Regulatory Overview

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Disclaimer and Conflict of Interest Statement

- This presentation reflects the views of the author and should not be construed to represent FDA's views or policies

- I have no conflicts of interest to disclose

Untreated ADHD among adults is associated with significant harms

Consequences of ADHD in adulthood include employment and financial difficulties (e.g., frequent job changes, unemployment, and lower socioeconomic status), interpersonal problems (e.g., social maladjustment and marital problems), and coexisting psychiatric disorders (e.g., depression and anxiety). There is also an increased risk of substance abuse, including smoking.

-Volkow, NEJM, 2013

Volkow ND, Swanson JM, Clinical practice: Adult attention deficit-hyperactivity disorder. Engl J Med. 2013 Nov 14;369(20):1935-44. doi: 10.1056/NEJMcp1212625

Multiple treatment options for people with ADHD

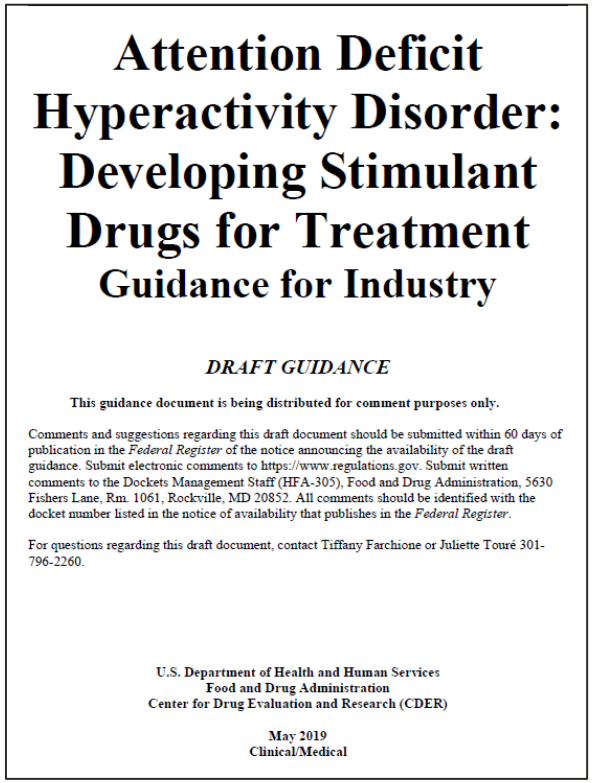
- Stimulant medications, e.g.,
  - Lisdexamfetamine
  - Mixed amphetamine salts
  - Methylphenidate
- Non-stimulant medications, e.g.,
  - Atomoxetine
  - Clonidine
  - Guanfacine
  - Viloxazine
- FDA has permitted marketing of one medical device for children ages 7-12
  - Monarch eTNS System
- Various options not overseen by FDA
  - Behavioral therapy

Efficacy of ADHD treatments is typically established based on < 12-week trials

Mixed amphetamine salts

- ADDERALL label: "The effectiveness of Adderall® for long-term use has not been systematically evaluated in controlled trials."

- ADDERALL XR efficacy was established in:
  - Children (ages 6-12): one 3-week outpatient, controlled trial and one analogue classroom, controlled trial in children with ADHD
  - Adolescents (ages 13-17) and adults: one 4-week controlled trial in each population



Attention Deficit Hyperactivity Disorder: Developing Stimulant Drugs for Treatment
Guidance for Industry

DRAFT GUIDANCE

This guidance document is being distributed for comment purposes only.

Comments and suggestions regarding this draft document should be submitted within 60 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit electronic comments to https://www.regulations.gov. Submit written comments to the Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. All comments should be identified with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions regarding this draft document, contact Tiffany Farchione or Juliette Touré 301-796-2260.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)

