APPROACH TO DEPRESSION

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Faculty/Presenter Disclosure

- **Faculty: Dr.** Jon Davine

- **Relationships with financial sponsors:**
  - **Any direct financial relationships including receipt of honoraria: Pri-Med Canada/Humber River Health, William Osler Health, Peterborough FHT, McMaster CME, KW Family Medicine, Ont. College of Family Physicians, Touchstone Institute, Trillium Health, CME Away by Sea Courses, Trillium Health Partners.**
  - **Memberships on advisory boards or speakers' bureau: No**
  - **Patents for drugs or devices**: No
  - **Other: financial relationships/investments: CAMH, Toronto, Co-Editor of Book, "Psychiatry in Primary Care"**

Disclosure of Financial Support

- **This program has not received financial support**
- **This program has NOT received in-kind support**

- **<u>Potential for conflict(s) of interest</u>:**
  - Jon Davine has not received payment

Objectives

- Describe a brief differential diagnosis of the sad state
- Describe how to choose, start, and increase antidepressant medication
- Describe recent recommendations re medications and augmentation techniques (CANMAT 2023)
- Describe ECT, TMS as treatment techniques

Sad State – Differential Diagnosis

- Rule out organic
- Adjustment disorder with depressed mood
- Unipolar depression
- Bereavement
- Bipolar disorder, depressed phase
- Dysthymic disorder (persistent depressive disorder)
- Postpartum Blues/Depression
- Seasonal Affective Disorder
- Premenstrual Dysphoric Disorder

R/O Organic

- TSH, CBC
- Anything else where history and physical take you
- Check re alcohol use– Choosing Wisely Canada says hold off on treatment and see if Etoh can be d/c'd

Bereavement

- Bereavement means grief after death of someone close to you
- I would include breakup of significant relationship (JAMA)
- Bereavement means you can have 2 months of SIGECAPS, and this is still normal bereavement
- Treatment is counselling ALONE
- After 2 months, graduates to depression
- Then treatment is counselling PLUS medication
- Risk factor is past history of depression
- DSM-V took out bereavement exemption. I totally disagree

Postpartum Blues

- 50-60% of women, thus NORMAL!
- Usually goes away within 7-14 days

- Treatment:
- Supportive counselling only

Postpartum Depression

- SIGECAPS +
- Within 30 days of delivery
- No past psych history: 10% risk
- Past depression : 50% risk

- Treatment is meds PLUS counselling

Persistent Depressive Disorder (Dysthymic)

- Chronic long term, low grade sadness.
- Minimum 2 years, often all one's adult life

- Treatment:
- Counselling alone. I add meds after a few months if counselling not working
- In research data, trend to improve with meds, but not statistically significant

Seasonal Affective Disorder

- Usually during winter months
- Reverse neurovegetative features
- Gets in way of one's life

- Treatment:
- Light therapy, 2 weeks prior to onset and two weeks post usual end of symptoms
- If light not successful, try antidepressant meds

Seasonal Affective Disorder

Premenstrual Dysphoric Disorder

- Treat 2 weeks on, 2 weeks off during luteal phase
- If not effective, try continuous treatment

Bipolar Disorder Type 2, Depressed Phase

- Always screen for past hypomanic episodes
- What looks like depression is actually bipolar type 2, depressed phase

- Treatment:
- Mood stabilizers NOT naked antidepressant

Adjustment Disorder with Depressed Mood

- Usually within 3 months of a stressor
- Usually goes away within 3 months of stressor getting dealt with
- Can go on for years if stressor continues

- Tx:

- Counselling ONLY!!

