# OST and Depression

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ST VINCENT'S HEALTH AUSTRALIA

# DR. McMUNN'S ELIXIR OF OPIUM.

## THIS IS THE PURE AND ESSENTIAL EXTRACT FROM THE NATIVE DRUG.

It contains all the valuable medicinal properties of Opium in natural combination, to the exclusion of all its noxious, deleterious and useless principles, upon which its bad effects depend.

It possesses all the sedative, anodyne, and anti-spasmodic powers of Opium.

*To produce sleep and composure. To allay convulsions and spasmodic action. To relieve pain and irritation, nervous excitement and morbid irritability of body and mind, etc., etc.*

And being purified from all the noxious and deleterious elements, its operation is attended by

*No sickness of the stomach, no vomiting, no costiveness, no headache.*

*Nor any derangement of the constitution or general health.*

Hence its high superiority over Laudanum, Paregoric, Black Drop, Denarcotized Laudanum, and every other opiate preparation.

## The Elixir of Opium is also greatly superior to Morphine.

1. In its containing all the active medicinal virtues of Opium in native combination, and in being its full representative, while Morphine, being only one of its principles, cannot alone, and that in an artificial state of combination too, produce all the characteristic effects of so triumphant a remedy, when four or five of its other valuable principles are excluded.
2. In its effects, the Elixir is more characteristic, permanent and uniform than any of the *artificial compounds* of Morphine.
3. And as a *Preparation*, it is not liable to decompose or deteriorate like the *Solutions* of Morphine: and thus is obviated a serious objection, which has prevented the latter from being used with precision and effect.

To speak summarily, the Elixir of Opium, as a remedy, may be adopted in all cases in which either Opium or its preparations are administered, with the certainty of obtaining all their salutary and happy effects, without being followed by their distressing and pernicious consequences.

All orders from the "Trade," must be addressed, as heretofore, to **A. B. & D. Sands,** Wholesale Druggists, 100 Fulton Street, corner of William, New York. Sold by J. B. Wilder & Bro. and Wilson, Starbird & Smith, Louisville; W. H. Harrison, Cincinnati, and H. Blakesley, St. Louis.

