Obesity Update 2020

Major Mental Health Comorbidities in Obesity

An Overview

Royal Alexandra HOSPITAL FOUNDATION
CASES
Centre for Advancement of Surgical Education & Simulation

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  - Pfizer, Lundbeck, Takeda, Sunovion, Allergan, Otsuka, Elysium, Eisai, Canopy
- Speaking
  - Pfizer, Lundbeck, Bausch, Otsuka, Purdue, Novo-Nordisk, Sunovion, Eisai, Alllergan
- Research funding
  - AstraZeneca, Sanofi-Aventis, Pfizer, Merck

Disclosure of Commercial Support

- **Potential for conflict(s) of interest:**
  - Dr. Atul Khullar has received payment/funding from companies exhibiting in this program AND/OR companies whose product(s) are being discussed in this program.
  - The exhibitors did not provide content for Obesity Update 2020 nor did they have any editorial input or involvement with the selection of Dr. Khullar as a speaker.
  - The Royal Alexandra Hospital Foundation and/or Centre for Advancement of Surgical Education & Simulation (CASES) has not developed /licensed / distributed/ benefited from the sale of any product that is discussed in this program

Mitigating Bias

- **The content has been developed based on needs assessment results**
- **The information presented is for educational purposes and includes balanced coverage of relevant therapies**
- **All data has been sourced from evidence that is clinically accepted**
- **All support used in justification of patient care recommendations conform to generally accepted standards, the 5A's of Obesity Management from Obesity Canada, and Canadian Clinical Practice Guidelines on the Management of Obesity in Adults**
- **Speakers are asked to clearly identify when they are making personal or off label recommendations as opposed to presenting information that is explicitly "evidence-based"**
- **Speakers have been informed that they must indicate all unapproved products and/or off-label data to the audience during their presentation**
- **Speakers completed the CFPC Mainpro® Declaration of Conflict of Interest form evidencing compliance with Mainpro® requirements, a requisite for this program to be given accredited status.**

Objectives

Following this session, participants will be able to:

- identify common psychiatric conditions found to be co-morbid with obesity:
  - mood disorders (major depressive disorder, generalized anxiety disorder)
  - eating disorders (binge eating disorder)
  - neurodevelopmental disorders (ADHD)
- explain why psychiatric conditions create barriers to weight loss that if left unmanaged may hinder a patients' effective participation in a weight management plan

The 60-Second Summary

- **Be aware of weight issue stigma**
  - **Approaching the topic is key**
- **Screen rigorously for and optimize mental health co-morbidities**
  - **Sleep apnea can mimic (Depression, ADHD)**
  - **Binge eating as a key co-morbidity in obesity**
  - **Consider bipolarity, mixed features or missed anxiety**
  - **May need to be sequential over a couple of visits**
- **Look carefully at medications**
  - **Weight gain can happen insidiously**
  - **Start with weight-neutral medications**
- **Excessive fatigue or sleep deprivation will derail any weight loss program**

PUT YOUR PATIENT FIRST

DO SAY

"Patients struggling with…"

- Weight
- Unhealthy weight
- Weight problems

DON'T SAY

"Obese patients"

- Obese
- Fat
- Extremely obese

~20%

of patients who perceive weight stigma from their health care provider would **avoid future appointments** or **seek out a new health care provider**[2]

Case: Candice

- 35-year-old single mother
- Always struggled with food
- History of yo-yo and fad dieting
- Now weighs 100 kg (220 lbs)
- Height 170 cm, BMI 34.6 kg/m^2 (class II obesity)
- Comorbidities: PCOS, Borderline HTN
- Post partum depression: On Sertraline
- Sleep issues: Mirtazapine added recently
- Appears very concerned about her weight
- Also very fatigued, inattentive, anger outbursts

Case: Candice

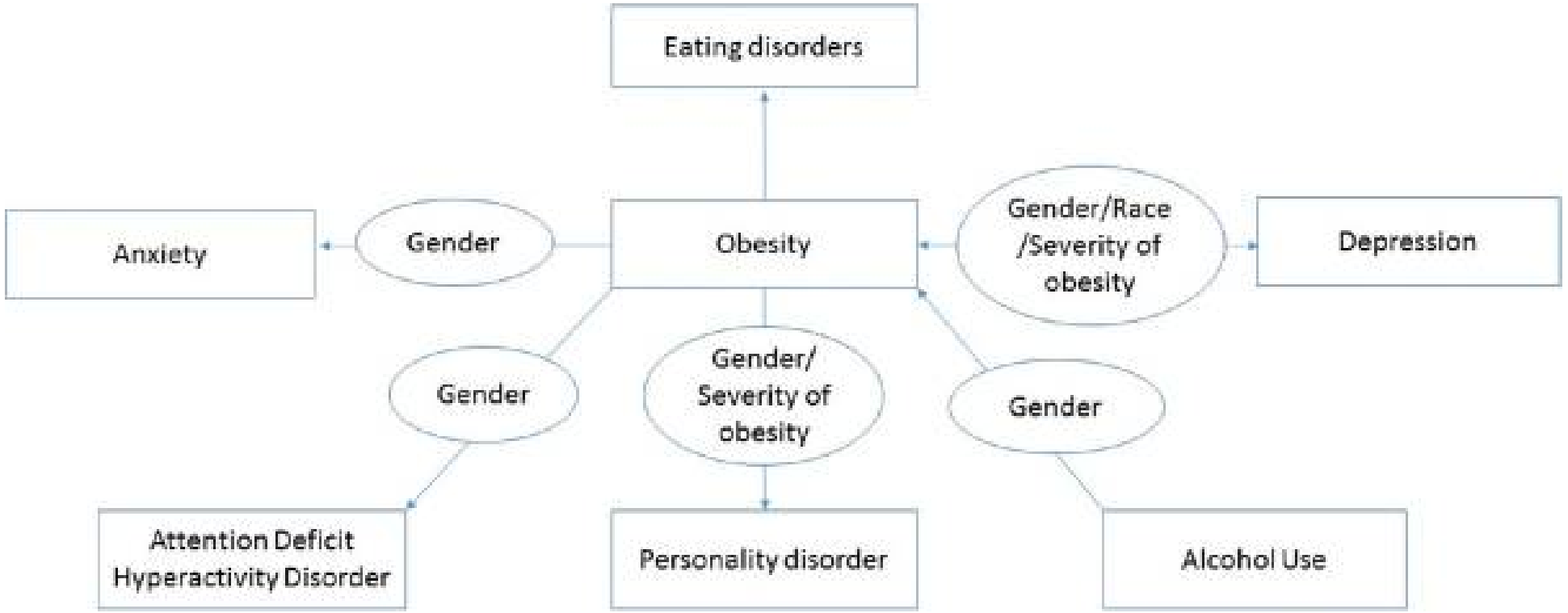
- **Psychosocial stressors (financial, stressors with father of child, behaviour of son)**
- **Son is being worked up for ADHD**
- **Tends to eat emotionally (coping strategy, cravings, doesn't listen to hunger**
- **Eats as habit**
- **Lots of bad habit foods and drinks (lots of soda, processed food, etc.)**

Thoughts on her depression treatment? How would we assess this?

What other mental/physical health co-morbidities do we need to screen for in Candice?

What instruments or scales would we consider?

