

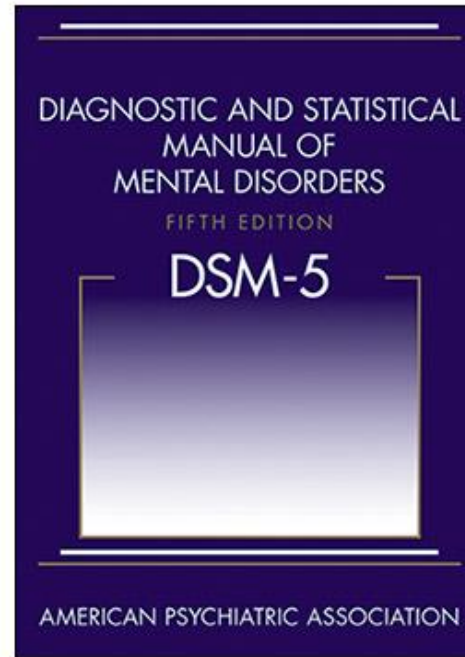
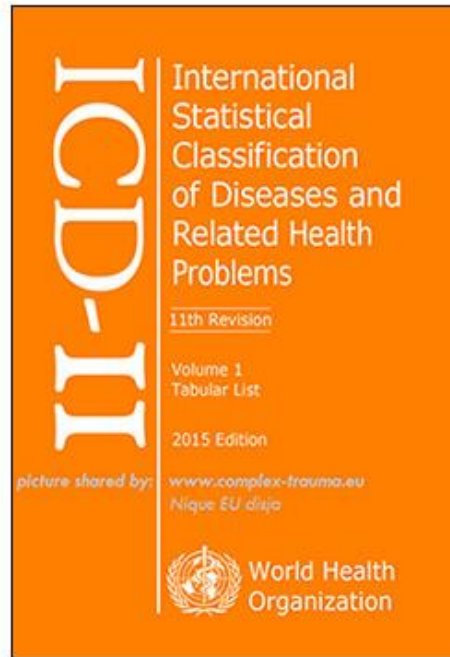


Psychiatric disorders

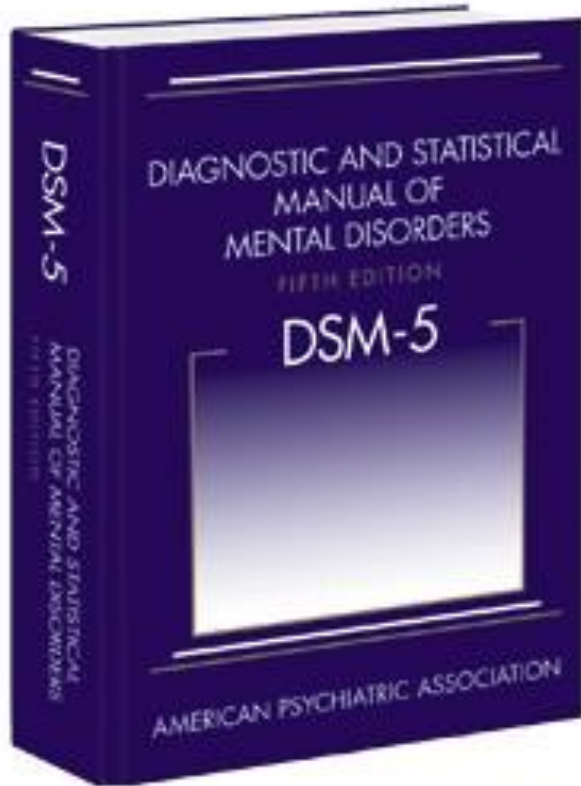
psychiatric disorders



How Are Diseases Classified?



The **DSM-5** and **ICD-11** are two of the most respected medical manuals in the world for classifying diseases & disorders



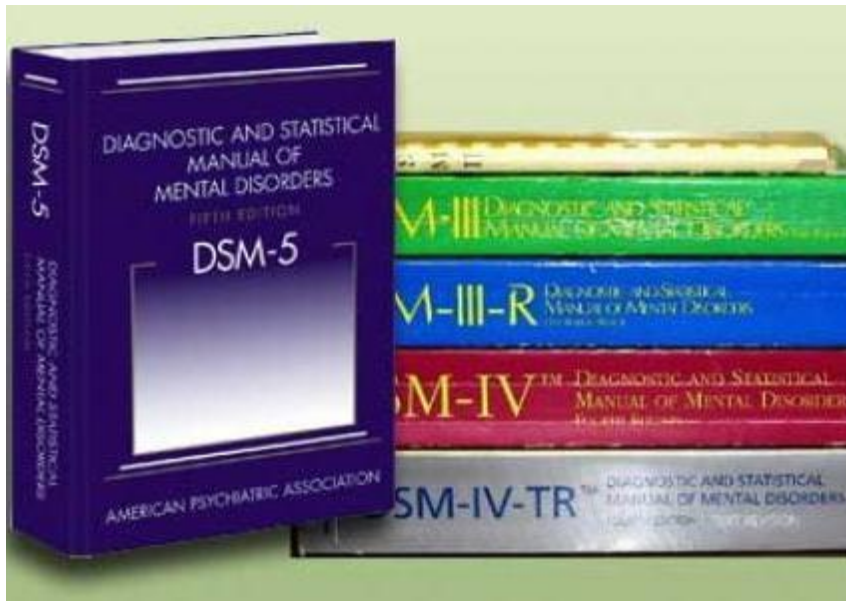
DSM-5
2013

- Alignment with ICD-11
- 12-year process by hundreds of people (literature reviews, international conferences, field trials)

Aims of the DSM5

- Summarising all psychiatric diagnoses
- Providing a “shared language” for mental health professionals
- Identifying patient groups for clinical and basic research
- Guiding treatment recommendation and reimbursement by insurance companies
- Documenting public health information such as morbidity and mortality rates

The science of mental disorders continues to evolve.



- The past decades there has been a durable progress in cognitive neuroscience, brain imaging, epidemiology and genetics

DSM5 : organisational structure

- Explicit diagnostic criteria
- DSM5 codes and harmonisation with ICD-11 (codes): schizophrenia
- Dimensional approach to diagnosis approaches the wide spread sharing of symptoms and risk factors across many disorders
- Developmental and lifespan considerations
- Information about diagnostic features, associated features, prevalence, development and course, risk and prognostic factors, culture-related diagnostic issues, gender related diagnostic issues, differential diagnosis, comorbidity

DSM5 : organisational structure

- **Explicit diagnostic criteria**
- DSM5 codes and harmonisation with ICD-11 (codes): schizophrenia
- Dimensional approach to diagnosis approaches the wide spread sharing of symptoms and risk factors across many disorders
- Developmental and lifespan considerations
- Information about diagnostic features, associated features, prevalence, development and course, risk and prognostic factors, culture-related diagnostic issues, gender related diagnostic issues, differential diagnosis, comorbidity

DSM5 criteria of schizophrenia

Criterion A. Two (or more) of the following (At least one of these should include 1-3):

1. Delusions
 2. Hallucinations
 3. Disorganized speech
 4. Grossly disorganized or catatonic behavior
 5. Negative symptoms (i.e., diminished emotional expression or avolition)
-

Criterion B. One or more major areas functioning, such as work, interp, are markedly below the level achieved prior to the onset.

Criterion C. Continuous signs of the disturbance persist for at least 6 months.

Criterion D. Schizoaffective disorder and depressive and bipolar disorder with psychotic features have been ruled out.

Criterion E. Substance / general medical condition exclusion.

Criterion F. If there is a history of autism spectrum disorder or other communication disorder of childhood onset, the additional diagnosis of schizophrenia is made only if prominent delusions or hallucinations are also present for at least 1 month (or less if successfully treated).

- Clinical training and experience are needed to use DSM for determining a diagnosis



- Harmful if used as a cookbook by not trained people: people of insurances and courts of law read it literally = danger

DSM5 : organisational structure

- Explicit diagnostic criteria
- *DSM5 codes and harmonisation with ICD-11 (codes): schizophrenia*
- Dimensional approach to diagnosis approaches the wide spread sharing of symptoms and risk factors across many disorders
- Developmental and lifespan considerations
- Information about diagnostic features, associated features, prevalence, development and course, risk and prognostic factors, culture-related diagnostic issues, gender related diagnostic issues, differential diagnosis, comorbidity

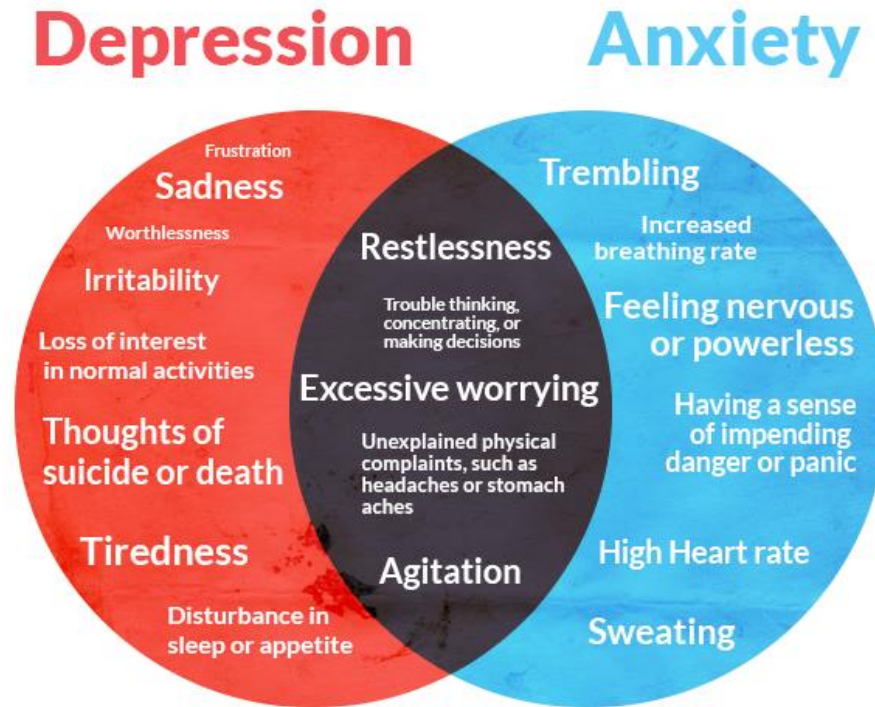
DSM5 : organisational structure

- Explicit diagnostic criteria
- DSM5 codes and harmonisation with ICD-11 (codes):
schizophrenia 295,90 DSM5 (F20,9) ICD11
- Dimensional approach to diagnosis approaches the wide spread sharing of symptoms and risk factors across many disorders
- Developmental and lifespan considerations
- Information about diagnostic features, associated features, prevalence, development and course, risk and prognostic factors, culture-related diagnostic issues, gender related diagnostic issues, differential diagnosis, comorbidity

