## Discussion

Thank you Angela for this excellent presentation. Certainly will catalyze much thought about the role of neuroscience, alcohol, and HIV.

Need to consider both, direct effects (DE) and indirect effects (IE) of alcohol use. For e.g., enhancing optimistic bias or disinhibition is an IE versus immune suppression as a DE. What about the interaction?

## **Key Finding**

Systems involved in adolescent sexual risk behavior

- Examined relationship of VOLUME of various areas to sexual risk
- Relationships of size of limbic areas (amygdala, hippocampus) to risk behavior. Size of reward and control regions was NOT related to risk behavior
- Pubertal development moderated these associations (may act as a risk censor)

#### **PrEP**

- No studies with youth under age 18. Interest generally low (Brian's study among YMSM 16-20).
- ➤ The regimen is an important factor simple is better. While this may not be the case at the moment, second generation PrEP delivery systems are being developed which will markedly simplify dosing. However, we should not consider this a panacea. If we examine the use of birth control, Norplant, for example, we still find significant non-adherence even though the drug is inserted under the skin and does not need replacement for months.

#### **ART Adherence**

## Key finding:

Literacy is unrelated to adherence.

This sounds a familiar bell ----- while knowledge or awareness may be important, it is, in and of itself, not sufficient to motivate the adoption or sustainment of health behaviors.

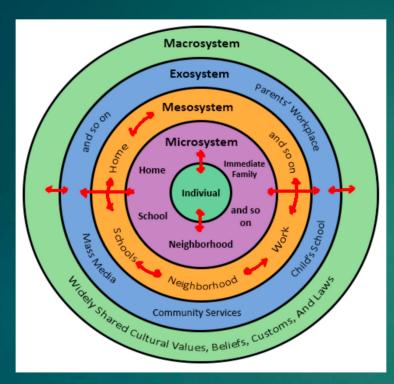
The key, once again, is motivation - motivating young people to utilize knowledge, attitude changes, and behavioral skills.

#### What do adolescents care about?

- Angela also raised another important point What do adolescents care about?
- Adolescents do weigh the cost and benefits of a decision; however, they may be more likely to experience what Weinstein terms, "optimistic bias".
- ▶ This bias is predicated on a platform of (1) few life experiences, (2) usually being in good health, (3) proximally focused or "here and now focused" rather than distally-focused, (4) less capacity to project into the future, and (4) poor capacity for assessing probabilistic outcomes.

#### **Area for Future Research**

- What are the mechanisms that govern adolescent risk-taking and how does alcohol and drug use facilitate risk – is it by dampening neuroscience control mechanisms or by enhancing optimistic bias?
- What is the impact of social context on adolescents' decisionmaking?
- Is there a mechanism through which adolescents' perception of their social context actually affects brain function or does brain function affect perception? This may not be a unidirectional or linear relationship.
- ▶ Is the relationship between brain, behavior, and environment "reciprocal" – can each can exert and effect the other resulting in changes in inclination, optimistic bias, neurocognitive perception.
- ▶ This needs to be disentangled.



Bronfenbrenner, U. (1979). The Ecology of Human Development. Cambridge: Harvard University Press.

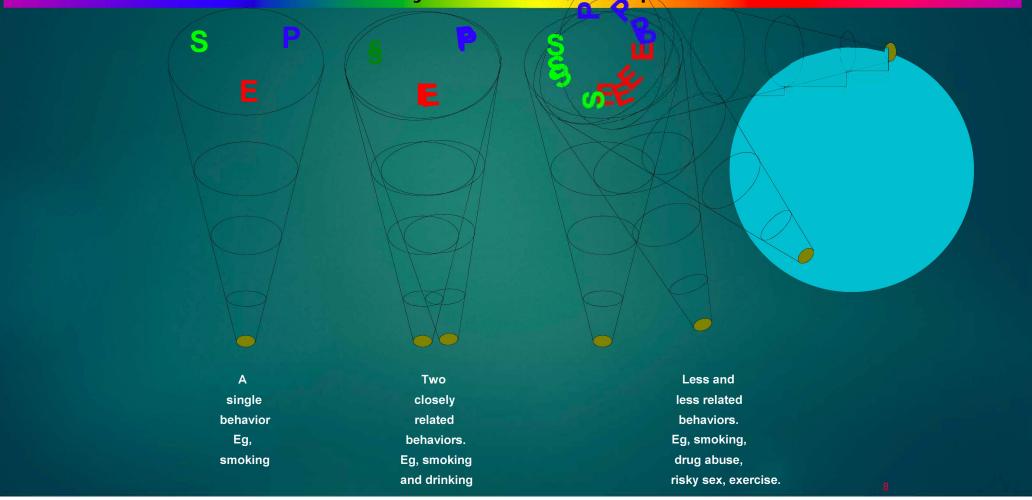


Ecological Model in Public Health

#### Area for Future Research

Defining the specificity of alcohol effects on closely and less related behaviors

Ultimate causes may be the same, distal predictors less so



### Area for Future Research Role of Alcohol in Immunity

- Alcohol modulates immune function
- Alcohol abuse associated with increased immunosupression and more rapid HIV progression to the end-stage disease
- Alcohol induces neuroinflammatory processes
- Chronic alcohol intake increases level of monocytes and is associated with diminished circulating CD4+ T cells

# Area for Future Research Biological mechanisms of alcohol withdrawal

Alcohol withdrawal and detoxification induce disturbances in the stress response system included hypothalamic-pituitary axis (HPA), sympathetic-adrenomedullary system (SAM), and immune response.

Stress induces hypersecretion of the catecholamines, epinephrine and norepinephrine, both associated with neuropeptide Y (NPY) deficiency.

Hypercortisolemia during withdrawal impaired cellular immunity (Th1) and facilitated humoral immunity (Th2), contribute to cognitive dysfunction.

Hypoproduction of NPY during first days of withdrawal results in lack of NPY ability to suppress inflammation

## Prudens quaestio dimidium scientiae Francis Bacon

- ► As in most of science, the more questions we answer, the more questions are raised that need answers.
- Our objective, then, is to marshal new data and begin to ask more precise questions using an integrated approach that combines behavioral and social sciences with neuroscience and immunology to develop testable mechanistic models of alcohol effects.