

# Why is Tobacco Use Disorder so Common in People with other Mental Disorders?

## The Dual Disorders Perspective

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# Nestor Szerman MD Faculty Disclosure

<i>Company Name</i>	<i>Honoraria/ Expenses</i>	<i>Consulting/ Advisory Board</i>	<i>Funded Research</i>	<i>Royalties/ Patent</i>	<i>Stock Options</i>	<i>Ownership/ Equity Position</i>	<i>Employee</i>	<i>Other (please specify )</i>
Otsuka			X					
Lundbeck			X					
Viartis	X							
Recordati	X		X					
Exeltis	x		X					



# Agenda

- **Tobacco Use Disorder (TUD) is a Mental Disorder**
- TUD in people with other Mental Disorders (**Dual Disorder**)
- Genetic and Neurobiological basis of **Dual TUD**
- **Common Dual TUDs: Depression, Psychosis, and ADHD**
- **Treatment of Dual TUD**
- **Conclusions.**

# Smoking / Tobacco Use Disorder (TUD)

- **Tobacco consumption (Smoking)** is a public health problem that worries society and health authorities.
- From a scientific perspective, **Smoking** should be distinguished from "TOBACCO USE DISORDER"
- "Tobacco Use Disorder" is a Mental Disorder recognized by all international classifications (DSM-5; and ICD-WHO) and therefore a disorder of the human brain, different from a custom or habit.\*

\* Szerman Néstor et al. TOBACCO USE DISORDER AND DUAL DISORDERS Joint statement by the Spanish Psychiatry Society and the Spanish Dual Disorders Society. Actas Esp Psiquiatr. 2022 Jun;50(Supplement):77-138.



# Tobacco Use Disorder (TUD) and Other Mental Disorders

Tobacco use particularly affects vulnerable populations, mainly people with Mental Disorders, who are three times more likely to develop TUD (addiction) compared to the general population.

- **TUD** is likely to be the main cause of a **20-25 year reduction in the life expectancy** of people with **severe mental disorders**.
- \* Parro C, .....and Szerman N. Viewpoint. Tobacco Use Disorder and Other Mental Disorders: The Neglected Dual Disorder. Position Statement by the Spanish Society of Psychiatry and Mental Health and the Spanish Society of Dual Disorders. Spanish Journal of Psychiatry and Mental Health . Article accepted for publication 2024



# The Imperative to Treat Tobacco Use Disorder

May 2024

## The Imperative to Treat Tobacco Use Disorder

According to the Centers for Disease Control and Prevention, tobacco use disorder remains the leading cause of preventable disease, disability, and death in the United States, killing close to 500,000 Americans each year. While significant public health efforts have resulted in fewer people smoking and less tobacco consumed, in 2021 an estimated 11.5% of U.S. adults still smoked cigarettes. Tobacco use disorder and related complications historically have disproportionately affected people with serious mental illness. For too long, mental health clinicians have believed they need to choose between treating serious mental illness and treating tobacco use disorder. It is a false choice: clinicians have a responsibility to treat both.


This month's [Editor's Choice Collection](#) reflects on the treatment of tobacco use disorder for people with mental illness, with a special emphasis on addressing barriers to accessing this life-saving care. Such barriers are discussed in detail in articles listed in the first section, and articles in the second section highlight the roles of peers and community health workers. The third section outlines key clinical interventions. As this collection illustrates, psychiatric providers should be leaders at the forefront of managing tobacco use disorder.

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**75** Psychiatric Services



Difficulty getting community mental health appointments for adolescents  
A tale of two taxes: paying for behavioral health services in two states  
Psychotropic prescribing across medical providers, 2016–2019  
The ultimate intercept for preventing criminal legal system involvement

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# TUD: Choosing appropriate language to reduce the stigma\*

- TUD: IS IT A VICE? IS IT A CUSTOM? IS IT A HABIT?
- The language we employ can either challenge or perpetuate stigmatizing attitudes and beliefs.
- **Labeling Tobacco Use Disorder (TUD) as “a habit”** perpetuates the notion that it is not a mental disorder.
- We should use language based on a neuroscientific perspective, which can contribute to a more effective approach to the treatment of TUD.
- \* Parro-Torres C.....and Szerman N. Tobacco use disorder and other mental disorders: The neglected dual disorder. Span J Psychiatry Ment Health. 2024 May 11:S2950-2853(24)00029-2.
- \*Volkow, N.D., Gordon, J.A. & Koob, G.F. Choosing appropriate language to reduce the stigma around mental illness and substance use disorders. Neuropsychopharmacol. 46, 2230–2232 (2021).



# Tobacco Use Disorder (TUD)\*

One of the main obstacles hampering therapeutic approaches to TUD is to **consider it a “behavioral problem” rather than a mental disorder** (i.e., a brain disorder) probably related to other mental disorders.