Unipolar Depression

- 15% lifetime prevalence
  - 10% men
  - 20% women

Diagnosis – SIGECAPS

- Low mood/irritable mood for at least 2 weeks, **but** I would say 3-4 weeks minimum

  - **S**leep
  - **I**nterests (and pleasure)
  - **G**uilt
  - **E**nergy
  - **C**oncentration
  - **A**ppetite
  - **P**sychomotor agitation/retardation
  - **S**ex, **S**uicide

Important to Remember

- r/o past depressive episodes
  - This has treatment implications: **length of time**

Recurrence and Treatment Length

- **1 episode: 50% recurrence rate**
  - Treat for 6-9 months of feeling good, overall ~1 year
  - 2023 CANMAT 6-12 months
- **2 episodes: 70% recurrence rate**
  - Treat for 12-18 months of feeling good
  - If 2 difficult episodes, treat indefinitely (possibly)
- **3 episodes: 90% recurrence rate**
  - Treat indefinitely (possibly), at least 2 years

Risk Factors for Prolonged Treatment >2y

- Persistent residual sx's
- Hx of childhood maltreatment (robust evidence)
- Greater severity of episodes
- Chronic depressive episodes
- Presence of medical co-morbidity (psychiatric or non)
- Greater number of previous episodes
- Poor social; supports
- Persistent stressful life events

- (CANMAT 2023)

