

Substance Abuse and Mental Illness: Effects of Marijuana and Other Drugs on Developing Psychosis

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Integrating Care: Addressing Mental Health and
Substance Abuse

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Introduction

- **Substance abuse is a problem in and of itself, and it is also a problem that exacerbates other problems**
- **This talk focuses on the latter role of substance abuse, as a type of maladaptive or toxic environmental exposure that exacerbates or hastens the development of serious mental illness in vulnerable individuals.**
- **A greater understanding of the role of substance abuse in mental illness will both shed light on the development of mental disorders themselves, and will identify new opportunities for therapeutic interventions**

Outline

- **Effects of marijuana in the general population**
- **Relationship of marijuana to psychosis**
- **Relationship of marijuana to cognition in clinical high risk individuals**

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Cannabis and Other Substance Use Numbers

- Most popular illicit drug worldwide
- 2.8 – 4.5% of the global adult population aged 15-64 uses cannabis – World Drug Report 2010, using UN Office on Drugs and Crime (UNODC); 10.7% in North America
- 0.3 – 0.5% for opioids worldwide; Same % in North America
- 0.3 – 1.3% for amphetamines worldwide; 1.1% in North America
- 0.3 – 0.5% for cocaine worldwide; 1.9% in North America

General Population Effects of Cannabis in Adolescents and Young Adults

- Brain function
 - Reduced volumes (e.g. hippocampal, amygdala, right medial orbitofrontal cortex), gyrification complexity and structure (possible atrophy, decreased dendritic branching)
 - Increased volumes (e.g. anterior cerebellum) that might reflect abnormal pruning or abnormal connections
 - Reduced white matter integrity (CB1 receptors on oligodendrocytes)
 - Impaired prefrontal cortex (PFC) and limbic neurotransmission for glutamate, GABA and dopamine neurons
 - Reduced blood flow (e.g. PFC, temporal and insular regions)

General Population Effects of Cannabis in Adolescents and Young Adults

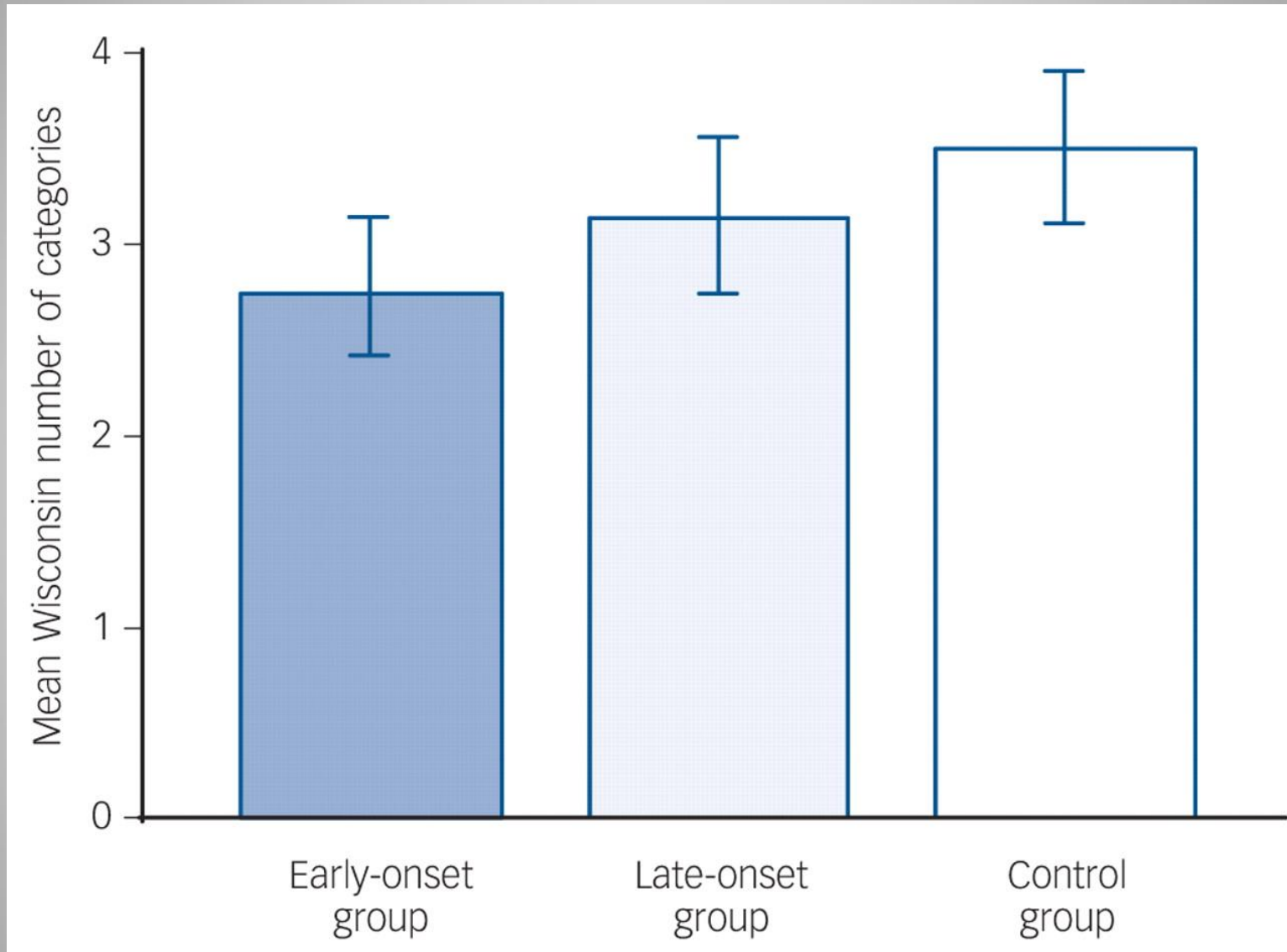
- Motivation

Cannabis amotivational syndrome (McGlothlin and West, 1968. Associated with reduced motivation for reward, educational underachievement (also reduced striatal dopamine synthesis)

