MILLIMAN REPORT

Treatment Patterns for Generalized Anxiety Disorder and Insomnia in Medicare Fee-for-Service

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Executive Summary

OVERVIEW & KEY FINDINGS FROM MILLIMAN'S ANALYSIS

Insomnia and generalized anxiety disorder (GAD) are common mental health conditions in the Medicare population.[1] Approximately 50% of older adults complain about poor sleep, and insomnia medications were prescribed to approximately 30% of beneficiaries.[2,3] Poor sleep quality has also been shown to contribute to the development and exacerbation of comorbidities such as cardiovascular disease, Type II diabetes mellitus, hypertension, and obesity.[4,5] Data shows that the prevalence of anxiety disorders, including GAD, panic disorder, social phobia, and other anxiety disorders, in the Medicare fee-for-service (FFS) population has steadily increased. In 2015, 15% of beneficiaries struggled with anxiety and that number increased to 18.75% by 2019.[6]

Clinical guidelines developed by professional associations recommend the provision of cognitive behavioral therapy (CBT) as first-line treatment for both GAD and insomnia, while pharmacotherapy (selective serotonin reuptake inhibitors/selective norepinephrine reuptake inhibitors (SSRIs/SNRIs)) is first-line only for GAD. The American College of Physicians (ACP) and American Academy of Sleep Medicine (AASM) guidelines on the management of insomnia recommend CBT as first-line treatment, followed by consideration of pharmacologic treatment if CBT alone is unsuccessful.[7,8] The Anxiety & Depression Association of America (ADAA) guidelines on the management of GAD recommend CBT as first-line psychotherapy treatment and SSRIs/SNRIs as first-line pharmacotherapy treatment.[9] Pharmacotherapy options for the management of GAD and insomnia include drugs that have the potential for adverse events, abuse, and dependence (e.g., benzodiazepines and hypnotics). For example:

- The use of benzodiazepines and hypnotics is associated with serious health risks, such as falls, fractures, and cognitive impairment in the elderly.[10–14]
- The American Geriatrics Society (AGS) Beers Criteria® for Potentially Inappropriate Medication Use in Older Adults recommends against the general use of first-generation benzodiazepines and hypnotic z-drugs in the elderly because the risks outweigh the benefits.[15,16]
- Polypharmacy poses a health risk when people are treated concurrently with specific psychoactive agents in combination with opioids (e.g., a combination of alprazolam and an opioid), yet the contemporaneous use of opioids with benzodiazepines and hypnotics is common.[17–19]

Milliman was engaged by Big Health to study the treatment patterns of Medicare FFS beneficiaries with GAD and insomnia, with a focus on how those patterns align with evidence-based clinical guidelines specified in US Food and Drug Administration (FDA) drug labels and those developed by professional organizations. More specifically, we studied the prevalence of GAD and insomnia in Medicare FFS, beneficiary use of psychotherapy as a proxy for CBT, whether beneficiaries receive psychotherapy prior to initiating non-SSRI/SNRI pharmacotherapy, and pharmacotherapy utilization patterns, including overall use, duration, and starting doses. We report on these patterns using information from large administrative medical and pharmacy claims databases spanning 2016 to 2020. While we summarize results here, deeper insights into the differences in findings by age (under 65 and 65+), race/ethnicity, and income status are identified throughout the report and in the appendices. Our key findings about GAD and insomnia are as follows:

1. Prevalence: In 2020, over one in five Medicare beneficiaries have GAD, and roughly one in twelve has insomnia. The prevalence of these conditions is higher in beneficiaries under age 65, who are eligible for Medicare due to their disability or end stage renal disease (ESRD) status, where nearly 38% of beneficiaries under age 65 have GAD and 12% have insomnia.
    - Select co-occurring medical conditions: Beneficiaries with GAD and insomnia have higher rates of co-occurring medical conditions such as chronic pain, depression, dementia, and cancer relative to the overall Medicare FFS population.
2. Treatment patterns and guideline-concordant care for GAD and insomnia
    - Overall Treatment Trends: As shown in Table 1, roughly a quarter of all beneficiaries 65+ with GAD and insomnia are untreated in 2020. For beneficiaries 65+ that are treated for GAD and insomnia, 3% receive psychotherapy only. Most beneficiaries (84% for GAD, 88% for insomnia) receive pharmacotherapy only, while a smaller share (13% for GAD, 10% for insomnia) receive both psychotherapy and pharmacotherapy.

