Anxiety Disorders and Obsessive-Compulsive Disorder :

conceptual and clinical aspects

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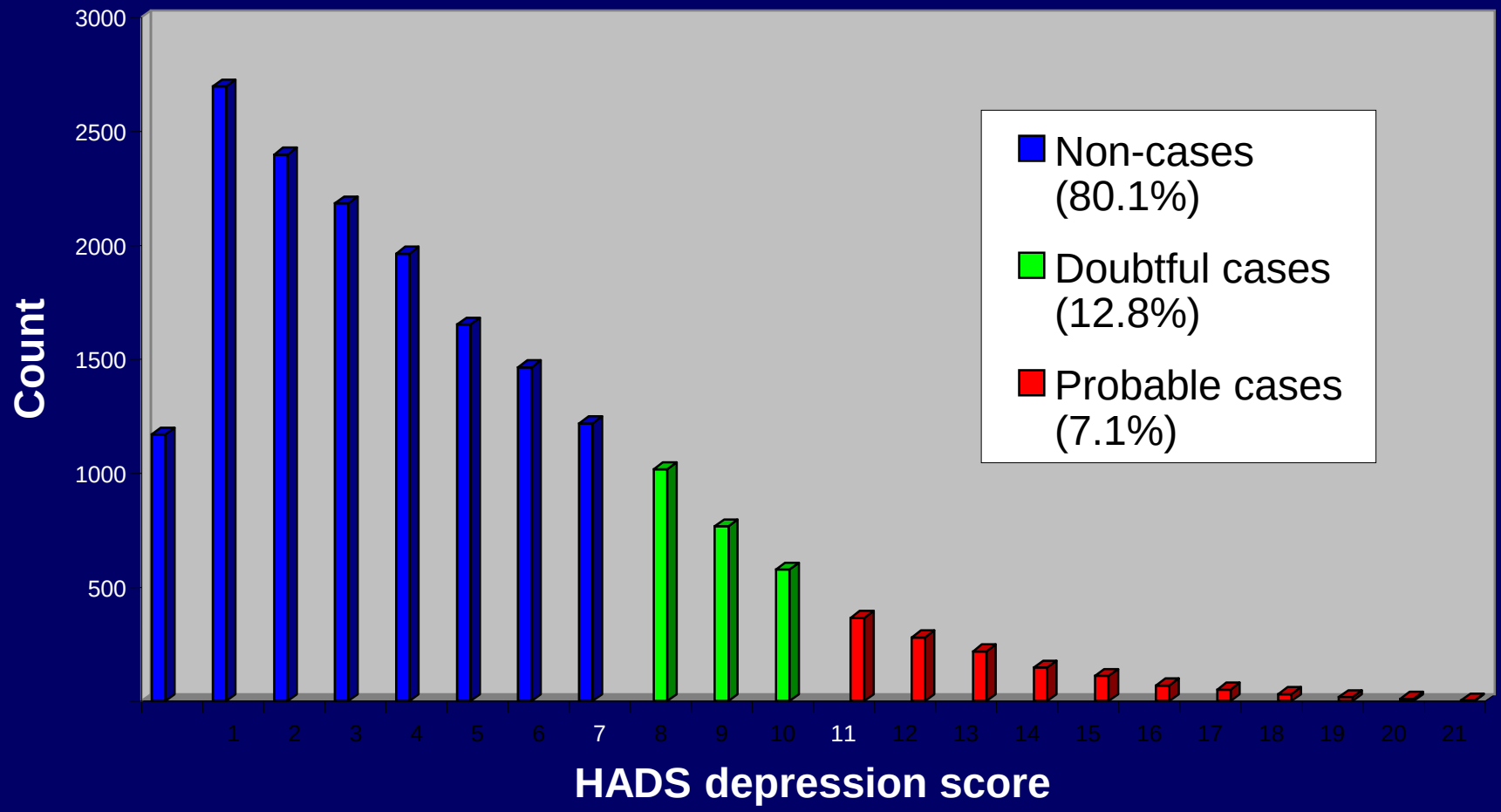
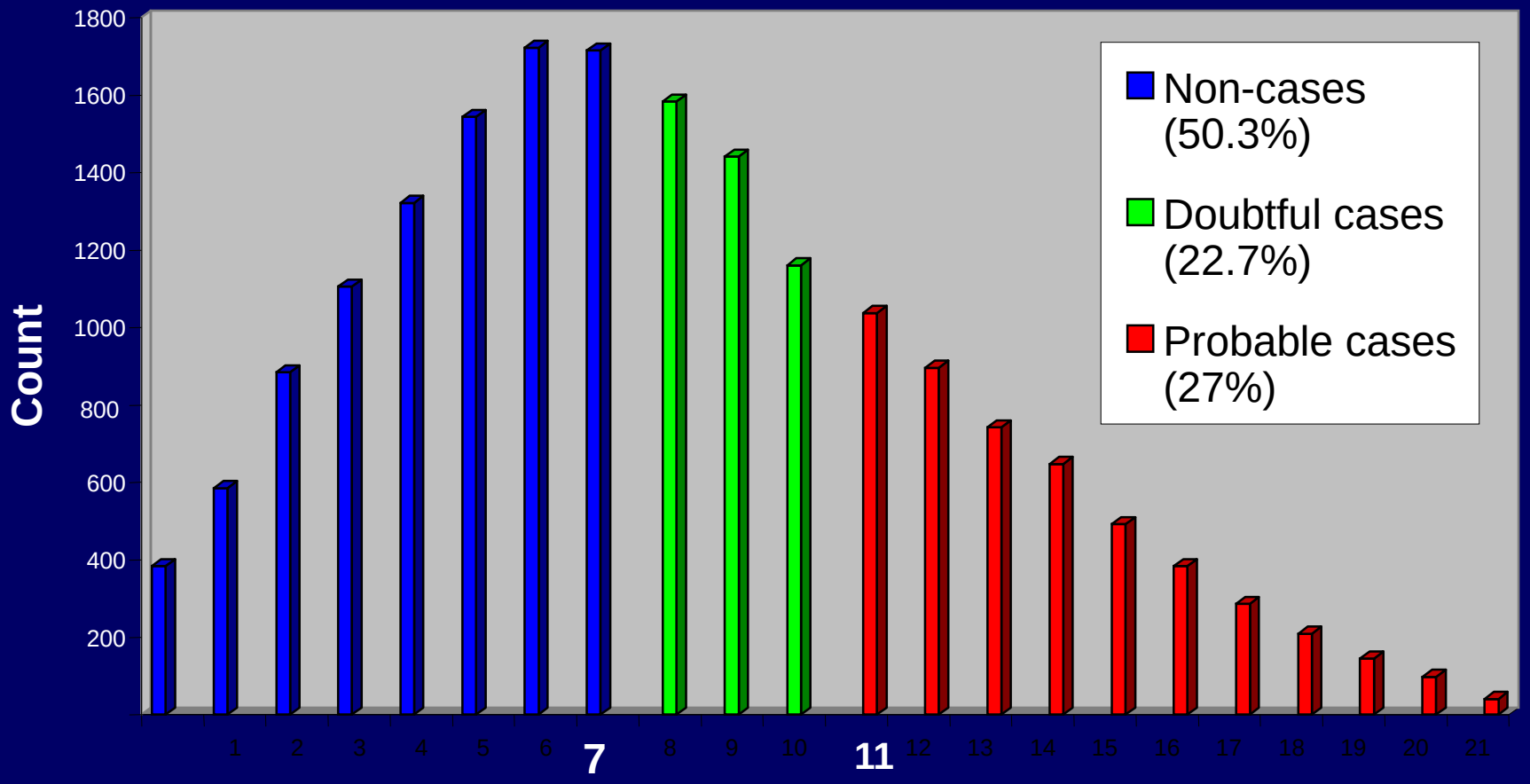
HADS depression score distribution : primary care