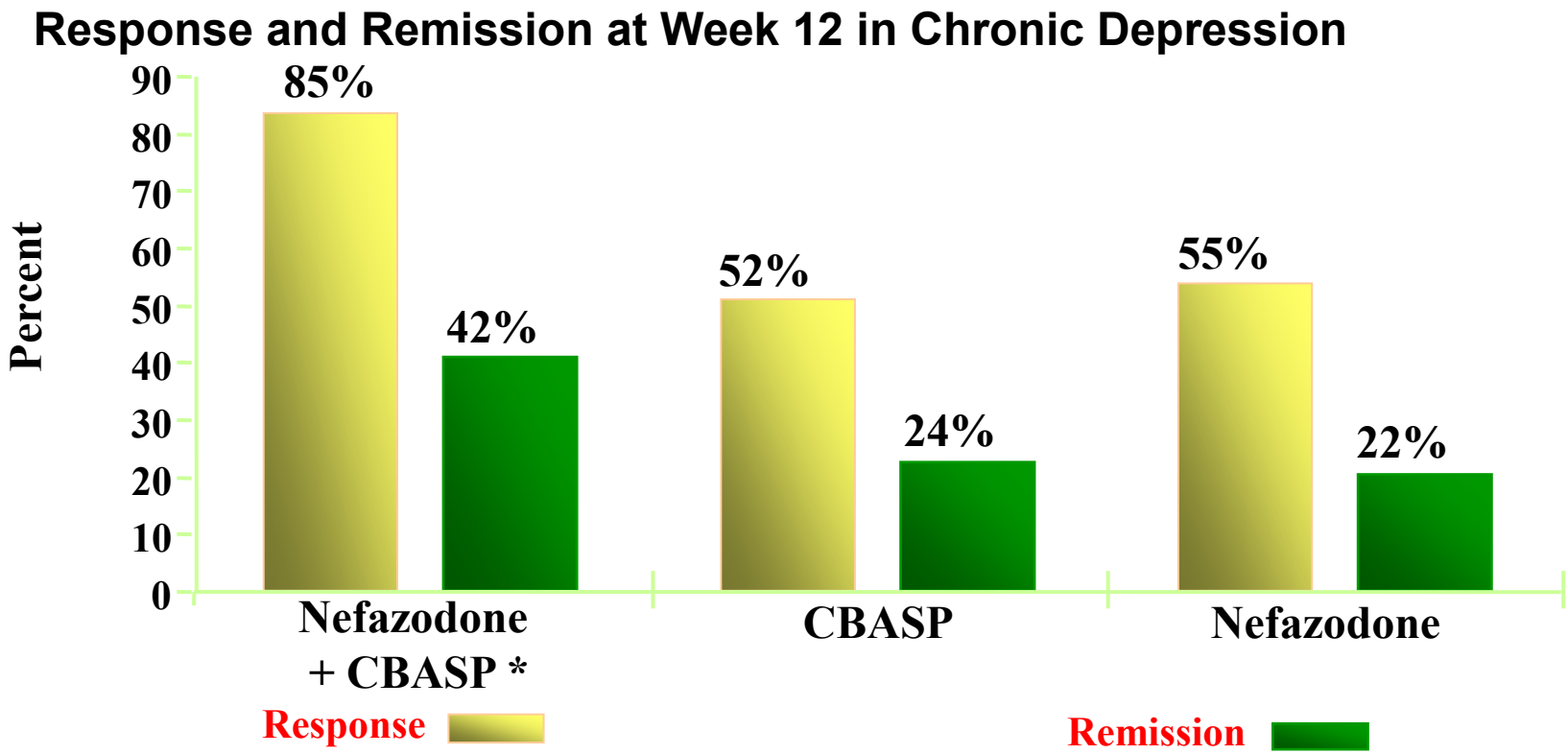
Counselling

- Stress diathesis model of depression
- Counselling can decrease stress, and increase supports
- Supportive therapy
- Cognitive Behaviour Therapy (CBT)
- Mind over Mood by Dennis Greenberger and Christine Padesky

Psychopharmacology

- So you've ruled out organic, it's not bipolar, it's not an adjustment disorder,
- You're going to start meds

Combination Pharmacotherapy and Psychotherapy is More Effective than Either Alone



$p \leq 0.001$ combined vs. treatment nefazodone

$p \leq 0.001$ combined treatment vs. psychotherapy

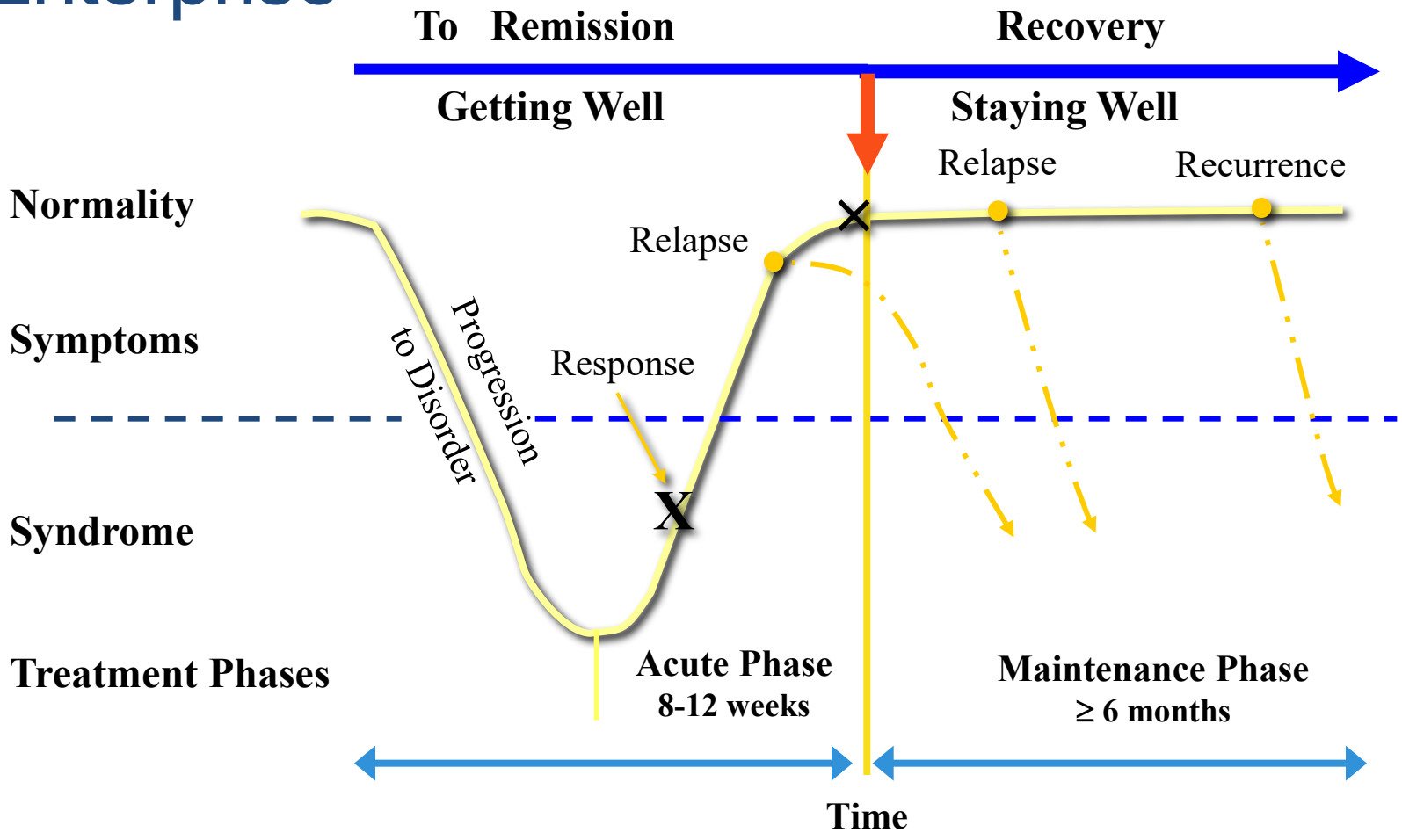
*Cognitive behavior and specific psychotherapy

