

“Medicine is Awesome”:
A Critical Look at the Factors that Shape
the Definition of, and Research on,
Depression and its Treatment

Allen F. Shaughnessy, Pharm.D., M.Med.Ed.
Professor and Vice Chair of Family Medicine for Research
Tufts University School of Medicine
Boston, Massachusetts

Conflicts of Interest

Financial:

- I receive payments for the work I do from Tufts University, Cambridge Health Alliance, John Wiley and Sons, publishers (Essential Evidence Plus), American Family Physician (editor, STEPS)
- I have a small production company, *Meducation*, that makes online CME programs

Intellectual:

- I have published research and editorials critical of depression guidelines and analyses of research into psychiatry drugs
- I am a big fan of medical nihilism, a topic I will discuss

Professional:

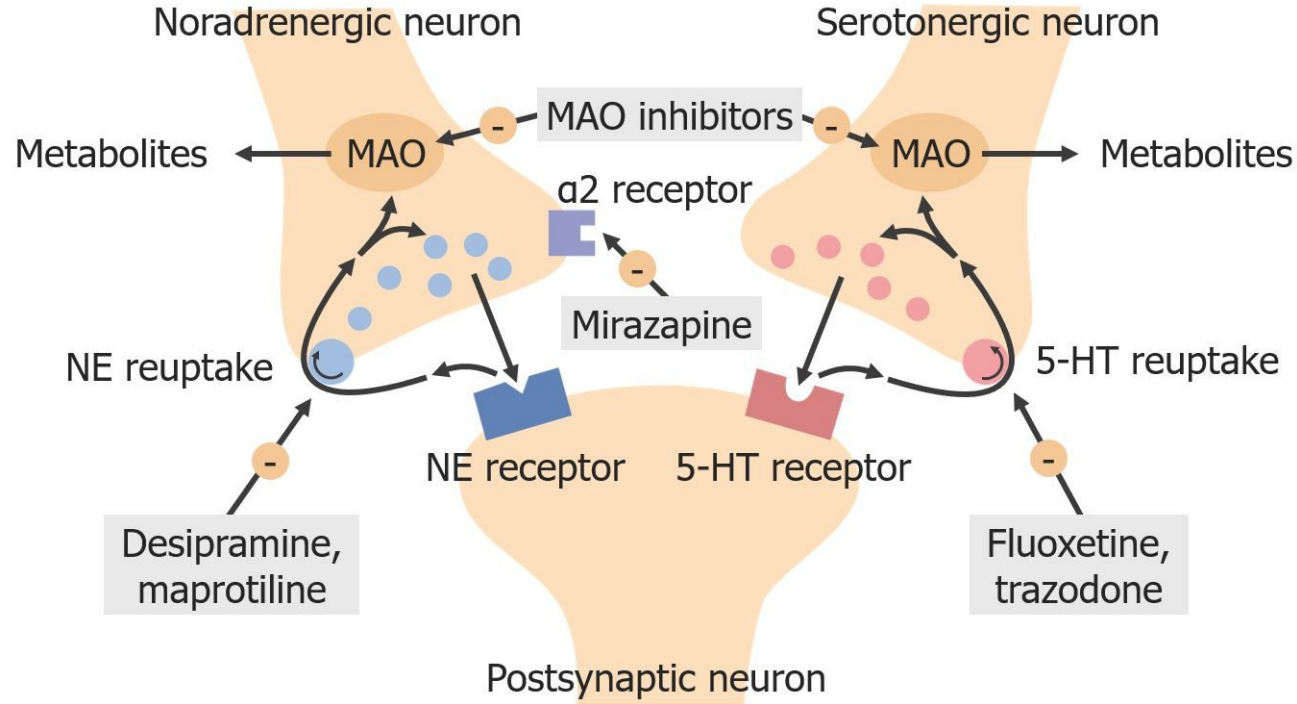
- I am a member of the following organizations: The Society of Teachers of Family Medicine and the N. American Primary Care Research Group (also the Am Institute for the History of Pharmacy and the American Association for the History of Medicine)

Where I'm going today

1. Depression: from maladaptation to a comprehensive disease
2. How institutional corruption promotes overdiagnosis and overtreatment of depression in primary care
3. The lack of evidence supporting the treatment of patients with mild to moderate depression
4. Tempering our use of medical interventions through “medical nihilism”

- 1. Depression: From maladaptation to a comprehensive disease**

TO:





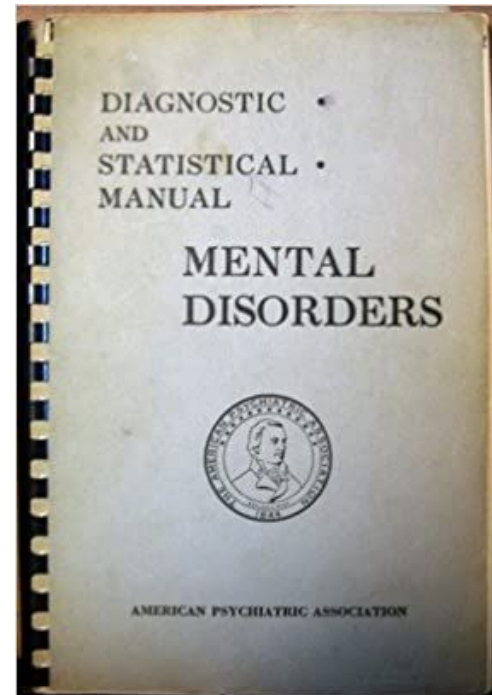
The evolution of the DSM

1952: DSM I: Mental Health Disorders (n=102)