Anderson I

HADS anxiety score distribution : primary care



HADS anxiety score

Anderson I

Anxiety

- Pendulum swings between body, mind and brain
  - From anatomy (inner ear/lungs/heart/g-i system) to psychology to anatomy (brain)
- Ongoing permutations and combinations of
  - Subjective complaints : fear, anxiety, phobias, obsessions, panic attacks
  - Objective complaints : skin, cardiovascular, gastrointestinal, nervous system
  - Behaviour : avoidance, agoraphobia,….
- From anxiety as a symptom of other disorders to anxiety disorders
- From unitary syndrome to a variety of anxiety disorders
  - The global concept of ‘neurasthenia’ versus DSM categorical disorders
  - GAD was a ‘residual’ category once panic disorder was identified

Berrios G, 1999

Terminology : DSM-I

- Anxiety
  - A danger signal sent and perceived by the conscious portion of the personality
    - supercharged repressed emotions, agressive impulses as hostility and resentment
- Discharged by / deflected into various expressions (symptoms)
  - **Anxiety reaction :**
    - Anxiety becomes diffuse and not restricted to different situation objects
  - **Dissociative reaction / conversion reaction :**
    - Impulse converted into functional symptoms in organs
  - **Phobic reaction :**
    - Anxiety becomes detached from a specific idea or object and displaced to some symbolic idea or situation
  - **Obsessive-compulsive reaction :**
    - Anxiety associated with the persistence of unwanted ideas and of repetitive impulses to perform acts
  - **Depressive reaction :**
    - Anxiety allayed and partially relieved by depression and self-depreciations

Terminology : DSM-5

Anxiety Disorders :

- Separation anxiety disorder
- Selective mutism
- Specific phobia
- **Social anxiety disorder**
- **Panic disorder**
- Agoraphobia
- **Generalized anxiety disorder**

Trauma- and stressor-related disorders :

- Reactive attachment disorder
- Disinhibited social engagement disorder
- **Posttraumatic stress disorder**
- Acute stress disorder
- Adjustment disorders

Obsessive-Compulsive and related disorders :

- **Obsessive-Compulsive Disorder**
- Body dysmorphic disorder
- Hoarding disorder
- Trichotillomania
- Excoriation

Impairment (SDS) in depression and anxiety

1-3 : mild **4-7 : moderate** **8-10 : severe**

	Work score	Social score	Family score
MDD	4.96	6.42	5.63
PD	4.29–5.42	5.88–6.14	3.76–5.18
GAD	3.97	4.41	4.40
SAD	3.83–6.67	5.67–7.17	2.93–4.57

Lader, 2004; Kennedy, 2002; Sheehan, 1993; Davidson, 1993; Leon, 1992

Drug nomenclature is confusing

The drug nomenclature is unprecise and confusing :

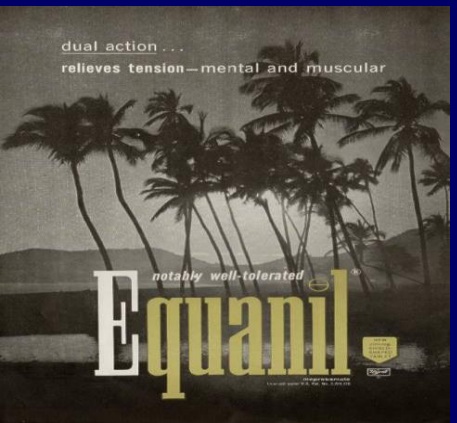
- Chlorpromazine : ‘Largactil’
- What’s in a word ?
  - Antidepressants are effective in anxiety disorders
  - Antipsychotics are effective in non-psychotic depression
  - Antipsychotics are effective in generalized anxiety disorder
  - Anti-epileptics are effective as mood stabilizers
  - **Many modern ‘antidepressants’ have more indications in anxiety disorders than in mood disorders**

