

# Mental Health and IBD

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# Conflicts of Interest

- Investigator-initiated grant from Allergan
- No other financial conflicts to disclose

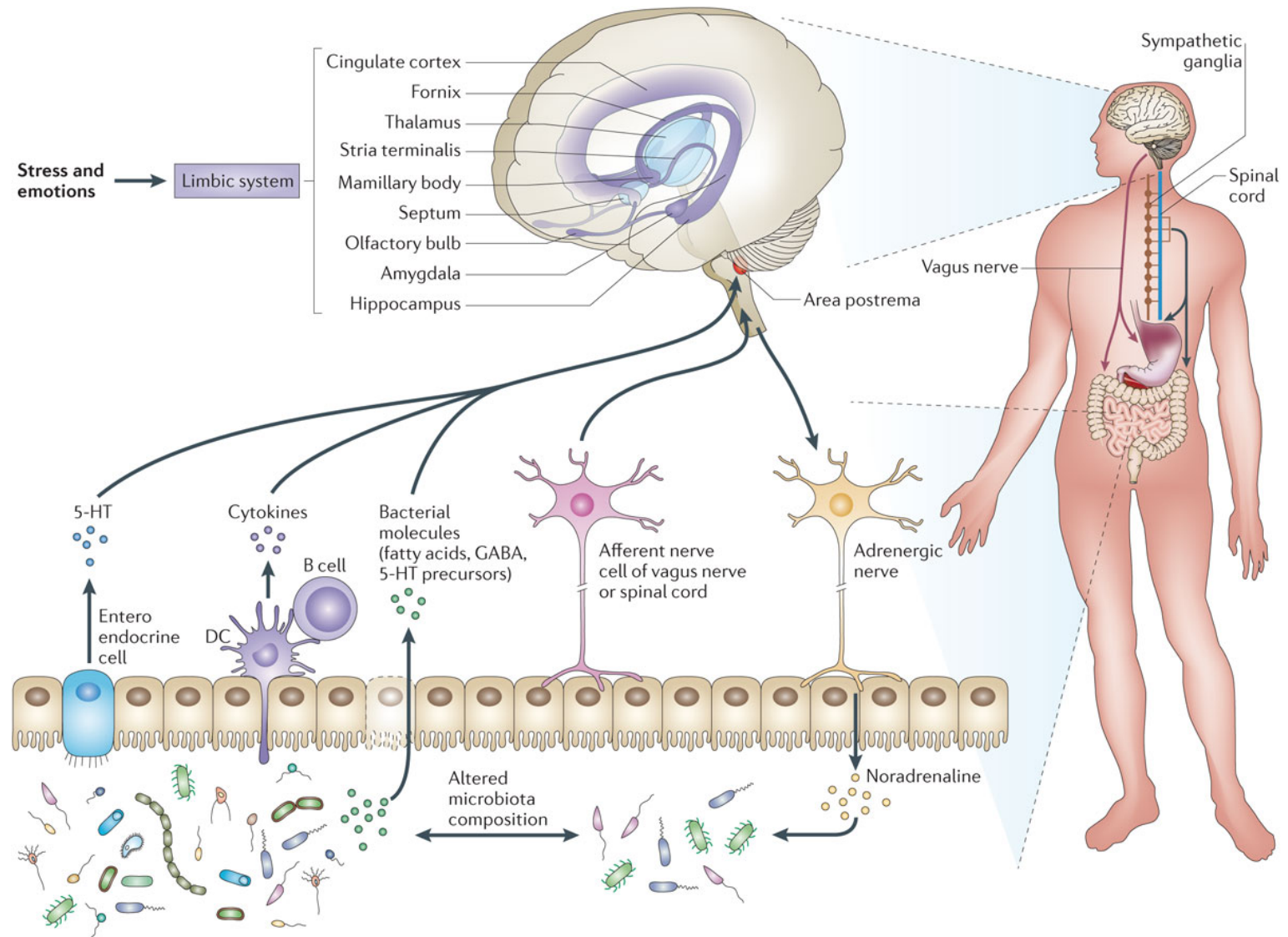
# Outline

- Review gut-brain axis
- Explore the relationship between mental health and IBD
- Discuss quick screening tools for anxiety and depression and when to refer to psychiatry
- Review of treatment of anxiety and depression in patients with IBD

“The results, as thousands of physicians and users testify, are nothing short of amazing. Not only a banishing of mental and physical depression, but a flooding of new vitality throughout the system”



