Anxiety and Depression

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Disclosure

- Anne Emmerich MD reports no personal or family financial conflict of interest related to the content of this session.

Educational Objectives

- Diagnosis of Anxiety and Depression
- Medication strategies
- ACT, CBT, DBT, ECT, TMS
- Treatment Resistant Depression
- Suicide Risk Assessment

Anxiety and Depression

Hirshfeld (2001):

10-20% of adults will visit primary care doctor during episode of anxiety or depression during any 12 month period

Greater than 50% will have comorbid second anxiety or depressive disorder

Comorbidity

- Slower recovery
- ↑ medical services utilization
- ↑ chronicity
- ↑ rate of recurrence
- Greater psychosocial disability

Hirshfeld, 2001

Anxiety

- Fear = response to awareness of actual threat.
  - MD tells you there is high likelihood the biopsy of your lesion will show cancer.
- Anxiety = worry about future event out of proportion to reality of any actual threat.
  - You have never visited your daughter since she moved to California because you are anxious about flying on airplanes.
- Anxiety Disorder = 6 months or more of sxs.

Anxiety Disorders

- **Specific Phobia**
- **Social Anxiety Disorder (social phobia)**
- **Generalized Anxiety Disorder**
- **Panic Disorder**
- **Agoraphobia**
- **Illness Anxiety Disorder** – excessive worry about health in absence of symptoms

Anxiety Disorders cont'd

- **Substance/Medication Induced Anxiety Disorder**
  - Cocaine, stimulants(amphetamines), caffeine, alcohol, nicotine, energy drinks
  - Albuterol, synthroid, SSRIs, prednisone, chemo
  - Withdrawal from alcohol, opiates
- **Anxiety Disorder due to Medical Condition**
  - Hyperthyroidism, pheochromocytoma, cardiac disease, arrhythmias, asthma, pneumonia, pulmonary embolism, B12 deficiency, CNS disorders (malignancy, encephalitis, vestibular dysfunction, seizures).

Screening Questions, Anxiety GAD-2

- “Over the past two weeks, how often have you felt unable to stop or control worrying”
- “Over the past two weeks, how often have you been bothered by feeling nervous, anxious, on edge.”

Phobias

- ***Simple phobia*** – needles, elevators, snakes

- ***Social phobia*** – situations in which one is exposed to possible scrutiny by others (eating in public, public speaking, going to a party)

Agoraphobia

Marked fear or anxiety about 2/5:

- Public transportation
- Open spaces
- Enclosed spaces
- Standing in line, crowds
- Away from home alone

Hallmark of agoraphobia is that patient will not go places alone. (DSM5)

Case 1

- 32 yo male. Physically healthy. No substances.
- Working full time, going to night school to get his MBA.
- Group projects, speaking in class trigger sweating, moist palms, need to go to the bathroom, worry he will faint in front of everyone.
- In college, avoided classes that involved public speaking.

Case 1 continued

- Dx: Social Anxiety Disorder.
- Treatment:
  - B-blocker: Propranolol, l0-30 mg. 30-60 minutes before public speaking or other anxiety producing event.
  - Self help group in which participants practice public speaking – “Toastmasters Club”.

Panic Attack

- “Abrupt surge of intense fear or intense discomfort that reaches a peak within minutes” (DSM5)
- Can be due to medical illness, intoxication, withdrawal, panic disorder, other anxiety disorders.

4 of the following

--Palpitations, pounding heart, rapid heart rate

– Sweating, trembling, shaking

– Sensations of shortness of breath or smothering

– Feelings of choking

– Chest pain or discomfort

– Nausea, GI distress

– Dizzy, unsteady, light headed, feeling of vertigo

– Paresthesia (numbness/tingling)

– Derealization or depersonalization

– Fear of losing control, going crazy, dying

Panic Disorder

- "Recurrent unexpected panic attacks" (DSM5)
- Not attributable to substances/medical cause
- At least one of the attacks has been followed by 1 month or more of:
  - Persistent worry about additional attacks &/or
  - A significant maladaptive change in behavior related to the attacks.