History of psychopharmacology : anxiety

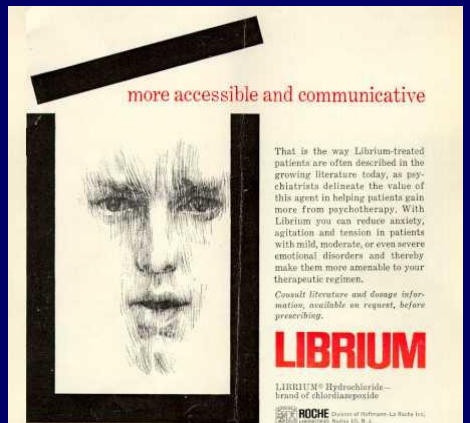
…..from ‘blaming mommy’ to the ‘broken brain’

‘minor tranquillizers’ and ‘major tranquillizers’

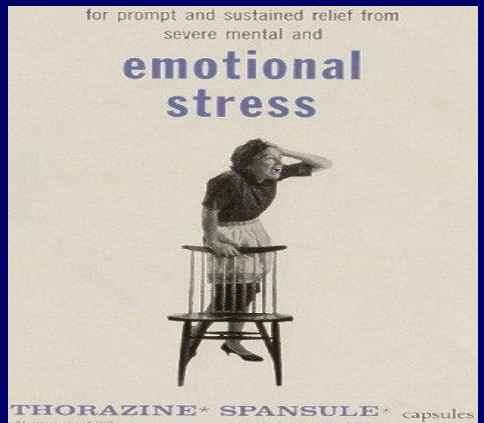
meprobamate

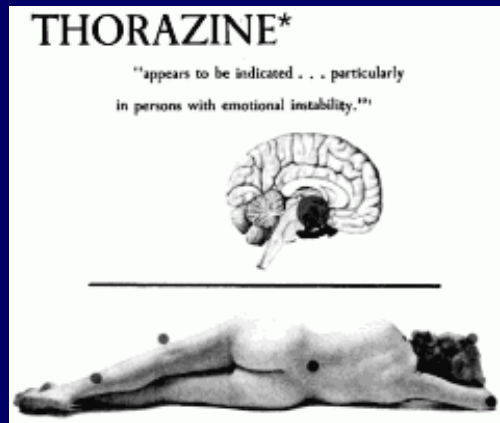


chlordiazepoxide



Chlorpromazine (Larg-actil, Thorazine)





Prevalence of anxiety disorders

	Per population (%)	
	Australia	New Zealand
Any anxiety disorder (including PTSD and OCD)	14.4	14.8
Social anxiety disorder	4.7	5.1
Generalised anxiety disorder	2.7	2
Panic disorder	2.6	1.7
Agoraphobia without panic	2.8	0.6