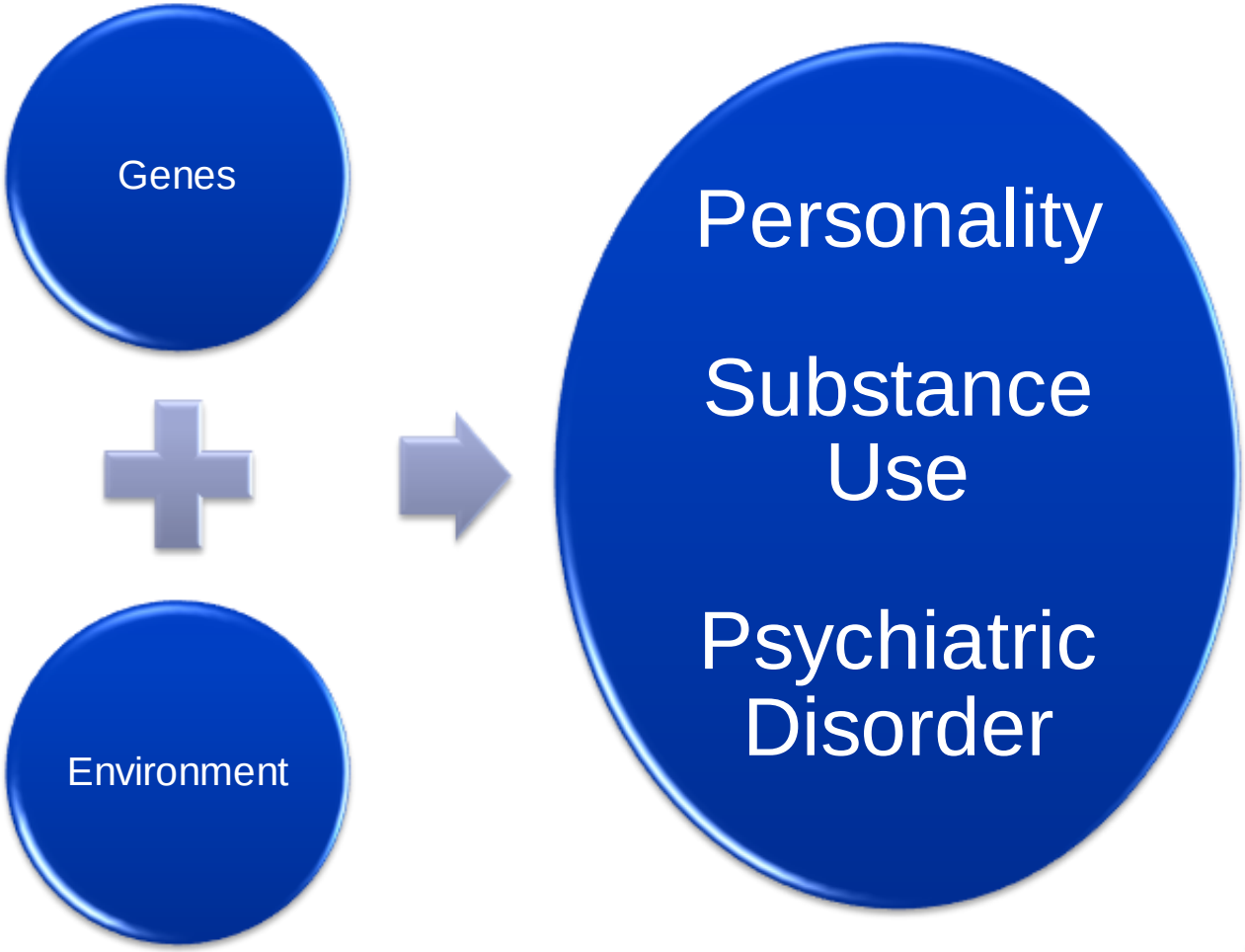
# Opioid use disorder and depression

- **Five times more likely than the general population to have a depressive disorder**
- **Three times more likely to have an anxiety disorder**
- **Rates are higher in women**
- **Depressive disorders are associated with worse treatment outcomes.**
- **Lifetime prevalence rates in dependent patients of 20% to 50%**

# Opioid use disorder and depression

- **Opioid**

# Comorbidity



# Social complications of opioid use

- **Vulnerability whilst substance affected**
- **Poverty**
- **Homelessness**
- **Conflict**
- **Loss of pleasure and normal activities of life**
- **High risk behaviours to obtain drugs; theft, dealing, sex work.**
- **Risks of misadventure via contact with criminals**
- **Risk of incarceration**
- **Difficulties of obtaining employment or housing with a criminal history**
- **Social and familial isolation**
- **Stigma**

# Depression – DSM 5 categories

**Unipolar major depression**

- **With anxious distress**
- **Melancholic features**
- **Atypical features**
- **Psychotic features**
- **Peripartum onset**
- **Mixed features**
- **Catatonia**

