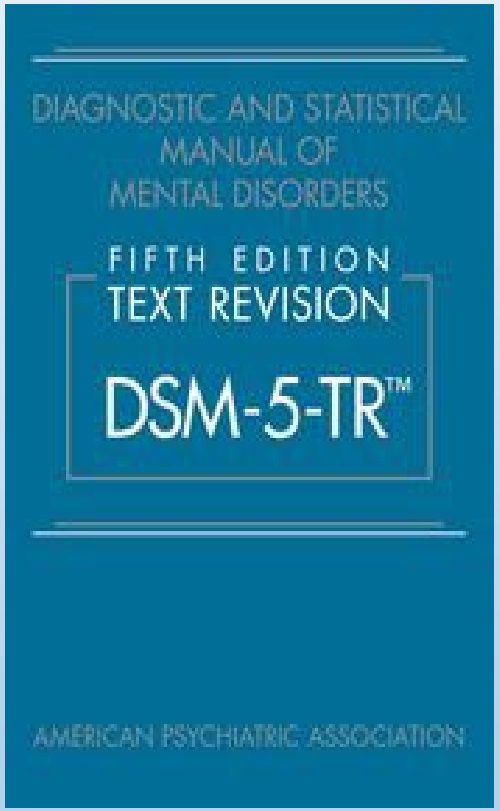
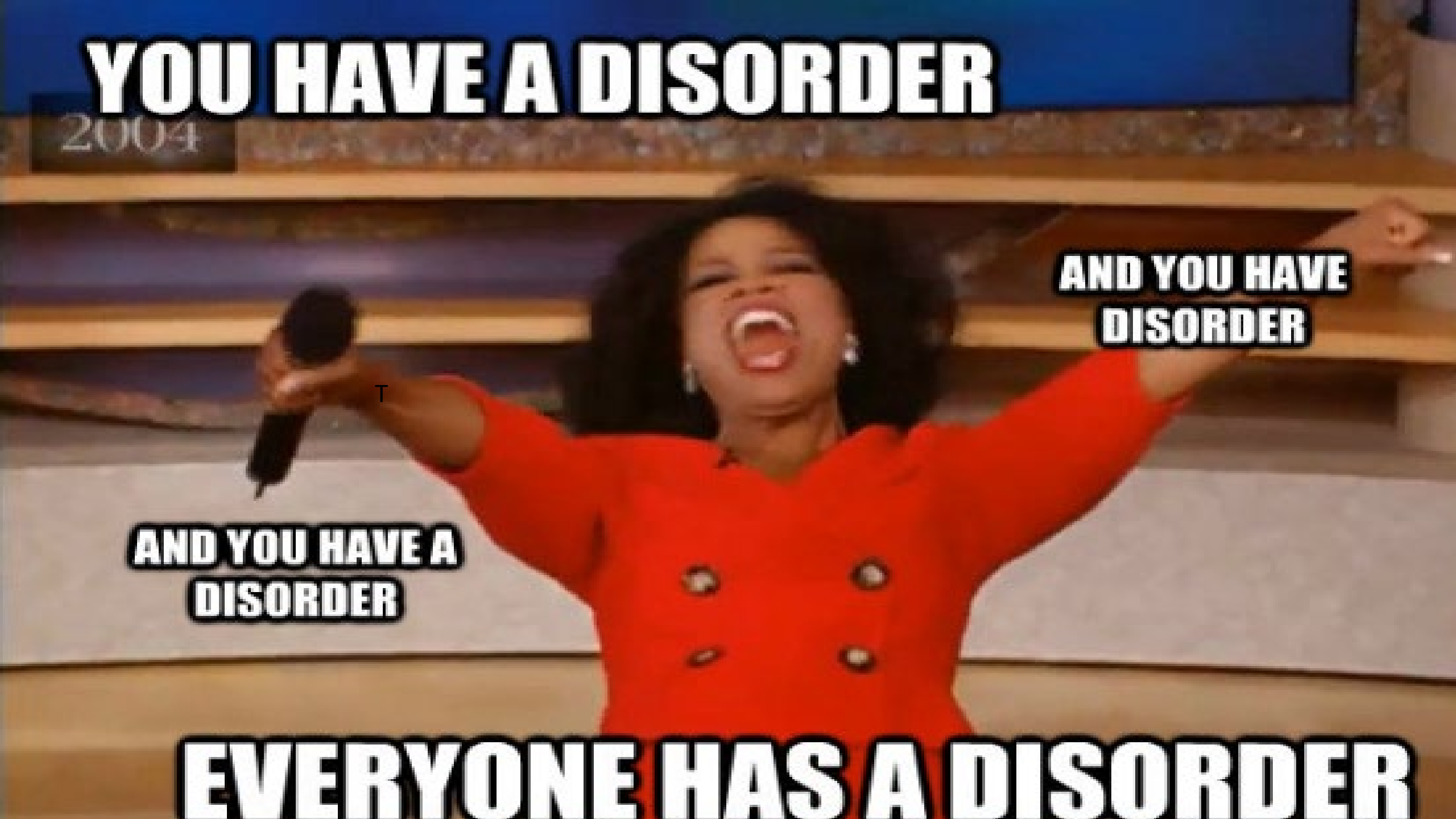
Industry Influence on the DSM 5 TR: Prolonged Grief Disorder and Treatment Resistant Depression