# Microbe-Gut-Brain Axis



# Social stress can change the microbiome

- Social disruption – mice exposed to 6 cycles of aggression
- Increased inflammatory biomarkers and changed the community structure of the microbiota



# Probiotics and Anxiety Model

- Mice infected with noninvasive parasite *T.Muris* resulting in chronic colonic inflammation
- Showed increased anxiety-like behaviour and decreased hippocampal BDNF
- *Bifidobacterium longum* NCC3001 normalized anxiety-like behaviour and BDNF expression in the hippocampus

# Mental Health and the Gut-Brain Axis

- Healthy women assigned to receive fermented milk product with probiotic (n=12), non-fermented milk product (n=11) or no intervention (n=13) BID x 4 weeks
- Measured brain response to an emotional faces attention task





# FMPP resulted in reduced response to emotional attention task

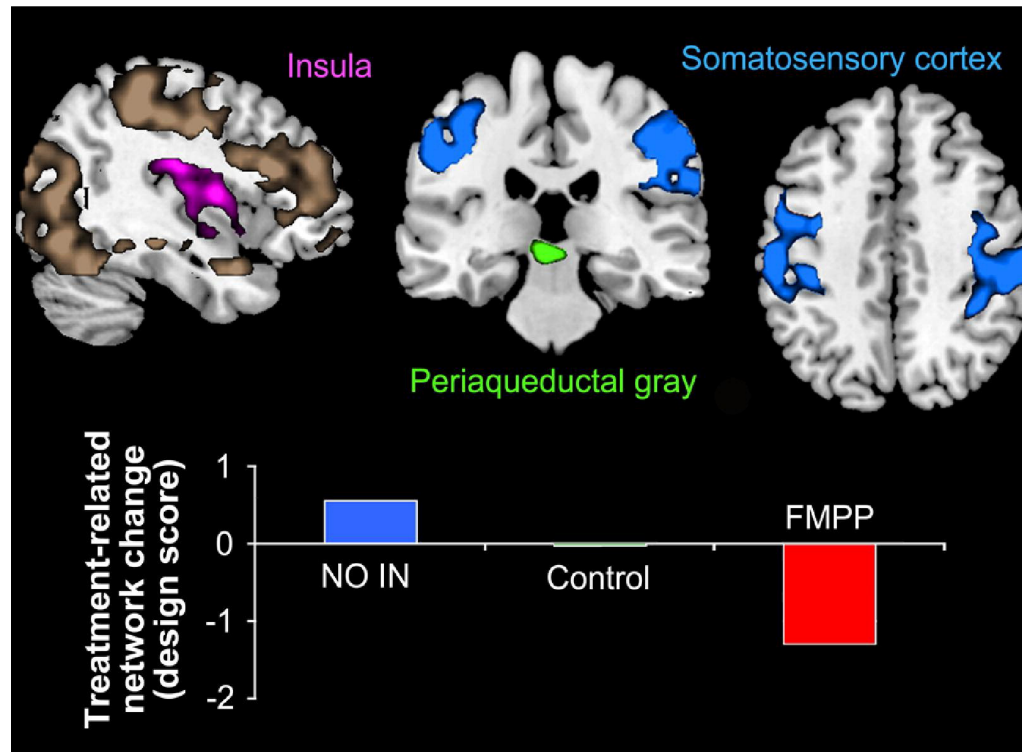


Figure 1 A distributed network of brain regions showing decreases in the FMPP group during the emotional faces attention task is shown in the shaded regions. Three regions of interest selected from the network for study in the resting state are highlighted...

Kirsten Tillisch , Jennifer Labus , Lisa Kilpatrick , Zhiguo Jiang , Jean Stains , Bahar Ebrat , Denis Guyonnet ,...

**Consumption of Fermented Milk Product With Probiotic Modulates Brain Activity**

Gastroenterology Volume 144, Issue 7 2013 1394 - 1401.e4

# Take Home Points

- Bidirectional pathways connecting the gut and the brain
- Stress, anxiety and depression can change GI function, inflammation and microbiota
- Changes in gut can change the brain and emotional processing

# **RELATIONSHIP BETWEEN MENTAL HEALTH & IBD**

# Psychiatric Comorbidity IBD

- Majority of clinical and population-based studies show elevated rates of anxiety and depression in patients with IBD

## Manitoba IBD Cohort

- Depression 2x more common in patients with IBD
- Anxiety 2-3x more common in patients with IBD

# Impact Mental Health on IBD

- Psychiatric symptomatology associated with increased symptom severity, disease exacerbations and poorer quality of life
- MDD risk factor for failure to achieve remission with infliximab
- Depression and anxiety are associated with an increased risk of surgery in CD (OR 1.28, 95%CI 1.03-1.57)

