

Novel Molecular Targets in Mood Disorders and Psychosis

A WORKSHOP

March 8-9, 2021

*The National
Academies of*

SCIENCES
ENGINEERING
MEDICINE

Hosted by the Forum on Neuroscience and Nervous System Disorders

The meeting materials, including the agenda and speaker biosketches,
are available on the workshop homepage. Navigate there via nas.edu/neuroforum.



Linda Brady (Chair), National Institutes of Health

Tiffany Farchione, Food and Drug Administration

David Gray, Cerevel Therapeutics

Magali Haas, Cohen Veterans Bioscience

John Krystal, Yale University School of Medicine

Carlos Larrauri, National Alliance on Mental Illness

Husseini Manji, Johnson and Johnson Pharmaceuticals

Sharon Mates, Intracellular Therapies, Inc.

Steve Paul, Karuna Therapeutics, Inc.

Morgan Sheng, The Broad Institute of MIT and Harvard

Greg Simon, Kaiser Permanente Washington Health Research Institute

Ilina Singh, University of Oxford



Day 1, March 8, 2-5 pm ET

Session 1: Introduction to Drugs and Drug Targets for
Mood Disorders and Psychosis

Session 2: Promising Developments with Glutamate Receptors (GluRs)

Day 2, March 9, 10 am - 5 pm ET

Session 3: Promising Developments with GABA Receptors (GABARs)

Break for Lunch

Session 4: The Road Ahead for Emerging Drug Targets

Session 5: Bioethical Considerations

Session 6: Synthesis and Next Steps

Novel Molecular Targets in Mood Disorders and Psychosis

Linda Brady, Ph.D.

