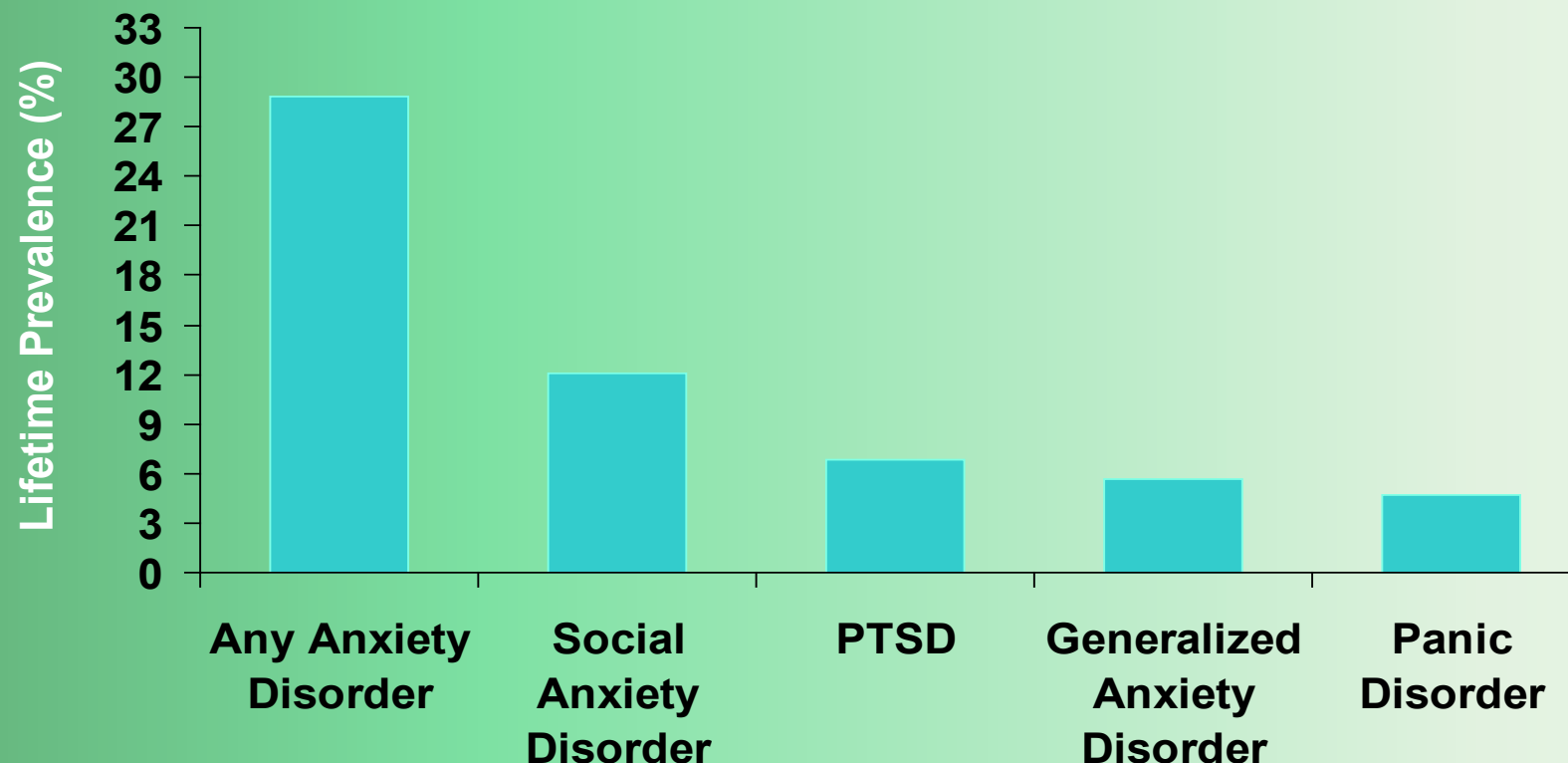


Psychopharmacology of Anxiety Disorders

Anxiety Disorders Are Common:

National Comorbidity Survey Replication



Kessler et al. *Arch Gen Psychiatry*. 2005;62:593-602

DSM-5 reorganized Anxiety Cluster

DSM-5 Disorders

Anxiety Disorders

- Separation Anxiety Disorder
- Selective Mutism
- Specific Phobia
- Social Anxiety Disorder (Social Phobia)
- Panic Disorder
- Panic Attack (Specifier)
- Agoraphobia
- Generalized Anxiety Disorder
- Substance/Medication-Induced Anxiety Disorder
- Anxiety Disorder Due to Another Medical Condition
- Other Specified Anxiety Disorder
Unspecified Anxiety Disorder



Anxiety Disorder Treatment Options

PSYCHOSOCIAL

- Exposure-Based
- Cognitive Behavioral Therapy
- Other psychotherapies
- Relaxation/mindfulness

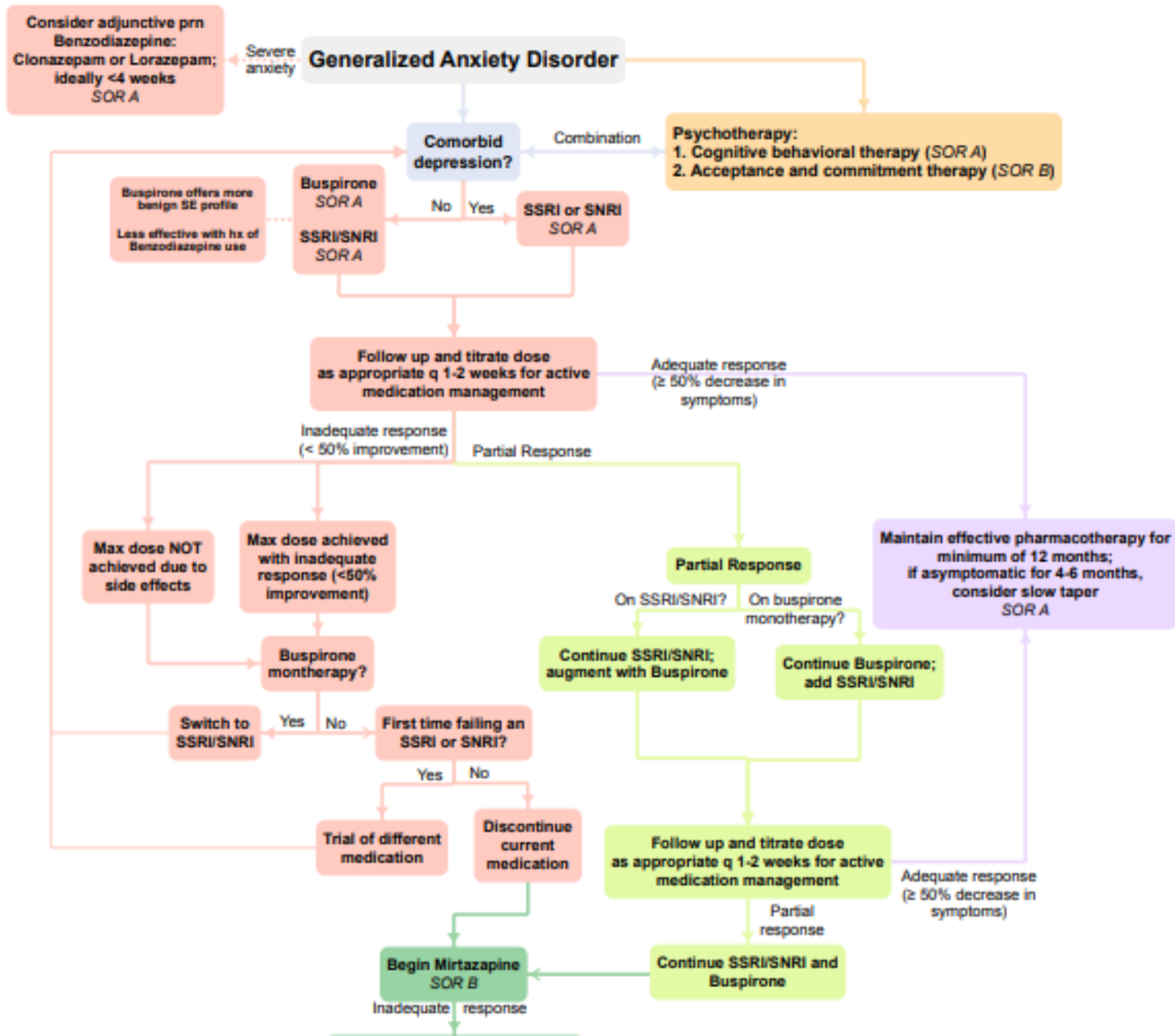
PHARMACOLOGICAL

- SSRIs/SNRIs