CASE 2

- 50 yo male, self employed accountant. Panic attacks since age 29. No substance use.
- Taking zoloft 100 mg, klonopin 1 mg bid, xanax 1 mg when acute attack occurs.
- Continues to have 10 panic attacks per year. Has been to ER 3 x this year with panic attack.

Case 2 cont'd

- Diagnosis: Panic Disorder, severe.
- Treatment:
  - Add Cognitive Behavioral Therapy

Cognitive Behavioral Therapy (CBT)

- Thesis: Our thoughts and behaviors influence our emotions.
- Treatment of choice for panic and phobias.
- Doesn’t focus on “talking about the past”.

CBT

- 1:1 therapy with PhD or LICSW who is trained in CBT techniques.
- Explicit goals, clear expectations
- Short term, 8-20 sessions
- Homework between sessions
- Cognitive restructuring, breathing exercises, progressive muscle relaxation, visualization, exposure

Generalized Anxiety Disorder

- Excessive anxiety and worry, more days than not, for at least 6 months about a # of issues.
- 3/6: restlessness, easily fatigued, hard to concentrate, irritability, muscle tension, disrupted sleep.
- Significant disruption of social or occupational function.
- Not attributable to another mental disorder

(DSM5)

Pharmacology: Anxiety Disorders

- Choose medication based on frequency of symptoms
  - Infrequent sxs: B-blocker, benzo
  - Frequent sxs: SSRI, neurontin, buspar
- Side effects can derail the treatment entirely
- START LOW, GO SLOW

SSRI/SNRI

- SSRI antidepressants - first line medication treatment for most anxiety disorders
- Dosage range and onset of action are identical to treatment of depression
- SNRIs venlafaxine (Effexor) and duloxetine (Cymbalta) also have FDA approval for treatment of anxiety

Benzodiazepines

- 1st line: Patients with symptoms that occur rarely or only in specific situations.
- Immediate reduction of distressing symptoms while waiting for SSRI to work.
- Some patients need long term benzos.
- Low potential for abuse if no history to suggest risk for this.

Benzodiazepine dosages

- **Clonazepam**: 0.5 mg, up to tid, titrate gradually, max 4 mg per day.
- **Lorazepam**: 0.5 mg, up to tid, titrate gradually, max 4-6 mg per day.
- **Alprazolam**: 0.5 – 1 mg for rare acute panic. Max 2-3 mg/24 hours.
- **Oxazepam**: 10 mg, titrate gradually, max 15 mg tid.

Prescribing Benzodiazepines

- Careful history re dependence on alcohol and sedative hypnotics, current use of any drugs.
- Set expectations (dosages, no lost scripts, no early refills).
- Only set conditions you are prepared to stand by. Know yourself and how you respond to insistent patients.
- Keep track of your prescriptions.

Benzodiazepine Risks

- Sedation – warn about driving.
- Memory/Balance – new concerns.
- Elderly at higher risk for sedation, falls, confusion – start lower, go slower, adjust dose down as pts age.
- Addiction – pay attention to warning signs (lost scripts, early refills, escalating dosages)

Alprazolam

- Short acting, highly addictive
- Rebound anxiety between doses
- Switch to klonopin: 0.5 mg klonopin per 1 mg xanax. Substitute half the doses with klonopin. Continue some xanax for 5-7 days to prevent withdrawal. After a few days re-evaluate and begin to taper remaining xanax increasing klonopin if needed.

Gabapentin (Neurontin)

- Popular off-label choice for anxiety.
- Well tolerated.
- Wide dose range (300-2400 mg).
- Mood stabilizing and anti-pain properties, useful for patients with co-morbid conditions.
- Start with 100 mg, increase q 2-3 days by 100 mg.

