REDUCING ALCOHOL PROBLEMS IN YOUNG DRINKERS: A FOCUS ON GENETIC PREDISPOSITION

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In Compliance with the ACCME Standards for **Commercial Support of CME, I do not have any relevant financial relationships to disclose in relation to this presentation.**

EDUCATIONAL OBJECTIVES

As a result of participating in this study, you should be able to:

- Analyze the data demonstrating that genes contribute to the development of alcohol problems
- Explain how complex genetically influenced disorders operate
- Discuss how information on genes and the environment contribute to the risk for alcohol problems and can be used for prevention

LECTURE COVERS

Background on AUD

Do genes affect the AUD risk?

What is inherited?

- Low alcohol response (low LR) ↑ risk
  - How environment contributes
  - Searching for genes?

Using low LR for prevention

LECTURE COVERS

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SUBSTANCE USE DISORDER Dx

In same year 2+ of:

Failed roles

Hazardous use

Social problems

Tolerance

Withdrawal

Use longer/more

Unable to ↓

Lots time use

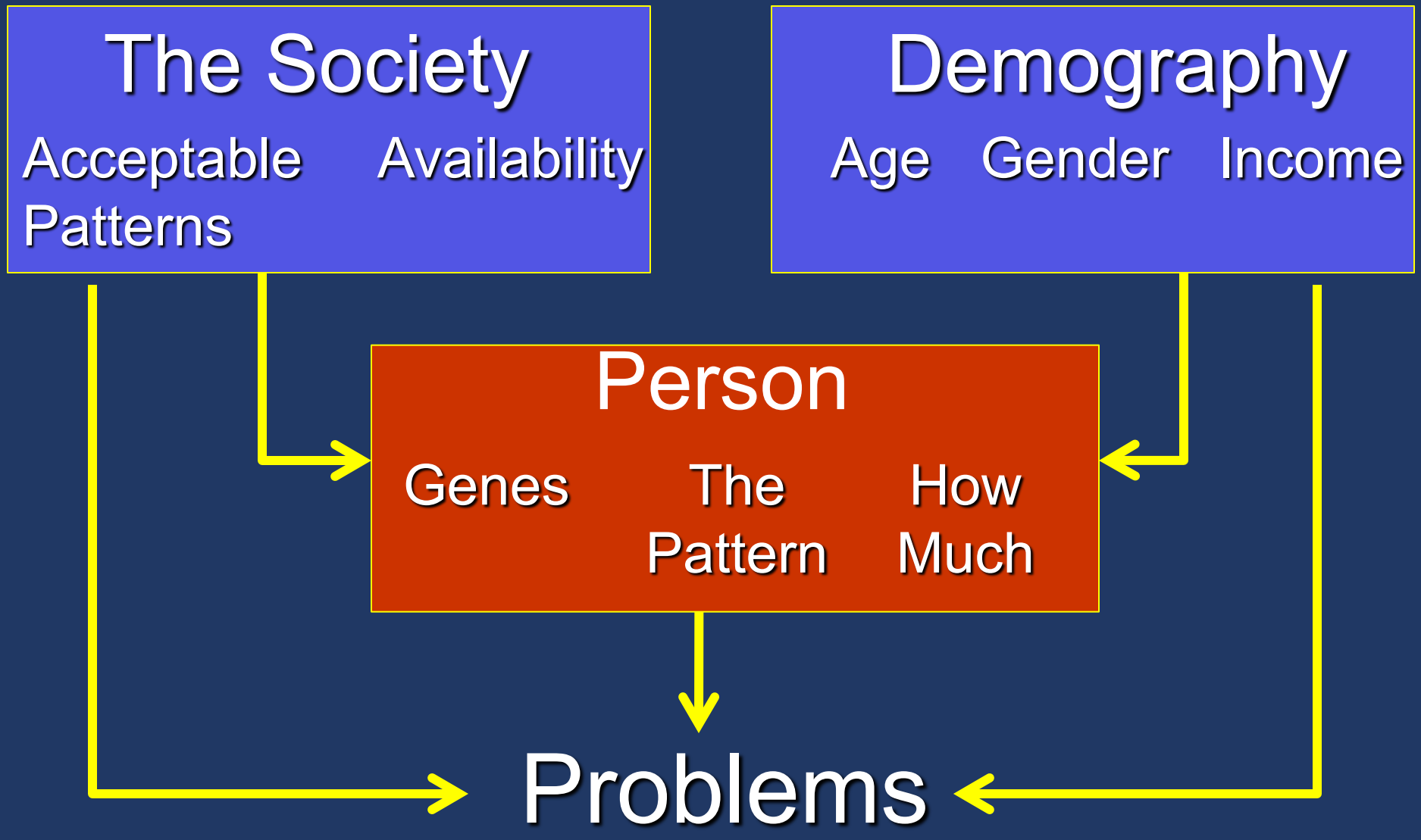
↓ activities

Use despite probs

Craving

If alcohol, is AUD, etc.