**Persistent depressive disorder**

**Substance induced depressive disorder**

**Medically induced depressive disorder**

**Grief**

**Bipolar Depression**

**Schizoaffective disorders**

# Treatment

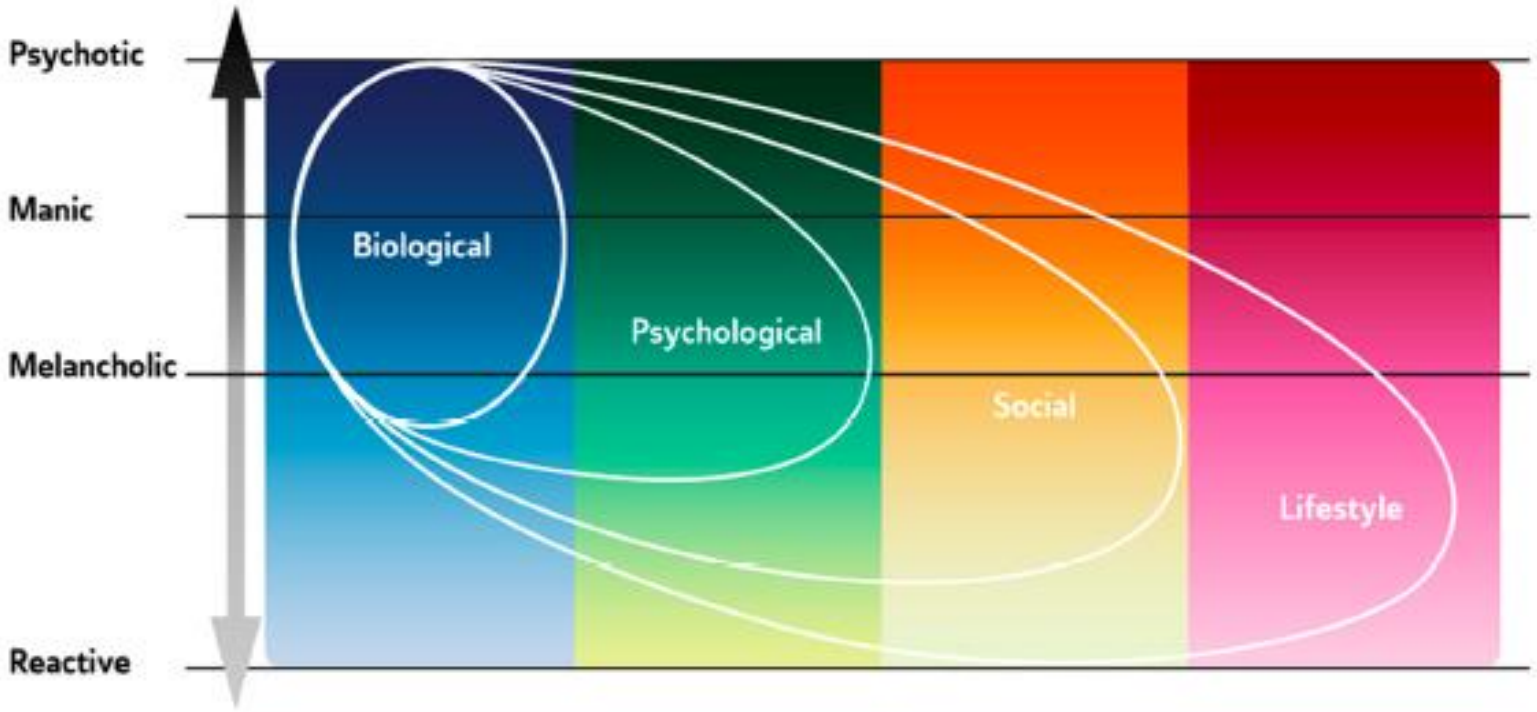
- **Treatment for opioid use disorder and reduction or cessation of use is associated with an improvement in depressive symptoms**
- **Stable appropriate dose of OST.**
- **Controlled trial of buprenorphine vs methadone showed equivalent efficacy (Mattick et al. , 2003)**
    - Reduced toxic effects of unknown substances
    - Treatment alliance and support
    - Reduced stress
    - Mu agonist maintenance agents, kappa antagonism by buprenorphine
    - Social stability
    - Improved health
    - Cessation of cycle of intoxication/withdrawal
    - Brain reward system - resensitisation

# Rate and risk factors of depression in MMT

- **already being in MMT**
- **female gender**
- **any DSM 4 axis I psychiatric diagnosis**
- **taking any psychotropic medication**
- **abuse or use of prescribed benzodiazepines**
- **methadone dose >120mg/day**

