Depression and Antidepressants: epidemiology and statistics

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Outline

• How common is depression, and how common is untreated depression?

• How commonly are antidepressants used? Are antidepressants always for depression?

• How effective are antidepressants? What effects do they have on the brain?
Depression Prevalence: overall

• 8.4% of community dwelling adults are currently depressed. (Olfson 2016)¹

• 10.6% of the population met DSM-IV criteria for Major Depression or Dysthymia in the last 12 months. (Alegria 2008)²,³,⁴

¹ Medical Expenditure Panel Surveys
² National Latino and Asian American Study
³ National Comorbidity Survey Replication
⁴ National Survey of African American Life
Past-year Depression Prevalence:

by race/ethnicity

11.2% of Whites*

10.8% of Latinos
8.0% of African-Americans
5.4% of Asians

* Significantly higher in whites than other groups (Alegria 2008)
2. National Latino and Asian American Study
3. National Comorbidity Survey Replication
4. National Survey of African American Life
Depression rates vs. Treatment rates

**Depression**
- 6.0%
- Current depression
- no past year treatment
- (n=2,775)

**Treatment**
- 5.7%
- Past year treatment
- No current depression
- (n=2,636)

2.4%
Depressed & past year treatment
(n=1,124)

Extrapolation from (Olfson 2016)
1. Medical Expenditure Panel Surveys
Non-treatment rates among depressed persons

- 71.5% of depressed persons received no depression treatment (in the survey year)
- Non-treatment was more prevalent among:
  - Males
  - Younger adults (<35 years old)
  - Older adults (>64 years old)
  - Non-whites
  - No high school diploma
  - No health insurance
- 78.5% of adults with untreated depressed saw a medical doctor (in the survey year)

(Olfson 2016)
1. Medical Expenditure Panel Surveys
Non-Treatment rates among depressed adults (in the past year)

(Alegria 2008)
2 National Latino and Asian American Study
3 National Comorbidity Survey Replication
4 National Survey of African American Life

*Adequate Treatment:
4+ healthcare visits & 30 days or more of antidepressant use;
8 + visits to a mental health provider lasting 30+ minutes with no antidepressant
Antidepressant use: community-dwelling adults

Antidepressants are the 3rd most common medication class, after antihypertensives (27%) and antihyperlipidemic agents (18%).

(Kantor 2015)
7. National Health and Nutrition Examination Survey
Over-treating depression?

• 70.1% of adults getting depression treatment* did not currently have depression (screened negative on the PHQ-2 for the 2 weeks before the survey) (Olfson 2016)

• 79.7% of adults receiving antidepressants did not currently have serious psychological distress (in the 30 days before the survey) (Olfson 2016)

• 9.5% of physician office visits (to non-psychiatrists) resulted in an antidepressant prescription but no psychiatric diagnosis (Mojtabai 2011)

1. Medical Expenditure Panel Surveys
8. National Ambulatory Medical Care Surveys

* 87% were using an antidepressant
Effectiveness of Antidepressants versus Placebo

<table>
<thead>
<tr>
<th>Hamilton Depression Rating Scale</th>
<th>Mild to Moderate Depression</th>
<th>Severe Depression</th>
<th>Very Severe Depression</th>
</tr>
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<tbody>
<tr>
<td>Antidepressants versus Placebo</td>
<td>18 or less</td>
<td>19-22</td>
<td>23+</td>
</tr>
<tr>
<td>Interpretation</td>
<td>Minimal effect over placebo</td>
<td>Minimal effect over placebo</td>
<td>Small effect over placebo</td>
</tr>
</tbody>
</table>

Antidepressants do not separate from Placebo (defined as 3 points off the Hamilton) until patients are starting with Hamilton scores of 25 or greater.