- Cognition

Accumulating evidence that cannabis impairs executive functions (e.g. mental flexibility, processing speed, fluency, learning), sustained concentration, memory and overall cognitive abilities (IQ). Level of impairment affected by multiple factors such as age of onset, duration of use, co-morbid substance use, other demographic variables and dose

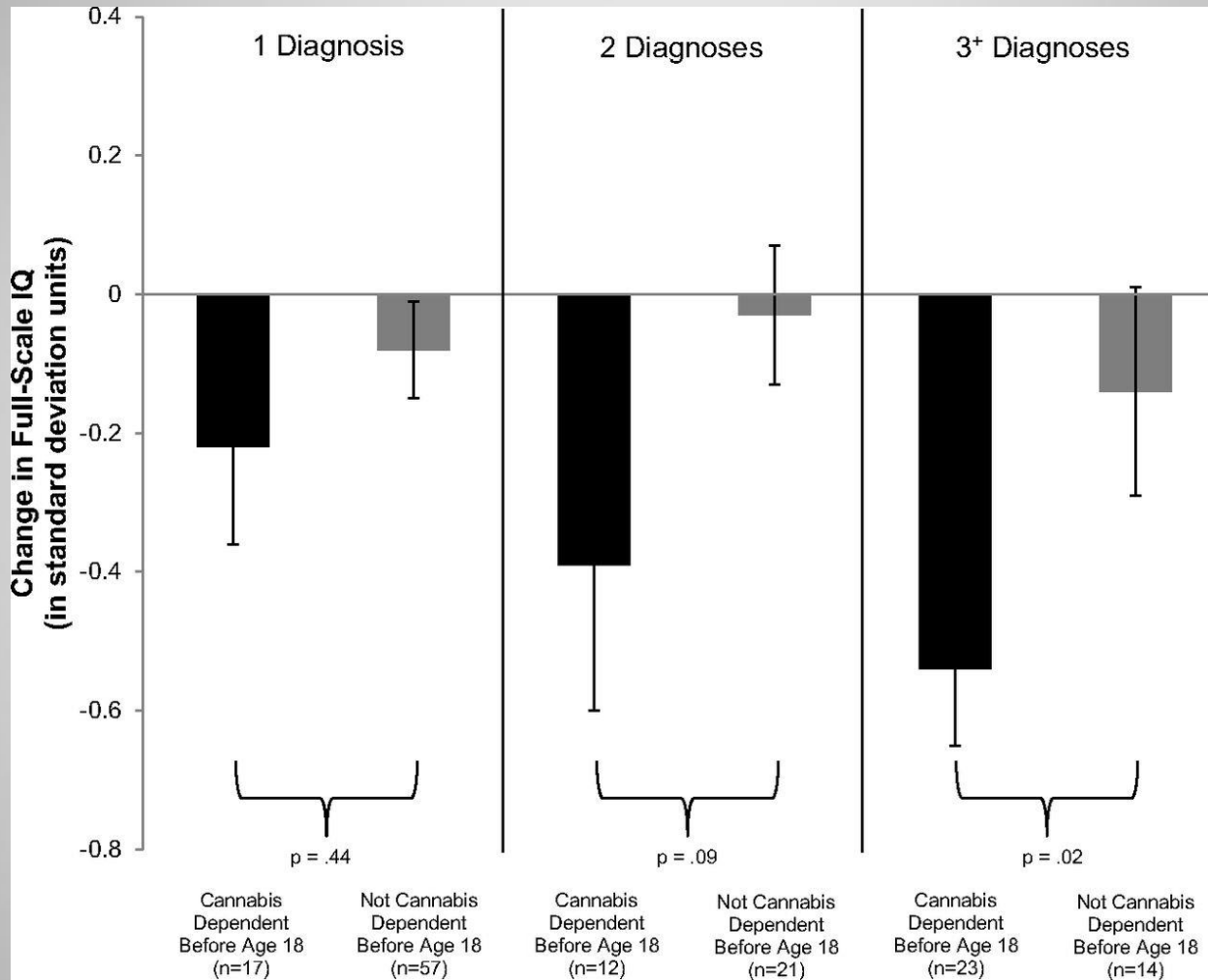
Wisconsin Card Sorting Test number of categories in early-onset, late-onset and control groups.



Maria Alice Fontes et al. *BJP* 2011;198:442-447

THE BRITISH JOURNAL
OF PSYCHIATRY

Longitudinal Study of Cannabis Dependent Users Comparing IQ Declines in Adolescent and Adult Onset Subject, and in Duration of Cannabis Dependence



Madeline H. Meier et al. PNAS 2012;109:E2657-E2664

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Severity of Substance Use in CHR as Measured with the Alcohol Use Scale (AUS) / Drug Use Scale (DUS) Buchy et al, 2015, Psychological Medicine

