

Depression Across the Lifecycle

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What Is Depression?

- A pathological alteration in mood/affect, behavior and thinking.
- The mental state changes represent a broad spectrum.
- Must take into account the individual's premorbid (baseline) temperament and personality.
- *Nothing is written in stone.*

Is It Depression, Or Is It Unhappiness?

- Acute unhappiness can look a lot like clinical depression.
- Clinical/pathological/psychiatric/major depression tends to have a life of its own.
 - Often autonomous of life events
 - *n.b.* Can be triggered and thus situational (stress diathesis model).
 - Persists despite positive events (“black cloud”, “wet blanket” states).

THE DEPRESSED CHILD

Childhood Depression

- Depression also tends to run in families.
- About 5 percent of children and adolescents in the general population suffer from depression at any given point in time.
- Children under stress, who experience loss, or who have attention, learning, conduct or anxiety disorders are at a higher risk for depression.
- Genetic and/or trauma based variables.

• [Amer Acad Child & Adol Psychiatry, 2008]

Signs & Symptoms

- Frequent sadness, tearfulness, crying spells.
- Decreased interest in activities; or inability to enjoy previously favorite activities.
- Hopelessness.
- Persistent boredom; low energy.
- Social isolation, poor communication.
- Low self esteem and guilt.
- Extreme sensitivity to rejection or failure.
- Increased irritability, anger, or hostility.
- Difficulty with relationships.

Signs & Symptoms

- Frequent complaints of physical illnesses such as headaches and stomach aches.
- Frequent absences from school or poor performance in school.
- Poor concentration.
- A major change in eating and/or sleeping patterns.
- Talk of or efforts to run away from home.
- Thoughts or expressions of suicide or self destructive behavior.

Bullying

- 29.2% of depression at age 18 could be explained by peer victimization in the UK.
- N=6719 evaluated for bullying by age 13;
1769 reported no bullying by 13:
 - 5.5% were depressed by age 18
- 1446 reported some bullying by 13:
 - 7.1% were depressed by 18
- 683 reported frequent bullying by 13:
 - 14.8% were depressed (ICD 10) at 18

Childhood Depression Treatment

- Controversial due to the 2004 FDA black box warning on suicide.
- The result:
 - Tremendous decrease in antidepressant prescribing (the bulk by pediatricians) and an increase in suicidal ideation and behavior.

Black Box Rebuttal

- Olfson, Shaffer, Marcus and Greenberg examined the trend in the number of suicides occurring from 1990 to 2000 and compared those to the number of youth prescribed antidepressants during that period.
 - This study found an inverse relationship between youth suicide and use of antidepressants noting that the increased rate of antidepressant use in children and adolescents from 1990 to 2000 was associated with a decrease in suicide rates.
 - Further, analysis indicated that SSRI use was associated with an even more notable decrease in the suicide rate in high-risk populations, older adolescents and males, and underserved populations, minorities and low income youth.

[Arch Gen Psychiatry. 2003 Oct;60(10):978-82]

What To Do?

- Weigh the risks and benefits of antidepressant therapy.
- Do not forget the critical role of individual and family therapy in treating the depressed child.
- Make the school aware.
- Don't forget the need for comprehensive medical assessment.

THE DEPRESSED TEEN

The Depressed Teen

- A period of tremendous psychological turmoil.
- A period of significant neurocellular remodeling (pruning) resulting in de novo neurocircuitry.
 - or, why the adolescent is like a puppy dog!
- How to differentiate the *sturm und drang* of adolescence from a primary biological state?
- A battle between frontal lobe and limbic circuitry.

Teen Treatment

- The challenge of recognition, lack of teen insight and getting he/she to see the doctor.
- Similar antidepressant controversies and issues as the child.
- Drug abuse is a major complicating variable.
- Parental involvement and unity is critical.
- Hormones, hormones, hormones!

THE DEPRESSED GROWN UP

Depression As Major Medical Illness

- 17-25% *lifetime U.S. prevalence* of a major depressive episode.
- Up to 15% of patients with major depressive disorder that require hospitalization *commit suicide*.
- Total annual cost to society – *\$44 billion*.
 - 55% due to lost productivity.