Biological causes: infection, cancer, heritable diseases, etc

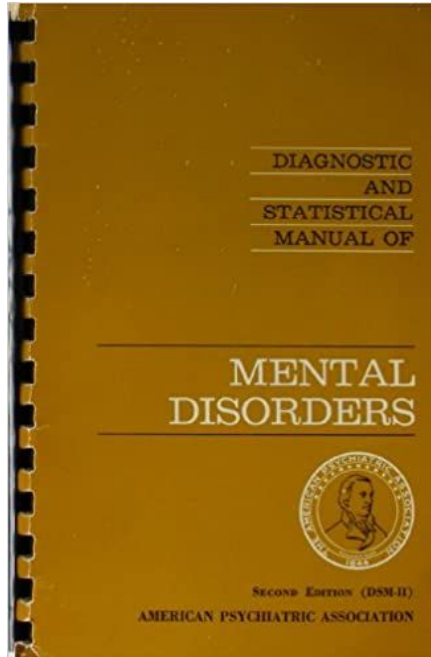
OR

Inability to adjust to one's environment



The evolution of the DSM

1968: DSM II: Mental Health Disorders (n=182)



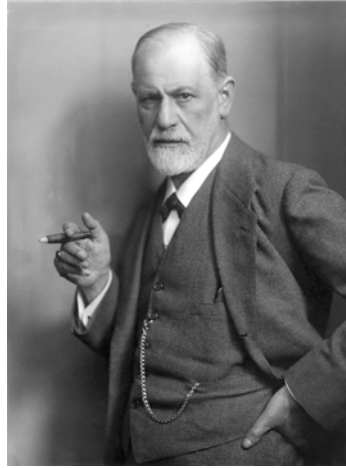
Problem #1



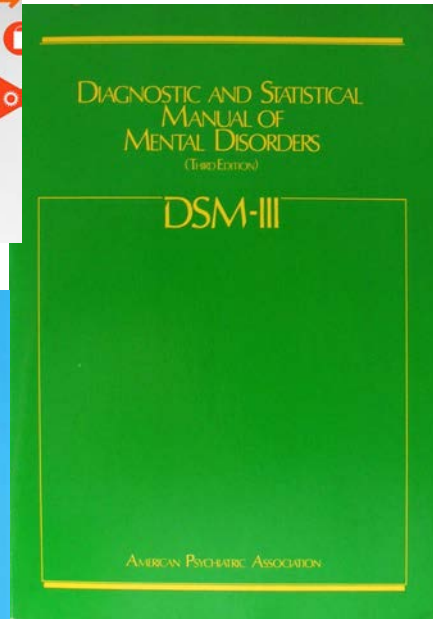
Problem #2



Pushback against talk therapy



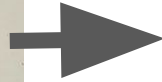
1980: DSM III (n = 265)







1994: DSM IV (n = 297)



2013: DSM 5: (n = 157)



Arabic numbers

 0 sifr	 1 wahid	 2 ithan	 3 thalaatha	 4 arbaa
 5 khamsa	 6 sitta	 7 saba	 8 thamaaniya	 9 tisa

DSM 5 (2013)



Hot takes on the value of biologic psychiatry

“I spent 13 years at NIMH really pushing on the neuroscience and genetics of mental disorders, and when I look back on that I realize that while I think I succeeded at getting lots of really cool papers published by cool scientists at fairly large costs—I think **\$20 billion**—I don’t think we moved the needle in reducing suicide, reducing hospitalizations, improving recovery for the tens of millions of people who have mental illness.”

[Tom Insel, Psychiatrist and former head of NIMH](#)

Wired Science Interview, May 11, 2017

Hot takes on the value of biologic psychiatry

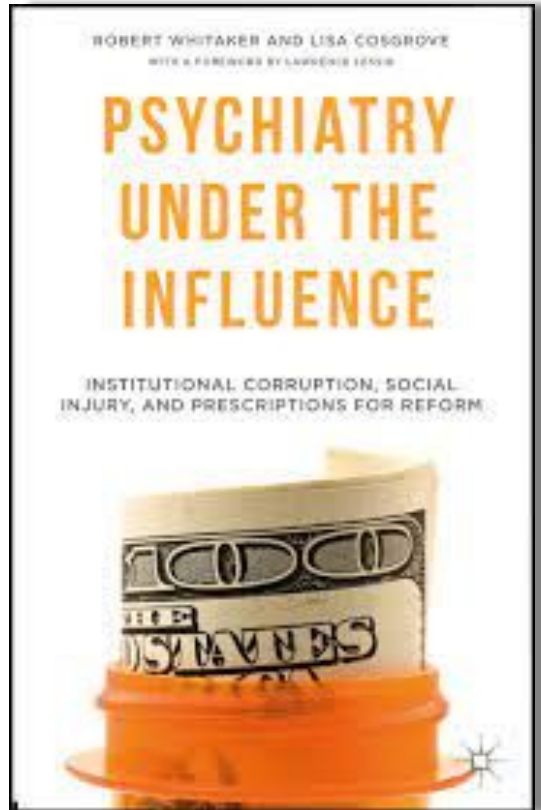
“I object to the National Institute of Mental Health (NIMH) research agenda that is narrowly brain reductionistic; it has achieved great intellectual masterpieces, but so far has not yet helped a single patient.”

