Benzodiazepine Overdose v2 Parsed Drug Overdose Surveillance and Epidemiology (DOSE) System Guidance Syndromic Surveillance Definition Factsheet and Technical Brief

Authors: Stephen Liu, PhD 1, Herschel Smith, MPH 1, Erin Stokes, MPH 1, Snehaa Krishnan, MPH 1,2

¹ CDC National Center for Injury Prevention and Control, Division of Overdose Prevention (DOP), Epidemiology and Surveillance Branch

²Oak Ridge Institute for Science and Education, Oak Ridge, TN

Point of contact: DOSE Team (DOSE@cdc.gov)

<u>Definition Purpose</u>: To assist state, local, tribal, territorial, and federal public health practitioners in monitoring emergency department (ED) visits for suspected nonfatal benzodiazepine-involved overdoses using syndromic surveillance data.

New or Revised Definition: Revision of CDC Benzodiazepine Overdose v1

Date Added to ESSENCE: June 18, 2023

<u>Definition Description</u>: The benzodiazepine overdose syndrome definition was designed to identify emergency department (ED) visits for suspected nonfatal benzodiazepine-involved overdoses of unintentional or undetermined intent. The query uses two fields from ED visit records to identify encounters that meet the definition criteria:

- (1) the chief complaint free text field is queried for terms indicating an overdose/poisoning and benzodiazepine involvement and for relevant exclusion terms (e.g., terms indicating benzodiazepine administration by medical personnel or withdrawal without acute intoxication, etc., which would exclude ED visit records from this syndrome definition), and
- (2) the discharge diagnosis parsed coded field is queried for International Classification of Diseases, 9th Revision (ICD-9-CM),¹ 10th Revision (ICD-10-CM),² and Systematized Nomenclature of Medicine Clinical Terms (SNOMED-CT)³ diagnosis codes indicating acute benzodiazepine poisoning of unintentional or undetermined intent.

Within ESSENCE, the syndrome query is applied to the Chief Complaint Discharge Diagnosis (CCDD) Parsed field, which combines these two fields of interest.

Use-Cases for Definition:

- □ Case-finding
- ☑ Trend monitoring
- □ Early outbreak detection

¹ World Health Organization. International Classification of Diseases, Ninth Revision, Clinical Modification. World Health Organization; 1980.

² World Health Organization. International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM). World Health Organization; 2015.

³ National Library of Medicine. SNOMED-CT. Accessed [Dec 5 2023]. https://www.nlm.nih.gov/healthit/snomedct/index.html

<u>Justification for Development</u>: Benzodiazepines are sedative/hypnotic agents used clinically to treat anxiety, seizures, and agitation. However, they are also being illegally made and diverted, and their use in combination with illegally made opioids has increased in the United States.^{4,5} This definition was developed to help public health practitioners track and understand trends of nonfatal benzodiazepine-involved overdoses treated in EDs in near real-time.

Data Source During Development: ED visits

Development methods:

This revision was developed to adapt the CDC Benzodiazepine Overdose v1 definition syntax to query the newly developed CCDD Parsed field which removes extraneous test from the discharge diagnosis portion of the CCDD.

CDC scientists first started developing the definition using lessons learned from jurisdictions funded by CDC's Overdose Data to Action (OD2A) and Enhanced State Opioid Overdose Surveillance (ESOOS) Programs. First, ICD-9-CM, ICD-10-CM, and SNOMED-CT diagnosis codes indicating acute benzodiazepine misuse/dependence and/or benzodiazepine poisoning were identified; this was followed by benzodiazepine-specific terms and overdose terms in the chief complaint field. Lastly, exclusion terms were identified (e.g., terms indicating benzodiazepine administration by medical personnel, withdrawal without acute intoxication, etc.) to avoid incorrectly capturing encounters that were not for a benzodiazepine-involved overdose.

Validation Methods: Three methods were employed to validate this new definition.