Kessler RC, et al. *Arch Gen Psychiatry*. 1994;51:8-19.

Depression Guideline Panel. AHCPR publication 93-0550. 1993.

Greenberg PE, et al. *J Clin Psychiatry*. 1993;54:405-418.

Stahl, S *J Clin Psychiatry*, 1993, 54 (1 supp), 33-38, 8-19

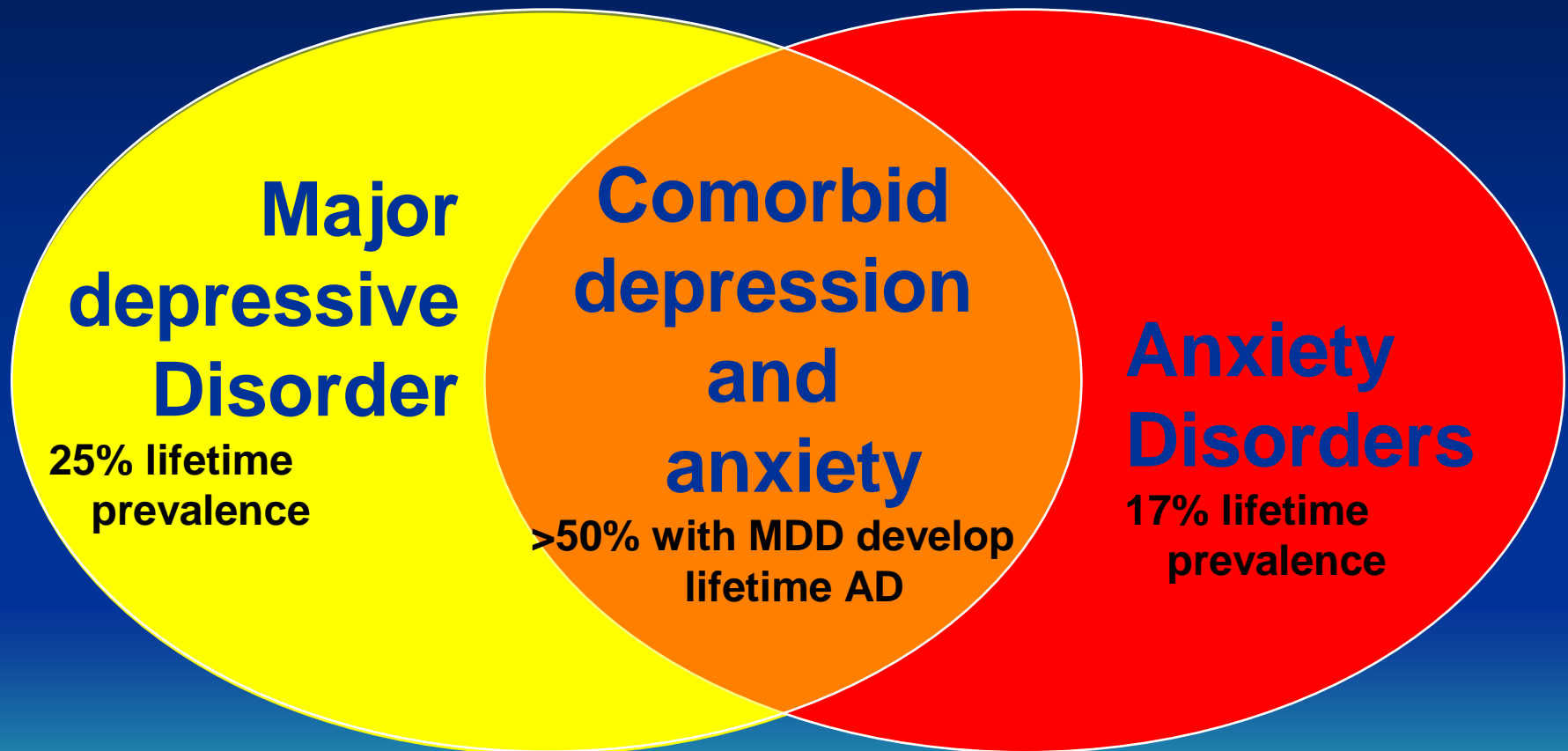
Major Depression: A Major Public Health Liability

- Leading cause of health-related disability in the US.
- 1 in 6 individuals may experience a major depressive episode per lifetime.
- The fourth greatest cause of global illness burden.