Buspirone (Buspar)

- Some effectiveness for GAD as second line agent. Uncertain usefulness in other anxiety disorders.
- Useful when benzos are contraindicated.
- Dose range: 30-60 mg. Start with 15 mg tab, 1/3 tab per day, increase by 1/3 tab q3-4 days. Intolerable GI side effects with rapid dose titration.
- 1-2 weeks to onset of action.
- Not useful as a “prn” although some patients use it this way.

Other meds

- **Hydroxyzine** : 50 mg, increase every few days, max 100 mg qid.
- **Trazadone**: 25 mg, increase every few days, max 300 mg (priapism, orthostatic hypotension).
- **Doxepin**: 25 mg, increase weekly, max 150 mg bid.
- Caution about sedation, no use of alcohol

Atypical Antipsychotics

- **LAST CHOICE** for sleep or anxiety
- Risperdone (Risperdal)1-4 mg, Quetiapine (Seroquel) 25-100 mg, others
- Risk of metabolic syndrome.
- Monitor lipids, blood sugar.
- Use only when all others have failed or short term if high risk and rapid response needed
- Document informed consent.

Anxiety Summary

- Rule out medical and substance induced sxs.
- CBT is treatment of choice for most anxiety disorders.
- Frequency of sxs guides choice of medication.

If treatment isn't working, re-evaluate

- Substances – use of them, withdrawal from them, excessive caffeine, excessive use of energy drinks, nicotine.
- Co-morbid psych: Axis II, substance abuse, other anxiety disorders, PTSD, agitated depression.
- Undisclosed social stressors (DV, legal, financial, gambling)

DEPRESSION

- Depressed mood most of the day, nearly every day.
- SIGECAPS – sleep, interest, guilty ruminations, energy, concentration, appetite, psychomotor, suicidal thoughts
- 5 or more sxs, 2 weeks or more, causing significant distress or impairment in functioning.

Screening Questions, Depression PHQ-2

- “Over past 2 weeks, how often have you felt down, depressed or hopeless”
- “Over past 2 weeks, how often have you felt little pleasure or interest in doing things”
- If answer to either of these is “yes”, ask about suicidal thoughts

U.S. Preventive Service Task Force, 2009

"Depression screening programs without substantial staff-assisted depression care supports are unlikely to improve depression outcomes. Close monitoring of all adult patients who initiate antidepressant treatment, particularly those younger than 30 years, is important both for safety and to ensure optimal treatment."

Follow Up

- 40% of patients who begin an antidepressant discontinue it within a month
- Only 25% of patients receive even minimal follow-up
- Of patients who begin psychotherapy only half attend 4 or more sessions

Simon et al, JAMA, 292(8), 25 August 2004

Initial treatment

- If patient sees MD, medication is the most common first treatment.
- Primary care doctors write 2/3 of all antidepressant prescriptions.
- First agent used has the best chance of success.

Set expectations

4-6 weeks for onset of action.

Response is not linear. *“There will be a phase of good days and bad days before you feel truly well. This does not mean the medicine is not working or that you will not get better”.*

How to start

Start low, titrate, to diminish side effects and improve compliance.

Contact in 2 weeks (sooner for more severe depression) *"I don't expect you to be feeling better in 2 weeks but I do want to know how you are tolerating the medication*".

DON'T LOSE FOCUS. Goal is to get to full dose and achieve remission.

Adequate Duration

- First depression – 6 to 9 months of medication after symptoms remit
- Two depressions – 18 months
- 3 or more depressions – long term treatment

Pharmacology: Depression

- All antidepressants have side effects.
- Use side effect profile of drug to patient's advantage.
- Clinical outcome correlates with adequate monitoring and follow up.

Antidepressant-Induced Mania

- Case reports with all antidepressants. Less likely with bupropion (Wellbutrin)
- Risk factors: prior symptoms, first degree family member with bipolar disorder
- ALWAYS ASK. If prior sxs of MANIA, no antidepressant without mood stabilizer
- SSRI induced restlessness can occur, differentiate from mania by presence of other sxs.