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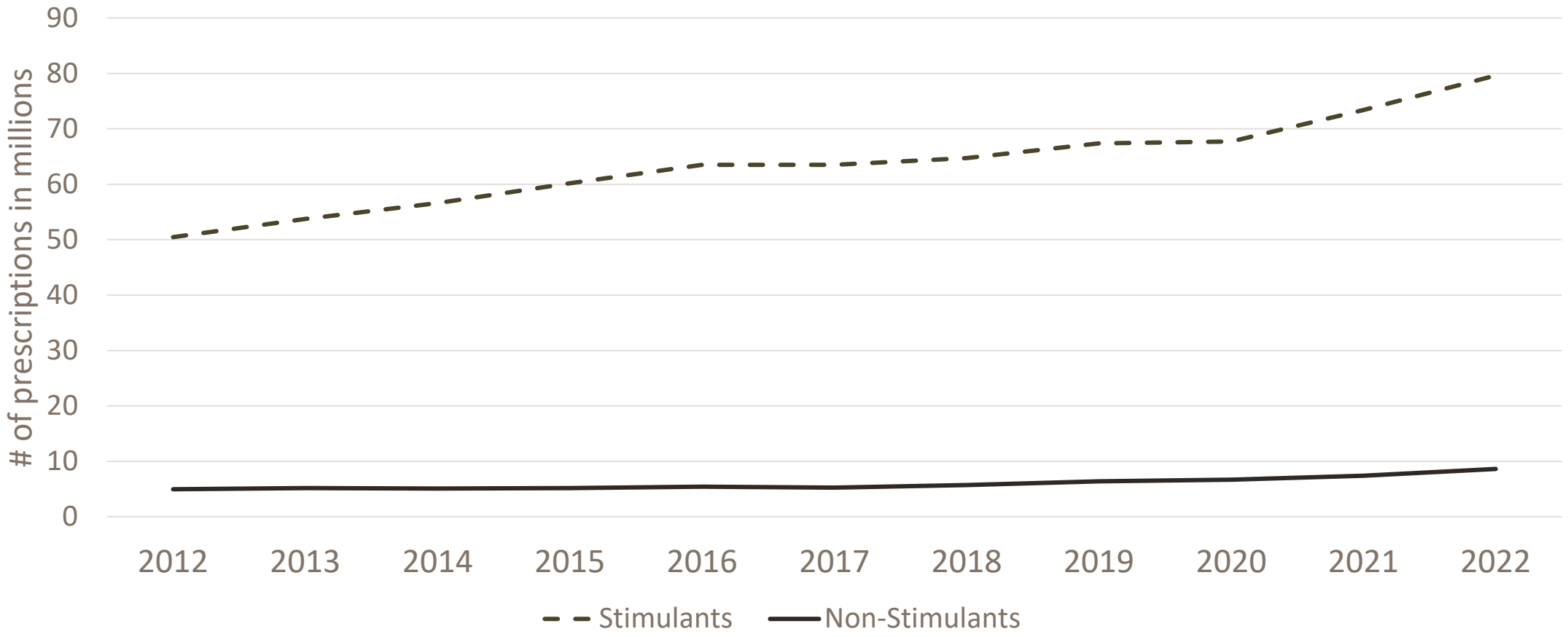
Balancing risks and benefits