ALCOHOL USE & PROBLEMS



SAN DIEGO PROSPECTIVE STUDY

Began 1978: 453 FHP/FHN ♂ age 21 students

Follow up every 5 years

Wives & children enter study over time (N=1620)

Genes and environment

~90% follow up

Followed probands (age ~65) & kids (age ~30)

COGA

Collab Study on the Genetics of Alcoholism

Began 1989 with AUD individuals in treatment

Most had ~ 12 years education; ↑impulsivity

Probands FH++ for AUD versus "controls"

Data by semi-structured interviews (SSAGAs)

2004 begin youth panel of kids, grandkids, etc.

Follow up every 2 years

ALSPAC

Avon Longit Study of Parents and Children

All children born in area over 18 months 1991

8000 selected age 7 and followed q 1.5 years

Data from birth through age 23

I joined ALSPAC when kids about age 12

Data included alcohol use and problems

SRE LR used to predict future alcohol problems

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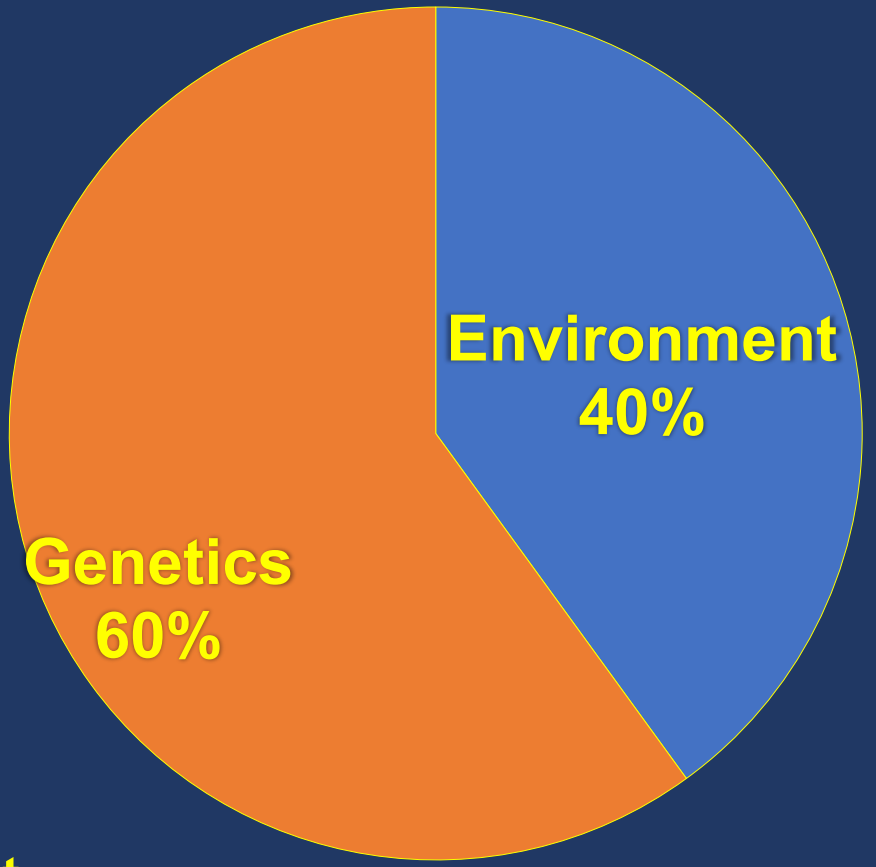
GENES AND AUDs

4 x ↑offspring risk

4 x ↑ if adopted out

Risk > for MZ vs DZ twins

ALCOHOLISM RISK



Multiple Characteristics

Each with Genes & Environment

PREDISPOSING RISK FACTORS

Alcohol metabolizing enzymes

Impulsivity

Psychiatric disorders

Sensitivity / Level of Response (LR)