Lisa Cosgrove, PhD



What are the iatrogenic consequences of understanding emotional distress qua disease?


YOU HAVE A DISORDER
AND YOU HAVE A DISORDER
AND YOU HAVE DISORDER
EVERYONE HAS A DISORDER

At its best a diagnosis should open up a future, not foreclose it

Medicalizing emotional distress, especially as codified in the DSM,

may (implicitly at least) encourage people to understand their complex life stories in terms of narrow and reductive psychological concepts


“I HAVE BEEN IN SORROW’S KITCHEN AND LICKED OUT ALL THE POTS. THEN I HAVE STOOD ON THE PEAKY MOUNTAIN WRAPPED IN RAINBOWS, WITH A HARP AND SWORD IN MY HANDS.”
ZORA NEALE HURSTON
© Lifehack Quotes

The DSM facilitates acronym formulations of an individual's complex life stories—which may be good for industry but not so much for public health

As psychiatrist Sami Timimi points out, **acronym formulations ("TRD"; "PGD") have powerful consequences.** They can act as "hypnotic suggestions" and change the way people see themselves and how others see them

Philosopher Ian Hacking makes a similar point:

Diagnostic classifications create and reify certain truths about people and frame their suffering in specific ways. **Classification changes people**.

Medicalizing distress

Medicalizing distress opens the door for industry influence on the DSM

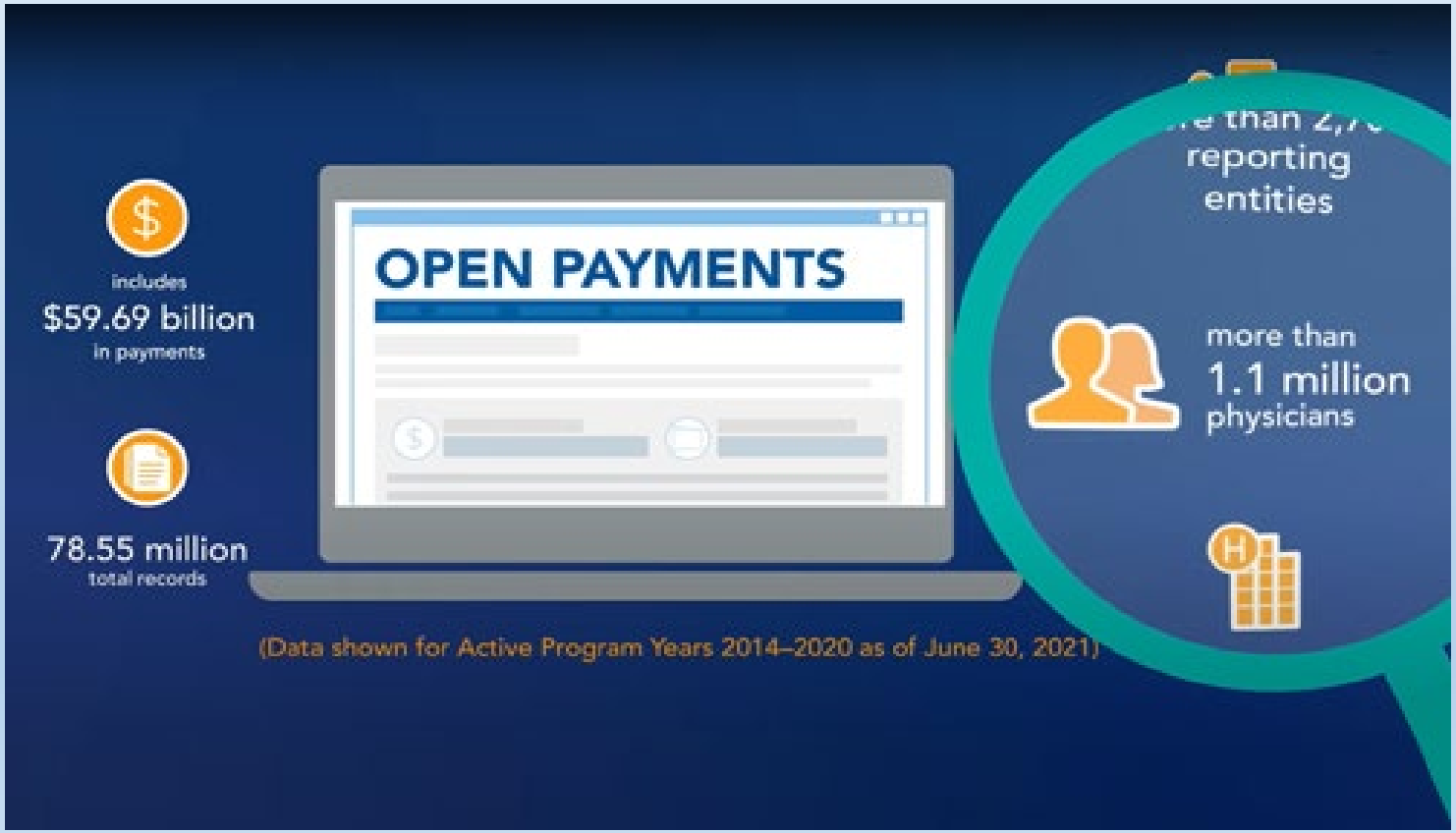
"The pharmaceuticals were delighted with the *DSM*"

Robert Spizter, Chair of the DSM III, discussing DSM III's shift to a medical model in an interview with Jon Ronson, New Scientist, June 2011

DSM IV and 5

***DSM*-IV Work Groups**		***DSM*-5 Work Groups**	
Group	**%FCOI**	**Group**	**%FCOI**
Mood disorder	100%	Mood disorders	67%
Schizophrenia and other psychotic disorders	100%	Psychotic disorders	83%
Sleep disorders	50%	Sleep-wake disorders	100%
Substance-related disorders	17%	Substance-related disorders	58%

Preliminary examination of FCOI in DSM 5 TR suggests that as with the DSM-IV and 5, financial conflicts of interest among DSM-5-TR panel members were prevalent



FCOI in DSM 5 TR (2022)

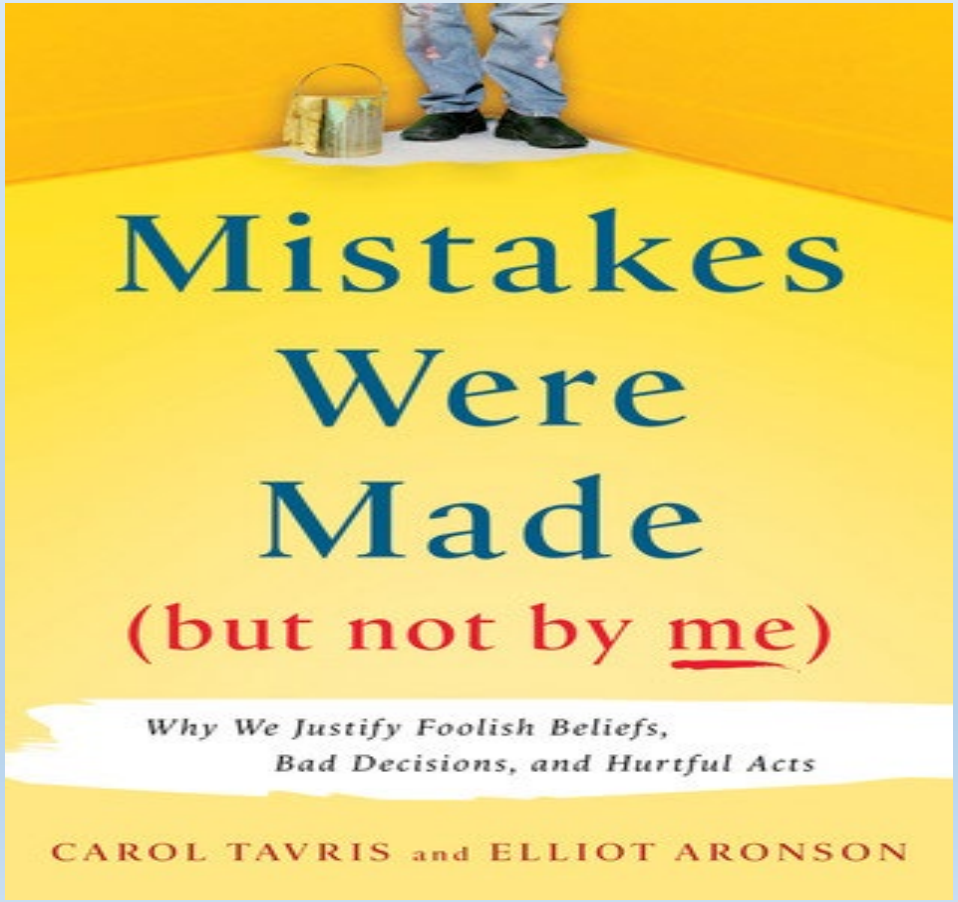
Almost 60% of the 92 panel members who met inclusion criteria had industry ties and collectively they received over 14 million dollars