Ananthakrishnan et al. Aliment Pharmacol Ther 2013; 37:445

Mittermaier C et al. Psychosom Med 2004; 66:79

**When asked about what factors contribute to worsening of their symptoms, 90% of patients with IBD identified stress as a significant factor (Drossman & Ringel, 2004).**



# Stress and IBD

- Stressful life events predict occurrence of a flare in the next 3 months
- ***Perceived stress*** is associated with increased GI symptoms, independent of inflammation

Bernstein CN et al. Am J Gastroenterol 2010 105(9):1994-2002

Targownik LE et al. Am J Gastroenterol 2015; 110:1001-1012

# Impact IBD on mental health

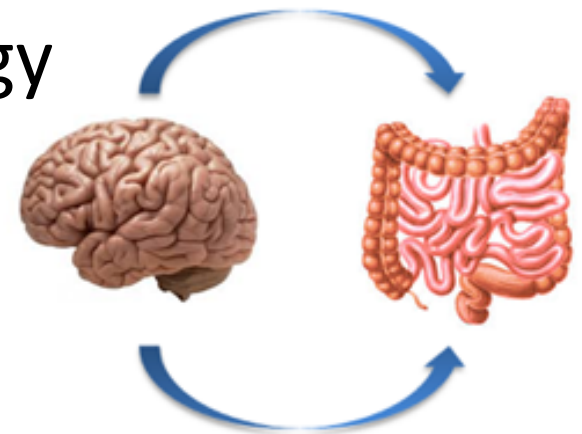
- Chronic illness generally associated with poorer quality of life
- Patients with IBD have lower psychological well-being and mastery than non-IBD controls
- Can be an impact of treatment (for example corticosteroids) on mental health



# TAKE HOME POINTS:

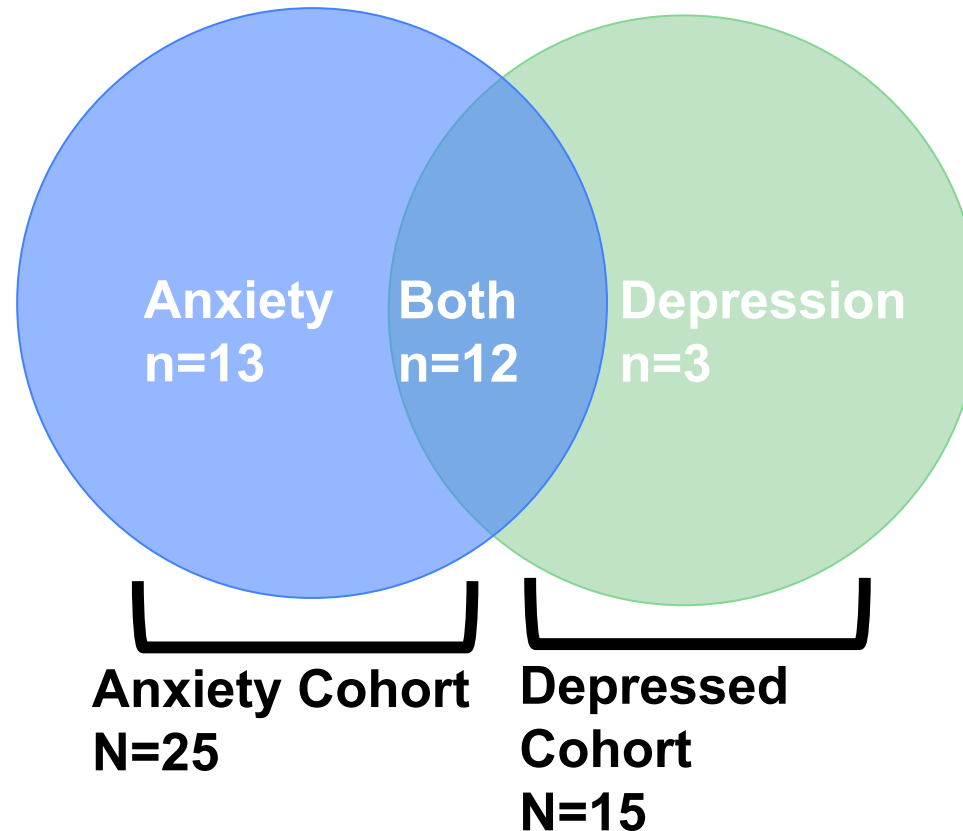
## Bidirectional Relationship

- Underlying anxiety, depression impacts on ability to cope with chronic illness and manifestation of symptoms
- Experience of chronic illness can worsen mental health and trigger or intensify psychiatric illness
- Potential shared pathophysiology