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LR RATIONALE

Youth drink for effects

If need more for effect

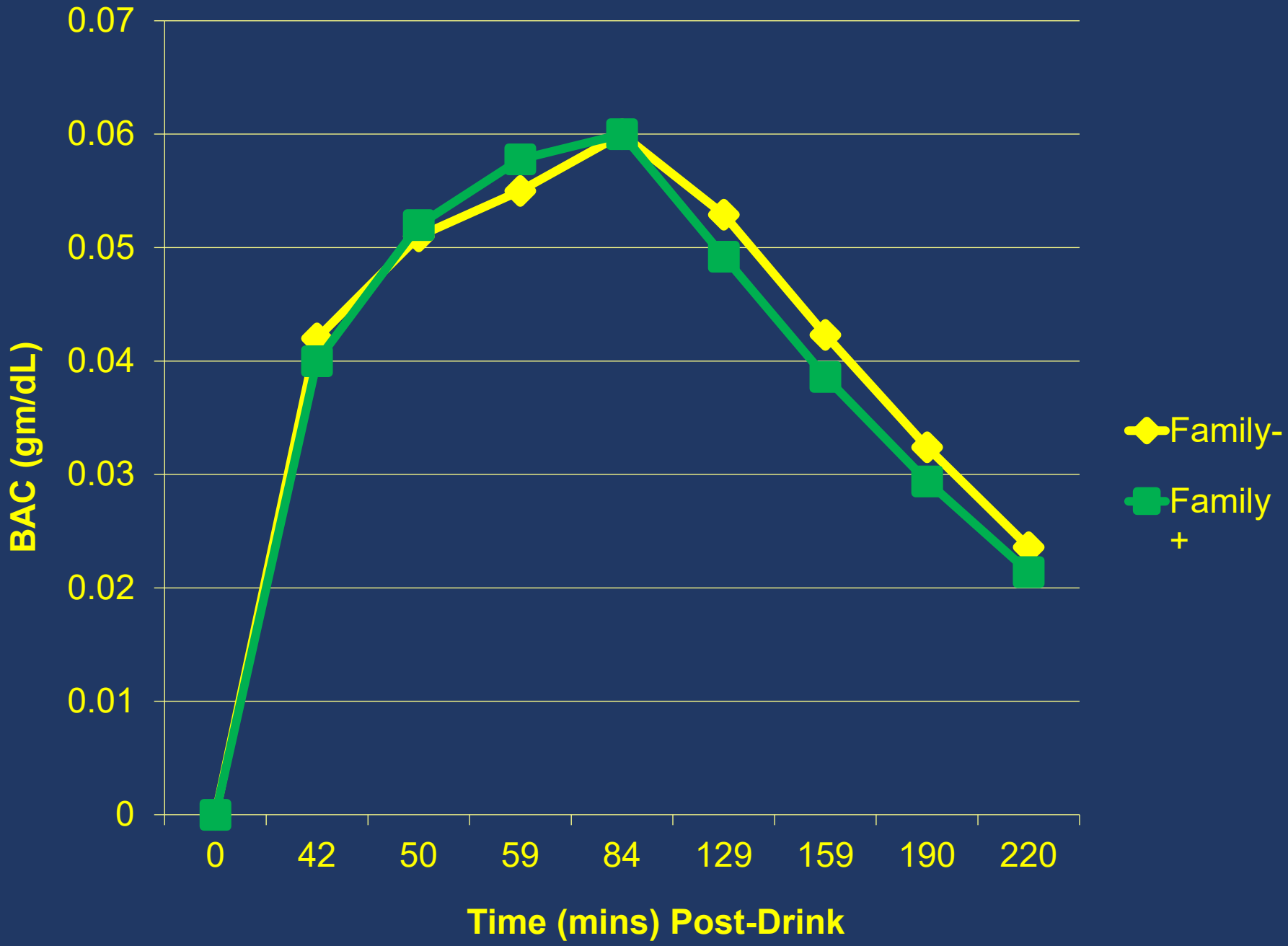
will drink more

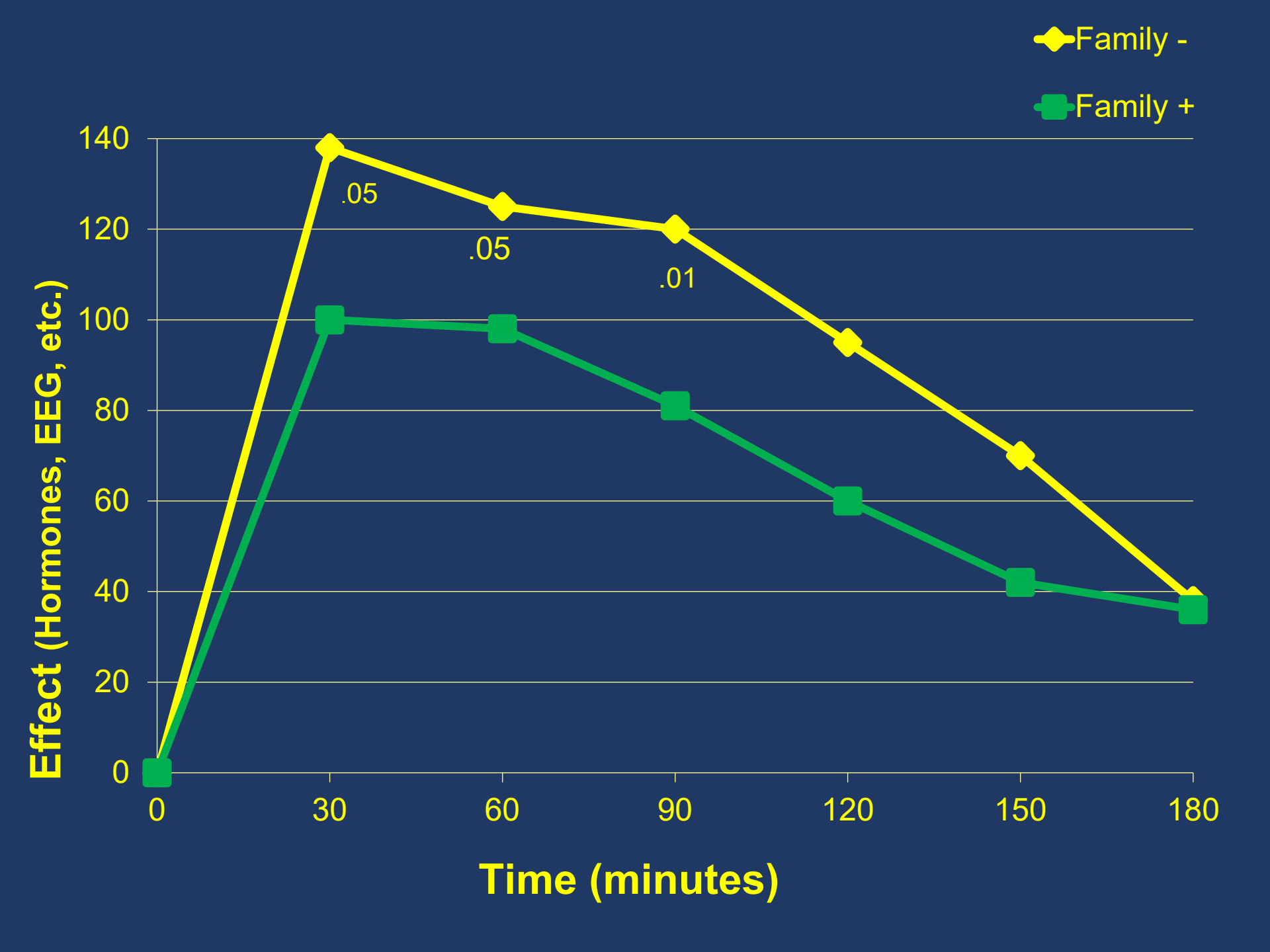
Then heavy drinking affects

Peers

Expectations

Stress