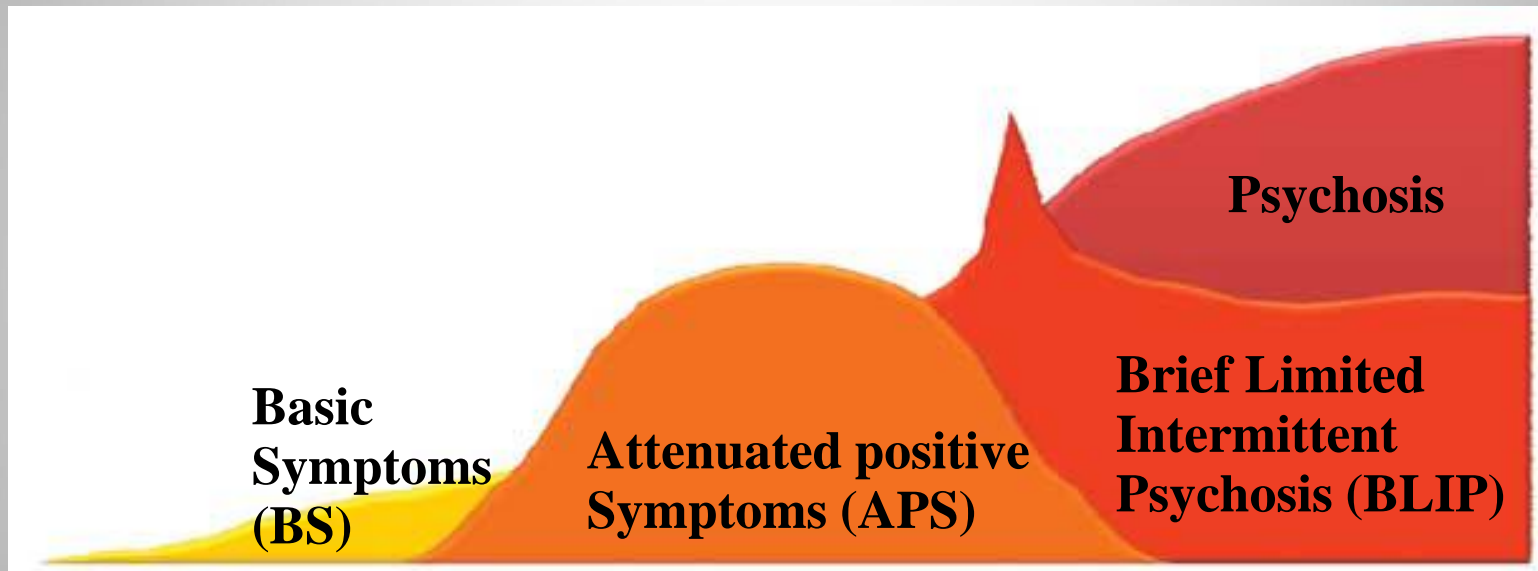
| Baseline AUS/DUS Assessment | CHR (n=735) | Controls (n=278) |
|--------------------------------|----------------|---------------------|
| Alcohol | | |
| Abstinent | 441 (60.0%) | 136 (49.1) |
| Use Without Impairment | 273 (37.1) | 141 (50.9) |
| Abuse | 16 (2.2) | 0 (0.0) |
| Dependence | 5 (0.7) | 0 (0.0) |
| Tobacco | | |
| Abstinent | 560 (76.2%) | 256 (92.1) |
| Use Without Impairment | 163 (22.2) | 20 (7.2) |
| Abuse | 5 (0.7) | 0 (0.0) |
| Dependence | 7 (1.0) | 0 (0.0) |

Severity of Substance Use in CHR as Measured with the Alcohol Use Scale (AUS) / Drug Use Scale (DUS)

Buchy et al, 2015, Psychological Medicine

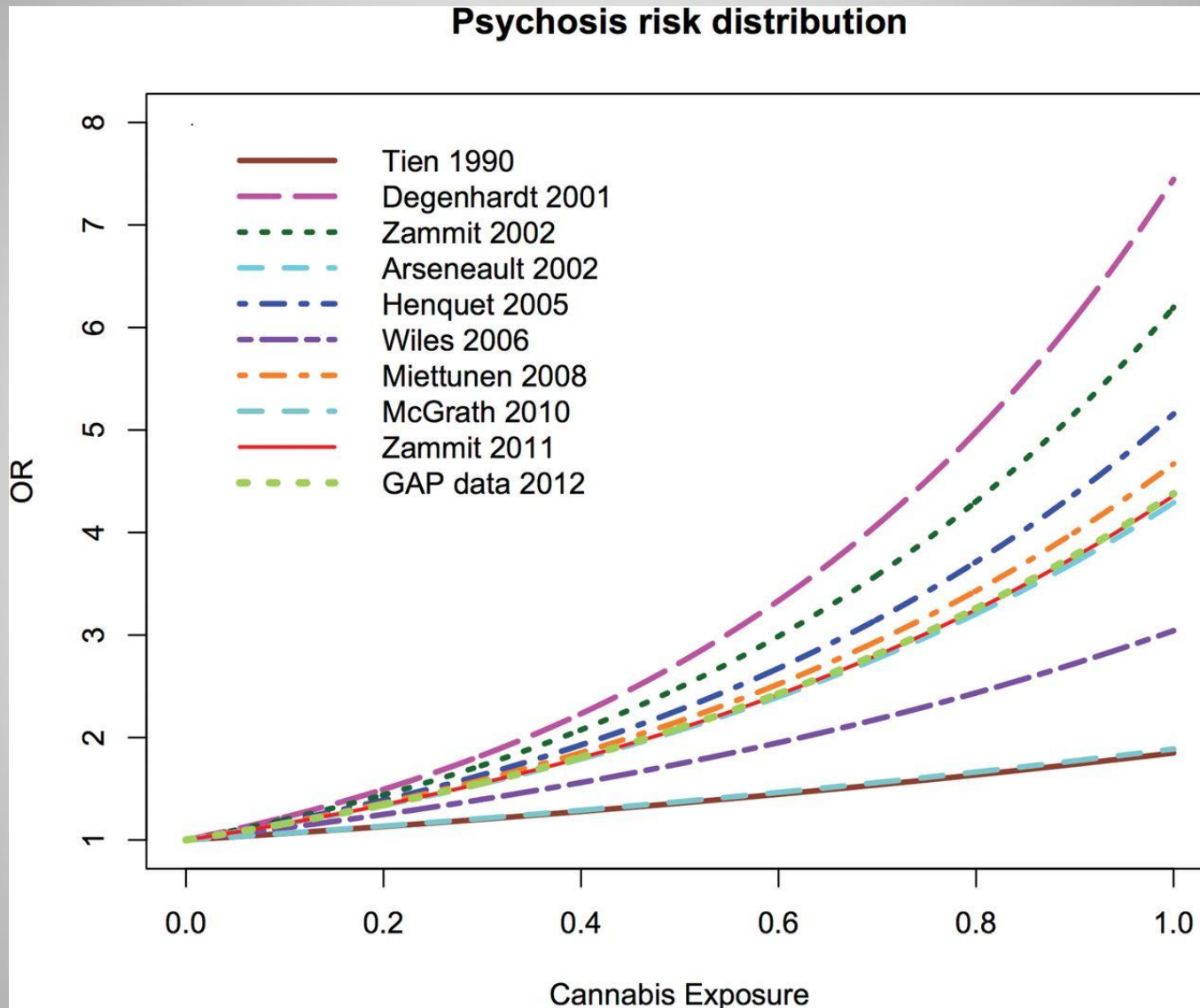
| Baseline AUS/DUS Assessment | CHR (n=735) | Controls (n=278) |
|-----------------------------|----------------|---------------------|
| Cannabis | | |
| Abstinent | 563 (76.6%) | 252 (90.6) |
| Use Without Impairment | 144 (19.6) | 26 (9.4) |
| Abuse | 26 (3.5) | 0 (0.0) |
| Dependence | 2 (0.3) | 0 (0.0) |