Director, NIMH Division of Neuroscience
and Basic Behavioral Science

National Academies of Sciences, Engineering, and
Medicine Virtual Workshop

March 8-9, 2021

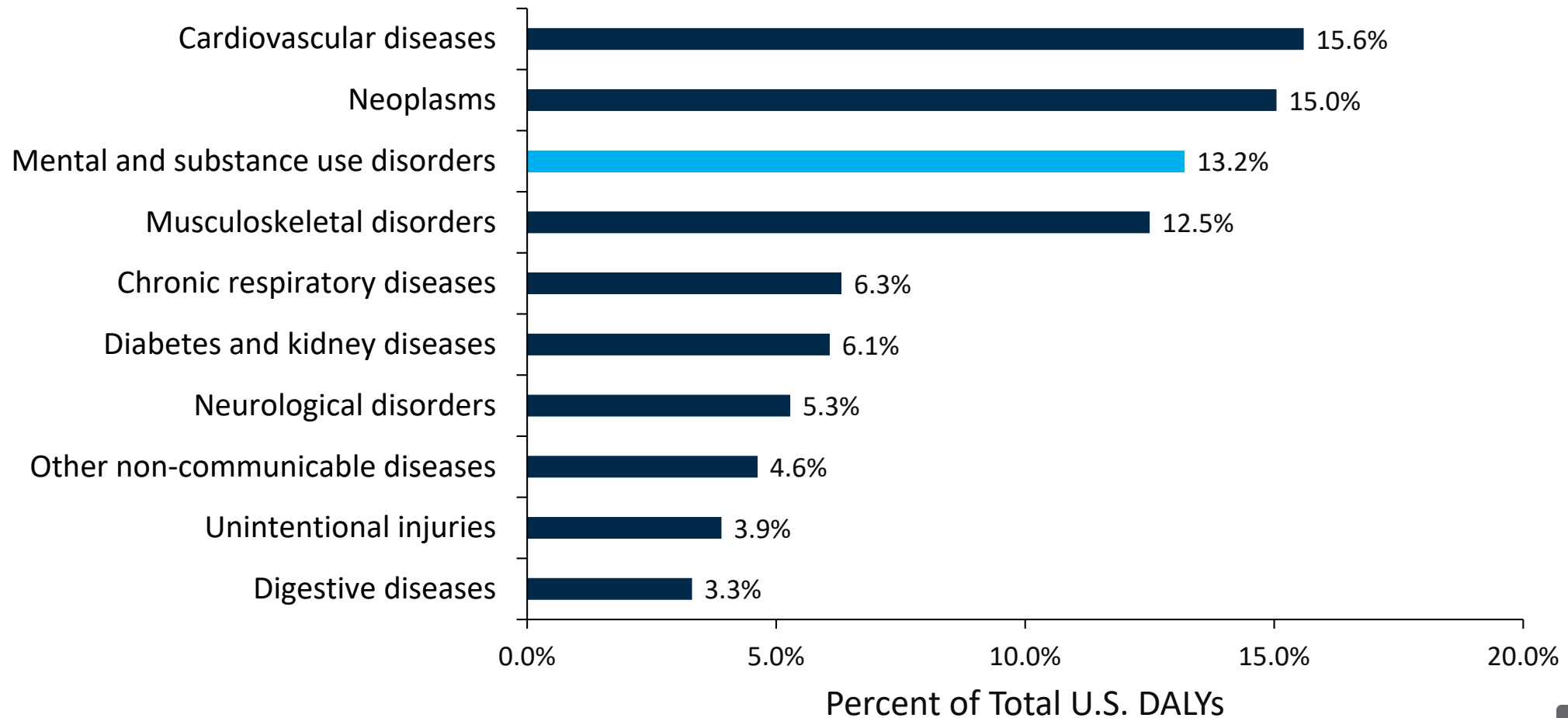


National Institute
of Mental Health

Burden of Mental Illness: U.S. Disability-Adjusted Life Years (DALYs)

Top Ten Leading Disease/Disorder Categories Contributing to all U.S. DALYs (2019)