Obesity And Mental Health Disorders Correlations



Rajan et al 2017

In some studies, what is the reported % of MDD patients that are overweight and obese

A. 40%

B. 60%

C. 75% 

D. 50%

E. 35%

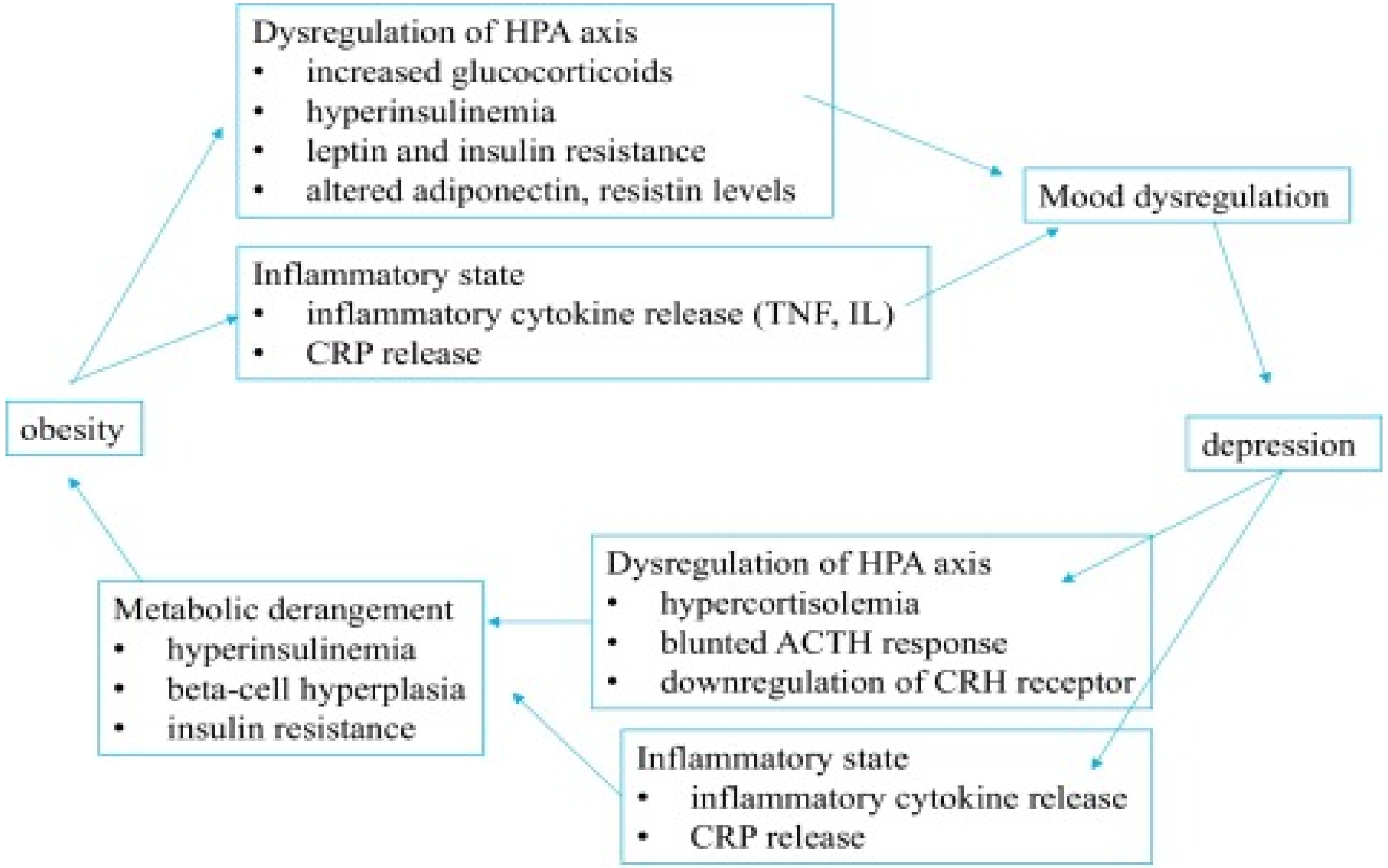
Relationship Between Depression and Unhealthy Weight

- A high proportion of depressed patients are overweight or obese
  - Obesity: MDD 45%, Controls 29%
  - Overweight + obesity: MDD 75.5%
- There is a bi-directional relationship between depression and obesity
- D>O OR=1.20, O>D OR=1.27
- Depression and obesity are interactive risk factors for metabolic syndrome (CV disease, diabetes)
- Overweight and obesity reduce response to antidepressants and other meds for mood disorder

SR Bornstein et al, Mol Psychiatry 2006; 11:892-902 Luppino Arch Gen Psychiatry 2010)

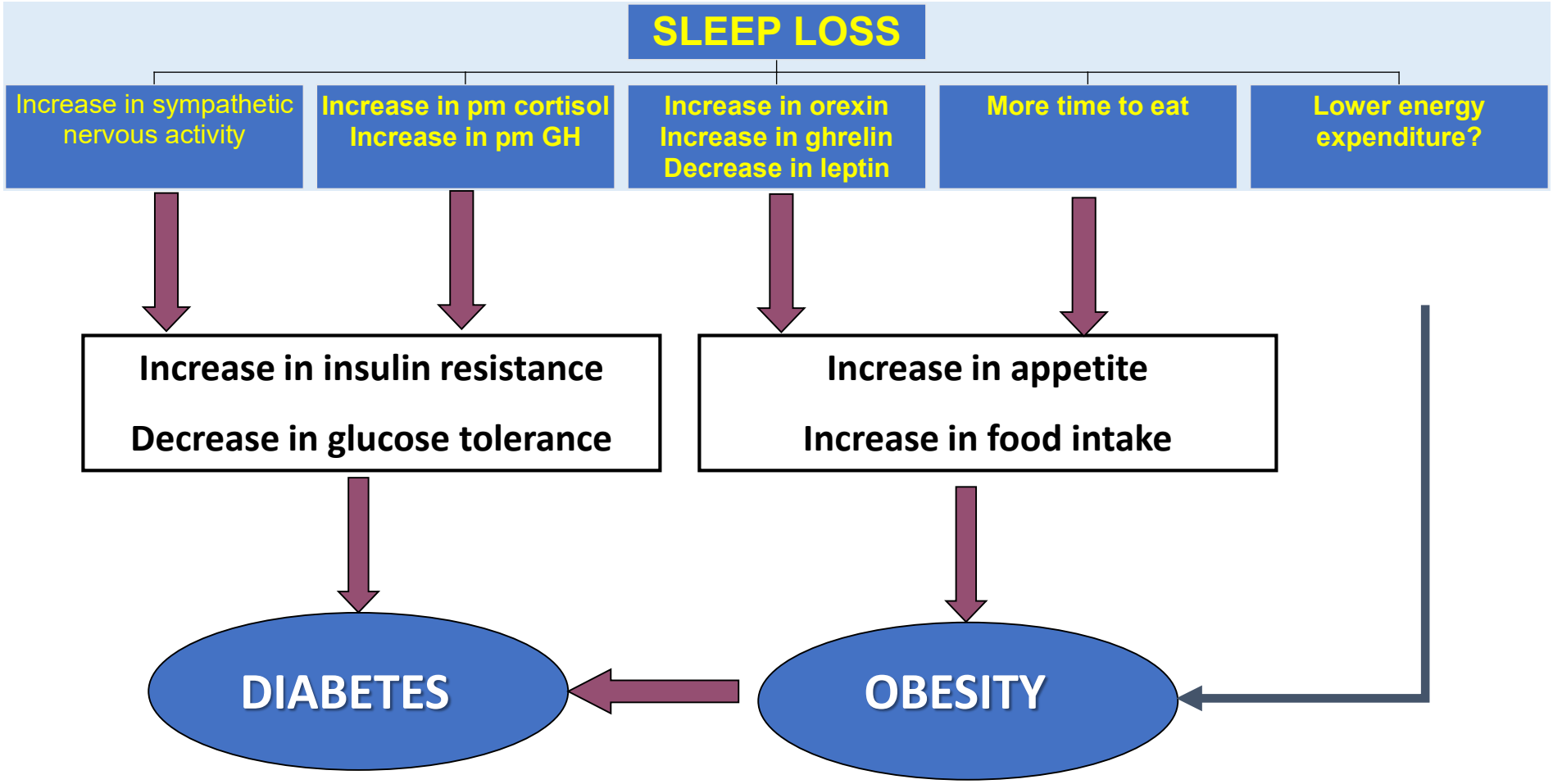
Why?