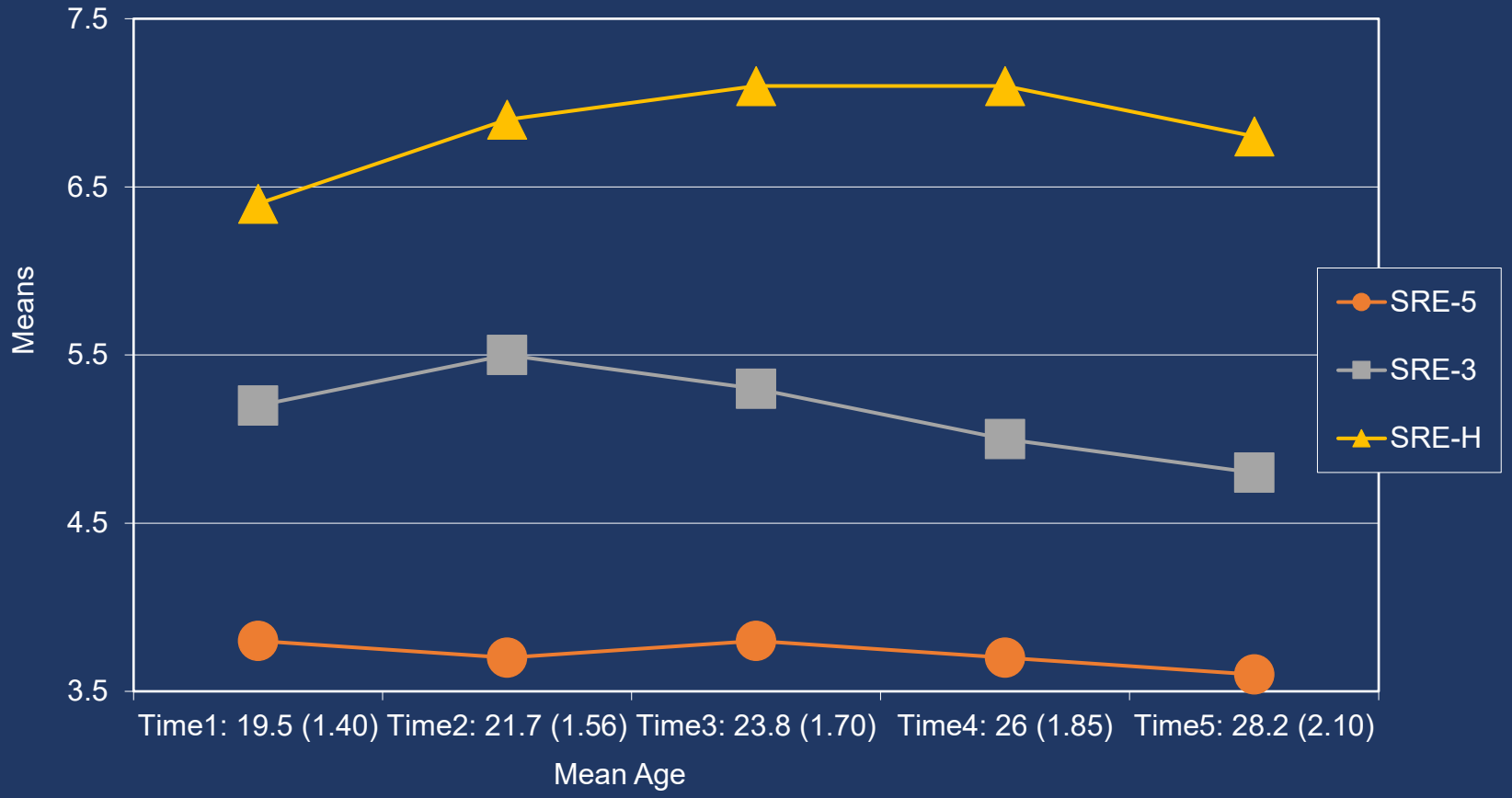

0.07
0.06
0.05
0.04
0.03
0.02
0.01
0
BAC (gm/dL)
0
42
50
59
84
129
159
190
220
Time (mins) Post-Drink
Family-
Family +


Family -
Family +
140
120
100
80
60
40
20
0
.05
.05
.01
Effect (Hormones, EEG, etc.)
0
30
60
90
120
150
180
Time (minutes)