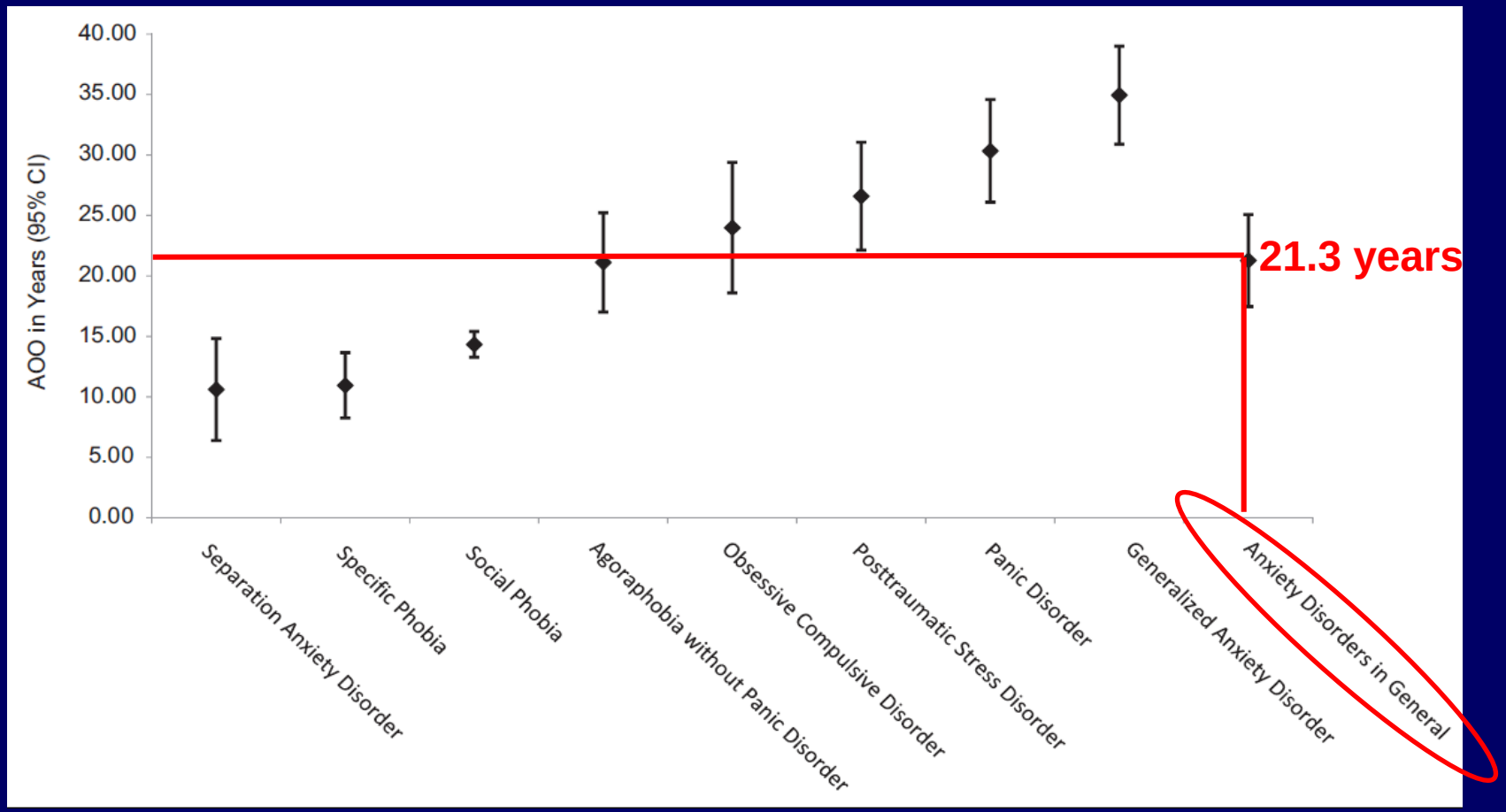
2.7%

6.0%

OCD	0.7-1.2%*
PTSD	6.4-6.8%*
Simple phobia	8.8%

ANZJP guidelines for anxiety disorders, 2019 ** Canadian Guidelines, 2014*

Age of onset of anxiety disorders



De Lijster J et al., Can J Psychiatry 2017

Under-treatment ?

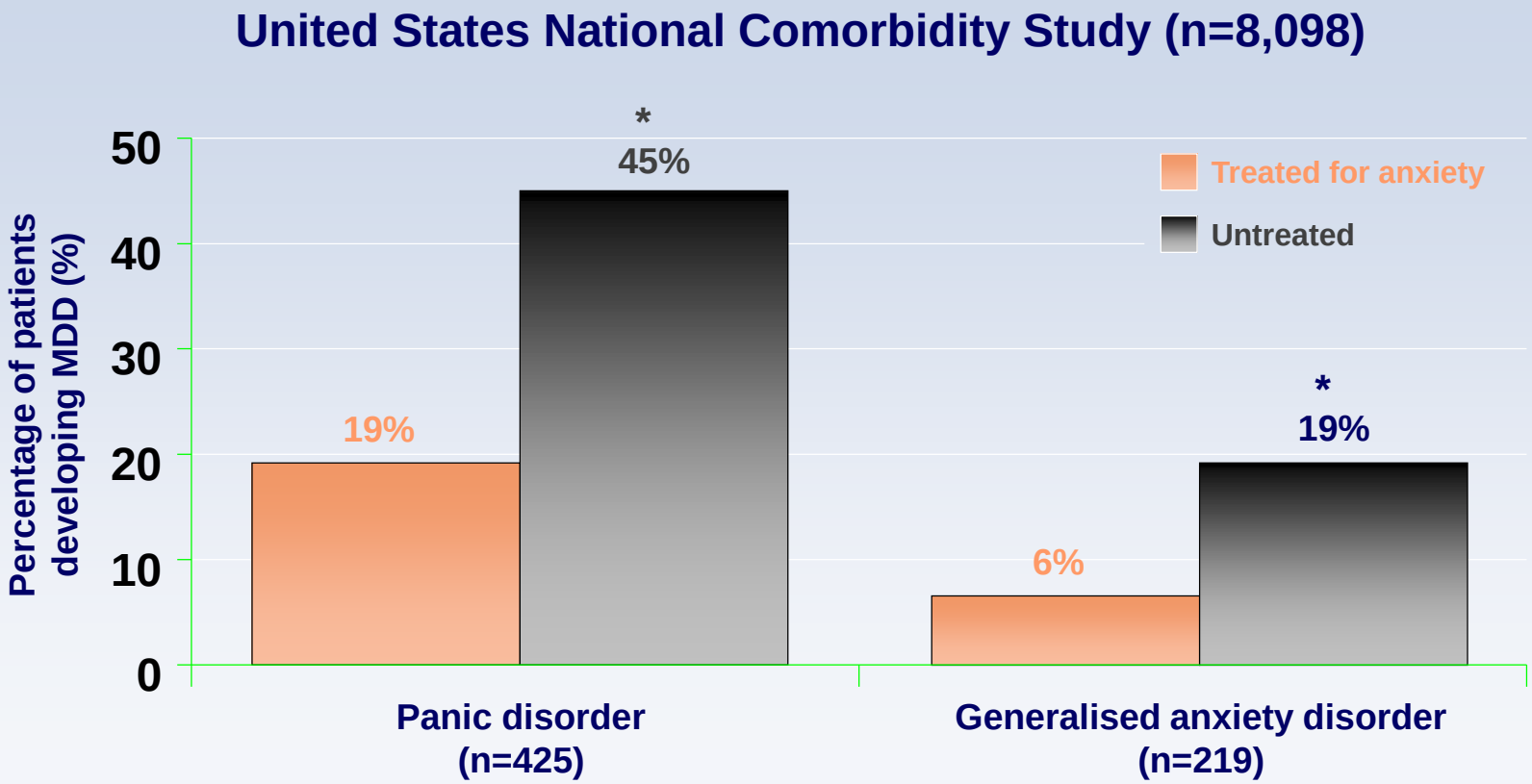
Median age of onset **: 11 years** (mainly due to simple phobia)