The stigma has been persistent, but the moralizing and punitive views of the past are giving way to a consensus in the scientific and even cultural community that

**Addiction (to Tobacco) is a chronic BRAIN DISORDER** that is influenced by social factors and is treatable.\*

\* Nora D. Volkow. Personalizing the Treatment of Substance Use Disorders. Am J Psychiatry 177:2, February 2020



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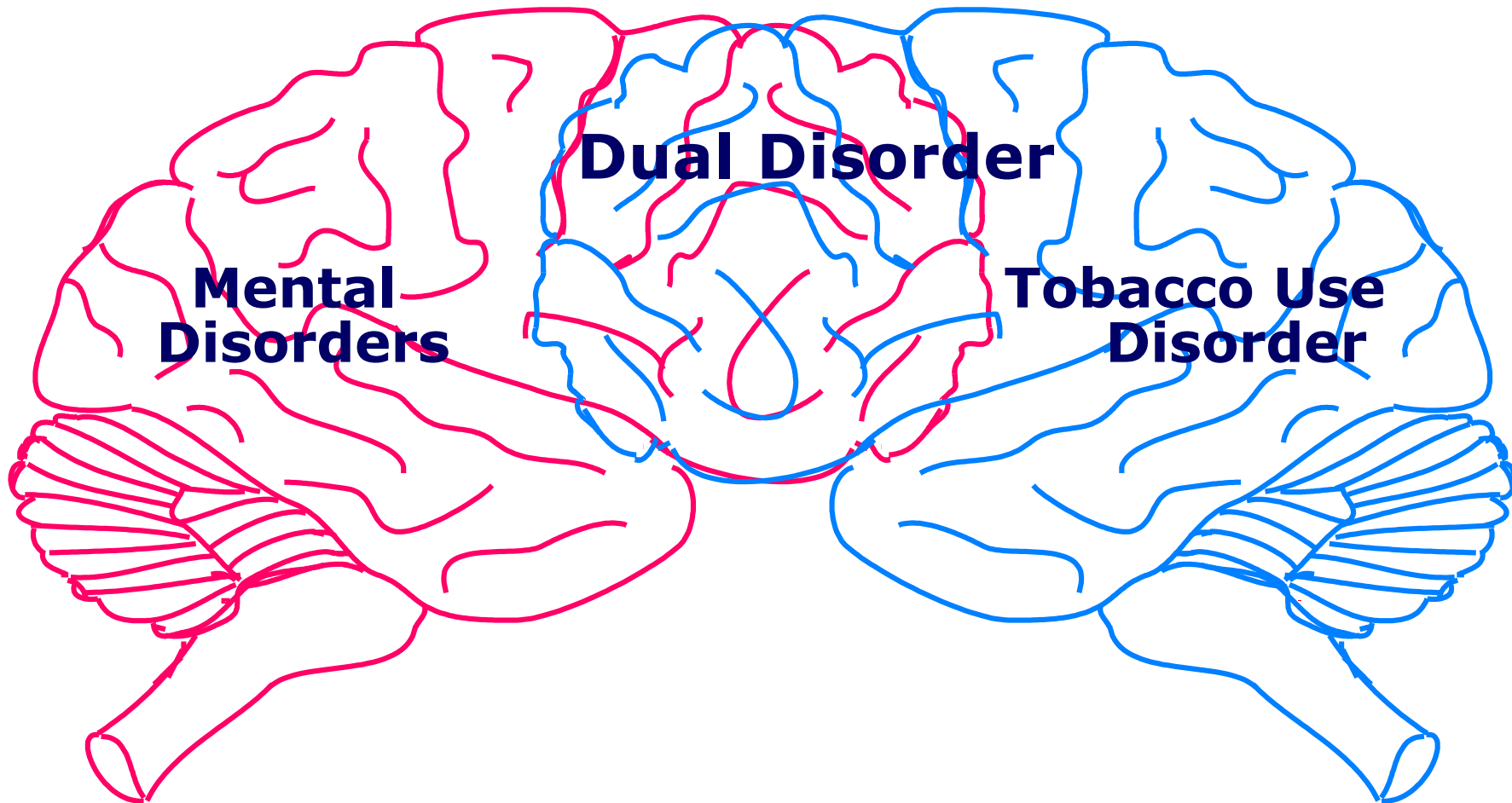


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# ***TUD: DUAL DISORDER?***

*Szerman et al. Rethinking dual disorders. ADTT. 2013*



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# **Neurobiological advances from the Brain Disease Model of Addiction\***

- *Only a minority of people who use drugs (TOBACCO) ultimately become addicted.*
- *In fact, the most severe phenotypic characteristics of addiction will develop in only a small percentage of people exposed to addictive drugs.*

## **Why is this?**

***Susceptibility differs because people differ in their VULNERABILITY to various GENETIC, neurodevelopmental and environmental factors.***

\* Volkow ND, Koob GF, McLellan AT. N Engl J Med 2016

# TOWARD PRECISION MEDICINE in ADDICTION TREATMENT.

## Vulnerability and GENETIC Factors\*

### Speaking of vulnerability. What does genetics tell us?

- Important advances in our understanding of genetic contributions have evolved with large-scale “**Genome-Wide Association Studies**” (GWAS) of smokers and non-smokers.
- Genetic factors have a role in **smoking initiation**, the development of **nicotine addiction** and the **likelihood of smoking cessation**.
- Indeed, heritability has been estimated to contribute to approximately **half of the variability** in TUD
- \* Le Foll, B., Piper, M.E., Fowler, C.D. et al. Tobacco and nicotine use. Nat Rev Dis Primers, 19 (2022).



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## Based on a recent **Genome-Wide Association (GWAS) meta-analysis\***

- A polygenic addiction risk score was associated with **SUD, Other Mental Symptoms or Psychiatric Disorders**, somatic conditions, and settings associated with addiction onset.
- This meta-analysis has identified **32 tobacco-specific loci**, including metabolic and receptor-encoding genes.
- These findings provide **insight into genetic risk sites for TUD and other mental disorders** that could be leveraged as treatment targets

\* Hatoum AS et al. Multivariate genome-wide association meta-analysis of over 1 million subjects identifies loci underlying multiple substance use disorders. *Nat Ment Health*. 2023 Mar;1(3):210-223.