Depression As Spectrum Disorder

- *Major* depression - single, recurrent
- *Dysthymia* - early, late onset (now *persistent depressive disorder*)
- *Adjustment* (now a stress/trauma) *Disorder*
- Depression NOS (neurotic depression, now *unspecified* or *other unspecified*)
- *Bipolar* depression (mood instability disorder)
- *Mixed* depression-anxiety states
- *Subsyndromal* (subclinical) depression?
- *Secondary* depression (due to medical condition)

Depression – Anxiety Continuum



National Comorbidity Survey Replication (NCS-R)

[Kessler, R et al, JAMA, 289;2003]

- N = 9,000 adults, studied 2/01-12/02.
- 16.2% (32 million) experienced major depression at some time in their life.
- 6.6% (14 million) experienced depression within the 12 months preceding the survey.
- Depression prevalence rates highest in younger individuals.
 - women age 18-29 were 3 times as likely and those 30-44 were 1.8 times as likely as those age 60 and older to be depressed.
 - *Those living below the poverty line were 3.8 times likely to be depressed.*

NCS-R: Functional Impairment

- Of those with depression in the past year:
 - 97% reported at least some impairment,
 - 87% reported moderate impairment
 - 59% reported severe or very severe impairment
 - 19% reported very severe impairment

[Kessler,R et al, JAMA, 289;2003]

NCS-R

- 72% of those with lifetime depression and 64% of those with depression in the past year met criteria for at least one other DSM-IV disorder, most commonly an *anxiety disorder*, *impulse control disorder*, or *substance abuse disorder*.
- Depression claims an average of 16 weeks per year from people's lives on a recurring basis.
- Over a lifetime, this accounts for 10 years lost to this disorder.

[Kessler, R et al, JAMA, 289;2003]

Depression May Worsen Outcome of Many General Medical Conditions

- Depression may worsen morbidity and mortality after myocardial infarction^{1,2}
- Depression increases morbidity and mortality in patients with CHF^{3,4}
- Depression increases risk of mortality in patients in nursing homes⁵
- Depression worsens morbidity post-stroke⁶
- Depression may worsen outcomes of cancer, diabetes, AIDS, and other disorders⁷

