Poster Code: MSR12

Variation in Conceptual and Operational Definitions of Depression in Real-World Research

Scan for poster + more

Jared Kamauu, BFA,[1] Michael Buck, PhD,[1] Craig Parker, MD, MS,[1] Allise Kamauu, MS,[1] Scott L. DuVall, PhD,[2] Aaron Kamauu, MD, MS, MPH[1]

[1]Navidence Inc., USA; [2]PurpleLab, USA

So What?

Awareness of the high variability in definitions for depression, MDD, and TRD are essential for clear understanding the interpretation of data.

BACKGROUND

Context
Conceptual and computable operational definitions (CODefs) are integral to Real-World Research (RWR), especially to define cohort phenotypes. Interpretation of results in RWR are directly dependent on the CODefs used.

The Gap / Problem
Variance in CODefs can create inconsistencies in research results and interpretation.

Pharmacoepidemiologic Relevance
Awareness of variation in definitions and code lists used to define clinical concepts is essential to having a clear understanding of study results.

OBJECTIVES

Primary Objective
To demonstrate variations in cohort-defining CODefs from reputable sources and publications on patients with depression.

METHODS

Study Design & Data Source
We reviewed definitions for depression, major depressive disorder (MDD), and treatment resistant depression (TRD) that were published in literature and clinical references (i.e. NICE). Those definitions were extracted and compared against each other to see the level of variation between the references. The analysis includes comparison of code lists (ICD-10-CM), scoring models, and treatment failure.

Study Population
24 references were reviewed and 33 distinct CODefs were extracted as definitions of depression, MDD, or TRD. The analysis includes comparison of code lists (ICD-10-CM), scoring models, and treatment failure.

Figure 1: Study Design

Targeted Literature Review
24 Published references with depression, MDD, and TRD CODefs

↓

Distinct Definitions Extracted
33 Definitions across depression, MDD, and TRD

↓

Distinct Code Lists Extracted
7 Diagnosis code lists 13 medication lists

↓

Compared Variation Between Definitions and Code Lists

Definitions Review
24 references were reviewed and 33 distinct CODefs were extracted as definitions of depression, MDD, or TRD. The most common definition was Diagnostic and Statistical Manual of Mental Disorders (DSM-5) criteria which appeared in 8 of the references. After that were two diagnosis code lists, one defining depression (3/24) and the other MDD (3/24), and the initiation of a third antidepressant defining TRD (3/24). 20 definitions only appeared in a single reference.

Code and Medication Review
13 TRD definitions across 8 references showed variance in the number of treatments and their definition for failure of treatment. 10 references published 7 distinct code list definitions for depression/MDD. Every code list included F32 and F33 codes but differed by the additional codes that were included or excluded. The most unique definition came from the depression deficit component of the Veterans Affairs Frailty Index (VA-FI) which included disorders related to depression such as bipolar disorder.

Computable Operational Definitions (CODefs™)

Study elements — exposures, outcomes, and covariates — were defined using Navidence CODefs™: rigorous, data source-agnostic algorithms that ensure precision and reproducibility across real-world data sources.

navidence.com

RESULTS

24	33	13
Total Published References Reviewed	Distinct Definitions for Depression, MDD, and TRD	Distinct Definitions for TRD Alone

Figure 2: # of Distinct Definitions Per Each Reference

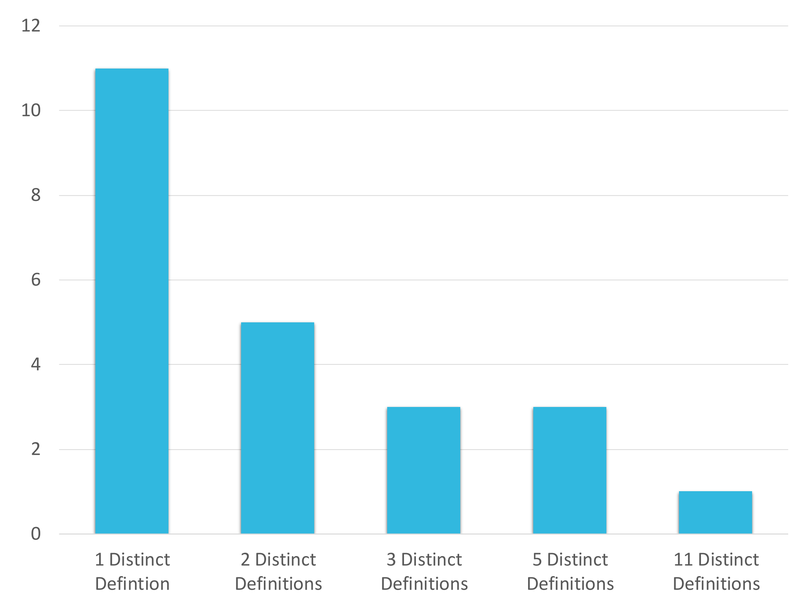
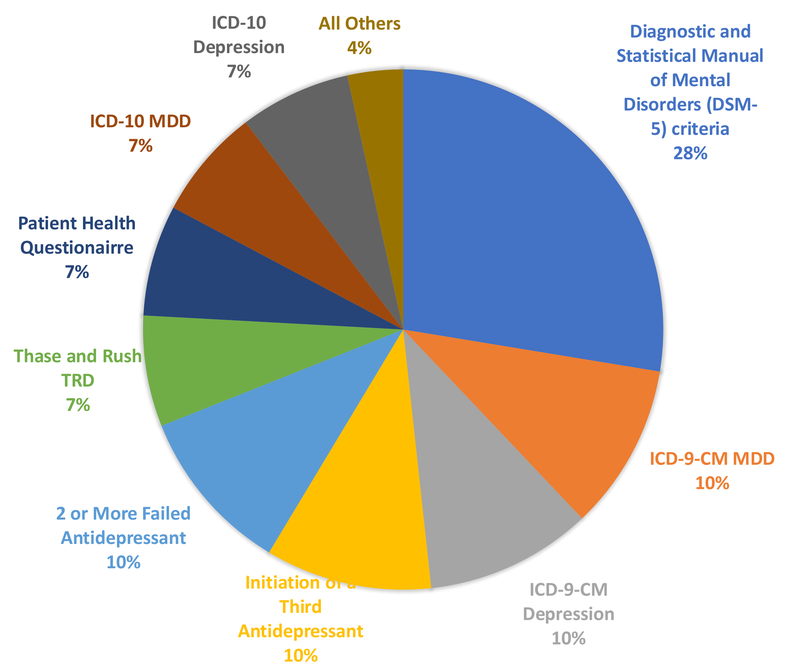