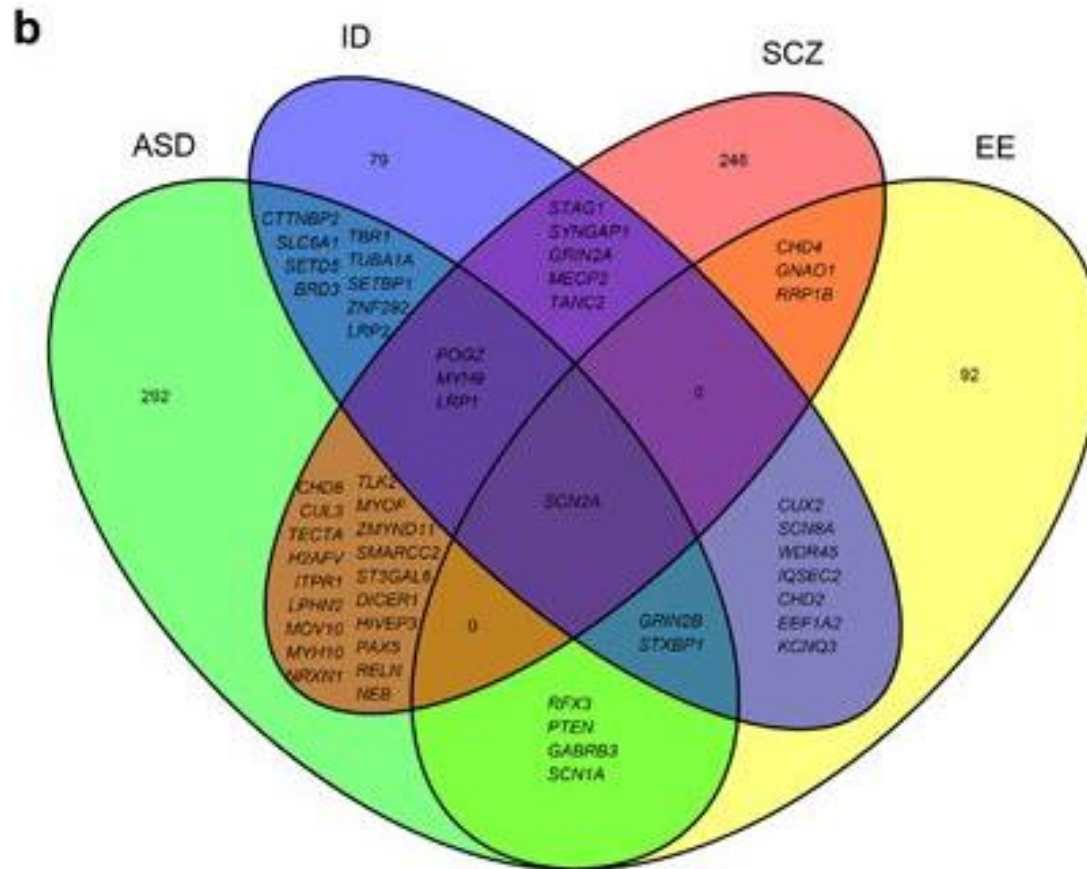
DSM5 : organisational structure

- Explicit diagnostic criteria
- DSM5 codes and harmonisation with ICD-11 (codes): schizophrenia
- ***Dimensional approach to diagnosis approaches the wide spread sharing of symptoms and risk factors across many disorders***
- Developmental and lifespan considerations
- Information about diagnostic features, associated features, prevalence, development and course, risk and prognostic factors, culture-related diagnostic issues, gender related diagnostic issues, differential diagnosis, comorbidity

Shared symptoms and risk factors between different psychiatric disorders



Shared risk factors

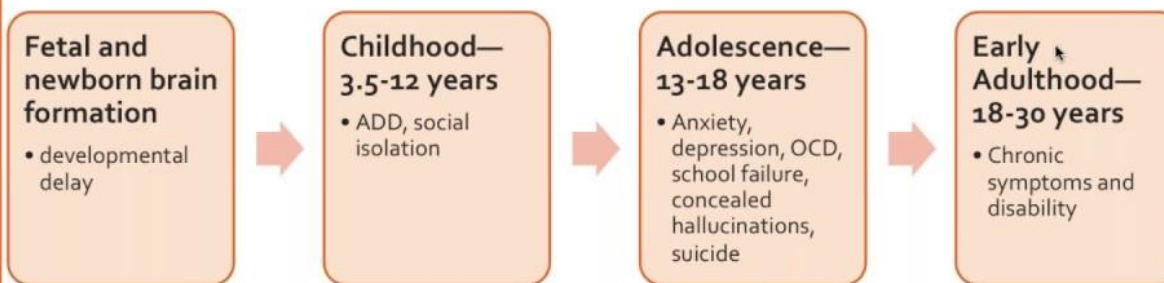


Genes with de novo mutations are shared by different neurodevelopmental disorders: intellectual disability, schizophrenia, epileptic encephalopathy and autism spectrum disorders (Li et al. 2016)

DSM5 : organisational structure

- Explicit diagnostic criteria
- DSM5 codes and harmonisation with ICD-11 (codes): schizophrenia
- Dimensional approach to diagnosis approaches the wide spread sharing of symptoms and risk factors across many disorders
- *Developmental and lifespan considerations*
- Information about diagnostic features, associated features, prevalence, development and course, risk and prognostic factors, culture-related diagnostic issues, gender related diagnostic issues, differential diagnosis, comorbidity

Critical Periods in Development and Schizophrenia—SYMPTOMS

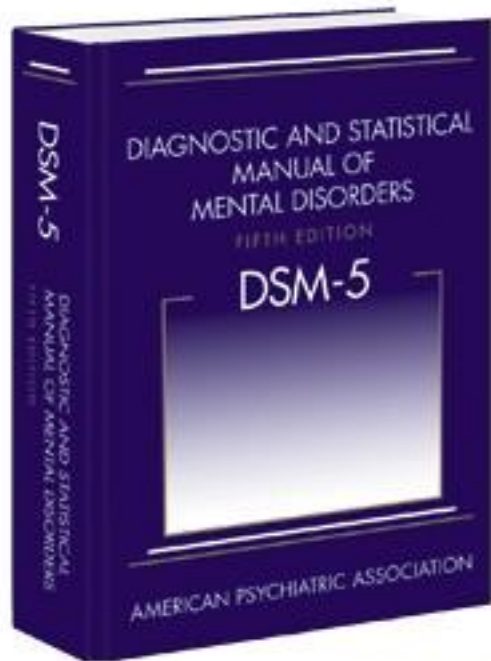


DSM5 : organisational structure

- Explicit diagnostic criteria
- DSM5 codes and harmonisation with ICD-11 (codes): schizophrenia
- Dimensional approach to diagnosis approaches the wide spread sharing of symptoms and risk factors across many disorders
- Developmental and lifespan considerations
- ***Information about diagnostic features, associated features, prevalence, development and course, risk and prognostic factors, culture-related diagnostic issues, gender related diagnostic issues, differential diagnosis, comorbidity***

- Schizophrenia affects around 0.3–0.7% of people at some point in their life

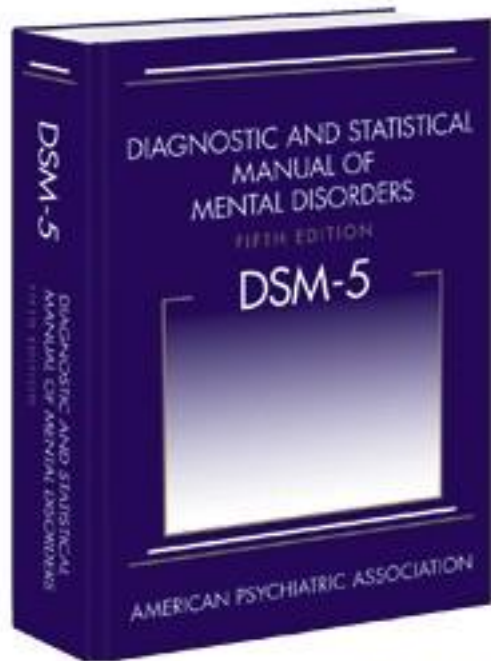
Contents of the DSM5



DSM-5
2013

- Three sections:
 - instructions for use
 - description of the psychiatric disorders
 - future developments

Contents of the DSM5



DSM-5
2013

- Three sections:
 - instructions for use
 - description of the psychiatric disorders
 - future developments

Section 2: Psychiatric disorders

- Neurodevelopmental disorders
- Schizophrenia spectrum and other psychotic disorders
- Bipolar and related disorders
- Depressive disorders
- Anxiety disorders
- Obsessive-compulsive and related disorders
- Dissociative disorders
- Somatic symptom disorders
- Feeding and eating disorders
- Elimination disorders
- Sleep-wake disorders
- Sexual dysfunctions
- Gender dysphoria
- Disruptive, impulse control and conduct disorders
- Substance use and addictive disorders
- Neurocognitive disorders
- Personality disorders
- Paraphilic disorders
- Other disorders

Section 2: Psychiatric disorders

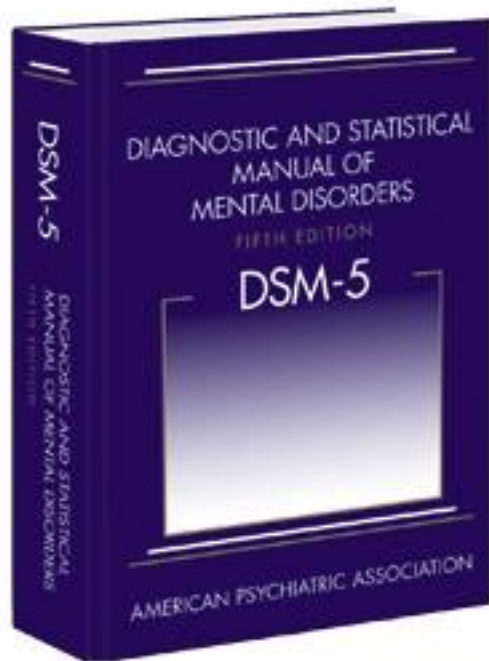
- Neurodevelopmental disorders
- Schizophrenia spectrum and other psychotic disorders
- Bipolar and related disorders
- Depressive disorders
- Anxiety disorders
- Obsessive-compulsive and related disorders
- Dissociative disorders
- Somatic symptom disorders
- Feeding and eating disorders
- Elimination disorders
- Sleep-wake disorders
- Sexual dysfunctions
- Gender dysphoria
- Disruptive, impulse control and conduct disorders
- Substance use and addictive disorders
- Neurocognitive disorders
- Personality disorders
- Paraphilic disorders
- Other disorders