(A cross-sectional analysis of undisclosed financial conflicts of interest in *DSM-5-TR*: Caveat emptor. Paper under review, *BMJ*)

These ties are not evidence of wrongdoing

Rather, they create “pro-industry habits of thought”

It is part of the human condition to have implicit biases—and remain blissfully ignorant of them



Medicalizing emotional distress and even minor changes in DSM criteria can have a profound effect on diagnosis and treatment

DSM 5 replaced the more stringent criteria of "**mixed episode"** with a **mixed-features specifier** that can now be applied to episodes of MDD.

In DSM IV, only patients who previously met the diagnostic criteria for a **Bipolar** Disorder could receive a "mixed episode" specifier (i.e., it could not be applied to **MDD**)

Medscape Psychiatry

First-Ever Guideline for Mixed Depression Released

Megan Brooks

May 16, 2017

One third or more of adults diagnosed with major depression have depressiosn with mixed features and probably would do better taking an antipsychotic than an antidepressant, concludes an international panel of experts.

Monotherapy with on-patent 2nd generation APs are recommended as the first-

Recommendation	*Drug Name*	*Cost per month*	*Manufacturer*
First-Line	**Latuda (lurasidone)** **No generic**	**$1055**	Sunovion (Sumitomo Dainippon Pharma)
First-Line	**Saphris (asenapine)** **No generic**	**$569.28**	Merck Sharp & Dohme B.V./Allergan

"Mixed depression **under-diagnosed** (especially in children): Ask every patient; every time"

- "When a patient has accepted treatment **for several years and remains very well**, he or she should be ***strongly advised to continue indefinitely"***
- Latuda from 8 to 80?
- 13/20 guideline panel members had multiple ties to the pharmaceutical companies whose products they endorse

How seemingly small changes in the DSM can lead to new disorders: Elimination of the bereavement exclusion and the medicalization of grief

DSM IV and IV TR

"The symptoms are not better accounted for by bereavement"

No statements about carefully considering whether grief might be MDD

DSM 5

"A diagnosis [of Major Depressive Disorder] based on a single episode is possible…Careful consideration is given to the delineation of normal sadness and grief from a major depressive episode… and *recovery* [from bereavement] *may be facilitated by antidepressant treatment."*

Note: "facilitated by ADM" was removed in DSM 5TR

Cymbalta for Depression as a Complication of Bereavement

ClinicalTrials.gov Identifier: NCT00658931

Recruitment Status : Unknown
Verified February 2010 by Jefferson Clinic, P.C..
Recruitment status was: Active, not recruiting
First Posted : April 16, 2008
Last Update Posted : February 12, 2010

View this study on Beta.ClinicalTrials.gov

Sponsor:
Jefferson Clinic, P.C.

Collaborator:
Eli Lilly and Company

Information provided by:
Jefferson Clinic, P.C.