Serotonin Reuptake Inhibitors

- Most common first step.
- Easy to use.
- Common side effects – insomnia, GI distress, sexual dysfunction.
- “Start in a.m. with food – ok to change these if tolerated”.

Serotonin Reuptake Inhibitors (SSRIs)

- Fluoxetine(Prozac) 20-40 mg
- Sertraline(Zoloft) 50-200 mg
- Citalopram(Celexa) 20-40 mg
- Escitalopram(Lexapro) 10-20 mg
- Paroxetine(Paxil) 20-40 mg

Issues to consider

- QTc prolongation: Citalopram, Escitalopram
- Cytochrome P450: Paroxetine and Fluoxetine, CYP2D6 inhibition (B-blockers, anti-psychotics, TCAs)
- Bleeding: Reports in combo with NSAIDS, aspirin, other anticoagulants (increasing evidence, no guidelines).

QTc prolongation – dose guidelines

Adults up to age 65: Maximum dose, 40 mg citalopram or 20 mg escitalopram.

Over age 65: maximum dose, 20 mg citalopram and 10 mg escitalopram.

Use the lower dose range if given with other meds that can prolong QTc

omeprazole, cimetidine, methadone, antivirals, others

Patients already on higher doses

- Evaluate risk of taper to patient
- If risk too high or taper unsuccessful and no other options: EKG for QTC monitoring and cardiology input are recommended
- There is no way to know for sure even with “normal” EKG – we are waiting for more guidance
- Discuss risk with patient/document

SSRI/Tricyclic combo

- Gilman, Br J Pharmacol, 2007. “No TCA/SSRI combination is sufficiently safe to be universally applicable without expert knowledge”.
- Prozac/Paxil + TCA particularly dangerous due to SSRI inhibition of cytochrome P450.
- Check EKGs and TCA levels
- Not for patients with SI or who overuse meds

SSRI/Triptan combo

- Triptans: serotonin receptor agonists
- 2006: FDA warned risk of serotonin syndrome when triptans combined with SSRIs.
- 2010: American Headache Society Position Paper. “Available evidence does not support limiting use of triptans with SSRIs or SNRIs. However, given the seriousness of serotonin syndrome, caution is warranted and clinicians should be vigilant.”

Serotonin Norepinephrine Reuptake Inhibitors (SNRI)

Usually tried after 2 failed trials of SSRI, but can be first agent.

Rapid titration = nausea, headache, often leads to patient terminating trial.

START LOW, GO SLOW but don't lose focus.

Venlafaxine

Serotonin Norepinephrine Reuptake Inhibitors (SNRI)

- **Venlafaxine (Effexor)** 225-300 mg/d target
- **Desvenlafaxine (Pristiq)** 50-100 mg/d target
- **Duloxetine (Cymbalt**a) 60-120 mg/d target
  - FDA approved for MDD, GAD, diabetic neuropathy, chronic musculoskeletal pain, fibromyalgia
- **Milnacipran**
  - FDA approved for fibromyalgia, not MDD

SNRI side effects

Venlafaxine – hypertension, cardiovascular fatalities reported in overdose especially with alcohol, headaches, GI distress

Duloxetine – hepatotoxicity (fatalities reported, avoid use in heavy drinkers), tachycardia, nausea, fatigue, sweats.

Bupropion (Wellbutrin)

- Start low (75 mg), target dose 300-400 mg per day. Once daily XL increases compliance.
- Energizing, weight gain uncommon.
- Seizures – ↑ risk with rapid titration, prior seizure, bulimia (purging), alcohol use.
- Hypertension – common, often missed as cause of new onset HTN in middle aged adults
- No sexual dysfunction.