Duration before help seeking **: 9-23 years**

- 21% seek help
- When asking help :
  - 23% no treatment
  - 20% psychotherapy
  - 31% drug treatment
  - 26 % combined treatment

Alonso J et al., 2007

Treatment of anxiety disorders is associated with a decreased risk of developing depression



Hazard ratio=0.52 for both; *p=0.001;
MDD=major depressive disorder

Goodwin & Olfson. Am J Psychiatry 2001;158:1146–1148;
Goodwin & Gorman. Am J Psychiatry 2002;159(11):1935–1937

2-year course trajectories of anxiety disorders

- 15% severe, chronic
- 43% moderate severity, chronic
- 42% mild severity

- Baseline severity, duration of anxiety, and disability better predict severe chronic course trajectories than DSM-categories (including comorbidities)
- Additionally, partner status, age at onset, childhood trauma, and comorbid depressive disorder predict chronic course

Batelaan NM et al., 2014

Canada approved drugs in anxiety disorders

	Anxiety disorders	Panic disorder	Social anxiety disorder	Obsessive–compulsive disorder	Generalized anxiety disorder	Posttraumatic stress disorder
ANTIDEPRESSANTS						
SSRIs						
Escitalopram (Cipralex®)				X	X	
Fluoxetine (Prozac®)				X		
Fluvoxamine (Luvox®)				X		
Paroxetine (Paxil®)		X	X	X	X	X
Paroxetine CR (Paxil® CR)		X	X			
Sertraline (Zoloft®)		X		X		
TCAs						
Clomipramine				X		
Other antidepressants						
Venlafaxine XR (Effexor® XR)		X	X		X	
Duloxetine (Cymbalta®)					X	
AZAPIRONES						
Buspirone (BuSpar®, Buspirex®)					X	
BENZODIAZEPINES*	X					

CANMAT guidelines : agomelatine is added for GAD

Katzman MA et al., BMC Psychiatry 2014

Pharmacological treatment recommendations in anxiety disorders

Medications					
		Efficacy shown in RCTs for			Daily dose
	Drug	PDA	GAD	SAD	
SSRIs	Citalopram[1]	x		x	20–40 mg
	Escitalo-pram[2]	x	x	x	10–20 mg
	Fluoxetine	x			
	Fluvox-amine	x		x	
	Paroxetine	x	x	x	20–50 mg
	Sertraline	x	x	x	50–150 mg
SNRIs	Duloxetine		x		60–120 mg
	Venlafaxine	x	x	x	75–225 mg
Tricyclic anti-depressant	Clomip-ramine	x			75–250 mg
Calcium modulator	Pregabalin		x	x	150–600 mg
Azapirone	Buspirone		x		15–60 mg
RIMA	Moclo-bemide			x	300–600 mg

Check local regulatory guidelines

Bandelow B et al., 2017

Meta-analysis : pre-post effect sizes pharmacotherapy and psychotherapy

(234 studies, N = 37.333)

- **Pharmacotherapy**
  - **ES : 2.02 (1.90-2.15)**

>>

- **Psychotherapy**
  - **ES : 1.22 (1.14-1.30)**

- SNRIs : 2.25
- BZD : 2.15
- SSRIs : 2.09
- TCAs : 1.83

- Mindfulness : 1.56
- Relaxation : 1.36
- Individual CBT : 1.30
- Group CBT : 1.22
- Psychodyn Rx : 1.17
- Internet Rx : 1.11
- EMDR : 1.03
- IPT : 0.78

Placebo pills : 1.29
Placebo psychoRx : 0.83
Waiting list : 0.20

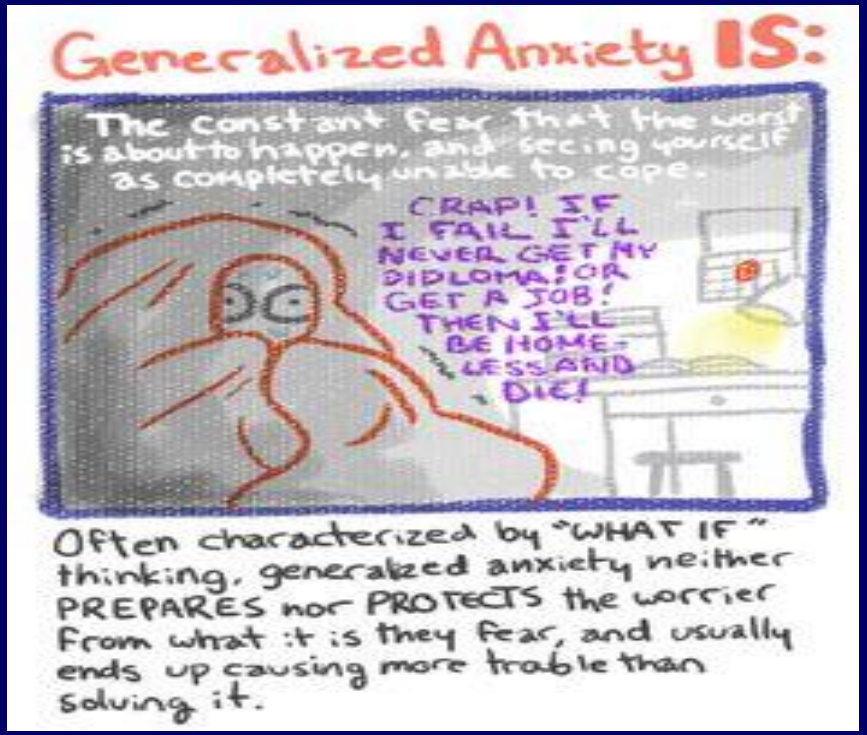
Bandelow B et al., 2015

Risk of relapse after antidepressant discontinuation in anxiety disorder, OCD and PTSD