1. Frasure-Smith N, et al. *JAMA*. 1993;270:1819-1825.

2. Penninx BW, et al. *Arch Gen Psychiatry*. 2001;58:221-227.

3. Jiang W, et al. *Arch Intern Med*. 2001;161:1849-1856.

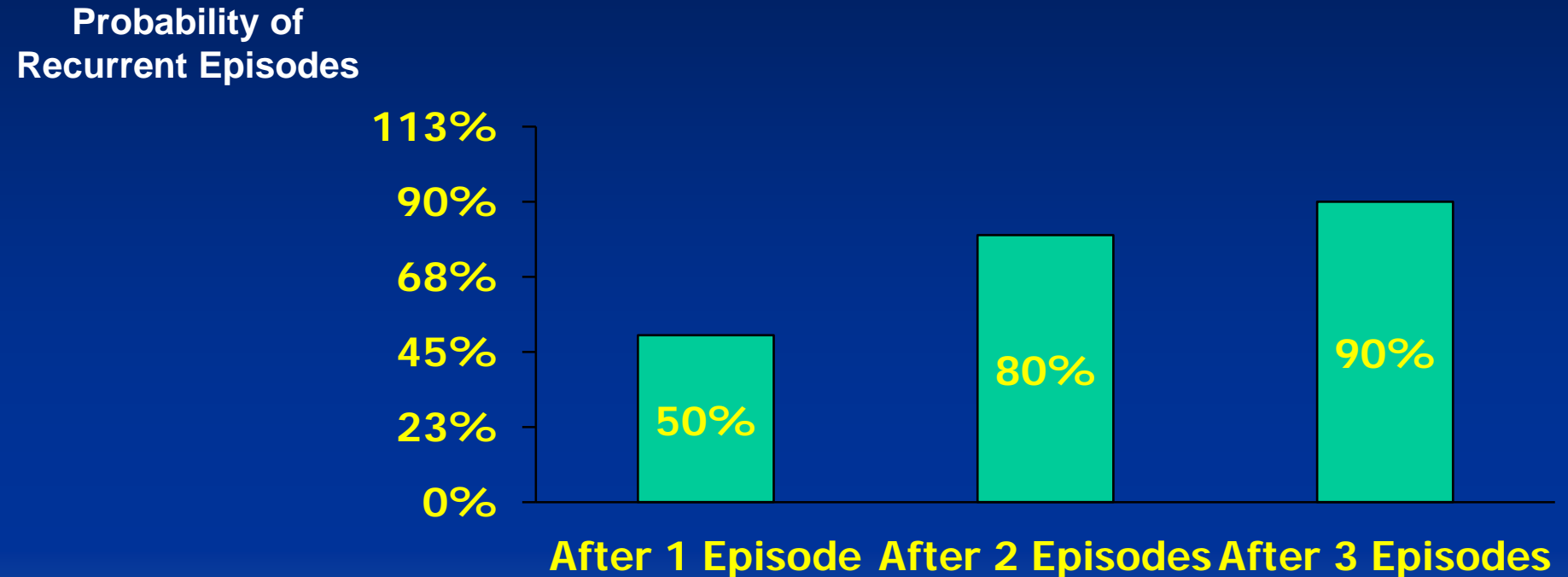
4. Vaccarino V, et al. *J Am Coll Cardiol*. 2001;38:199-205.

5. Rovner BW, et al. *JAMA*. 1991;265:993-996.

6. Pohjasvaara T, et al. *Eur J Neurol*. 2001;8:315-319.

7. Petitto JM, Evans DL. *Depress Anxiety*. 1998;8(suppl 1):80-84.

Depression Is a Chronic Illness





Major Depression — Underdiagnosis

Prevalence

- About 1/3 of people experiencing major depression do not seek treatment
- Approximately 1/3 to 1/2 of patients with depression who present in primary care do not receive a diagnosis of depression

Implications

- Increased time spent on history taking and physical examination
- Unnecessary diagnostic procedures, particularly in response to patients' vague somatic complaints

Primary Care Screening Questions

- *Over the past two weeks, have you felt down, depressed, or hopeless?*
- *Over the past two weeks, have you felt little interest or pleasure in doing things?*



Common Presenting Somatic Complaints in Patients with Depression

- Tired all the time, “blahs”
- Headache
- Malaise
- Vague abdominal or joint pains
- Back pain
- Disturbed sleep
- Sexual dysfunction or loss of sexual interest
- “Stressed out”
- GI complaints (eg, constipation, diarrhea)



Common Presenting Psychological Symptoms in Patients with Depression

- Hopelessness
- Low self-esteem
- Impaired memory
- Difficulty concentrating
- Anhedonia
- Anxiety
- Preoccupation with negative thoughts

Risk Factors for Depressive Disorder

- Family history of depressive disorders
- Prior history of depressive disorder
- Female gender
- Life stressor, eg, bereavement, chronic financial problems *[practicing medicine in South Florida]*
- Personality traits
- Death of parents or childhood abuse
- Anxiety disorders
- Neurologic disorder, eg, Parkinson's, Alzheimer's, stroke
- Primary sleep disorder

Medical Mimics

- Hypothyroidism
- B12 , folate deficiency
- Cancer
- Autoimmune disorders
- Medications
- Drugs of abuse
- Various neurological disorders

LATE LIFE DEPRESSION

Late Life Depression

- Among elderly in the community:
 - 1-2% prevalence major depression
 - 3% prevalence of dysthymia
 - 13-27% prevalence of subsyndromal depression

[Johnson, JAMA,267:1992; Judd, JClinPsy, 55s:1994]

- Among nursing home residents, up to 50% suffer from subsyndromal depression.