- Benzodiazepines
- Mood Stabilizers
- Antipsychotics
- Adrenergic Blockers
- Sleep agents

Anxiety Disorders Management



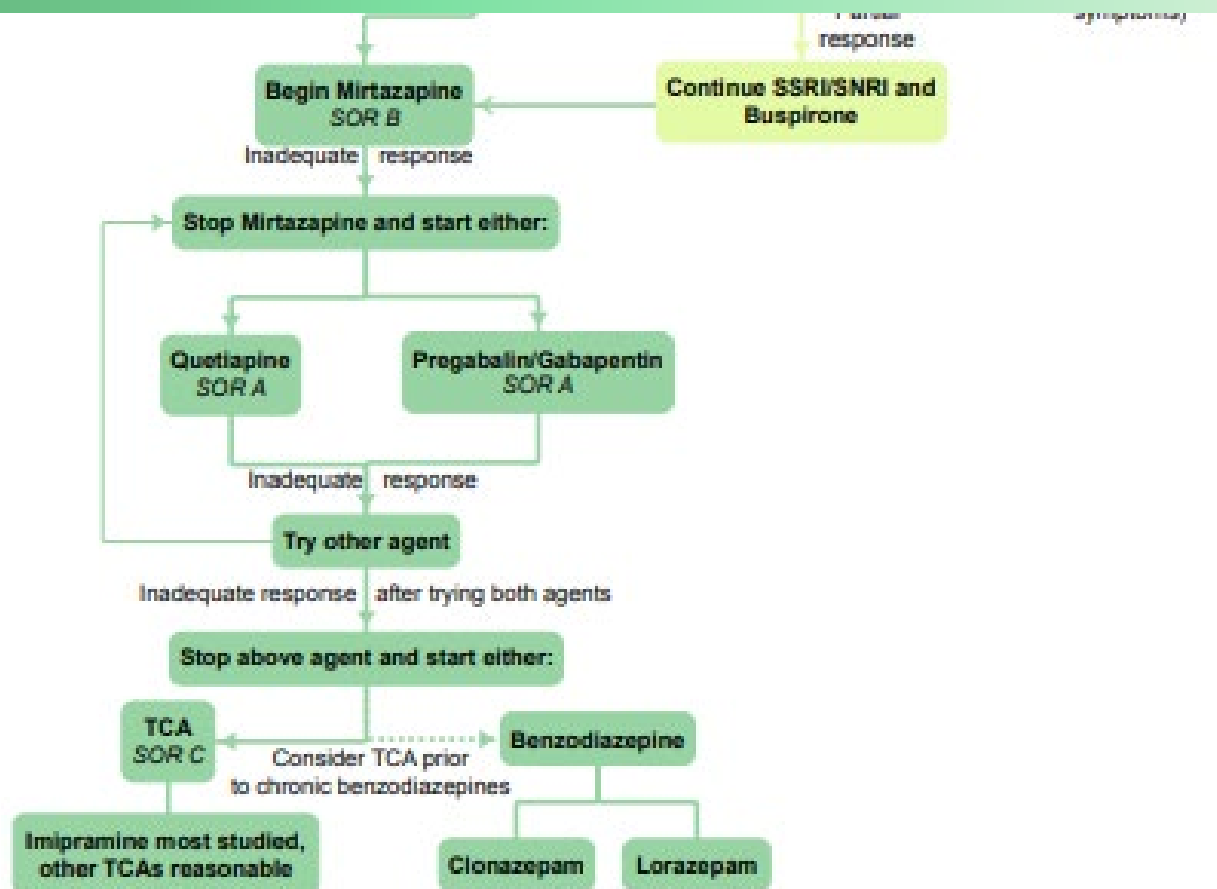
- Exercise, mindfulness, diet, time in nature
- Evaluate medical/psychiatric/substance comorbidity
- RCT data together suggest comparable efficacy for SSRIs, SNRI, TCAs (except SAD, PTSD), Benzos (except PTSD), and CBT
 - SSRI/SNRIs and CBT are first line due to side effects and broad spectrum efficacy
 - Longer acting high potency benzos optimal (but not PTSD)
- Anticipate side-effect sensitivity
- Mixed support combining CBT and meds first line (benzos may interfere CBT, esp. prn)
- → anticipate plan to d/c meds if start together
- Encourage return to avoided situations for all