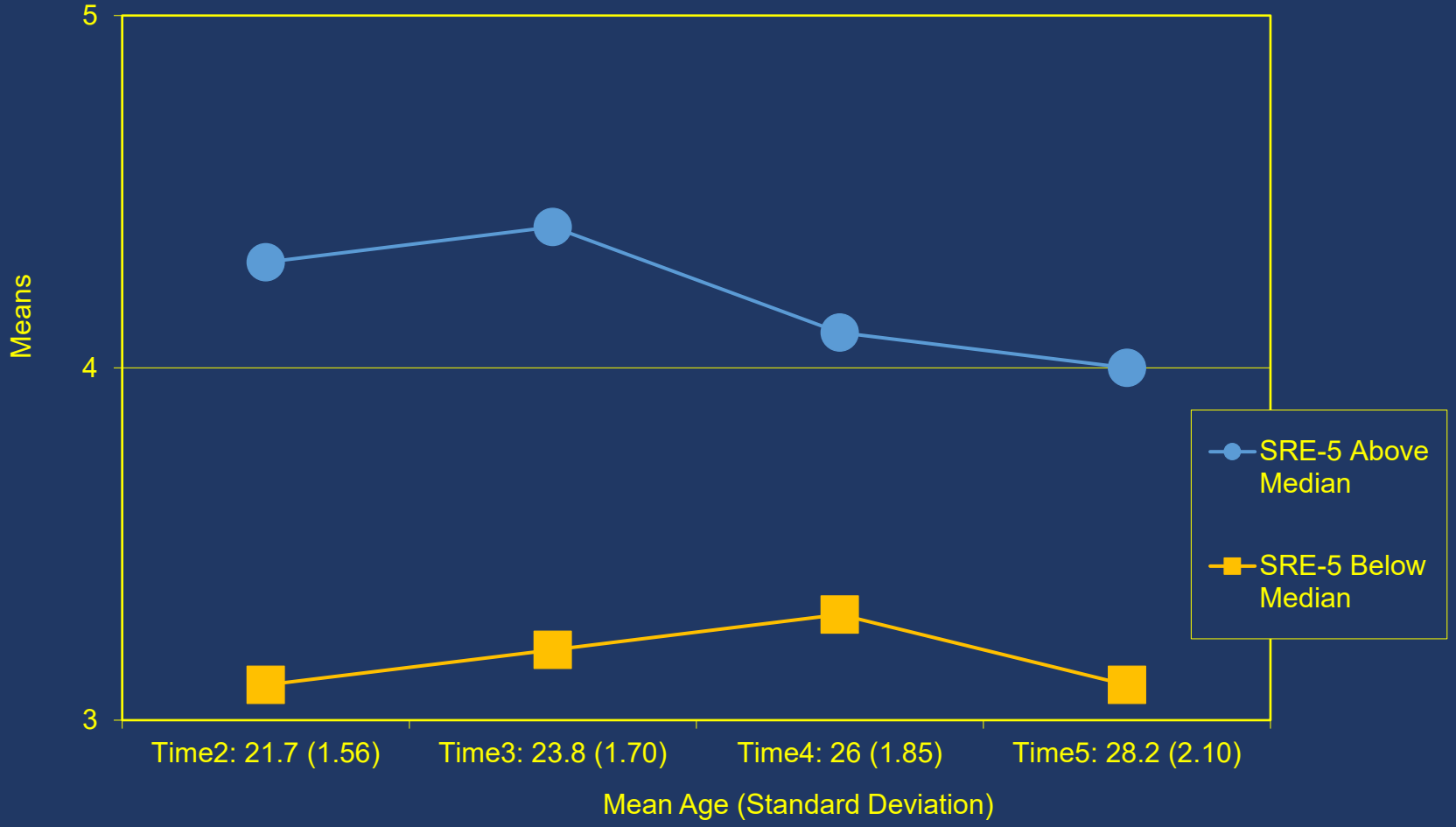
SELF REPORT OF EFFECTS

	1st 5 Times	Recent 3 Months	Heaviest
Feel Effect			
Feel Dizzy or Slur Speech			
Stumble			
Fall Asleep			