# Do opiate dependent patients respond to antidepressant medication?

## Figure 3. Biopsychosocial & Lifestyle Model (BPSL).




| Biological Treatments | Psychological Treatments | Social Treatments | Lifestyle Treatments |
|---|---|---|---|
| · Antidepressants<br>· Antipsychotics<br>· Mood stabilisers<br>· Electroconvulsive therapy<br>· Transcranial magnetic stimulation | · Brief cognitive behavioural therapy<br>· Formal cognitive behavioural therapy<br>· Interpersonal therapy<br>· Mindfulness<br>· Acceptance and commitment therapy<br>· Schema therapy | · Family psychoeducation<br>· Family / friends<br>· Formal support groups<br>· Community groups<br>· Caregivers<br>· Employment<br>· Housing | · Exercise<br>· Diet<br>· Smoking cessation<br>· Alcohol cessation<br>· Ceasing drugs<br>· Managing substance misuse<br>· Sleep |

# Treatment and management

- **Screen for depression.**
- **Treat opioid use disorder - stable appropriate dose.**
- **Monitor mood - feedback to patient.**

- **Avoid benzodiazepines.**
- **Avoid pregabalin and other sedating substances**
- **Ask about alcohol use and monitor.**

- **Stable housing**
- **Safety**
- **Patient goals**

# Treatment and management 2

- **Depression – review symptoms**
- **Medical comorbidities – consider**
- **Consider antidepressant medication.**
- **Lack of response – review diagnosis**
- **Psychiatry referral for assessment?**
    - Risk Issues
    - Other psychiatric comorbidities
    - Complex personality structure
    - Lack of response to treatment
- **Focal psychological input**
- **Support groups**
- **Lifestyle changes**
- **Social and familial supports**

# Kappa opioid receptor antagonism

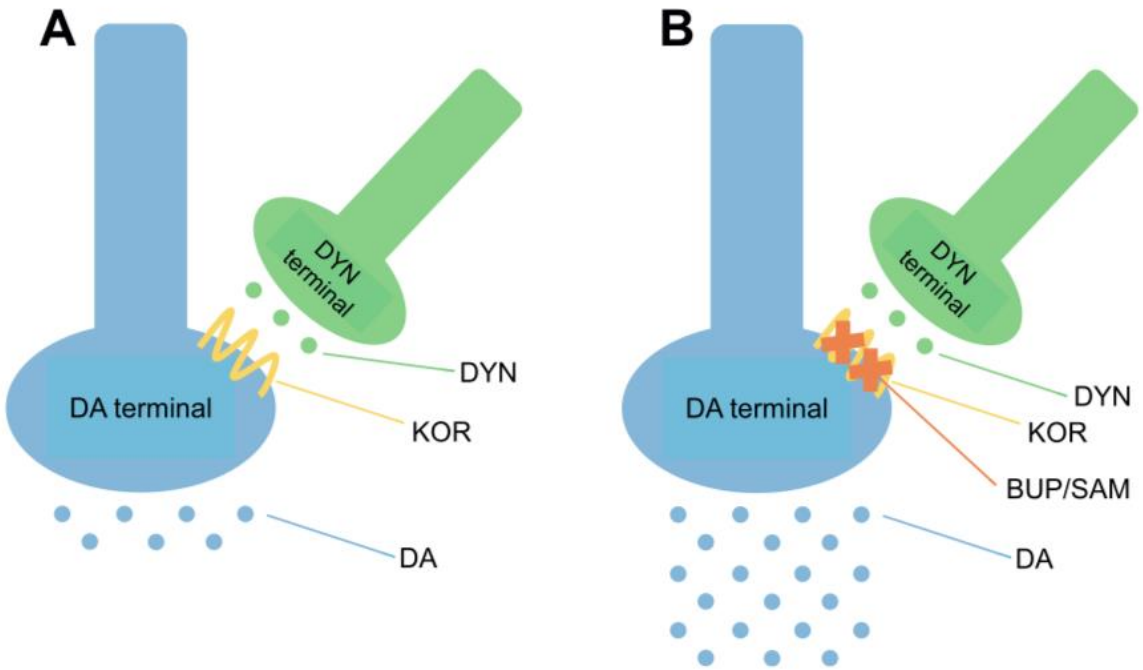



**FIGURE:** Mechanism of action of buprenorphine/samidorphan (BUP/SAM) (A) In the absence of kappa opioid receptor (KOR) antagonism, endogenous dynorphin (DYN) activates KOR-mediated dopaminergic inhibition, which may lead to depressive-like symptoms of dysphoria and anhedonia. (B) In the presence of KOR antagonism via BUP/SAM, KOR-mediated dopaminergic inhibition is blocked, facilitating increased dopamine (DA) release, which may lead to a reduction in depressive-like symptoms

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# Kappa opioid receptor antagonism: Are opioids the answer for treatment resistant depression?