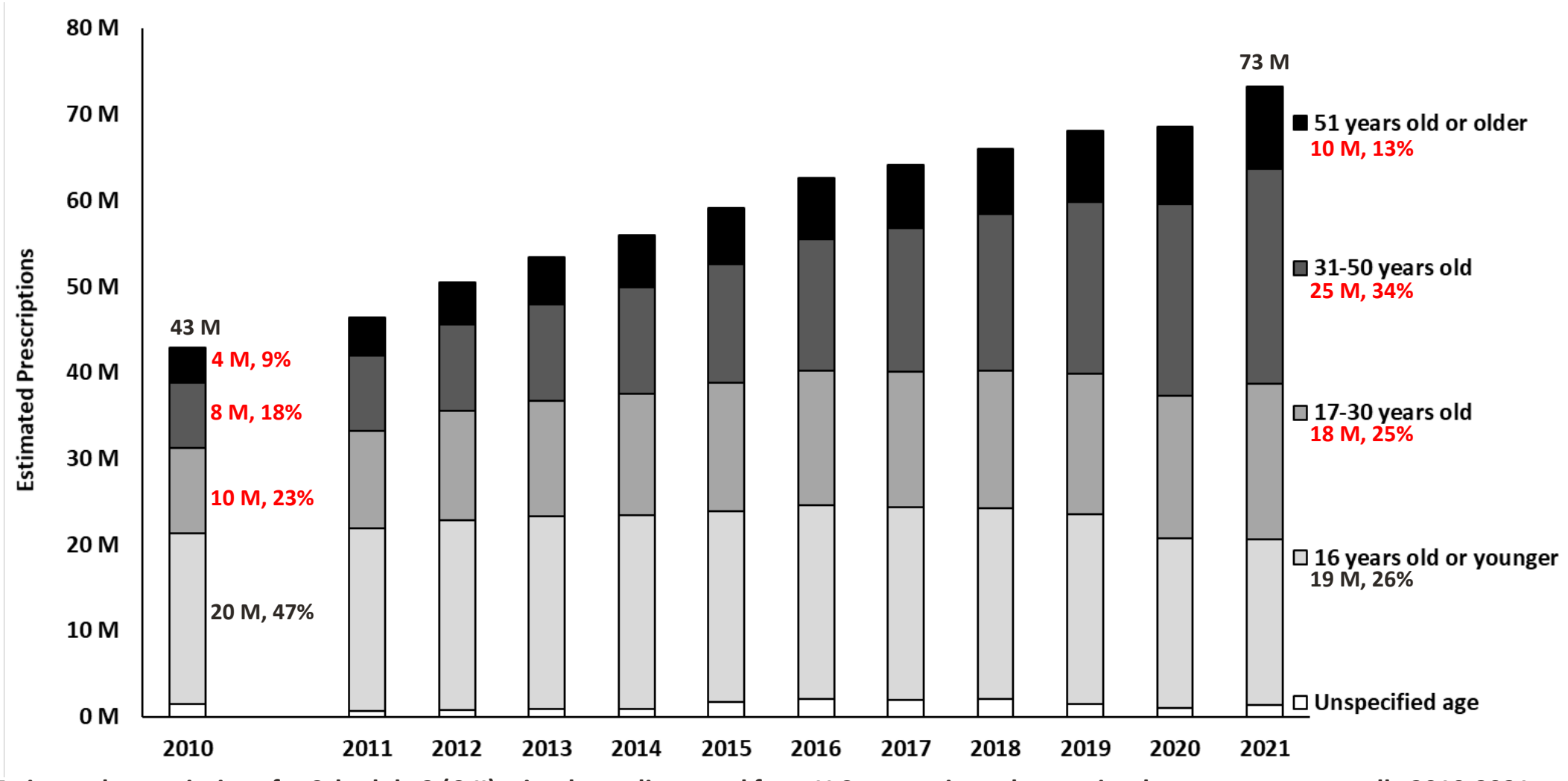
- Both stimulant and non-stimulant treatments for ADHD are associated with significant risks (boxed warnings):
  - Stimulants for ADHD have a high potential for abuse and misuse, which can lead to the development of a substance use disorder, including addiction
  - Atomoxetine use is associated with an increased risk of suicidal ideation in children or adolescents
  - Viloxazine treatment is associated with higher rates of suicidal thoughts and behaviors in pediatric and adult patients with ADHD

Dispensed prescriptions for stimulant and non-stimulant ADHD treatments from 2012 to 2022



Adopted from: https://www.deadiversion.usdoj.gov/drug_chem_info/stimulants/IQVIA_Report_on_Stimulant_Trends_from_2012-2022.pdf

Increases in Stimulant Use Driven by Prescriptions to Adults



Estimated prescriptions for Schedule 2 (C-II) stimulants dispensed from U.S. outpatient pharmacies, by age group, annually 2010-2021.
Source: Symphony Health Metys™. Study period 2010-2021, data extracted March 2022. M = millions. Outpatient pharmacies include retail and mail-order pharmacies. Data include all dosage formulations.

Absence of Adult ADHD Clinical Practice Guidelines Created Potential Opportunities for Inappropriate Prescribing

The New York Times

The Hazards of Prescribing A.D.H.D. Drugs Online

Buzzy start-ups promising easy access to mental health medication found an eager market on social media. Should anyone be looking for treatment on TikTok, though?

Quora
https://www.quora.com › What-can-I-do-say-to-my-psyc...

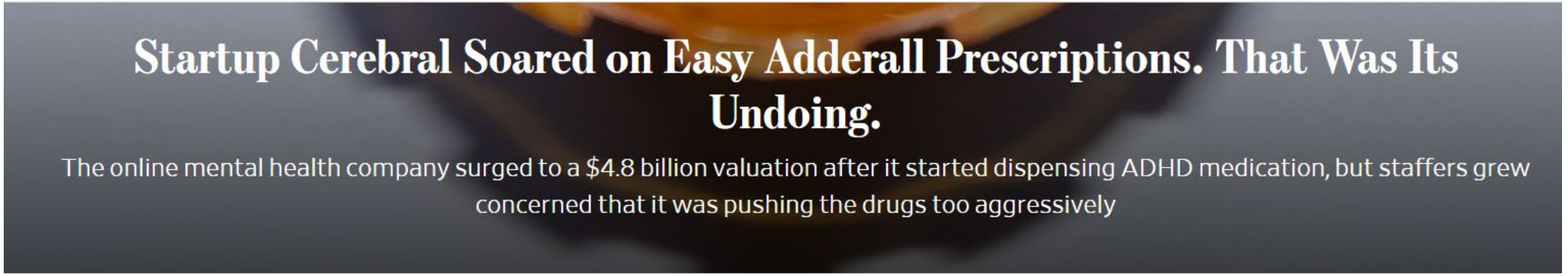
What can I do/say to my psychiatrist to get my hands on ...