[Allen Frances, MD, Chair, DSM IV committee](#)

Interview, Psychiatric Times 2019; 36(10)

<https://www.psychiatrictimes.com/view/conversations-critical-psychiatry-allen-frances-md>

2. Institutional corruption, overdiagnosis, overtreatment



Epistemic Corruption, the Pharmaceutical Industry, and the Body of Medical Science

Sergio Sismondo *

Department of Philosophy, Queen's University, Kingston, ON, Canada

When a knowledge system importantly loses integrity, ceasing to provide the kinds of trusted knowledge expected of it, we can label this *epistemic corruption*. Epistemic corruption often occurs because the system has been co-opted for interests at odds with some of the central goals thought to lie behind it. There is now abundant evidence that the involvement of pharmaceutical companies corrupts medical science. Within the

Institutional corruption (Whitaker and Cosgrove)

“When the *institution* – the system or process – allows or encourages *legal* systematic practices that draw the institution away from its mission and undermine its integrity.”

WHITAKER, R., & COSGROVE, L. (2015). Psychiatry under the influence: institutional corruption, social injury and prescriptions for reform. 2015; Palgrave MacMillan.

Epistemic corruption (Sismondo)

“When a *knowledge system* importantly loses integrity, ceasing to provide the kinds of trusted knowledge expected of it . . . (which) often occurs because the system has been co-opted for interests at odds with some of the central goals thought to lie behind it.”

Sismondo S (2021) Epistemic Corruption, the Pharmaceutical Industry, and the Body of Medical Science. Front. Res. Metr. Anal. 6:614013. doi: 10.3389/frma.2021.614013

It's not that there are bad apples; it's the barrel that is rotten



How? Conflicts of interest

Financial

Intellectual

Professional

Financial conflicts of interest

Community Mental Health Journal (2022) 58:619–623
<https://doi.org/10.1007/s10597-021-00906-6>

FRESH FOCUS



Conflicts of Interest in Psychopharmacology Textbooks

Lisa Cosgrove¹ · Farahdeba Herrawi¹ · Allen F. Shaughnessy²

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Abstract

While most textbooks and editors

Conflicts of interest and the quality of recommendations in clinical guidelines[†]

Lisa Cosgrove, PhD^{1,2} Harold J. Bursztajn, MD⁴ Deborah R. Erlich, MD, MmedEd⁵, Emily E. Wheeler, MS³ and Allen F. Shaughnessy, PharmD, MmedEd⁶

¹Research Lab Fellow, The Edmond J. Safra Center for Ethics, Harvard University, Cambridge, MA, USA

²Associate Professor, ³Doctoral Candidate, Department of Counseling and School Psychology, University of Massachusetts Boston, Boston, MA, USA

⁴Associate Clinical Professor, Department of Psychiatry, Harvard Medical School, Cambridge, MA, USA

⁵Assistant Professor, ⁶Professor, Department of Family Medicine, Tufts University School of Medicine, Boston, MA, USA

Keywords

clinical practice guidelines, conflict of interest, depression

Abstract

Background There is increasing concern that conflicts of interest affect the development process of clinical practice guidelines. We evaluated The American Psychiatric Association's Practice Guideline for the Treatment of Patients with Major Depressive Disorder to determine the existence of financial and intellectual conflicts of interest and examine their

Correspondence

Psychother Psychosom 2012;81:186–188

DOI: [10.1159/000335523](https://doi.org/10.1159/000335523)

The American Psychiatric Association's Guideline for Major Depressive Disorder: A Commentary

Lisa Cosgrove^{a, d}, Allen F. Shaughnessy^e, Emily E. Wheeler^d, Kirsten E. Austad^{a, b}, Irving Kirsch^{b, f}, Harold J. Bursztajn^c

^aEdmond J. Safra Center for Ethics, Harvard University,

^bHarvard Medical School, and ^cDepartment of Psychiatry, Beth Israel Deaconess Medical Center, Harvard Medical School, Cambridge, Mass., ^dDepartment of Counseling and School Psychology, University of Massachusetts, and ^eDepartment of Family Medicine, Tufts University School of Medicine, Boston, Mass., USA; ^fSchool of Psychology, University of Plymouth, Devon, UK

ACCOUNTABILITY IN RESEARCH

2017, VOL. 24, NO. 2, 99–115

<http://dx.doi.org/10.1080/08989621.2016.1251319>



Taylor & Francis
Taylor & Francis Group

Conflict of Interest Policies and Industry Relationships of Guideline Development Group Members: A Cross-Sectional Study of Clinical Practice Guidelines for Depression

Lisa Cosgrove, Ph.D.^a, Sheldon Krinsky, Ph.D.^b, Emily E. Wheeler, M.S.^a, Shannon M. Peters, M.S.^a, Madeline Brodt, M.S.^a, and Allen F. Shaughnessy, Pharm.D., M.Med.Ed.^{c, d}

^aDepartment of Counseling and School Psychology, University of Massachusetts Boston, Boston, Massachusetts, USA; ^bDepartment of Urban and Environmental Policy and Planning, Tufts University, Medford, Massachusetts, USA; ^cDepartment of Family Medicine, Tufts University School of Medicine, Boston, Massachusetts, USA; ^dTufts University Family Medicine Residency at Cambridge Health Alliance, Malden, Massachusetts, USA

ABSTRACT

Because of increased attention to the issue of trustworthiness of clinical practice guidelines, it may be that both transparency and management of industry associations of guideline development groups (GDGs) have improved. The purpose of the present study was to assess a) the disclosure requirements of GDGs in a cross-section of guidelines for major depression;

KEYWORDS

clinical practice guidelines; conflict of interest; depression; disclosure policies; public trust; research bias

Example: APA guidelines on the treatment of depression

Financial ties to industry were disclosed by all members (100%) of the guideline development committee with members reporting a mean 20.5 relationships (range 9–33). The majority of the committee participated on pharmaceutical companies' speakers' bureaus.