Prodromal Syndromes and Psychosis



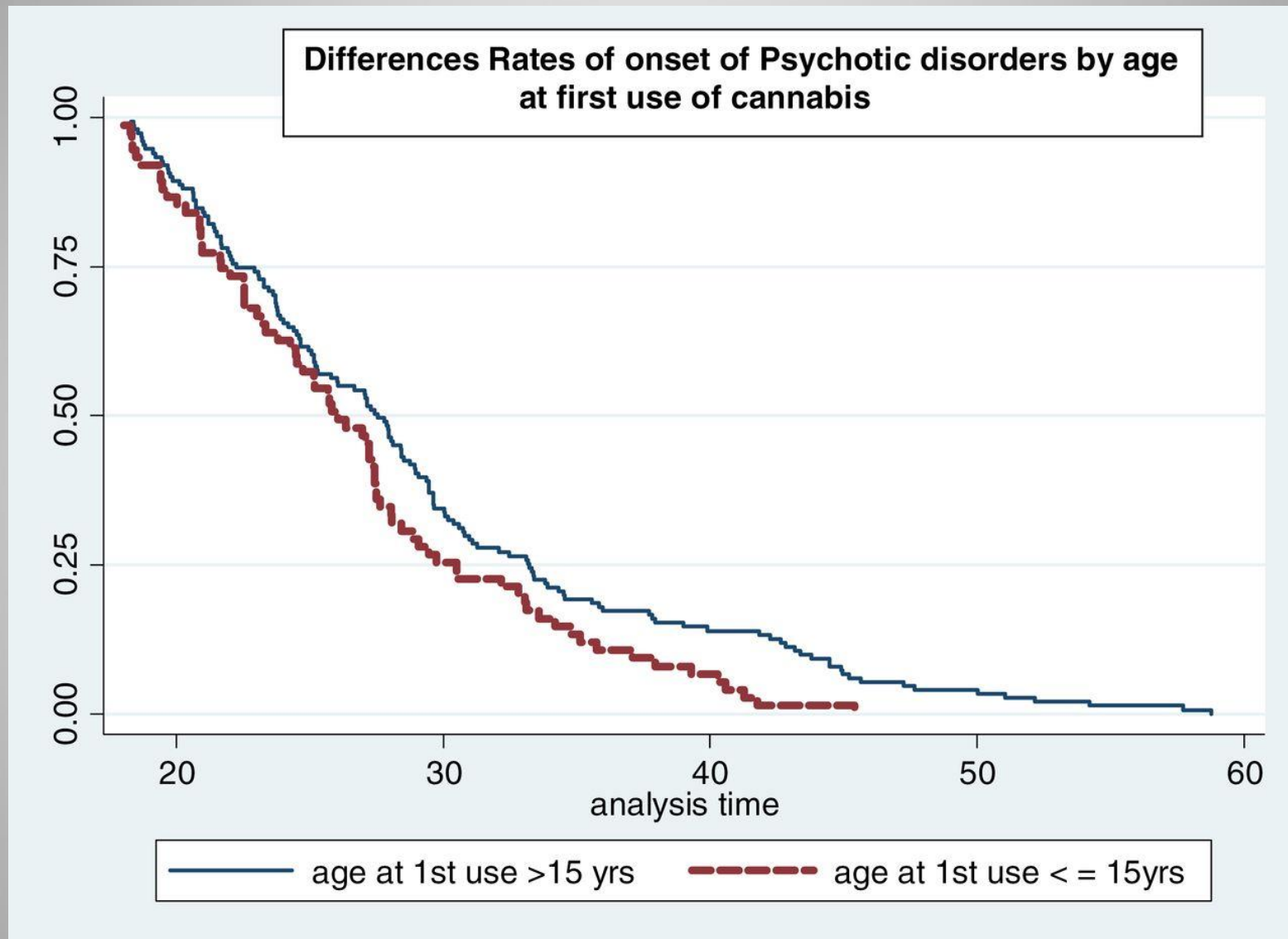
**Genetic Risk and
Deterioration Syndrome (GRDS)**

Estimated risk ratio of psychosis by level of cannabis use in original studies.



