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Title: Buprenorphine and Naloxone Combinations and Dopamine

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Abstract: Background: Opioid dependence and death in America have reached epidemic proportions. Since 2000, we have seen an increase of over 3,000 percent in patients seeking treatment for substance use disorders. The “gold standard” for medically –assisted treatment, that is, Buprenorphine (a partial opioid agonist), combined with Naloxone, an opioid antagonist. Unfortunately, the relapse rates for Buprenorphine programs are high, and withdrawal reactions are common when Buprenorphine is precipitously discontinued. We must find approaches to treating substance use disorders that are more effective.

Objectives: This report reviews the neuropharmacology of neurotransmitters involved in brain reward circuitry to increase understanding of the effect of Buprenorphine/Naloxone treatment on patients with substance use disorders.

Discussion: We provide evidence, from animal and human models, regarding the acute and chronic effects of Buprenorphine on Dopaminergic reward processing. Microdialysis in animal models reveals that acute Buprenorphine tends to increase mesolimbic dopamine release. However, longterm use tends to decrease dopamine release. Cessation of Buprenorphine combination treatment increases drug reinstatement and relapse.

Conclusions: This review of both the acute and chronic effects of Buprenorphine naloxone

combination therapy on neurotransmission and behavior suggests new treatment targets and clinical options. “Pro-Dopamine Regulation” to induce dopaminergic homeostasis, via new options, other than the current, underutilized FDA approved Medication Assisted Treatments, which favor dopamine antagonism is proposed. We hypothesize that dopamine homeostasis is a crucial process that suppresses withdrawal symptoms, drug seeking and relapse in abstinent individuals.