Cosgrove L, Bursztajn HJ, Erlich DR, Wheeler EE, Shaughnessy AF. Conflicts of interest and the quality of recommendations in clinical guidelines. *J Eval Clin Pract.* 2013 Aug;19(4):674-81. doi: 10.1111/jep.12016.

Financial conflicts of interest: Psychopharm textbooks

Table 1 FCOI of Editors of psychopharmacology textbook

Textbook	Editor	Payments from 2 years prior to textbook publication to 2020 ^a	Total payments
The American Psychiatric Association Publishing Textbook of Psychopharmacology 5th edition (2017)	Editor #1 M.D.	\$85,457.00	\$162,976.00
	Editor #2 M.D., Ph.D.	\$77,519.00	
Clinical Manual of child and Adolescent Psychopharmacology Revised 3rd Edition (2017)	Editor #3 M.D.	\$2389.00	\$137,899.00
Essential Psychopharmacology: Neuroscientific Basis and Practical Applications 5th edition (2013)	Author #12 M.D., Ph.D.	\$10,616,165.00	\$10,616,165.00
Manual of Clinical Psychopharmacology 9th edition (2019)	Author #13 M.D.	\$63,016.00 ^b	\$89,308.00
	Author #14 D.M.H., M.D.	\$26,292.00	

Cosgrove L, Herrawi F, Shaughnessy AF. Conflicts of Interest in Psychopharmacology Textbooks. Community Ment Health J. 2022 ;58(4):619-623. doi: 10.1007/s10597-021-00906-6.

Intellectual conflicts of interest

When we love our own ideas: “Academic activities that create the potential for an attachment to a specific point of view that could unduly affect an individual’s judgment about a specific recommendation.”

Guyatt G, Akl EA, Hirsh J, Kearon C, Crowther M, Gutterman D, Lewis SZ, Nathanson I, Jaeschke R, Schönemann H. The vexing problem of guidelines and conflict of interest: a potential solution. *Ann Intern Med.* 2010 Jun 1;152(11):738-41. doi: 10.7326/0003-4819-152-11-201006010-00254.



Conflicts of interest and the quality of recommendations in clinical guidelines[†]

Lisa Cosgrove, PhD^{1,2} Harold J. Bursztajn, MD⁴ Deborah R. Erlich, MD, MEd, MS³ and Allen F. Shaughnessy, PharmD, MmedEd⁶

¹Research Lab Fellow, The Edmond J. Safra Center for Ethics, Harvard University

²Associate Professor, ³Doctoral Candidate, Department of Counseling and Applied Behavioral Science, Boston College, Chestnut Hill, MA, USA

⁴Associate Clinical Professor, Department of Psychiatry, Harvard Medical School

⁵Assistant Professor, ⁶Professor, Department of Psychiatry, Harvard Medical School

“Seventeen (13%) of the 130 papers supporting the recommendations were published by one of the guideline developers.”

Key
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Background There is increasing concern that conflicts of interest affect the development process of clinical practice guidelines. We evaluated The American Psychiatric Association's Practice Guideline for the Treatment of Patients with Major Depressive Disorder to determine the existence of financial and intellectual conflicts of interest and examine their possible effects. We selected this guideline because of its influence on clinical practice and

Professional conflicts of interest

- Official statements from a professional group or society
“Approved by,” “official guidance from,” etc.
- “Although it is true that individual medical providers care deeply about their patients, the guild of health care professionals – including their specialty societies – has a primary responsibility to promote its members’ interests.”

Quanstrum KH, Hayward RA. Lessons from the mammography wars. N Engl J Med. 2010 Sep 9;363(11):1076-9. doi: 10.1056/NEJMsb1002538. PMID: 20825322.

Example: subclinical hypothyroidism

“Although good evidence is **unavailable** [to support our recommendation], *there is a sizable amount of fair evidence* **and an abundance of opinion by experts** . . . The [scientific panel recommendations] are **contrary to the practice of many. . . experts**”

Gharib H, et al. Consensus statement: Subclinical thyroid dysfunction: A joint statement on management from the American Association of Clinical Endocrinologists, The American Thyroid Association, and The Endocrine Society. J Clin Endocrinol Metab 2005;90:581-5.

It's not that there are bad apples; it's the barrel that is rotten



The result: Diagnostic creep



“An ill for every pill”

Overdiagnosis

Overtreatment

Ignoring root causes

3. The lack of evidence supporting the treatment of patients with mild to moderate depression

Antidepressant medication works. . . but so does placebo

Antidepressant Drug Effects and Depression Severity

A Patient-Level Meta-analysis

Jay C. Fournier, MA

Robert J. DeRubeis, PhD

Steven D. Hollon, PhD

Sona Dimidjian, PhD

Context Antidepressant medications represent the best established treatment for major depressive disorder, but there is little evidence that they have a specific pharmacological effect relative to pill placebo for patients with less severe depression.

Objective To estimate the relative benefit of medication vs placebo across a wide

Conclusions The magnitude of benefit of antidepressant medication compared with placebo increases with severity of depression symptoms and may be minimal or non-existent, on average, in patients with mild or moderate symptoms. For patients with very severe depression, the benefit of medication over placebo is substantial.