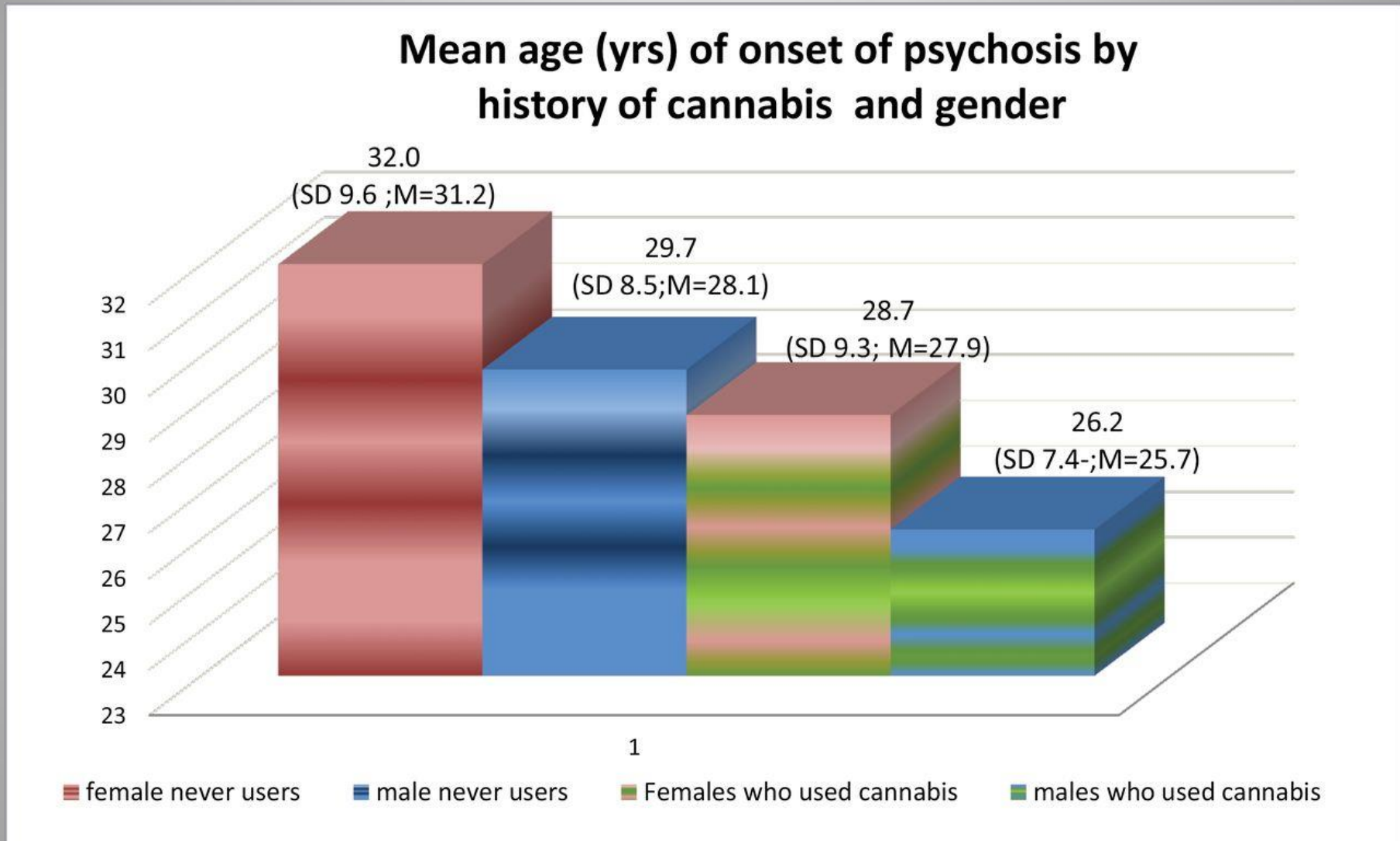
Arianna Marconi et al. Schizophr Bull 2016;schbul.sbw003

Kaplan–Meier survival curves showing rate (y axis) of onset for participants grouped by age at first use of cannabis



Marta Di Forti et al. Schizophr Bull 2014;40:1509-1517

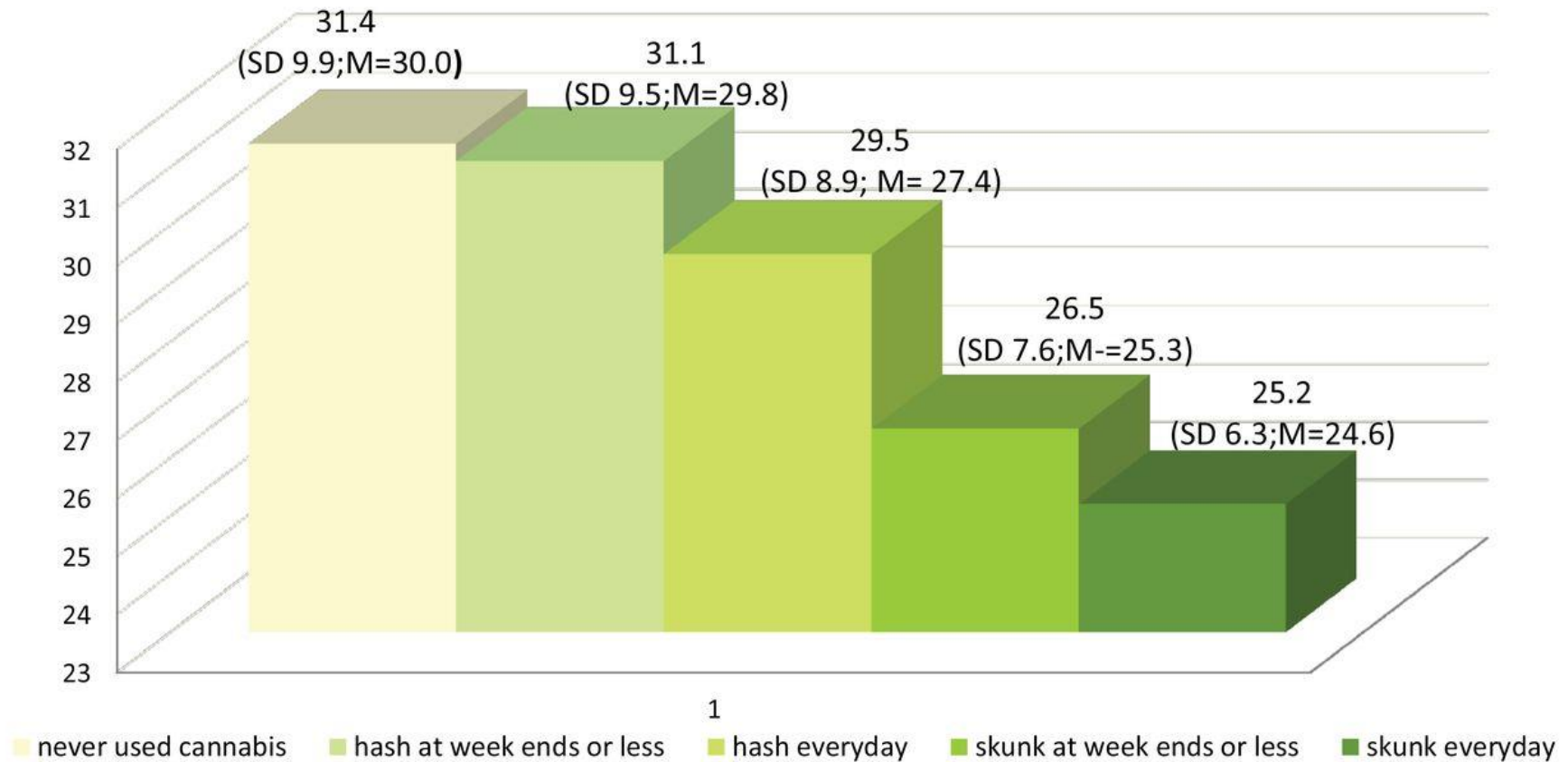
Cannabis use is associated with an earlier age of onset of psychosis in both males and females