(Fournier 2010)

Cohen d definitions: 0.2 = small effect, 0.5 = medium effect
Effectiveness of Antidepressants: Number Needed to Treat

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<tr>
<td>Hamilton Depression</td>
<td>16</td>
<td>11</td>
<td>4</td>
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</tbody>
</table>

Aspirin:
Number needed to treat to prevent 1 myocardial infarction is 67.
Number needed to harm: If 1000 persons receive daily aspirin for 5 years, expect 1.9 cerebral hemorrhages, 1.7 major bleeds, 7.6 non-minor bleeds.

(Fournier 2010), (Sanmuganathan 2001)
Effectiveness of Antidepressants: STAR*D

• Multi-center randomized controlled trial
• Enrolled 3,671 adults with major depression
• 33% never achieved remission of symptoms
• 50% who achieved remission suffered a relapse within 12 months

Star*D Treatment Sequence:
1) Citalopram
2) Bupropion, Sertraline, Venlafaxine, Citalopram & Bupropion, Citalopram & Buspirone, Citalopram & Cognitive therapy, Cognitive Therapy
3) Nortriptyline, Mirtazapine, Lithium, T3, Bupropion, Venlafaxine
4) Tranylcypromine, Venlafaxine & Mirtazapine, Nortriptyline, Mirtazapine, Lithium, T3

(Rush 2006)
Brain Changes amidst Antidepressant use

**Structural Changes:**
Antidepressants enlarged the middle frontal gyrus, dorsolateral prefrontal cortex and orbitofrontal cortex; Geriatric patients previously exposed to antidepressant treatment had larger orbitofrontal cortex volumes compared to drug-naïve patients; Female responders (after 8 weeks of fluoxetine) had larger caudate nucleus compared to male responders and to female non-responders; Increased right hippocampal volumes were found in female responders after 8 weeks of fluoxetine treatment; Patients who remitted with antidepressants had less hippocampus shrinkage at 3 year follow up (Dusi 2015)

**Functional Changes: (R- right, L-left)**
Activation of: anterior cingulate cortex (R), Insula (R&L), Middle frontal gyrus (L), Precentral (L), postcentral gyrus (L), cingulate gyrus (L), caudate nuclei (R&L), putamen (L), declive (L), precuneus (L) (Boccia 2016)
Brain Changes amidst Depression

Whole brain volume; Whole gray matter volume; White matter hyperintensities appear; reduced volume in prefrontal/orbitofrontal cortex; reduced volume of anterior cingulate; Shrinkage of medial prefrontal cortex in drug naïve patients; Anterior cingulate volume reduction progresses faster than in healthy controls; Orbitofrontal cortex, cingulate cortex, insula, and temporal operculum have less cortical folding; Reduced temporal gray matter; Superior temporal gyrus volume gets smaller the longer the illness lasts among unmedicated patients; Paralimbic areas in the temporal lobes have greater cortical thickness in first episode and child-adolescence depression; Putamen and Caudate nucleus have reduced volume; Hyperintensities in putamen and globus pallidus (mostly in elderly patients); Reduced volume of thalamus; Smaller hippocampal volumes among chronic, acute, and non-remitting patients (with progressive reduction over time); Amygdala is reduced, especially in unmedicated and recurrent patients; Larger volume of third ventricle, lateral ventricles, and CSF enlargement; Smaller hippocampal volume is associated with depression severity, early onset, refractory illness, longer duration of untreated depression, comorbidity with childhood abuse, and high levels of disease burden

(Dusi 2015)
Brain Changes amidst Psychotherapy

Functional Changes: (R- right, L-left)
Activation of: precentral gyrus (R&L), culmen (R), superior and inferior frontal gyri (L), lingual and fusiform gyri (L), middle temporal gyrus (L)

(Boccia 2016)
Conclusions:

• How common is depression?
  • 1 in 10 adults has depression
  • 1 in 20 adults has untreated depression

• How commonly are antidepressants used?
  • 13% of adults use antidepressants
  • Sometimes it’s not clear why

• How effective are antidepressants?
  • They are better than placebo, but only for very severe depression

• What effects do they have on the brain?
  • Medication changes your brain, so does psychotherapy, so does untreated depression


References

Mojtabai R, Olfson M. Proportion of antidepressants prescribed without a psychiatric diagnosis is growing. Health Affairs. 2011; 30(8): 1434-1442.