A

(ADM) represents the current standard of treatment for

proved by the Food and Drug Administration in the treatment of major or minor depressive disorder were selected. Studies were included if their authors provided the requisite original data; they comprised adult outpatients; they included a medication

Fournier JC, DeRubeis RJ, Hollon SD, Dimidjian S, Amsterdam JD, Shelton RC, Fawcett J. Antidepressant drug effects and depression severity: a patient-level meta-analysis. JAMA. 2010 Jan 6;303(1):47-53. doi: 10.1001/jama.2009.1943. PMID: 20051569

Initial Severity and Antidepressant Benefits: A Meta-Analysis of Data Submitted to the Food and Drug Administration

Irving Kirsch^{1*}, Brett J. Deacon², Tania B. Huedo-Medina³, Alan Scoboria⁴, Thomas J. Moore⁵, Blair T. Johnson³

1 Department of Psychology, University of Hull, Hull, United Kingdom, **2** University of Wyoming, Laramie, Wyoming, United States of America, **3** Center for Health,

Drug-placebo differences in antidepressant efficacy increase as a function of baseline severity, but are relatively small even for severely depressed patients. The relationship between initial severity and antidepressant efficacy is attributable to decreased responsiveness to placebo among very severely depressed patients, rather than to increased responsiveness to medication.

and BTJ have no
interests.

placebo treatment, and when unpublished trial data are included, the benefit falls below

Kirsch I, Deacon BJ, Huedo-Medina TB, Scoboria A, Moore TJ, Johnson BT. Initial severity and antidepressant benefits: a meta-analysis of data submitted to the Food and Drug Administration. PLoS Med. 2008 Feb;5(2):e45. doi: 10.1371/journal.pmed.0050045. PMID: 18303940

Comparative efficacy and acceptability of 21 antidepressant drugs for the acute treatment of adults with major depressive disorder: a systematic review and network meta-analysis



We found that all antidepressants included in the meta-analysis were more efficacious than placebo in adults with major depressive disorder and the summary effect sizes were mostly modest. Some antidepressants, such as

work to compare and rank antidepressants for the acute treatment of adults with unipolar major depressive disorder.

Methods We did a systematic review and network meta-analysis. We searched Cochrane Central Register of Controlled Trials, CINAHL, Embase, LILACS database, MEDLINE, MEDLINE In-Process, PsycINFO, the websites

See [Comment page 1333](#)

*Joint first authors

Department of Psychiatry,

Cipriani A, Furukawa TA, Salanti G, et al. Comparative efficacy and acceptability of 21 antidepressant drugs for the acute treatment of adults with major depressive disorder: a systematic review and network meta-analysis. *Lancet*. 2018 Apr 7;391(10128):1357-1366. doi: 10.1016/S0140-6736(17)32802-7

Why?

The expectation effect (placebo response)

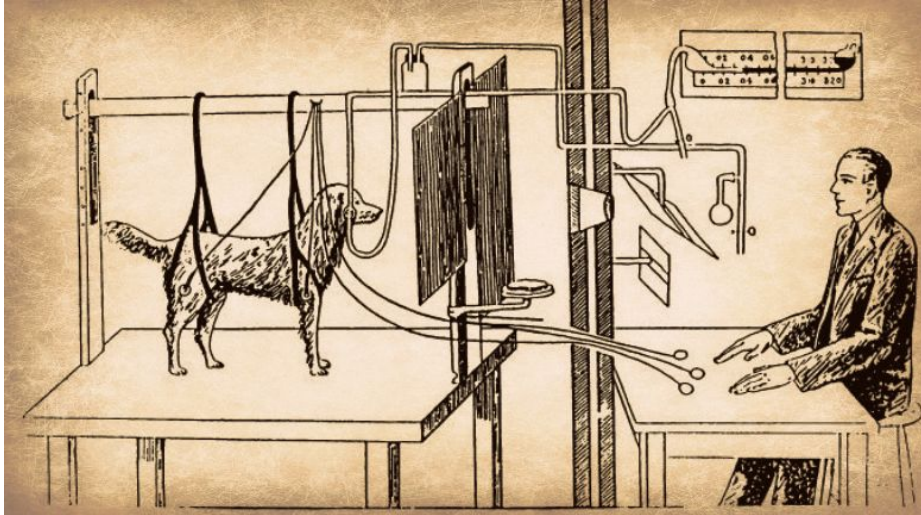


- 610 patients with pain: Pain 4.3 -5.7 out of 10
- “ionized” bracelet or un-ionized bracelet
- At 4 weeks:
 - Q-ray: average score 1.7 - 2.6 lower
 - Placebo: average score 1.3 -2.5 lower
 - 77% of patients reported pain relief
- 50% had heard of the bracelet; 80% felt it would work

• Cuff style makes it easy to clin bracelet on and off: great for daily wear

Bratton RL, Montero DP, Adams KS, et al. Effect of "ionized" wrist bracelets on musculoskeletal pain: a randomized, double-blind, placebo-controlled trial. Mayo Clin Proc 2002;77:1164-8.

Conditioning



51 patients receiving oxy/APAP or hydrocodone/APAP after spine surgery

Half also received placebo with the analgesic – this group took 30% less analgesia

Flowers KM, Patton ME, Hruschak VJ, et al. Conditioned open-label placebo for opioid reduction after spine surgery: a randomized controlled trial. *Pain* 2021;162(6):1828-1839.

Natural history of depression

The natural history of symptoms

Without antidepressant therapy, episodes of clinical depression last from 2 months to several years, with an average of around 5 to 6 months. One-third of the patients recover within a year.