$p \leq 0.001$ combined vs. treatment nefazodone

$p \leq 0.001$ combined treatment vs. psychotherapy

Keller *et. al.* The New England Journal of Medicine, May, 2000

Treating Depression is a Long-Term Enterprise



Depression is associated with high rates of relapse and recurrence

Adapted from Kupfer. 1991. Adapted from CANMAT Guidelines, June 2001.

SSRIs

Drug (Brand name)	Initial Dose (per day)	Range (per day)
Citalopram (Celexa)	20 mg	20-40 mg
Escitatalopram (Cipralex)	10 mg	10-20 mg
Fluoxetine (Prozac)	20 mg	20-60 mg
Fluvoxamine (Luvox)	50 mg	100-300 mg
Paroxitene (Paxil)	20 mg	20-60 mg
Sertraline (Zoloft)	50 mg	50-200mg

Other Antidepressants

- **SNRI**
  - Venlafaxine (Effexor)
    - Range: 75-225 mg per day
  - Desvenlafaxine (Pristiq)
    - Range: 50 mg per day
  - Duloxetine (Cymbalta)
    - Range 30-60 mg per day
- **NaSSA** (Noradrenergic and Serotonergic Specific Antidepressant)
  - Mirtazapine (Remeron)
    - Range: 15-45 mg per day

Other Antidepressants (2)

- **DNRI**
  - bupropion (Wellbutrin)
    - Range: 150-300 mg per day

New Antidepressant

- Vortioxetine (Trintellix) 10-20 mg./day

- It is felt to function much as an SSRI

Even Newer Antidepressants

- Vilazodone (Vibryd)
- SSRI plus partial serotonin agonist (SPARI)
- 10 mg. po od x 7 days, then increase to 20 mg.
- Range is 20-40 mg. With Food.