- Binge, emotional eating and craving are common in mental health disorders
- Weight gaining medications
- Increased unhealthy lifestyles/behavior
- Poor cognition/motivation to manage weight
- Causation unclear but mental health disorders, obesity and diabetes run together and worsen each illness
- Many mental health disorders (especially mood) linked with decreased insulin sensitivity
  - Shared pathways with diabetes
  - Other endocrine/brain structure abnormalities



* ACTH, adrenocorticotrophic hormone; CRH, corticotropin-releasing hormone; CRP, C-reactive protein; HPA, hypothalamic-pituitary-adrenal; IL, interleukin; TNF, tumor necrosis factor

Potential relationships between sleep glucose metabolism, obesity, and diabetes



Rating Scales

- Standard of mental health care
- Compare to BP for hypertension or A1C for diabetes
- Patient-rated are less accurate, but more practical in clinical practice
- Depression: Beck, PHQ-9
- Bipolar: MDQ
- Anxiety: GAD-7
- ADHD: ASRS (short and long form)
- Sleep Apnea: STOPBANG

Screen for OSA: STOP BANG

- **S**nore
- **T**ired and fatigued almost every day
- **O**bserved apneas
- **P**ressure (hypertension)

- **B**MI > 35 (30)
- **A**ge > 50 (40)
- **N**eck circumference > 40
- **G**ender (male)

- 2 of STOP or 3 of STOPBANG = high risk for OSA

PHQ-9

The Patient Health Questionnaire (PHQ-9)

Patient Name _____ Date of Visit _____

Over the past 2 weeks, how often have you been bothered by any of the following problems?	Not At all	Several Days	More Than Half the Days	Nearly Every Day
1. Little interest or pleasure in doing things	0	1	2	3
2. Feeling down, depressed or hopeless	0	1	2	3
3. Trouble falling asleep, staying asleep, or sleeping too much	0	1	2	3
4. Feeling tired or having little energy	0	1	2	3
5. Poor appetite or overeating	0	1	2	3
6. Feeling bad about yourself - or that you're a failure or have let yourself or your family down	0	1	2	3
7. Trouble concentrating on things, such as reading the newspaper or watching television	0	1	2	3
8. Moving or speaking so slowly that other people could have noticed. Or, the opposite - being so fidgety or restless that you have been moving around a lot more than usual	0	1	2	3
9. Thoughts that you would be better off dead or of hurting yourself in some way	0	1	2	3
Column Totals	_____	+ _____	+ _____	
Add Totals Together	_____			

10. If you checked off any problems, how difficult have those problems made it for you to Do your work, take care of things at home, or get along with other people?

☐ Not difficult at all ☐ Somewhat difficult ☐ Very difficult ☐ Extremely difficult

Kroenke, K., J. et al., 1999; Kroenke, K. et al. 2001

GAD-7

Generalized Anxiety Disorder 7-item (GAD-7) scale

Over the last 2 weeks, how often have you been bothered by the following problems?	Not at all sure	Several days	Over half the days	Nearly every day
1. Feeling nervous, anxious, or on edge	0	1	2	3
2. Not being able to stop or control worrying	0	1	2	3
3. Worrying too much about different things	0	1	2	3
4. Trouble relaxing	0	1	2	3
5. Being so restless that it's hard to sit still	0	1	2	3
6. Becoming easily annoyed or irritable	0	1	2	3
7. Feeling afraid as if something awful might happen	0	1	2	3
Add the score for each column	+	+	+	
Total Score *(add your column scores)* =				

If you checked off any problems, how difficult have these made it for you to do your work, take care of things at home, or get along with other people?

Not difficult at all _____
Somewhat difficult _____
Very difficult _____
Extremely difficult _____

Spitzer RL et al, 2006; Ruiz MA et al, 2011

The Adult ADHD Self-Report Scale (ASRS-V1.1)[1] Symptom Checklist

- **A checklist of 18 questions about symptoms that are based on the diagnostic criteria for ADHD from the DSM-IV**
- **Developed in conjunction with the World Health Organization and the Workgroup on Adult ADHD.**

Your Name: Today's Date:

Please answer the questions below, rating yourself on each of the criteria shown using the scale on the right side of the page. As you answer each question, place an X on the box that best describes how you have felt and conducted yourself over the past 6 months. Please give this completed checklist to your healthcare professional to discuss during today's appointment.

		Never	Rarely	Sometimes	Often	Very Often
1.	How often do you have trouble wrapping up the final details of a project, once the challenging parts have been done?					
2.	How often do you have difficulty getting things in order when you have to do a task that requires organization?					
3.	How often do you have problems remembering appointments or obligations?					
4.	When you have a task that requires a lot of thought, how often do you avoid or delay getting started?					
5.	How often do you fidget or squirm with your hands or feet when you have to sit down for a long time?					
6.	How often do you feel overly active and compelled to do things, like you were driven by a motor?					
						Part A
7.	How often do you make careless mistakes when you have to work on a boring or difficult project?					
8.	How often do you have difficulty keeping your attention when you are doing boring or repetitive work?					
9.	How often do you have difficulty concentrating on what people say to you, even when they are speaking to you directly?					
10.	How often do you misplace or have difficulty finding things at home or at work?					
11.	How often are you distracted by activity or noise around you?					
12.	How often do you leave your seat in meetings or other situations in which you are expected to remain seated?					
13.	How often do you feel restless or fidgety?					
14.	How often do you have difficulty unwinding and relaxing when you have time to yourself?					
15.	How often do you find yourself talking too much when you are in social situations?					
16.	When you're in a conversation, how often do you find yourself finishing the sentences of the people you are talking to, before they can finish them themselves?					
17.	How often do you have difficulty waiting your turn in situations when turn taking is required?					
18.	How often do you interrupt others when they are busy?					
						Part B