Neurodevelopmental disorders:

group of disorders with onset in in the developmental period, often before the child enters school

- Intellectual disabilities
- Communication disorders
- Autism spectrum disorder
- Attention-deficit/hyperactivity disorder
- Specific learning disorder
- Other neurodevelopmental disorders

Contents of the DSM5



DSM-5
2013

- Three sections:
 - instructions for use
 - description of the psychiatric disorders
 - future developments

Intellectual Disability



DSM IV TR

- IQ 70 or below
- Concurrent deficits or impairments in present adaptive functioning
- The onset is before age 18 years
- Severity: Mild, Moderate, Severe, Profound, Based on IQ level

DSM 5

- Deficits in general mental abilities
- Impairment in adaptive functioning for the individual's age and sociocultural background
- All symptoms must have an onset during the developmental period
- Severity: Mild, Moderate, Severe, based on Adaptive Behavior

Diagnostic Criteria for Intellectual Disability

TABLE 5.2 | Diagnostic Criteria for Intellectual Disability (Intellectual Developmental Disorder)

Intellectual disability (intellectual developmental disorder) is a disorder with onset during the developmental period that includes both intellectual and adaptive functioning deficits in conceptual, social, and practical domains. The following three criteria must be met:

DSM-5

- (A) Deficits in intellectual functions, such as reasoning, problem-solving, planning, abstract thinking, judgment, academic learning and learning from experience, confirmed by both clinical assessment and individualized, standardized intelligence testing.
- (B) Deficits in adaptive functioning that result in failure to meet developmental and sociocultural standards for personal independence and social responsibility. Without ongoing support, the adaptive deficits limit functioning in one or more activities of daily life, such as communication, social participation, and independent living, across multiple environments, such as home, school, work, and community.
- (C) Onset of intellectual and adaptive deficits during the developmental period.

Note: The diagnostic term *intellectual disability* is the equivalent term for the ICD-11 diagnosis of *intellectual developmental disorders*.

Specify current severity (see Table 5.3): Mild, Moderate, Severe, or Profound

Section 2: Psychiatric disorders

- Neurodevelopmental disorders
- Schizophrenia spectrum and other psychotic disorders
- Bipolar and related disorders
- Depressive disorders
- Anxiety disorders
- Obsessive-compulsive and related disorders
- Dissociative disorders
- Somatic symptom disorders
- Feeding and eating disorders
- Elimination disorders
- Sleep-wake disorders
- Sexual dysfunctions
- Gender dysphoria
- Disruptive, impulse control and conduct disorders
- Substance use and addictive disorders
- Neurocognitive disorders
- Personality disorders
- Paraphilic disorders
- Other disorders



- a 16 year-old with strange behaviour:
school refusal
dermatological problems (itching)
flies in the neck
- Second child of healthy parents
vocational training

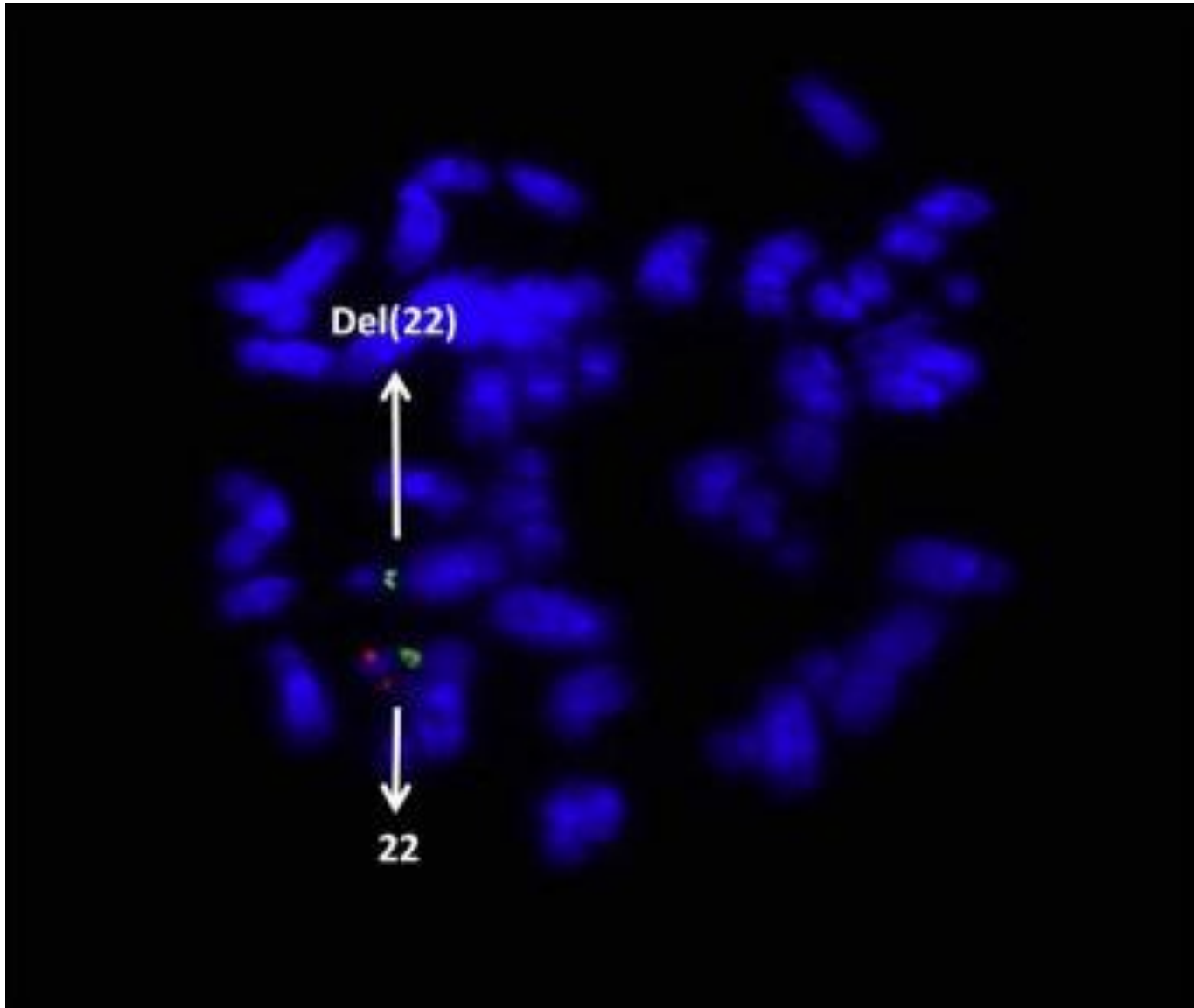


- a 16 year-old with strange behaviour:
school refusal **ANXIETIES**
dermatological problems (itching)
flies in the neck **HALLUCINATIONS**
- Second child of healthy parents
vocational training **BORDERLINE**
INTELLIGENCE

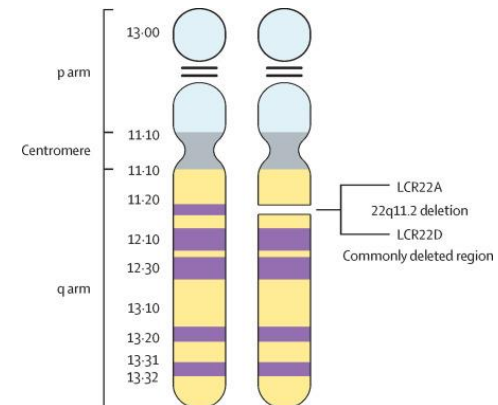
Velo-cardio-facial syndrome with psychotic symptoms



- a 16 year-old with strange behaviour:
school refusal **ANXIETIES**
dermatological problems (itching)
flies in the neck **HALLUCINATIONS**
- Second child of healthy parents
vocational training **BORDERLINE**
INTELLIGENCE



Psychotic symptoms, borderline intelligence, facial dysmorphism



Section 2: Psychiatric disorders

- Neurodevelopmental disorders
- Schizophrenia spectrum and other psychotic disorders
- Bipolar and related disorders
- Depressive disorders
- Anxiety disorders
- Obsessive-compulsive and related disorders
- Dissociative disorders
- Somatic symptom disorders
- Feeding and eating disorders
- Elimination disorders
- Sleep-wake disorders
- Sexual dysfunctions
- Gender dysphoria
- Disruptive, impulse control and conduct disorders
- Substance use and addictive disorders
- Neurocognitive disorders
- Personality disorders
- Paraphilic disorders
- Other disorders

General characteristics of psychotic disorders:

- Delusions
- Hallucinations
- Disorganised thinking (speech)
- Disorganised or abnormal behaviour (including catatonia)
- (Negative symptoms: diminished emotional expression and avolition, alogia, anhedonia, asociality)

Schizophrenia spectrum and other psychotic disorders: key features that define the psychotic disorders

- Delusions

Grandiose delusions

The Power of Delusion



growthink

Erotomaniac delusions



psychotic disorders

- Delusions
- Hallucinations

Auditive hallucinations



Visual hallucinations



Tactile hallucinations

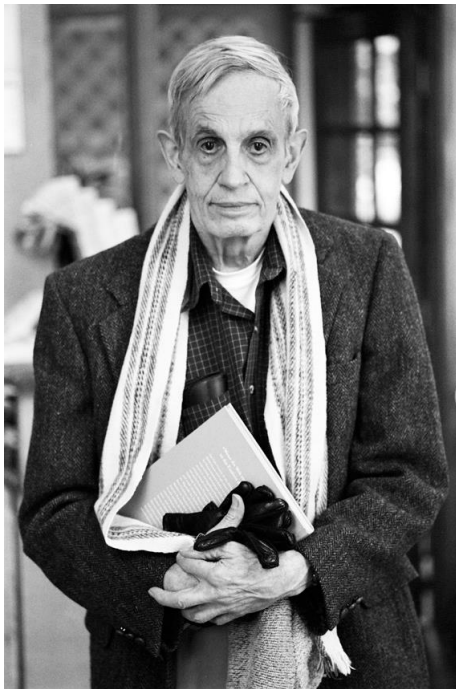


psychotic disorders

- Delusions
- Hallucinations
- Disorganised thinking (speech)