Study Descriptions

[1] Medical Expenditure Panel Surveys. Dates of data collection: 2012-2013. Sample: Nationally representative sample of household adults (n=46,417). Assessment methods: Data were collected by face-to-face interviews. The Patient Health Questionnaire-2 (PHQ-2) was used to screen for depressed mood and anhedonia during the past 2 weeks. Participants screened positive for depression if they had a PHQ-2 score of 3 or less. Psychological distress was assessed using the Kessler 6 scale, which asks about the frequency of mental health symptoms in the past 30 days.

[2] National Latino and Asian American Study. Dates of data collection: 2002-2003. Sample: Nationally representative survey of household residents, ages 18 and older, among Latino and Asian populations in the United States. The response rate was 73.2%. Assessment methods: Interviews were conducted by professional interviewers. Depression was assessed using the World Health Organization Composite International Diagnostic Interview, which generates DSM-IV diagnoses for conditions occurring over the past 12 months. Functional impairment was assessed using the World Health Organization Psychiatric Disability Assessment Schedule.
Study Descriptions

[3] National Comorbidity Survey Replication. Dates of data collection: 2001-2002. Sample: Nationally representative study of non-institutionalized adults ages 18 or older, living in the United States. The response rate was 70.9%. Assessment methods: Interviews were conducted by professional interviewers. Depression was assessed using the World Health Organization Composite International Diagnostic Interview, which generates DSM-IV diagnoses for conditions occurring over the past 12 months. Functional impairment was assessed using the World Health Organization Psychiatric Disability Assessment Schedule.

[4] National Survey of African American Life. Dates of data collection: 2001-2003. Sample: Nationally representative survey of household residents in the non-institutionalized Black population. The response rate was 70.9%, and included 3,570 African-Americans and 1,621 Black respondents of Caribbean descent. Assessment methods: Interviews were conducted by professional interviewers. Depression was assessed using the World Health Organization Composite International Diagnostic Interview, which generates DSM-IV diagnoses for conditions occurring over the past 12 months. Functional impairment was assessed using the World Health Organization Psychiatric Disability Assessment Schedule.
Study Descriptions

[5] National Comorbidity Survey – Adolescent Supplement. Dates of data collection: 2002-2003. Sample: Nationally representative sample of 10,123 adolescents age 13-18. The response rate was 82.9%. Assessment methods: Data were collected by face to face surveys in households and in schools. Depression was identified using the World Health Organization Composite International Diagnostic Interview Version 3.0 (CIDI), which is a structured interview administered by trained lay interviewers that generates DSM-IV diagnoses. Respondents were asked whether they had received treatment in the last 12 months. Psychotropic medication use was assessed by presenting participants with a list of 215 names of psychotropic medications. Participants were asked which medications they had taken during the past 12 months. Participants were asked to check the medication bottle for the exact name of the medications they used.

[6] Medicare Current Beneficiary Survey. Dates of data collection: 2001-2005. Sample: Nationally representative sample of Medicare beneficiaries ages 65 and older, including those who live in long-term care facilities. The final sample was 12,353 unique persons contributing 33,708 person-years of observations. Assessment methods: Data came from beneficiary interviews and from Medicare claims. Depression was defined as having a medical care claim during the observation year with depression listed as a diagnosis. Depression was also assessed during interviews by administering a modified version of the Patient Health Questionnaire (PHQ-2). Depression assessment questions were: “In the past 12 months how much of the time did you feel sad, blue, or depressed?” and “In the past 12 months, did you have 2 weeks or more when you lost interest or pleasure in things that you usually cared about or enjoyed?” Treatment was defined as receiving either psychotherapy or antidepressant medications in the same observation year. During interviews, interviewers reviewed medication containers, reviewed explanations of benefits, and collected data on filled prescriptions. Treatment was also assessed by reviewing medical claims from that year.
Study Descriptions

