Cannabinoids and Health

Module 10

Lecture 3: Etiology of Mood Disorders and Psychosis

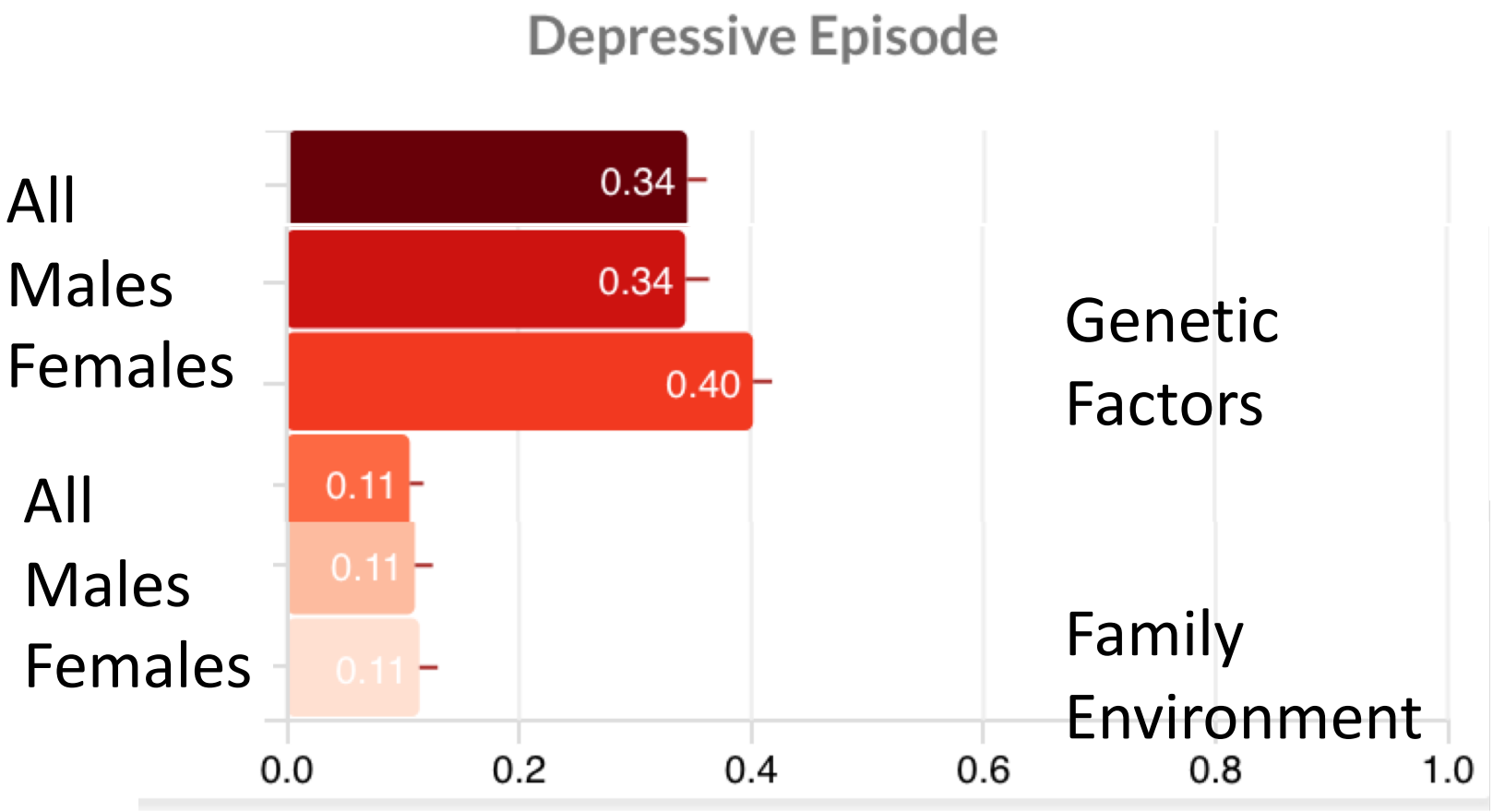
Etiology: Depression

- Family studies suggest that genetic factors are important in depression
  - The rates of mood disorders are 2-3x higher if a person's relative with a mood disorder
  - Severity in relatives is relevant (more severe = more risk).
- Twin studies further support to this genetic hypothesis
  - For depression (heritability = 35-45%; environment = 55-65%)
    - Non-identical twin concordance: 20%
    - Identical twin concordance: 46%