- Levomilnacipran (Fetzima)
- SNRI plus partial serotonin antagonist (SARI)
- 20 mg./ po od x 2 days then increase to 40 mg. po od
- Range is 40-120 mg./day

CANMAT 2023---- First Line

Escitalopram, Sertraline, Paroxetine, Citalopram, Fluoxetine, Fluvoxamine

Venlafaxine and Desvenlafaxine

Duloxetine

Buproprion

Mirtazapine

Vortioxetine

Levomilnacipran

Vilazodone

CANMAT 2023---Superior Efficacy (5-15% better)

Escitalopram

Sertraline

Venlafaxine XR

Mirtazapine

Paroxetine

Buproprion

Vortioxetine

(CANMAT 2023)

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Optimizing Dose

- Increase dose q2-3weeks depending on response
- Increment of increase = starting dose
- If doing better, don't adjust
- Once they plateau, increase, unless back to normal
- If not improved with 1st dose and 1 bump---X-Crossover, except Venlafaxine XR

X-Crossover

- For use when switching to a different antidepressant
- Lower first drug by typical increment q7days
- Start 2nd drug at half dose along with starting dose of first drug for 7 days
- Increase second drug to full starting dose while discontinuing the 1st drug

Compliance with Antidepressants in General Practice

Reasons for Drop Out & Time of Event			
Proportion of respondents	**Reason**	**Time of drop out**	**Potential MD strategies**
35%	Feel better	6.1 weeks	Reminder to stay on
30%	Side effects	4.5 weeks	Ask/address side effects
17%	Other (e.g., fear of dependence)	8 weeks	Explain antidepressants are non-addictive
15%	Told by doctor	3.2 weeks	Stay on medication, if well
15%	Lack of Efficacy	1-4 weeks	Remind efficacy begins later

"52% stopped taking their medication during a 12 week period. Two-thirds did not inform their GP"

Psychoeducation makes a difference in improving response rates

Side Effects

- GI upset (Give with meals)
- Sedation (after supper)
- Insomnia (after breakfast). Fluoxetine, Buproprion.
- Agitation
- Sexual (Mirtazapine, Wellbutrin, Desvenlafaxine, Vortioxetine, Vilazodone have less).

Interesting Facts (CANMAT 2023)

- In the over 65 group, SSRI<SNRI

- Fluoxetine 1st line for <25

Augmentation – Increasing Dose

- For partial response
  - Defined as 25% of the usual range or greater
- Go above the usual range
  - Often take meds one to two increments higher, as long as side effects are not a problem (except Escitalopram and Citalopram)

Augmentation – CANMAT 2023

- **First-Line Options:**
  - Aripiprazole – Level 1 2-10 mg.
  - Brexiprazole—Level 1 0.5-2.0 mg.

- **Second-line:**
  - Buproprion 150-450 mg.
  - Intranasal esketamine 56-84 mg. intranasally
  - IV racemic ketamine 0.5-1.0 mg./kg. IV
  - Olanzapine 2.5-10 mg.
  - Quetiapine XR 150-300 mg.
  - Risperidone 1-3 mg.
  - Lithium 600-1200 mg. (0.5-0.8mmol/L)
  - .

Augmentation Strategies – Atypicals

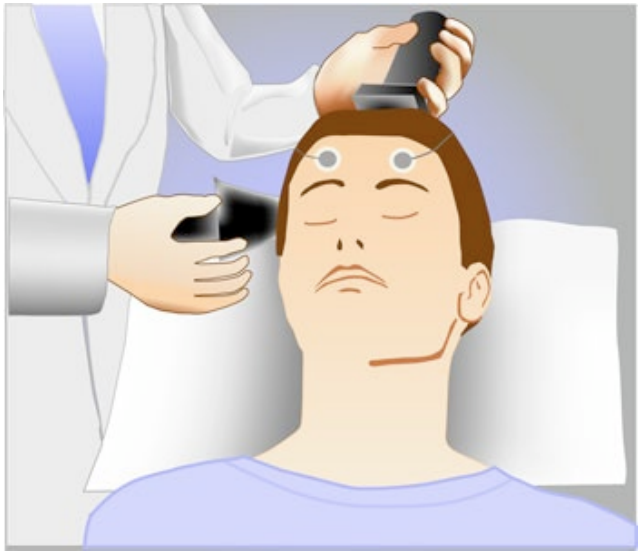
- Options
  - FIRST LINE:
  - Aripiprazole (Abilify) 2-4-6- up to 15 mg. po hs
  - Brexiprazole (Rexulti) 0.5--1--1.5—2mg. po qhs
  - SECOND LINE:
  - Quetiapine (Seroquel) 50-100-150 mg po daily (150-300 mg.)
  - Wellbutrin XL (Buproprion) 150-450 mg. po QAM
  - Wait 2-3 weeks between raises

