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COMMENTARY

Use of gabapentinoid medications among US adults with cancer, 2005–2015

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Abstract

Background Gabapentinoid use for long-term cancer pain control may be problematic, given unclear mechanisms of action and increased concerns for physical dependence. The purpose of this report is to examine trends of gabapentinoid use among US adults with cancer from 2005 to 2015.

Methods We conducted a serial, cross-sectional study using data from the Medical Expenditure Panel Survey (MEPS). We performed multiple logistic regression to examine the annual percentages of gabapentinoid users, which were adjusted for age, sex, and US region of residence. The amount of gabapentinoid prescriptions filled in 2015 was also estimated.

Results The adjusted percentage of gabapentinoid users in 2015 was 5.60% (3.79%, 7.41%), 2.39 times greater than the percentage in 2005 ($p < .001$). By 2015, the number of gabapentinoid prescriptions had grown to approximately 3.52 million (2.40 million, 4.65 million).

Conclusion We observed greater than a twofold increase in the trend of gabapentinoid medication use among US adults with cancer. Investigations on the long-term efficacy of gabapentinoids for complex pain syndromes, and mitigation of risks, is essential to guide informed clinical management and keep patients safe.

Keywords Cancer · Supportive care · Gabapentin · Practice pattern

Patients with cancer often present with complex pain syndromes that vary in etiology. The estimated prevalence of chronic pain in patients undergoing primary cancer treatment, without advanced disease, ranges from 33 to 59% [1]. First-line pain treatment with opioids has varied effectiveness and faces additional scrutiny amidst the opioid crisis [2, 3]. Moreover, clinicians are prescribing alternative treatments to manage complex cancer pain [4]. The drugs gabapentin and pregabalin (i.e., gabapentinoids) were developed originally for anticonvulsant therapy, but demonstrate efficacy for treating neuropathic pain and other chronic pain syndromes [5, 6]. Gabapentinoid use for cancer pain syndromes may be problematic, given unclear mechanisms of action for pain control and concerns for physical dependence [7]. The purpose of this report is to examine trends of gabapentinoid medications among US adults with cancer from 2005 to 2015.

We conducted a serial, cross-sectional study using data from the Medical Expenditure Panel Survey (MEPS). The sampling frame of the MEPS was non-institutionalized US adults (age 18 and older), therefore excluding adults in medical facilities, inmates, and those serving in the armed forces. The survey collection procedures of the MEPS have been described elsewhere [8].

Individuals with a cancer diagnosis in the MEPS, which was self-reported, were included for analysis. Using previously validated approaches, we used the MEPS prescription medication data files to identify adults who received a gabapentinoid [9]. Users of gabapentinoid were identified by with the National Drug Code (NDC) classifications for "gabapentin" or "pregabalin."

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The MEPS allowed for complex survey design methods to adjust for the probability of selection, clustering of observations, and multiple stages of selection to yield national estimates [8]. We examined the crude percentage of US adults with cancer who used a gabapentinoid from 2005 to 2015. Next, we used multiple logistic regression to examine the annual adjusted percentages of users of a gabapentinoid from 2005 to 2015, adjusting for age, sex, and US region of residence. The amount of gabapentinoid prescriptions filled in 2005, 2010, and 2015 was also estimated with complex survey design. All analyses were performed with Stata, version SE 15 (StataCorp, LLC).

We observed that the crude percentages of adults with cancer who used a gabapentinoid in 2005 and 2015 were approximately 3.28% (95% confidence interval 2.10%, 4.23%) and 8.26% (6.98%, 9.84%), respectively ($p < .01$) (see Supplemental Table 1). By 2015, the crude percentages of adults who used a gabapentinoid increased across all age, sex, and US region of residence groups.

In 2015, the crude percentages of females with cancer who used a gabapentinoid was greater than the percentage of males (8.86% (6.97%, 11.4%) and 7.54% (5.46%, 10.2%)). The percentage of adults with cancer who used a gabapentinoid was the greatest in the 18–44 age group, 15.3% (9.59%, 24.6%) compared with that of adults age 45–64 and 65–85. The Southern US region had the highest percentage of adults with cancer who used gabapentinoid (11.1%) (8.73%, 14.1%). The greatest increase in the percentage who used gabapentinoid from 2005 to 2015 occurred in adults residing in the West, 1.56% (0.45%, 5.02%) to 7.91% (5.85%, 10.7%), respectively ($p = .11$).

We found that the age-, sex-, and US region–adjusted percentage of adults who used gabapentinoid in 2015 was 5.60% (3.79%, 7.41%), whereas the adjusted percentage in 2005 was 2.34% (1.28%, 3.40%; rate ratio 2.39; $p < .001$) (see Fig. 1). Additionally, the adjusted percentages in 2013 and 2014 surpassed 5% (6.52% (4.60%, 8.45%); 6.18% (4.35%, 8.01%), respectively).