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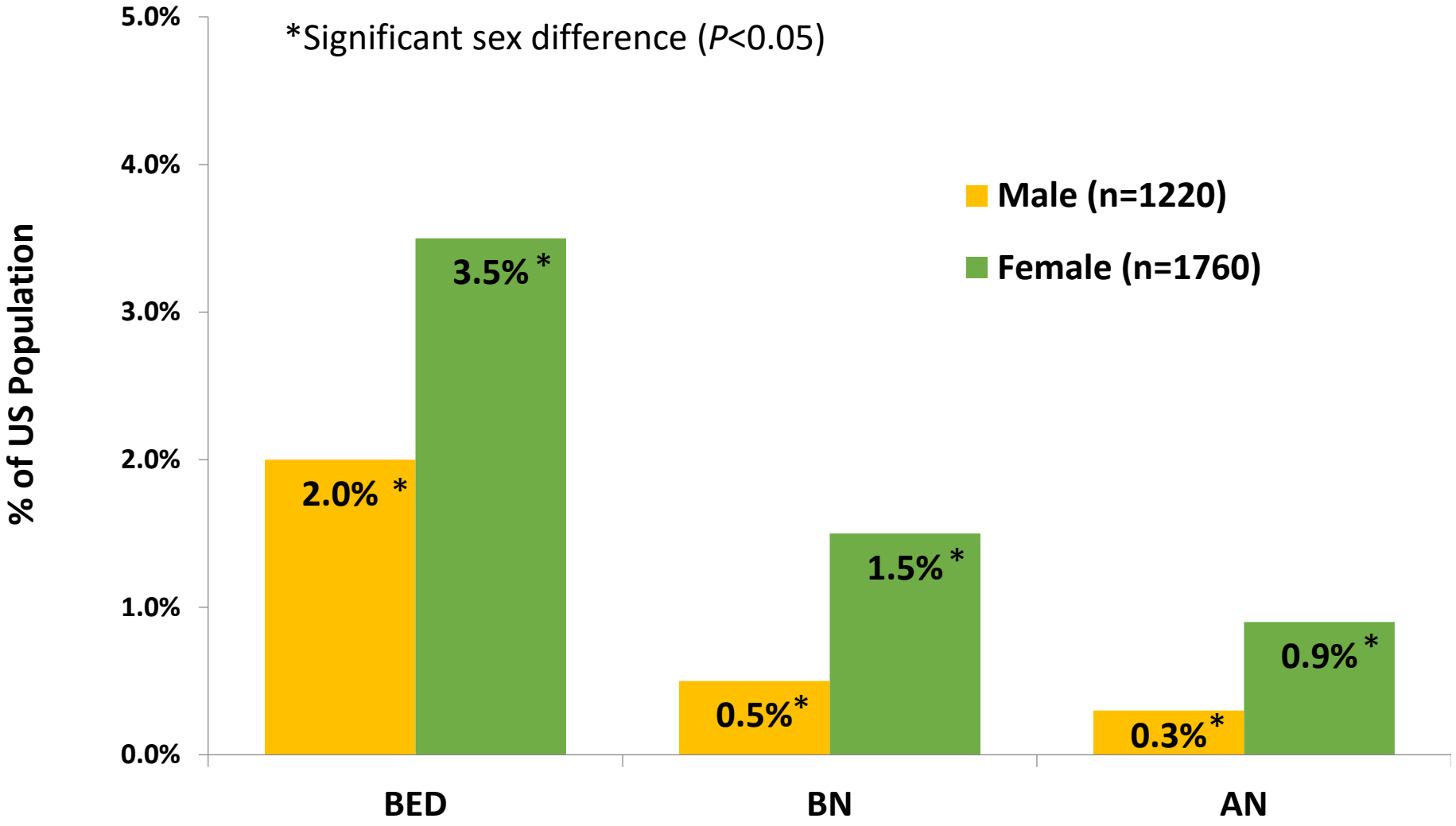
Eating Disorder Prevalence



The 7-item BED Screener

Help identify your patients with BED using the 7-item BED Screener (BEDS-7)

This tool is intended *for screening use only*. It should not be used as a diagnostic tool.

1. During the last 3 months, did you have any episodes of excessive overeating (*i.e.,* eating significantly more than what most people would eat in a similar period of time)? **YES** **NO**

NOTE: if you answered "no" to question 1, you may stop. The remaining questions do not apply to you.

2. Do you feel distressed about your episodes of excessive overeating? **YES** **NO**

WITHIN THE PAST 3 MONTHS…	**NEVER OR RARELY**	**SOMETIMES**	**OFTEN**	**ALWAYS**
3. During your episodes of excessive overeating, how often did you feel like you had no control over your eating (*e.g.,* not being able to stop eating, feel compelled to eat, or going back and forth for more food)?	○	○	○	○
4. During your episodes of excessive overeating, how often did you continue eating even though you were not hungry?	○	○	○	○
5. During your episodes of excessive overeating, how often were you embarrassed by how much you ate?	○	○	○	○
6. During your episodes of excessive overeating, how often did you feel disgusted with yourself or guilty afterward?	○	○	○	○
7. During the last 3 months, how often did you make yourself vomit as a means to control your weight or shape?	○	○	○	○

Scoring the BEDS-7: if the response to Q1 is "YES," Q2 through Q7 are answered. If the response to Q1 is "NO," the remaining questions do not apply as the screening result is negative. If the response to Q2 is "YES" and a shaded box is checked for each of the items Q3 through Q7, the screening result is positive.

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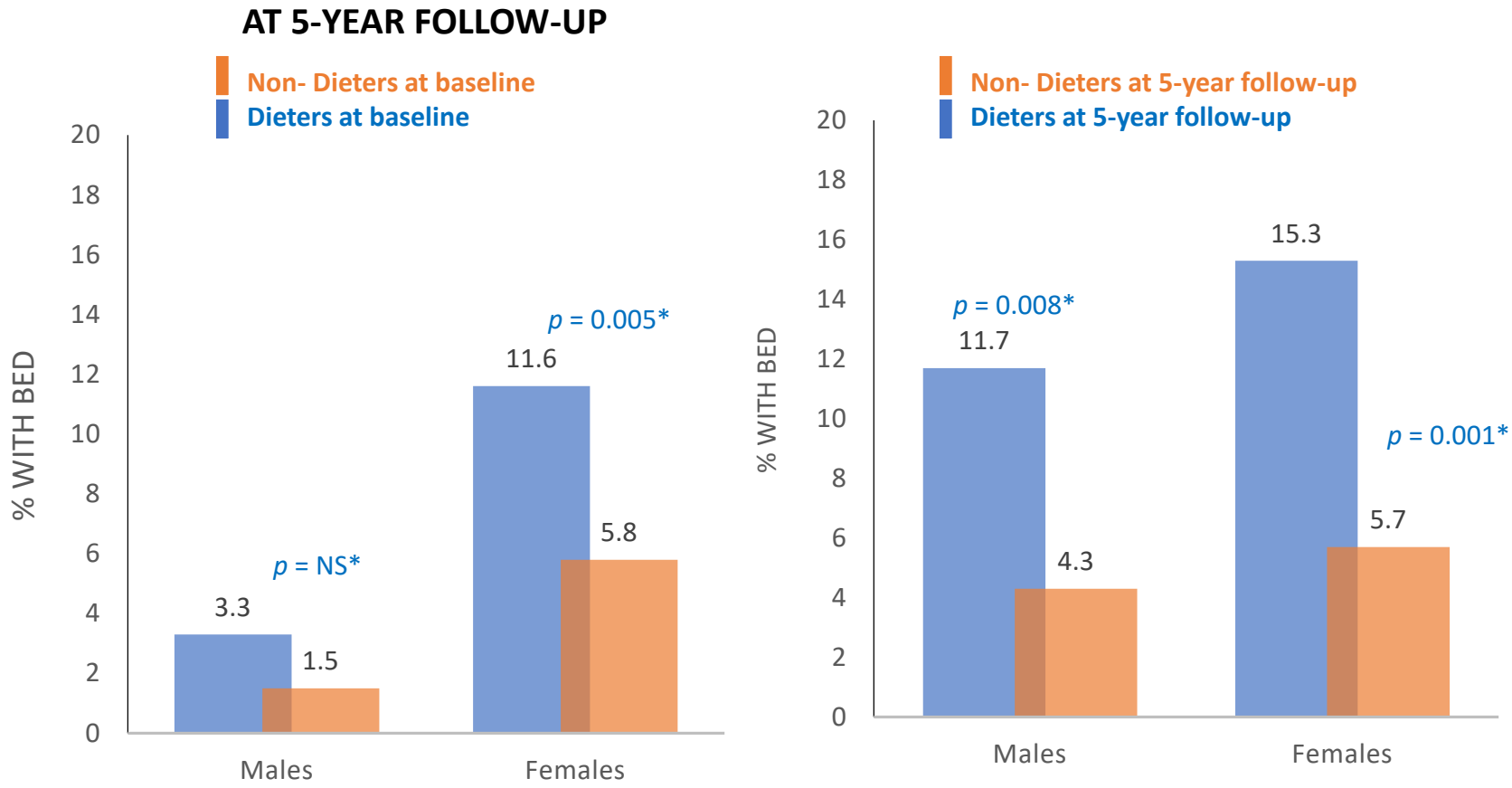
Herman BK, et al. Prim Care Companion CNS Disord 2016; 18(2).

