

Depressive Disorders: General

- Egyptian, 4000 years ago (from Kay Redfield Jameson)

Lo, my name is abhorred,
Lo, more than the odour of carrion
On summer days when the sky is hot.

Lo, my name is abhorred,
Lo, more than the odour of crocodiles,
More than sitting under the bank of crocodiles.

Lo, my name is abhorred,
Lo, more than a woman
Against whom a lie is told her husband

Death is before me today
As the odour of myrrh,
As when one sitteth under the sail on a windy day.

Death is before me today
As the odour of lotus flowers,
As when one sitteth on the shore of drunkenness.

Death is before me today
As a man longs to see his house
When he has spent years in captivity

- Emily Dickinson:

I can Wade Grief
I CAN wade grief,
Whole pools of it,
I'm used to that.

I Felt a Cleavage in My Mind
I FELT a cleavage in my mind
As if my brain had split;
I tried to match it, seam by seam,
But could not make them fit.

The thought behind I strove to join
Unto the thought before,
But sequence raveled out of reach
Like balls upon a floor

- General

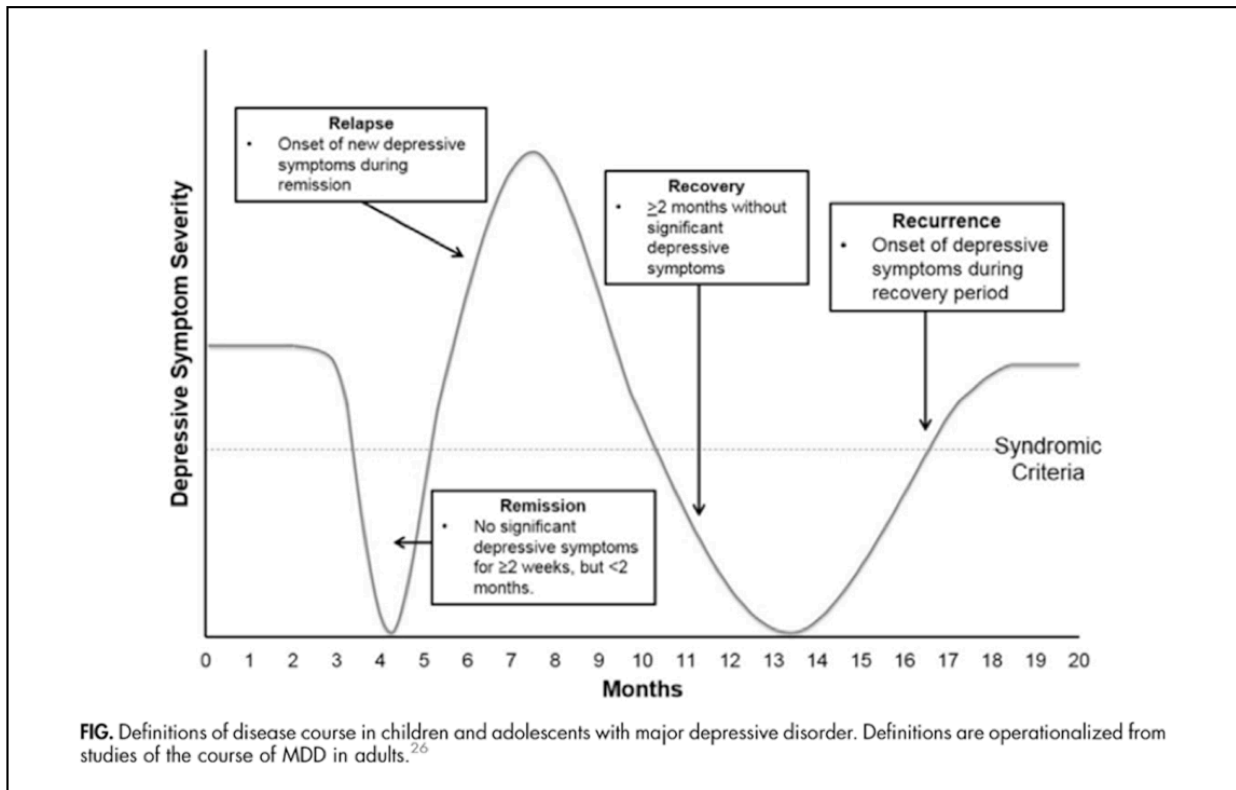
- Depression is an illness, not a choice, and is just as socially debilitating as coronary artery disease and more debilitating than diabetes mellitus or arthritis.
- More than 40 million Americans suffer from depression, about 3.5 million of whom are children and adolescents (per a 1999 US Surgeon General's report).
- There are 18 million office visits/year due to depression.
- Depression is currently the fourth major cause of disability worldwide and is estimated to become the second major cause of disability (and the leading cause in the developing world) by 2020
- It is the most disabling condition for females
- Total estimated direct and indirect costs of depression are estimated to be over \$130 billion/year
- Increased risk of cardiovascular disease/inflammatory disease
- Increased morbidity of comorbid general medical conditions and increased rate of suicide as percent of total mortality (of these medical conditions)
- Increased risk of cardiovascular events, strokes, life-shortening medical conditions
- Bi-directional comorbidity with

- Other psychiatric disorders
- Inflammation, which is associated with decreases in dopamine and glutamate
- Cardiovascular disease
- Autoimmune disorders
- Chronic pain
- Infectious disease
- Insulin resistance
- Chronic obstructive pulmonary disease
- Functional gastrointestinal disorders/irritable bowel syndrome
- Cancer
- Criteria for major depressive episode
 - Depressed mood or lack of pleasure almost all day, every day for 14 days or more
 - At least 5 of the following, during the same 14 days, representing a marked change in function:
 - Depressed mood
 - Decreased interest or pleasure most of the time
 - Insomnia or hypersomnia
 - Poor or increased appetite with 5% weight loss or gain in month
 - Psychomotor slowing or agitation
 - Fatigue
 - Decreased concentration, indecisiveness
 - Negative thinking—worthlessness, inappropriate guilt, hopelessness
 - Recurring thoughts of death or suicide
 - Not organically caused, not uncomplicated bereavement
 - Cannot be superimposed on:
 - Schizophrenia
 - Schizophreniform disorder
 - Delusional disorder
 - Diagnosis of depression should be excluded if depressive symptoms last less than 2 months after the death of a loved one (aka, the bereavement exclusion)
 - This was started in DSM-V, since it is recognized that grief can last 1-2 years and many of the symptoms overlap
 - Depending on context and symptoms, one can nonetheless experience a major depressive episode even in the context of active grief
 - Specify the following:
 - Single or recurrent episode
 - With (vs. without) melancholic features
 - Almost complete loss of pleasure in almost all activities, including previously highly desired events that would normally brighten mood
 - Three or more of the following:
 - Depressed mood characterized by profound despondency, despair, or moroseness or by “empty mood”
 - Depression typically worse in the AM
 - Morning awakening at least two hours before usual waking
 - Change in psychomotor activity (retardation or agitation)
 - Weight loss or anorexia
 - Guilt that is inappropriate or excessive
 - With (vs. without) atypical features (when mood brightens during positive events (aka mood reactivity); two or more of the following:
 - Significant weight gain or increase in appetite
 - Heavy leaden feeling in arms and legs
 - Longstanding pattern of interpersonal rejection sensitivity, not occurring exclusively during the mood disorder, that results in occupational or social impairment
 - Hypersomnia
 - With (vs. without) psychotic features, which includes catatonia, involving three or more of these features
 - Waxy flexibility, catalepsy, or stupor
 - Motor overactivity that is purposeless and not in response to external stimuli
 - Negativism or mutism
 - Peculiarities of movement (posturing, grimacing, stereotypy, and mannerisms)
 - Echolalia or echopraxia
 - With (vs. without) (high levels of) anxiety/anxious distress
 - Feeling tense or keyed up
 - Feeling unusually restless
 - Difficulty concentrating because of worry
 - Fear that something awful might happen
 - Feeling that individual might lose control of him or herself
 - With (vs. without) mixed features (hypomanic or manic symptoms), with at least three of the following

- Elevated or expansive mood
 - Inflated self-esteem or grandiosity
 - More talkative than usual or pressure to keep talking
 - Flight of ideas or subjective experience that thoughts are racing
 - Increase in energy or goal-directed activities that have a high potential for painful consequences
 - Decreased need for sleep
 - With seasonal pattern
 - With menstrual/late luteal phase pattern
 - With peripartum onset
- Overt irritability/anger present in 54.5% of cases of unipolar depression in Judd et al, 2013. The presence of this symptom is associated with
 - Increased depression severity
 - Longer duration of episode
 - Poorer impulse control
 - More chronic and severe long-term course of illness
 - Higher rates of lifetime comorbid substance abuse and anxiety disorder
 - Higher risk of antisocial personality disorder
 - Reduced life satisfaction
 - Higher rate of bipolar II disorder in relatives
- In adolescents (but see below) (Frost et al, 1999; Rao et al, 1995, 1999; Weissman et al, 1999a)
 - 3-8% affected by a depressive disorder, with a lifetime prevalence of 20% by the end of adolescence (Costello et al, 2003; Lewinsohn et al, 1998; Reinhertz et l, 1993)
 - Strong continuity between adolescent and adult depression (Frombonne et al, 2001; Harrinton et al, 1990; Weissman et al, 1999a, 1999b)
 - Often chronic, recurrent, and serious
 - Increased rate of suicide attempts and medical hospitalization (Kovacs, 1994)
 - Over 50% of depressed adolescents had a recurrence within 5 years (Birmaher et al, 1996; Lewinsohn et al, 2000)
 - Persistent boredom, lack of motivation
 - Extreme sensitivity to rejection/failure
 - Increased irritability, anger, hostility
 - Lack of social development and skills
 - Difficulty with relationships, loss of friendships, withdrawal from peers
 - Frequent physical complaints: headaches, dizziness, nausea, lightheadedness, back pain, vomiting, stomachaches, menstrual problems
 - Truancy
 - Poor school performance/poor concentration
 - Thoughts of running away
 - Obsession with suicide
 - Self-destructive behaviors, self-injury
 - High comorbidity with anxiety disorders
 - Alcohol and other drug abuse
 - Less than optimal career and marriage choices
- In pre-pubertal children (but see below)
 - 1-5% affected by a depressive disorder, with a lifetime prevalence of 20% by the end of adolescence (Costello et al, 2003; Lewinsohn et al, 1998; Reinhertz et l, 1993)
 - Continuity into adolescence (which shows strong continuity into adulthood) (Kovacs, 1994)
 - Unexcited, anhedonic
 - Withdrawn
 - Afraid to leave home
 - Irritable mood > sad mood (usually co-existing)
 - Physical complaints
 - Male predominance
 - High co-morbidity with disruptive behavior disorders (Biederman et al, 1995; Leibenluft et al, 2003) and neurodevelopmental disorders
- Differentiating major depression from ADHD in youths with ADHD
 - Symptoms suggestive of major depression separate from ADHD, in order of decreasing degree of differentiation
 - Anhedonia
 - *Not enjoying anything (anhedonia)
 - *Not happy, even when praised
 - Not having fun at school
 - Not wanting to see friends
 - Depressive/cognitive symptoms
 - **Thoughts that life is not worth living
 - **Thoughts about killing self