A beautiful mind (2001)

John Nash wiskundige en nobelprijs voor de economie



General characteristics of psychotic disorders:

- Delusions
- Hallucinations
- Disorganised thinking (speech)
- Disorganised or abnormal behaviour (including catatonia)
- (Negative symptoms: diminished emotional expression and avolition, alogia, anhedonia, asociality)

catatonia

- Psychomotor disturbance
- In the context of several disorders:
 - medical: neurological conditions (like headtrauma, encephalitis, neoplasms, cerebrovascular disease) and metabolic conditions (hypercalcemia)
 - psychiatric: psychotic, bioplar, depression or other mental disorder

catatonia





“Psychological pillow”



Awakenings (1990, Penny Marshall)



Table 1

DSM-5 diagnostic criteria for catatonia

The clinical picture is dominated by 3 (or more) of the following symptoms:

1. Stupor (ie, no psychomotor activity; not actively relating to environment)
2. Catalepsy (ie, passive induction of a posture held against gravity)
3. Waxy flexibility (ie, slight, even resistance to positioning by examiner)
4. Mutism (ie, no, or very little, verbal response [exclude if known aphasia])
5. Negativism (ie, opposition or no response to instructions or external stimuli)
6. Posturing (ie, spontaneous and active maintenance of a posture against gravity)
7. Mannerism (ie, odd, circumstantial caricature of normal actions)
8. Stereotypy (ie, repetitive, abnormally frequent, non-goal-directed movements)
9. Agitation, not influenced by external stimuli
10. Grimacing
11. Echolalia (ie, mimicking another's speech)
12. Echopraxia (ie, mimicking another's movements)

Source: Reference 2

Clinical examination (Rooseleer en Sienaert, 2011)

- Bush-Francis Catatonia Screening Instrument (BFCSI)
- Bush-Francis Catatonia Rating Scale (BF CRS)

catatonia

- Good response to treatment:

benzodiazepines

ECT

Section 2: Psychiatric disorders

- Neurodevelopmental disorders
- Schizophrenia spectrum and other psychotic disorders
- Bipolar and related disorders
- Depressive disorders
- Anxiety disorders
- Obsessive-compulsive and related disorders
- Dissociative disorders
- Somatic symptom disorders
- Feeding and eating disorders
- Elimination disorders
- Sleep-wake disorders
- Sexual dysfunctions
- Gender dysphoria
- Disruptive, impulse control and conduct disorders
- Substance use and addictive disorders
- Neurocognitive disorders
- Personality disorders
- Paraphilic disorders
- Other disorders

Schizophrenia and other psychotic disorders

ICD-11	DSM-5
Schizophrenia and other primary psychotic disorders	Schizophrenia spectrum and other psychotic disorders
7A50 Schizophrenia	Schizophrenia
7A51 Schizoaffective disorder	Schizoaffective disorder
7A52 Schizotypal disorder	Schizotypal personality disorder
7A53 Acute and transient psychotic disorder	Brief psychotic disorder
7A54 Delusional disorder	Delusional disorder
7A5Y Other specified schizophrenia and other primary psychotic disorders	Other specified schizophrenia spectrum and other psychotic disorders
7A5Z Schizophrenia and other primary psychotic disorders, unspecified	Unspecified schizophrenia spectrum and other psychotic disorders
	Schizophreniform disorder
	Substance/medication induced psychotic disorder
	Psychotic disorder due to another medical condition
	Catatonia associated with another mental disorder (catatonia specifier)
	Catatonic disorder due to another medical condition
	Unspecified catatonia

schizophrenia

- Prevalence: 1%
- High risk of suicide, unemployment, substance abuse
- Economic burden
- Recognized as one of the most burdening disabilities globally by the World Health Organisation (WHO, 2008)

Deinstitutionalization of the mentally ill out of the large state mental hospitals when they closed during the 1980s. For schizophrenics it was the start of a cycle through the jail, shelter, and mental health systems and supportive housing.

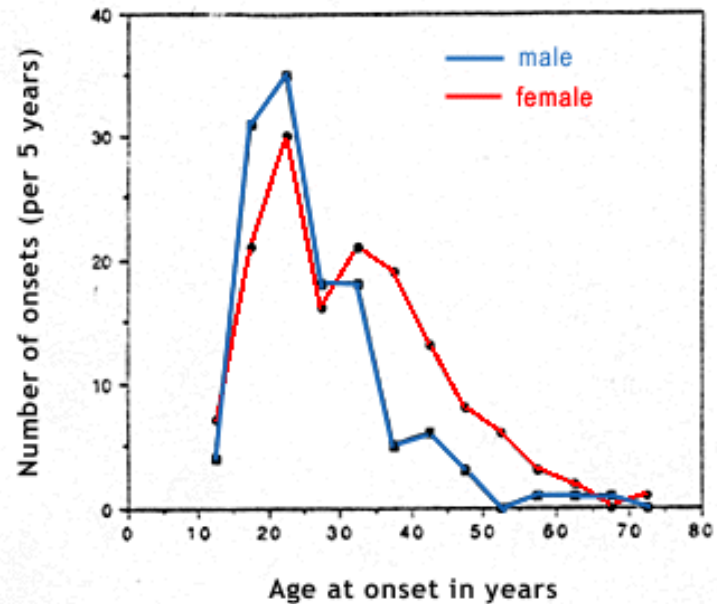


Where are the People with Schizophrenia?

Approximately:

- 6% are homeless or live in shelters
- 6% live in jails or prisons
- 5% to 6% live in Hospitals
- 10% live in Nursing homes
- 25% live with a family member
- 28% are living independently
- 20% live in Supervised Housing (group homes, etc.)

Onset of schizophrenia



- In men, schizophrenia symptoms typically start in the late 20s. It's uncommon for children to be diagnosed with schizophrenia and rare for those older than age 45. In women, symptoms typically start in the late 20s. It's uncommon for children to be diagnosed with schizophrenia and rare for those older than age 45.

[A typological model of schizophrenia based on age at onset, sex and familial morbidity. Acta Psychiatr. Scand. 89, 135-141 \(1994\).](#)

Schizophrenia: DSM5 criteria

Criterion A. Two (or more) of the following (At least one of these should include 1-3):

1. Delusions
2. Hallucinations
3. Disorganized speech
4. Grossly disorganized or catatonic behavior
5. Negative symptoms (i.e., diminished emotional expression or avolition)

Criterion B. One or more major areas functioning, such as work, interp, are markedly below the level achieved prior to the onset.

Criterion C. Continuous signs of the disturbance persist for at least 6 months.

Criterion D. Schizoaffective disorder and depressive and bipolar disorder with psychotic features have been ruled out.

Criterion E. Substance / general medical condition exclusion.

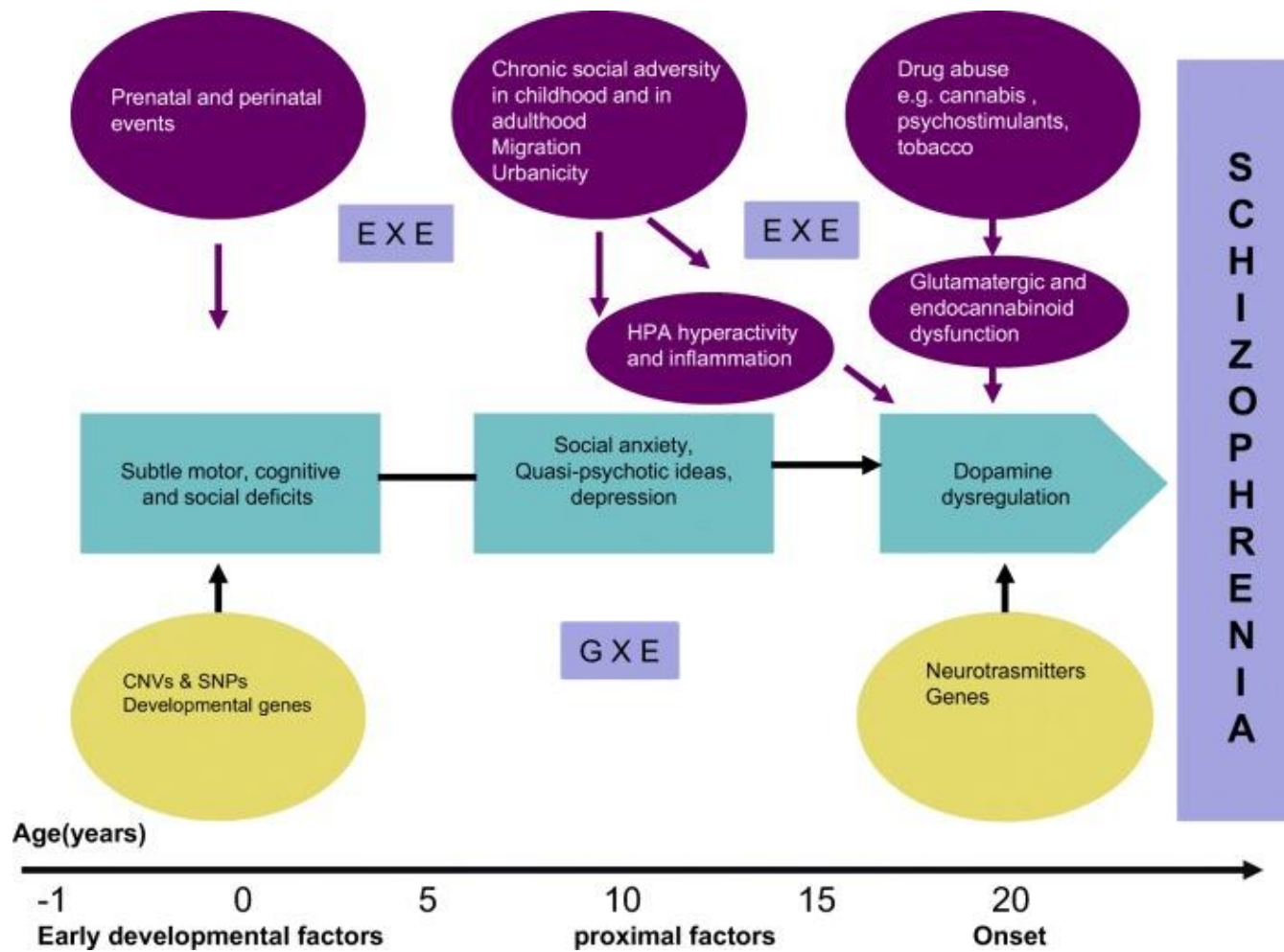
Criterion F. If there is a history of autism spectrum disorder or other communication disorder of childhood onset, the additional diagnosis of schizophrenia is made only if prominent delusions or hallucinations are also present for at least 1 month (or less if successfully treated).