History of dieting predicts onset of BED



***After controlling for demographic/anthropometric variables/based on data collected from survey completed by 1827 individuals**

BED=binge eating disorder; NS=non-significant

Goldschmidt AB *et al. J Adolesc Health* 2012;51(1):86–92.

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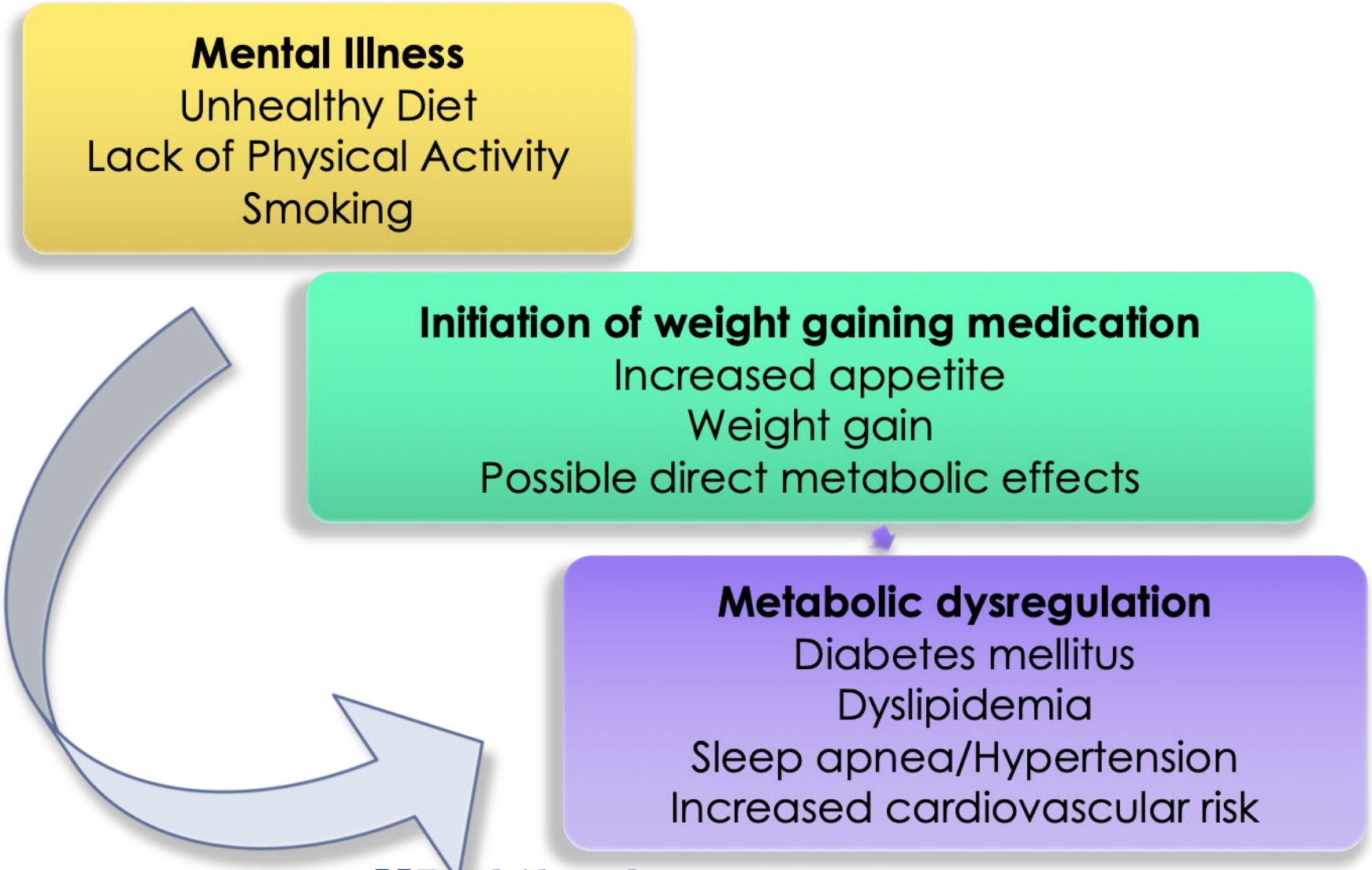
Case: Candice

- PHQ-9 and GAD7 show significant symptoms
- ADHD and BED scales positive
- Screened for sleep apnea – moderate
- CPAP started
- Sleeping better
- Making behavioural changes
- Drops 5kg (BMI = 32.9)
- Next steps?

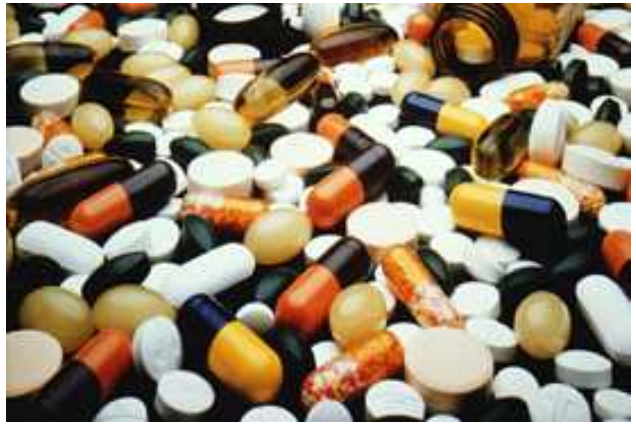
THE SPIRAL OF WEIGHT GAIN



Hasnain et al (2010)

Drugs in Psychiatry Made Ridiculously Simple

1. Antidepressants (AD)
   - Also low dose for sleep and pain (trazodone, doxepin, amitryptline, nortryptyline)
2. Antipsychotics (AP)
3. Anti-epileptic drugs (AED)
   - Used for bipolar/behavior control (Lamotrigine, Valproic Acid)
4. Other
   A. Hypnotics (Zopiclone, Zolpidem)
   B. Benzodiazepines
   C. Lithium
   D. Stimulants
   E. Opiates /Cannabinoids



Why Patients Stop Their Medications for Mood Disorders

Table 3
Adverse effects reported that caused discontinuation of a treatment in the past. Respondents could provide more than one answer.

Adverse effects that cause discontinuation of medications Answer options	Depression group $N = 316$ Response percent	Bipolar group $N = 384$ Response percent	P value
Weight gain	43.7%	56.9%	<0.001
Feeling lethargic/sleepiness	36.7%	49.7%	<0.001
Blunted emotions	35.4%	31.0%	0.218
Anxiety	34.2%	43.7%	0.010
Suicidal thoughts	27.8%	38.5%	0.003
Sexual dysfunction	27.5%	33.8%	0.073
Shaking/trembling	26.6%	43.1%	<0.001
Dry mouth	26.3%	22.0%	0.185
Irritability	24.4%	35.7%	0.001
Insomnia	23.7%	33.8%	0.004
Gastrointestinal issues	23.7%	26.4%	0.413
Headaches/blurred vision	21.8%	29.7%	0.018
Loss of balance/dizziness	21.8%	33.5%	<0.001
Other	17.4%	21.2%	0.206
Impact on pregnancy/nursing	4.1%	5.5%	0.392