- **Feeling unloved
 - *Feeling that one is a bad person
 - *Thoughts that bad things will happen
 - *Feeling that nothing good will come in the future
 - *Hating self
 - *Thoughts about death/dying
 - *Thoughts that family will be better off without them
 - Feelings that does everything wrong
 - Blames self
 - Thoughts that looks ugly
- Physical/vegetative symptoms
 - **Talking more slowly
 - *Moving/walking slowly
 - Feeling like talking less
- Symptoms that do NOT differentiate between either disorder
 - Mild irritability
 - Miserable/unhappy moods
 - Sleep symptoms
 - Appetite symptoms
 - Energy levels
 - Concentration
- Preschoolers with depression have increased rates of co-morbid:
 - ADHD
 - ODD
 - Anxiety
- Major depression with atypical features
 - Diagnosis
 - Mood reactivity
 - Intensified mood reactivity/lability
 - Crashes or brightens in response to events: 74% with atypical depression vs. 72% if typical
 - Anxiety/irritability (not distinguishing factor with typical depression)
 - At least two of the following:
 - Chronic interpersonal/rejection sensitivity 83% with atypical depression vs. 54% if typical
 - Heavy, leaden feelings in arms or legs: 75% with atypical depression vs. 38% if typical
 - Increased weight or appetite: 47% increased weight and 46% increased appetite with atypical depression vs. 17% and 18% if typical
 - Hypersomnia: 44% with atypical depression vs. 21% if typical
 - Often associated with anxiety
 - Social anxiety disorder: 55% with atypical depression vs. 32% if typical
 - Panic disorder with agoraphobia: 32% with atypical depression vs. 19% if typical
 - Also seen frequently with (or associated with)
 - Seasonal affective disorder (SAD); 80% of cases of SAD are female
 - Premenstrual dysphoric disorder
 - Bipolar depression, especially rapid cycling (85% female)
 - Earlier onset of depression
 - 15-20% of depressive episodes have atypical features
 - 80% of cases are atypical depression female
 - Prevalence of 22-25% of in women vs. 11-13% in men; prevalence of all types of depression is ~30% in women and 15% in men
- Dysthymia
 - Now classified as persistent depressive disorder
 - Depressed (or irritable in teens) mood most days, more days than not, for at least 2 years (1 year in youth)
 - Can never be symptom free for more than 2 months during the period of persistent depression
 - At least two of the following:
 - Poor appetite or overeating
 - Insomnia or hypersomnia
 - Low energy or fatigue
 - Poor concentration, indecisiveness
 - Low self-esteem
 - Hopelessness
 - Major depressive episodes may precede dysthymia or occur during a period of dysthymia (at which point it's called double depression)
 - Should not be diagnosed if
 - Due directly to a substance or medication
 - Is a general medical condition
 - Is occurring during the course of a psychotic disorder

- Equals or exceeds major depression in:
 - Suicide rate
 - Loss of marriage or job due to depression
 - Overall impairment
- Prevalence in youth (Birmaher, 1996)
 - 0.6-1.7% in prepubertal children
 - 1.6-8% in teens
- Symptoms of Depression
 - Depressed mood most of the day
 - YOUTH: irritable or cranky mood, preoccupation with nihilistic song lyrics
 - Decreased interest/enjoyment in once-favorite activities
 - YOUTH: lost of interest in sports, video games, activities with friends
 - Significant weight loss/gain
 - YOUTH: failure to gain weight as normally expected, anorexia or bulimia, frequent complaints of physical illness (e.g., stomach ache, headache)
 - The presence of physical symptoms generally predicts greater severity of depression; there is a direct correlation between the degree of physical symptoms improvement and ability to achieve remission
 - Insomnia or hypersomnia
 - YOUTH:
 - Insomnia in 88% of depressed youth
 - E.g., excessive late night TV; refusal to wake for school in the morning
 - sleep-onset and sleep-maintenance insomnia in 2/3
 - terminal insomnia with early morning awakenings in 1/2
 - delayed sleep onset and decreased sleep efficiency predicts recurrence—a nearly 3-fold increased risk with delayed sleep onset
 - hypersomnia in 1/4 of depressed youth
 - Psychomotor agitation or retardation
 - YOUTH: talk of running away from home, or efforts to do so
 - Fatigue or loss of energy (70-100% of adults suffering from depression, even in the absence of depressed mood)
 - YOUTH: persistent boredom
 - Low self-esteem; feelings of guilt
 - YOUTH: oppositional and/or negative behavior
 - Decreased ability to concentrate; indecisive
 - 16% of adult subjects have a lifetime history of ADHD
 - YOUTH: poor performance in school; frequent absences
 - Recurrent suicidal ideation or behavior
 - YOUTH:
 - Looking at 6 studies from 1995-2017 (De Crescenzo et al, 2017), with 2303 participants diagnosed with mood disorder, aged 3-18 y.o., rates of suicide attempts were as follows:
 - 31.5% of those with bipolar disorder
 - 20.5% of those with major depressive disorder
 - Diurnal mood variation (mood worse in the AM) or reversed diurnal mood variation (mood worse in the PM)
 - Anxiety
 - 57.5% of individuals with depression also have an anxiety disorder (in any given year)
 - 50% of those with anxiety also suffer from depression.
 - In those with co-morbid anxiety and depression, anxiety precedes the depression 80% of the time.
 - Antecedent anxiety disorders in youth are risk factors for the subsequent onset and/or recurrence of depressive disorders.
 - Sareen, 2005: pre-existing anxiety disorder is an independent risk factor for subsequent onset of suicidal ideation and attempts
 - Sareen, 2005: co-morbid anxiety disorders increase the risk of suicide attempts in persons with mood disorders
- Patients with dysthymia
 - After 7 years, in one study, 70% recovered, 30% not recovered.
 - After > 10 years, 75% recovered, 25% not.



Hathaway, E. et al. Curr Probl Pediatr Adolesc Health Care 2018;48:31-39

- The lifetime prevalence of a major depressive episode is estimated to be:
 - 13.23-17% overall for adults (Older studies and Hasin, 2005: 13.23% lifetime and 5.28% 12-month).
 - broken down by gender in the age range 15-54:
 - 7-12% of men lifetime prevalence; 3% point prevalence
 - 21% (20-25%) of women.; 5-6% point prevalence
 - Mean age of onset 25.5 years.
 - This difference in prevalence rates exists across cultures with higher rates in London, Athens, Edinburgh, Cranberra
 - Additional 2.5% annual prevalence of dysthymia
 - 3-7% in the community
 - 5-10% of primary care patients
 - 10-15% of patients with chronic medical illness
 - 33% of hospitalized patients
 - 36% of geriatric inpatients
 - 33-47% of patients with one or more of the following: cancer, stroke, heart attack, Parkinson's disease
 - Prevalence rates in children overall: 0.4-7.8%
 - 2-5% in children
 - 8.3-15.3% in adolescents; lifetime prevalence up to 25 % by age 18
 - These rates account for approximately 2.6 million youth aged 6-17
 - Diagnoses of depressive disorders rose 2.4-fold from 1990-2001, and the rate of antidepressant use rose from 44% to 59% in that same period
 - Prevalence of dysthymic disorder (chronic, low level depression):
 - 3-6%, 0.6-1.7% in children
 - 1.6-8% in adolescents
 - 42-75% have superimposed major depression.
- High Incidence of Mood and Anxiety Disorders in Offspring of Depressed and Anxious Patients: A Prospective Cohort Study
 Petra J Havinga, Lynn Boschloo, Annelene J P Bloemen, Maaïke H Nauta, Sybolt O de Vries, Brenda W J H Penninx, Robert A Schoevers, Catharina A Hartman
Journal of Clinical Psychiatry 2016 November 22
OBJECTIVE: Early recognition of individuals at risk for depressive and anxiety disorders is key in influencing onset and course of these disorders. Parental history is a potent risk factor for the development of these disorders in offspring. However, knowledge about the magnitude of this risk is limited as large-scale longitudinal studies with a follow-up into adulthood are scarce. Those offspring at highest risk may possibly be identified by easy-to-determine parental psychiatric characteristics, family context, and offspring characteristics.
METHODS: From 2000-2002, we recruited 523 offspring (age 13-25 years) of 366 patients who had received specialized treatment for depressive and/or anxiety disorder. Offspring DSM-IV mood (major depressive disorder, dysthymia, and bipolar disorder) and anxiety

disorders (generalized anxiety disorder, social phobia, panic disorder, and agoraphobia) were assessed at baseline and at 4-, 6-, 8-, and 10-year follow-up.

RESULTS: Kaplan-Meier analysis showed that the cumulative incidence of mood and/or anxiety disorder was 38.0% at age 20 years and 64.7% at age 35 years. Parental early disorder onset (hazard ratio [HR] = 1.33; 95% CI, 1.00-1.77), having 2 affected parents (HR = 1.58; 95% CI, 1.10-2.27), and offspring female gender (HR = 2.34; 95% CI, 1.74-3.15) were independent predictors of offspring mood and/or anxiety disorder. Balanced family functioning (HR = 0.73; 95% CI, 0.56-0.96) was found to be protective against offspring risk.

CONCLUSIONS: Offspring of depressed and anxious patients are at very high risk of a mood and/or anxiety disorder themselves.

Parental early onset, having 2 affected parents, female gender, and family functioning are important additional markers that can be used in clinical practice to identify those offspring at greatest risk.