TABLE 1: DISTRIBUTION OF GAD AND INSOMNIA TREATMENT MODALITIES FOR BENEFICIARIES 65+ IN 2020

	GAD	Insomnia
Untreated	**24%**	**25%**
Treated	**76%**	**75%**
Psychotherapy Only	*3%*	*3%*
Pharmacotherapy Only	*84%*	*88%*
Both	*13%*	*10%*

- Psychotherapy Prior to Initiating Pharmacologic Treatment: Clinical guidelines recommend the provision of CBT as first-line treatment for both GAD and insomnia, while pharmacotherapy (SSRIs/SNRIs) is also first-line only for GAD.[7–9] In contrast to those guidelines, we found that only 9% of beneficiaries with GAD and 5% of beneficiaries with insomnia receive psychotherapy in the 30 days prior to initiating pharmacologic treatment with drugs like non-hypnotic benzodiazepines and hypnotic z-drugs.
- Pharmacologic Treatment Patterns: The use of drugs to treat GAD and insomnia is common in the Medicare population, and providers continue to prescribe drugs that may pose safety risks to elderly patients with these conditions. In 2019, the year prior to the initiation of the COVID-19 public health emergency (PHE), approximately 1 million Medicare beneficiaries were treated with non-hypnotic benzodiazepines (e.g., alprazolam, clonazepam, lorazepam, etc.) for GAD and hypnotic z-drugs (e.g., zolpidem, eszopiclone, zolpidem ER, etc.) for insomnia. However, we found declines in the use of non-hypnotic benzodiazepines to treat beneficiaries with GAD (6% decline), as well as declines in the use of hypnotic benzodiazepines (7% decline) and hypnotic z-drugs to treat beneficiaries with insomnia (14% decline) during the 2016-2020 period. We note that filled prescriptions of other insomnia-related drugs (e.g., gabapentin, trazodone, quetiapine) increased by 9% over the same period.
- Drug Use Duration: For certain drug groups such as benzodiazepines and hypnotic z-drugs, FDA labels and clinical guidelines from professional organizations recommend against prolonged drug use beyond 4 weeks because of concerns of abuse and dependence, as well as seizures when patients discontinue or decrease use.[20,21] Despite these concerns, continuous drug treatment beyond 30 days for these drug groups is common in both the GAD (65% for non-hypnotic benzodiazepines) and insomnia (73% for hypnotic benzodiazepines and 74% for hypnotic z-drugs) populations. Continuous use beyond 30 days is even higher for those Medicare beneficiaries under 65: in 2020, 76% for beneficiaries with GAD using non-hypnotic benzodiazepines and 81% for beneficiaries on hypnotic z-drugs. For beneficiaries 65+ with GAD who have continuous drug treatment beyond 30 days, the median number of continuous days of treatment of non-hypnotic benzodiazepines is 143. The median number of continuous days of treatment of hypnotic z-drugs for 65+ beneficiaries with insomnia who have continuous drug treatment beyond 30 days is 184.
- Select Initial Drug Dosing: Clinical guidelines recommend lower drug dosing in people 65+ for some drugs used to treat GAD or insomnia due to the increased potential for harmful side effects. Nevertheless, beneficiaries 65+ with GAD and insomnia who are new to drug treatment seldom receive lower initial doses of these drugs, especially for the subgroup of drugs used to treat insomnia.[10–14,20,21] For example, we found that beneficiaries 65+ prescribed zolpidem generally receive similar initial doses as those under 65, despite the lower dose recommendation for users 65+. In addition, we found that only one quarter of new temazepam users under 65 in the insomnia population are on the FDA-recommended dose, and an even smaller percentage of users 65+ are on the reduced dose recommended for this age group.

Our findings demonstrate several shortcomings in the treatment of Medicare beneficiaries with GAD and insomnia:

- Nearly one quarter of beneficiaries with GAD and insomnia are diagnosed but untreated.
- Beneficiaries who receive treatment frequently receive care that is not concordant with evidence-based guidelines that balance the potential benefits and harms of pharmacologic treatment.
- Beneficiaries commonly receive pharmacologic treatment as first-line, without a trial of psychotherapy (CBT) first. Moreover, beneficiaries often receive initial drug doses that are too high and treatment courses that are too long relative to guideline recommendations.

METHODOLOGY

Population Identification

Using administrative medical and pharmacy claims data of all Medicare FFS beneficiaries, we identify beneficiaries with GAD and insomnia and evaluate their treatment patterns between 2016 and 2020.