BRIDGES TO MENTAL HEALTH



BRIDGES TO MENTAL HEALTH



Medications for Anxiety Disorders



Antidepressants

- Serotonin Selective Reuptake Inhibitors (SSRIs)
- Serotonin-Norepinephrine Reuptake Inhibitors (SNRIs)
- Atypical Antidepressants
- Tricyclic Antidepressants (TCAs)
- Monoamine Oxidase Inhibitors (MAOIs)

Benzodiazepines

- High Potency Benzodiazepines
- Low Potency Benzodiazepines

Other Agents

- Azaspirones
- Beta blockers
- Anticonvulsants
- Atypical Antipsychotics

SSRI and SNRI Antidepressants First Line for Anxiety Disorders



- Due to safety and tolerability and broad efficacy
- No clear within-class efficacy differences anxiety disorders
- Start low, go slow, but go
 - start citalopram 10 mg, sertraline 25 mg, venlafaxine 37.5 mg
 - -Minimize early exacerbation of anxiety and overlapping side effects, but MAY NEED HIGHER DOSES
- Lack abuse but serotonin withdrawal, initial activation, insomnia, sexual dysfn, GI, weight gain
- AUGMENTATION STRATEGIES: Adjunctive benzodiazepine, beta-blocker, anticonvulsant

Tricyclic Antidepressants and Anxiety

- No longer first line due to side effect profile (e.g., cardiovascular, anticholinergic) and lethal in overdose
- Imipramine most RCT data in panic
- No evidence lesser efficacy SSRIs/SNRIs panic but lack efficacy Social Anxiety Disorder
- No RCT refractory data but clinical SSRI augmentation
- Initial anxiety worsening (initiate with “test” dose - e.g., 10 mg/d imipramine)

Bakker A et al. *Acta Psychiatrica Scand.* 2002.

This information concerns a use that has not been approved by the US FDA.

Buspirone



- Non-benzodiazepine anxiolytic
- Non-sedating
- Effects on serotonin and dopamine receptors
- Indicated for generalized anxiety; weak antidepressant effects at higher doses but generally reserve milder cases or if no depression comorbidity
- Potentially useful as augmentation GAD or augment:
 - Panic
 - Social phobia
 - Depression
 - Sexual dysfunction
- Dosing: 30-60 mg/d

This information concerns a use that has not been approved by the US FDA.

Beta-Blockers



- Propranolol: 10-40 mg PO QD
- Atenolol: 50-150 mg PO QD
- Effective for discrete “performance anxiety” taken 1-2 h before event
- Propranolol meta-anal. panic (n=130), social (n=16), spec phobia (n=37) found insufficient evidence for anxiety disorders¹
- Not effective for depression/comorbidities
- Decreases physiologic symptoms of arousal, not emotional experience of anxiety

This information concerns a use that has not been approved by the US FDA

¹Steenen et al . J psychopharmacology, 2016

Anticonvulsants for SAD



- None “first line”
- Some RCT support for:
 - Gabapentin (900-3600 mg/d)
 - Pregabalin (at 600 mg)
- Other anticonvulsants have demonstrated possible efficacy for SAD on the basis of open and anecdotal experience
 - Valproate
 - Tiagabine
 - Negative results for Levetiracetam (3,000 mg/day)

This information concerns a use that has not been approved by the US FDA.