Figure 3: Common Definitions



CONCLUSIONS

Key Findings
This review showcases a large amount of variety in definitions for depression. This variance creates difficulty in consistent interpretation of results. Awareness of this variance in definitions is essential to understanding the impact on RWR studies

Clinical & Policy Implications
It is recommended to always publish the exact definition and codes used to define depression so that interpretation of data can become clear and consistent.

REFERENCES

1. Sforzini L, et al. A Delphi-method-based consensus guideline for definition of treatment-resistant depression for clinical trials. Mol Psychiatry. 2022 Mar;27(3):1286-1299. doi: 10.1038/s41380-021-01381-x. Epub 2021 Dec 15. PMID: 34907394; PMCID: PMC90954752.

2. Solberg LI, et al. Are claims data accurate enough to identify patients for performance measures or quality improvement? The case of diabetes, heart disease, and depression. Am J Med Qual. 2006 Jul-Aug;21(4):238-45. doi: 10.1177/1062860606288243. [PMID: 16849780]

3. Xu R, Bode L, Geva A, Mandl KD, McMurry AJ. Accuracy of ICD-10 codes for suicidal ideation and action in pediatric emergency department encounters. medRxiv [Preprint]. 2024 Jul 24:2024.07.23.24310777. doi: 10.1101/2024.07.23.24310777. Update in: Pediatr Emerg Care. 2025 May 1;41(5):378-382. doi: 10.1097/PEC.0000000000003328. [PMID: 39211891; PMCID: PMC11361224]

4. Tolentino JC, Schmidt SL. DSM-5 Criteria and Depression Severity: Implications for Clinical Practice. Front Psychiatry. 2018 Oct 2;9:450. doi: 10.3389/fpsyt.2018.00450. [PMID: 30333763; PMCID: PMC6176119]

5. National Institute of Mental Health. Major Depression. Available at: https://www.nimh.nih.gov/health/statistics/major-depression

6. Patel RK, Aslam SP, Rose GM. Persistent Depressive Disorder. [Updated 2024 Aug 11]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2026 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK541052/

7. Löwe B, Spitzer RL, Gräfe K, Kroenke K, Quenter A, Zipfel S, Buchholz C, Witte S, Herzog W. Comparative validity of three screening questionnaires for DSM-IV depressive disorders and physicians' diagnoses. J Affect Disord. 2004 Feb;78(2):131-40. doi: 10.1016/s0165-0327(02)00237-9. [PMID: 14706723]

8. Park LT, Zarate CA Jr. Depression in the Primary Care Setting. N Engl J Med. 2019 Feb 7;380(6):559-568. doi: 10.1056/NEJMcp1712493. [PMID: 30726688; PMCID: PMC6727965]

9. Smith KM, Renshaw PF, Bilello J. The diagnosis of depression: current and emerging methods. Compr Psychiatry. 2013 Jan;54(1):1-6. doi: 10.1016/j.comppsych.2012.06.006. Epub 2012 Aug 15. [PMID: 22901834; PMCID: PMC5502713]