Apr 28, 2019 — 1. **Go** look up the DSM criteria for **ADHD**. Study it, know it. 2. **Get** a new Psychiatrist (someone who specializes in **ADHD** is preferred or a Dr.

How to get Adderall from a doctor - Quora	Apr 12, 2021
What do I **tell** a doctor in order to **get** a **prescription** for **Adderall** ...	Dec 23, 2017
How to ask my therapist to **prescribe** me **Adderall**? Should I ...	Jul 3, 2020
How do I **get** a doctor to **prescribe** me **Adderall**? - Quora	Jun 14, 2017

More results from www.quora.com

THE WALL STREET JOURNAL.

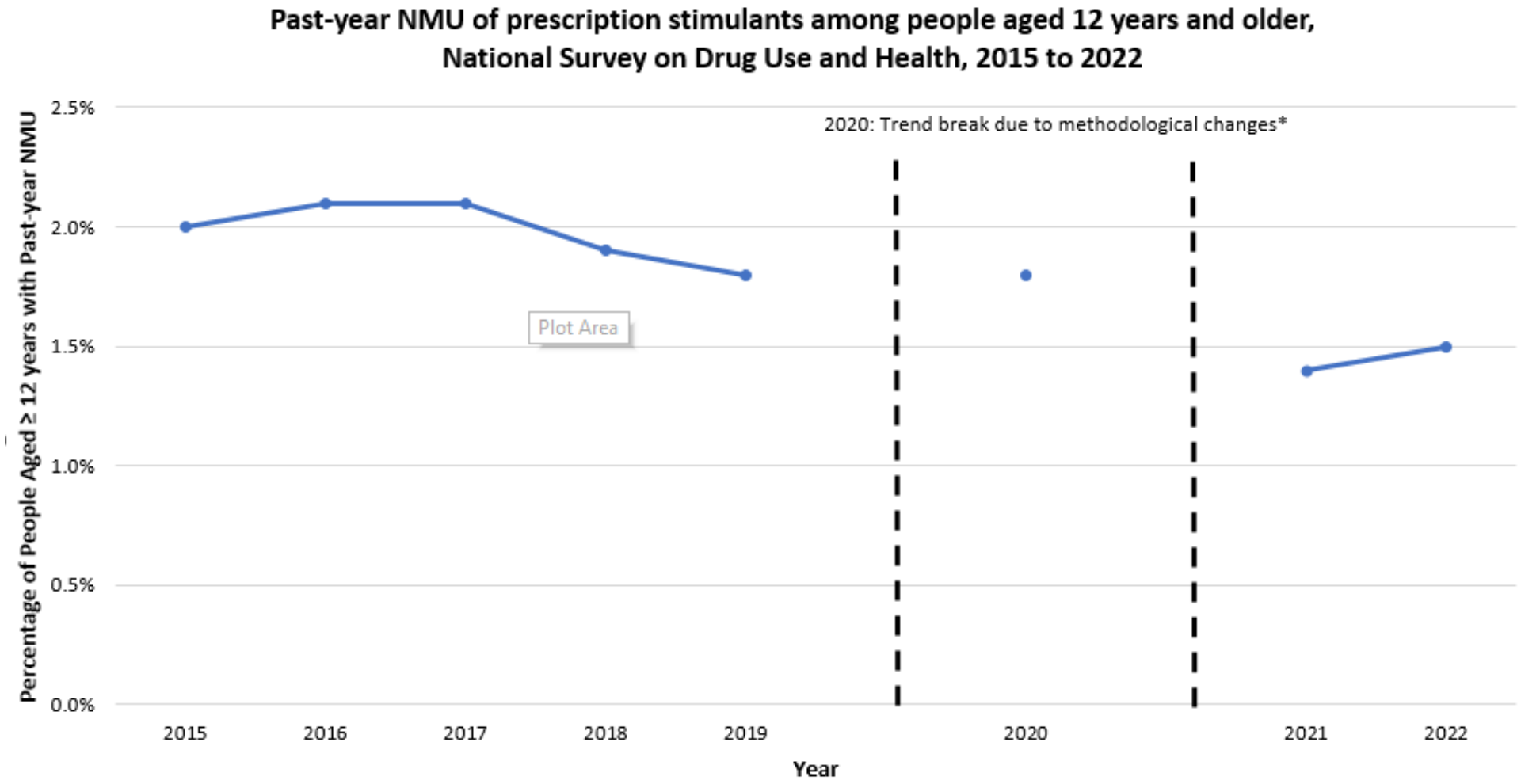


Startup Cerebral Soared on Easy Adderall Prescriptions. That Was Its Undoing.

The online mental health company surged to a $4.8 billion valuation after it started dispensing ADHD medication, but staffers grew concerned that it was pushing the drugs too aggressively

Adderall prescriptions fueled Cerebral's rise. COLIN TEMPLE/ALAMY

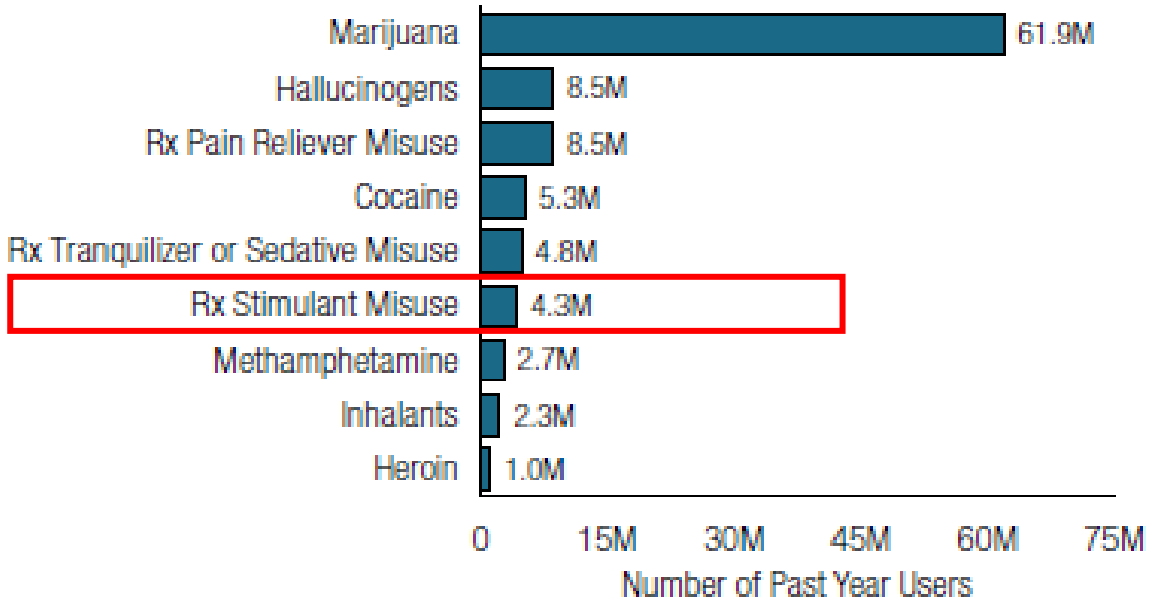
Monitoring for changes in non-medical use