ECT – Electroconvulsive Therapy

- Highest rate of therapeutic success
- No absolute contraindications
- Chief side effects are cognitive
  - Memory impairment typically resolves in a few weeks after cessation of treatment
  - Rarely, more pervasive and persistent cognitive disruption
- Method
  - Unilateral, non-dominant
  - Fewer side effects (e.g., cognition disruption)

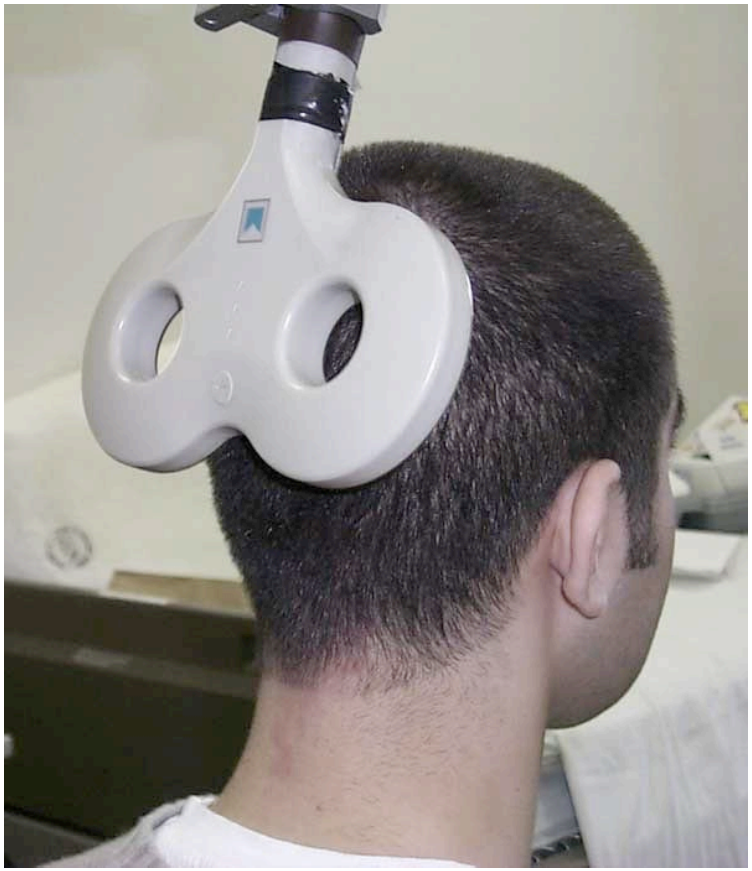
ECT – Indications

- Non-response to antidepressant medication
- Food refusal leading to nutritional compromise
- Unable to tolerate antidepressant medications
- Past response to ECT



TMS

- Transcranial Magnetic Stimulation
- Has helped some people



TMS

- Health Quality Ontario
- Recommends TMS when ECT has failed or contraindicated

- rTMS vs. ECT favoured ECT (Weighted mean difference 5.97) Risk ratio for remission and response were 2.20 and 1.72 favouring ECT

Pediatric Depression

- Watch for decreased school performance
- Use Fluoxetine (RCT evidence)
- Increased suicidal ideation and behaviours (not completed suicides)
  - True in kids, not in adults
- NNH-143

Patient Health Questionnaire (PHQ)

- Self report
- Does not replace clinical interview
- Supports diagnosis and can follow treatment effects

- Questions?

End