10. McIntyre RS, Alsuwaidan M, Baune BT, Berk M, Demyttenaere K, Goldberg JF, Gorwood P, Ho R, Kasper S, Kennedy SH, Ly-Uson J, Mansur RB, McAllister-Williams RH, Murrough JW, Nemeroff CB, Nierenberg AA, Rosenblat JD, Sanacora G, Schatzberg AF, Shelton R, Stahl SM, Trivedi MH, Vieta E, Vinberg M, Williams N, Young AH, Maj M. Treatment-resistant depression: definition, prevalence, detection, management, and investigational interventions. World Psychiatry. 2023 Oct;22(3):394-412. doi: 10.1002/wps.21120. [PMID: 37713549; PMCID: PMC10503923]

11. U.S. Department of Veterans Affairs (VA). VA/DOD Clinical Practice Guidelines. Management of Major Depressive Disorder (MDD) (2022). Available at https://www.healthquality.va.gov/guidelines/MH/mdd/

12. National Institute for Health and Care Excellence (NICE). Depression in adults: treatment and management. Reference number: NG222. Published: 29 June 2022. Available at: https://www.nice.org.uk/guidance/ng222

13. Zhdanava M, Pilon D, Ghelerter I, Chow W, Joshi K, Lefebvre P, Sheehan JJ. The Prevalence and National Burden of Treatment-Resistant Depression and Major Depressive Disorder in the United States. J Clin Psychiatry. 2021 Mar 16;82(2):20m13699. doi: 10.4088/JCP.20m13699. PMID: 33989464.

14. Engels A, König HH, Magaard JL, Härter M, Hawighorst-Knapstein S, Chaudhuri A, Brettschneider C. Depression treatment in Germany - using claims data to compare a collaborative mental health care program to the general practitioner program and usual care in terms of guideline adherence and need-oriented access to psychotherapy. BMC Psychiatry. 2020 Dec 14;20(1):591. doi: 10.1186/s12888-020-02995-1. [PMID: 33317480; PMCID: PMC7737360]

15. Pilon D, Joshi K, Sheehan JJ, Zichlin ML, Zuckerman P, Lefebvre P, Greenberg PE. Burden of treatment-resistant depression in Medicare: A retrospective claims database analysis. PLoS One. 2019 Oct 10;14(10):e0223255. doi: 10.1371/journal.pone.0223255. Erratum in: PLoS One. 2021 Apr 1;16(4):e0249731. doi: 10.1371/journal.pone.0249731. [PMID: 31600244; PMCID: PMC6786597]

16. Märtens C, Stapel B, Heitland I, Zeidler J, Bauersachs J, Stahmeyer JT, Kahl KG. Depression severity and major cardiovascular events: Findings from German insurance claims data. J Psychosom Res. 2026 May;204:112579. doi: 10.1016/j.jpsychores.2026.112579. Epub 2026 Feb 9. [PMID: 41689971]

17. Hwang S, Jayadevappa R, Zee J, Zivin K, Bogner HR, Raue PJ, Bruce ML, Reynolds CF 3rd, Gallo JJ. Concordance Between Clinical Diagnosis and Medicare Claims of Depression Among Older Primary Care Patients. Am J Geriatr Psychiatry. 2015 Jul;23(7):726-34. doi: 10.1016/j.jagp.2014.08.009. Epub 2014 Aug 27. [PMID: 25256215; PMCID: PMC4634645]

18. Amos TB, Tandon N, Lefebvre P, Pilon D, Kamstra RL, Pivneva I, Greenberg PE. Direct and Indirect Cost Burden and Change of Employment Status in Treatment-Resistant Depression: A Matched-Cohort Study Using a US Commercial Claims Database. J Clin Psychiatry. 2018 Mar/Apr;79(2):17m11725. doi: 10.4088/JCP.17m11725. [PMID: 29474009]

19. Pilon D, Sheehan JJ, Szukis H, Singer D, Jacques P, Lejeune D, Lefebvre P, Greenberg PE. Medicaid spending burden among beneficiaries with treatment-resistant depression. J Comp Eff Res. 2019 Apr;8(6):381-392. doi: 10.2217/cer-2018-0140. Epub 2019 Feb 8. [PMID: 30734581]

20. U.S. Food and Drug Administration. Major Depressive Disorder: Developing Drugs for Treatment Guidance for Industry. Available at: https://www.fda.gov/media/113988/download

21. European Medicines Agency. Guideline on clinical investigation of medicinal products in the treatment of depression. Available at: https://www.ema.europa.eu/en/documents/scientific-guideline/guideline-clinical-investigation-medicinal-products-treatment-depression-revision-3_en.pdf

22. Thase ME, Rush AJ. When at first you don't succeed: sequential strategies for antidepressant nonresponders. J Clin Psychiatry. 1997;58 Suppl 13:23-9. [PMID: 9402916]

23. National Library of Medicine. Clinicaltrials.gov. Prospective Clinical Cohort Study of Depression. Available at: https://clinicaltrials.gov/study/NCT05775809

DISCLOSURES & ACKNOWLEDGMENTS

Aa Kamauu, J Kamauu, Al Kamauu, M Buck & C Parker: Employees of Navidence Inc. Aa Kamauu, C Parker: Co-Founders of Navidence Inc. S DuVall: Employee of PurpleLab. No conflicts of interest to disclose.