- Obtaining/access to mental health treatment for depression
 - Only 50% of those with depression ever receive any treatment
 - It is estimated that only 1 in 10 people with depression receives appropriate treatment.
 - Fewer than 10% of individuals with depression have ever seen a psychiatrist
 - 10-20% of individuals with depression state that they do not want an antidepressant
 - Approximately 1 in 5 patients with depression do not fill their first antidepressant prescription
 - Only half of patients who fill their first prescription continue to take the medication after 5-6 months
- Solomon and colleagues demonstrated that
 - 92% of clients with depression remain symptomatic 1 month after treatment begins
 - 63% 3 months after treatment begins
 - 42% 6 months after treatment begins
 - 30% after one year
 - 12% after 2 years
 - 33% of clients with depression have episodes that last more than two years duration
 - 27% of patients never had an asymptomatic week during a 12-year follow-up in one study.
- Peak age of onset 20-40 years.
- Recurrence/relapse
 - Depression tends to be an episodic, recurrent illness
 - Clients experiencing
 - one major depressive episode have a 50% chance of experiencing another
 - 10% chance in the first 12 weeks since recovery
 - after 2 episodes, the chance of a third is 70-90%
 - 10% chance in the first 12 weeks since recovery
 - after 3 or more episodes, the chance of future episodes rises to >90%
 - 45% chance in the first 12 weeks since recovery
 - Identifying and treating the episodes early and intensively may reduce the risk of future episodes
 - Clients with residual symptoms are three times more likely to relapse
 - Treating to full remission (e.g., stably good mood, normal energy, sleep, concentration, etc) is critical to obtaining and maintaining full functioning
- Youth (Costello and Maughn, 2015)
 - Recovery in half of all youth cases
 - 50% with poor adult functioning
 - Family systems issues increase recurrence risk
 - Comorbidities increase recurrence risk
 - Protective factors
 - Positive emotional style
 - Family bonding
 - Good parent/child relationships
- 23 year follow-up (2005) confirms that individuals who achieve and maintain remission from depression have long-term health outcomes comparable to those of nondepressed individuals
- Keller, 1998, relapse rates among patients who received continuation treatments for placebo
 - Celexa, 24 wks 11% vs. 31% placebo
 - Prozac, 52 wks 26% vs. 57% placebo
 - Remeron, 30 wks 4% vs. 28% placebo
 - Serzone, 36 wks 17% vs. 33% placebo
 - Paxil, 52 wks 16% vs. 43% placebo
 - Zoloft, 44 wks 13% vs. 46% placebo
- Children
 - Relapse (during remission—2 wks-2 months from well point): 50%
 - Recurrence: 50% by 1-2 years, 70% by 5 years
 - Protracted, chronic course in 10%
 - Childhood onset depression has a 60-70% risk of recurrence in adulthood
- Long-term outcome of adolescent depression (Melvin et al, 2013); over 3-9 years after episode (average 6 years)
 - 93% full remission (which means 7% don't fully remit an average of 6 years later)
 - 53% recurrence of depressive disorder

- 79% develop non-mood disorder (e.g., anxiety, eating disorder, substance use disorder)
 - 15% had no subsequent depressive episode or other non-mood disorder
- Major depression in youth is associated with cortical gray matter volume loss and thinning (Luby et al, 2016)
- Clinical factors associated with treatment-resistance in major depressive disorder from the Group for the Study of Resistant Depression, based on 702 patients with major depression, 356 of which were resistant to treatment:
 - Panic disorder co-morbidity increases risk 3.2-fold
 - Anxiety (in general) co-morbidity increases risk 2.6-fold
 - Suicidality risk increases risk 2.2-fold
 - Social anxiety disorder co-morbidity increases risk 2.1-fold
 - Early age of onset increases risk 2-fold
 - Severity (high degree) increases risk 1.7-fold
 - Personality disorder co-morbidity increases risk 1.7-fold
 - More than one hospitalization increases risk 1.6-fold
 - Nonresponse to first antidepressant received lifetime increases risk 1.6-fold
 - Recurrent episodes increase risk 1.5-fold
 - Melancholia (as one subtype of major depression) increases risk 1.5-fold
- Clinical factors associated with treatment resistance in youth (Weissman et al, 2015; Lewinsohn et al, 1995)
 - Parental depression
 - Child abuse
 - Bullying
 - Substance abuse
- Seasonal affective disorder (SAD)
 - Prevalence increases as move from the equator (e.g., 1.5% in Florida) towards the poles (e.g., 9% in New Hampshire)
 - *Winter Blues*, Norman Rosenthal, MD
 - Winter nadir in serotonin levels
 - Reduced serotonin transporter in thalamus and hypothalamus and dopamine transporter in striatum in SAD
 - Abnormal behavioral effects of serotonin agonist mCPP which normalize after light treatment and in summer
 - Depletion of tryptophan (which is a building block of serotonin) reverses the therapeutic effect of light treatment in SAD
 - Depletion of brain catecholamines (e.g., norepinephrine and dopamine) reverses therapeutic effect of light treatment in SAD
 - May be related to abnormal retinal response to light
 - Melatonin more effective than placebo in augmenting light therapy in SAD.
 - Light therapy
 - Morning light treatment more effective than evening light treatment (which is more effective than no treatment)
 - Fluorescent light box, 10,000 lux white light, no ultraviolet wavelengths
 - 30 minutes daily
 - 1-3 weeks minimum for response
 - Side effects: headache, wired feeling, eyestrain, nausea, dizziness, hypomania
 - No evidence of toxicity or eye damage
 - Begin 1-2 weeks prior to usual onset of SAD; treat for the duration of the season
 - For more info: www.UBCsad.ca; www.SLTBR.org; www.CET.org.
- Premenstrual dysphoric disorder
 - Diagnosis:
 - One plus of:
 - Mood lability
 - Irritability/anger (76% of those with PMDD experience worse anger)
 - Depressed mood, hopelessness
 - Anxiety/tension
 - Some of these (to total 5 including above)
 - Decreased interest
 - Subjective concentration impairment
 - Lethargy, reduced energy
 - Change in appetite
 - Sleep disturbance
 - Feeling overwhelmed
 - Physical symptoms
 - During last week of luteal phase (leading into period) (usually the 7-10 days prior to one's period)
 - Begins to remit within a few days after onset of follicular phase
 - Minimal or absent in the week after menses
 - Happens in most menstrual cycles
 - Confirmed by prospective symptom ratings across at least two cycles
 - Causes marked distress and/or interferes with functioning
 - Prevalence estimates for 12 months suggest 1.8-5.8% of women are affected by this disorder
- Treatment
 - Aerobic exercise
 - CBT
 - SSRI's

- Yaz
- Vitex agnus castus extract (VACE)
 - Aka chaste tree berry
 - Equal in efficacy to Prozac, but Prozac better for mood
 - Superior to placebo
 - Side effects (affect less than 2%)
 - Nausea
 - Rash
 - Fatigue
 - Headache
 - Dry mouth
 - Tachycardia
 - Agitation
 - Menstrual changes
 - Acne
 - One case of multiple follicular development
 - Calcium 1200 mg/day
- Children and adolescents:
 - Average age of onset in children
 - 11.6 yo (10 years ago)
 - 9.9 yo (for children born 1973-1975)
 - Course of childhood depression:
 - Average duration 9 months
 - 90% remission by two years
 - Relapse rates
 - as high as 50%
 - 40% recur in two years
 - 70% in five years
 - 2013 study
 - 93% full remission
 - 53% recurrence of depressive disorder
 - 79% develop non-mood disorder (e.g., anxiety, substance use, eating disorder)
 - 15% had no subsequent depressive episode or non-mood disorder
 - 6-10% have a chronic course
 - Suicidality in adolescents with depression (2015 study)
 - 27.3% have suicidal thoughts
 - 9.6% have plan for suicide
 - 10.8% attempt suicide
 - **Meta-analysis by Bridge et al, 2017**
 - Antidepressants with response rate of 61%
 - Placebo with response rate of 50% (!)
 - **Keep in mind, it's impossible NOT to provide basic psychosocial engagement and services/support for kids in studies, so placebo rate is naturally higher than in adult studies**
 - **FDA-approved meds as of 5/6/2018**
 - Prozac in 8-17 yo, based on 3 trials
 - Lexapro in 12-17 yo, based on 1 trial
 - **Childhood depression increases the risk for future mood disorders by up to 70%.**
 - **Depression in childhood can result in social dysfunction and academic underachievement.**
 - **Depression in childhood is co-morbid with other psychiatric disorders 40-70% of the time:**
 - **Anxiety disorders 40-90%**
 - **Dysthymia 30-80%**
 - **Disruptive behavior disorders 10-80%**
 - **Personality disorders 60%**
 - **Substance abuse 20-30%**
 - **Suicidal behavior in adolescents (from NCS survey of 6,483 adolescents)**
 - **Suicidal ideation 12.1%**
 - **Suicide plans 4%**
 - **Suicide attempts 4%**
 - **Suicidal behavior in depressed adolescents (Nock, et al, 2013)**
 - **Suicidal ideation 56.8%**
 - **Suicide plans 69.7%**
 - **Suicide attempts 75.7%**
 - 13% of children with major depression with psychotic features may go on to experience a mania (and thus meet criteria for bipolar disorder); treatment of the depression with antidepressants decreased the risk fourfold, although this is controversial. Antidepressants can precipitate mania.

- **Maternal and paternal depression increases the risk of mood, anxiety and behavior problems in children. Children of currently depressed mothers:**
 - 34% with current psychiatric diagnosis, 45% with lifetime diagnosis
 - 22% with disruptive behavior disorder
 - 16% with anxiety disorder
 - 10% with depressive disorder
 - Maternal atypical depression associated with 3-fold increased risk of depressive or of anxiety disorder
 - History of maternal suicide attempts associated with 3-fold increased risk of depressive disorder
 - Presence of maternal panic disorder with agoraphobia associated with 8-fold increased risk of depressive disorder
 - More likely to develop depression in response to family strife
- 20-40% eventually are diagnosed with bipolar disorder
- **If treatment resistant, consider**
 - **Parental depression/strife**
 - **Child abuse**
 - **Ongoing bullying; ask “how much are you getting bullied?” vs. “are you getting bullied?”**
 - **Substance abuse**
 - **Other psychiatric diagnosis (e.g., ADHD, bipolar disorder)**
 - **Other learning/neuropsychological diagnosis**
 - **Medical issues**
 - **Genetic issues of metabolism, etc**
 - **Adherence**
 - **Absence of therapy**
 - **True treatment resistance (see below)**
- Treatment resistant pediatric depression algorithm
 - Start with SSRI (response rates ~60%)
 - Prozac
 - Lexapro
 - (Zoloft)
 - If no response to maximal dose at 8 wks minimum, try alternate SSRI (response rates ~50%)
 - Prozac
 - Lexapro
 - Zoloft
 - Celexa
 - If response to alternate SSRI is...
 - Partial
 - Augment with
 - Abilify
 - Lithium
 - Wellbutrin
 - No response
 - Change to different class
 - Wellbutrin
 - Effexor
 - Cymbalta
 - If response to different class antidepressant is...
 - Partial
 - Augment with
 - Abilify
 - Lithium
 - No response to maximum dose at 8 wks minimum, try newer antidepressant
 - Pristiq
 - Viibryd
 - Levomilnacipram
 - Addition of CBT (increases response rate by 10%)
 - 2005
 - Atypical antipsychotic
 - Case series of 10 adolescents
 - 70% responded to augmentation with Seroquel
 - Antidepressants
 - Wellbutrin XL
 - Remeron
 - Mood stabilizer
 - Lithium
- Texas Medication Algorithm for pediatric depression
 - SSRI monotherapy