Mirtazapine (Remeron)

- Start with 15 mg, target dose 30-60 mg.
- Sedation and weight gain are common
- Dry mouth, weight gain(10-20lbs), edema
- Lowest sexual dysfunction of SS/NRIs.
- Favorable med interaction profile.
- Paradoxical sedation (more at lower doses): *"if it makes you too sleepy at first, do not cut it in half".*

Newer Agents

- **Vilazodone (Vibryyd**): 40 mg/d, diarrhea, n/v, insomnia, risk of bleeding.
- **Vortioxetine (Brintellix**): 2.5-5 mg/d, n/v, diarrhea, headache, dizziness, ↓sexual dysfunction.
- **Tedatioxetine** (**Lu AA24530**): Phase II clinical trials, triple reuptake inhibitor (ser/ne/dop)
- **NMDA receptor modulators:** early trials, Ketamine,Glyx13

SSRI/SNRI induced sexual dysfunction

- Decrease dose – not always dose dependent though
- Switch to another agent
- Drug holiday
- Placebo controlled trials:
  - Sildenafil 50-100 mg, evidence that it works for both men and women but not FDA approved for women
  - Bupropion, 100-200 mg
- Other:
  - Buspar, conflicting results
  - Cyproheptadine, stimulants, amantadine, yohimbine – anecdotal evidence only
  - 1 small trial of loratadine was promising

Insomnia

- Anxiety: Difficulty falling asleep (DFA)
- Depression: Difficulty staying asleep (EMA)
- Antidepressants: Cause insomnia frequently. Need for sleep aid is common.
- Insomnia can be first sign of recurrence of illness or even trigger it. Educate patients.
- Common sleep aids:
  - Trazodone, 50-100 mg (priapism, postural hypotension, falls in elderly)
  - Prazosin (Minipress), 2-15 mg, for patients with comorbid PTSD related nightmares.

Comorbid Treatment

- **SSRI**'s: PTSD, PMDD, OCD, bulimia, GAD, Panic D/O, Social Anxiety D/O, pain
- **Bupropion**: ADD/ADHD, smoking cessation, sexual dysfunction
- **SNRI**: PTSD, PMDD, OCD, GAD, Social Anxiety D/O, pain
- **TCA**s: diarrhea, urinary incontinence, sleep, diabetic neuropathy, ADD

Next Steps

- Good response at 6 weeks
  - continue 6-9 months (first episode), then taper
- Partial response at 6 weeks
  - increase dose as tolerated; combination therapy or augmentation
- No response or minimal response at 6 weeks
  - switch within category or change category (ie SSRI to SNRI)

Treatment Resistant Depression

- No consensus definition
- Research study definition: 1 failed trial at 6 weeks.
- Insurance definition: 2-4 failed trials of meds before ECT/TMS.
- ICSI: “failure to achieve remission with an adequate trial of therapy and 3 different classes of antidepressants at adequate duration and dosage”

Combination Therapy

- Use of two antidepressants when the first one is not providing full desired benefit
- Use an antidepressant from another category so side effects do not compound, reduce risk of serotonin syndrome
  - SSRI/SNRI with Wellbutrin
  - SSRI with Trazadone
  - Venlafaxine with Mirtazapine

Augmentation

- Adding a second agent that is NOT an antidepressant.
- Implies that first agent is FULL DOSE.
- Two meds, both at inadequate doses, is not augmentation – it is inadequate treatment.