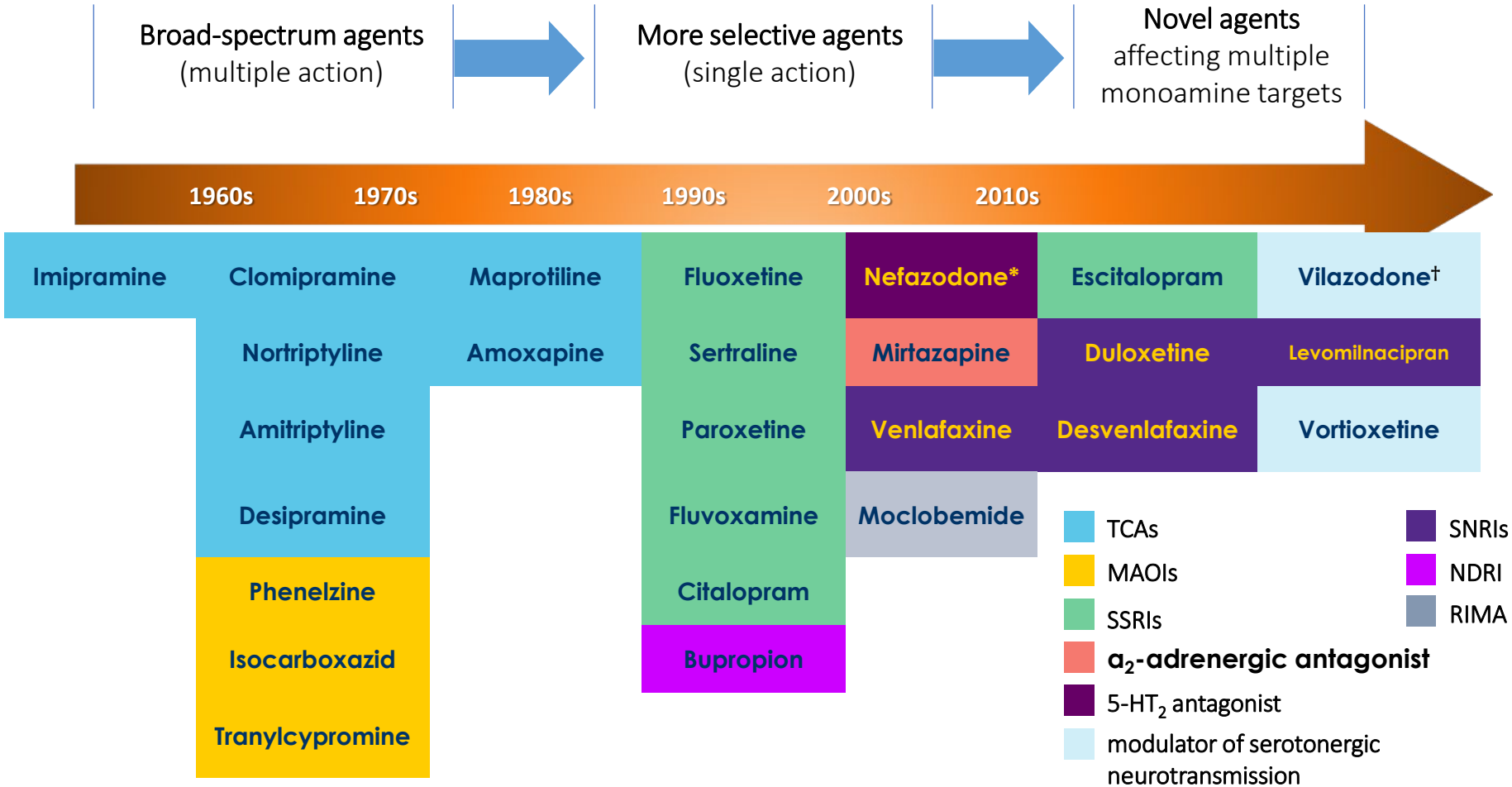
JD Rosenblat et al (2019)

PROPOSED WEIGHT GAIN MECHANISMS OF MEDICATIONS

- **Food cravings/appetite stimulation:** antidepressants, mood stabilizers, and antipsychotics
- **Altered metabolic rate:** tricyclic antidepressants, SSRIs, and monoamine oxidase inhibitors
- **Activation of hypothalamic-pituitary-adrenal axis** changes insulin sensitivity, hyperprolactinemia, and gonadal dysfunction
- **Interaction** with dopamine, serotonin 5-HT_{2C}, and histamine H1 receptors
- **Gene polymorphisms:** individual variation

Jensen (2008)

Evolution of Antidepressants



TCA: Tricyclic antidepressant; MAOI: Monoamine oxidase inhibitor; SSRI: Selective serotonin reuptake inhibitor; SNRI: Selective norepinephrine reuptake inhibitor; RIMA: Reversible Monoamine Oxidase Inhibitor

*** Withdrawn from the Canadian Market; † Not available in Canada**

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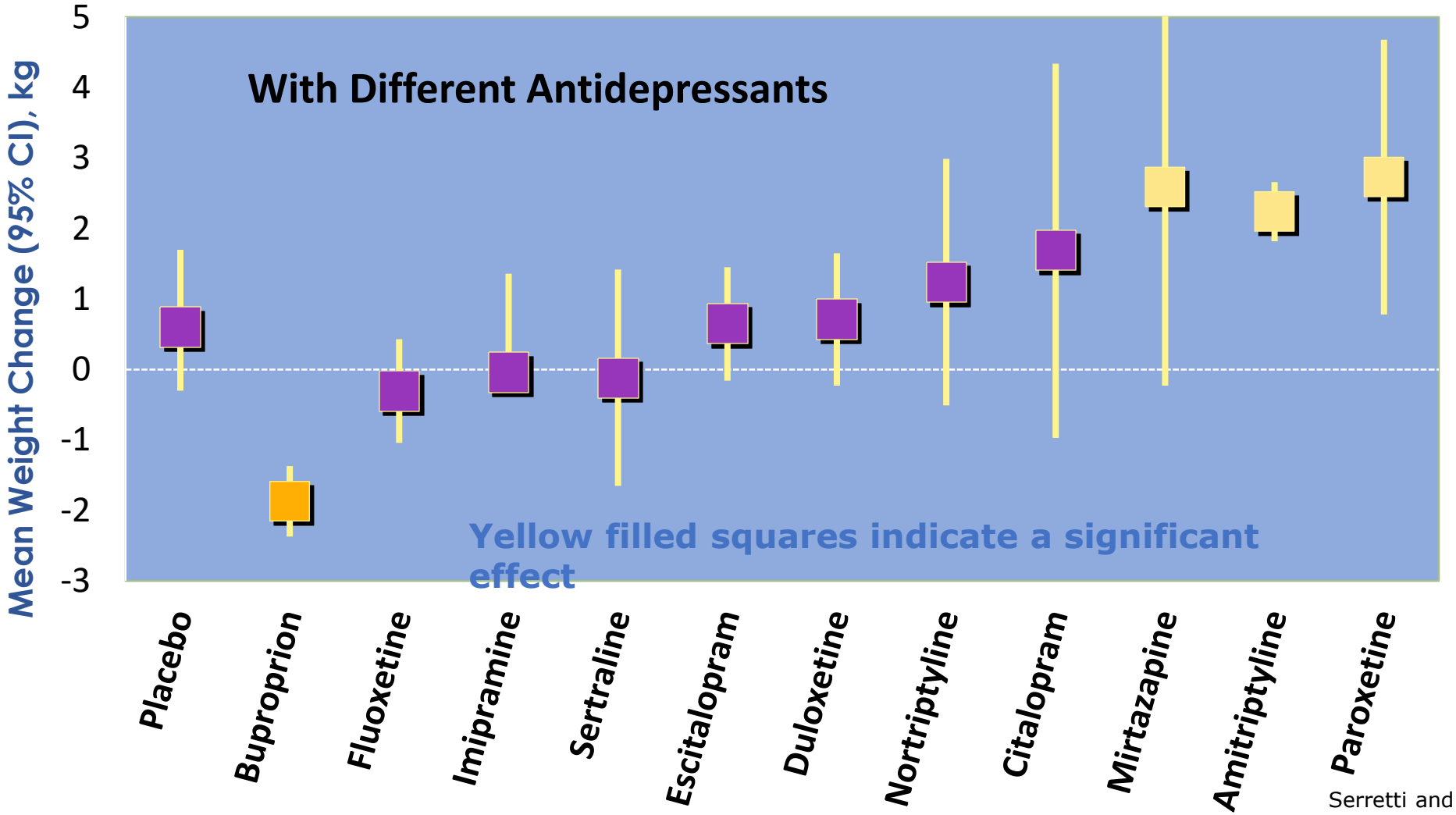
CURRENTLY ON
EXIT 58A-B
95
1
Zoloft
TP
9
Prozac
Paxil
LAST EXIT BEFORE TOLL
Buspar
Wellbutrin
Celexa
Xanax

Which antidepressants have been mostly seen to be weight neutral?