Lehmann HE. Clinical evaluation and natural course of depression. J Clin Psychiatry. 1983 May;44(5 Pt 2):5-10. PMID: 6406462.

Regression (return) to the mean

Outlying findings tend to return to average

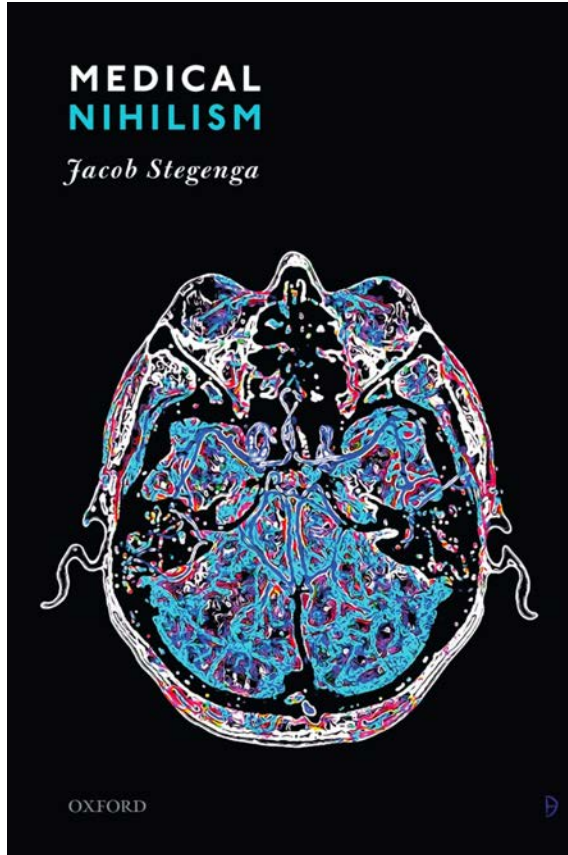


Morton V, Torgerson DJ. Effect of regression to the mean on decision making in health care. *BMJ*. 2003 May 17; 326(7398): 1083–1084. doi: 10.1136/bmj.326.7398.1083



4. How a “medical nihilism” approach can lead to a more temperate approach to the use of medicines and medical interventions

Medical Nihilism— Jacob Stegenga, PhD



PhiSci

Conversations about
Philosophy and Science



Medical Nihilism— Jacob Stegenga, PhD

Change our baseline assumption:

We should have little confidence in the effectiveness of medical interventions

Medical Nihilism— Jacob Stegenga, PhD



Medical Nihilism— Argument 1

Research is Malleable



Medical Nihilism— Argument 1

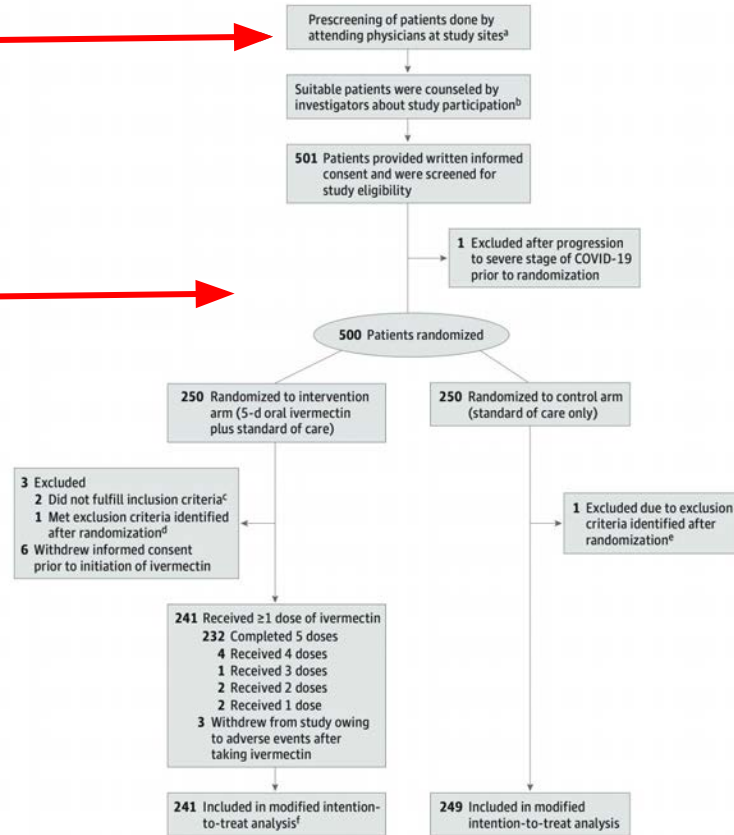
Recruitment



Design

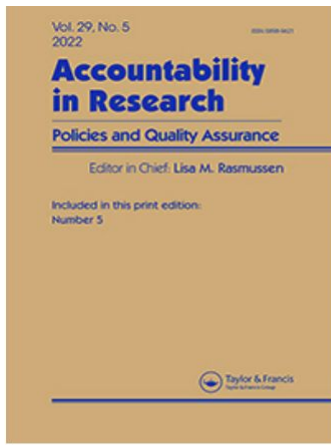


Analysis



Enriched design

Short-duration



Accountability in Research

Policies and Quality Assurance

ISSN: (Print) (Online) Journal homepage: <https://www.tandfonline.com/loi/gacr20>

Industry Effects on Evidence: A case study of long-acting injectable antipsychotics

Lisa Cosgrove, Barbara Mintzes, Harold J. Bursztajn, Gianna D'Ambrozio & Allen F. Shaughnessy

