# From Bench to Bedside and Back Again:

## *Translational bridges in adolescent nicotine dependence research*

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# Nicotine Dependence: Big Picture

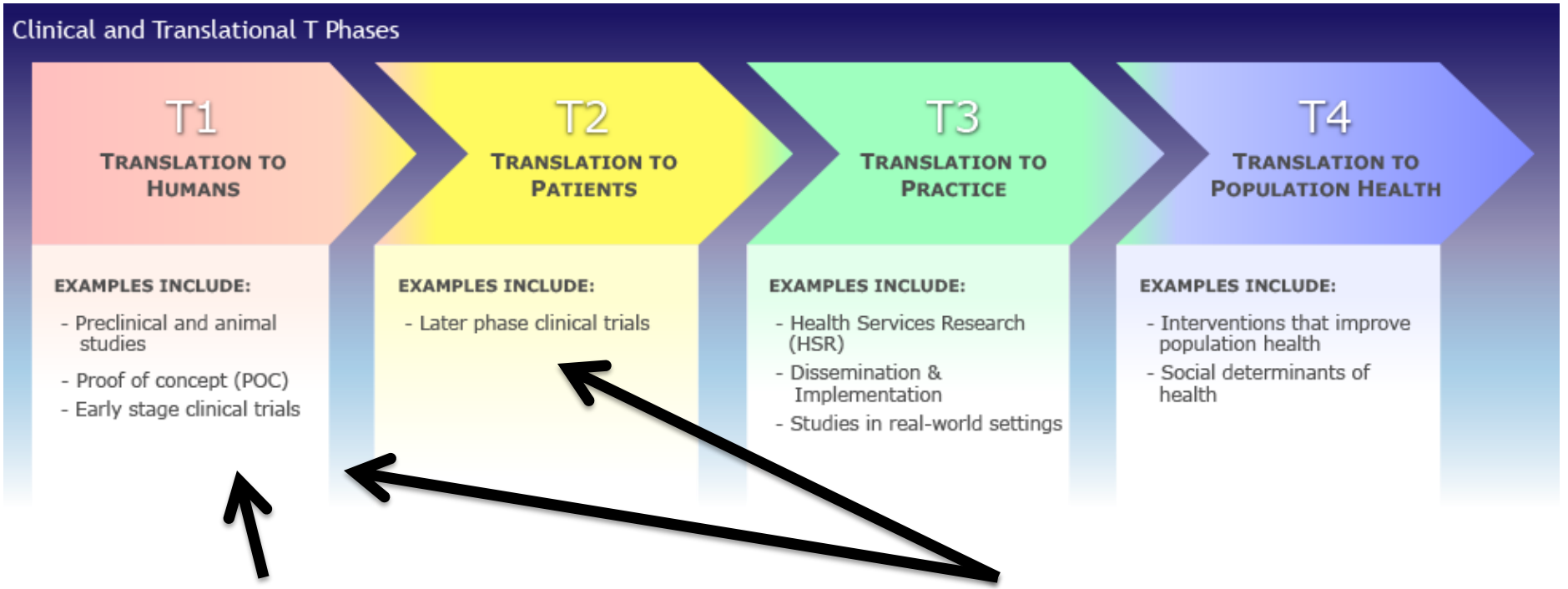
- Tobacco use remains the leading global cause of preventable disease and premature death (Word Health Organization, 2011)

- Over 80% of adults with nicotine dependence started smoking tobacco during adolescence (USDHHS,1994)


**"In the case of smoking, children and adolescents hold the key to progress toward curbing tobacco use in future generations"**

**- U.S. Surgeon General, 1994**

# Translational Approaches: Bench to Bedside and Back Again




**Mineur Laboratory**:

-preclinical/animal studies of nicotinic acetylcholine receptors (α7 and β4) and feeding behaviors

**Krishnan-Sarin Laboratory**:

-Early and Late stage clinical trials, neural (fMRI) and behavioral (impulsivity) correlates of treatment

https://www.ctsi.ucla.edu/about/pages/featured

# Translational Implications: Better Treatments and Targeted Interventions

Using translational approaches to better understand the molecular mechanisms behind the nicotine receptor system will assist in:

- Mechanism-based Drug Targets for Nicotine Dependence (e.g. α4β2), Obesity (e.g. β4 or α7), and subgroups of smokers who smoke to lose/maintain weight

- Personalized Medicine: *Pharmacogenetics* = Genotype-targeted treatments to Improve Outcomes in subgroups
  - Example: CHRNA5, CHRNA4, CHRNB2 gene SNPs and Treatment Response to Varenicline (Chantix) in smoking adults (King et al. 2012)

# Translational Implications: Development of Biobehavioral Markers

- A major challenge for the field of addiction moving forward is the development of **biobehavioral markers** that convey addiction vulnerability in at-risk populations and that are associated with treatment-response, prognosis, and recovery in addicted youth.
- Candidate intermediate phenotypes:
  - **Impulsivity**, delay discounting, stress-reactivity/responsiveness, **fMRI**, & EEG biomarkers
- In vivo neuroimaging 'challenge' studies involving behavioral challenges that require cognitive control in the presence of appetitive cues or affective stimuli may be useful assays

*Hammond, Mayes, Potenza. Adolescent Medicine: STARS, 25(1), 2014*

# Translational Implications: Neurobiologically-Informed Behavioral Interventions and Public Policy

- Prevention and interventional strategies should take into account the specific biological vulnerabilities and strengths of adolescents.
- Adolescents are biologically **more responsive to rewards** and **less responsive to aversive stimuli/losses**, relative to adults:
  - Positive reinforcement > punishment or negative reinforcement
  - Providing access to exciting activities under controlled settings may help replace or limit harmful risk-taking opportunities (Casey, 2008)
  - Contingency management using positive reinforcers for prosocial behavior, engagement, and negative urine drug tests (Budney et al. 2009)
- Attempting to enhance cognitive control by cognitive training or cognitive behavioral therapy (CBT)

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# Understanding Recovery: Neurodevelopmental implications


*Cosgrove, K.P. et al. Archives of General Psychiatry* 66(6): 666-676, 2009.