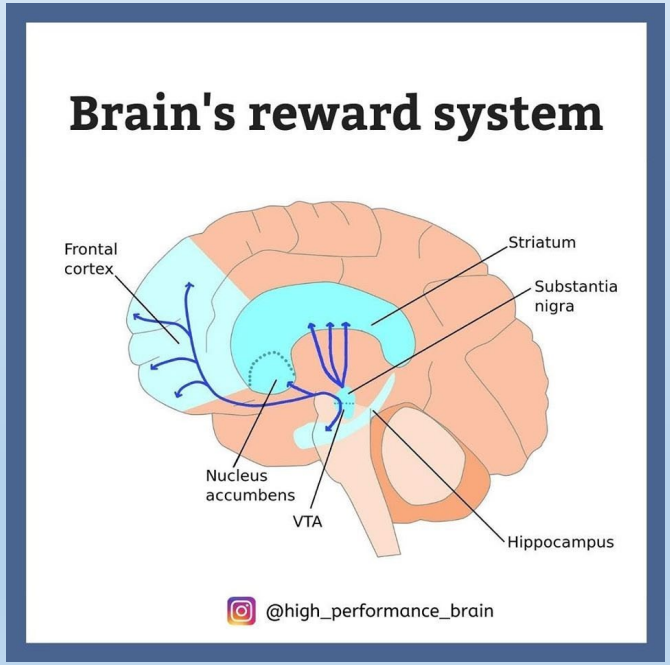
No Study Results Posted on ClinicalTrials.gov for this Study

About Study Results Reporting on ClinicalTrials.gov

New to DSM 5 TR Prolonged Grief Disorder: “A maladaptive grief reaction” akin to addiction

“Patients with PGD continue to “crave” their loved ones after they have died, due to the positive reinforcement provided by their memories of loved ones. The absence of the deceased creates a feeling of withdrawal.”

Gang, J., Kocsis, J., Avery, J., Maciejewski, P. K., & Prigerson, H. G. (2021). Naltrexone treatment for prolonged grief disorder: Study protocol for a randomized, triple-blinked, placebo-controlled trial. *Trials*, *22*.



"PGD may be conceptualized as a reward dysfunction disorder, with the deceased person as the rewarding stimulus for whom the bereaved person yearns."

Gang, J., Kocsis, J., Avery, J., Maciejewski, P. K., & Prigerson, H. G. (2021). Naltrexone treatment for prolonged grief disorder: Study protocol for a randomized, triple-blinked, placebo-controlled trial. *Trials*, *22*.

"At its core, PGD is a disorder of attachment and a craving and yearning for the deceased from whom they are separated…. the primary gateway symptom required for diagnosis is yearning, persistent longing, pining for, or preoccupation with, the deceased."

Naltrexone is prescribed based on the idea that PGD resembles addiction
"wherein the bereaved person continues to seek a connection with the deceased."

"Naltrexone may disrupt this [addictive] behavior, reducing core symptoms of PGD, such as yearning."

Eisma, M.C (2023) Prolonged grief disorder in *ICD*-11 and *DSM*-5-TR: Challenges and controversies *Australian & New Zealand Journal of Psychiatry*

"Detachment from the deceased is a necessary first step towards being able to connect with living others…we predict that naltrexone will provide a pharmacological way to dampen the benefits of social bonding" Gang et al., 2021

"Studies have shown that *naltrexone reduces feelings of social connection*, especially to one's closest others.

Reduced positive associations with significant others, especially the deceased, may make bereavement feel less lonely and isolated while diminishing the reward derived from reminiscing about the deceased."

(emphasis added)

Medicalizing grief, codifying it as a DSM disorder, and conceptualizing PGD as a "reward dysfunction disorder" is deeply problematic

Gang et al's suggestion that naltrexone be used to intentionally disrupt feelings of social bonding is problematic at many levels—philosophical, ethical, and empirical. Indeed, in bereavement social connection is critical and as Thieleman et al 2023 note,

Naltrexone will not selectively target bonds with the loved one who died.