28 studies N=5233

- Duration of treatment and of follow-up (for both : 8 to 52 wks)
- **Relapses : 36.4% for placebo, 12.6% for antidepressants**
- **OR for relapses : 3.11 (2.48-3.89) for discontinuation**
  - No difference
    - between GAD, OCD, PD, PTSD, SAD
    - between SSRIs and SNRIs
    - Between longer or shorter duration of previous Rx
    - between abrupt discontinuation and tapering
    - between concurrent psychotherapy or not
- **OR for time to relapse : 3.63 (2.58-5.10)**

Batelaan NM et al., 2017



GENERALIZED ANXIETY DISORDER

Comorbidity MDD and GAD

- **MDD** : 5/9 symptoms 14 days
  - Depressed mood
  - Diminished interest/pleasure
  - Weight changes
  - Sleep disturbance
  - Agitation/retardation
  - Fatigue
  - Worthlessness/guilt
  - Difficulty concentrating
  - Suicidal ideation
- **GAD** : 3/6 symptoms 6 months
  - Excessive anxiety/worry, difficult to control
  - Restlessness/on the edge
  - Fatigue
  - Difficulty concentrating
  - Irritability
  - Muscle tension
  - Sleep disturbance

Worrying about the nature of … GAD

- Excessive, pervasive, uncontrollable : ??
- Cognitive dysfunction :
  - Intolerance to uncertainty (Karl Rickels)
- Better categorized as
  - a prodrome, residual or severity marker ?
  - a ‘general neurotic disorder’ ?
    - Focusing on the ‘worries’ distracts the patient from more disturbing underlying concerns ?
- Lifetime comorbidity : 90% (62% MDD, 40% dysthymia)

Depression with anxious distress in DSM-5

- Major depressive disorder / persistent depr disorder
  - Specifier : **with anxious distress** :
    - Anxious distress is defined as the presence of at least two of the following symptoms during the majority of days of a major depressive episode or persistent depressive disorder (dysthymia):
      1. Feeling keyed up or tense
      2. Feeling unusually restless
      3. Difficulty concentrating because of worry
      4. Fear that something awful may happen
      5. Feeling that the individual might lose control of himself or herself

Efficacy of SSRIs/ SNRIs in GAD : Rank order
Probabilistic analysis (Bayesian approach)

- Rank order for remission :
  - Fluoxetine, escitalopram, venlafaxine, paroxetine, sertaline, duloxetine
- Rank order for adherence (completer):
  - Duloxetine, escitalopram, venlafaxine, paroxetine, fluoxetine, sertraline

Gale CK and Millichamp. Clinical Evidence, 2011

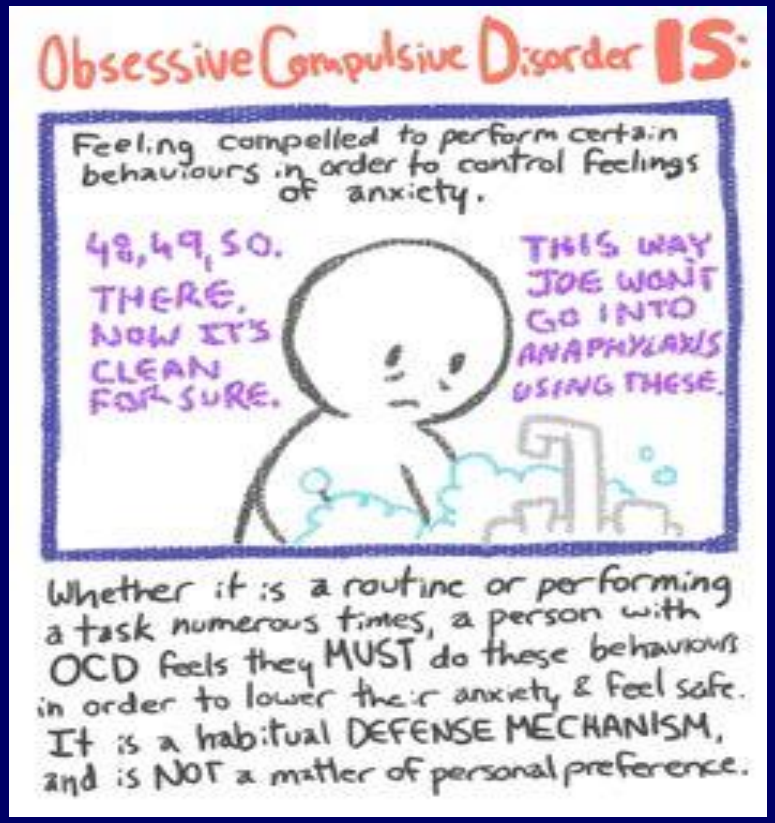
Pharmacotherapy or Psychotherapy in GAD ?