In 2005, the total number of gabapentinoid prescriptions filled among US adults with cancer was approximately 1.19 million (0.61 million, 1.78 million). By 2015, the number of gabapentinoid prescriptions had grown to approximately 3.52 million (2.40 million, 4.65 million), an estimated increase of 0.46 million annually (95% CI 0.22 million, 0.70 million; $p < .01$ for monotonic trend).

Amidst an opioid epidemic, the observed upward pattern of gabapentinoid use may reflect public recognition of unwanted consequences of long-term opioid use [10]. Yan and colleagues suggested that multiple well-designed clinical trials of gabapentin for reduced pain and analgesic use following various surgical procedures demonstrated efficacy, but the evidence of efficacy is less clear in cancer pain syndromes [11]. We were surprised to find the crude percentage of adults who used gabapentinoid in the 18–44 age group was much greater than that of the other age groups, which may indicate that clinicians perceive gabapentinoids as a prominent non-opioid therapy among younger adults diagnosed with cancer.

Additionally, the increased use of gabapentinoids may reflect the growing incidence of chemotherapy-induced neuropathic pain in cancer survivors [12, 13]. Gabapentinoid prescribing for chronic, non-cancer pain conditions has risen dramatically since 2012 [14]. Significant late effects of chemotherapy-induced neuropathic pain may persist from 2 to 5 years following the first course of neurotoxic chemotherapy, which necessitates long-term prescription of analgesic therapy [13].

To our knowledge, this is the first evidence of a consistent, upward trend of gabapentinoid medication use among adults with cancer in the US. Evidence from Johansen observed a smaller percentage of gabapentinoid users in the general US adult (age >

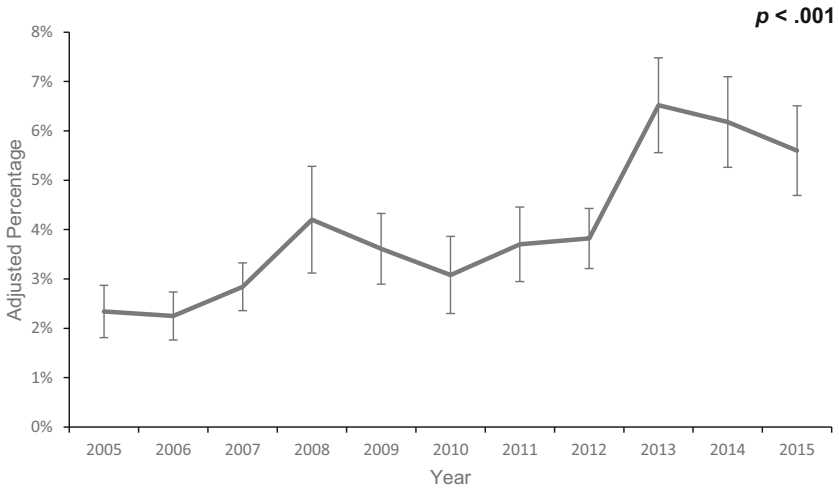

Fig. 1 Trend in percentage of US adults with cancer who used a gabapentinoid medication with 95% confidence intervals, adjusted for age, sex, and US region, 2005–2015

17) population, although a nearly threefold increase was observed from 2002 to 2015 [15]. Gabapentinoid use for cancer pain is off-label with conflicting evidence for benefit [6]. A deeper understanding of dosages, drug interactions, and adverse effects of gabapentinoid therapies would provide clinicians with needed data to personalize pain management. In addition to physical dependence, gabapentinoids increase respiratory depression risks in patients who are opioid tolerant or who receive it in a post-operative setting [16, 17]. Gabapentinoids in combination with opioids increase overall mortality compared with either drug alone [18, 19].

There are several study limitations. First, the indications of medication use for MEPS participants were unknown. Therefore, we could not determine if gabapentinoids were used for cancer pain syndromes or anticonvulsant therapy. However, gabapentin and pregabalin are not considered first-line therapies for seizures or epilepsy [20]. Secondly, the MEPS data include self-reported measures, which limits our ability to identify errant reporting. Finally, the analyses were limited to outpatient prescription medications only, which may not fully represent the trends of inpatient, unprescribed, or unfilled medications used. Despite these limitations, to our knowledge, this was the first study to examine trends over recent time in the use of gabapentinoids among adults with cancer in the US.

Over time, we observed greater than a twofold increase in crude and adjusted percentages of adults with cancer who used a gabapentinoid medication. In recent years, adults with cancer are more likely to use a gabapentinoid. Investigations on the long-term efficacy of gabapentinoids for complex pain syndromes, and mitigation of risks, are essential to guide informed clinical management and keep patients safe.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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