A. Mirtazapine (Remeron RD)
B. Nortyptyline (Aventyl)
C. Vortioxetine (Trintellix)
D. Paroxetine (Paxil)
E. Desvenlafaxine (Pristiq)
F. C and E
G. B and C
H. B and E

Weight Change in Maintenance Treatment



Serretti and Mandelli (2010)

Effects of Newer Antidepressants on Weight

Drug class	Drug name	Weight change at >12 weeks (95% CI)*
SSRI	Citalopram	+1.69 kg (-0.97, 4.34)[1]
	Escitalopram	+0.65 kg (-0.16, 1.45)[1]
	Fluoxetine	**-0.31 kg (-1.04, 0.43)[1]**
	Fluvoxamine	**-0.02 kg (-0.49, 0.45)[1,†]**
	Paroxetine	+2.73 kg (0.78, 4.34)[1]
	Sertraline	**-0.12 kg (-1.65, 1.42)[1]**
SNRI	**Desvenlafaxine**	**-0.5 kg[2]**
	Duloxetine	+0.71 kg (-0.23, 1.65)[1]
	Levomilnacipran	**-0.59 kg[3]**
	Venlafaxine	**-0.50 kg (-0.74, -0.27)[1,†]**
Other	**Bupropion**	**-1.87 kg (-2.37, -1.37)[1]**
	Vortioxetine	**+0.4 kg[4]**
	Vilazodone	**+0.5 kg[4]**

Weight loss >0.5 kg **Weight change ≤0.5 kg** **Weight gain >0.5 kg**

***These data do not include all recorded adverse events. They are presented as guidance and should be considered in the context of individual patients.**
[†]Evidence based on exposure <12 weeks.

CI, confidence interval; SNRI, selective norepinephrine reuptake inhibitor; SSRI, selective serotonin reuptake inhibitor.

1. Dent R, et al. *PLoS One* 2012;7(6):e36889.
2. PRISTIQ® desvenlafaxine succinate product monograph. August 28, 2018.
3. FETZIMA® levomilnacipran extended-release capsules product monograph. September 13, 2018.
4. TRINTELLIX® vortioxetine (as vortioxetine hydrobromide) product monograph. December 19, 2018.

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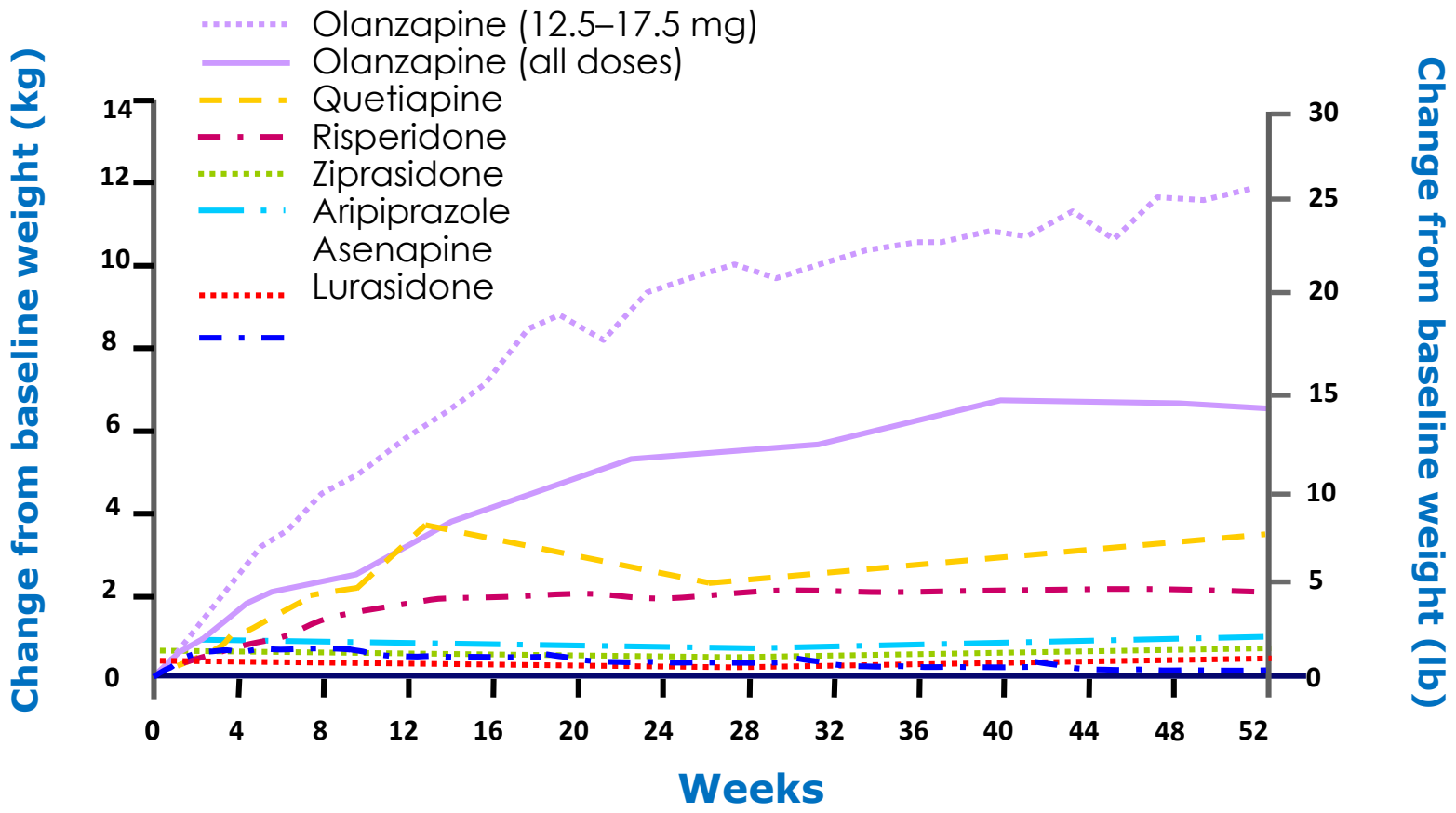
Anti-Psychotics

- Older anti-psychotics used effectively in resistant cases (Chloropromazine, Haloperidol, Loxapine, etc)
  - Can cause depression with increased side effects
- Atypical antipsychotics used as mood stabilizers, behavioral control and to improve response in sleep, anxiety and depression now
- Traditional atypicals : Quetiapine (Seroquel), Olanzapine (Zyprexa), Risperidone (Risperidal), Clozaril (Clozapine), Ziprasidone (Zeldox),
- Newer ones: Aripipazole (Abilify), Lurasidone (Latuda), Brexipipazole (Rexulti)
- Some may have independent anti-depressant effects
- Varying degrees of weight and metabolic disruption
  - Not always correlated

Which antipsychotics have been associated with a lower risk of weight gain?