## Nicotinic Cholinergic Receptors (CHRN)

- One of the most striking findings has been that allelic variation in the CHRNA5–CHRNA3–CHRN4 gene cluster correlates with an increased vulnerability for tobacco addiction\*
- Genes variants related to CHRNA5 **predict individuals who smoke more heavily\*\***
- \*\*Volkow ND, Boyle M. Neuroscience of Addiction: Relevance to Prevention and Treatment. Am J Psychiatry. 2018 Aug 1;175(8):729-740.
- \* Le Foll, B., Piper, M.E., Fowler, C.D. et al. Tobacco and nicotine use. Nat Rev Dis Primers, 19 (2022). <https://doi.org/10.1038/s41572-022-00346-w>

## Nicotine Metabolism: slow or fast metabolizers

- Allelic variation in **CYP2A6 (this enzyme metabolizes nicotine)** has also been associated with differential vulnerability to TUD.
- **CYP2A6 is highly polymorphic**, resulting in variable enzymatic activity, determining whether individuals are **slow or fast metabolizers** of nicotine
- “Fast nicotine metabolizers are genetically predisposed to smoke more and have more trouble quitting.
- Fast nicotine metabolizers respond better to Varenicline than to Nicotine Replacement Therapy alone.
- \*\*Volkow ND, Boyle M. Neuroscience of Addiction: Relevance to Prevention and Treatment. Am J Psychiatry. 2018 Aug 1;175(8):729-740.
- \* Le Foll, B., Piper, M.E., Fowler, C.D. et al. Tobacco and nicotine use. Nat Rev Dis Primers, 19 (2022).
- Lee SS, Chang Y, Rigotti NA, et al. Can Treatment Support Mitigate Nicotine Metabolism-Based Disparities in Smoking Abstinence? Secondary Analysis of the Helping HAND 4 Trial. Nicotine Tob Res. 2023 Aug 19;25(9):1575-1584.

# Could TOBACCO USE DISORDER be a single disorder? \*

- Neuroscience has revealed that
- Addiction involves a set of interconnected Brain processes that can be targeted strategically,
- rather than being a disorder defined principally by a single behavior (uncontrollable excessive drug (TOBACCO) use).\*
- These “**Brain processes**” are also expressed with different symptoms of other mental disorders.

\* Nora D. Volkow. Personalizing the Treatment of Substance Use Disorders. Am J Psychiatry 177:2, February 2020



# TOBACCO USE DISORDER: A single disorder? \*

- A recent study demonstrated that Mental Health problems during childhood and adolescence
- **Predict the onset of tobacco use among youth and young adults,**
- \*\_Green, V. R. et al. Mental Health Problems and Onset of Tobacco Use Among 12- to 24-Year-Olds in the PATH Study. J Am Acad Child Adolesc Psychiatry 57, 944-954 e944 (2018).  
<https://doi.org:10.1016/j.jaac.2018.06.029>



## ***Can tobacco use cause schizophrenia? “correlation does not imply causation”***

- An alternative theory is that tobacco smoking plays a role in the development of schizophrenia. This theory is in line with the high prevalence of smoking in patients with first-onset psychosis.
- A study<sup>1</sup> was shown that participants who smoked over 10 cigarettes per day were 2.28 times more likely to develop schizophrenia (95%CI = 1.19-4.34) than those who did not.
- Isuru A. et al Tobacco smoking and schizophrenia: re-examining the evidence. *BJPsych Advances* . 2019;25(6):363–372.
- <sup>1</sup>Weiser M., et al Higher rates of cigarette smoking in male adolescents before the onset of schizophrenia: a historical-prospective cohort study. *American Journal of Psychiatry* . 2004;161(7):1219–1223.

# **Nondaily Cigarette Smoking Is Increasing Among People With Mental Health problems in the United States\***

In the US, the prevalence of nondaily cigarette smoking is increasing among adults with **MENTAL HEALTH PROBLEMS**,

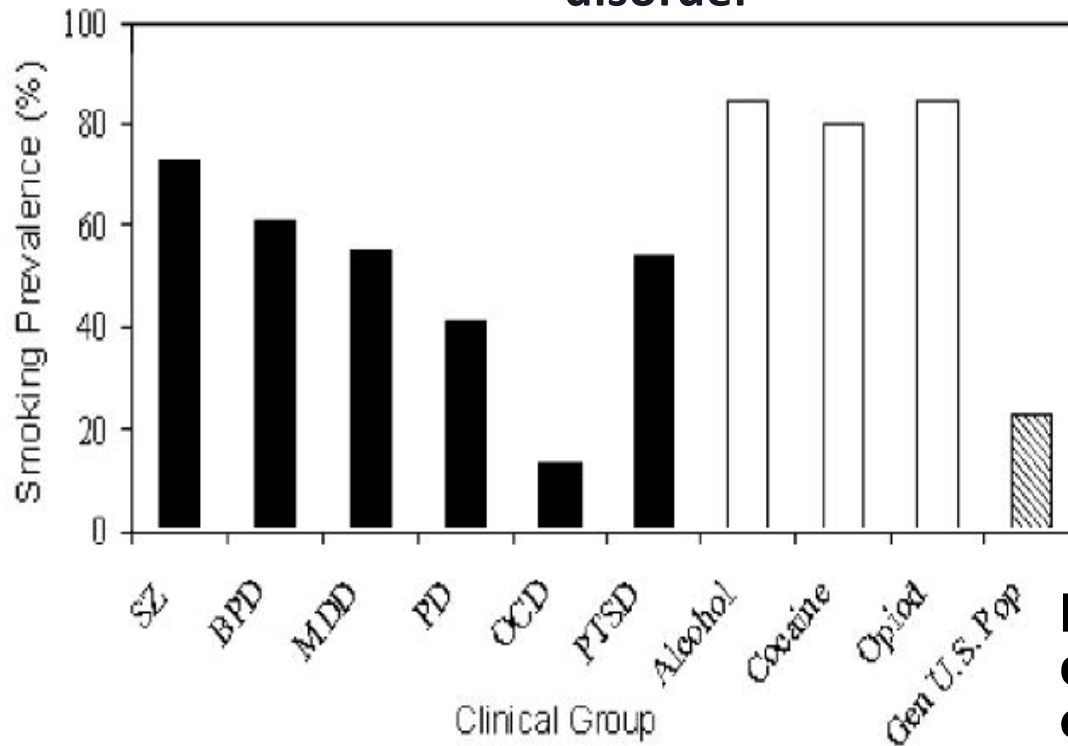
while it continues to decline among those without these vulnerabilities.