- 1) CDC NSSP scientists used R code to convert syntax from (A) the previous Benzodiazepine Overdose versions that queried the Chief Complaint Discharge Diagnosis (CCDD) field to (B) syntax that would more effectively query the Chief Complaint Discharge Diagnosis (CCDD) Parsed field. These conversions focused on changes to diagnostic code formatting within the syntax. The CDC DOSE team checked to see whether the syntax converted correctly (i.e., did not eliminate codes or terms that were intended to capture benzodiazepine-involved overdose).
- 2) CDC scientists in DOP piloted the draft definition by manually reviewing records that were captured after aforementioned conversion of syntax.
- 3) Overall summary counts over time comparing benzodiazepine overdose syndrome definitions v1 and v2 were analyzed to determine whether there were large deviations in trends.

Validation steps 2 and 3 were iterative processes and were repeated until, as a result of the syntax changes, most new ED records that were included and excluded were a result of syntax conversion only. In addition, and the large picture trends during 2021-2022 were similar.

For more information on initial development of the CDC Benzodiazepine Overdose version 1, please refer to its accompanying documentation.⁶

⁴ https://www.who.int/docs/default-source/controlled-substances/43rd-ecdd/final-flubromazolam-a.pdf?sfvrsn=887bdf43 4

⁵ https://cesar.umd.edu/sites/cesar.umd.edu/files/pubs/DEA-Emerging-Threat-Report-2022-Annual.pdf

⁶ CDC Benzodiazepine Overdose version 1 Brief:

<u>Definition Fields and Structure</u>: The CCDD Parsed field is used to query both the diagnosis codes and chief complaint free text with exclusions (as necessary) to develop the syndrome definition.

- Automatic inclusion:
 - If a diagnosis code indicating a benzodiazepine poisoning is present, the ED visit is automatically included in the syndrome.
- Conditional inclusion:
 - If the ED visit does not include a diagnosis code for benzodiazepine poisoning, then the visit is not automatically included.
 - The visit is captured only if it includes two components:
 - 1) chief complaint text indicating an overdose or poisoning AND
 - 2) chief complaint text indicating benzodiazepine involvement **OR** a SNOMED-CT code for benzodiazepine misuse or dependence.
 - The list of exclusions is applied to the chief complaint text only when a discharge diagnosis code is not present for benzodiazepine poisoning, or for any of the conditional inclusions mentioned above.

<u>For Consideration</u>: A large number of commonly used benzodiazepine types and names are included. The team attempted to identify most drug names used for benzodiazepines; however, it is likely that some drug names and slang terms should be added to the next version of the definition. The use of large amounts of benzodiazepines in isolation does not often lead to serious symptoms such as respiratory depression or cardiopulmonary instability. However, opioids and benzodiazepines have complex drug interactions with each other and, when used in combination, can increase risk for synergistic respiratory depression. Persons experiencing this symptom are more likely to receive care at EDs. It is important to consider that persons treated for benzodiazepine-involved overdoses in EDs may have co-used other drugs.

Limitations:

This definition is subject to both misclassification, overreporting, and underreporting for several reasons, including limited point-of-care confirmatory testing to identify the drug(s) involved in the overdose and reliance on self-report, bystander reports, and/or clinical presentations to determine the drug(s) involved in an overdose. The codes provided in the discharge diagnosis field from the ED visit record do not necessarily represent the final diagnosis of a patient and should be considered preliminary. Additionally, some hospitals may enter all diagnosis codes from a patient's entire medical history, including codes for previous benzodiazepine-involved overdose visits; the definition may incorrectly capture such encounters that were not for a true benzodiazepine-involved overdose and thus result in overreporting. Benzodiazepines may be administered by medical personnel in the ED setting or by emergency medical services technicians as a sedative en route to the ED, and this information could have been added into the chief complaint field. We attempted to identify all possible exclusion terms to avoid capturing encounters that describe benzodiazepines administered in a medical setting and not a benzodiazepine-involved overdose; however, it is possible that some of these encounters were erroneously captured, leading to overreporting. The team attempted to identify all appropriate inclusion and exclusion terms to capture any suspected nonfatal benzodiazepine-involved overdoses while avoiding capturing encounters that were not for an acute benzodiazepine-involved

⁷ Jones CM, McAninch JK. Emergency Department Visits and Overdose Deaths From Combined Use of Opioids and Benzodiazepines. Am J Prev Med. 2015 Oct;49(4):493-501. doi: 10.1016/j.amepre.2015.03.040. Epub 2015 Jul 3. PMID: 26143953.

overdose or poisoning, but it is possible that some of these encounters were erroneously captured, leading to overreporting.