Core symptom:

Cognitive decline precedes the onset of psychotic symptoms

(Mayo Clinic)

- Schizophrenia symptoms in teenagers are similar to those in adults, but the condition may be more difficult to recognize. This may be in part because some of the early symptoms of schizophrenia in teenagers are common for typical development during teen years, such as:
 - Withdrawal from friends and family
 - A drop in performance at school
 - Trouble sleeping
 - Irritability or depressed mood
 - Lack of motivation
- Also, recreational substance use, such as marijuana, methamphetamines or LSD, can sometimes cause similar signs and symptoms.
- Compared with schizophrenia symptoms in adults, teens may be:
 - Less likely to have delusions
 - More likely to have visual hallucinations



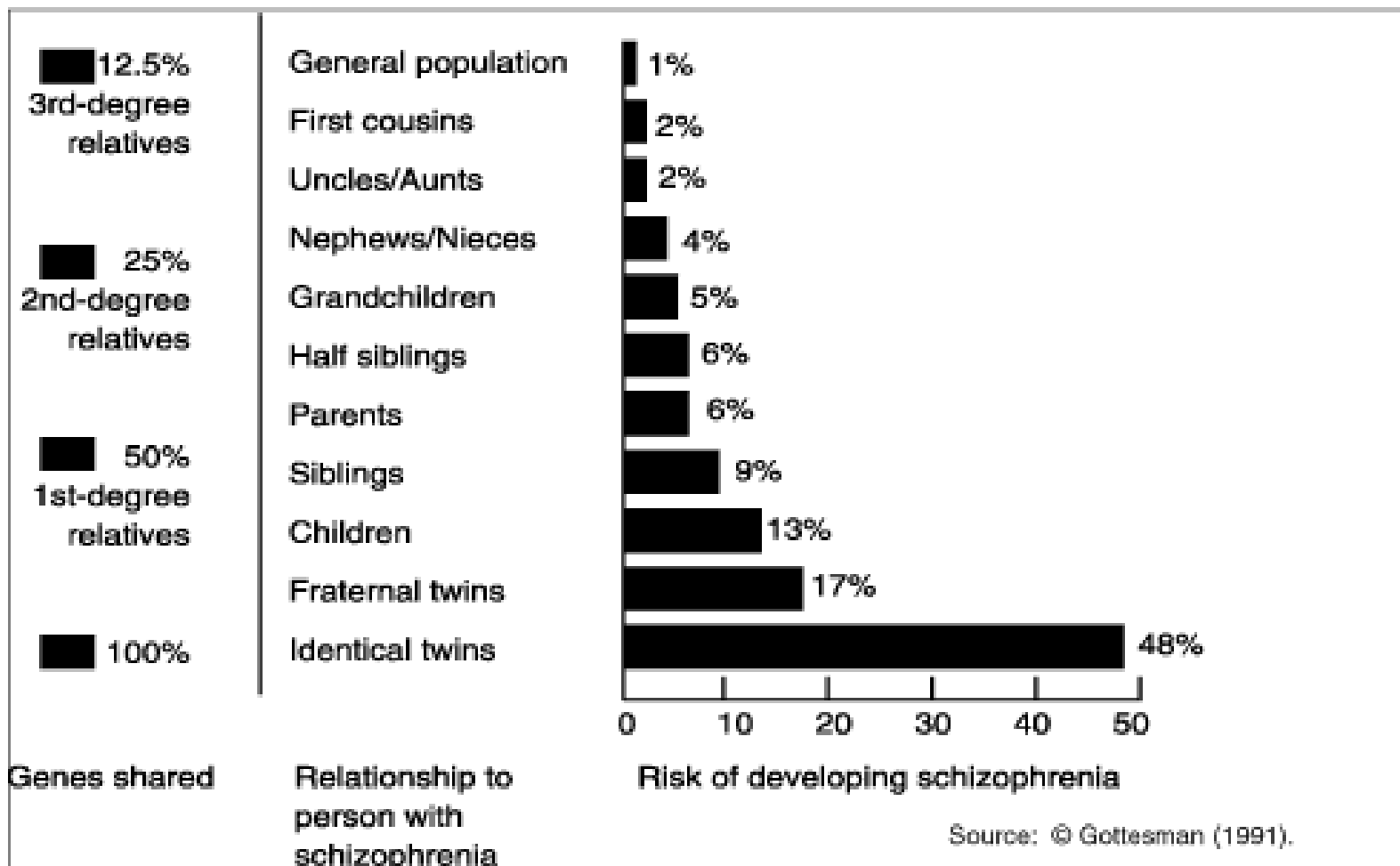
- Stilo SA and Murray RM, Curr Psychiatry Rep 2019

Developmental cascade towards schizophrenia.

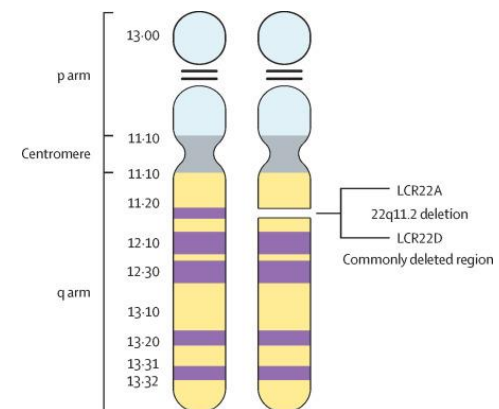
Schizophrenia: genetics

- Concordance monozygotic twins: 85%
- Concordance dizygotic twins: 25%
(franzek and Beckman 1998)

- Heritability: 80%



Velocardiofacial syndrome: 30% risk of schizophrenia



- 2017 May;30(3):191-196.
- 2017 May;30(3):191-196.

- Patients with velocardiofacial syndrome have 30% risk for developing schizophrenia. The strongest molecular genetic factor for schizophrenia
- 0.5–1% of individuals with schizophrenia in the general population have the associated 22q11.2 deletion syndrome.
- Recognition of 22q11.2DS is important for
 - clinical management, including treatment and genetic counseling
 - for the opportunity such a molecular model presents for understanding schizophrenia

Van, Boot and Basset
Curr Opin Psychiatry 2017 May;30(3):191-196

Section 2: Psychiatric disorders

- Neurodevelopmental disorders
- Schizophrenia spectrum and other psychotic disorders
- Bipolar and related disorders
- Depressive disorders
- Anxiety disorders
- Obsessive-compulsive and related disorders
- Dissociative disorders
- Somatic symptom disorders
- Feeding and eating disorders
- Elimination disorders
- Sleep-wake disorders
- Sexual dysfunctions
- Gender dysphoria
- Disruptive, impulse control and conduct disorders
- Substance use and addictive disorders
- Neurocognitive disorders
- Personality disorders
- Paraphilic disorders
- Other disorders



- Intellectual disability
- Regression
- Bipolar disorder
- catatonia



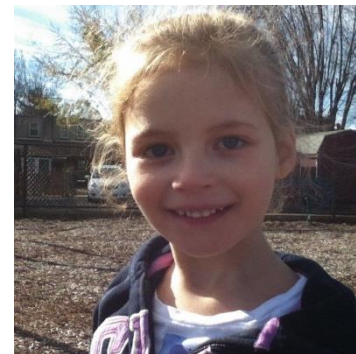
Time course: The boy pictured above hasand went from speaking relatively normally to saying only "yes" or "no" as he grew older.

Phelan Mc Dermid Syndrome

- The major neurodevelopmental features of PMS are caused by deletions or mutations of the *SHANK3* gene, which encodes a scaffolding protein of the postsynaptic density of glutamatergic synapses

Phelan McDermid Syndrome (SHANK3)

- neonatal hypotonia, global developmental delay, intellectual disability (ID), severely delayed or absent speech, and frequent autism spectrum disorder (ASD)
- The neurobehavioral phenotype of PMS is usually severe: 77% manifested severe-to-profound ID and 84% met criteria for ASD
- Dysmorphic features are usually mild and include long eyelashes, large or prominent ears, bulbous nose, pointed chin, fleshy hands, and dysplastic toenails
- Additional features include gastrointestinal problems, seizures, motor deficits, structural brain abnormalities, renal malformations, lymphedema, and recurrent infections



Phelan-Mc Dermid Syndrome: psychiatric disorders

“we conducted a systematic literature review and identified 56 PMS cases showing signs of behavioral and neurologic decompensation in adolescence or adulthood (30 females, 25 males, 1 gender unknown).

*Clinical presentations included features of **bipolar disorder, catatonia, psychosis, and loss of skills,** occurring at a mean age of 20 years”*

Neuropsychiatric decompensation in adolescents and adults with Phelan Mc Dermid Syndrome: a systematic review of the literature
Kolevzon et al., 2019

Section 2: Psychiatric disorders

- Neurodevelopmental disorders
- Schizophrenia spectrum and other psychotic disorders
- Bipolar and related disorders
- Depressive disorders
- Anxiety disorders
- Obsessive-compulsive and related disorders
- Dissociative disorders
- Somatic symptom disorders
- Feeding and eating disorders
- Elimination disorders
- Sleep-wake disorders
- Sexual dysfunctions
- Gender dysphoria
- Disruptive, impulse control and conduct disorders
- Substance use and addictive disorders
- Neurocognitive disorders
- Personality disorders
- Paraphilic disorders
- Other disorders

Bipolar disorder

- Prevalence: 1-4%
- Onset: 18-24y (earlier or later)
- Episodes: frequent or separated by many years or periods of hours or days (rapid cycling).
- Comorbid anxieties, psychotic symptoms, alcohol abuse
- High suicide risk: 15%

DSM5 Bipolar and related disorders

- Bipolar I disorder
- Bipolar II disorder
- Cyclothymic disorder
- Substance/medication-induced bipolar and related disorder
- Bipolar and related disorder due to another medical condition
- Other specified bipolar and related disorder
- Unspecified bipolar and related disorder

Types of bipolar disorder

- **Bipolar I disorder (classic manic depressive disorder):** at least one manic episode that may be (major depression is NOT a requirement) preceded or followed by hypomanic or major depressive episodes. In some cases, mania may trigger a break from reality (psychosis).
- **Bipolar II disorder.** at least one major depressive episode (typically accompanied by serious impairment in work and social functioning) and at least one hypomanic episode, but never a manic episode.
- **Cyclothymic disorder.** at least two years — or one year in children and teenagers — of many periods of hypomania symptoms and periods of depressive symptoms (though less severe than major depression), without ever fulfilling the criteria for an episode of mania, hypomania or major depression
- **Other types.** These include, for example, bipolar and related disorders induced by certain drugs or alcohol or due to a medical condition, such as Cushing's disease, multiple sclerosis or stroke.