Etiology: Depression

Meta-analysis of the heritability of human traits based on fifty years of twin studies

Tinca J C Polderman[1,10], Beben Benyamin[2,10], Christiaan A de Leeuw[1,3], Patrick F Sullivan[4–6], Arjen van Bochoven[7], Peter M Visscher[2,8,11] & Danielle Posthuma[1,9,11]



Etiology: Depression

- Biology plays an important role
  - Monoamine theory of depression is based on the efficacy of early monoaminergic drugs in treating depression.
    - Insufficient activity of **monoamines (e.g., serotonin, dopamine)** are a proposed cause of depression.
    - Some suggest low levels of serotonin lead to broad dysregulation
  - Evidence of monoamine theory
    - Depletion of precursors to serotonin can cause depression in those in remission
    - Enzymes that break down serotonin linked to depression
  - However, these theories are flawed/incomplete.
    - Drugs that target serotonin may be no better than placebo.
    - Serotonin depletion does not seem to cause depression.

Etiology: Depression

- Other theories focus on cognitive styles
  - Learned helplessness: anxiety is a first response to stress, and depression follows if one feels they can't control the stressor
  - Negative Cognitive Style of Depression
    - Depression is comprised of the cognitive triad:
      - Thinking negatively about themselves
      - Thinking negatively about their immediate world
      - Thinking negatively about their future
  - These cognitive styles have been linked to the neurobiological causes of depression (last slide) – chicken/egg: which is first?

