Evaluation of utilization patterns of cough medications in ambulatory care settings in the United States: 2003-2018

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Background & Objective

- Cough is one of the most common reasons for seeking medical attention in the United States (US)[1]
- Medications commonly used as cough medications (CM) include opioid antitussives, benzonatate, and dextromethorphan[2-3]
- Gabapentinoids, such as gabapentin, are potential pharmacological options for unexplained chronic cough[4]
- Little is known about the utilization patterns of CM over time in the context of the opioid crisis in the US
- **Objective:** To examine the trends and characteristics of CM use in US ambulatory care settings

Methods

- **Design:** Repeated cross-sectional analyses
- **Source:** 2003-2018 National Ambulatory Medical Care Survey (NAMCS) for office-based ambulatory settings (excluding 2017 due to data unavailability) and National Hospital Ambulatory Medical Care Survey (NHAMCS) for emergency department (ED) settings
- **Cohort:** Adult (≥18 years) visits with any cough-related diagnosis or reason for visit (ie, cough, acute upper respiratory tract infections [URTI], chronic upper respiratory tract diseases [URTD], influenza, bronchitis, pneumonia) using the first 3 diagnosis codes or reason-for-visit codes
- **Exclusion criteria:** Visits with any malignant cancer or any benign respiratory tumor diagnoses
- **Statistical analysis**

1. Eligible cough-related visits served as the final analytical sample and denominator for estimating the annual proportion of visits reporting CM use (using the first 8 medication codes) among cough-related visits for each year
2. We estimated the annual proportion of visits reporting use of CM among cough-related visits using complex survey design procedures in SAS version 9.4, with sampling weights from NAMCS/NHAMCS to obtain national estimates
3. We examined the trends in those annual proportions over time using multivariable logistic regression adjusted for age, sex, race, and payment source
4. The National Center for Health Statistics (NCHS) recommends excluding the results from analyses for unweighted count values less than 30 or when the relative standard error is greater than 30% due to the unreliability of these estimates.[5] The results for gabapentinoids based on NHAMCS analysis were, thus, not presented in this study

CM categories (Multum Lexicon Plus®)
1. Opioid antitussives: Codeine-, hydrocodone-, and dihydrocodeine-containing formulations
2. Benzonatate
3. Dextromethorphan-containing antitussives (including prescription and over-the-counter drugs)
4. Gabapentinoids: Gabapentin and pregabalin
5. Opioid analgesics (comparison group)

Results

Characteristics of cough-related visits by CM type

- Among a weighted estimate of 11.1 billion adult office-based ambulatory visits from 2003 to 2018, we identified 819.9 million (7.4%) cough-related visits
- Among a weighted estimate of 1.6 billion adult ED visits from 2003 to 2018, we identified 155.5 million (9.9%) cough-related ED visits
- Overall, the characteristics of cough-related ambulatory visits with benzonatate or dextromethorphan-containing antitussives were similar to visits involving opioid antitussives (**Table 1**)
- By contrast, cough-related office-based ambulatory visits with gabapentinoids were more likely from patients aged ≥65 years (41.2%) and having ≥2 chronic conditions (64.8%) (**Table 1A**)
- Common diagnoses in cough-related ambulatory visits with CM use were bronchitis and acute upper respiratory tract infections (**Table 1**)

Table 1. Characteristics of cough-related visits by CM type

A. 2003-2018 NAMCS (weighted estimate of 819.9 million)

Characteristics	Opioid antitussives 63.3 million (7.7%)	Benzonatate 20.9 million (2.5%)	Dextromethorphan 29.7 million (3.6%)	Gabapentinoids 13.3 million (1.6%)	Opioid analgesics 41.1 million (5.0%)
Age ≥65 years	23.5%	25.7%	21.5%	41.2%	24.7%
Female	64.8%	71.3%	62.6%	62.9%	61.6%
Race					
White	81.0%	84.1%	78.9%	87.5%	83.1%
Non-White	19.0%	15.9%	21.1%	12.5%	16.9%
Smoking status[a]					
Current	15.3%	12.9%	14.8%	19.7%	24.6%
Non-current	81.5%	83.0%	81.3%	78.0%	72.0%
Payment source[b]					
Governmental	27.7%	30.4%	31.7%	53.2%	44.6%
Commercial	62.7%	60.1%	54.9%	37.3%	45.5%
Others	7.5%	6.3%	11.4%	5.0%	7.7%
≥2 Chronic conditions[c]	39.7%	41.1%	30.7%	64.8%	45.5%
Top 3 diagnoses	Bronchitis 39.1%	Acute URTI 39.8%	Acute URTI 53.4%	Bronchitis 22.6%	Acute URTI 30.8%
	Acute URTI 36.8%	Cough 30.0%	Bronchitis 27.0%	Acute URTI 21.9%	Bronchitis 25.8%
	Cough 15.8%	Bronchitis 26.1%	Cough 14.9%	Chronic URTD 17.7%	Chronic URTD 16.4%
Prescriber as primary care physician	88.7%	89.0%	88.6%	76.7%	80.1%
Geographic region[d]					
Northeast	12.4%	11.1%	21.7%	12.4%	10.9%
Midwest	19.5%	16.2%	14.4%	22.4%	20.9%
South	44.6%	53.8%	42.0%	43.1%	41.4%
West	23.5%	19.0%	21.8%	22.1%	26.9%
Metropolitan area	86.7%	90.9%	88.5%	76.4%	83.6%