Manic episodes

Inflated self esteem or grandiosity



Manic episodes



- Inflated self esteem or grandiosity
- Decreased need for sleep
- Racing thoughts

Manic episodes



Excessive involvement in activities that have a high potential for painful consequences (e.g. going on buying sprees, taking sexual risks or making foolish investments)

Manic episodes



Psychomotor agitation (purposeless), increase in goal-directed activity (socially, at work, sexually)

Manic episodes

Both a manic and a hypomanic episode include three or more of these symptoms:

- Inflated self esteem or grandiosity
- Decreased need for sleep
- Unusual talkativeness
- Racing thoughts
- Distractibility (attention drawn to unimportant or irrelevant stimuli)
- Psychomotor agitation (purposeless), increase in goal-directed activity (socially, at work, sexually)
- Excessive involvement in activities that have a high potential for painful consequences (e.g. going on buying sprees, taking sexual risks or making foolish investments)

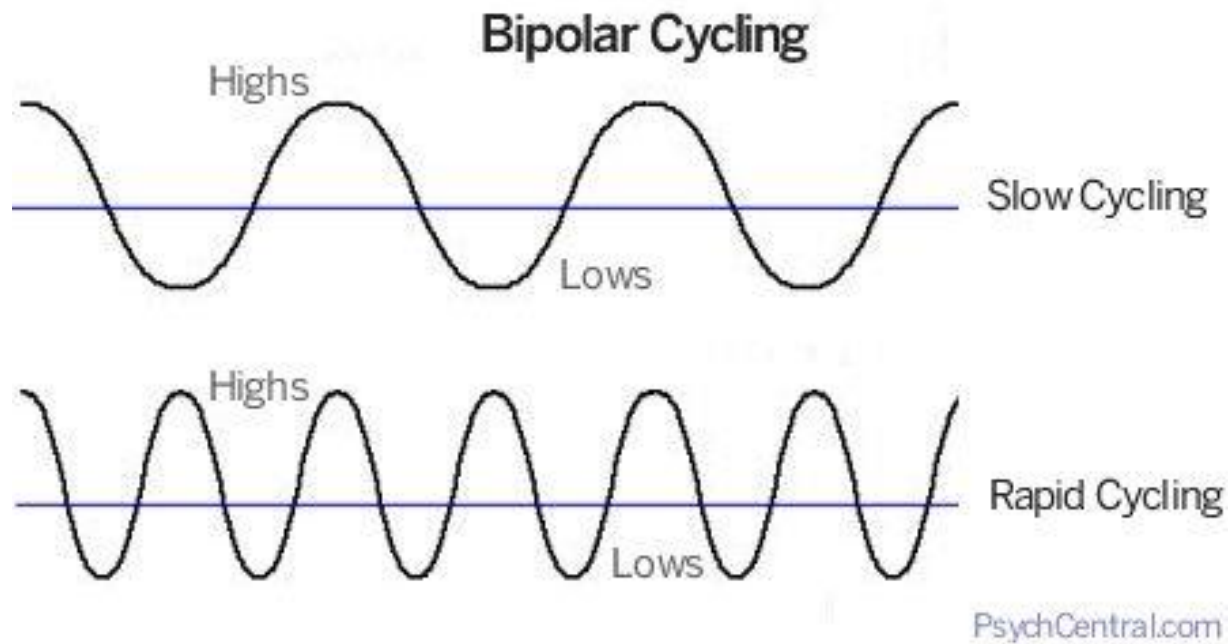
Major depressive episode



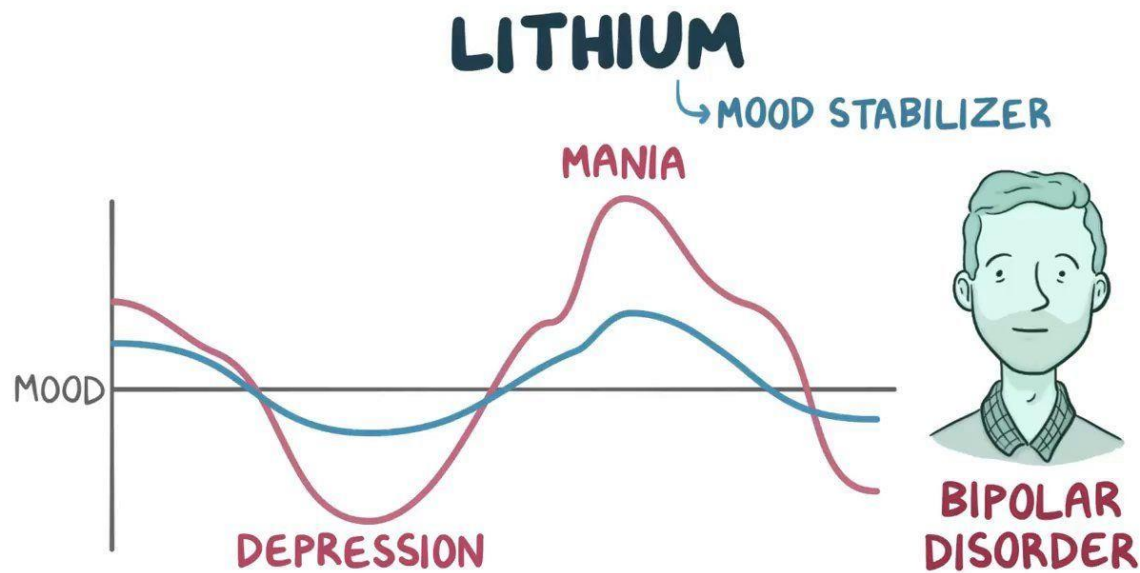
Major depressive episode

- An episode includes five or more of these symptoms:
- Depressed mood, such as feeling sad, empty, hopeless or tearful (in children and teens, depressed mood can appear as irritability)
- Marked loss of interest or feeling no pleasure in all — or almost all — activities
- Significant weight loss when not dieting, weight gain, or decrease or increase in appetite (in children, failure to gain weight as expected can be a sign of depression)
- Either insomnia or hypersomnia
- Either psychomotor agitation or retardation
- Fatigue or loss of energy nearly every day
- Feelings of worthlessness or excessive or inappropriate guilt nearly every day
- Decreased ability to think or concentrate, or indecisiveness nearly every day
- Recurrent thoughts of death, recurrent suicidal ideation or suicide attempt

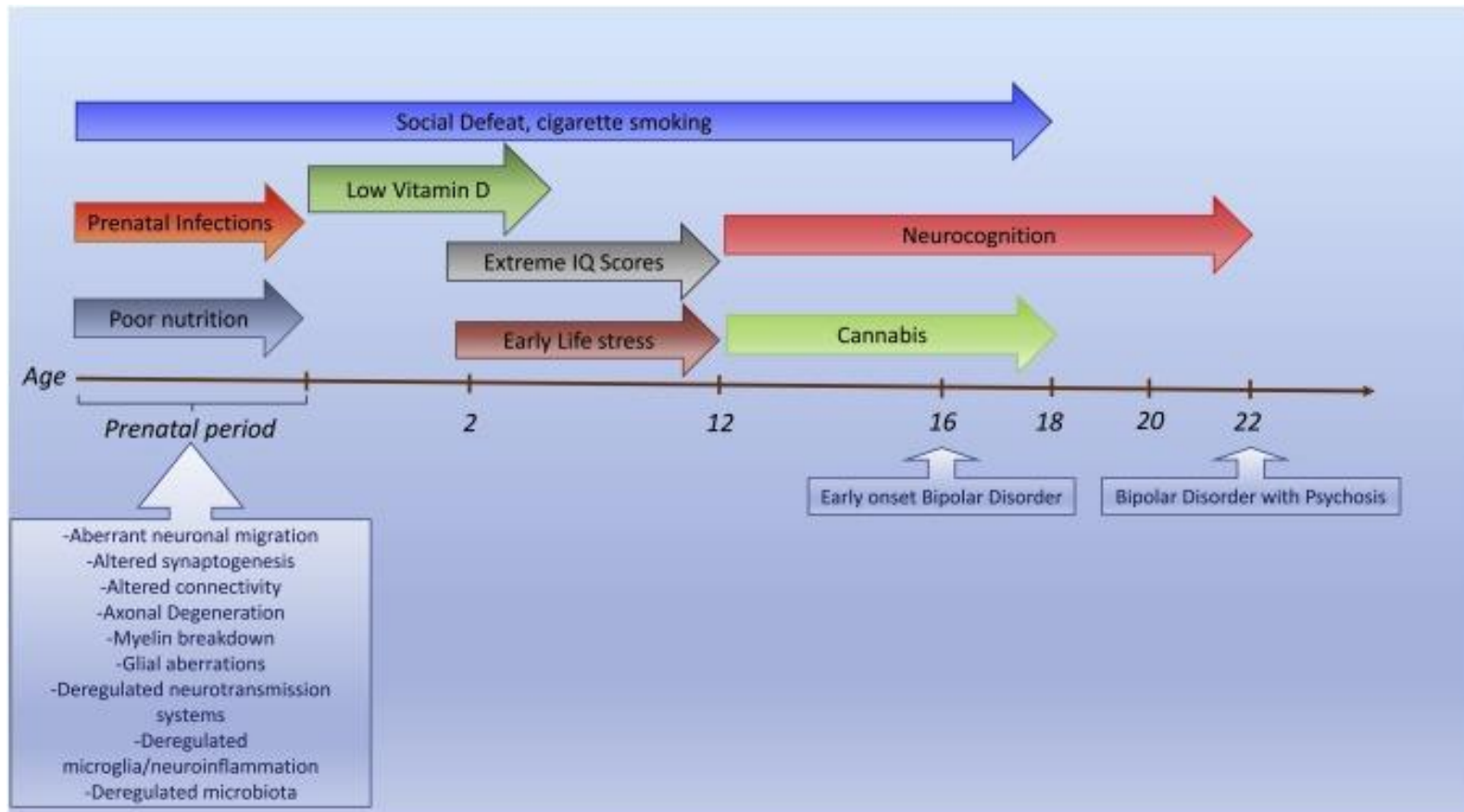
Core feature: Cycling



Core feature: response to lithium



Neurodevelopmental model for bipolar disorder



Bipolar disorders and genetics

- One of the most heritable psychiatric disorders
- Polygenic architecture overlapping with that of schizophrenia, major depression and other mental disorders
- Genome wide significant loci reported to date
Three genes are highlighted:
ANK3 on 10q21,2 (axonal myelinisation)
CACNA1C on 12p13 (neuronal development and synaptic signalling)
TRANK1 on 3p22 (maintenance blood-brain barrier)
- CNV's play a major role in schizophrenia but a smaller role in BPD:
16p11,2 duplication and 3q29 deletion