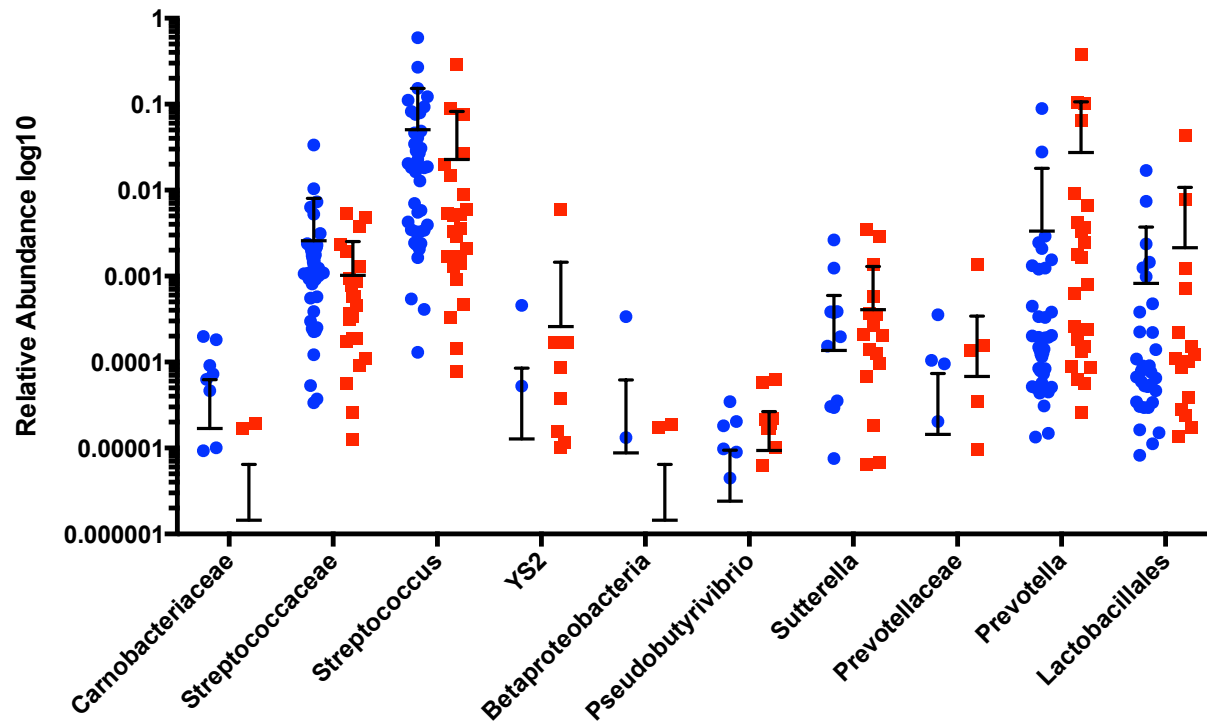


# IBD, Mental Health, Microbiome

- 68 patients with UC, Mayo Clinic score  $\geq 4$  and endoscopic score  $\geq 1$ ) on stable treatment



***Differential abundance testing reveals statistically significant taxa at the L6 level.***



**SCREENING**

# Anxiety

- The most common anxiety disorder is **Generalized anxiety disorder (GAD)**
- This is characterized by EXCESSIVE anxiety and worry most days that INTERFERES WITH FUNCTION
- They find it DIFFICULT TO CONTROL THE WORRY
- They feel restless, fatigued, have trouble concentrating, feel irritable and tense

# Key Questions to ask for GAD

- Have you been having problems with anxiety, worry or stress?
- Have you been feeling nervous, jittery, or tense most of the time?
- Do you find it difficult to control your worry?



# Depression

- Depression is characterized by sad or depressed mood OR loss of interest in activities
- Feelings of hopelessness, worthlessness, guilt
- Changes in sleep, energy, appetite, concentration
- Suicidal ideation
- At least 2 weeks, interfering with function

# Key Questions for Depression

- On a scale where 0 = “down and hopeless” and 10 = “good mood”, how would you rate your mood during the past week?
- Do you feel depressed or down most of the day?
- Have you found that you’ve lost interest or enjoyment in most things?