[7] National Health and Nutrition Examination Survey (NHANES). Dates of data collection: 1999 was the first year of continuous sampling, 2012 is the most recent cycle for which data are available. Sample: Nationally representative cross-sectional survey of civilian noninstitutionalized persons living in the United States. The response rate was 73.6%. The final sample size was 37,959 (the sample size for individual NHANES cycles ranged from 4,861 to 6,212). Assessment methods: Information about prescription drug use was collected during face-to-face household interviews. Participants were asked if they had taken prescription drugs over the prior 30 days. Those who said “yes” were asked to show the containers of all products used (84% of the medication containers were seen by interviewers).

[8] National Ambulatory Medical Care Surveys. Dates of data collection: 1996-2007. Sample: National sample of visits by patients (age 18 or older) to office-based physicians. The survey design randomly selects a one-week period in each year and solicits a systematic sample of visits from each physician surveyed. The response rate ranged from 62.9%-77.1% (median 67.7%). Total n=233,144. Assessment methods: Each physician or a staff member completing the survey provides information about the patient’s social, demographic, and clinical characteristics and the medications prescribed at the visit. Antidepressant use was gathered from the doctor’s documentation of what medicines were prescribed (respondents can list up to 6 medications per visit). The reason for the visit was discerned by reviewing patient’s complaints (the “reason for visit” code), or by reviewing the diagnoses associated with each visit (providers could list up to three diagnoses, using ICD-9 codes). For this analysis, the authors excluded psychiatry visits, and focused instead on primary care visits and other non-psychiatrist physician visits.
ADHD and Stimulants: epidemiology and statistics

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"Like many of my friends, I spent years using prescription stimulants to get through school and start my career. Then I tried to get off them."

By CASEY SCHWARTZ
Outline

• How common is ADHD?
• How common are stimulant use and abuse?
• Are stimulants effective for treating ADHD?
ADHD Prevalence:

Adolescents (ages 13-18)
• 8.7% have ADHD
• 13.0% of males, 4.2% of females
• 4.2% (half) of all ADHD cases are severe

Adults (ages 18-44)
• 4.4% have ADHD

(Merikangas 2010) (Kessler 2006)
1. National Comorbidity Survey – Adolescent Supplement
2. National Comorbidity Survey - Replication
ADHD Prevalence (adults)

Risk Factors Associated w ADHD
- Male 5.4% (vs. female 3.2%)
- White 5.4% (vs. Black 1.9%, Hispanic 2.1%)
- Previously Married 6.9% (vs. married-cohabiting 3.9%)

Factors not associated with ADHD
- Age
- Education level
- Income

(Kessler 2006)
2. National Comorbidity Survey - Replication
ADHD Treatment Rates

Current treatment:

• Youths (ages 4-17) ⁵ (Visser 2007)
  • 56.3% (half) of youths with ADHD are taking medication
  • 4.3% of all youths have ADHD and are taking medication

• Adults² (Kessler 2006)
  • 10.9% of adults with ADHD received treatment in the past 12 months

2. National Comorbidity Survey - Replication
5. National Survey of Children’s Health
Stimulant prescriptions among youths

- 2.8 million children received stimulants in 2008
- Higher rates among:
  - Whites (vs. African Americans & Hispanics)
  - Insured (vs. uninsured)
  - Publicly insured (vs. private)
  - Northeast (vs. West)

(Zuvekas 2012)

6. Medical Expenditure Panel Survey
Stimulant Use among Adults

(Kantor 2015)
7. National Health and Nutrition Examination Survey

(Offson 2013)
8. National Ambulatory Medical Care Survey
1.7 million (0.6% of people aged 12 or older) were currently misusing stimulants in 2015.

