Prevalence of Concurrent Opioid and Benzodiazepine Use Among ~15 million Commercial members

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Background

- Concurrent use of benzodiazepines with opioids can result in increased risk of respiratory depression that can lead to death.[1]
- The 2016 Centers for Disease Control (CDC) Guideline for Prescribing Opioids for Chronic Pain recommends clinicians should avoid prescribing the combination of an opioid and benzodiazepine whenever possible.[2]
- In 2016, the FDA announced its intent to develop enhanced warnings and safety information for immediate-release opioid labeling including risks due to interactions with central nervous system depressants including benzodiazepines.[3]
- The 2017 Final Center for Medicaid and Medicare Services (CMS) Call Letter discussed concerns about concurrent use of opioids and benzodiazepines and encouraged Part D sponsors to evaluate their claims data and use available drug utilization management tools to help address the concurrent use of these drug classes.[4]
- In December 2016, the Pharmacy Quality Alliance (PQA) membership endorsed a new measure called "Concurrent Use of Opioids and Benzodiazepines".[5] Past PQA measures have been adopted by CMS as Star Rating measures.
- A 2016 CMS analysis found concurrent opioid and benzodiazepine occurred in 24 percent of Part D opioid users without evidence of cancer or enrolled in hospice.[1]
- Advanced knowledge around prevalence of concurrent opioid and benzodiazepine use can help insurers plan for potential quality measures or other prescribing restrictions and improve member safety.

Objective

- Describe the prevalence of concurrent opioid and benzodiazepine use in a commercial population and examine how prevalence changes when analysis methods are modified.

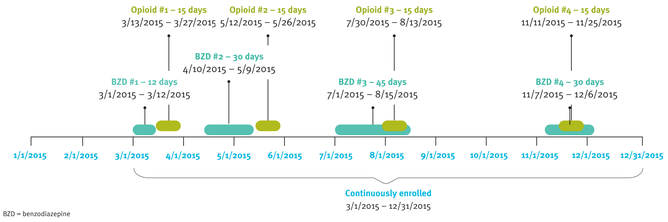
Methods

- Pharmacy claims data from approximately 15 million commercial members was first queried to identify members with one or more opioid or benzodiazepine claims filled in 2015.
- Members were assigned an index date based on the earliest opioid or benzodiazepine claim in 2015 (index date).
- Members were required to be continuously enrolled from their index date through Dec. 31, 2015 or disenrollment, whichever came first.
- Members included in the analysis were limited to those 18 years and older as of Jan. 1, 2015 AND with two or more opioid claims filled on two or more separate days, for which the sum of the days supply was 15 or more. **(Table 1)**
- Medical claims data in 2015 was used to identify members with one or more cancer diagnosis code in any field of their medical claims.
- Opioids used in the analysis were based on a list obtained from the CDC that excludes cough and cold, injectable formulations, and buprenorphine products used to treat opioid use disorder. **(Table 3)**
- To determine concurrent benzodiazepine use among opioid users, members were also required to have two or more benzodiazepine claims on two or more separate days in 2015. **(Table 1)**
- Consistent with the PQA quality measure requirements, concurrent use of opioids and benzodiazepines was defined as 30 or more cumulative days of overlap based on days supply found on the claims.[5] **Figure 1** shows an example member and their enrollment, opioid claims and benzodiazepine claims.
- Additional variations of analysis methods to determine concurrent opioid and benzodiazepine use included:
  - Excluding members with cancer diagnosis code
  - Requiring only one benzodiazepine in 2015 instead of two claims, OR
  - Requiring only seven days of cumulative concurrent opioid and benzodiazepine use instead of 30 days, OR
  - Requiring only one benzodiazepine claim and seven cumulative days of concurrent use.

Results

- In 2015, 3,992,900 (26.6 percent) out of approximately 15 million commercially insured members had at least one opioid or benzodiazepine claim. **(Figure 2)**
  - 2,668,934 (66.8 percent) had only opioid claims.
  - 674,880 (16.9 percent) had only benzodiazepine claims.
  - 649,086 (16.3 percent) had both opioid and benzodiazepine claims.
- 3,949,782 (98.9 percent) members were continuously enrolled from their index date through Dec. 31, 2015 or disenrollment.
- 3,723,372 (94.3 percent) of the opioid and/or benzodiazepine users were 18 or older as of Jan. 1, 2015.
- 884,407 (23.8 percent) members of 3,723,372 had two or more opioid claims filled on separate days with 15 days supply or more in 2015 – the analysis population.
- 234,966 (26.6 percent) of the 884,807 members also had two or more benzodiazepine claims on separate days in 2015.
- 221,264 (25 percent) of the 884,407 members had at least one day of overlapping opioid and benzodiazepine supply.
- 152,083 (17.2 percent) of the 884,407 members had 30 or more cumulative overlapping days of opioids and benzodiazepines in 2015.
- 107,372 (12.1 percent) of the 884,407 members had one or more medical claim cancer diagnosis codes in 2015.
- After excluding the cancer members, the rate of concurrent opioid and benzodiazepine use for 30 or more cumulative days did not change, 132,308 (17.0 percent) of 777,035.
  - Nine per 1,000 overall commercial members (132,308 of 15 million)
- The rate of concurrent use increased when methods of identification were modified. **(Table 2)**
  - The number of members identified with concurrent opioid and benzodiazepine use with only one or more benzodiazepine claims filled in 2015 and 30 or more cumulative overlapping days was 0.6 percent higher than when two or more benzodiazepines were required.
    - 136,995 (17.6 percent) of 777,035 members without cancer had overlapping opioid and benzodiazepine use.
  - The number of members identified with concurrent opioid and benzodiazepine use with only seven or more overlapping days of opioid and benzodiazepine was 5.8 percent higher (22.8 percent vs. 17.0 percent) than when 30 more days were required.
    - 177,522 (22.8 percent) of 777,035 members without cancer had overlapping opioid and benzodiazepine use.
  - The number of members identified with concurrent opioid and benzodiazepine use with only one benzodiazepine and only seven or more overlapping days was 8.7 percent higher (25.7 percent vs. 17.0 percent) than when two benzodiazepines and 30 or more days were required.
    - 199,861 (25.7 percent) of 777,035 members without cancer had overlapping opioid and benzodiazepine use.