# Screening of anxiety and depression (PHQ4)

Over the past 2 weeks, how often have you been bothered by the following problems? (not at all, several days, more than half the days, nearly every day)

- Feeling nervous, anxious or on edge
- Not being able to stop or control worrying
- Little interest or pleasure in doing things
- Feeling down, depressed, or hopeless

# Other screening tools

- Luebeck Interview for Psychosocial Screening (LIPS)
- Hospital Anxiety and Depression Scale (HADs)
- 5-item Anxiety and Depression Detector

All take 5-10 minutes to administer

Kunzendorf S *Inflamm Bowel Dis* 2007; 13:33-41

Zigmond AS et al. *Acta Psychiatr Scand* 1983; 67(6):361-70

Means-Christensen AJ et al. *Gen Hosp Psychiatry* 2006; 28:108-118

# When to screen?

- Initial Diagnosis
- Active disease
- Refractory symptoms despite adequate therapy and absence of disease activity
- Patient presentation suggestive of anxiety or depression
- Consider routine screening

# **TREATMENT PRINCIPLES**

# Treatment Mental Health in IBD

- Explain condition and common comorbidity in patients with IBD
- Emphasize importance dealing with symptoms, impact on health, functioning, quality of life
- Treatment can be pharmacological or psychological

# Antidepressant Treatment IBD

- Case reports and open studies suggest that antidepressants may improve IBD symptoms as well as mood and anxiety
- Lack of evidence from RCTs to guide treatment
- Treatment often limited by GI side effects



# Antidepressant Primer

TYPES of antidepressants:

- Tricyclic Antidepressants (TCAs)  
Selective Serotonin Re-uptake Inhibitors (SSRIs)
- Serotonin and Norepinephrine Reuptake Inhibitors (SNRIs)
- Monoamine-Oxidase Inhibitors (MAOIs)
- Others – Bupropion, mirtazapine

# Tricyclic Antidepressants

- Amitriptyline, Imipramine, Doxepin, Desipramine, Nortriptyline
- Side Effects: Sedation, constipation, dry eyes/mouth, weight gain, hypotension, sexual dysfunction

CAUTION – can be fatal in overdose so require risk assessment prior to prescribing, cardiac side effects need to be taken into consideration prior to prescribing



# SSRIs

- Fluoxetine, sertraline, fluvoxamine, paroxetine, citalopram, escitalopram
- Side effects: insomnia, diarrhea, night sweats, agitation, sexual dysfunction, upper GI bleeding, osteoporosis, possible increased risk suicidality, QT prolongation (citalopram)

# SNRIs

- Duloxetine, venlafaxine
- Side effects: nausea, agitation, dizziness, fatigue, liver dysfunction (duloxetine), hypertension (venlafaxine)

# Antidepressant Tips



- SSRIs generally cause diarrhea but can still be tolerated in many IBD patients
- Escitalopram is often prescribed due to its favourable side effect profile and limited drug-drug interactions
- Generally sertraline should be avoided as it causes the most GI side effects