(Center for Behavioral Health Statistics and Quality 2016)
10. National Survey on Drug Use and Health
Effectiveness of Stimulants for ADHD

Stimulants reduce ADHD symptoms (measured by rating scales)

<table>
<thead>
<tr>
<th>Stimulant</th>
<th>Number needed to treat</th>
<th>Implied failure rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amphetamine</td>
<td>2</td>
<td>50% don’t respond</td>
</tr>
<tr>
<td>Methylphenidate</td>
<td>2.6</td>
<td>62% don’t respond</td>
</tr>
</tbody>
</table>

(Faraone 2010)
Stimulants change the brain

• Stimulants cause ADHD brains to look and function more like normal controls (on MRI)

• Brain regions affected:
  • Striatum
  • Anterior cingulate cortex
  • Prefrontal cortex
  • Connectivity between ventral anterior cingulate cortex and lateral prefrontal cortex

(Spencer 2013)
Limitations of Stimulants

Stimulants do improve:
• Ability to sit still and do classwork

Stimulants do not improve:
• Long-term academic achievement
• Standardized test scores
• College Grade Point Averages
• College graduation rates

(Advokat 2009)
Conclusions

• How common is ADHD?
  • 8.7% of adolescents, 4.4% of adults

• How common are stimulants?
  • 3.5% of youths, 1.8% of adults are currently prescribed stimulants
  • 0.6% of persons over 12 currently abuse stimulants

• Are stimulants effective?
  • They improve ADHD symptoms
  • They do not affect long-term achievement


References


1. The National Comorbidity Study – Adolescent Supplement was a face-to-face interview of 10,123 adolescents (ages 13-18), combined with a self-administered questionnaire about the adolescent completed by a parent or adult surrogate. The sample was a nationally representative group of adolescents in the continental United States. Data were collected from 2001-2004. The response rate was 82.9%. DSM-IV diagnoses were generated by using the WHO-CIDI structured interview.

2. The National Comorbidity Survey – Replication was a face-to-face interview of 9,282 English speaking, household-dwelling adults (ages 18-44) in the United States. The sample was nationally representative. Data were collected from 2001-2003. The response rate was 70.9%. Final sample of adults who completed the ADHD evaluation was 154. Interview tools included the Diagnostic Interview Schedule for DSM-IV, Adult ADHD Clinical Diagnostic Scale (which included the ADHD Rating Scale), the WHO-CIDI, and the WHO Disability Assessment Schedule.
Study Descriptions

3. The National Health Interview Survey enrolled civilian non-institutionalized persons in the USA. The study uses a multistage cluster sample design. Trained interviewers from the US Census Bureau visited homes and administered the survey in person. A knowledgeable adult provides survey answers for the sample child. Data were collected in 2012 for 13,275 sample children. The response rate was 69.7%. ADHD was assessed by asking “have you ever been told the child has attention deficit hyperactivity disorder.”

4. The Monitoring the Future study surveyed a cross-sectional nationally representative sample of high school seniors annually in the coterminous United States using self-administered paper-and-pencil questionnaires in classrooms. This analysis includes 10 cohorts annual cohorts, from 2005-2014. The mean response rate was 82.5 from 2005-2014. The sample was 40,358 individuals who completed the questionnaire in the spring of their senior year. The modal age was 18. Participants were asked if they had ever taken a prescription stimulant medication under a doctor’s supervision for ADHD, how old they were when they first started using one of these prescription stimulant medications for ADHD under a doctor’s supervision, and if they had ever taken a non-stimulant prescription medication under a doctor’s supervision for ADHD. 3,539 individuals were ever prescribed stimulant medication therapy for ADHD and 1,332 individuals were prescribed only non-stimulant medication therapy.
Study Descriptions

5. The National Survey of Children’s Health was a nationally representative survey involving face-to-face interviews with an adult most knowledgeable about the target youth. Data were collected in 2003. The adult provided information on ADHD diagnosis, which was inferred from a positive response to the question “Has a doctor or other health professional ever told you that [child] had Attention Deficit Disorder or Attention Deficit Hyperactivity Disorder, that is, ADD or ADHD?” If ADHD was endorsed by the adult, current medication treatment for ADHD was queried with the question, “Is [child] currently taking medication for ADD or ADHD? The final sample included 79,264 youth ages 4-17 years of age. 6,497 youths had a reported ADHD diagnosis and 3,786 were reported to be “currently” taking medication for ADHD at the time of the survey.