Table 1. Descriptions of discharge diagnosis codes, concepts, and chief complaint terms included or excluded in the CDC Benzodiazepine Overdose v2 Parsed definition.

	Automatic		Description (discharge
Variable Type	inclusion?	Terms	diagnosis codes only)
Inclusions			
Discharge Diagn	osis codes		
			Poisoning –
			benzodiazepine-based
ICD-9-CM ¹	Yes	9694	tranquilizers
ICD-10-CM ¹			Poisoning by
			benzodiazepines,
			accidental
			(unintentional), initial
	Yes	T424X1A	encounter
			Poisoning by
			benzodiazepines,
	.,		undetermined, initial
	Yes	T424X4A	encounter
			Accidental poisoning
			caused by
	Voc	216520001	benzodiazepine-based
	Yes	216530001	tranquilizer (disorder)
	W	200052004	Benzodiazepine
	Yes	296053004	overdose (disorder) Accidental overdose
			of benzodiazepine
	Yes	296128004	(disorder)
	163	230128004	Overdose of
			benzodiazepine of
	Yes	296129007	undetermined intent
	163	230123007	Benzodiazepine
	Yes	712742003	intoxication
			Poisoning caused by
			benzodiazepine-based
SNOMED-CT	Yes	81914009	tranquilizer (disorder)
	No, must use in		Benzodiazepine
	combination with	231473004	dependence (disorder)
	overdose		,
	term AND no		Benzodiazepine
SNOMED-CT	exclusion terms	428406005	misuse
Chief Complaint	terms		
	No, must use in		
	combination	Poisoning (poison), Overdose (overdose,	
	with benzodiazepi	overdoes, averdose, averdoes, over does, overose),	
Overdose-	ne term or	nodding off, snort, ingestion (ingest, injest),	
related term	SNOMED-CT term	unresponsive (unresponsiv), loss of consciousness	

	for benzodiazepine misuse or dependence AND no exclusion terms	(syncope, syncopy), shortness of breath (SOB), altered mental status (AMS)	
Benzodiazepine -related term	No, must use in combination with overdose term AND no exclusion terms	prosom, niravam, tranxene, oxazepam, byfavo, flurazepam, Dalmane, downers, Xanax (with slang terms: xanny, xannies, xans, xan bars), Z bars, K Pin, Phennies, BZD, roofies, benzodiazepine, benzo, benzos, benezos, clorazepate, diazepam, clonazepam, midazolam, alprazolam, temazepam, alprazolam, helex, trankimazin, onax, alprox, misar, restyl, tafil, frontin, librium, solanax, klonopin, valium, iktorivil, paxam, rivatril, antenex, apaurin, apzepam, apozepam, hexalid, normabel, pax, ronal, vival, stesolid, stedon, valaxona, hipnosedon, vulbegal, fluscand, flunipam, rohydorm, hypnodorm, loraz (for lorazepam misspellings), ativan, zolam, bromazepam, diazepoxide, zolam, serax, temazepam, restoril, halcion	
Exclusions			
Chief complaint	Exclude	Prescribed or given benzodiazepine by a medical professional. See list below in ESSENCE code	

¹ICD-9-CM and ICD-10-CM code punctuation is removed when querying the CCDD Parsed field.

Table 2. ESSENCE syntax, CDC Benzodiazepine Overdose v2 Parsed

(,^;9694;^,OR,^;T424X[14]A;^,OR,^;296128004;^,OR,^;216530001;^,OR,^;296129007;^,OR,^;296053004;^,OR,^;712742003;^,OR,^;81914009;^,),OR,(,(,(,^poison^,OR,^verdo[se][es]^,OR,^overdose^,OR,^overose^,OR,^nodding^,OR,!nod!,OR,^snort^,OR,^in[gj]est^,OR,^intoxic^,OR,^unresponsiv^,OR,^los s of consciousness^,OR,^syncop^,OR,^shortness of breath^,OR,^short of breath^,OR,^altered mental status^,),AND,(