Pande et al. J Clin Psychopharmacol. 1999;19:341; Pande. J Clin Psychopharmacol. 2004.
Feltner et al. Int Clin Psychopharmacol. 2011 26;213-220

Atypical Antipsychotics: Role Refractory Anxiety?

- NOT a first line intervention!
- May have role for refractory patients or more complex comorbidity:
 - bipolar and anxiety
- Better side effect and safety profiles than typicals but not side effect free
- Caution re: weight gain and metabolic syndrome

Krystal et al [JAMA](#). 2011 Aug 3;306(5):493-502.

This information concerns a use that has not been approved by the US FDA.

Pharmacotherapy Augmentation: Limited Data

- Potential benefits
 - Enhance initial partial response
 - No lost time tapering
 - Combine agents differing in mechanism
- Potential downsides
 - Side-effect burden
 - Cost
 - Unclear which drug to discontinue and when

Focus on Remission: Pharmacotherapy Options for Patients Remaining Symptomatic

- Optimize dose, duration, and tolerability
- Augmentation
- Switch

Pharmacotherapeutic treatment regimen should reflect the adequacy of prior treatments and other patient variables (such as comorbidity)

Social Anxiety and Pharmacotherapy Meta-analysis (n = 52 studies)



Pooled effect sizes for pharmacotherapy trials by drug category		
<u>Drug Category (Type)</u>	<u>Pooled Effect Size (<i>g</i>)</u>	<u>No. Studies</u>
SSRI (Paroxetine, Fluvoxamine, Sertraline, Fluoxetine, Citalopram, Escitalopram)	0.44	26
SNRI (Venlafaxine ER)	0.45	5
MAOI (Phenelzine, Moclobemide)	0.36	9
MAO-A (Brofaromine)	0.60	6
Benzodiazepines (Clonazepam, Alprazolam)	0.82	2
Antipsychotics (Olanzapine)	0.72	1
Anticonvulsant (Gabapentin, Pregabalin, Levetiracetam)	0.21	5
Beta-blockers (Atenolol)	0.08	1
Herbal (St. John's Wort)	-0.07	1
NaSSA (Mirtazapine)	0.13	1
NK1 (Gr205171)	0.46	1