Peckham AM[1], De La Cruz A[2], Dufresne RL[3].

Author information

## Abstract

**INTRODUCTION:** Past trials of buprenorphine (BUP) in the treatment of major depressive disorder (MDD) have displayed favorable results, although its clinical utility was limited by the risk of abuse or physical dependence. By combining BUP with samidorphan (SAM), the euphoric high is negated by an opposing mechanism, which theoretically reduces addictive-like properties while allowing the antidepressant properties to remain. As such, the objective of this article is to analyze the results of BUP/SAM premarketing clinical trials as adjunctive treatment for treatment-resistant MDD.

**METHODS:** A comprehensive PubMed/MEDLINE search was conducted through November 9, 2017, using the following search terms: depression, samidorphan, buprenorphine, ALKS-5461. Additional data were obtained from Clinicaltrials.gov and resources included in the present study. All English-language clinical trials evaluating the combination of BUP/SAM in the treatment of MDD were included.

**RESULTS:** A few premarketing studies have evaluated the efficacy and safety of BUP/SAM combination as adjunctive treatment in patients with treatment-resistant MDD. The FORWARD-1 through FORWARD-5 trials concluded (1) the most effective dosing ratio of BUP/SAM to reduce abuse potential was 1:1; (2) statistically significant changes in scores from baseline on the Montgomery-Asberg Depression Rating Scale were noted for the 2 mg/2 mg dose compared with placebo; and (3) the most commonly reported adverse effects were nausea, dizziness, and fatigue.

**DISCUSSION:** Buprenorphine/samidorphan has shown favorable results for efficacy and tolerability in premarketing studies evaluating its use as adjunctive therapy for treatment-resistant MDD. Its novel mechanism targeting the opioid pathway may serve as a promising

Int J Mol Sci. 2018 Aug 15;19(8). pii: E2410. doi: 10.3390/ijms19082410.

# The Efficacy of Buprenorphine in Major Depression, Treatment-Resistant Depression and Suicidal Behavior: A Systematic Review.

Serafini G[1,2], Adavastro G[3,4], Canepa G[5], De Berardis D[6], Valchera A[7], Pompili M[8], Nasrallah H[9], Amore M[10,11].

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## Abstract

Although several pharmacological options to treat depression are currently available, approximately one third of patients who receive antidepressant medications do not respond adequately or achieve a complete remission. Thus, novel strategies are needed to successfully address those who did not respond, or partially respond, to available antidepressant pharmacotherapy. Research findings revealed that the opioid system is significantly involved in the regulation of mood and incentives salience and may be an appropriate target for novel therapeutic agents. The present study aimed to systematically review the current literature about the use of buprenorphine (BUP) for major depression, treatment-resistant depression (TRD), non-suicidal self-injury (NSSI) behavior, and suicidal behavior. We investigated Pubmed and Scopus databases using the following keywords: "buprenorphine AND depression", "buprenorphine AND treatment resistant depression", "buprenorphine AND suicid*", "buprenorphine AND refractory depression". Several evidence demonstrate that, at low doses, BUP is an efficacious, well-tolerated, and safe option in reducing depressive symptoms, serious suicidal ideation, and NSSI, even in patients with TRD. However, more studies are needed to evaluate the long-term effects, and relative efficacy of specific combinations (e.g., BUP + samidorphan (BUP/SAM), BUP + naloxone (BUP/NAL), BUP + naltrexone) over BUP monotherapy or adjunctive BUP treatment with standard antidepressants, as well as to obtain more uniform guidance about the optimal BUP dosing interval.

**KEYWORDS:** buprenorphine; endocannabinoid system; major depression; suicidal behavior; treatment-resistant depression

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