Etiology: Bipolar/Psychosis

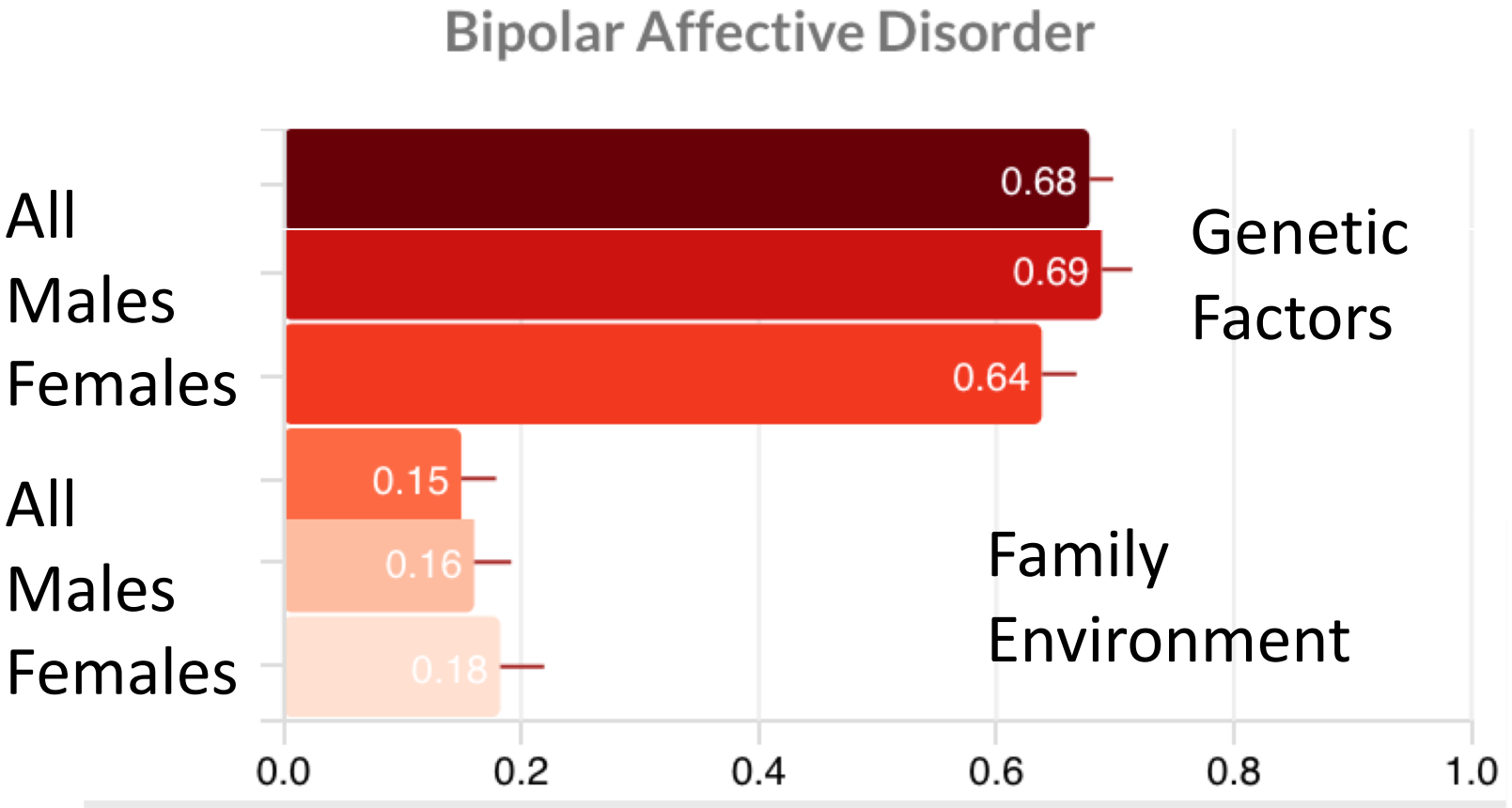
- Of all psychiatric conditions, bipolar/psychosis have the strongest link to genetic factors
  - The rates of mood disorders are 2-3x higher if a person has a relative with a mood disorder
  - Severity in relatives is relevant (more severe = more risk)

- Twin studies further support to this genetic hypothesis
  - For bipolar (heritability = 60-70%)
    - Non-identical twin concordance: 19%
    - Identical twin concordance: 67%