- If fails, switch to alternate SSRI
 - Prozac
 - Zoloft
 - Celexa
 - Lexapro
 - Paxil (adolescent only)
- If fails, SSRI + augmentation
- If fails, switch to alternate antidepressant

- Dimensional conceptualizations

- Major depression, unipolar
- Major depression with or alternating with
 - Dysthymia: double depression
 - Cyclothymic temperament: bipolar II-b mixed state; typically non-psychotic
 - Irritability, anxiety, agitation, mood/energy/sleep/focus swings common
 - Cyclothymic disorder, and atypical depressive features: bipolar IV disorder subtype or pseudo-unipolar depression
 - Irritability, anxiety, agitation, mood/energy/sleep/focus swings common
 - 50-70% of patients with borderline personality disorder meet criteria for bipolar spectrum disorders
 - Hyperthymic temperament: bipolar IV disorder subtype or hyperthymic depression or excited depression or pseudo-unipolar depression
 - Irritability, anxiety, agitation common
 - often males in their 50's whose life-long drive, ambition, high energy, confidence, and extroverted interpersonal skills helped them advance in life, to achieve success in a variety of business domains and/or political life
- Medication-induced mixed states: bipolar III-b mixed states
 - Consists of hyperthymia, hypomania, mania, or depression caused by medication
 - Suggests vulnerability to and high risk of bipolar disorder or cyclothymia
 - increasingly seen following the overzealous treatment of psychomotor retarded, seemingly unipolar depressions arising from a stable hyperthymic temperamental background without hypomanic episodes
 - Common features
 - Family history of bipolar disorder
 - Habitual short sleep—less than six hours per day
 - Cheerful, optimistic personality style
 - Extraverted and sociable
 - Tendency to become irritable easily
 - Unrelenting sadness and irascibility
 - Recurrent depressions
 - Agitation against a background of psychomotor retardation
 - Extreme fatigue with racing thoughts
 - Panic
 - Insomnia

- Suicidal obsessions and impulses
 - Unendurable sexual excitement
 - Histrionic countenance with genuine expressions of intense suffering
 - Abuse of stimulants and alcohol
- Hypomania(s): bipolar II disorder
- Hypomania and underlying cyclothymia: bipolar II-1/2 disorder
 - Consists of periods of
 - Bipolar depression or double depression
 - Cyclothymic/bipolar dysthymia
 - Cyclothymia/bipolar hyperthymia
 - Bipolar hypomania
 - Euthymia
- Protracted hypomania: bipolar I-1/2 disorder
- Mania(s): bipolar I disorder
 - Consists of periods of
 - Bipolar depression or double depression
 - Cyclothymic or bipolar dysthymia
 - Cyclothymic or bipolar hyperthymia
 - Bipolar hypomania
 - Bipolar mania
 - Euthymia
- Dysthymia temperament/dysthymia: unipolar, cyclothymic or bipolar dysthymia
 - Overlaps with dysphoria from borderline personality disorder
- Euthymia: “Normal” range
 - Extraversion, introversion; pessimism, optimism; exuberance, stoicism
- Hyperthymic temperament/hyperthymia
 - Borderland between extraversion and hypomania.
 - Creativity common and heritable in familial bipolar disorder (and to a lesser extent in ADHD).
 - Common in bipolar disorder, men > women
 - Associated with more frequent manic switches
 - Irritable temperament could be variation of hyperthymia
 - common in bipolar disorder
 - associated with higher risk of psychotic features
 - associated with higher frequency of manic episode at the start of the illness.
- Cyclothymic temperament/cyclothymia
 - Borderland between normal mood swings and bipolar disorder
 - Consists of periods of
 - Hyperthymia
 - Dysthymia
 - Euthymia
 - Common in bipolar disorder
 - Associated with higher co-morbidity
 - Overlaps with intermittent explosive disorder (highly co-morbid with mood, anxiety and substance use disorders)
- Mania, unipolar/hypomania unipolar
 - Consists of periods of
 - Hypomania and/or mania
 - Euthymia
- Bipolar 1/2 disorder
 - AKA schizobipolar disorder; similar to schizoaffective disorder, bipolar type.

○ [A systematic review and meta-analysis of prospective transition from major depression to bipolar disorder](#)

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OBJECTIVE: Some people with major depressive disorder (MDD) may be at a pre-onset stage for bipolar disorder (BD), where early identification or prevention efforts may be feasible. We aimed to identify rates and characteristics predictive of transition to BD in prospective follow-up studies of people with MDD.

METHODS: Using a systematic search strategy, we identified studies with a diagnostic ascertainment of MDD and BD of an adequate standard, and where the minimum length of follow-up was 6 months. We examined the incidence and point prevalence of BD and the pooled odds ratios (OR) for baseline predictors.

RESULTS: From 5554 unique publications, 56 were included. Nearly a quarter of adults (22.5%) and adolescents with MDD followed up for a mean length of 12-18 years developed BD, with the greatest risk of transition being in the first 5 years. The meta-analysis identified that transition from MDD to BD was predicted by family history of BD (OR = 2.89, 95% CI: 2.01-4.14, N = 7), earlier age of onset of depression ($g = -0.33$, SE = 0.05, N = 6) and presence of psychotic symptoms (OR = 4.76, 95% CI: 1.79-12.66, N = 5).

CONCLUSIONS: Participants with the identified risk factors merit closer observation and may benefit from prevention efforts, especially if outcomes broader than BD are considered.

- Gender
 - Epidemiology/prevalence
 - Depression/dysthymia: 30% vs. 16% in men
 - 52.7% of women with depression have 1 or more co-morbid psychiatric disorders
 - Two-fold increased risk of depression in females seen across all cultures
 - Among women with depression,
 - More than half will have suicidal thoughts
 - ~25% will attempt suicide
 - Exposure to child physical abuse is one of the most significant risk factors for suicidal ideation
 - Women with a history of child sexual abuse are 2-4X more likely to attempt suicide
 - Women with a history of child physical or sexual abuse 3-4X more likely to suffer from depression
 - Presence of one or more co-morbid conditions is most predictive of suicide attempts
 - More likely to have “atypical” depression or seasonal affective disorder
 - Less likely to respond to endogenous opioids
 - Greater heritability in women (42% vs. 29% in men)
 - Women are 3 times more likely to attempt suicide.
 - Estrogen-induced depression (from OCP)
 - Estrogen may cause low vitamin B6 activity
 - Low B6 affects neurotransmitter activity
 - Treatment is vitamin B6 25-50 mg twice-a-day
 - Three-fold increased risk of anxiety in women; this may be 50% of increased risk of depression in women
 - Phobia: 16% vs. 5% in men
 - Social phobia: 15% vs. 12% in men
 - Panic disorder with or without agoraphobia: 12% vs. 5% in men
 - PTSD: 10% vs. 5% in men
 - Agoraphobia without panic: 6-7% vs. 2-3% in men
 - Generalized anxiety disorder: 5% vs. 2-3% in men
 - Obsessive compulsive disorder (narrowly defined): 2% vs. 1% in men
 - Rate of childhood sexual abuse is ~13% of women and 4% of men
 - Pregnancy/Breastfeeding (see separate packet for more updated information)
 - Depression during pregnancy
 - 14-23% of pregnant women are depressed
 - 7.4% in first trimester
 - 12.8% in second trimester
 - 12% in third trimester
 - Often co-morbid with 1 or more of the following
 - Anxiety disorders
 - Eating disorders
 - Substance disorders
 - Personality disorders
 - Roughly 7% of all American women experience episodes of major depression during their first pregnancy
 - Cohen et al 2004, 2004, 2006, depressed women who continued vs discontinued maintenance treatment of depression before or during their pregnancy (201 patients):
 - Relapse rates in women who continued treatment: 26%
 - Relapse rates in women who discontinued treatment: 68%
 - Throughout pregnancy, rates of depression are the same or higher than in women when they are not pregnant
 - Pregnant women with depression have higher levels of cortisol and adrenocorticotrophic hormone levels (stress hormones)
 - Risks of untreated depression in pregnancy
 - Poor prenatal care
 - Risk of medical/obstetric complications (e.g., hyperemesis gravidarum, pre-eclampsia)
 - Self-medication/substance abuse
 - Impaired bonding
 - Postpartum exacerbation
 - Risks of untreated depression to developing fetus/infant
 - Increased risk of preterm labor and birth/earlier gestational age
 - Increased risk of low birth weight/reduced infant growth
 - Relative right frontal EEG asymmetry
 - Altered fetal neurobehavioral function
 - Poorer quality of movement
 - Increased hypotonia
 - Elevated fetal stress hormones
 - Infant
 - Increased fussiness/crying, more inconsolable
 - Decreased time awake and alert
 - Poor growth
 - More infections

- More difficult temperament—more distress, sadness, fear, shyness, frustration
 - Poorer health-related quality of life
 - Higher rates of depression (via stress/stress hormone effects on hypothalamic-pituitary-adrenal axis?)
 - Behavioral, emotional, and social difficulties in children, potentially via adverse effects on the developing fetal brain
 - Long term cognitive effects
- Omega-3 fatty acids (up to 2.8 g/day) may boost mood in pregnant women.
- Post-partum blues:
 - 50-70% of women experience this transient condition within 10-14 days of childbirth.
 - This is not considered pathologic.
- Post-partum depression (PPD):
 - Defined as occurring within 12 months of childbirth
 - 13% of pregnant women (and 20% of pregnant adolescents) will experience a post-partum depression
 - Usually by 6 weeks postpartum
 - Postpartum depression is serious and disabling
 - Potentially damaging to the mother-child attachment.
 - Risk of post-partum depression is very high (25-60%) when a client has a history of a prior post-partum depression
 - Restarting antidepressant treatment at the end of the third trimester or in the first 24-48 hours post-partum reduces relapse by 90%
 - bipolar spectrum
 - Elsewhere: 13.87% of women with PPD in the first 30 days post-partum go on to develop bipolar disorder (so that prior depression is relabeled as bipolar disorder) within 15 years
 - 4.69% of women with PPD in the 31-365 days post-partum go on to develop bipolar disorder (vs. 4.04% outside of pregnancy/post-partum (past 365 days)
 - Women with bipolar I or II disorder have a 25-40% risk of developing mood symptoms in the postpartum period
 - In post-partum exacerbation of bipolar disorder, there is a risk of psychotic symptoms:
 - Usually considered a bipolar spectrum illness, rather than a primary psychotic disorder
 - Non-affective psychotic cases occur in less than 10% of cases
 - 50-80% have episode(s) outside the perinatal period, usually in the bipolar spectrum context
 - Rule out
 - Eclampsia
 - Delirium
 - Thyroid disorder
 - Infections
 - 1-2/1000 deliveries have postpartum psychosis
 - more common in first time moms
 - relative risk for 1st onset is 23X higher within 4 weeks after delivery
 - usually occurs within 2 weeks of delivery
 - mean duration of illness is 40 days
 - if one has a prior history of bipolar disorder (prior to pregnancy), risk of psychosis is 100 times higher
 - symptoms include
 - insomnia
 - mood fluctuations
 - obsessive concerns regarding newborn
 - severe mood symptoms (manic, depressive, or mixed symptoms)
 - delusions
 - hallucinations
 - disorganized behavior, confusion, perplexity
 - women with a history of postpartum psychosis have a risk of recurrence between 30-50%
 - this is a psychiatric emergency
 - ESPECIALLY if delusion is one in which the parent believes the baby has been replaced
- Suicide
 - Leading cause of maternal deaths in pregnancy and postpartum
 - Rate (3/100,000) is similar to rate in in general female population (3.4/100,000)
- Infanticide
 - Maternal infanticide is rare, but not well reported
 - Estimated rate is 8 per 100,000 live births
 - Most cases associated with postpartum mental illness
 - Among women admitted for postpartum psychosis
 - Infant mortality 3%
 - Most infant deaths preceded admission
- Post-partum obsessional thoughts/OCD
 - Obsessional thoughts or images
 - Ego-dystonic (which means highly uncomfortable/unwanted)
 - Distressing
- Maternal depression negatively correlates with infant growth Pregnancy
 - The baseline rate of significant infant malformations is 2-4% in the absence of psychiatric medication treatment.
 - SSRI's and pregnancy
 - Fetal serum levels of antidepressants may approach 50% of the maternal levels
 - Louik et al, 2007, case control study with 9,849 infants with congenital malformations and 5,860 infants without congenital malformations:
 - No association found between SSRIs overall exposure and
 - Craniosynostosis