- Is there a similar trend in France? Europe?

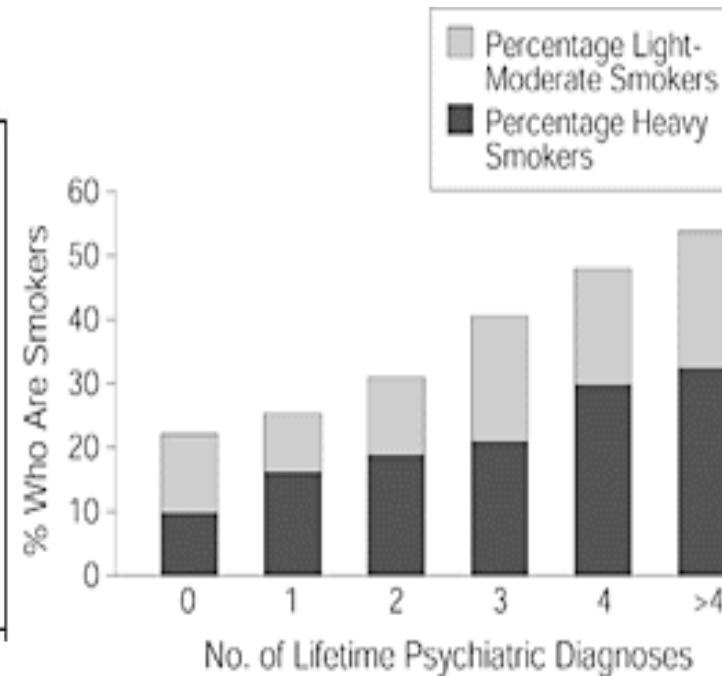
\*Andrea H. Weinberger, et al. Nondaily Cigarette Smoking Is Increasing Among People With Common Mental Health and Substance Use Problems in the United States:Data From Representative Samples of US Adults, 2005–2014. *J Clin Psychiatry* 2018;79(5):17m11945

# Dual Disorders: TUD and Other Mental Disorders

Prevalence of TUD in Individuals  
with SUD and other Psychiatric  
disorder



Kalman et al., Am J Addict. 2005



Persons with a mental  
disorder consumed 44.3%  
of cigarettes smoked in US.

Lasser et al., JAMA 2000



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## TUD and Other Mental Disorders

- This high prevalence of TUD among patients with Other Mental Disorders
- makes it reasonable to explore the assertion that both conditions are in some ways causally linked.

- \*Szerman N et al. Rethinking dual disorders. ADTT. 2013
- \* \*Szerman N. et al Tobacco use disorder and dual disorders. Actas Españolas de Psiquiatria. 2022. Jun;50(Supplement):77-138.



# Nicotinic Acetylcholine Receptor (nAChR) System and Mental Disorders

- Contributing to the potential shared vulnerability between Tobacco Use Disorder and Other Mental Disorders
  - is a dysregulation of the Nicotinic Acetylcholine Receptor (nAChR) System.

\* Mackowick KM, Barr MS, Wing VC et al. Neurocognitive endophenotypes in schizophrenia: modulation by nicotinic receptor systems. Prog Neuropsychopharmacol Biol Psychiatry. 2014 Jul 3;52:79-85