[Koenig, AMJGerPsy, 4s:1996]

Late Life Issues

- The senior citizen with their first lifetime episode of depression probably represents a different entity than major depression disorder.
 - Aging brain (may be harbinger for dementia)
 - Aging body systems (thyroid, immune, cardiovascular, etc.)
 - Polypharmacy
 - Psychosocial stressors

Vascular Depression: Cerebral Small Vessel Disease (CSVD)

- Longitudinal study of 1,949 dementia and depression free Icelanders >75 yo.
- MRI markers of CSVD (white matter hyperintensity volume, subcortical infarcts, micro bleeds, total brain parenchyma volume, perivascular space) measured at baseline ('02-'06) and in followup ('07-'11).
- CSVD markers were associated with higher incidence of depressive symptoms.
- CSVD located in *deep brain regions* were more strongly associated with a higher incidence of depressive symptoms.

[van Sloten, TT, et al, Am J Psychiatry, 172:6, 2015]

LLD & Dementia

- Prospective (1997-2002) cohort study of 2488 community dwelling older (mean age 74) adults free of dementia assessed repeatedly for depression.
 - Having a high and increasing depressive symptom trajectory associated with significantly increased risk of dementia.
 - The longitudinal depressive course is more accurate for dementia prediction than one-time depressive symptom assessment.

[Kaup, AR et al. JAMA Psychiatry, 2016, 73 (5), 525-530]

GENDER ISSUES

Male

- Testosterone syndromes.
- Is there a *maleopause*?
- Medication issues.
- Mid life crisis.

Female

- PMS
- Post partum states
- Premenstrual Dysphoric Disorder (PMDD)
- Perimenopause
- Menopause
- Thyroid

TREATMENT ISSUES

Treatment Goals

- Response alone is not sufficient.
- Remission is the goal.
- Prevention is the ultimate goal because of the recurrent nature of depressive illness
- Do not ignore the possibility that lack of response may represent a diagnostic failure; think bipolar disorder, medical mimic.

Treatment Trials

- How to evaluate treatment response?
- How long to treat?
- Role of talking therapy?
- Family involvement?
- Stigma?

Treatment

- ECT
- Repetitive transcranial magnetic stimulation (rTMS)
- Deep brain stimulation (DBS)
- Psychotherapy
- Attention to co-morbid issues

Antidepressants

- Tricyclic, tetracyclic
- MAOI
- SSRI
- SNRI
- Bupropion
- Mirtazapine
- OTC agents: St John's Wort, SAMe

SSRI Cardiovascular/Cerebrovascular Risks

- 5 year prospective study of 238,963 primary care (UK) patients, age 20-64 with a first diagnosis of depression between 2001-2
- MI-772, CVA/TIA-1106, arrhythmia-1452.
- SSRIs as a class are not associated with an increased risk of arrhythmia, CVA, TIA and may be associated with an decreased risk of MI (especially fluoxetine)
 - high dose citalopram not associated with arrhythmia.

[Coupland, C et al. BMJ, 2016, 352:1350]

Augmenting Agents

- T3
- Lithium
- Buspirone
- Activated folate
- Aripiprazole, Brexpiprazole
- Quetiapine
- Lurasidone
- Psychostimulants
- Full spectrum light
- Psychotherapy/CBT
- Exercise

Glutamine

- Dysregulation of glutamine neurotransmission and neuroplasticity effects may be a core component of the pathophysiology of depression.
- Ketamine's rapid antidepressant action.
- Role of N-methyl-D-aspartate (NMDA) receptor antagonism.

[Sanacora, G. JAMA Psychiatry, 2016 73(7), 651-652]

Inflammation

- Depression as an inflammatory process.
- Cytokine elevation.
- May be the tie in between life stress and depressive disorders.
- SSRI-Statin combination more effective than the antidepressant alone?

[Yan, J. Psychiatric News, July 2016; Kohler, O et al. Amer J Psychiatry, online 5/3/16]

“In times of change, the learners may inherit the earth, while the learned find themselves exquisitely prepared to inherit a world that no longer exists”

Eric Hoffer