Stahl et al., Nat Genet 2019; 51(5):793-803

Approximative genetic risks in schizophrenia and bipolar disorder

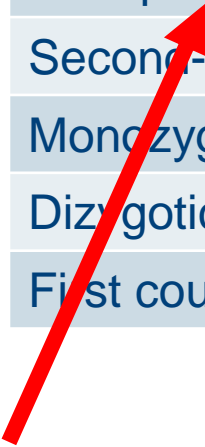
Harper's practical genetic counseling, Angus Clarke

Affected relative	schizophrenia	Bipolar disease
General population	1	2-3
Sib	9	13
Parent	13	15
Sib and one parent	15	20
Both parents	45	50
Second-degree relative	3	5
Monozygotic twin	40	70
Dizygotic twin	10	20
First cousin	1-2	2-3

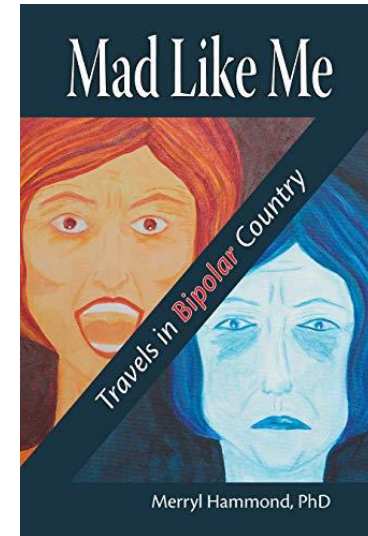
Approximative genetic risks in schizophrenia and bipolar disorder

Harper's practical genetic counseling, Angus Clarke

Affected relative	schizophrenia	Bipolar disease
General population	1	2-3
Sib	9	13
Parent	13	15
Sib and one parent	15	20
Both parents	45	50
Second-degree relative	3	5
Monozygotic twin	40	70
Dizygotic twin	10	20
First cousin	1-2	2-3



Assortative mating



- Assortative mating across psychiatric and other traits like educational and social status
- Assortative mating can lead to accumulation of risk alleles in subsequent generations with consequent increase in rates or severity of illness across generations of a family known as anticipation

Section 2: Psychiatric disorders

- Neurodevelopmental disorders
- Schizophrenia spectrum and other psychotic disorders
- Bipolar and related disorders
- Depressive disorders
- Anxiety disorders
- Obsessive-compulsive and related disorders
- Dissociative disorders
- Somatic symptom disorders
- Feeding and eating disorders
- Elimination disorders
- Sleep-wake disorders
- Sexual dysfunctions
- Gender dysphoria
- Disruptive, impulse control and conduct disorders
- Substance use and addictive disorders
- Neurocognitive disorders
- Personality disorders
- Paraphilic disorders
- Other disorders

DSM5: Depressive disorders

- Disruptive mood dysregulation disorder (6-18y)
- Major depressive disorder
- Persistent depressive disorder (dysthymia)
- Premenstrual dysphoric disorder
- Substance/medication-induced depressive disorder
- Depressive disorder due to another medical condition
- Other specified depressive disorder
- Unspecified depressive disorder

Major depressive episode

- An episode includes five or more of these symptoms during a two week period:
- Depressed mood, such as feeling sad, empty, hopeless or tearful (in children and teens, depressed mood can appear as irritability)
- Marked loss of interest or feeling no pleasure in all — or almost all — activities
- Significant weight loss when not dieting, weight gain, or decrease or increase in appetite (in children, failure to gain weight as expected can be a sign of depression)
- Either insomnia or hypersomnia
- Either psychomotor agitation or retardation
- Fatigue or loss of energy nearly every day
- Feelings of worthlessness or excessive or inappropriate guilt nearly every day
- Decreased ability to think or concentrate, or indecisiveness nearly every day
- Recurrent thoughts of death, recurrent suicidal ideation or suicide attempt

Major Depressive Disorder: DSM-5

- A. 5 (or more) of the following symptoms have been present during the same 2-week period and represent a change from previous functioning; at least one of the symptoms is either (1) depressed mood or (2) loss of interest or pleasure.
 - Note:** do not include symptoms that are clearly attributable to another medical condition
 - (1) Depressed mood most of the day, nearly every day
 - (2) Markedly diminished interest or pleasure in all, or almost all, activities most of the day, nearly every day
 - (3) Significant weight loss when not dieting or weight gain (e.g., a change of more than 5% of body weight in a month), or decrease or increase in appetite nearly every day.
 - (4) Insomnia or Hypersomnia nearly every day
 - (5) Psychomotor agitation or retardation nearly every day
 - (6) Fatigue or loss of energy nearly every day
 - (7) Feelings of worthlessness or excessive or inappropriate guilt nearly every day
 - (8) Diminished ability to think or concentrate, or indecisiveness, nearly every day
 - (9) Recurrent thoughts of death (not just fear of dying), recurrent suicidal ideation without a specific plan, or a suicide attempt or a specific plan for committing suicide
- B. The symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.
- C. The episode is not attributable to the physiological effects of a substance or another medical condition
- E. There has never been a manic episode or a hypomanic episode
- **Note:** This exclusion does not apply if all of the manic-like or hypomanic-like episodes are substance-induced or are attributable to the physiological effects of another medical condition. The symptoms are not better accounted for by Bereavement

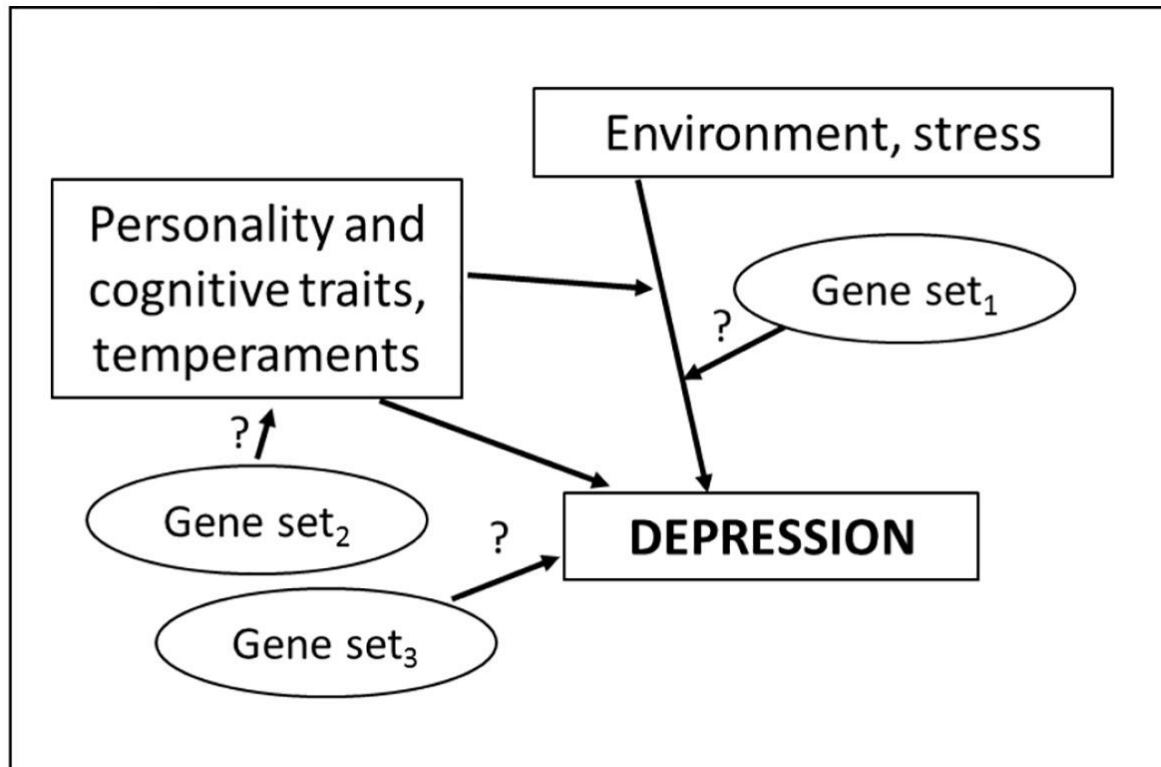
Core feature of a major depressive episode

- Depressed mood is a normal human emotion; in major depressive disorder, however, depressed mood becomes nearly unremitting, unshakable and associated with cognitive and physical symptoms.
- It is clinically heterogeneous and individuals vary greatly in their symptom severity, treatment response, and outcome.

Depression and genetics

- Heritability: modest: 40%
- Prevalence: high
 - medical students: 26% (Rotenstein et al., 2016)
 - physicians in training: 28% (Mata et al., 2016)
- Role of environmental factors: high
- Phenotypic heterogeneity

genetic research is lagging behind



Gene sets include certain genes and Gene x Gene interactions

Proposed mechanism for the development of depression (Bagdy, Juhasz, & Gonda, 2012). The figure depicts possible interrelations that may shape depression. Genes that may influence the disease directly (Gene set₃) are rare and are usually involved in basic functions thus are unfeasible as therapeutic targets. Gene set₂ contains genes that contribute to personality traits, whose different combination in different individuals may results in the disease and can represent a subset of therapeutic targets in the future. The personality traits, temperaments and cognitive functions act together with environmental stress, for which individuals are sensitized through a different set of genes (Gene set₁) in shaping depression

Depression in intellectually disabled

- Poor verbal skills
- Based on non-verbal signs: behaviour and daily living skills

Major depressive episode in intellectually disabled: DSM5 criteria are based on normal verbal capacities

- An episode includes five or more of these symptoms during a two week period:
- Depressed mood, such as feeling sad, empty, hopeless or tearful (in children and teens, depressed mood can appear as irritability)
- Marked loss of interest or feeling no pleasure in all — or almost all — activities
- Significant weight loss when not dieting, weight gain, or decrease or increase in appetite (in children, failure to gain weight as expected can be a sign of depression)
- Either insomnia or hypersomnia
- Either psychomotor agitation or retardation
- Fatigue or loss of energy nearly every day
- Feelings of worthlessness or excessive or inappropriate guilt nearly every day
- Decreased ability to think or concentrate, or indecisiveness nearly every day
- Recurrent thoughts of death, recurrent suicidal ideation or suicide attempt