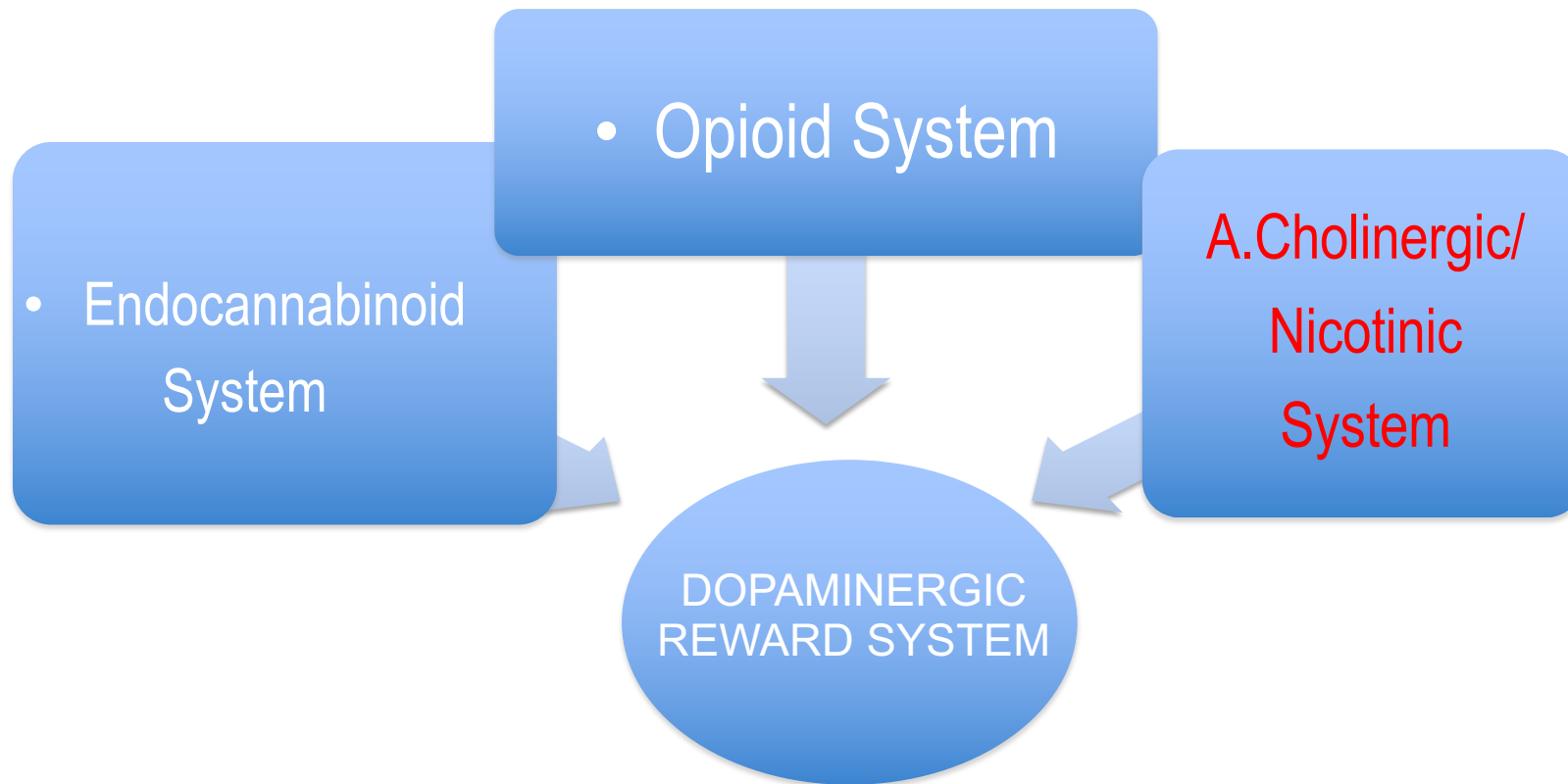
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# All psychoactive substances with abuse potential, bind to some endogenous systems

\*Szerman et al, ADTT, 2013



## NICOTINE'S EFFECT ON THE BRAIN

- Nicotinic nAChR stimulation drives attention, which is necessary for learning and memory. \*
- Comparative studies have shown that rats may learn to increase their nicotine intake before a cognitively-demanding task. \*
- In human smokers, cognitive abilities usually decline after smoking cessation. This effect can be reversed by a new nicotine dose. \*
- Accumulating research suggests that the cognitive-enhancing effects of nicotine may also significantly **contribute to the initiation and maintenance of TUD, especially in individuals with pre-existing cognitive deficits** \*\*

- \* Müller CP. Drug instrumentalization. Behav Brain Res. 2020 Jul 15;390:112672. doi: 10.1016/j.bbr.2020.112672. Epub 2020 May 19. PMID: 32442549.
- \*\*Valentine G, Sofuoglu M. Cognitive Effects of Nicotine: Recent Progress. Curr Neuropharmacol. 2018;16(4):403-414.



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## TUD AND DEPRESSIVE SYMPTOMS: MAO INHIBITION

- Monoamine oxidase (MAO) inhibition is significant in smokers but **does not** appear to be related to nicotine.
- People with depressive symptoms might relieve their symptoms due to this MAOI effect of Tobacco, independent of nicotine
- This could explain why the modulation of the cholinergic/nicotinic system with Varenicline or Nicotine Replacement is not sufficient in some patients

Truman P, Grounds P, Brennan KA. Monoamine oxidase inhibitory activity in tobacco particulate matter: Are harman and norharman the only physiologically relevant inhibitors? *Neurotoxicology*. 2017;59:22-26.

Hogg RC. Contribution of Monoamine Oxidase Inhibition to Tobacco Dependence: A Review of the Evidence. *Nicotine Tob Res*. 2016;18(5):509-23.





# Tobacco Use Disorder and Psychosis\*

- A recent **meta-analysis** indicated that the pooled worldwide prevalence of **TUD among people with a primary diagnosis of schizophrenia, is 65%.\***
- These data could reach **78% on the schizophrenia spectrum\*\***
- They also **smoke more cigarettes per day** and inhale more deeply than other smokers, **achieving higher blood levels of nicotine** than smokers without serious mental illnesses (Ruther et al, 2014)
  
- Fornaro M, Carvalho AF, De Prisco M *et al.* The prevalence, odds, predictors, and management of tobacco use disorder or nicotine dependence among people with severe mental illness: Systematic review and meta-analysis. *Neurosci Biobehav Rev* 2022; 132:289-303.
- Szerman N. et al. Tobacco use disorder and dual disorders Joint statement by the Spanish Psychiatry Society and the Spanish Dual Disorders Society. *Actas Esp Psiquiatr.* 2022 Jun;50(Supplement):77-138.

## Nicotinic Receptors and Schizophrenia\*.

Research assesses the involvement of the NICOTINIC SYSTEM in schizophrenia and suggests ways in which this system may participate in the pathophysiology of this disease.