Average SRE Assessments Over Time



Average SRE-5 for Above and Below Median At Baseline



SRE CORRELATES: AGE 12*

Maximum drinks	.49
Frequency	.11
Problems	.28

* Avon Longitudinal Study of Parents and Children

LR PREDICTS: AUD ONLY

San Diego Prospective Study

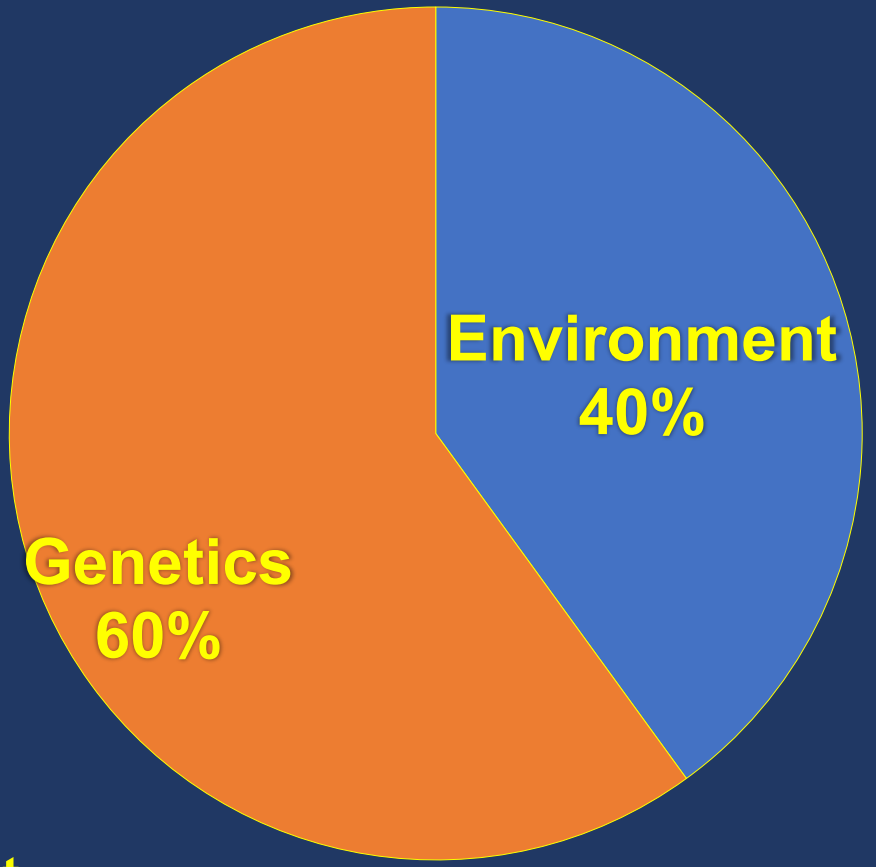
San Diego Prevention Study

Collaborative Study of Genetics AUDs

Avon Longit Study Parents & Children

Plus Australian twins, Danish cohort

ALCOHOLISM RISK



Multiple Characteristics

Each with Genes & Environment

ENVIRONMENT/ATTITUDE MEASURES

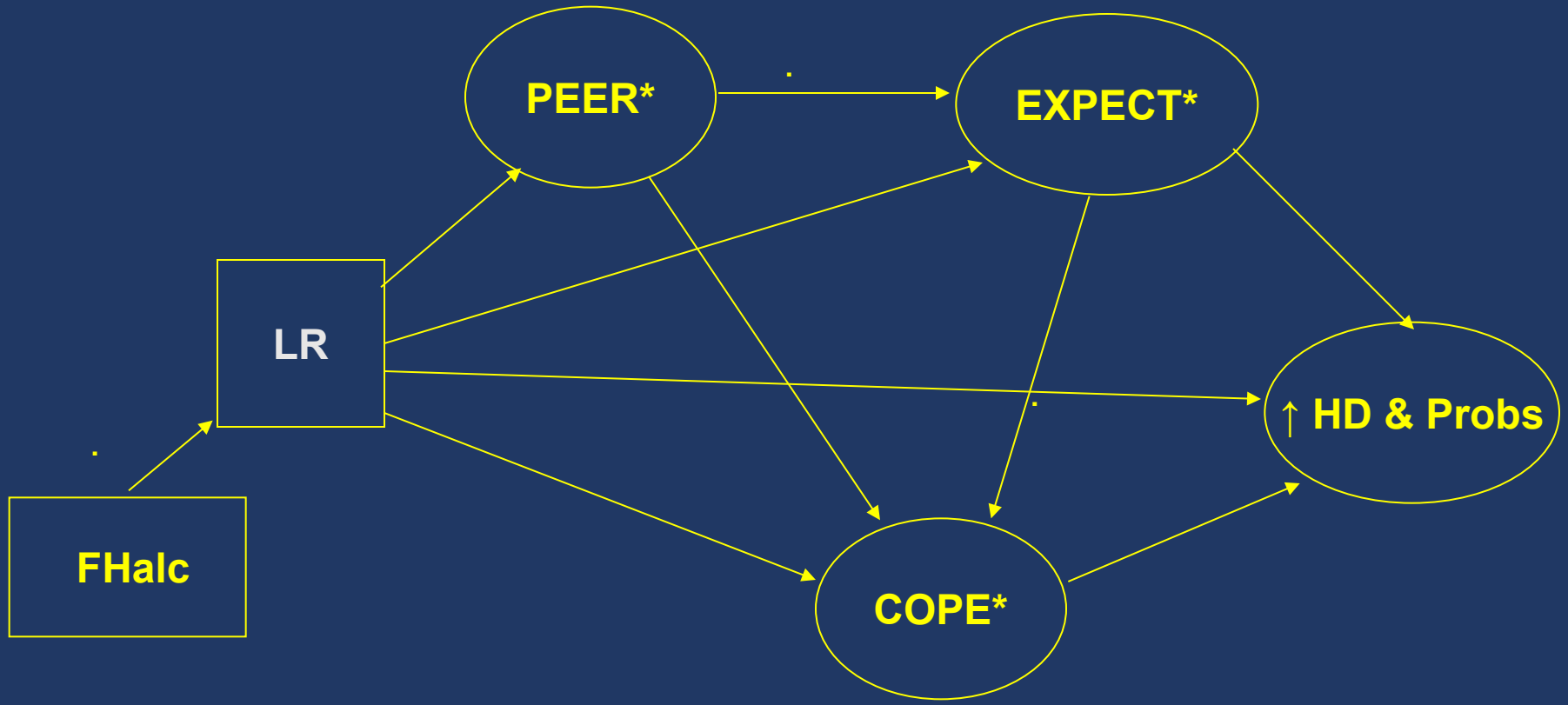
History: Renard Dx Interview & SSAGA

Impulsivity: Karolinska

Expectancies: AEQ

Coping: Drinking to Cope

Peer drinking: Important People Scale


PEER*
EXPECT*
LR
↑ HD & Probs
FHalc
COPE*

RELEVANT GENE VARIANTS?

Alc Metabolizing

ALDH2,2*
ALDH1B*

Stress

CRH1

GABA

GABRA1

Potassium

KCNMA1

Glutamate/NDMA

GRLK1 (GluR5)
GRM3

Opioids/Dop

OPRM1
OPRK1

Serotonin

5-HTTLPR -L

Cholinergic

CHRNA5/B2

More Genes

PRMT3*
HTATIP2*
DBX1*
SLC6A5*
AFDN*
KIF25*
ZNF699

STIMULATION AT RISING BAC

AUD risk based on Heavy Drinking (HD) vs LD

↑ stim on rising BAC if frequent HED history

in mid young adulthood

measured with BAES

Best prediction if also like and want more alcohol

Stimulation+ predicts future alcohol problems

Sessions also support low LR at later timepoints

Can use Alcohol Sensitivity Questionnaire

PERSONALITY PREDICTS ALC PROBS

Especially externalizing

- High impulsivity/disinhibition
- High sensation seeking
- Low conscientiousness

But studies not control for Time substance use!

Schuckit (2023) ACER 47:1179 (COGA)

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PREVENTION STUDY (N=500)