Lisa Cosgrove, Barbara Mintzes, Harold J. Bursztajn, Gianna D'Ambrozio & Allen F. Shaughnessy (2022) Industry effects on evidence: a case study of long-acting injectable antipsychotics, *Accountability in Research*, DOI: [10.1080/08989621.2022.2082289](https://doi.org/10.1080/08989621.2022.2082289)

Medical Nihilism— Argument 2

Small effect sizes

Clinically-relevant difference (HDRS) $\geq 3^*$

Nightly difficulty falling asleep \rightarrow no difficulty: 2 points

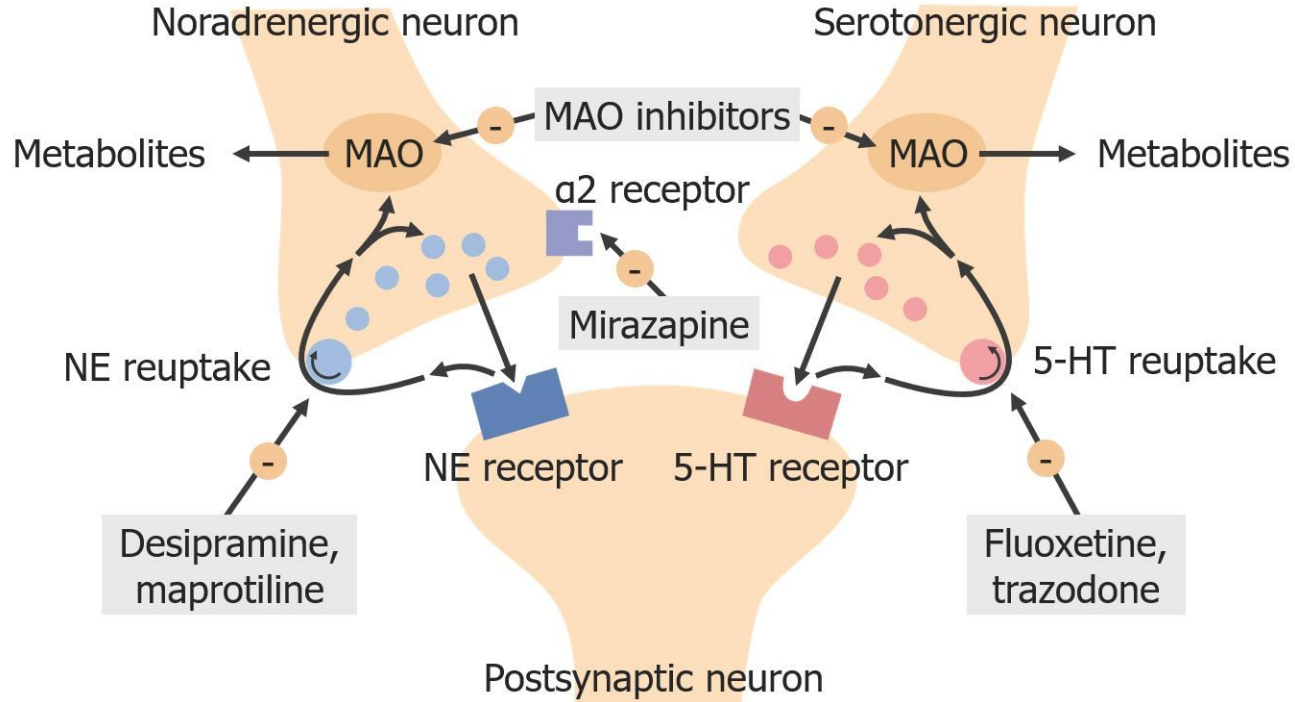
Denies being ill \rightarrow acknowledges being ill: 2 points

Medical Nihilism— Argument 3

No “magic bullets”

Specific + Effective

Medical Nihilism— Argument 3



Medical Nihilism— Argument 3

To illustrate how extensive non-selective binding can be, consider the drug aripiprazole (Abilify), a widely prescribed antipsychotic used for treating schizophrenia, bipolar disorder, and depression. Aripiprazole is a ligand for the following receptors: 5-HT_{1B}, 5-HT_{1D}, 5-HT_{2A}, 5-HT_{2B}, 5-HT_{2C}, 5-HT₃, 5-HT_{5A}, 5-HT₆, 5-HT₇, D₁, D₂, D₃, D₄, D₅, α_{1A} , α_{1B} , α_{2A} , α_{2B} , α_{2C} , β_1 , β_2 , H₁, M₁, M₂, M₃, M₄, M₅₁, among others. This drug is extremely non-selective.

Medical Nihilism— Argument 3

Action and site	Trazodone	Fluoxetine
<i>Uptake inhibition:</i>		
5-HT	189	12
NE	5000	280
DA	14100	1590
<i>Binding affinity:</i>		
5-HT ₁ receptor	60	24000
5-HT ₂ receptor	7.7	210
Muscarinic receptor	320000	2000
Histamine-H ₁ receptor	340	6250
Alpha-1 adrenergic receptor	36	5880
Alpha-2 adrenergic receptor	500	13000
Dopamine D ₂ receptor	3800	—

Pushback to Stegenga:

**Medicine
is
Awesome**

Pushback: Medicine is Awesome

Sanitation

Antibiotics

Anesthesia

Vaccines

Discovery of DNA structure

Germ theory

Oral contraceptive pill

Evidence-based medicine

Medical imaging

Computers

Oral rehydration therapy

Risk of smoking

Immunology

Chlorpromazine

Tissue culture

BMJ poll of the most important medical advances since 1840.

https://www-bmj-com.content/suppl/2007/01/18/334.suppl_1.DC3

Solutions

The solution, part 1 (Conceptual approach)

Epistemic humility

- Becoming an epistemically virtuous clinician

Epistemic humility

“The threat to medicine is not that we do not know things. The threat is that we create a sense of certainty out of uncertain knowledge—that we profess to know things that we do not.”