**Expression of NICOTINE RECEPTOR is REDUCED in SCHIZOPHRENIA and given these findings; it has been suggested that vulnerability to both disorders may be related.**

\* Neves GA, Grace AA.  $\alpha$ 7 Nicotinic receptor-modulating agents reverse the hyperdopaminergic tone in the MAM model of schizophrenia. *Neuropsychopharmacology*. 2018 Jul;43(8):1712-1720. doi: 10.1038/s41386-018-0066-0.

# Precision Psychiatry and Dual Disorders\*

“One man’s meat is another man’s poison.”



Due to the diversity in genotype and environment

- The effects of substances are not the same among different individuals, including those of a different sex.
- Psychoactive drugs can also have distinct effects depending on the mental state, based on the brain’s individual differences.
- \* Szerman N, Peris L J of Dual Diag. 2019



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## “Nicotine effect is different in schizophrenia and in non-schizophrenia populations”\*

- Nicotine can have different effects on different brains
- Nicotine administration normalized (Default Mode Network -DMN) hyperconnectivity in schizophrenia.
- The results suggest the high prevalence of nicotine use in schizophrenia may be an attempt to correct a network deficit known to interfere with cognition. (Self Medication Hypothesis)
- \*Heather Burrell Ward, et al Evidence for Schizophrenia-Specific Pathophysiology of Nicotine Dependence. Frontiers, 2022

# Neurocognitive endophenotypes in schizophrenia: modulation by Nicotinic Receptor Systems\*

- Neurocognitive deficit (NCD) (problems with *reaction time, spatial working memory, sustained attention, and sensory gating*) is a **specific phenotype or endophenotype** of schizophrenia, present in **80% of cases**
- It's stable in all phases of the illness and it's heritable
- NCD could be a vulnerability factor for starting and continuing smoking
  
- Pre-clinical evidence established a relationship between NCD and nAChR and other neurotransmitters ( DA; Glutamate, GABA)
  
- These deficits improved with the administration of nicotine in patients with schizophrenia.
  
- Mackowick, et al Neurocognitive endophenotypes in schizophrenia: modulation by nicotinic receptor systems. Prog Neuropsychopharmacol Biol Psychiatry. 2014 Jul 3;52:79-85.

# TUD and ADHD\*

- **ADHD** is a highly prevalent disorder and one of the most striking Dual Disorder is **TUD**.
- Youth diagnosed with ADHD are 2-3 times more likely to smoke than their peers without ADHD, initiate smoking earlier in life and progress more quickly and more frequently to regular use and dependence.
- **Possible explanations:**
  - (a) self-medication of ADHD symptoms with nicotine;
  - (b) common genetic or environmental determinants for ADHD and TUD.
- **You should note that Bupropion, Varenicline and Nicotine can also improve ADHD\*\***
- \* van Amsterdam J, et al Causal Factors of Increased Smoking in ADHD: A Systematic Review. *Subst Use Misuse*. 2018 Feb 23;53(3):432-445.
- \*\*Verbeeck W, et al. Bupropion for attention deficit hyperactivity disorder (ADHD) in adults. *Cochrane Database Syst Rev*. 2017 Oct 2;10(10):CD009504

# Why do people with severe mental disorder smoke so much?

- Nicotine use might be a form of self-medication
- Improve **cognition and mood\*** (Heather Burrell Ward\*, et al. Frontiers in Psychiatry. 2022)
- Reduce **dysphoria, stress and agitation** (Allen MH et al Am J Psychiatry 2011)
- Reduce **the negative symptoms.** (Tidey JW et al. Prev Med. 2018)
- Reduce **the severity of the side effects** of the antipsychotic medication (Mobascherand Winterer, 2008; Kelly et al, 2011)
  
- Regulate **appetite and food intake** (Schwartz A, Bellissimo N. Nicotine and energy balance: A review examining the effect of nicotine on hormonal appetite regulation and energy expenditure. Appetite. 2021 Sep 1;164:105260)
  
- And regulate a **dysfunctional brain nicotinic/cholinergic system**

# Tobacco Use Disorder and Other Mental Disorders: The Neglected Dual Disorder\*

- Assuming that **people with severe mental disorders will not be able to quit**, mental health professionals do not commonly address TUD.
- For a long time, psychiatry and addiction services have ignored, or even promoted, the use of tobacco among patients.
- Recently some measures have been implemented, but interventions are commonly limited to nicotine replacement therapy **during admissions**.
- Therefore, **TUD** treatment programs within mental health settings remain scarce.
- \* Parro-Torres C.....and Szerman N. Tobacco use disorder and other mental disorders: The neglected dual disorder. Span J Psychiatry Ment Health. 2024 May 11:S2950-2853(24)00029-2.



## A randomized controlled trial of combined behavioral and pharmacological intervention targeted TUD Patients WITH OTHER SEVERE MENTAL ILLNESS\*

- The proportion of participants who quit smoking at 6 months was higher in **the intervention group** than in the **usual care group** (32 [14%] of 226 vs 14 [6%] of 217
- **but the waning of this effect by 12 months means that continued treatment is needed for sustained quitting.**
- \*Gilbody S, et al. Smoking cessation for people with severe mental illness (SCIMITAR+): a pragmatic randomized controlled trial to test the effectiveness of a combined behavioral and pharmacological smoking cessation intervention targeted specifically at people with severe mental illness. Lancet Psychiatry 2019.