Marta Di Forti et al. Schizophr Bull 2014;40:1509-1517

Subjects who never used cannabis experience their first episode of psychosis at the oldest ages (mean ages in years) compared to those who used cannabis

Mean age (yrs) of onset of psychosis by degree of exposure to cannabis

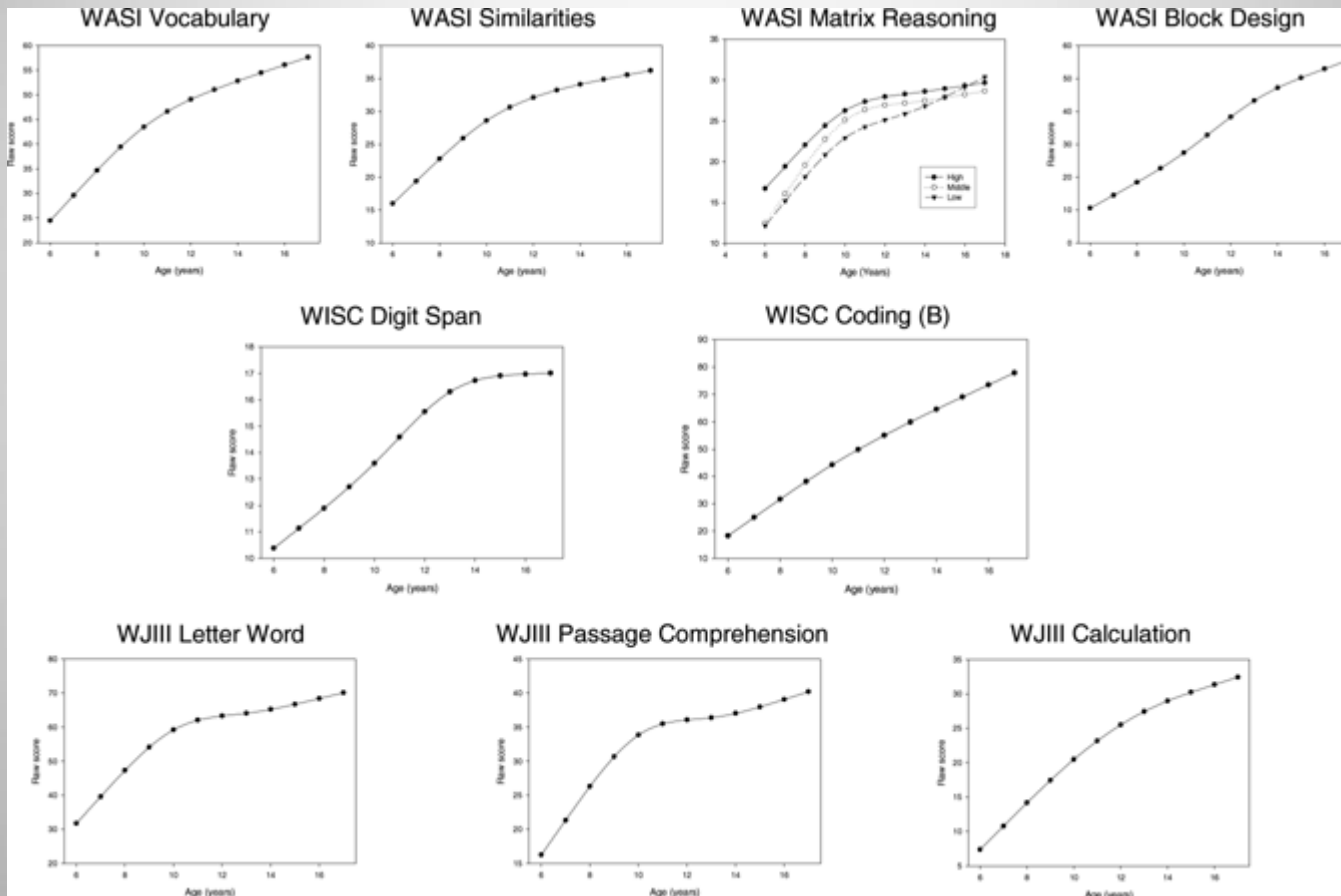


Marta Di Forti et al. Schizophr Bull 2014;40:1509-1517

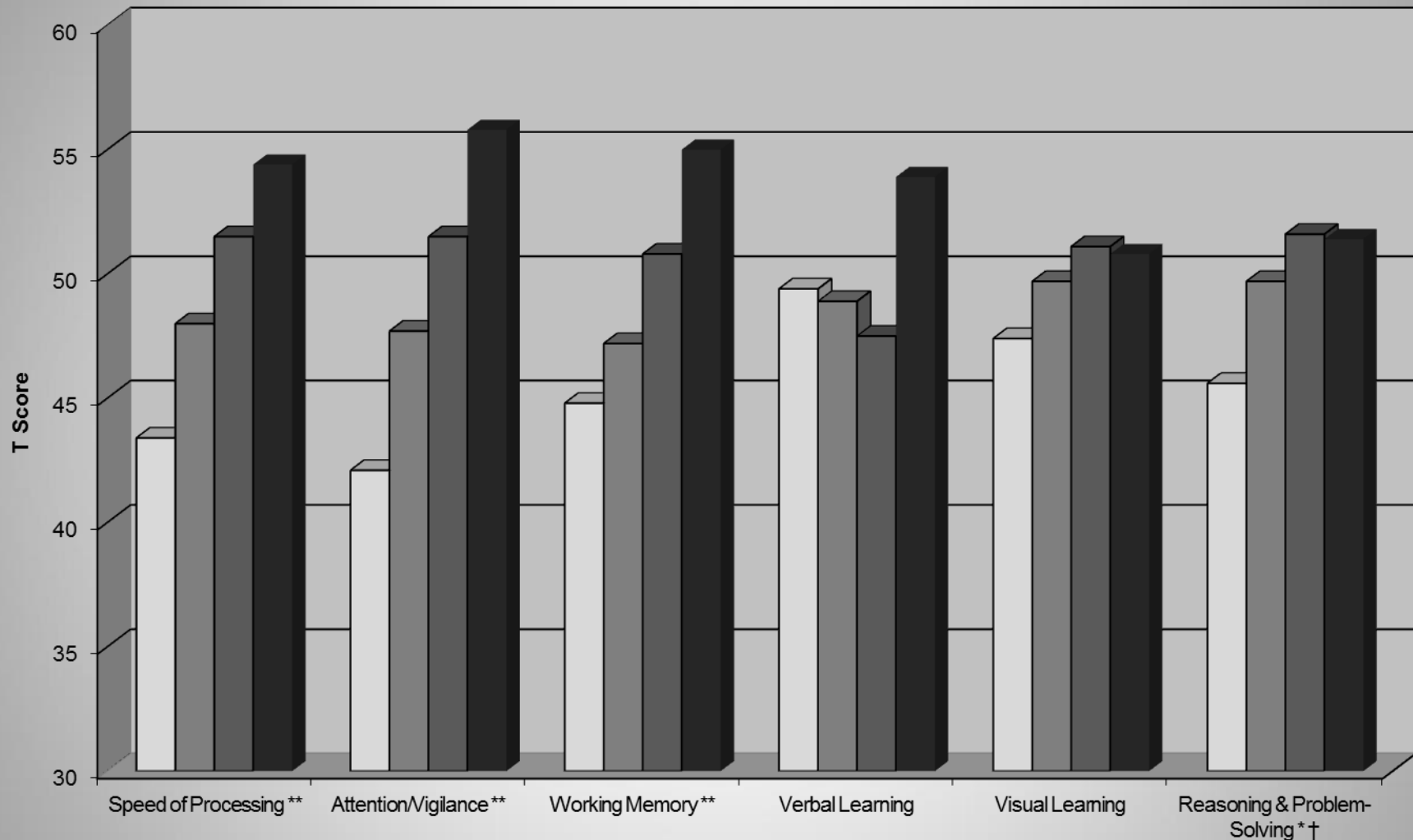
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Normal Cognitive Development