Augmenters

- Mood stabilizer: Lithium 300-600 mg or Lamictal 25-100 mg
- Buspirone (Buspar) 15-30 mg
- Atypical neuroleptics: Aripiprizole (Abilify) 2-10 mg, Quetiapine (Seroquel) 25-100 mg
- Psychostimulant: Ritalin 10-20 mg or Adderall 13-30 mg
- T3, SAMe, modafinil

L-methyl folate

Medical Food

Mixed studies re use as augmentation agent

? crosses blood-brain barrier better than folate

? MTHFR C677T mutation predicts likelihood of benefit

Re-examine your diagnosis

- Substances – illicit benzos, opiates, use of them, withdrawal from them (cocaine)
- Testosterone use increasing and with it some cases of increased depression and increased irritability
- Medical – TSH, cancer screen, fibromyalgia
- Co-morbid psych: Axis II, substance abuse, dysthymia (double depression), anxiety disorders, PTSD

Psychotherapy

- For more severe depression, studies show that medication plus therapy is better than either alone.
- For moderate-severe depression WITH functional impairment and WITHOUT suicidal PLAN, partial hospital program (php) offers option of daily psychotherapy groups for first few weeks of treatment.

ACT therapy

- “Acceptance and Commitment”
- Mindfulness practice
- Pts work toward acceptance of emotions they find painful and commitment to a vision of a goal they value.

CBT

Cognitive restructuring: changing thought patterns

Behavioral activation: overcome obstacles to participation in meaningful activities

Dialectical Behavioral Therapy (DBT)

"Emotional Skills Training".

Initially developed by Marsha Linehan PhD for treatment of patients with borderline personality disorder.

Structured group setting, workbook, homework.

Useful in depression especially when there is chronic suicidal thinking, Axis II.

Psychosomatic Therapies

- ECT (electroconvulsive therapy): 8-15 sessions, maintenance monthly therapy needed for some pts. Memory loss and H/As most common side effects.
- TMS (Transcranial Magnetic Stimulation: FDA approved, no anesthesia, approx 1 hour per day for 30 days.

Black Box Warning re Young Adults

- **"Antidepressants increased the risk compared to placebo of suicidal thinking and behavior (suicidality) in children, adolescents, and young adults in short-term studies of major depressive disorder (MDD) and other psychiatric disorders. Anyone considering the use of ….. or any other antidepressant in a child, adolescent, or young adult must balance this risk with the clinical need. Short-term studies did not show an increase in the risk of suicidality with antidepressants compared to placebo in adults beyond age 24; there was a reduction in risk with antidepressants compared to placebo in adults aged 65 and older. Depression and certain other psychiatric disorders are themselves associated with increases in the risk of suicide. Patients of all ages who are started on antidepressant therapy should be monitored appropriately and observed closely for clinical worsening, suicidality, or unusual changes in behavior. Families and caregivers should be advised of the need for close observation and communication with the prescriber." (FDA)**

SSRI/SNRI discontinuation

- Whenever possible, taper slowly.
- Discontinuation symptoms – flushing, headache, nausea, muscle aches, “electric jolt”
- Reported with all SSRIs and SNRIs (paroxetine, venlafaxine especially)
- Some patients need to go back to full dose and taper more slowly.

Pharmacogenomics

- No current FDA algorithms for genetic testing when using antidepressants
- ? If there is a role for pts who fail to respond to multiple meds/have intolerable side effects to multiple meds