Mercuri M. Humility in the face of uncertainty. J Eval Clin Pract. 2019;25:173–175. <https://doi.org/10.1111/jep.13116>: (DOI: 10.1111/jep.13116)

The slide to certainty

“We have a tendency to find solace in scientific findings. Average effects are codified into best practices. Those best practices become benchmarks for quality of care. Failing to meet those benchmarks is conceived as a sign of poor decision-making and ultimately poor patient care. Best practices and quality benchmarks may provide support for clinicians and may even provide a sense that healthcare decisions are grounded in objective science and not arbitrary, but such practices and benchmarks do not eliminate the uncertainty of the patient's outcome. “

The epistemically virtuous clinician James A. Marcum Theor Med Bioeth (2009) 30:249–265 DOI 10.1007/s11017-009-9109-1

The solution, part 2 (Political)

Re-conceptualizing depression as a social disorder

“Mental health and well-being cannot be defined by the absence of a mental health condition, but must be defined instead by the social, psychosocial, political, economic and physical environment that enables individuals and populations to live a life of dignity, with full enjoyment of their rights and in the equitable pursuit of their potential.”

D. Pūras, Report of the Special Rapporteur on the right of everyone to the enjoyment of the highest attainable standard of physical and mental health, UN Doc. A/ HRC/41/34 (2019).

The Solution, part 3 (individual)

Ask:

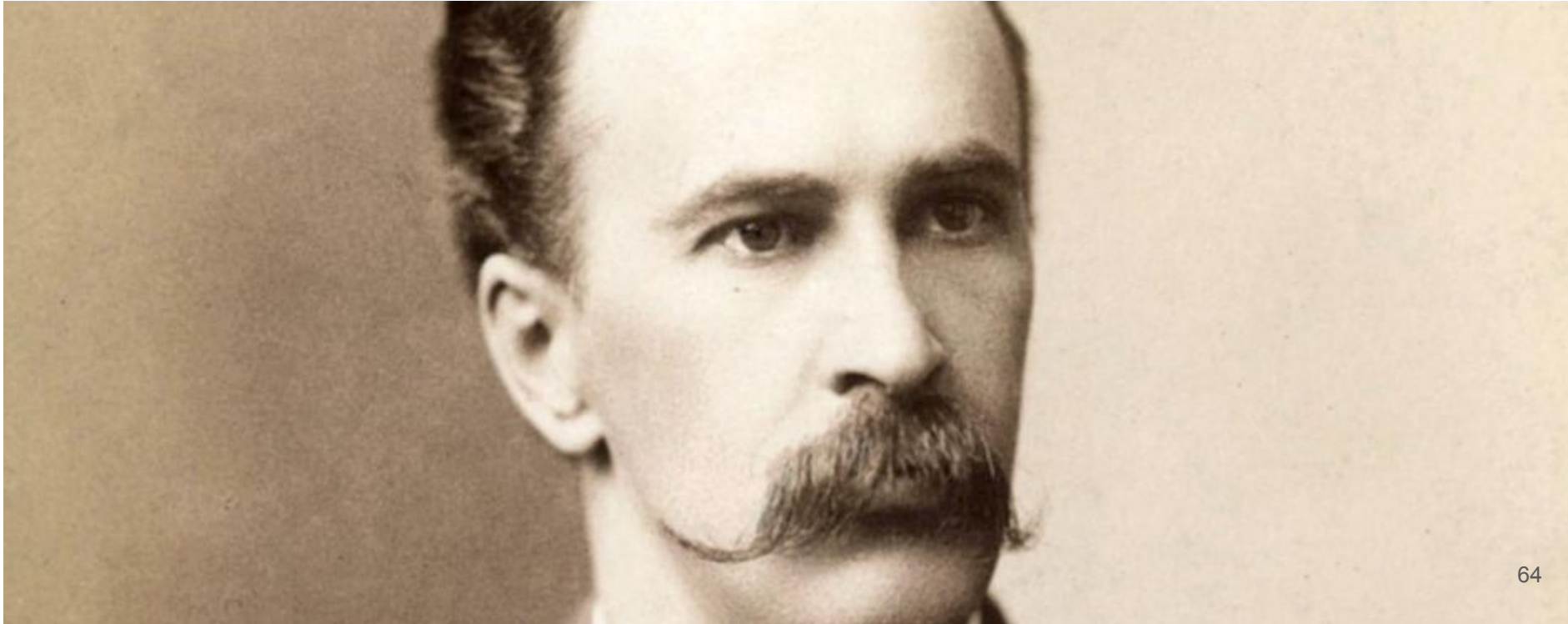
How **well** does it work?

In **whom** does it work?

Do the benefits **outweigh** the risks?

Are the benefits **worth** the cost?

“One of the first duties of the physician is to educate the masses not to take medicine.”



Wrap-up

- Is depression a chemistry problem or the result of one's environment?
- Our medical institutions promote overdiagnosis and overtreatment of depression
- Antidepressants work for depression, but so does placebo – what to do?
- While medicine is awesome, we have to focus more on social approaches to helping patients live longer and live better