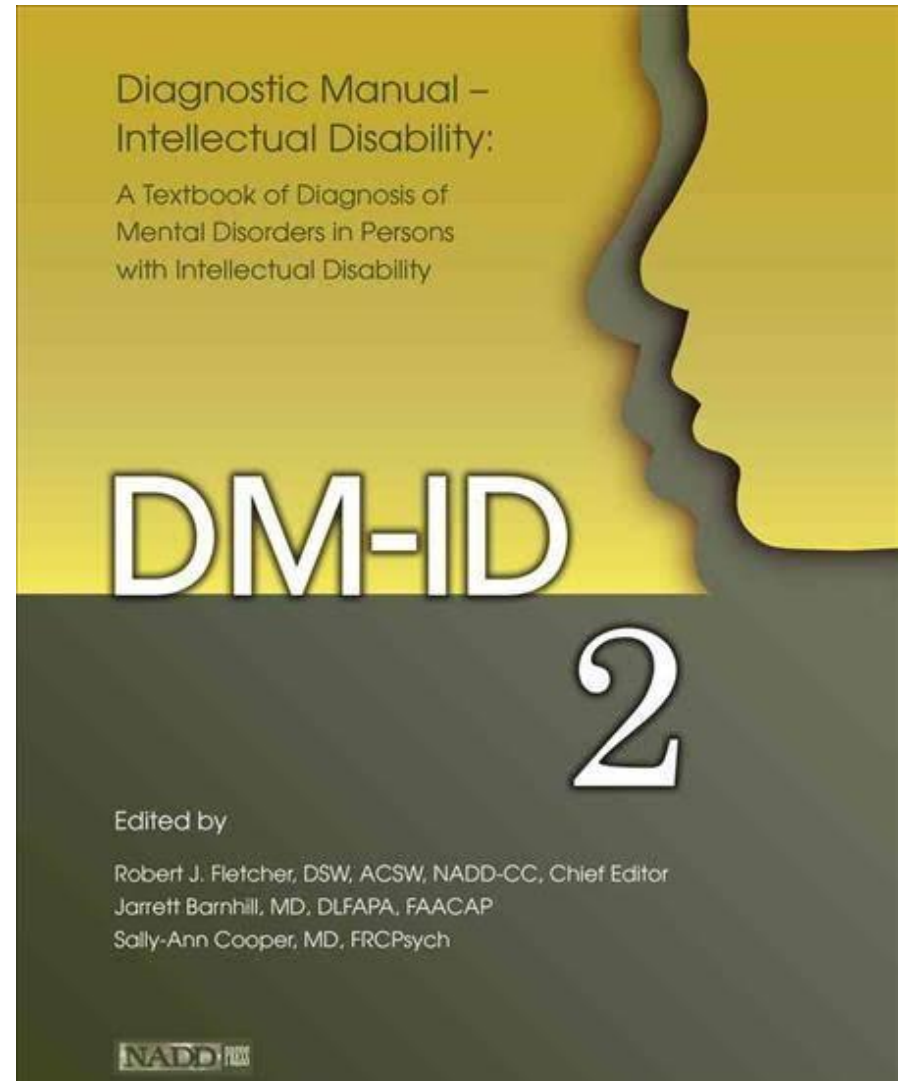
Symptoms in intellectually disabled

NADD An association for persons with developmental disabilities and mental health needs.

**Modification of DSM-5 Criteria
Change in Count and Symptom Equivalent
Major Depressive Disorder**

DSM-5 Criteria	Applying Criteria for Mild to Profound IDD
A. Five or more of the following symptoms have been present during the same 2 week period and represent a change from previous functioning. At least one of the symptoms is either (1) depressed mood or (2) loss of interest or pleasure.	A. Four or more symptoms have been present during the same 2 week period and represent a change from previous functioning. At least one of the symptoms is either (1) depressed mood or (2) loss of interest or pleasure or (3) irritable mood .

(DM-ID-2, 2016)



Over the past year there have been increasing problems with self-reliance and under

16j

Over the past year there have been increasing **problems with self-reliance** and understanding assignments.

He can no longer wash himself, dress himself or eat alone.

He has gradually become **less talkative** and now says nothing.

He **no longer has any interest** in his family members, his friends, nor in any activity.

His appetite has decreased and there has been a **weight loss** of seven kg.

He falls asleep very late. At night he sits on his bed, rocking while talking to himself.

His mother describes him as anxious and says that he often **starts laughing or crying** for no apparent reason.

It happens that he suddenly **can no longer perform acquired skills** such as cycling, going down stairs, etc



alamy stock photo

RJWXTW
www.alamy.com

Depressie bij het syndroom van Down

16j

Het afgelopen jaar zijn er toenemende problemen met zelfredzaamheid en het begrijpen van opdrachten. Hij slaagt er niet meer in zich te wassen, zich te kleden noch alleen te eten. Hij is geleidelijk aan minder spraakzaam geworden en zegt nu niets meer. Hij heeft geen interesse meer voor zijn familieleden, zijn vrienden, noch voor enige activiteit. Zijn eetlust is verminderd er is een gewichtsverlies van zeven kg. Hij slaapt zeer laat in. 's Nachts zit hij op zijn bed te wiegen terwijl hij in zichzelf praat. Zijn moeder beschrijft hem als angstig en vertelt dat hij vaak zonder enige duidelijke aanleiding begint te lachen of te huilen. Het gebeurt het dat hij verworven vaardigheden plots niet meer kan uitvoeren zoals fietsen, de trap afgaan,...



alamy stock photo

RJWXTW
www.alamy.com

Schizophrenia in intellectually disabled with psychiatric disorders

-Belgium, Leuven: inpatient unit for adults with a dual diagnosis admitted to a psychiatric unit for intellectually disabled (n=272)

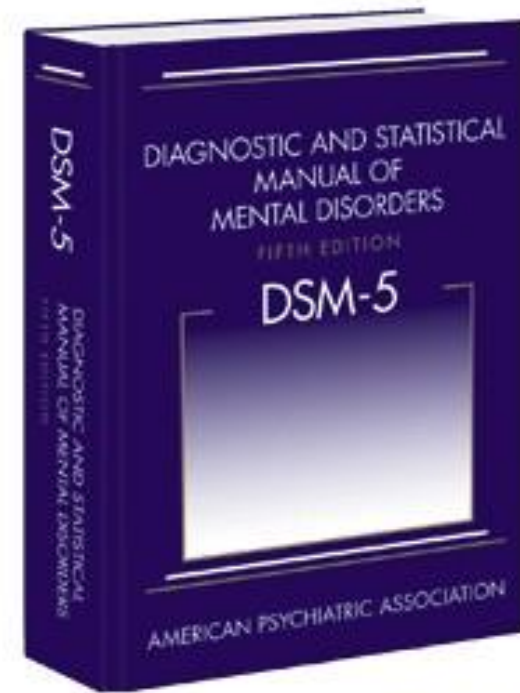
- velo-cardio-facial syndrome: 11/272

22q11deletion

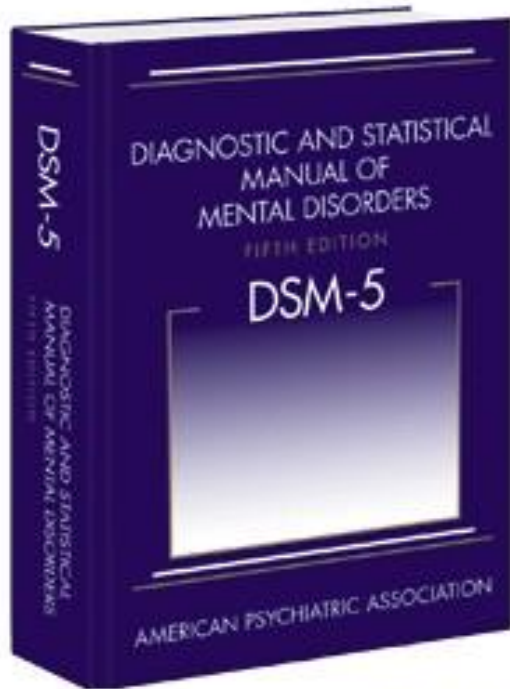
	Presenting symptoms	Psychiatric diagnosis	Age at diagnosis	During /before admission Systematic screening	Size deletion (F/M)	Sex (F/M)	Level of intellectual disability
1	Verbal & Physical aggression Depressive mood Anxiety	Schizo-affective disorder	58 y	During admission		F	Severe
2	Verbal & Physical aggression Selfneglect Depressive mood	Mood disorder NOS Personality disorder NOS Alcohol abuse	50 y	During admission	3 Mb (aCGH)	M	Mild
3	Sexual misconduct Mood swings	Paraphilia NOS Personality disorder NOS	3 y	Before admission	3Mb (aCGH)	M	Moderate
4	Physical aggression Anxiety	Personality disorder NOS	39 y	During admission	1,5Mb (aCGH)	M	Severe
5	Verbal aggression Paranoïd thoughts Logorrhea	Schizo-affective disorder	34 y	During admission	3Mb (aCGH)	F	Moderate
6	Verbal & Physical aggression Paranoïd thoughts	Psychotic disorder NOS Borderline personality disorder	49 y	During admission	3Mb (aCGH)	M	Mild
7	Runaway behavior Stealing	Reactive attachment disorder	19 y	During admission	3Mb (aCGH)	M	Mild
8	Mood swings Panic attacks Alcohol dependence	Mood disorder NOS	54 y	During admission	3Mb (aCGH)	M	Moderate
9	Behavioral problems Depressive mood	Diagnosis unknown	39 y	During admission, before screening		M	
10	Verbal & Physical aggression Mood swings	Borderline personality disorder	35 y	During admission, before screening		F	Mild
11	Depressive mood Sleeping problems	Paranoïd schizophrenia	17 y	Before admission		F	Mild

Section 2: Psychiatric disorders

- Neurodevelopmental disorders
- Schizophrenia spectrum and other psychotic disorders
- Bipolar and related disorders
- Depressive disorders
- Anxiety disorders
- Obsessive-compulsive and related disorders
- Dissociative disorders
- Somatic symptom disorders
- Feeding and eating disorders
- Elimination disorders
- Sleep-wake disorders
- Sexual dysfunctions
- Gender dysphoria
- Disruptive, impulse control and conduct disorders
- Substance use and addictive disorders
- Neurocognitive disorders
- Personality disorders
- Paraphilic disorders
- Other disorders



DSM-5
2013



DSM-5
2013