## The four available drugs with the capacity to modulate the Endogenous Nicotinic System

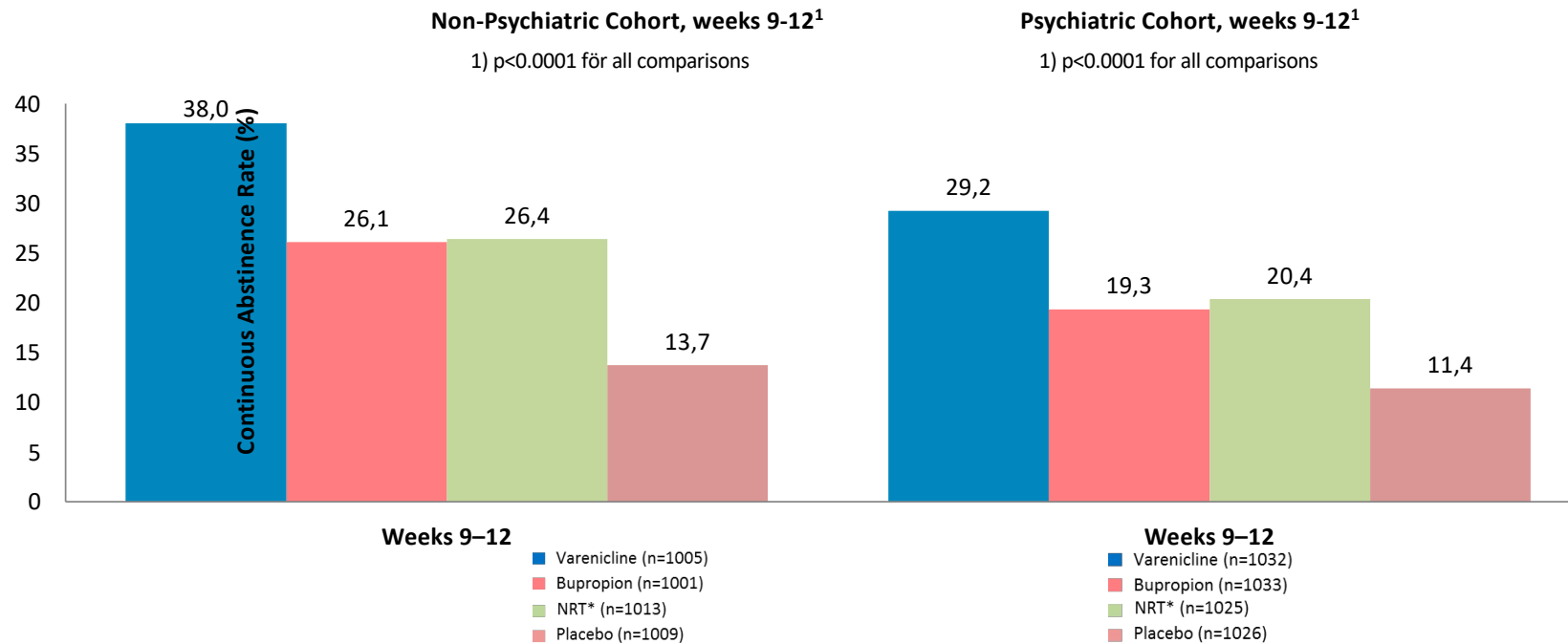
- For TUD, full and partial agonists, and noncompetitive antagonists of nACh receptor (approved by the FDA/EMA) are nicotine, varenicline, cytisine and bupropion.
- Deep TMS has been added to this biological treatment, and has been approved by the FDA for short-term smoking cessation
- \*All these therapies have proven to be effective, but only in the short term: trials show that a high percentage of people who quit smoking relapse within a year.
- But **in people with severe mental disorders**, a significant percentage **do not respond to this type of treatment**.
- \*Hajek P, et al Relapse prevention interventions for smoking cessation. Cochrane Database Syst Rev. 2013 Aug 20;(8):CD003999.

# Neuropsychiatric safety and efficacy of **varenicline, bupropion, and nicotine patch** in smokers with and without **psychiatric disorders (EAGLES)**: a **double-blind, randomised, placebo-controlled clinical trial**\*

- The study did not show a significant increase in neuropsychiatric adverse events attributable to varenicline or bupropion relative to nicotine patch or placebo.
- **Varenicline was more effective than placebo, nicotine patch, and bupropion** in helping smokers achieve abstinence, whereas bupropion and nicotine patch were more effective than placebo.

\* Anthenelli RM, et al Neuropsychiatric safety and efficacy of varenicline, bupropion, and nicotine patch in smokers with and without psychiatric disorders (EAGLES): a double-blind, randomised, placebo-controlled clinical trial. Lancet. 2016 Jun 18;387(10037):2507-20.

## Efficacy: Continuous Abstinence Rates (CARs)\*



**Varenicline** resulted in significantly more continuously smoke-free patients than all other treatment options during weeks 9-12 – both among patients **with stable mental illness** (p<0.0001) and patients without mental illness (p<0.0001).

\* Anthenelli RM, et al Lancet. 2016 Jun 18;387(10037):2507-20.

## Combinations of pharmacotherapies may be more effective for the treatment of TUD in people with mental disorders.

- Combining different forms of nicotine delivery: patches with gum is more effective than a single form of NRT\*.
- Combining drugs with different mechanisms of action, such as varenicline and NRT, has increased quit rates compared with use of a single product\*
- The current evidence suggests that **Electronic Nicotine Delivery systems (ENDS)** are an effective treatment tool, but more research is needed to confirm its long-term effectiveness and safety\*\*
- Combining **varenicline and ENDS** among varenicline non-responders in treatment for mental health illnesses\*\*\*
- \*\*Wadgave U, Nagesh L. Nicotine Replacement Therapy: An Overview. Int J Health Sci (Qassim). 2016 Jul;10(3):425-35.
- \*Rigotti NA, et al. Treatment of Tobacco Smoking: A Review. JAMA. 2022 Feb 8;327(6):566-577.
- \*\*\* Bullen C, et al. BMC Public Health. 2018 May 4;18(1):596.