- Omphalocele
 - Overall congenital heart anomalies
- Specific agents
 - Zoloft was associated with
 - 5.7-fold increased risk of omphalocele
 - 2-fold increased risk of septal defects
 - Anal atresia
 - Limb-reduction defects
 - Paxil was associated with
 - 3.3-fold increased risk of right ventricular outflow tract obstruction defects
 - Neural tube defects
 - Club foot
 - Undescended testes
 - Non-SSRI antidepressants were associated with anal atresia
- Alwan et al, 2007, case-control study looking at 9,622 with birth defects vs. 4,092 without birth defects
 - SSRI was found to be associated with a 2.4-fold to 2.8-fold increased risk of
 - Anencephaly
 - Craniosynostosis
 - Omphalocele
 - None of the individual SSRIs were associated with overall risk of birth defects or combined totals of cardiac or non-cardiac defects
 - Paxil and Celexa were each associated with the combined group of anencephaly, craniosynostosis, and omphalocele
- Meta-analysis, Rahimiet al, 2006, 9 studies looking at Celexa, Prozac, Paxil, Zoloft vs. general population:
 - No association with increased risk of major malformations
 - No association with cardiovascular malformations
 - No association with minor malformations
 - However, increased risk of spontaneous abortions (but is this related to depression or treatment?)
- King et al, 2006; looking prospectively at 19,691 cases
 - In general population the risk of major congenital malformation is 3-4%
 - In exposed cases the risk is 2.6%
- There may be an association between SSRI use in pregnancy and
 - premature delivery
 - low birth weight (e.g. 2002: Prozac associated with somewhat increased risk of low-birthweight baby)
 - low Apgar scores at 15 minutes
 - lower prolactin cord-blood levels (associated with respiratory distress)
 - higher serotonin-related symptoms scores at 4 days (in Prozac but not Celexa in one study)
 - respiratory functions (in women taking SSRI's after 29 weeks (not before))
 - ?pulmonary vasoconstriction
 - Respiratory distress
 - Oberlander et al, 2006: gestational age, birth weight, feeding difficulties, convulsions, and jaundice all happened in the same proportions in depressed women whether or not they were being treated with antidepressants; HOWEVER, respiratory distress WAS associated with SSRI use
 - mild motoric difference
 - post-natal bleeding/neonatal bleeding
 - post-natal neonatal hypertension
 - SSRI discontinuation syndrome in infants
 - Levinson-Castiel et al, 2006: 30% of infants exposed to SSRIs (18 of 60 such infants in this study) had evidence of the syndrome; Paxil was associated with 6 of the 18 cases.
 - **11/05: Celexa (20-40 mg/day) associated with 228 adverse events since 1998, 120 of which involved developmental events, 38 of which occurred during peri- or post-natal period, 31 of which in early neonatal period (first week of life), 18 of which involved neonatal withdrawal: jitteriness, rigidity, tremor**
 - In a study of 93 cases withdrawal due to SSRI exposure, 64 associated with Paxil, 14 with Prozac, 9 with Zoloft, 7 with Celexa.
- Malm et al, 2005; SSRI's purchased (by pregnant women) in the 3rd trimester associated with
 - Increased rates of admission to special units or ICU's (15.7%; 11.2% if exposed in first trimester)
 - Not associated with
 - Increased rate of preterm
 - Small for gestational age
 - Low birth weights
 - Perinatal death
 - Need for C-Section
 - Malformations
- 2005: self-resolving thalamic cysts in 6 SSRI-exposed infants
- Chambers et al, 1996: Prozac during pregnancy
 - Not associated with major structural anomalies
 - Not associated with pregnancy loss
 - Was associated with
 - increased rates of prematurity
 - admission to special-care nurseries
 - Poor neonatal adaptation

- Decreased weight
 - Decreased size
 - Minor structural anomalies (three or more)
 - HOWEVER, it is difficult to tease apart the risk on pregnancy outcome due to depression from the risk due to the treatment of depression.
- There is no association between Prozac or TCA use in pregnancy (in 135 children) with mental development.
- Maternal psychiatric history, prenatal SSRI use and the association with infant temperament
 - Reddy et al, 2006: 302 parent-infant pairs, 11/302 mothers took SSRIs during pregnancy, 13/302 had a history of serious psychiatric illness
 - Women with psychiatric illness who took SSRIs during pregnancy had infants with less fear behavior than those with psychiatric illness who did not take SSRIs during pregnancy
- Congenital anomalies
 - Studies demonstrating lack of increased risk:
 - 12/05 (Malm, 2005): 1782 pregnancies in Finland
 - First trimester SSRI use
 - major malformations were not associated with first trimester SSRI use (in the 1398 women who were prescribed SSRI's in the first trimester)
 - 11.2% of infants of moms with first trimester SSRI use were treated in special or intensive care units
 - Third trimester use:
 - 15.7% of infants of moms with third trimester SSRI use were treated in special or intensive care units
 - No increased risk of preterm birth, birth 32 weeks of gestation or less, small for gestational age, or low birth weight in women with second or third term SSRI use compared to women with only first trimester use.
 - In studies through 2004:
 - tricyclic antidepressants and Prozac do not appear to increase risk for congenital malformations.
 - there has not appeared to be an association between use of SSRI's in pregnancy and major congenital malformations or clear behavioral sequelae, including over 2000 women on Prozac in a national data-base.
 - Newport, 2004: 2219 reports of SSRI use in pregnancy; no association with congenital anomalies.
 - Kalra, 2005: review assessed more than 1700 pregnancies described in literature: Prozac was not associated with elevated risk of major congenital malformations, with other adverse pregnancy outcomes, or with long-term developmental delays.
 - **Studies demonstrating increased risk:**
 - **12/05: first trimester Paxil use may be associated with 1.5-2% risk of cardiac defect (vs. 1% in general population) and 1.8-fold increased risk in congenital malformations overall.**
 - **9/05: first trimester Paxil use may be associated with 4% incidence of birth defects (including ventricular septal defects) versus 2% in those taking other antidepressants.**
 - **8/05 analysis of new data at Teratology Society meeting:**
 - **5,357 SSRI-exposed (22% Paxil) infants (exposure b/w 1 mo prior and 3 mo after conception)**
 - **3,366 non-exposed infants**
 - **SSRI use associated with:**
 - **3.3-fold increased risk of omphalocele (highest with Paxil--increased risk is 6.4-fold)**
 - **6.3-fold increase in risk of tetralogy of Fallot**
 - **no other major congenital malformations.**
 - The baseline rate of omphalocele is 2.5/10,000 in one study, 30/10,000 in another (so that the increased risk from SSRI exposure is 7-90/10,000 overall (and 15-180/10,000 from Paxil exposure).
 - The risk(s) of fetal exposure to SSRIs must be balanced with the risk of relapse upon stopping medication during pregnancy or upon birth; post-partum depression and anxiety may negatively affect attachment
 - Misri et al, 2006: 4 yo children exposed to psychotropic medications in utero do not exhibit internalizing (e.g., anxiety) symptoms; maternal depression is associated with internalizing symptoms.
 - Animal evidence suggests Wellbutrin safe in pregnancy
 - Fetal serum levels of anticonvulsants are around 50-80% of the maternal dose
 - Lamictal, Topamax, and Neurontin have little evidence.
 - First generation antipsychotic medications appear to be safe in pregnancy
 - Second generation antipsychotic medications do not have evidence
 - More information on effects of medications on the fetus
 - California Teratogen Information Service: 800-532-3749
 - Organization of Teratology Information Services—www.otispregnancy.org
 - Illinois Teratogen Information Service—www.fetal-exposure.org
- Breast feeding
 - Overall
 - less than 1% of maternal dose of antidepressants is present in breast milk
 - levels in infants who are breastfed by mom's taking antidepressants often have undetectable levels.
 - a recent study looked at 22 breast feeding women on Celexa (9 women), Zoloft (5 women), Paxil (4 women), Prozac (1 woman), and Effexor (3 women) and found very low infant serum concentrations for all medications.
 - Another study (AJP, 6/04) confirmed low levels of Zoloft, Paxil and Nortriptyline in breast milk and nursing infants.
 - Zoloft
 - does not appear to be passed into the breast milk

- maximum daily infant dose in one study 0.026-0.044 mg/kg
- nursing infants exposed to Zoloft in breast milk: no problems on growth charts, number of illnesses, milestones; no adverse effects
- Prozac is passed into the breast milk but at low levels
- Paxil may be passed into the breast milk at high levels and is more associated with discontinuation syndrome when tapered in pregnancy or after delivery (in the newborn) than other SSRIs