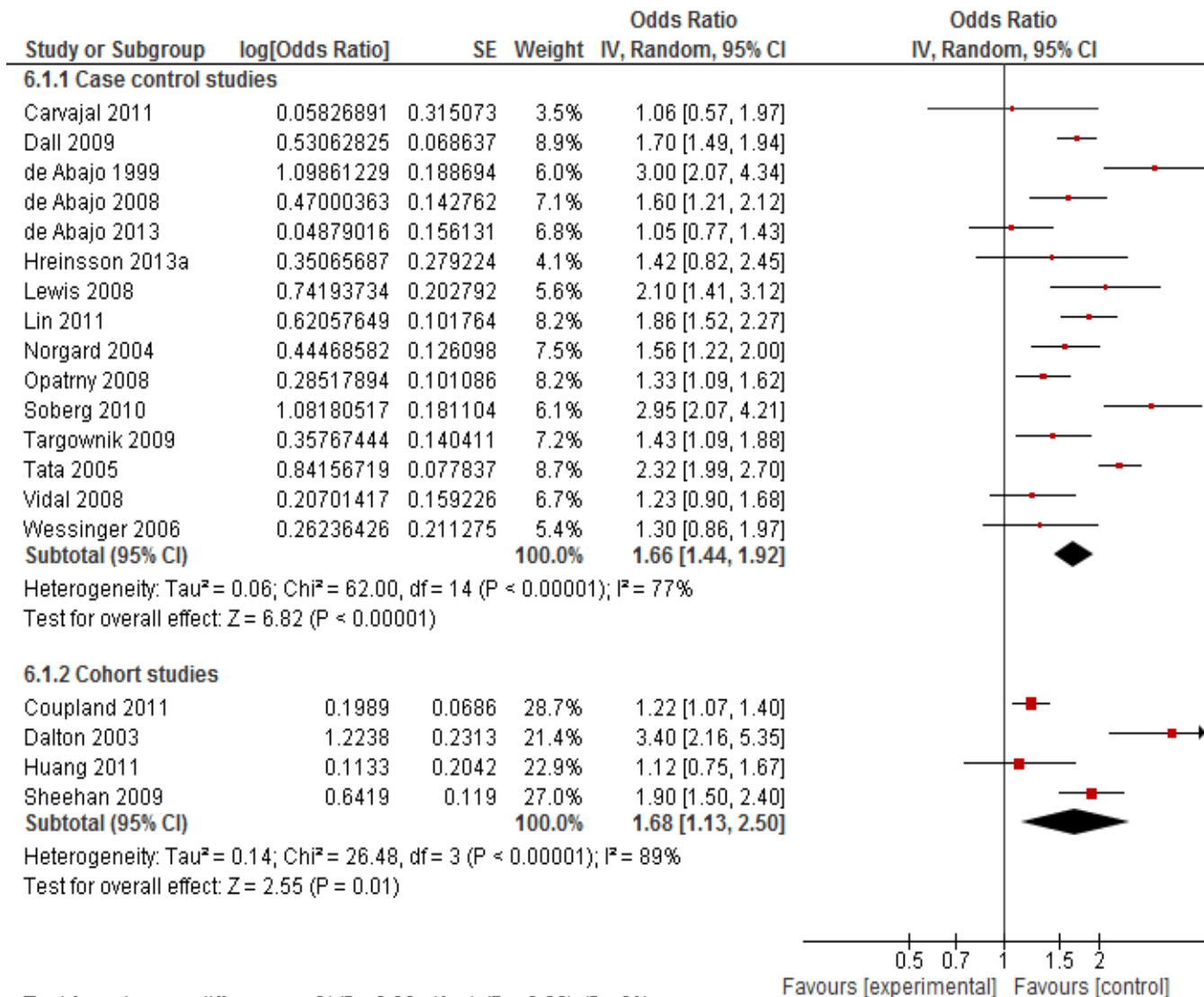
# Antidepressant Tips

- Patients with significant pain and anxiety/ depression may benefit from duloxetine which is also indicated for chronic pain
- Decreased sexual functioning is a relatively common dose-related side effect of the antidepressant medications, and may be a concern for IBD patients given disease-related difficulties with intimacy and sexual functioning

# UGIB with SSRIs

- Updated systematic review and meta-analysis
- 15 case-control studies (including 393,268 participants) and 4 cohort studies
- Increased risk of UGIB with SSRIs in the case-control studies (OR 1.66, 95% CI 1.44,1.92) and cohort studies (OR 1.68, 95% CI 1.13,2.50)
- NNH in low-risk population 3177 (Netherlands), high risk 881 (US)

# UGIB with SSRIs



Test for subgroup differences: Chi<sup>2</sup> = 0.00, df = 1 (P = 0.96), I<sup>2</sup> = 0%

# Managing Antidepressants

- Educate patient regarding
  - (a) expected clinical benefit delay of 2-4 weeks after start of treatment
  - (b) potential side effects, particularly GI, sexual functioning, and weight gain effects
  - (c) potential transient nature of the side effects
- Initiate treatment, gradually increasing dose to therapeutic level.

**Antidepressants should ideally be prescribed by a family physician or psychiatrist or in collaboration with psychiatry or the family physician**

**Despite improvements, studies in primary care settings suggest that many patients do not fill the first prescription.**

Of those who do, 40%–50% discontinue treatment within the first weeks or months, due to side effects, limiting effectiveness of the treatment, particularly given recommendations that medication treatment continue for at least a year



# Managing Antidepressants

Patients are often able to manage side effects or tolerate therapy during the initiation of treatment if they are **aware of the potential side effects, as well as the potential benefits** of persisting until they have adapted to the medication.