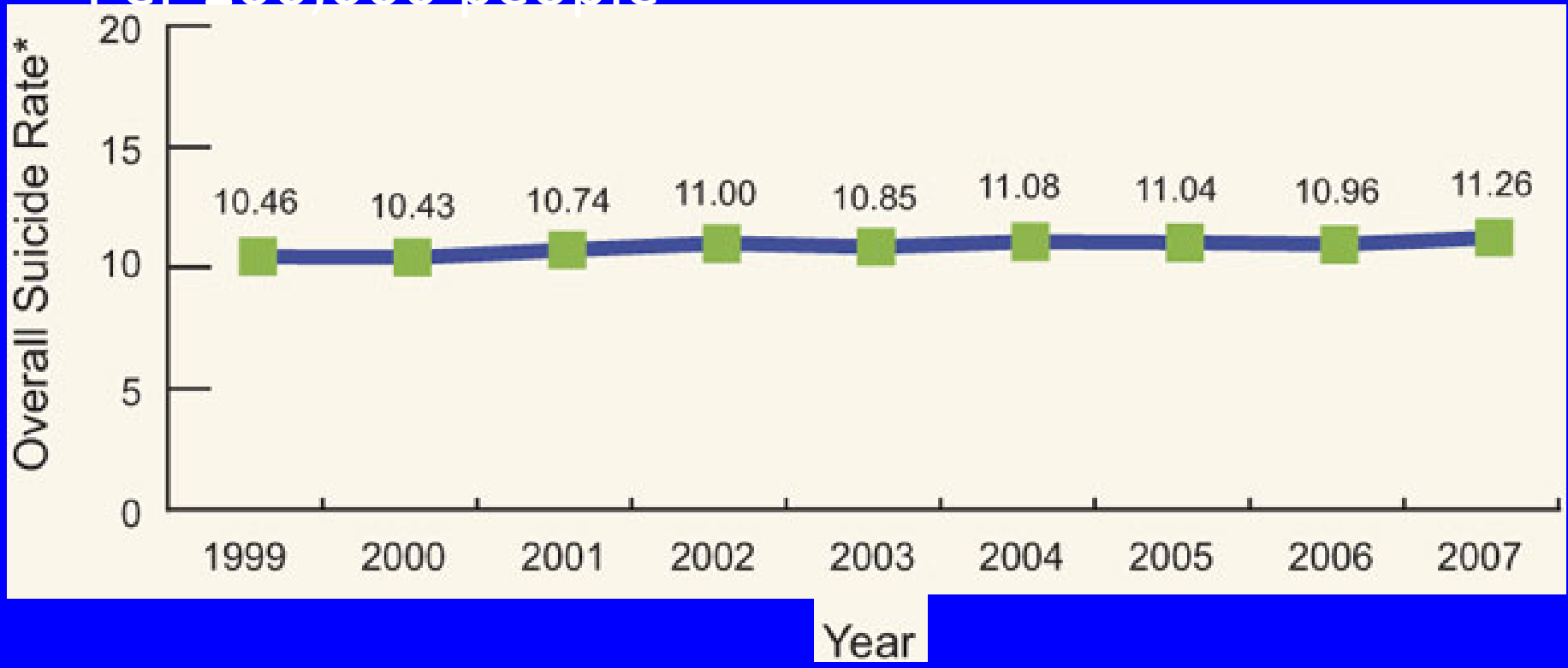
Pregnancy

- No psychotropic meds FDA approved during pregnancy.
- 20% women have episode of mood or anxiety disorder during pregnancy.
- High % relapse in women who discontinue meds with prior history of depression/bipolar.
- Useful website: MGH Center for Womens' Mental Health.

SUICIDE RISK ASSESSMENT

CDC Suicide Rates per year

- Per 100,000 people



Suicide Risk Assessment

- Protective Factors (family, friends, religion)
- Modifiable Risk Factors (depression, lack of day structure, support system, weapons)
- Static Risk Factors (head injury, age, loss)
- “Appropriate for continued outpatient care” vs “needs evaluation for higher level of care”

Suicidal Thoughts with Plan

- Suicidal thoughts plus plan: CONSTANT observation until safely in emergency room

Intermittent Suicidal Thoughts, No Current Plan, Not Committable:

- Eliminate access to firearms
- Reduce access to meds
- Increase frequency of contact
- Speak with family, supports
- If patient does not cooperate with above, refer for ER evaluation re hospitalization
- Start treatment and referral to psych immediately

Firearms

- During your annual wellness exam have a "what if" conversation with patients/family about what conditions would cause them to feel they should get rid of their weapons
  - Their own mental health
  - Mental health of family members
  - Children, grandchildren in home

Help

- National Suicide Prevention Line: 1-800-273-TALK (8255)
- Samaritans Hotline: 1-212-673-3000
- Veterans Suicide Helpline: 1-800-273-8255