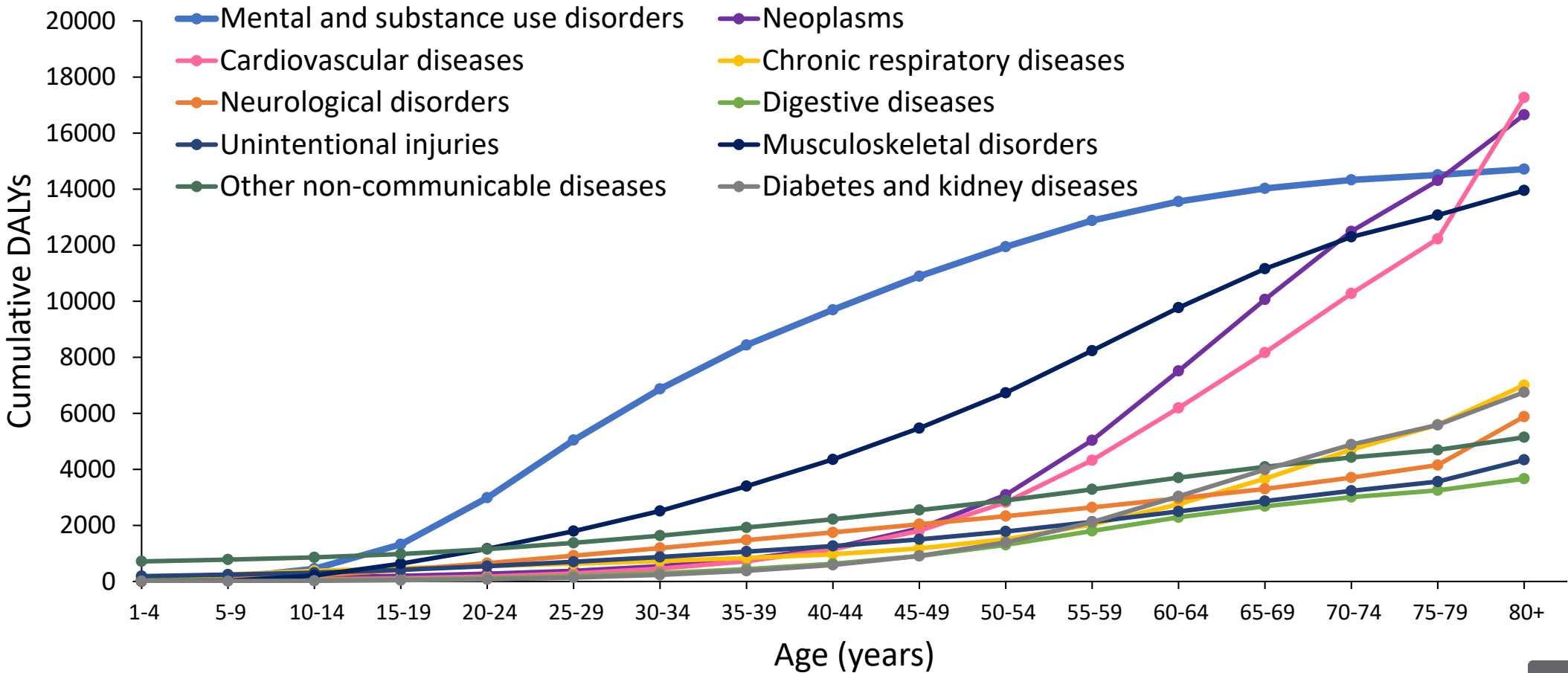
Data Courtesy of IHME, GHDx



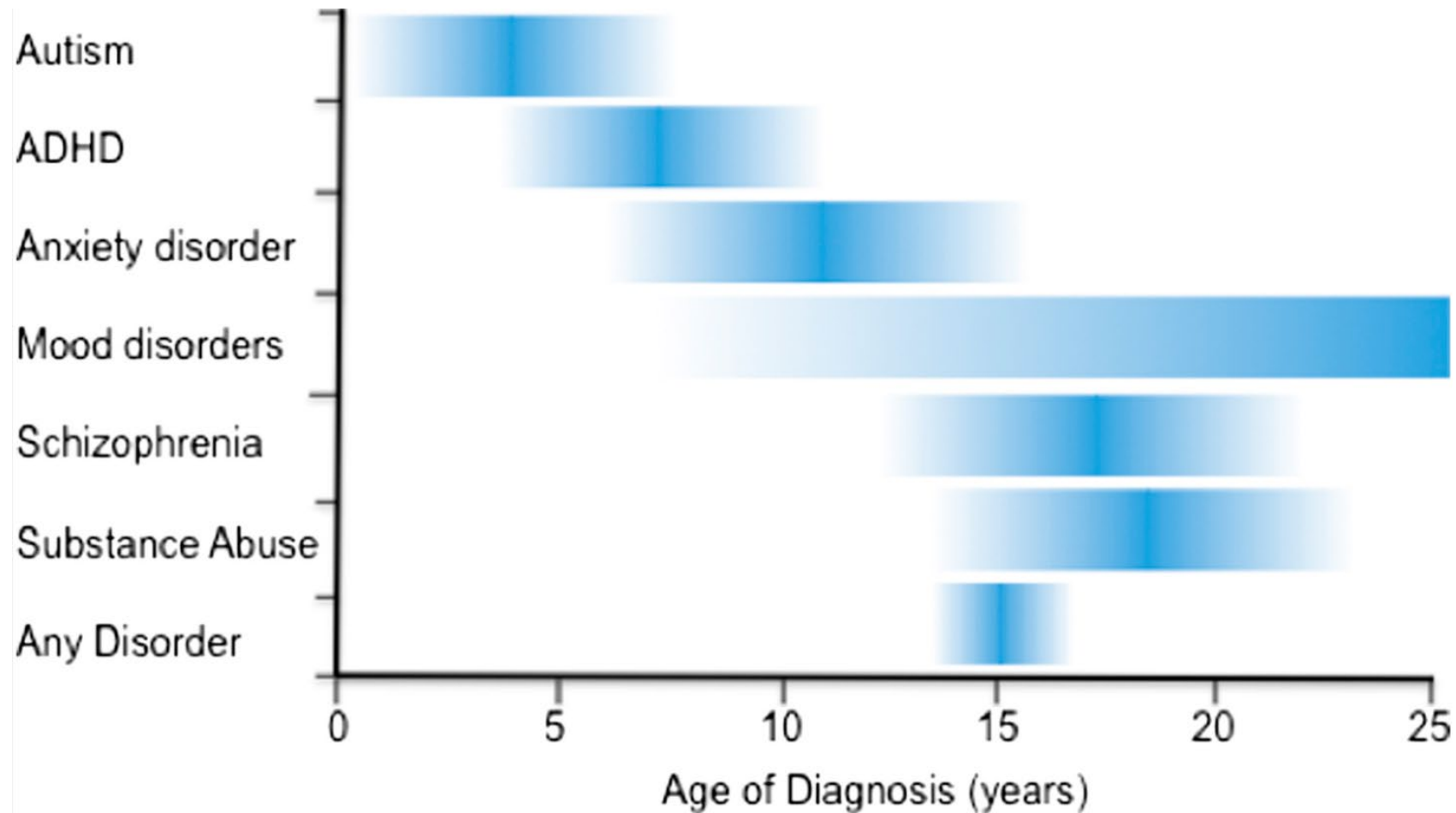
Burden of Mental Illness: U.S. Disability-Adjusted Life Years (DALYs)

Cumulative U.S. DALYs for the Leading Disease/Disorder Categories by Age (2019)