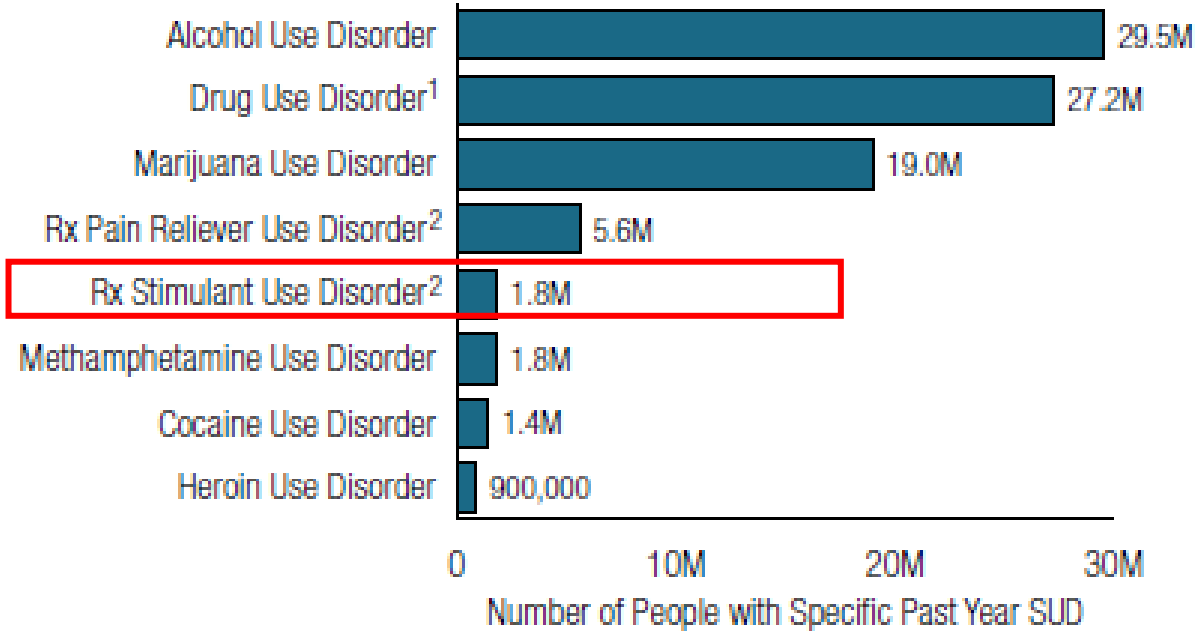
Key Substance Use and Mental Health Indicators in the United States: Results from the 2022 National Survey on Drug Use and Health | Published November 2023 (https://www.samhsa.gov/data/sites/default/files/reports/rpt42731/2022-nsduh-nnr.pdf)

Overview of illicit drug use & substance use disorder among people aged 12 or older in the U.S. in 2022

Past Year Illicit Drug Use



Past Year Substance Use Disorder



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Select recent FDA actions

- Issued joint FDA/DEA letter to the public on actions to address shortages in prescription stimulants (Aug 2023)
- Approved multiple first generics of lisdexamfetamine (Aug 2023)
- Updated label warnings to improve safe use of Rx stimulants used to treat ADHD and other conditions to emphasize serious risks with misuse, abuse, addiction, and sharing these drugs (May 2023)
- Approved new non-stimulant drug, viloxazine, for treatment of ADHD in pediatric patients (April 2021) and adult patients (April 2022)
- Approved new formulation of amphetamine extended-release tablets for treatment of ADHD in pediatric and adult patients (Nov 2021)
- Granted marketing authorization of the first medical device treatment for ADHD (April 2019)

Select recent FDA actions

- Issued joint FDA/DEA warning letters to online pharmacies illegally selling Adderall to consumers (April 2022)
- Issued warning letter to Outlook Pharmaceuticals, Inc. (Feb 2020)
- Continued funding research to evaluate non-medical use of Rx stimulants (Sept 2020 – present)

Knowledge gaps

- Limited studies of comparative effectiveness (e.g., cognitive performance) and safety profile of stimulants, non-stimulants and behavioral health in adults with ADHD
- Assessment of risk associated with long-term use of the medication
  - Behavioral changes
  - Healthcare outcomes (e.g., cardiovascular)
  - Non-medical use of Rx stimulants and development of substance use disorder among adults with ADHD
- Best approaches to address barriers and improve access to the treatments including impact of telemedicine

Next steps

- Continue to work on addressing stimulant shortages
  - Pediatric and adult patients with ADHD should be able to get needed treatments
- Emphasize the need for evidence-based adult ADHD clinical practice guidelines to facilitate clinician and patient understanding of the risks and benefits of various treatment options for ADHD, including no treatment
- Continue assessment of safety of ADHD medications to determine whether additional regulatory actions are appropriate
- Provide oversight and facilitate development of new treatment options for ADHD

Adult ADHD: Diagnosis, treatment, and implications for drug development – a workshop

- Discuss the criteria for diagnosis and treatment of adults with ADHD
- Consider what is known and unknown about the risks and benefits of ADHD medication use in adult populations
- Share perspectives on the causes, perceptions, consequences, and health equity implications of non-medical use of prescription stimulants, including misuse potential, overdosage, and toxicity
- Explore challenges and opportunities for the development of new and improved therapeutics for the treatment of ADHD
- Consider potential strategies for assessing the risks and benefits of ADHD medication treatment in adult populations, including the intersection with opioid use, that support the public health goal of safely and effectively treating adults with ADHD

Thank you