Information on Suicide

- General
 - National trends in suicide attempts from 2004→ 2013 (%)
 - Total 0.62→0.79
 - Men 0.52→0.64
 - Women 0.72→0.92
 - 21-34 yo 1.02→1.48
 - White 0.6→0.81
 - HS Educ 0.59→1.01
 - Suicide-related behavior is far more prevalent than suicide.
 - Risk factors
 - Psychiatry inpatient admission in the past year; 68.5-fold in 2001 study
 - The presence of mood disorders increases the risk 30-70 fold (18.1-fold in 2001 study)
 - The highest risk is when depression occurs at the same time as generalized anxiety disorder—the risk increases 469-fold
 - Severe psychic anxiety (in intensity and/or pervasiveness)
 - Hopelessness
 - Enduring/persistent depression
 - Panic attacks
 - Global insomnia
 - Agitation
 - Severe absence of pleasure in all things
 - Alcohol abuse
 - Substance abuse in the setting of anxiety or depression also greatly increases the risk (4.1-fold in 2001 study)
 - Prior suicide attempt(s)
 - 20.1-fold in 2001 study
 - 5.4% prevalence of death by suicide in a community cohort of people who have attempted suicide in the past (Bostwick et al, 2016)
 - Interpersonal, occupational, legal, financial conflict/stress (5.9-fold in 2001 study)
 - Antisocial behavior (3.9-fold in 2001 study)
 - Outpatient treatment, lifetime (7.4-fold in 2001 study)
 - Seasonal effect
 - Precipitous increase beginning March
 - Rate remains high through July
 - Rate begins to decrease beginning August
 - High risk period
 - Following suicide attempts
 - Following psychiatric hospital discharge; risk during 1st 90 days after discharge
 - Male 1.5-fold increased risk
 - Female 1
 - White 5.3
 - Latino 2
 - Black 1
 - 18-34 yo 1
 - 35-44 yo 1.4
 - 45-64 yo 1.6
 - High risk:
 - White, non-Latino
 - Male
 - Older adult
 - Divorced
 - Prior suicide attempt, especially if via violent means
 - Family history of suicide
 - Psychiatric history with inpatient admission, mood disorder, comorbid substance use, comorbid anxiety
 - History of sexual abuse
 - Access to firearms
- Suicidal behavior is, among many things, an attempt to solve problems that are viewed as
 - Inescapable—even when problems, one way or another, can be solved
 - Interminable—even when the negative feelings can and will end

- Intolerable—even when the client can stand the negative feelings
- Interpersonal theory of suicide/vulnerabilities:
 - thwarted belongingness
 - perceived burdensomeness
 - capability of suicide (not afraid to die)
- Suicidal behavior is not effective in solving problems, generally increases the very same problems, and usually brings about new problems
- Suicide is a permanent solution to a problem that requires a more temporary solution
- Feeling suicidal is a valid, understandable response to emotional pain
- It is acceptable to talk openly and honestly about suicide
- Often critical is honing one's
 - Interpersonal skills
 - Stress management skills
 - Problem-solving skills
 - Assertiveness training
 - Self-control skills
 - Ability to reconcile opposites—feelings, moral judgments about feelings or situations
 - Ability to reconcile the need for and to honor and value opposites, gray zones, imperfections, etc as an essential part of the human/life experience
 - Ability to separate thought, feeling, and action
- Establishing a humanizing clinical framework
 - Awareness of the “halo effect” where catharsis in early sessions leads to relief that shifts over time
 - Self-monitoring
 - Reframe the function of the behavior
 - Understand and explore rather than judge the behavior
 - Explore the costs of emotional avoidance in terms of valued life goals
 - Develop a crisis management framework
 - Exploration and disengagement from futile, costly emotional control “rules”
 - Shifting focus from the search for what will work to the stopping of what doesn't
 - Explore and deepen one's sense of suicidal behavior as a choice, not a decision, a choice for emotional control
 - Experiential exercises to flesh out mindfulness, “wise mind”, acceptance
 - Detachment from rigid, inflexible, unworkable rules, from mandates on how to live
 - Identification and clarification of valued ends and goals in basic sectors of living
 - Emphasis on accumulated positives
 - Sprinkle self-forgiveness on self-blame
 - Emphasis on committed action as a process, not an outcome
 - Learn and master early warning signs
 - Increasing social withdrawal
 - Self-preoccupation
 - Low acceptance of feelings
 - Insomnia
 - Anxiety/agitation
 - Mood changes
 - Threats to harm self
 - Actively planning suicide
 - Writing or talking about suicide
 - Rage, seeking revenge, or anger
 - Severe agitation or anxiety
 - Dramatic mood changes
 - Feeling trapped
 - Escalating alcohol or drug use
 - Feeling no purpose in living
 - A Safety Plan
 - Recognize your warning signs
 - Use your coping strategies
 - Socialize with others who may offer support or distract you from the crisis
 - Contact family members who may help you resolve the crisis; make a list of people with phone numbers
 - Contact mental health professionals for help; list names and numbers, crisis hotlines (e.g., National Suicide Prevention Lifeline—1-800-273-TALK (8255))
- Death by suicide
 - General
 - Approximately 30,000 people die annually by suicide in the United States; in 2004, 32,439 people took their lives.
 - US Trends in leading causes of age-adjusted mortality (from 2000 → 2015)
 - Suicide has increased from 10.4/100,000 population-year in 2000 → 13.3 in 2015

- Heart disease has decreased from 257.6 → 167
- Stroke has decreased from 186.8 → 98.8
- Cancer from 199.6 → 161.2
- COPD from 44.2 → 40.5
- AIDS/HIV 5.2 → 2
- Suicide is the
 - 2nd leading cause of death internationally in females between 15-44 yo
 - 2nd leading cause of death in 13-17 yo's (CDC 2013), 15-24 yo's, and 25-34 yo's
 - 3rd leading cause of death internationally in those under the age of 44 yo
 - 3rd leading cause of death in 10-19 yo's and 10-14 yo's
 - 3rd leading cause of death in 13-19 yo's (CDC 2013)
 - 4th leading cause of death internationally in males between 15-44 yo
 - 4th leading cause of death in 35-44 yo's
 - 4th leading cause of death in children
 - 5th leading cause of death in 45-54 yo's
 - 7th leading cause of death in the United States, resulting in more deaths annually than HIV disease
- 10th leading cause of death for persons aged 14-64
- 11th leading cause of death across all age groups
 - In Germany in the year 2000, suicide killed more people than did traffic accidents, drugs, and violence together, and around 60% of those suicides were related to depression
 - In 1995, more teens and young adults died by suicide than from cancer, heart disease, AIDS, pneumonia, influenza, birth defects and stroke
 - 66% of those with depression contemplate suicide; 15% will actually commit suicide
 - National suicide rate: 12.87/100,000
 - This represents an increase of 31% from 9.8/100,000 in 1957
 - Beginning in 1987, the rate began to decline and has continued to do so ever since
 - Prozac was introduced to the American market in 1988
 - The rate in Denmark is 20/100,000
- Rates
 - Youth:
 - General
 - National Youth Risk Behavior High School Survey (CDC 2012), in the past year:
 - 15.8% seriously considered suicide attempt
 - 7.8% made one or more suicide attempts
 - 2.4% were medically treated for a suicide attempt
 - 5-10% of depressed adolescents will die by suicide in the 10-15 years of diagnosis
 - 2-5% of depressed youth will die by suicide in the 10-20 years following an initial attempt
 - Depressed youth have increased risk for suicidality when they become adults—5-fold increase in suicide attempts in adulthood
 - Pediatric depression leads to an increased risk for substance abuse, conduct disorder, impaired functioning, long-term psychiatric and medical conditions
 - In Virginia
 - Suicide counted for 16.8% of the 2818 cases of unnatural death in children and adolescents in Virginia between 1987-2003
 - The youngest case was 9 yo
 - Rates were highest for Caucasians
 - Gender in adolescent suicidality
 - 19.3% of females experience suicidal ideation vs. 12.5% of males
 - 15% of females have made a suicide plan vs. 10.8% of males
 - 9.8% of females have made a suicide attempt vs. 5.8% of males
 - 10-14 yo
 - 1.6/100,000
 - 330 suicides in 1997, representing 1% of all suicides that year
 - The suicide rate for children 10-14 years of age has more than doubled over the last 10 years.
 - The ratio of boys to girls is 3:1
 - Adolescents (and older children)
 - National Comorbidity Survey, Nock et al, 2013; 6843 adolescents surveyed
 - 12.1% lifetime prevalence of suicidal ideation; this increased to 56.8% in those with depression
 - 4% lifetime prevalence of suicidal plans; this increased to 69.7% in those with depression
 - 4.1% lifetime prevalence of suicide attempts; this increased to 75.7% in those with depression
 - Attempts
 - Nationwide, there are more than 1,000 suicide attempts (by adolescents) each day, over 500,000 each year.
 - Each year,

- ~2 million adolescents attempt suicide, ~700,000 of which require medical attention for their attempt
 - 8.3% of 9th-12th graders (YRBS study) reported at least one suicide attempt, of which 2.6% enacted at least one medically serious attempt within the year of survey
 - Up to 35% of depressed youth attempt suicide
 - Over 50% of depressed youth will attempt suicide in their lifetime
- Suicide completion
 - 90% of adolescents who die by suicide have a psychiatric disorder at the time of their death
 - Suicide is the leading cause of death in adolescents.
 - Overall rate 9.5/100,000, representing 6% of all suicides
 - Girls: 2-3.4/100,000; ratio of attempts to completed suicide is 6000:1
 - Boys: 12-15.2/100,000; ratio of attempts to completed suicide is 400:1
 - ~2,000 American teenagers kill themselves each year, which is more than all other medical illnesses in that age group combined. Only traffic accidents and homicides take more adolescents than suicide.
 - The ratio of boys to girls is 4.5:1
 - **The suicide rate in youth aged 15-19 from the early 1960's through the late 1980's increased threefold, mostly in males, to a peak in 1987.**
 - **BUT: The suicide rate in children aged 10-19 has decreased by 25% over the last 10 or so years.**
 - **This decade has been associated with a dramatic increase in the prescription rates of SSRI antidepressants.**
 - **A recent study has demonstrated that a 1% increase in prescription of antidepressant medication was associated with a 0.23 per 100,000 decrease in adolescent suicides**
- Adults aged 20-24
 - 13.6/100,000, representing 8% of all suicides
 - The ratio of young men to women in this age group is over 6:1
- Adults, overall
 - Males, North American: annual rate of 20.7/100,000
 - Females, North American an annual rate of 4.9/100,000
- Thoughts of suicide
 - 17-19.3% of 9th-12th graders in the US reported suicidal ideation (CDC; Youth Risk Behavior Surveillance study).
 - Other data suggests 60% of high schoolers have contemplated suicidal thoughts at one time or another
 - 40-80% of depressed youths experience thoughts of suicide
 - Sudak and Brent, 2005: 107 depressed adolescents were in psychotherapy study (**WITH NO MEDICATION TREATMENT**);
 - 17 experienced current suicidal ideation the week before the evaluation
 - 88 denied current suicidal ideation the week before the evaluation
 - 11 of the 88 developed suicidality during therapy treatment
 - One adolescent attempted suicide
- Depression and suicide
 - ~60% of suicides occur during a mood disorder, mostly untreated
 - 16,000 suicides each year are associated with depression
 - Approximately 30% of clinically depressed people attempt suicide
 - 2.5-15% of those with depression eventually die from suicide (15% of those with recurrent depressive illness commit suicide).
 - In girls, the risk of suicide is increased 20-fold by depression
- Anxiety and suicide
 - There is a 6-fold increase in the risk of suicide attempts if one has panic disorder or generalized anxiety disorder or post-traumatic stress disorder.
 - There is a 2-fold increase in the risk if one has social anxiety disorder.
- Self-harm and suicide
 - There is a 30-fold increase in the risk of completed suicide, compared with the general population, in the four years following a deliberate self-harm episode in adults
 - There is a 38-fold increase in the risk of complete suicide in individuals with a history of suicide attempts.
- Disruptive behavior disorders
 - ~1/3 of males who suicide have evidence of conduct disorder, frequently co-morbid with a mood, anxiety, or substance-abuse diagnosis
- Often driven by anger, loss, depression, panic, anxiety, rejection, self-hate, disconnectedness, and stress
- Often related to wishing to be free of anguish
- A genetic variant of the SSAT gene (SSAT342C) increases risk of completed suicide by 2.7-fold. SSAT is an enzyme that breaks down pyramines.
- Impulsivity of suicide