Figure 1. Example Member Timeline — Member has 2 periods of concurrent opioid and benzodiazepine use — each for 15 days



BZD = benzodiazepine

Table 1. Member Identification Criteria

Members included in analysis	1. Members 18 or older as of Jan. 1 2015, **AND** 2. Continuously enrolled from first opioid or benzodiazepine claim through Dec. 31, 2015 or disenrollment, **AND** 3. Two or more opioid pharmacy claims filled on two or more separate days for which the sum of the days supply was 15 days or more during 2015.
Concurrent opioid and benzodiazepine use definition	1. Members included in analysis (above), **AND** 2. Two or more benzodiazepine pharmacy claims filled on two or more separate days in 2015, **AND** 3. Concurrent use of opioid and benzodiazepine for 30 or more cumulative days during their enrollment period.

Table 2. Prevalence of Concurrent Opioid and Benzodiazepine Use Among ~15 Million Commercial Members; Using Different Criteria in 2015

Criteria	Concurrent opioid and benzodiazepine users	Opioid users*	%
Cancer diagnosis inclusion**	152,083	884,407	17.2%
Cancer diagnosis exclusion	132,308	777,035	17.0%
Only one benzodiazepine claim	136,995	777,035	17.6%
Seven (or more) days of concurrent use	177,522	777,035	22.8%
One benzodiazepine claim and seven (or more) days of concurrent use	199,861	777,035	25.7%

*Two or more opioid claims filled on two or more dates with a sum of 15 days supply or more.
**Criteria as defined in Table 1.

Figure 2. Member Flow

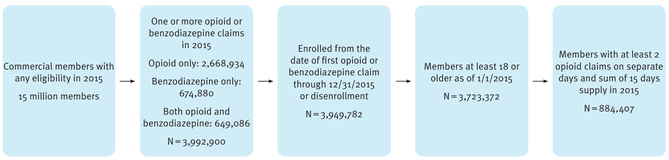


Table 3. Opioid and Benzodiazepine Drugs Used in Concurrent Opioid and Benzodiazepine Analysis

Opioids[a]		Benzodiazepines[a]	
buprenorphine[b]	butorphanol	alprazolam	chlordiazepoxide
codeine	dihydrocodeine	clobazam	clonazepam
fentanyl[c]	hydrocodone	clorazepate	diazepam
hydromorphone	levorphanol	estazolam	flurazepam
meperidine	methadone	lorazepam	midazolam
morphine	opium	oxazepam	quazepam
oxycodone	oxymorphone	temazepam	triazolam
pentazocine	tapentadol		
tramadol			

[a]Excludes injectable formulations.
[b]Excludes single-agent and combination buprenorphine products used to treat opioid use disorder (i.e., buprenorphine sublingual tablets, Probuphine® implant kit subcutaneous implant, and all buprenorphine/naloxone combination products).
[c]Excludes Ionsys® (fentanyl transdermal patch), as it is only for inpatient use and is only available through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS).

Conclusions

- As the CDC recommends against combination opioid and benzodiazepine use and the PQA has developed a pharmacy performance measure, it is anticipated that health insurers quality of care will be assessed by the prevalence of combination use among their membership. Health insurers should consider identifying at risk members and developing clinical programs with the goal of reducing combination use.[2,5]
- Combination opioid and benzodiazepine use for 30 or more cumulative days was found at a rate of nine per 1,000 or 0.9 percent of the entire commercially insured population. An alarming one of every six opioid users with no evidence of cancer had concurrent opioid and benzodiazepine use for 30 or more cumulative days in 2015.
- The rate of concurrent use increased as the analysis was modified to require fewer claims and fewer overlapping days. Health insurers need to understand their own data and member use patterns to determine intervention thresholds of concurrent opioid and benzodiazepine use.
- Future research could include an investigation of prescribers with high volumes of concurrent opioid and benzodiazepine users within their discipline.

Limitations

- Data are limited to commercial populations in the United States; therefore findings may not be generalizable to Medicare or Medicaid populations.
- Administrative pharmacy and medical claims have the potential for miscoding and include assumptions of member actual drug use and diagnosis.
- Members may have paid for opioid or benzodiazepines claims out of pocket or obtained them through friends and family. In addition, our analysis excluded certain opioids like opioid containing cough and cold products. This could have resulted in underestimation of the number of members concurrently using opioid and benzodiazepines.
- Members solely utilizing high dose opioids, a risk for overdose and negative outcomes, without benzodiazepines would not be included in the analysis.
- We did not evaluate doctor or pharmacy shopping for the opioid and benzodiazepine claims; a known risk factor for inappropriate use.

References

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