**Tip!**

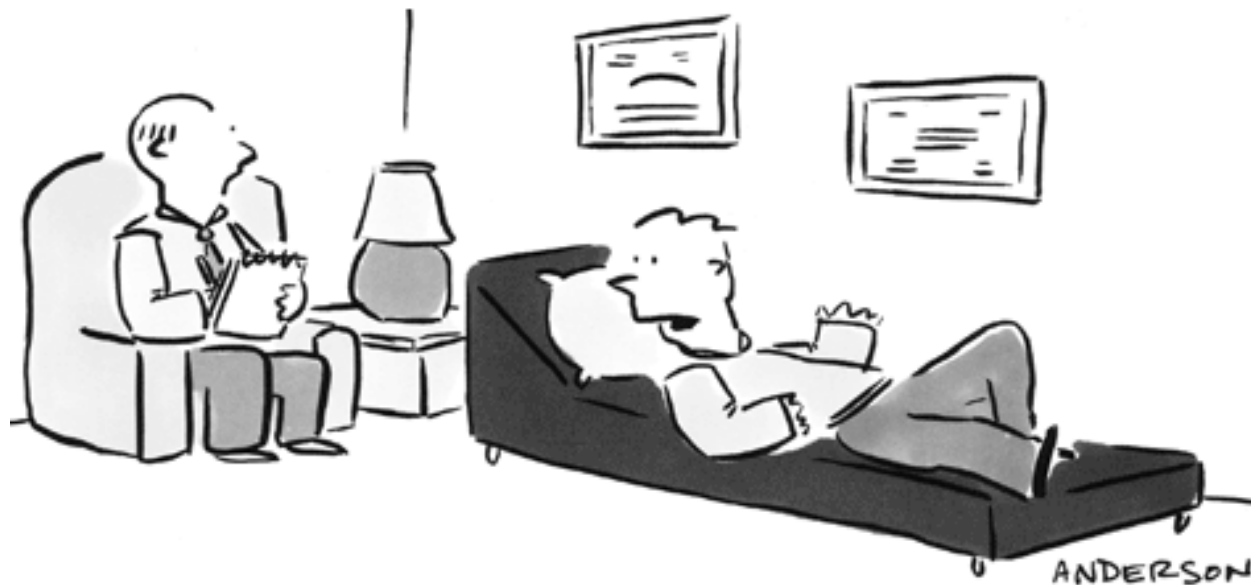
# Psychological Therapies IBD

- Over 16 studies of psychological therapies in IBD, largely stress management and CBT
- CBT showed generally consistent benefits in anxiety and depression, inconsistent evidence for IBD symptoms

Knowles et al. Inflamm Bowel Dis 2013; 19(12)

McCombie et al Inflamm Bowel Dis 2015 In Press

# What is CBT?



"Don't hold back. I want you to feel like you can say anything that comes into my mind."

# Principles of CBT

- Active and collaborative
- Homework exercises
- Focused on the here and now
- Time-limited
- Structured format
- Skills-based

- “I can’t handle this”
- “I’m going to have an accident”
- “Everyone will think I’m disgusting”

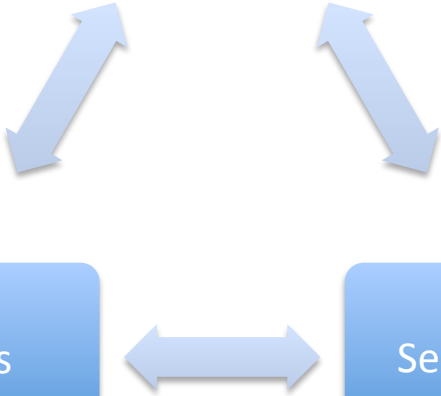
Thoughts

- Leave/avoid the situation
- Safety behaviors (e.g., taking extra medication, staying with a “safe” person, awareness of nearest washrooms)

Behaviours

Physical Sensations and Emotions

- Nausea
- Stomach pain
- Feeling hot



- Behavioural exposure to avoided situations
- Exposure to feared physical sensations
- Increase problem solving skills
- Enhance stress management/coping skills

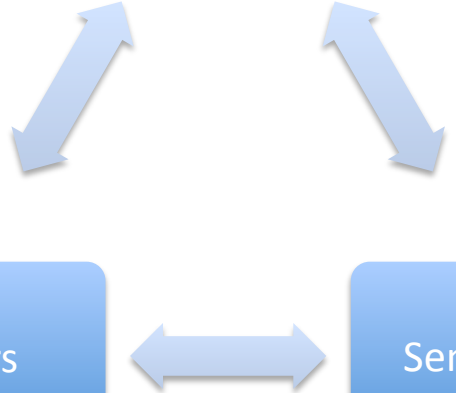
Thoughts

- Identify maladaptive thinking patterns
- Evaluate negative automatic thoughts
- Develop balanced/rational statements

- Relaxation strategies

Behaviours

Physical Sensations and Emotions



# Illustrative Case

- 32 year old woman, single, works part-time as a cleaner at the hospital
- Past history of generalized anxiety disorder and Crohn's disease
- Treated with citalopram 20mg for 2 years and uses over the counter laxatives when constipated and Gas-X prn.