[a]The percentage of missingness for smoking status among cough-related visits involving 5 medication groups was ≤5.4% from 2003 to 2018. Non-concurrent smoker includes never smoker, former smoker, and unknown.
[b]The percentage of missingness for payment source among cough-related visits involving 5 medication groups was ≤2.5% from 2003 to 2018. Governmental payment source included Medicare and Medicaid. Others included all other types of insurance, uninsured, and unknown.
[c]The number of chronic conditions was available in NAMCS since 2005. The percentage of missingness for the variable of ≥2 chronic conditions among cough-related visits involving 5 medication groups were ≤1.7% from 2005 to 2018.
[d]The region was unavailable in NAMCS in 2018.

B. 2003-2018 NHAMCS (weighted estimate of 155.5 million)

Characteristics	Opioid antitussives 9.7 million (6.2%)	Benzonatate 7.5 million (4.8%)	Dextromethorphan 2.9 million (1.9%)	Opioid analgesics 22.7 million (14.6%)
Age ≥65 years	10.6%	10.8%	10.5%	15.4%
Female	63.2%	65.8%	62.1%	63.0%
Race				
White	71.3%	68.0%	59.1%	72.7%
Non-White	28.7%	32.0%	40.9%	27.3%
Payment source[a]				
Governmental	37.8%	40.2%	40.7%	46.1%
Commercial	31.9%	31.5%	26.6%	27.8%
Others	28.6%	27.7%	31.5%	24.5%
≥2 Chronic conditions[b]	24.9%	26.5%	27.8%	31.9%
Top 3 diagnoses	Bronchitis 44.6%	Bronchitis 40.9%	Acute URTI 37.0%	Acute URTI 28.4%
	Acute URTI 28.8%	Acute URTI 33.3%	Bronchitis 34.5%	Bronchitis 24.7%
	Cough 14.4%	Cough 23.1%	Cough 16.3%	Pneumonia 18.6%
Geographic region				
Northeast	12.8%	16.0%	9.5%	10.0%
Midwest	20.0%	23.0%	19.8%	22.6%
South	51.3%	47.8%	54.3%	42.2%
West	15.9%	13.2%	16.4%	25.2%
Metropolitan area[c]	77.8%	83.2%	78.2%	86.2%

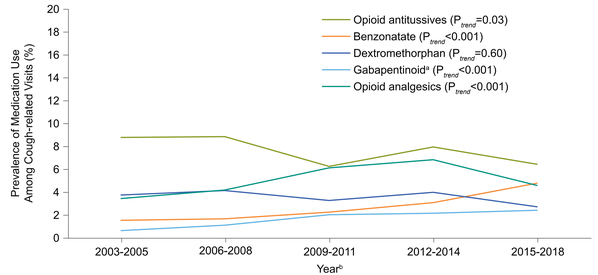
[a]The percentage of missingness for payment source among cough-related visits involving 4 medication groups was ≤1.7% from 2003 to 2018. Governmental payment source included Medicare and Medicaid. Others included all other types of insurance, uninsured, and unknown.
[b]The number of chronic conditions was available since 2012. The percentage of missingness for the variable of ≥2 chronic conditions among cough-related visits involving 4 medication groups was ≤1.1% from 2012 to 2018.
[c]The metropolitan area was unavailable in NHAMCS in 2012.