Questionnaire to students

- ~73% response
- Select matched low and high LR

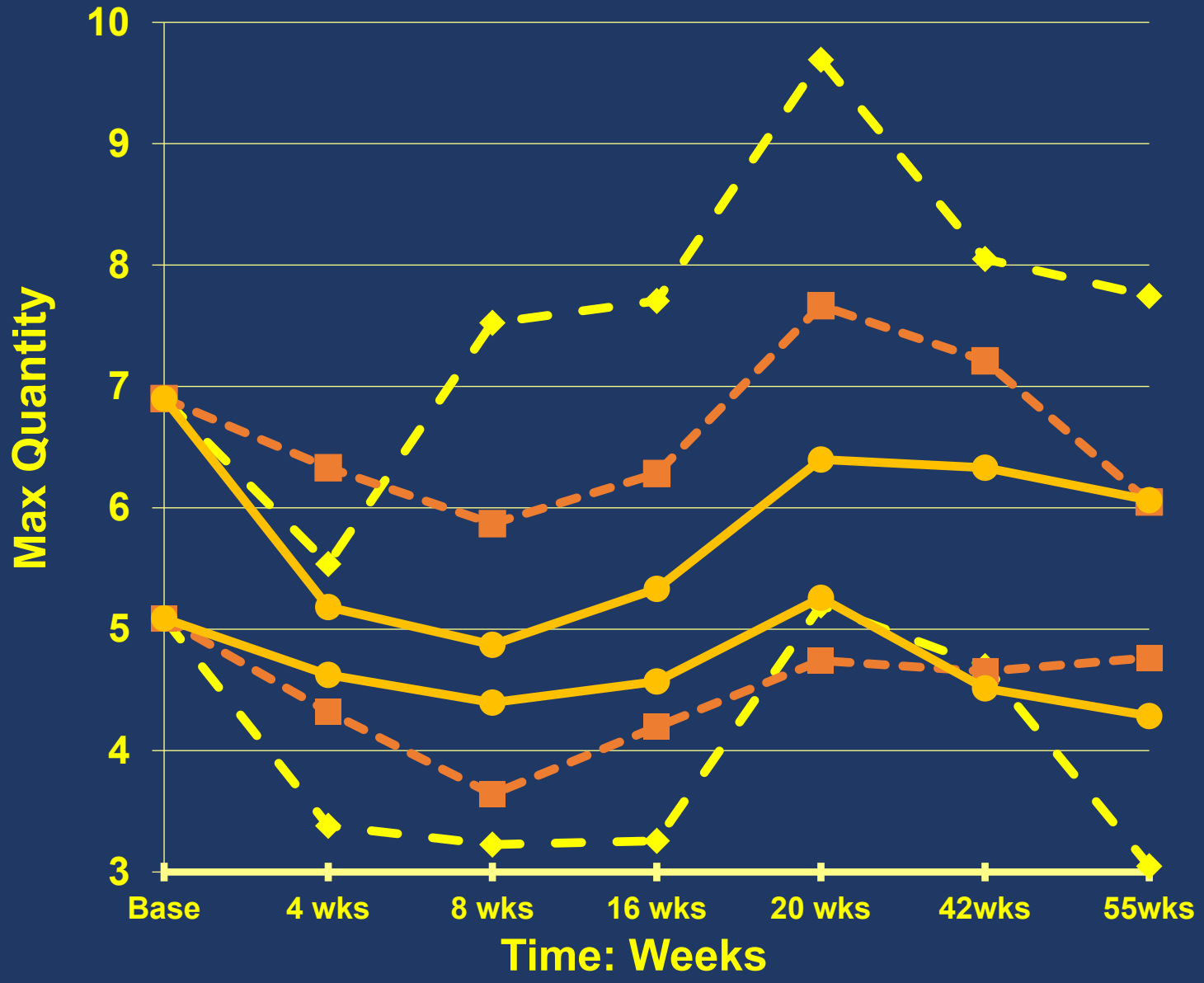
3 prevention groups

- LR-Based (LRB)
- State of the Art (SOTA)
- Control

Four 45-min Internet videos

Follow for 55 weeks

Maximum Drinks



VCU PREVENTION STUDY

231 students age 18 in “Spit for Science” (72% ♀)

State of art & LR-based groups

Control group selected separately in SFS records

Education used UCSD videos

Modest compliance across 6-month follow up

If complied, videos related to better outcomes

Savage ACER (2015) 49:2215

CONROD PREVENTION STUDIES

31 schools 7th grade students, age 13, 49% ♀

>1 SD high impulsivity, SS, anxiety, or hopeless

2 CBT 90 min sessions vs none for each risk

Led by counselor with 2 days training

Followed yearly for 5-years

~FU 60% show 21% lower SUD if trained

No sig effect on anxiety or hopelessness

Conrod et al (2025) AJP 182:473

SOME CONCLUSIONS

50%+ of AUD risk relates to genes

There is no “AUD gene”

Many genes relate to each risk characteristic

None are classically dominant or recessive

Low LR is one such characteristic

LR measured by alcohol challenges or SRE

Some environment & attitudes related to LR & AUD

These facts can be used for prevention

SOME KEY REFERENCES

Schuckit, et al; The 10-year stability of three subscale scores of the Self-Report of the Effects of alcohol measure and their relationship to changes in drinking quantities over the same period. Alcohol Clin exp Res, March 2026.

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King, et al: Subjective Responses to Alcohol in the Development and Maintenance of Alcohol Use Disorder. Am J Psychiatry 2021