A. Aripipazole (Abilify)
B. Quetapine (Seroquell)
C. Risperidone (Risperidone)
D. Lurasidone (Latuda)
E. Olanzapine (Zyprexa)
F. C and D
G. A and D
H. A and B

One-year Weight Gain: Mean Change from Baseline Weight



[1]Nemeroff CB. J Clin Psychiatry 1997; 58(suppl 10):45-9; [2]Kinon BJ, et al. J Clin Psychiatry 2001; 62:92-100; [3]Brecher M et al. Neuropsychopharmacology 2004; 29(suppl 1):S109; [4]Geodon® [package insert]. New York, NY: Pfizer Inc; 2005; [5]Risperdal® [package insert]. Titusville, NJ: Janssen Pharmaceutical Products, LP; 2003; [6]Abilify® [package insert]. Princeton NJ: Bristol-Myers Squibb Company and Rockville, Md: Otsuka America Pharmaceutical, Inc.; 2005; [7]Boyda HN. PLoS One. 2013; (8):e53459, Latuda product monograph, June 2012.


YOUR'E FREAKIN ME OUT
STOP DOING THAT
makeameme.org

Medication Management When Considering METABOLIC EFFECTS

AVOID USING	CAUTION IF USING	CONSIDER USING
Paroxetine Mirtazapine Tertiary Tricyclic Valproic Acid Olanzapine	Lithium Quetiapine Risperidone Pregabalin Gabapentin Secondary Tricyclic	Buproprion Vortioxetine Levomilancipran Lamotrigine Ziprasidone Aripiprazole Brexipipazole Topiramate Asenapine Lurasidone

Always be aware of idiosyncratic weight gain with other SSRI/SNRI medications

Case: Candice

- Switched to Vortioxetine (weight neutral antidepressant)
- Sleeping better, discontinued Mirtazapine (Remeron RD)
- Drops 4 kg (BMI = 31.5)
- Better energy, still scattered, inattentive
- Working hard on food changes, but sometimes "I still just lose control"

Medication Overview in ADHD

- **First-line treatments**
  - **Long-acting psychostimulants (amphetamine-based and methylphenidate-based)**
- **Second-line treatments**
  - **Non-stimulants (atomoxetine, guanfacine XR) and short/intermediate acting psychostimulants**
  - **Option for those who do not tolerate or respond to first-line treatment**
- **Third-line treatments**
  - **Off-label (e.g., bupropion, clonidine, imipramine, modafinil)**
  - **Reserved for treatment-resistant cases**

Guanfacine XR is not indicated for adults (≥18 years) in Canada.

Canadian ADHD Resource Alliance (CADDRA). Canadian ADHD Practice Guidelines, 4th Edition, Toronto, ON; CADDRA, 2018.

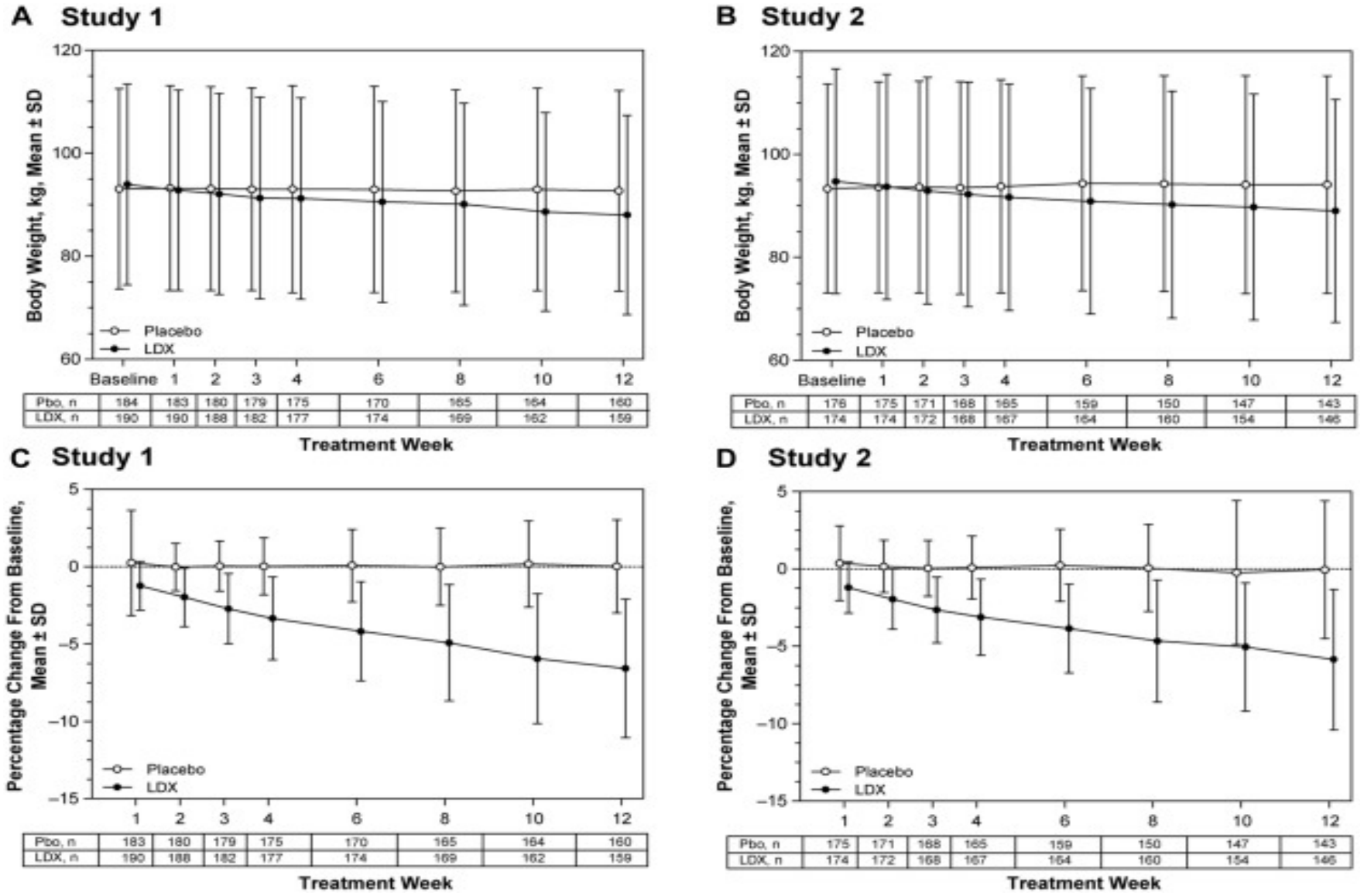
Treatment of Binge Eating Disorder

- **Therapy**
  - **Cognitive Behavioural Therapy**
  - **IPT**
- **Medications**
  - **Approved**
    - **Lisdexamfetamine (Vyvanse)**
  - **Off Label**
    - **Antidepressants**
    - **Anticonvulsants - Topiramate**

Case: Candice

- ADHD scale and BED scale positive
- Starts Vyvanse
- More focused, brighter
- Can control my urges to eat
- Appetite is the same, just can control better and stick to healthy choices
- More efficient at work and more time to exercise and make food at home
- Loses another 4 kg (BMI 30.1)
- ***Next steps?***

Lisdexafetamine (Vyvanse) weight loss only in BED



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McElroy et al 2017

Who to Potentially Refer Onwards for Psychiatric Assessment

- Psychotic, agitated, severely anxious or suicidal patients
- Unstable bipolar or suspected bipolar patients
  - People on Lithium, Epival, Lamotrigine
- Average stable depressed patient on one or two antidepressants DOES NOT NEED a psychiatric consult
  - Also if on antidepressant for sleep or chronic pain
  - Or single-therapy hypnotic/benzodiazepine
- Unclear ADHD/BED diagnosis (treat simple, uncomplicated ones)
- If mental health is stable and there are above issues, a GLP-1 agonist can be considered
  - no real clinical interaction with psychotropics


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