6. The Medical Expenditure Panel Survey (MEPS) is a nationally representative household survey of health care use and costs conducted by the Agency for Healthcare Research and Quality and has been used extensively to track trends in mental health treatment in the United States. Households for each panel are interviewed five times over a 2-year period. The sample for each panel is drawn from the sample of all households responding to the National Health Interview Survey in the year prior to the panel start date in the MEPS. Overall response rates for the MEPS for 1996–2008 ranged from 56.9% to 70.2%. The analytic sample for this study includes all individuals age 18 and younger in each year. Final annual sample sizes varied with the number of households sampled each year in the MEPS and ranged from 6,595 to 11,713. The sample is poststratified to the Current Population Survey and is representative of the civilian noninstitutionalized population in each year. Data on prescription drug use were collected both directly from households and from a follow-back survey of all pharmacies reported by the household, for which a signed permission form was obtained. Detailed information obtained from responding pharmacies (85% response rate), including National Drug Code, drug name, strength, and form for each drug fill, were matched back to the prescription drug fills reported by the household. Stimulants were defined to include the following compounds in various formulations: methylphenidate, dexamethylphenidate, pemoline, amphetamines, and dextroamphetamine. The current study uses data from 1996-2008.
Study Descriptions

7. The National Health and Nutrition Examination Survey is a nationally representative cross-sectional survey of civilian noninstitutionalized persons living in the United States. Information about prescription drug use was collected during face-to-face household interviews. Participants were asked if they had taken prescription drugs over the prior 30 days. Those who said “yes” were asked to show the containers of all products used (84% of the medication containers were seen by interviewers). 1999 was the first year of continuous sampling, and 2012 is the most recent cycle for which data are available. The response rate was 73.6%. The final sample size was 37,959 (the sample size for individual NHANES cycles ranged from 4,861 to 6,212).

8. The National Ambulatory Medical Care Survey, which is conducted annually by the National Center for Health Statistics (NCHS), samples a nationally representative group of visits to physicians in office-based practice. For this analysis (following NCHS recommendations) data from contiguous survey years were combined to derive more stable estimates (1994–1997, 1998–2001, 2002–2005, and 2006–2009). Across the 16 survey years, response rates varied between 58.9% (2006) and 72.8% (1995) with a mean of 66.1%. For each visit (n = 372,702), the treating physician or member of the physician’s staff provided information about patient sociodemographic and clinical characteristics as well as the medications prescribed or supplied to the patient. Diagnoses were made by treating physicians according to the International Classification of Diseases, Ninth Revision, Clinical Modification. Each visit includes up to 3 diagnoses, and the diagnostic groups were not mutually exclusive. The proportions of office-based visits that included stimulant treatment were determined overall and stratified by patient age (18–29, 30–49, 50+ years), sex, race/ethnicity, primary payment source, physician specialty, mental disorder group, coprescribed psychotropic medication, and presence of psychotherapy for each time period (1994–1997, 1998–2001, 2002–2005, 2006–2009).
10. The 2010 National Survey on Drug Use and Health surveyed a nationally representative sample of the civilian non-institutionalized population aged 12 years and older residing in the United States. The final respondent sample was approximately 67,500, with a weighted interview response rate of 66.3%. In-person interviews were done, which included some computer-assisted interviewing to promote honesty and confidentiality among respondents. Respondents are asked to report only "nonmedical" use of drugs, defined as use without a prescription of the individual's own or simply for the experience or feeling the drugs caused. Use of over-the-counter drugs and legitimate use of prescription drugs are not included. (Note: This describes the 2010 data; for this powerpoint presentation I used recently released 2015 data.)