Data Courtesy of IHME, GHDx

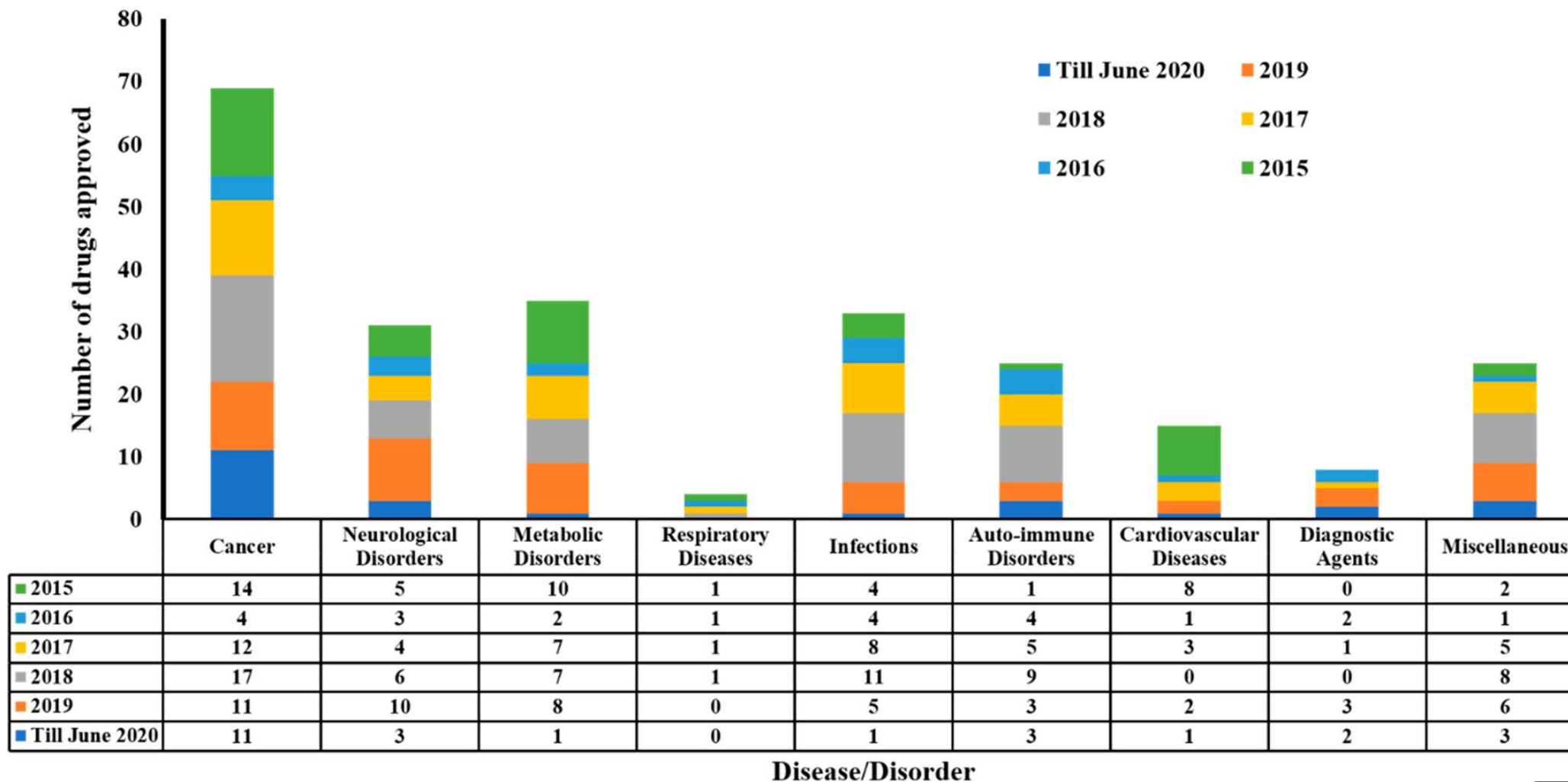


Psychiatric Disorders Onset During Childhood and Adolescence



U.S. FDA Approved Drugs from 2015 - June 2020

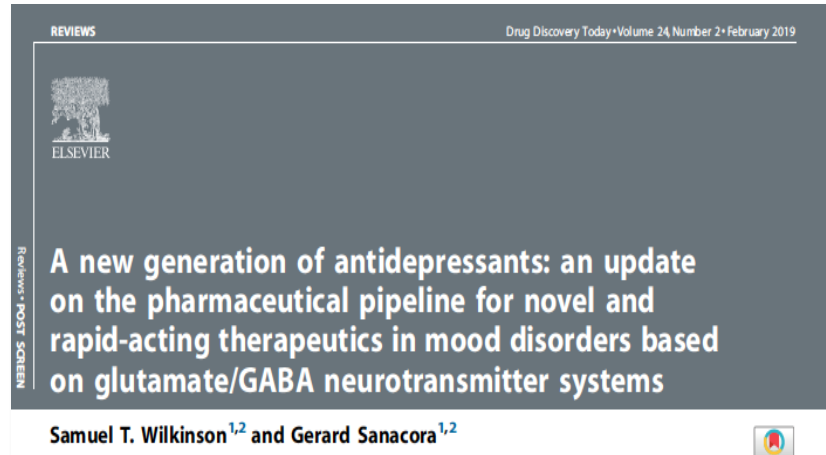
Drug approved from year 2015 – June 2020



U.S. FDA Drug Approvals for Depression and Psychosis (2015-2020)

Drug	Sponsor	Properties	Receptor Target(s)	Indication	Year
none					2020
Esketamine (Spravato)	Johnson & Johnson	Rapid-acting antidepressant	Noncompetitive NMDA receptor antagonist	Treatment-resistant depression	2019
Brexanolone (Zulresso)	Sage Therapeutics	Rapid-acting antidepressant	Neuroactive steroid, GABA-A receptor positive allosteric modulator	Postpartum depression	2019
Lumateperone (Calyptra)	Intra-Cellular Therapies	Atypical antipsychotic	Dopamine phosphoprotein modulator (D1 and D2 receptors), 5-HT2A receptor antagonist, SERT inhibitor	Schizophrenia	2019
none					2018
none					2017
Pimavanserin (Nuplaxid)	Acadia Pharmaceuticals	Atypical antipsychotic	5-HT2A receptor inverse agonist, less so at 5-HT2C receptor	Hallucinations and delusions associated with Parkinson's disease psychosis	2016
Brexipiprazole (Resulti)	Otsuka	Atypical antipsychotic	5-HT1A receptor and D2 receptor partial agonist, and 5-HT2A, alpha 1B & 2C receptor antagonist	MDD and schizophrenia	2015
Cariprazine (Vraylar)	Forest	Atypical antipsychotic	D2 receptor and D3 receptor partial agonist	Schizophrenia and bipolar disorder	2015
Aripiprazole lauroxil (Aristada)	Alkermes	Extended-release atypical antipsychotic	D2 & 5-HT1A receptor partial agonist, 5-HT2A receptor antagonist	Schizophrenia	2015

