



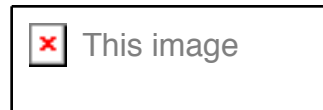
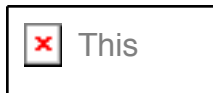
**UW PACC**

Psychiatry and Addictions Case Conference

UW Medicine | Psychiatry and Behavioral Sciences

# USING PSYCHOSTIMULANT TO AUGMENT DEPRESSION TREATMENT

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# GENERAL DISCLOSURES

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# GENERAL DISCLOSURES

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# SPEAKER DISCLOSURES

I have no conflicts of interest

# PLANNER DISCLOSURES

The following series planners have no relevant conflicts of interest to disclose:

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# OBJECTIVES

Review evidence of psychostimulant use in treatment of depression

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# FIRST LINE ANTIDEPRESSANTS

SSRI

- Except Fluvoxamine

SNRI

- Except Milnacipran (Fibromyalgia)

Bupropion

Mirtazapine





# ADEQUATE TRIAL

- 4-8 weeks on therapeutic dose
- If partial improvement in 6-12 weeks then increase the dose
  - Continue for 6-12 months
  - Long term use for second or third episode of depression

# TREATMENT RESISTANT DEPRESSION

Unsatisfactorily response to at least 2 trials (> 6 weeks) of antidepressant monotherapy

## Switch

**Intolerance of  
adverse effects**

No improvement in  
symptoms

## Augment

**Partial benefit**

Adverse effects but  
improved symptoms

# AUGMENTATION: OPTIONS

Bupropion or  
Mirtazapine

Atypical  
Antipsychotics

Lithium

Thyroid  
Hormone (T3)

Psychostimulants  
(Amphetamine  
Methylphenidate  
Modafinil)

# WHEN TO THINK ABOUT PSYCHOSTIMULANTS

Trials of FDA approved  
meds did not work

Fatigue, lack of energy,  
apathy, sleep  
disturbance, cognitive  
difficulties

# WHAT IS THE HESITATION?

- Misuse/abuse?
- Dependence?
- Is there evidence?

# PSYCHOSTIMULANTS

Modafinil

Amphetamines

Methylphenidate

# COCHRANE REVIEW 2008

- 24 studies
- Little data to support psychostimulant use as antidepressant augmentation
- No evidence to support modafinil use



# MODAFINIL

- FDA approved: narcolepsy, OSA and shift work sleep disturbance
- Armodafinil is R-enantiomer and longer half life
- Inhibit DA and NE transporters
- Less potential of abuse and addiction

# AUGMENTATION THERAPY IN DEPRESSION

- 4 RCT double blind studies

Results:

- Support the use of modafinil augmentation
- Improvement in depression score
- Improved remission rate
- Positive effects in first week
- Improved fatigue and sleepiness
- Increased SI (2 cases in Dunlop et al 2007)

Goss et al. J Clin Psychiatry. 2013

# METHYLPHENIDATE

- 16 wk RCT
- Geriatric depression N 143
- Citalopram + methylphenidate
  - Faster decrease in symptoms (at 4 wks)
  - Greater remission rate (60.4%)

Lavretsky et al. Am J Psych 2015 June

# LISDEXAMFETAMINE

## Meta-Analysis

- Superiority in treating for depression
- Well tolerated
- Not associated with SI

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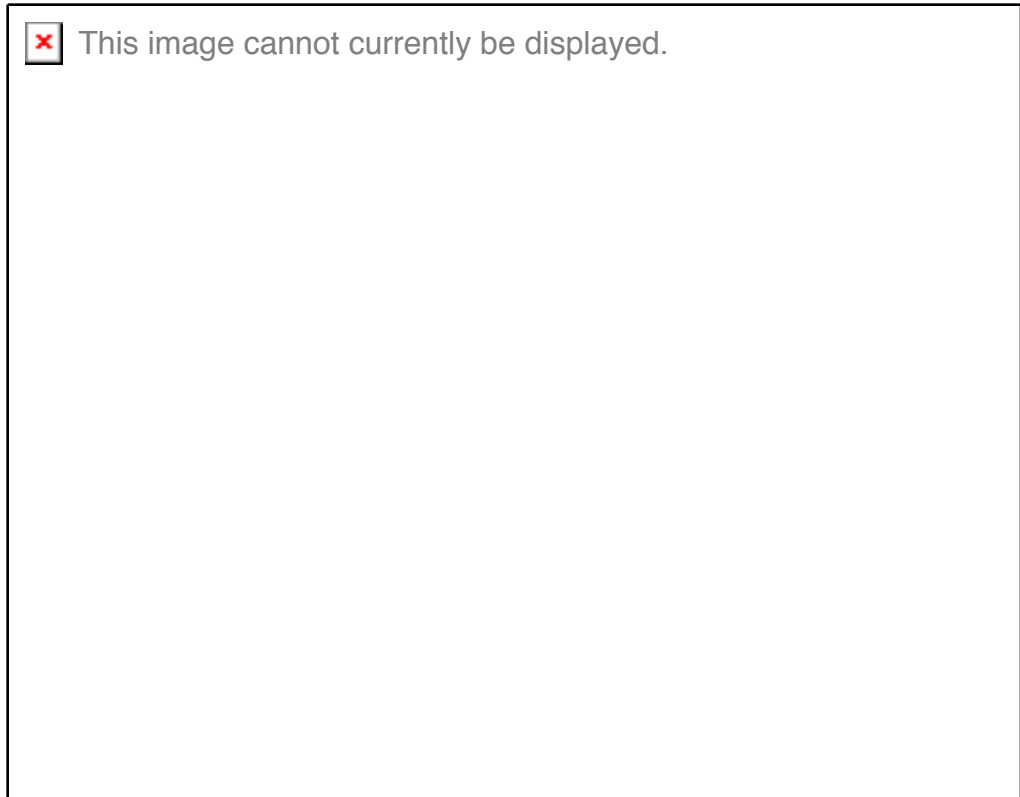
Giacobbe et al. J of Affective disorder. 2018

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# SUMMARY OF FINDINGS

- 21 articles
- Meds: armodafinil, modafinil, Lisdex-, Dex-, Amphetamine and methylphenidate
- Diagnosis: MDD and major depressive episode in bipolar disorder

Ar/modafinil	Clinically significant improvement OR 1.47;95% CI, 1.20-1.81
Dextroamphetamine	N= 22 , trial for 2 wks(OR 7.11;95% CI, 1.09- 46.44)
Lisdexamphetamine	Response but not statistically significant
Methylphenidate	Response but not statistically significant



# SUMMARY AND LIMITATIONS

- Overall greater response rate in mood disorders
- Adjunctive therapy is associated with clinically significant improvement
- Heterogeneity in diagnosis
- Challenge successful blinding
- Small sample sizes



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# FINDINGS

- No clear evidence supporting the use of stimulants as a supplement
- Reduction in psychiatric admission and bed days with methylphenidate and modafinil
- 54% reduction in intentional self harm and SA (< 30 yr old) with methylphenidate

# LIMITATIONS

- Study was based on register data
- Could not assess compliance of stimulants
- Diagnosed with depression in hospital
- Small sample size (modafinil and amphetamines)

# TAKE HOME POINTS

- Limited Evidence
- Off label use for depression
- Need for higher quality studies
- Consider as adjunct treatment when evidence-based treatment don't work
- Target Symptoms: Fatigue, low energy, concentration disturbance, hypersomnolence
- Consider modafinil first