Trends in CM use among cough-related visits (Figure 1)

- Opioid-containing antitussive use decreased over time in office-based visits (8.8% in 2003-2005 to 6.4% in 2015-2018, P_{trend}=0.03), while their use remained stable in ED visits (6.3% to 5.9%, P_{trend}=0.99)
- Benzonatate use more than tripled in both settings (office-based: 1.6% in 2003-2005 to 4.8% in 2015-2018; ED: 1.5% to 8.0%; both P_{trend}<0.001)
- Dextromethorphan-containing antitussive use increased in ED visits (1.8% in 2003-2005 to 2.6% in 2015-2018, P_{trend}=0.003), whereas their use stayed stable in office-based visits (3.8% to 2.7%, P_{trend}=0.60)
- Gabapentinoid use doubled in office-based visits (1.1% in 2006-2008 to 2.4% in 2015-2018, P_{trend}<0.001) but was negligible in ED visits
- Opioid analgesic use increased and then decreased in both settings

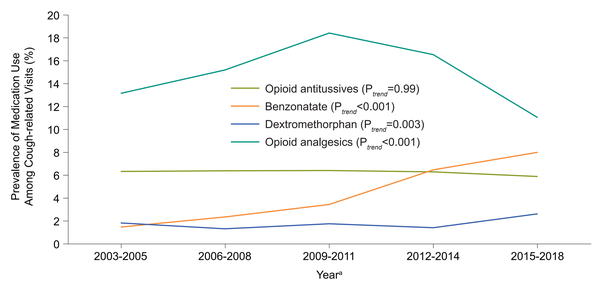
Figure 1. Trends in CM use among cough-related visits

A. 2003-2018 NAMCS



[a]The weighted estimate for gabapentinoid in 2003–2005 is unreliable based on NCHS's recommendation.
[b]The weighted estimate of the denominator (ie, adult cough-related visits) for each time period in NAMCS is 183.7 million, 171.9 million, 179.7 million, 152.8 million, and 131.8 million for 2003–2005, 2006–2008, 2009–2011, 2012–2014, and 2015–2018, respectively.

B. 2003-2018 NHAMCS



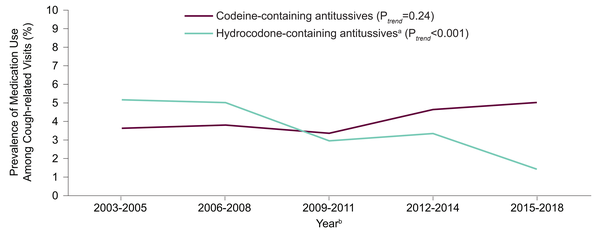
[a]The weighted estimate of the denominator (ie, adult cough-related visits) for each time period in NHAMCS is 25.2 million, 25.8 million, 30.1 million, 30.7 million, and 43.7 million for 2003–2005, 2006–2008, 2009–2011, 2012–2014, and 2015–2018, respectively.

Trends in hydrocodone- and codeine-containing antitussive use among cough-related visits (Figure 2)

- We further examined individual components in opioid antitussive class in both settings (dihydrocodeine-containing antitussive use was negligible, thus, not presented)
- In both office-based and ED ambulatory care settings, hydrocodone-containing antitussive use declined over 50%
- In ED settings, a decreasing trend in hydrocodone-containing antitussive use (3.8% in 2003–2005 to 1.8% in 2015–2018, P_{trend} =0.004) was offset by an increasing trend in codeine-containing antitussive use (2.6% to 4.1%, P_{trend} =0.008)

Figure 2. Trends in hydrocodone- and codeine-containing antitussive use among cough-related visits

A. 2003-2018 NAMCS



[a]The weighted estimate for hydrocodone-containing antitussives in 2015–2018 is unreliable based on NCHS's recommendation.
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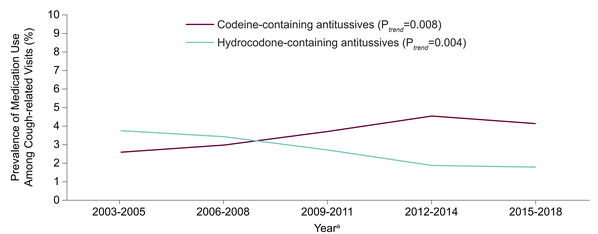
B. 2003-2018 NHAMCS



[a]The weighted estimate of the denominator (ie, adult cough-related visits) for each time period in NHAMCS is 25.2 million, 25.8 million, 30.1 million, 30.7 million, and 43.7 million for 2003–2005, 2006–2008, 2009–2011, 2012–2014, and 2015–2018, respectively.

Discussion & Conclusions

- Cough-related visits with CM use were generally low (<9%), regardless of setting
- CM utilization trends varied by medication among cough-related ambulatory care settings from 2003 to 2018. In US office-based and ED ambulatory care settings, hydrocodone-containing antitussive use substantially declined from 2003 to 2018, while benzonatate use more than tripled, and dextromethorphan-containing antitussive and gabapentinoid use remained low (<3%)
- Nearly one-third of cough-related ambulatory visits with opioid antitussive had a diagnosis of acute upper respiratory tract infections, which do not warrant their use due to limited evidence
- Further studies are warranted to examine CM use in each subtype of cough or cough-related condition

References

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