- Pharmacological trials :
  - Baseline HAMA : 22.1 – 27.6
  - LOCF analysis

Hidalgo et al., 2007

- Psychotherapeutical trials :
  - Baseline HAMA : 14.2 – 20.8
  - Completer analysis (20% drop-outs not taken into account)

Wetherell et al., 2003
Borkovec et al., 1993



OBSESSIVE-COMPULSIVE DISORDER

OCD :
Yale-Brown Obsessive-Compulsive Scale (Y-BOCS)

- Impact :

YALE-BROWN OBSESSIVE COMPULSIVE SCALE (Y-BOCS)

Patient's name _____ **Date** _____

Item	None	Mild	Moderate	Severe	Extreme
1. Hours/day spent on obsessions	0	0 to 1	>1 to 3	>3 to 8	>8
Score	0	1	2	3	4
2. Interference from obsessions	None	Mild	Definite but manageable	Impaired	Incapacitating
Score	0	1	2	3	4
3. Distress from obsessions	None	Mild	Moderate but manageable	Severe	Near constant, disabling
Score	0	1	2	3	4
4. Resistance to obsessions	Always resists	Much resistance	Some resistance	Often yields	Completely yields
Score	0	1	2	3	4
5. Control over obsessions	Complete control	Much control	Moderate control	Little control	No control
Score	0	1	2	3	4
					Obsession Subscale (0–20)
6. Hours/day spent on compulsions	0	0 to 1	>1 to 3	>3 to 8	>8
Score	0	1	2	3	4
7. Interference from compulsions	None	Mild	Definite but manageable	Impaired	Incapacitating
Score	0	1	2	3	4
8. Distress from compulsions	None	Mild	Moderate but manageable	Severe	Near constant, disabling
Score	0	1	2	3	4
9. Resistance to compulsions	Always resists	Much resistance	Some resistance	Often yields	Completely yields
Score	0	1	2	3	4
10. Control over compulsions	Complete control	Much control	Moderate control	Little control	No control
Score	0	1	2	3	4
Comments:					Compulsion Subscale (0–20)
					Total Score (0–40)

Date:									
Total previous score:									

Range of severity: 0–7 Subclinical 8–15 Mild 16–23 Moderate 24–31 Severe 32–40 Extreme
Ratings include observations during interviews as well as average occurrence for each item during the last 7 days.

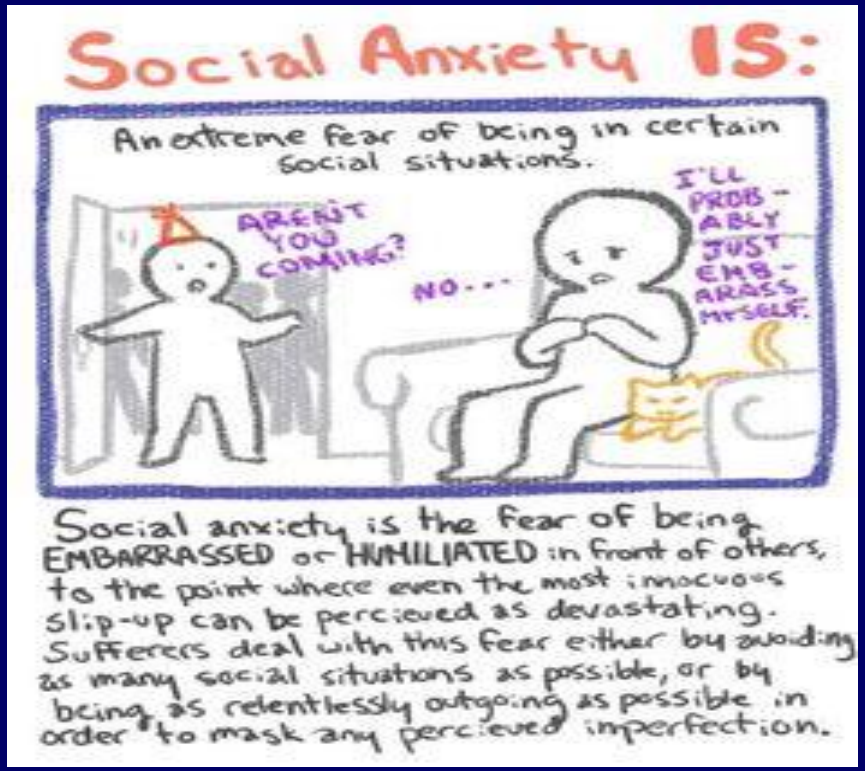
Source. Adapted with permission from Wayne K. Goodman, M.D. Goodman WK, Price LH, Rasmussen SA, et al.: "The Yale-Brown Obsessive Compulsive Scale." Arch Gen Psychiatry 46:1006–1011, 1989.

Targeting family accomodation in OCD

- CBT + family intervention (focusing on reducing family accomodation) *versus* psychoeducation / systematic relaxation training