# Illustrative Case cont.

- Describes difficulty working as she has overwhelming anxiety that she will have an accident and not be able to get to a washroom in time. Keeps track of nearest bathroom at all times. Feels she can't handle continuing to work as a result of the stress.
- Avoids social situations as she won't go to a new restaurant and is afraid she will "pass gas" in front of others and they will think she is disgusting. When she has to go to an appointment she takes Gas-X as she describes having nausea, bloating and stomach pain.
- Worries excessively about her finances as she fears she may have to stop working.
- Fears that she may develop colon cancer.



- “I can’t handle this”
- “I’m going to have an accident”
- “I will pass gas and everyone will think I’m disgusting”
- “I’m going to have to stop working and I will be broke”
- “I may develop colon cancer”

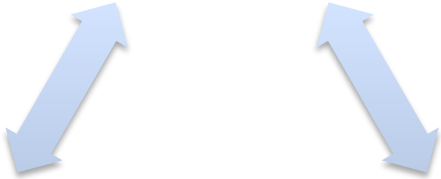
Thoughts

- Avoids social situations
- Safety measures: Takes Gas-x before interactions, Keeps track of bathrooms
- Frequently requesting colonoscopies to rule out new polyps, colon cancer

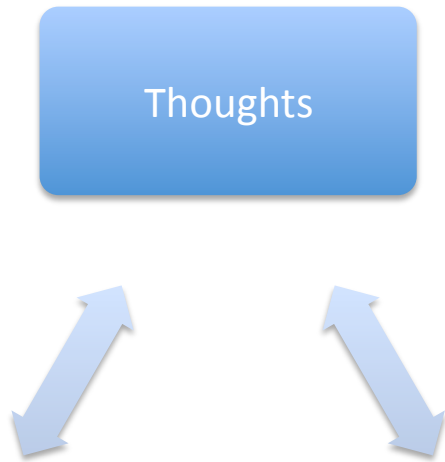
Behaviours

Physical Sensations and Emotions

- Nausea
- Stomach pain
- Bloating

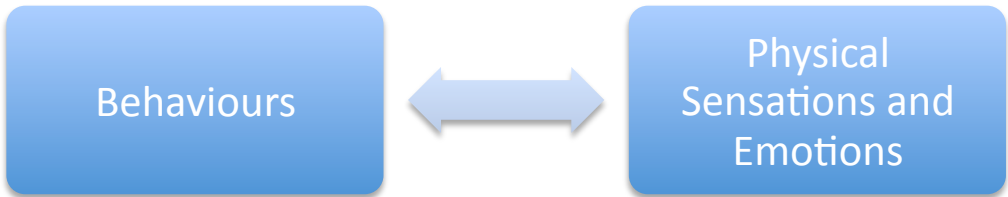


- Behavioural exposure – going to new restaurant, not taking Gas-X
- Exposure to feared physical sensations
- Increase problem solving skills
- Enhance stress management/coping skills



- Identify maladaptive thinking patterns (Catastrophizing, over-estimating the probability, mind-reading)
- Evaluate negative automatic thoughts (people will think I'm disgusting)
- Develop balanced/rational statements

- Relaxation strategies



# Who benefits the most from CBT?

*Capacity to identify and articulate thoughts and feelings and to share them in a nondefensive, focused way*

# Treatment Mental Health in IBD

- Risk stratify based on severity, acute safety concerns
- Discuss patient preference, available options
- Options: initiate pharmacological treatment, refer back to GP, refer to counselor/psychology, refer to psychiatry
- Community resources in your area

# When to refer

- Severe anxiety or depression
- Any acute risks (consider form 1 criteria, ER, community crisis teams, police, rapid consults)
- Comfort level of GI, GP treating psychiatric illness
- Patient refractory to initial treatment
- Complex comorbidity
- Patient preference

# Referrals

- Consider developing a relationship with both psychology and psychiatry in your area
- Integrated care works best – enhanced communication, reduced stigma, specialized care
- Become aware of the community resources in your area

# Summary

- Gut-brain axis likely plays an important role in bidirectional relationship between mental health and IBD
- Mental health aspects important in IBD disease expression, functioning of patients and quality of life
- Screen patients for anxiety and depression and refer for appropriate follow-up when indicated
- In the future we may have an enhanced understanding of common pathophysiological pathways between psychiatric illness and IBD which may lead to improved treatment options

**DISCUSSION AND QUESTIONS?**