Emerging Drug Targets for Mood Disorders and Schizophrenia



Expert Review | [Open Access](#) | Published: 15 February 2021

Update on GPCR-based targets for the development of novel antidepressants

Ioannis Mantas, Marcus Saarinen, Zhi-Qing David Xu & Per Svenningsson

CNS Spectrums (2019), 24, 41–68. © Cambridge University Press 2019
doi: [10.1017/S109285291900124X](https://doi.org/10.1017/S109285291900124X)

REVIEW ARTICLE

Keeping up with the therapeutic advances in schizophrenia: a review of novel and emerging pharmacological entities

Amanda Krogmann,^{1,†} Luisa Peters,^{1,†} Laura von Hardenberg,¹ Katja Bödeker,¹ Viktor B. Nöhles,¹ and Christoph U. Correll^{1,2,3*}

> [Curr Drug Targets](#). 2020;21(15):1593–1605. doi: [10.2174/1389450121666200615150429](https://doi.org/10.2174/1389450121666200615150429).

A Review on Emerging Drug Targets in Treatment of Schizophrenia

Hemen S Ved¹, Gaurav M Doshi¹

Review

Emerging therapeutic targets for schizophrenia: a framework for novel treatment strategies for psychosis

Susan F. Sonnenschein & A Grace

Pages 15–26 | Received 10 Jul 2020, Accepted 05 Nov 2020, Accepted author version posted online: 10 Nov 2020, Published online: 26 Nov 2020



**The lived experience and unmet needs of individuals with
schizophrenia and depression**

CARLOS LARRAURI, The National Alliance for Mental
Illness

ASHLEY CLAYTON, Yale University

**Scientific perspective on the history of drug treatments
for mood disorder and psychosis**

STEVE PAUL, Karuna Therapeutics

Audience Q&A