Etiology: Bipolar/Psychosis

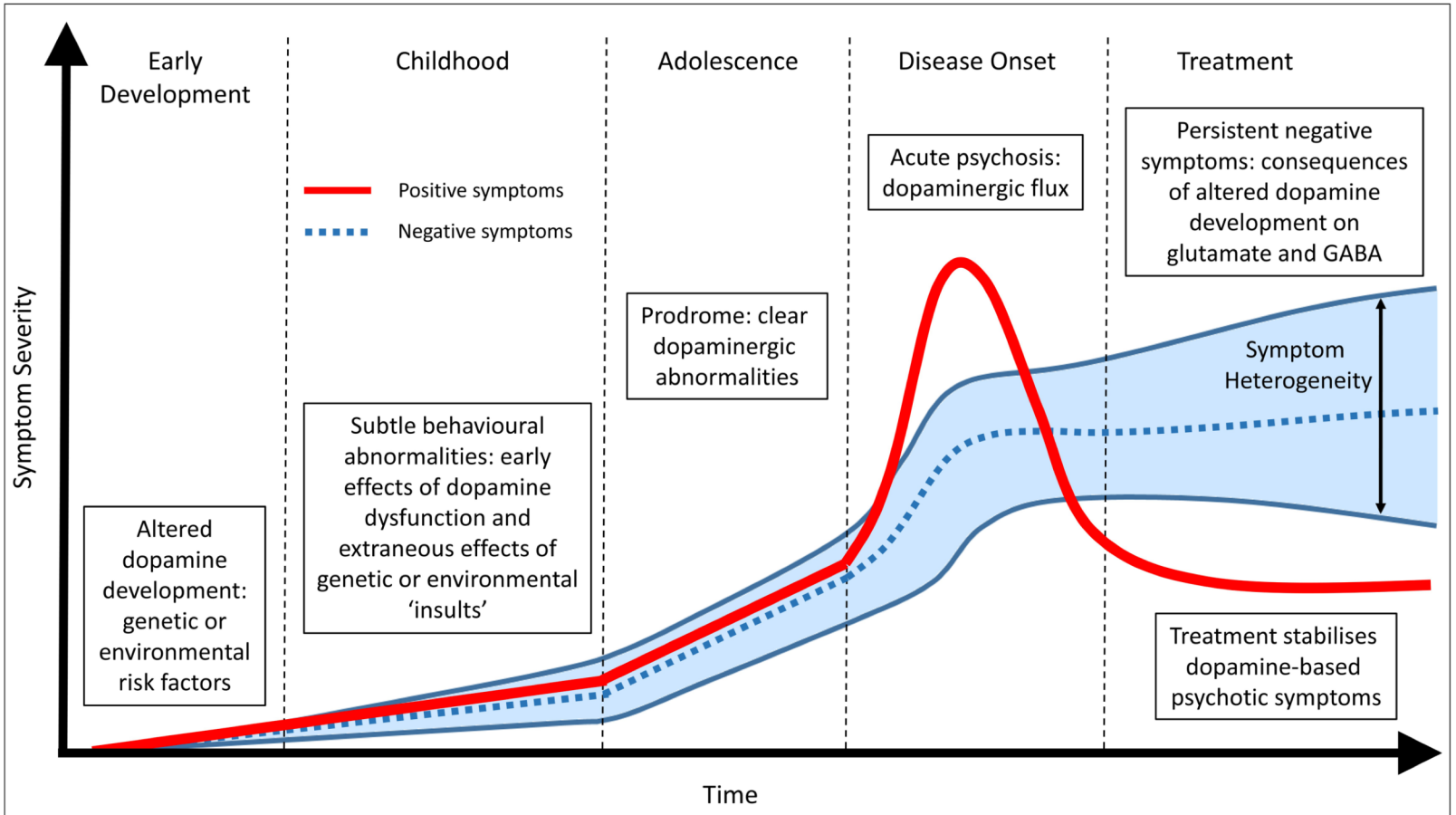
Meta-analysis of the heritability of human traits based on fifty years of twin studies

Tinca J C Polderman[1,10], Beben Benyamin[2,10], Christiaan A de Leeuw[1,3], Patrick F Sullivan[4–6], Arjen van Bochoven[7], Peter M Visscher[2,8,11] & Danielle Posthuma[1,9,11]



Etiology: Bipolar/Psychosis

- Dopamine in Bipolar Disorder
  - Dopamine is broadly related to mood cycling
  - Has been shown to have increased transmission during the manic phase
  - Findings that dopamine agonists can stimulate mania in people with bipolar disorder further supports this hypothesis



Temporal profile of developing schizophrenia symptoms. Early alterations in dopamine development due to genetic, environmental or a combination of both lead to abnormalities in dopamine function (positive symptoms) and subsequent alterations in other neurotransmitter systems (negative symptoms). During adolescence and the prodromal phase of the disease clear changes in dopamine function can be observed. Kesby et al., 2013, Frontiers in Neuroscience, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3713405/pdf/fncel-07-00111.pdf

Etiology: How Does Cannabis Fit In?

- Mood disorders and psychosis have clear neurobiological links.
  - Some are concerned that cannabis can play a causal role in exacerbating, or precipitating, these conditions.
  - In future lectures the evidence for causality, for cannabis and psychiatric conditions
  - We also look at current treatments, including their efficacy and side effects
  - Finally, we'll evaluate the evidence on whether cannabis or its constituents might be able to treat these conditions