- 51% of suicide attempters attempted suicide after 10 minutes or less of consideration
- 16% attempted after 30 minutes or less of consideration
- 29% used alcohol prior to the attempt
 - 93% of which attempted suicide after 10 minutes or less of consideration
- 79% no longer feel suicidal after an attempt

- **Biology and Genetics of Anxiety and Depression:** see other handout

- **Resources**

- www.depression-primarycare.org
- www.dr_mark_wilson.medem.com
- “More than Moody” by Harold Koplewicz
- “Depression in Children & Adolescents” by Harold Koplewicz
- “Straight Talk about Your Child’s Mental Health,” Stephen Faraone, PhD
- “Your Child,” AACAP
- “Your Adolescent,” AACAP

- **History**

- Hippocrates, 460-370 BC:
 - Thought that the origin of mental diseases lay in the disturbed interaction of bodily fluids with the brain.
 - “People ought to know that the brain is the sole origin of pleasure and joy, laughter and jests, sadness and worry, as well as dysphoria and crying. Through the brain we can think, see, hear and differentiate between feeling ashamed, good, bad, happy...Through the brain we become insane, enraged, we develop anxiety and fear, which can come during the night or during the day, we suffer sleeplessness, we make mistakes, and have unfounded worries, we lose the ability to recognize reality, we become apathetic and we cannot participate in social life. We suffer all those things above through the brain when it is ill.”
 - Agitated depressions: “the patient feels something like a thorn stinging his innards. He flees from light and from people, loves the dark and his caught by panic...he is terrified and sees frightening visions, dreadful nightmares and sometimes dead people. The disease strikes most people in spring.”
 - Formulated the first classification of mental disorders, namely into melancholia, mania, and paranoia.
 - He also described organic and toxic deliria, postpartum psychoses, phobias, personality disorders, and temperaments.
 - Assumed that long-lasting anxiety, fear (phobos) and moodiness as basic characteristics of melancholia.
 - “in Thesus, a woman, of a melancholic turn of mind, from accidental cause of sorrow, while still going about, became affected with loss of sleep, aversion to food, and had thirst and nausea...”
- Aretaeus of Cappadocia, 120-180 AD: patients with melancholia are “dull or stern, dejected or unreasonably torpid, without manifest cause...and they also become peevish, dispirited, sleepless, and start up from a disturbed sleep...”
- Persia, 860-1136 AD
 - Based on 4 humors (maza) theory
 - Dam (blood)
 - Balgham (phlegm)
 - Safra (yellow bile)
 - Sauda (black bile)
 - Malikholia (melancholia)
 - with or without
 - haziyan (delusions; e.g., grandeur (to be a king), influence (controlled by Satan), somatic (to be an animal or an industrial tool))
 - hallucinations
 - visionariness
 - grief
 - continuous obsession
 - hatred of people
 - intense, persistent, unreasonable fear cued by the presence of or anticipation of a specific object or situation (e.g., wild animal, thief, genie, destruction/collapse of the sky)
 - desire to die
 - fear of death
 - vertigo
 - ringing in ears
 - nightmares
 - changed sexual desire
 - tremor
 - stare
 - changed appetite
 - stomach upset
 - weight loss
 - spring considered the season most disposing to melancholia
 - swarthy, shaggy, and thin people were believed to be predisposed to melancholia
 - young men were thought to be at greater risk but women were thought to suffer from more complicated or difficult-to-treat types
 - Mania and daol-kalb (“dog’s sickness”)
 - state of raving madness with exalted mood with or without
 - severe anxiety
 - irritability
 - excitability
 - sleep disturbances
 - violent behavior
 - fluctuating nature—prone to change mind and personality readily
 - Ibn Sina: the appearance of anger, restlessness, and violence heralded the transition from melancholia to mania.
 - Ghotrab (persecutory psychosis, paranoia)

- Depression
- Secluded
- Averse to contact with people
- Irritable
- Walked about only at night, walking, barking, howling at graves, mortuary and deserts
- Lack of sleep, pale, dehydrated, hollow eyes, scabbed legs and thighs
- Most commonly occurring in midwinter
- Ishgh (“passionate love disease”; lovesickness with anxiety and depression)
 - Ibn Sina: “an obsessive disorder like melancholia, which man brings upon himself by concentrating his thinking totally on valuing some images and qualities.”
 - Love defined as an assiduous thought of depressive nature, born as a result of one’s thinking again and again of the features, gestures, or behavior of a person of the opposite sex.
 - Pale and wan complexion
 - Palpitations of the heart; irregular pulse
 - Swelling of the face
 - Interrupted breathing
 - Sense of grief
 - Sighing
 - Causeless tears
 - Fast blinking
 - Insomnia
 - Headaches
- Griesinger, mid-1800’s: mental illness stemmed from brain changes
- Kraepelin, early 1900’s: classification and delineation of psychiatric disorders
- Freud: depression as hostility against a psychologically internalized lost object (e.g., idealized parent)
- Jaspers:
 - “Its central core is formed from an equally unmotivated and profound sadness to which is added a retardation of psychic events, which is subjectively painful as it is objectively visible. All instinctual activities are subjected to it. The patient does not want to do anything. The reduced impulse to move and to do things turns into complete immobility. No decision can be made and no activity begun. Associations are not available. Patients have no ideas. They complain of a complete disruption of memory. They feel their poverty of performance and complain of their inefficiency, lack of emotion, and emptiness. They feel profound gloom as a sensation in their chest or body as if it could be laid hold of there. The depth of their melancholy makes them see the world as grim and gray. They look for the unfavorable and unhappy elements in everything. They accuse themselves of much past guilt (self-accusations, notions of having sinned). The present has nothing for them (notion of worthlessness) and the future lies horrifyingly before them (notions of poverty).
 - Block, 1954: used iproniazid for tuberculosis—helped mood → first antidepressants (MAOI’s)
- Famous People with Depression and/or Bipolar Disorder; those that attempted or committed suicide asterisked
 - Writers/Poets
 - *Spaulding Gray—depression (committed suicide)
 - *Virginia Woolf—depression, possible bipolar disorder; committed suicide
 - *Sylvia Plath—poet and author of The Bell Jar—bipolar disorder (committed suicide)
 - *Robert Lowell—bipolar disorder
 - *Anne Sexton—bipolar disorder
 - *Ernest Hemmingway—probably bipolar disorder
 - *Robert Schumann—bipolar disorder
 - *Hugo Wolf—bipolar disorder
 - William Blake—bipolar disorder
 - Lord Byron—bipolar disorder
 - Hans Christian Anderson—depression and/or bipolar disorder
 - Samuel Beckett—depression and/or bipolar disorder
 - William Blake—depression and/or bipolar disorder
 - Art Buchwald—depression and/or bipolar disorder
 - Albert Camus—depression and/or bipolar disorder
 - Truman Capote—depression and/or bipolar disorder
 - Ralph Waldo Emerson—depression and/or bipolar disorder
 - William Faulkner—depression and/or bipolar disorder
 - Rainer Maria Rilke—depression and/or bipolar disorder
 - Charles Dickens—depression and/or bipolar disorder
 - Emily Dickenson—depression and/or bipolar disorder
 - TS Eliot—depression and/or bipolar disorder
 - F. Scott Fitzgerald
 - Michel Foucault—depression and/or bipolar disorder
 - Victor Hugo—depression and/or bipolar disorder
 - Ibsen—depression and/or bipolar disorder
 - Nick Hornby—depression and/or bipolar disorder
 - Franz Kafka—depression and/or bipolar disorder
 - John Keats—depression and/or bipolar disorder
 - Jack London—depression and/or bipolar disorder
 - Robert Lowell—depression and/or bipolar disorder
 - Herman Melville—depression and/or bipolar disorder
 - Musicians
 - *Kurt Cobain—depression, polysubstance abuse and dependence (committed suicide)
 - Sting—bipolar disorder
 - Honore de Balzac—depression and/or bipolar disorder
 - Samuel Barber—depression and/or bipolar disorder
 - Beethoven—depression and/or bipolar disorder
 - Irving Berlin—depression and/or bipolar disorder
 - Hector Berlioz—depression and/or bipolar disorder
 - Ray Charles—depression and/or bipolar disorder
 - Chopin—depression and/or bipolar disorder
 - Billy Corgan—depression and/or bipolar disorder
 - John Denver—depression and/or bipolar disorder
 - Peter Gabriel—depression and/or bipolar disorder
 - Hector Berlioz—bipolar disorder
 - Brian Wilson—probably bipolar or schizoaffective disorder
 - George Frederick Handel—bipolar disorder
 - Handel—depression and/or bipolar disorder
 - Juliana Hatfield—depression and/or bipolar disorder
 - Jack Irons—bipolar disorder
 - Janet Jackson—depression and/or bipolar disorder
 - Billy Joel—depression and/or bipolar disorder
 - Elton John—depression and/or bipolar disorder
 - Daniel Johnston—bipolar disorder
 - Ashley Judd—depression and/or bipolar disorder
 - John Lennon—depression and/or bipolar disorder