Mean T-scores of MCCB Cognitive Domains by Age Group

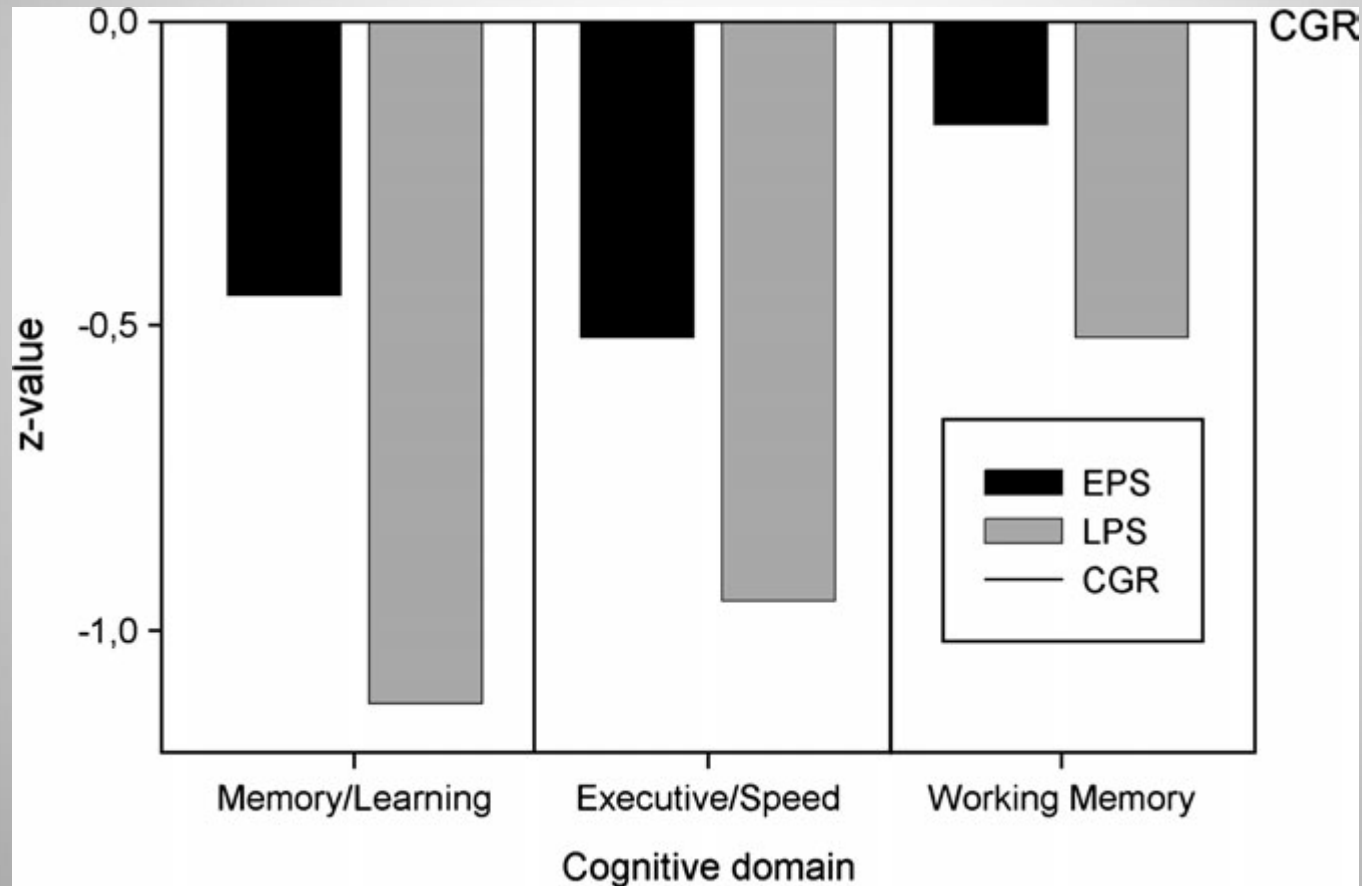


Note: Significant age effects corrected by IQ: * $p < .05$, ** $p < .001$

†: Main effect for sex, $p < .001$

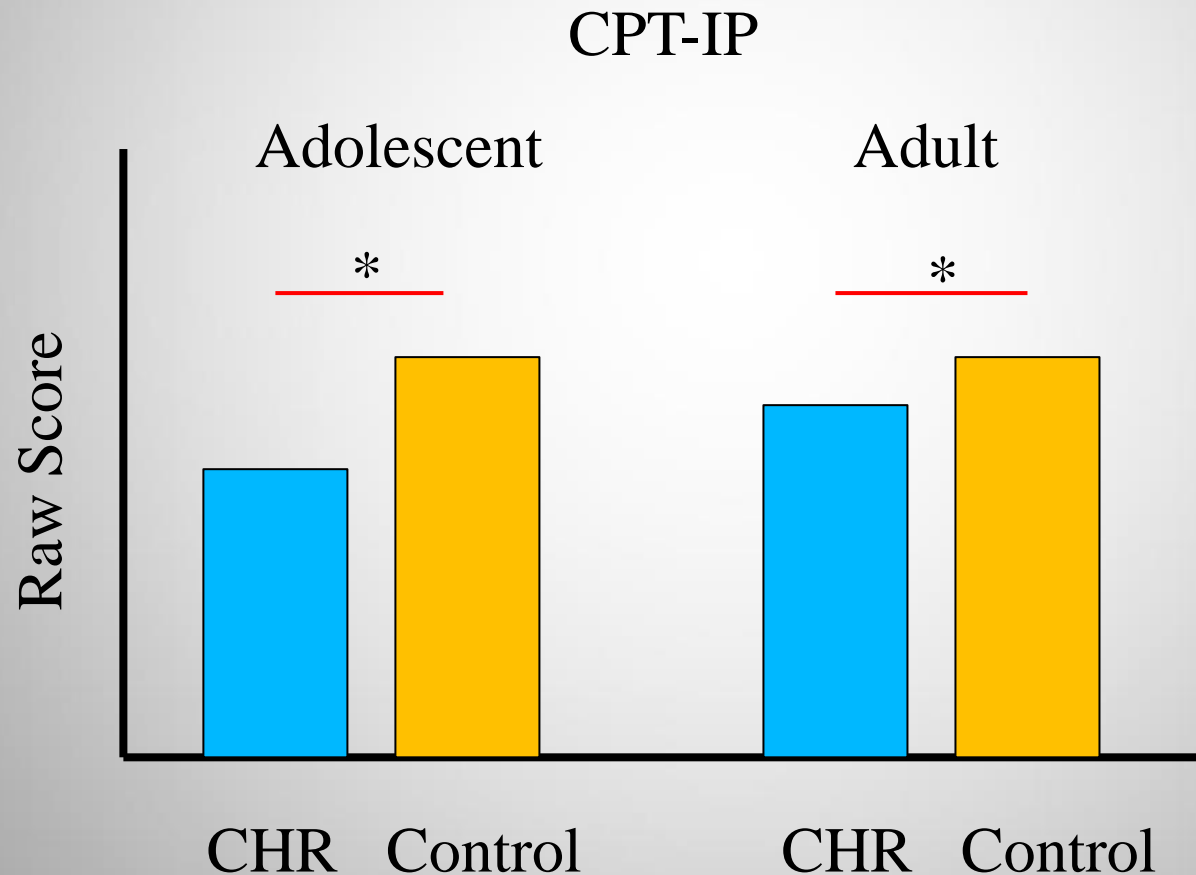
□ 12-13 years old
 ■ 14-15 years old
 ■ 16-17 years old
 ■ 18-19 years old

Cognitive Deficits in CHR Individuals Increase Over the Prodrome



Adolescent CHR Subjects Show Greater MCCB Deficits Compared to Controls than Adult CHR Subjects

Cui et al, in preparation



Cannabis-Induced Deficits in Cognition in CHR are Related to Multiple Factors

- Duration of prodromal period (Frommann et al, 2011, Fusar-Poli et al, 2012)
- Degree of exposure
- Age of onset of cannabis use. CHR late-onset users showed higher IQ scores than early onset users. Age of onset was significantly and positively correlated with IQ in CHR only, not in control subjects (Buchy et al., 2015)

Conclusions I

- **Cannabis is the most widely used illicit drug in the world**
- **Rates of cannabis use are approximately 2 times greater in persons with psychosis**
- **Cannabis has negative effects on cognition that are qualitatively similar in the general population, in people with psychotic disorders and in people at risk for psychotic disorders**
- **Adolescence is an important but vulnerable period of development for both the general population and especially for individuals at high risk for psychotic disorders**

Conclusions II

- **Our growing understanding of normal cognitive development offers opportunities to both assess the development of cognitive problems early, prior to the development of psychosis, and increasingly, to intervene therapeutically**
- **Studies of cannabis effects on psychosis and on cognition show there are many remaining unanswered questions about how and under what circumstances its effects are exerted. For example, sometimes it contributes to the development of psychosis, and sometimes it does not. Similarly, its relationships to other demographic variables such as comorbid substance use and SES, and its constellation of effects (e.g. it is associated with greater positive symptoms but lower negative symptoms and better premorbid social functioning) requires additional research**
- **Cannabis effects thus reflect both a serious clinical mental health challenge, but hopefully, also a window into the nature of vulnerability for serious mental disorders**

Thank You