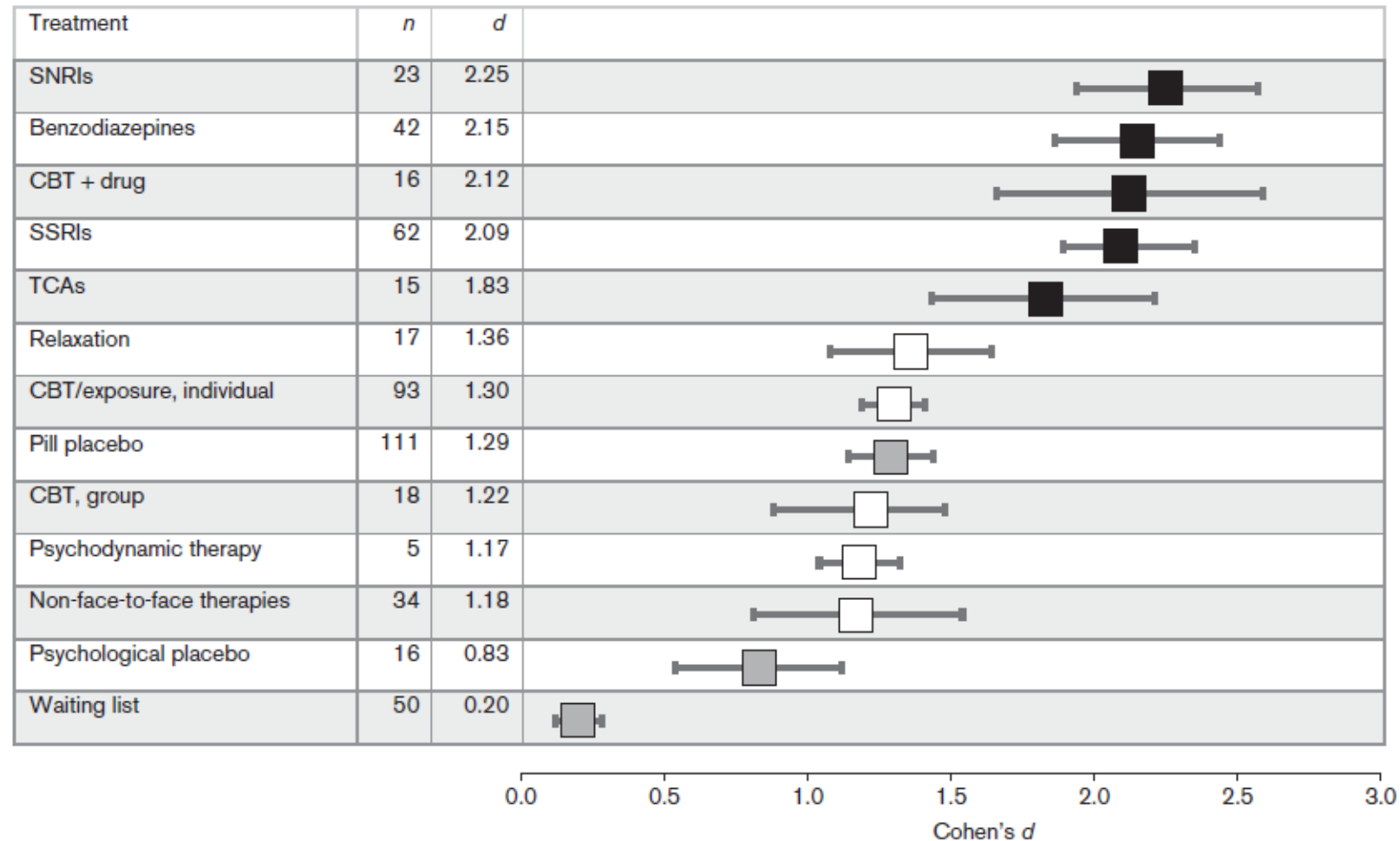
Curtiss J et al. Exp. Opin. Pharmacother. 2017;18:243-251.

Panic, Social, & GAD Meta-Analysis RCTS



BRIDGES TO MENTAL HEALTH

Fig. 2



Bandelow B et al. Int Clin Psychopharmacol. 2015;30:183-92.

Cost



Drug ^a	Average Daily Dose (mg)	Cost Per Day (\$)	References
Antidepressant			
Escitalopram	19.1	3.60	6, 7, 8, 13
Fluoxetine	37.8	1.17	6, 7, 8, 13
Paroxetine	44.3	0.57	6, 7, 8, 13
Sertraline	142.8	0.76	6, 7, 8, 13
Venlafaxine XR	209.1	9.60	6, 7, 8, 13
All antidepressants		4.13 ^b	
Aripiprazole with ADT	9.2	20.31	6, 7, 8, 13
Quetiapine 150 mg with ADT	150.0	12.28	9,13
Quetiapine 300 mg with ADT	300.0	15.90	10,13
Olanzapine/fluoxetine	8.6/48.8 ^c	19.21	11,13
Pharmacotherapy for akathisia			
Lorazepam	1.0	0.14	13
Propranolol	10.0	0.04	13
Benztropine mesylate	1.0	0.12	13
ADT = antidepressant therapy; XR = extended release.			
^a Aripiprazole, dosage 2-20 mg/day; olanzapine/fluoxetine, fixed-dose combination of 6-18/50 mg/day.			
^b Calculated by weighting the mean dosages of the antidepressants by the proportion of patients receiving each agent.			



Thank you!