- Courtney Love—depression and/or bipolar disorder
- Sinead O'Connor—depression and/or bipolar disorder
- Alanis Morissette—depression and/or bipolar disorder
- Morrissey—depression and/or bipolar disorder
- Thelonius Monk—depression and/or bipolar disorder
- Gustav Mahler—depression and/or bipolar disorder
- Mussorgsky—depression and/or bipolar disorder
- Charles Mingus—depression and/or bipolar disorder
- Sarah McLachlan—depression and/or bipolar disorder
- Syd Barrett—?schizophrenia or severe bipolar disorder/schizoaffective disorder
- Artists
 - *Marek Rothko—bipolar disorder (committed suicide)
 - *Vincent van Gogh—bipolar disorder
 - Paul Gauguin—bipolar disorder
 - Alvin Ailey—depression and/or bipolar disorder
 - Francisco de Goya—depression and/or bipolar disorder
 -
- Historical figures
 - *Meriwether Lewis (of Lewis and Clarke fame)—?bipolar disorder, “hypochondriasis”, ?syphilis
 - John Adams—bipolar disorder
 - Abraham Lincoln—debilitating, melancholic depressions with severe suicidality and psychotic features; might have been bipolar.
 - Theodore Roosevelt—bipolar disorder
 - Lyndon Johnson—bipolar disorder
 - Christopher Columbus—bipolar disorder
 - John Winthrop—possible bipolar disorder
 - Roger Williams—possible bipolar disorder
 - William Penn—possible bipolar disorder
 - Alexander Hamilton—bipolar disorder
 - Alexander the Great—depression and/or bipolar disorder
 - Menachem Begin—depression and/or bipolar disorder
 - Napoleon—depression and/or bipolar disorder
 - John Brown, abolitionist—depression and/or bipolar disorder
 - Churchill—depression and/or bipolar disorder
 - Barbara Bush—depression and/or bipolar disorder
 - Calvin Coolidge—depression and/or bipolar disorder
 - Kitty Dukakis—depression
 - Queen Elizabeth I of England—depression and/or bipolar disorder
 - King George III of England—depression and/or bipolar disorder
 - Kit Gingrich (Newt's mother)—depression and/or bipolar disorder
 - Tipper Gore—depression
 - Thomas Jefferson—depression and/or bipolar disorder
 - Jeremiah, biblical figure—depression and/or bipolar disorder
 - Joan of Arc—depression and/or bipolar disorder
 - Job, biblical figure—depression and/or bipolar disorder
 - Andrew Jackson—depression and/or bipolar disorder
 - Henry James—depression and/or bipolar disorder
 - Robert E. Lee—depression and/or bipolar disorder
 - Primo Levi—depression and/or bipolar disorder
 - Martin Luther—depression and/or bipolar disorder
 - Imelda Marcos—depression and/or bipolar disorder
 - Robert McFarlane—depression and/or bipolar disorder
 -
- Actors/Actresses
 - Carrie Fisher—bipolar disorder
 - Ann-Margaret—depression and/or bipolar disorder
 - Roseanne Barr—depression and/or bipolar disorder
 - Drew Barrymore—depression and/or bipolar disorder
 - Ned Beatty—depression and/or bipolar disorder
 - Marlon Brando and child—depression and/or bipolar disorder
 - Tim Burton—depression and/or bipolar disorder
 - Drew Carey—depression and/or bipolar disorder
 - Jim Carrey—depression and/or bipolar disorder
 - John Cleese—depression and/or bipolar disorder
 - Francis Ford Coppola—depression and/or bipolar disorder
 - Rodney Dangerfield—depression and/or bipolar disorder
 - Sandra Dee—depression and/or bipolar disorder
 - Ellen DeGeneris—depression and/or bipolar disorder
 - Richard Dreyfuss—depression and/or bipolar disorder
 - Patty Duke—depression and/or bipolar disorder
 - Carrie Fisher—bipolar disorder
 - Harrison Ford—depression and/or bipolar disorder
 - Judy Garland—depression and/or bipolar disorder
 - Margaux Hemingway—depression and/or bipolar disorder
 - Audrey Hepburn—depression and/or bipolar disorder
 - Sir Anthony Hopkins—depression and/or bipolar disorder
 - Margot Kidder—bipolar disorder
 - Jessica Lange—depression and/or bipolar disorder
 - Vivian Leigh—depression and/or bipolar disorder
 - Kristy McNichol—depression and/or bipolar disorder
 - Marilyn Monroe—depression and/or bipolar disorder
 - Deborah Norville (newscaster)—bipolar disorder
 -
- Sports figures
 - Tai Babilonia—depression and/or bipolar disorder
 - Oksana Baiul—depression and/or bipolar disorder
 - Dwight Gooden—depression and/or bipolar disorder
 - Greg Loughanis—depression and/or bipolar disorder
 -
- Others
 - Andrew Carnegie—possible bipolar disorder
 - Edwin “Buzz” Aldrin—depression and/or bipolar disorder
 - Louie Anderson—depression and/or bipolar disorder
 - Dick Cavett—depression and/or bipolar disorder
 - Sigmund Freud—depression and/or bipolar disorder
 - Stan Getz—depression and/or bipolar disorder
 - Stephen Hawking—depression and/or bipolar disorder
 - Nathaniel Hawthorne—depression and/or bipolar disorder
 - Abby Hoffman—depression and/or bipolar disorder
 - Howard Hughes—depression and/or bipolar disorder
 - Kay Redfield Jameson—bipolar disorder
 - Pat LaFontaine—depression and/or bipolar disorder
 -
 - John Stuart Mill—depression and/or bipolar disorder
 - Spike Milligan—depression and/or bipolar disorder
- Claude Monet—depression and/or bipolar disorder
- Edvard Munch—depression and/or bipolar disorder
- Mussolini—depression and/or bipolar disorder
- Ralph Nader—depression and/or bipolar disorder

- Nebuchadnezzar, biblical figure—depression and/or bipolar disorder
- Sir Isaac Newton—depression and/or bipolar disorder
- Florence Nightingale—depression and/or bipolar disorder
- Georgia O'Keefe—depression and/or bipolar disorder
- Eugene O'Neill—depression and/or bipolar disorder
- John Ogden—depression and/or bipolar disorder
- Laurence Olivier—depression and/or bipolar disorder
- Ozzie Osbourne—depression and/or bipolar disorder
- Donny Osmond—depression and panic disorder
- Marie Osmond—depression and/or bipolar disorder
- Charles Parker—depression and/or bipolar disorder
- Dorothy Parker—depression and/or bipolar disorder
- Dolly Parton—depression and/or bipolar disorder
- George Patton—depression and/or bipolar disorder
- William Pitt—depression and/or bipolar disorder
- Walker Percy—depression and/or bipolar disorder
- Sylvia Plath—depression and/or bipolar disorder
- Jackson Pollock—depression and/or bipolar disorder
- Edgar Allen Poe—depression and/or bipolar disorder
- Cole Porter—depression and/or bipolar disorder
- Ezra Pound—depression and/or bipolar disorder
- Rachmaninoff—depression and/or bipolar disorder
- Lou Reed—depression and/or bipolar disorder
- Joan Rivers—depression and/or bipolar disorder
- Norman Rockwell—depression and/or bipolar disorder
- Theodore Roethke—depression and/or bipolar disorder
- Theodore Roosevelt—depression and/or bipolar disorder
- Axl Rose—bipolar disorder
- Phillip Roth—depression and/or bipolar disorder
- Yves Saint Laurent—depression and/or bipolar disorder
- Robert Schumann—depression and/or bipolar disorder
- Charles Schultz—depression and/or bipolar disorder
- Monica Seles—depression and/or bipolar disorder
- Anne Sexton—depression and/or bipolar disorder
- Mary Shelley—depression and/or bipolar disorder
- Percy Bysshe Shelley—depression and/or bipolar disorder
- William Tecumseh Sherman—depression and/or bipolar disorder
- Paul Simon—depression and/or bipolar disorder
- Phil Spector—depression and/or bipolar disorder
- Rod Steiger—depression and/or bipolar disorder
- George Stephanopoulos—depression and/or bipolar disorder
- Robert Louis Stevenson—depression and/or bipolar disorder
- Daryl Strawberry—depression and/or bipolar disorder
- William Styron—depression and/or bipolar disorder
- James Taylor—depression and/or bipolar disorder
- Tchaikovsky—depression and/or bipolar disorder
- Alfred Lord Tennyson—depression and/or bipolar disorder
- Christopher Columbus—bipolar disorder
- Dylan Thomas—depression and/or bipolar disorder
- Tolstoy—depression and/or bipolar disorder
- Spencer Tracy—depression and/or bipolar disorder
- Ted Turner—bipolar disorder
- Mark Twain—depression and/or bipolar disorder
- Mike Tyson—bipolar disorder
- Jean-Claude Van Damme—depression and/or bipolar disorder
- Kurt Vonnegut—depression and/or bipolar disorder
- Tom Waits—depression and/or bipolar disorder
- Mike Wallace—depression and/or bipolar disorder
- George Washington—depression and/or bipolar disorder
- Damon Wayans—depression and/or bipolar disorder
- Walt Whitman—depression and/or bipolar disorder
- Dar Williams—depression and/or bipolar disorder
- Robin Williams—bipolar disorder
- Tennessee Williams—depression and/or bipolar disorder
- William Carlos Williams—depression and/or bipolar disorder
- Thomas Wolfe—depression and/or bipolar disorder
- Ed Wood—depression and/or bipolar disorder
- Natalie Wood—depression and/or bipolar disorder
- Virginia Woolf—depression and/or bipolar disorder
- Tammy Wynette—depression and/or bipolar disorder
- Boris Yeltsin—depression and/or bipolar disorder
- Rosemary Clooney—depression and/or bipolar disorder
- Ty Cobb—depression and/or bipolar disorder
- Leonard Cohen—depression and/or bipolar disorder
- James Madison—depression
- John Quincy Adams—depression
- Rutherford B. Hayes—depression
- James Garfield—depression
- Woodrow Wilson—depression, anxiety, personality change due to stroke
- Calvin Coolidge—depression, social phobia, hypochondriasis
- Herbert Hoover—depression
- Dwight Eisenhower—depression
- Lorraine Bracco—major depression
- Tipper Gore—major depression
- Thomas Jefferson—social phobia
- Franklin Pierce—depression, alcohol dependence
- Ulysses S. Grant—social phobia, specific phobia (blood), alcohol dependence
- Warren Harding—somatoform disorder
- Richard Nixon—alcohol abuse
- Mary Todd—may have also had OCD
- George Stephanopolous—panic disorder
- Greg Louganis
- Delta Burke
- Beethoven
- Samuel Barber
- Frederic Chopin
- Eric Clapton
- Dolly Parton
- Sheryl Crow
- Jack London
- F. Scott Fitzgerald
- Edgar Allen Poe
- Walt Whitman
- Elvis Presley—polysubstance abuse
- And so many more it's impossible to list