Medicalizing depression: Treatment Resistant Depression (TRD)

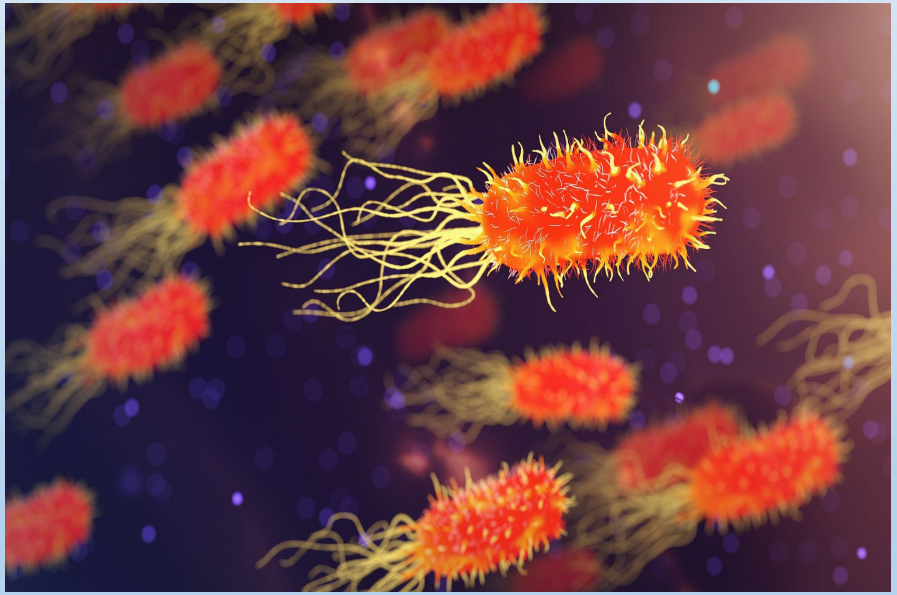
There is no agreed upon definition of TRD (e.g., how many antidepressants must be tried or if psychotherapy or other interventions should be tried before applying the label)

and little—but growing—discussion about whether TRD is a valid construct.

But the question remains: Is the disorder resistant to treatment?

Or, is it is more accurate to acknowledge that antidepressants are not as effective as we originally hoped that they would be?

Indeed, the infectious disease model is inappropriate here; depression is not like a bacterial infection, and we do not have strands of depression that are resistant to antidepressants.



The conceptualization of TRD reinforces the search for a one-size-fits-all intervention that will quickly and easily ’cure’ TRD (the search for ‘magic bullets”)

The FDA recently approved Janssen’s application for Spravato (Esketamine) through the agency’s breakthrough pathway designation. The FDA’s innovation Act introduced a **breakthrough therapy designation** where “a complete set of clinical data is not required.”

In contrast, the National Institute for Health and Clinical Excellence (NICE) in the United Kingdom has recommended against its use:

“….the evidence only considers a small number of people from the full trial population. The long-term effects of esketamine are also uncertain because the trials were short.”

https://www.nice.org.uk/guidance/ta854/documents/final-appraisal-determination-document#:~:text=2.1%20Esketamine%20nasal%20spray%20(Spravato,treatments%20with%20antidepressants%20in%20the

It is noteworthy that a recent business report described the **expansion of ketamine clinics**:

"In the U.S. ketamine clinics market size was valued at **USD 3.1 billion** in 2022 and is expected to grow at a compound annual growth rate (CAGR) of 10.63% from 2023 to 2030… The growth of this segment is expected to be driven primarily by the increasing prevalence of major depressive disorder."

https://www.grandviewresearch.com/industry-analysis/us-ketamine-clinics-market-report

(a market research and consulting company)

What's the solution?

Epistemic humility and "gentle medicine" as a possible solution

If psychiatry is to take the idea of gentle medicine (Jacob Stegenga, 2020) seriously,

the field would need to acknowledge that psychotropics are overprescribed (and their harms have been glossed over), embrace a greater tolerance for uncertainty, stop searching for "magic bullets," and focus more on the socio-political determinants of health.

Societies cannot improve the health status of their populations and reduce significant health inequalities solely or primarily by increasing the resources devoted to medical services. While necessary and significant, investments to improve availability of health services and enhance their quality and relevance cannot compensate for significant disparities in access to the social determinants of health.

Chapman 2010 The social determinants of health, health equity, and human rights. HHHR

Structural competency calls for a new approach to the relationships among race, class, and symptom expression and prepares trainees to act on systemic causes of health inequalities.

https://structuralcompetency.org/structural-competency/

"NEW MEDICINE FOR INEQUALITIES THAT ARE MAKING US SICK"

Psychiatrist Helen Hanson was one of the co-creators of the Structural Competency