## Preventive Medicine

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# Tobacco harm reduction: Past history, current controversies and a proposed approach for the future

Dorothy K. Hatsukami<sup>a</sup>  , Dana M. Carroll<sup>b</sup>



## TUD: Cessation vs Replacement Therapy\*

- The term “**CESSATION**” could exclude alternative treatment options beneficial to people with severe Mental Disorders, such as harm reduction or the less stigmatizing term “**SUBSTITUTION THERAPY.**”
- \*\* Parro-Torres C.....and Szerman N. Tobacco use disorder and other mental disorders: The neglected dual disorder. Span J Psychiatry Ment Health. 2024 May 11:S2950-2853(24)00029-2.

# Other tobacco products and nicotine substitutes, although not regulated, should be considered when treating people with severe mental disorders.

E-cig



Heated Tobacco



Snus





## SAMPLE OF SNUS PRODUCTS



The Swedish path to harm reduction:  
A type of moist powdered tobacco, typically held in the mouth between the lips  
and gums.

## A UK report highlights the potential of e-cigarettes to reduce the harms of TUD\*

- \*[www.thelancet.com](http://www.thelancet.com) Vol 400 November 19, 2022
- **Nicotine Vaping in England: an Evidence Update Including Health Risks and Perceptions\***: this report provides the most rigorous and comprehensive review on this topic to date.
- **Evidence on biomarkers of potential harm** (e.g. those that cause oxidative stress and inflammation) was limited
- Conclusions: Vaping poses a small fraction of the health risks of smoking. **Encouraging people with TUD to switch completely to vaping is likely an effective way to reduce the harms.**
- Most **major tobacco companies now include e-cigarettes in their product range.** Such industry involvement is a cause for concern.
- \* A report commissioned by the Office for Health Improvement and Disparities. Ann Mc Neill et al. Kings College London. 2022.



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# **Biomarkers of Exposure and Biomarkers of Potential Harm in Adult Smokers Who Switch to e-Vapor Products Relative to Cigarette Smoking in a 24-week, **Randomized, Clinical Trial\*****

- Long-term health effects of e-vapor products (EVPs) are not well-established.
- We compared biomarkers of exposure (BoE) to select harmful and potentially harmful constituents and biomarkers of potential harm (BoPH) in adult smokers who switched to EVPs versus continued smoking for 24 weeks.
- **This study demonstrates significant reductions in biomarkers of exposure (except for nicotine) accompanied with favorable changes in various biomarkers of potential harm (oxidative stress and inflammation) including pulmonary function.**
- **The totality of evidence suggests that exclusive EVPs use may present lower health risks compared with smoking cigarettes.**

\* Edmiston JS, et al Nicotine Tob Res. 2022 Jun 15;24(7):1047-1054.

## Is there a cardiovascular risk from the use of nicotine, like that of tobacco?\*

- The findings of this systematic review and meta-analysis indicate that:
- with moderate certainty, there are no significant associations between the use of Nicotine and the risk of clinically diagnosed adverse cardiovascular events
- \*Kim MM, et al. Study title: A systematic review of RCTs to examine the risk of adverse cardiovascular events with nicotine use. Front Cardiovasc Med. 2023 Mar 21;10:1111673.

## Examining the association of habitual e-cigarette use with inflammation and endothelial dysfunction in young adults: The VAPORS-Endothelial function study

- **Acute exposure to e-cigarette aerosol** has been shown to have potentially deleterious effects on the cardiovascular system.
- However, the cardiovascular effects of habitual e-cigarette use have not been fully elucidated.
- The findings suggest that **e-cigarette use may not be significantly associated with endothelial dysfunction and systemic inflammation** in healthy individuals. Longer term studies with larger sample sizes are needed to validate these findings.
- Boakye E, et al. Tob Induc Dis. 2023 Jun 10;21:75. Johns Hopkins Ciccarone Center for Prevention of Cardiovascular Disease, The Johns Hopkins University, Baltimore, United States.

## Tobacco end games\*

Some people have proposed getting rid of commercial tobacco products in this century and hastening **the demise of the tobacco industry**.

Some **tobacco companies** are responding with a strategy of switching to less harmful nicotine delivery systems.

Some countries are moving towards this goal; for example, New Zealand has set a target of less than 5% of New Zealanders being smokers by 2025.

## Could people with Severe Mental Disorders live without Nicotine?

\* Le Foll B, Piper ME, Fowler CD, Tonstad S, Bierut L, Lu L, Jha P, Hall WD. Tobacco and nicotine use. Nat Rev Dis Primers. 2022 Mar 24;8(1):19.



## TAKE HOME MESSAGE

- 1- **TUD** occurs with OTHER MENTAL DISORDERS (**Dual Disorders**) and the most frequent diagnosis is people with **Severe Mental Disorders**
- 2- TUD should be explored and diagnosed in all patients with **Severe Mental Disorder** as the same clinical condition, a Dual Disorder.
- 3- The treatment must be started jointly from the first moment, to be integrated.
- 4- We need to start with an approved medication or deep TMS for our patients.
- 5- For people who are failing, the goal should be **harm reduction (replacement therapy)** on the path to possible quitting.
- 6- According to the perspective of **Neuroscience and Precision Psychiatry**, treatment must be personalized and may include more than one therapeutic option.
- 7- This treatment **must be maintained for long periods of time**, as is done with antipsychotic medication.

\*Szerman N. et al Tobacco use disorder and dual disorders. Actas Españolas de Psiquiatria. 2022



**SEPD**





Thank you for your attention



**WADD**  
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