,!prosom!,OR,!niravam!,OR,!tranxene!,OR,!oxazepam!,OR,!byfavo!,OR,!flurazepam!,OR,![zx]ans!,OR,![zx]anny!, OR,![zx]annies!,OR,!dalmane!,OR,!downers!,OR,![zx]an bar!,OR,![zx]anbar!,OR,!z bar!,OR,!k pin!,OR,!phennies!,OR,!B[ZD][ZD]!,OR,!BZ!,OR,^roofies^,OR,^benzos^,OR,^benzodiazepine^,OR,^benezos^,OR, ^clorazepate^,OR,^diaz[aei]pa[mn]^,OR,^clonazepam^,OR,^midazolam^,OR,^alprazolam^,OR,^temaz[aei]pam^,OR,^alprazolam^,OR,^

xan^,OR,xan^,OR,Xan^,OR,^[zx]an[oae]x^,OR,^helex^,OR,^trankimazin^,OR,!onax!,OR,!alprox!,OR,!misar!,OR,!r estyl!,OR,!tafil!,OR,!frontin!,OR,!librium!,OR,^solanax^,OR,^[ck]lon[ae]z[ea]p[eoa]m^,OR,^[ck]lon[iao]pin^,OR,^ valium^,OR,^valum^,OR,^iktorivil^,OR,^paxam^,OR,^riv[oa]tril^,OR,^antenex^,OR,^apaurin^,OR,^apzepam^,O R,^apozepam^,OR,^hexalid^,OR,^normabel^,OR,!pax!,OR,!ronal!,OR,!vival!,OR,^stesolid^,OR,^stedon^,OR,^val axona^,OR,^hipnosedon^,OR,^vulbegal^,or^fluscand^,OR,^flunipam^,OR,^rohydorm^,OR,^hypnodorm^,OR,^lo raz^,or!ativan!,OR,^zolam^,OR,^bromazepam^,OR,^diazepoxide^,OR,^serax^,OR,^temazepa[nm]^,OR,^restor[aie]l^,OR,^halcion^,OR,^;428406005;^,OR,^;231473004;^,),ANDNOT,(,^ plan to overdose on benzo^,OR,Plan to overdose on benzo^,OR,!plan to overdose on [zx]an[oae]x!,OR,!plan to overdose on Ativan!,OR,!plan to overdose on valium!,OR,^ xanthogranulomatous ^,OR,!acetazolamide!,OR,^placed on ativan^,OR,^placed on valium^,OR,^placed on [zx]an[oae]x^,OR,^ran out of ativan^,OR,^ran out of valium^,OR,^ran out of [zx]an[oae]x^,OR,^ativan prn^,OR,^valium prn^,OR,^[zx]an[oae]x prn^,OR,^treated by ativan^,OR,^treated with ativan^,OR,^given ativan^,OR,^gave ativan^,OR,^ativan given^,OR,^treated by valium^,OR,^treated with valium^,OR,^treated by [zx]an[oae]x^,OR,^treated with [zx]an[oae]x^,OR,^given valium^,OR,^gave valium^,OR,^valium given^,OR,^[zx]an[oae]x given^,OR,^given [zx]an[oae]x^,OR,^gave [zx]an[oae]x ^,OR,^rec[ie][ei]ved ativan^,OR,^does not have any ativan left^,OR,^does not have any valium left^,OR,^does not have any [zx]an[oae]x left^,OR,^stopped using valium^,OR,^stopped using [zx]an[oae]x^,OR,^stopped using ativan^,OR,^out of valium^,OR,^out of [zx]an[oae]x^,OR,^out of ativan^,OR,^benzonatate^,OR,^no loss of consciousness^,OR,^denie[sd] loss of consciousness^,OR,^negative loss of consciousness^,OR,^denies any loss of consciousness^,OR,^denies drug^,OR,^deny drug^,OR,^denied drug^,OR,^denying drug^,OR,^denies any drug^,OR,^ with dra^,OR,^withdra^,OR,^detoxification^,OR,^detos^,OR,^detoz^,OR,^dtox^,),),