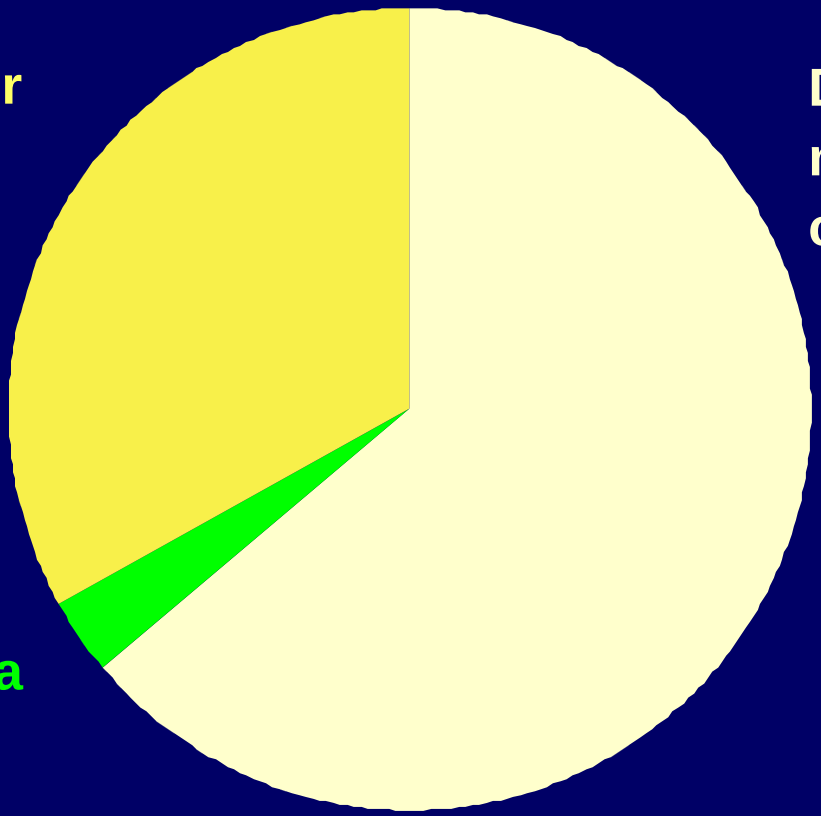
- Responders (CGI-I : very much or much improved)
  - 57.1% (with target on family accomodation) versus 27.3%
- Reduction in CYBOCS (children):
  - 42.5% (with target on family accomodation) versus 17.6%
- Influence of family accomodation on functioning :
  - **Reduction in family accomodation precedes improvement**
  - For each point reduction in family accomodation :
    - 1.2 improvement in functioning (family intervention)
    - 0.5 improvement in functioning (no family intervention)

Piacentini J et al., 2011



SOCIAL ANXIETY DISORDER

Social Anxiety Disorder (SAD) – help seeking…



Saw doctor for other psychological problems

33%

Did not seek medical consultation

64%

Admitted seeking help for social phobia

3%

Duke ECA study, Davidson et al. 1993

SAD :
Liebowitz Social Anxiety Scale

Liebowitz Social Anxiety Scale Liebowitz MR. Social Phobia. Mod Probl Pharmacopsychiatry 1987;22:141-173

Pt Name: Pt ID #:

Date: Clinic #: Assessment point:

Fear or Anxiety:
0 = None
1 = Mild
2 = Moderate
3 = Severe

Avoidance:
0 = Never (0%)
1 = Occasionally (1—33%)
2 = Often (33—67%)
3 = Usually (67—100%)

	Fear or Anxiety	Avoidance	
1. Telephoning in public. (P)			1.
2. Participating in small groups. (P)			2.
3. Eating in public places. (P)			3.
4. Drinking with others in public places. (P)			4.
5. Talking to people in authority. (S)			5.
6. Acting, performing or giving a talk in front of an audience. (P)			6.
7. Going to a party. (S)			7.
8. Working while being observed. (P)			8.
9. Writing while being observed. (P)			9.
10. Calling someone you don't know very well. (S)			10.
11. Talking with people you don't know very well. (S)			11.
12. Meeting strangers. (S)			12.
13. Urinating in a public bathroom. (P)			13.
14. Entering a room when others are already seated. (P)			14.
15. Being the center of attention. (S)			15.
16. Speaking up at a meeting. (P)			16.
17. Taking a test. (P)			17.
18. Expressing a disagreement or disapproval to people you don't know very well. (S)			18.
19. Looking at people you don't know very well in the eyes. (S)			19.
20. Giving a report to a group. (P)			20.
21. Trying to pick up someone. (P)			21.
22. Returning goods to a store. (S)			22.
23. Giving a party. (S)			23.
24. Resisting a high pressure salesperson. (S)			24.

Impairment (SDS):

Occupational	: 5.4
Social	: 6.8
Family	: 3.3

Antidepressants in social anxiety disorder :
meta-analysis : escitalopram 5mg, 10mg and 20 mg vs placebo

- Continuous endpoint (LSAS score):
  - Baseline : 94.0- 96.0
  - Endpoint : 69 for placebo, 56-64 for escitalopram,
    27.8% decrease for plc, 33%-41% for escitalopram
    (30% decrease is considered clinically significant)
    (**global score: 30 =SAD unlikely; 60 = SAD likely** !!)

- Response rate : CGI-I ≤ 2 (much or very much improved)
  - Escitalopram superior (37.8% to 41.2% !!) to placebo (10.2% to 20.8%)
  - NNT : 9 (10mg) and 6 (20mg)

Duration of illness : 14-24 years !!
Duration of trial : 12-24 weeks !!

Baldwin DS et al., 2016

PANIC DISORDER

Common conditions associated with panic attacks or panic-like symptoms

Substance-induced

- Intoxication (e.g. stimulants)
- Withdrawal (e.g. alcohol, benzodiazepines)
- Adverse effects of over-the-counter medications (e.g. decongestants, beta-adrenergic inhalers, stimulants)
- Effects of caffeine-related products (e.g. coffee, energy drinks/supplements)

Medical conditions

More common

- Hyperthyroidism and (less common) hypothyroidism
- Cardiac arrhythmias
- Vestibular dysfunction
- Seizure disorders (e.g. complex partial seizures)
- Hypoglycaemia

Less common

- Hypoparathyroidism and hyperparathyroidism
- Phaeochromocytoma
- Pulmonary embolus
- Electrolyte disturbance
- Cushing syndrome
- Menopause/oestrogen deficiency

Andrews G et al., ANZJP 2018

But…..do not overpromise

	Placebo	Escitalopram
Panic attacks / week	from 5.1 to 3.7	from 5.0 to 3.4
Anticipatory anxiety % of time	from 42.4% to 31.7%	from 45.7% to 21.4%
0 attacks per week at endpoint	38%	50%

Stahl SM et al., 2003

In conclusion :

don’t worry, be happy