We define the yearly GAD population as beneficiaries with one or more diagnosis codes for GAD (Appendix A: Condition Diagnosis Codes) in any position on any claim within that year or the year prior. We define the insomnia population as beneficiaries with one or more diagnosis codes for insomnia (Appendix A: Condition Diagnosis Codes) in any diagnosis code position on any claim or a prescription fill for hypnotic z-drugs or hypnotic benzodiazepines. Beneficiaries remain in the insomnia population from the date of the first claim or qualifying prescription, through the 90 days immediately following, at which point they are removed from the insomnia population. Beneficiaries can requalify into the insomnia population upon their next insomnia diagnosis or prescription fill for hypnotic z-drugs or hypnotic benzodiazepines.

We segment the results by race/ethnicity and income status. Research has shown that Medicare beneficiaries' race/ethnicity is often misclassified and may be imprecise for races other than Black and white.[22] To the extent that the race/ethnicity data provided in the Medicare 100% Research Identifiable Files is not accurate, the results provided by race/ethnicity in this report may likewise be inaccurate. Additionally, each beneficiary has only one value for this field, so we are unable to identify beneficiaries with more than one race. A beneficiary was considered low-income for a given year if they had at least one month of eligibility for the Part D low-income subsidy in the year.

Treatment Identification

We identify prescription fills for seven prescription drug groups of interest across the GAD and insomnia populations. Note that over-the-counter (OTC) drugs are not considered treatments for the purpose of this analysis because they cannot be identified in claims data. To increase our confidence that a prescription fill is related to the individual's GAD or insomnia, we require that the beneficiary have a claim reporting a diagnosis code of GAD or insomnia, respectively, within the 30 days prior to or 30 days following the first fill of a drug group other than hypnotic benzodiazepines and hypnotic z-drugs. Once a beneficiary with GAD or insomnia has been identified as a drug group user, future prescription fills for drugs in the same drug group are attributed to GAD or insomnia treatment (the proximate diagnosis code requirement does not apply). The drug groups are:

- **GAD**: Non-hypnotic benzodiazepines; SSRIs/SNRIs; other anxiety-related drugs.
- **Insomnia**: Hypnotic benzodiazepines; hypnotic z-drugs; other hypnotics; other insomnia-related drugs.

Each drug group is composed of multiple drugs; Appendix C.3.1 lists the generic drug names in each drug group. A beneficiary is considered a user of a drug group in a given year if they have at least one day's supply of a drug in that group during that year. This is ascertained using the days supply reported on pharmacy claims where the first fill has the associated diagnosis code. Beneficiaries with no days supply of a drug in a drug group for at least 60 days prior to a prescription fill are considered new drug group users.

We identify beneficiaries with psychotherapy treatment based on outpatient encounters reported with HCPCS codes that specify psychotherapy. CBT is a form of psychotherapy and is typically billed using psychotherapy procedure codes. While there is no individual procedure code or family of codes that is specific to CBT, we use psychotherapy encounters as a proxy for CBT. It is likely that there are psychotherapy visits captured in our data set in which techniques other than CBT are used. On the other hand, it is possible that psychiatrists or other physicians billing for evaluation and management visits (not used in this analysis to identify psychotherapy) may provide CBT during the encounter, which we do not identify as CBT. When a psychiatrist or other physician provides CBT during an evaluation and management encounter, they usually report a psychotherapy add-on code, all of which are included on our list of HCPCS codes used to identify psychotherapy. We believe our conservative definition of outpatient psychotherapy comprehensively reflects what is most likely to include CBT, taking into consideration the lack of psychotherapy modality-specific HCPCS codes.

DISCLOSURES & LIMITATIONS

This report was commissioned by Big Health Inc. The findings and conclusions reflect the opinion of the authors; Milliman does not endorse any product or organization. If this report is reproduced, it should be reproduced in its entirety as sections taken out of context can be misleading. Milliman does not intend to benefit any third-party recipient of its work product. Our analysis is based on populations, practice patterns, and treatments present in the administrative claims databases specified in the Data Sources and Methodology section of this report. To the extent that clinical conditions are under-identified in administrative claims data compared to survey data or other sources of information, the analysis may not represent the entire population with each condition but, rather, a potentially more severe condition population who seek medical care for the

condition. Additionally, less than half of American adults with mental illness seek treatment for their condition, which further contributes to the underrepresentation of the GAD and insomnia populations studied.[23] To the extent that there is a misdiagnosis, erroneous diagnosis, or no longer applicable diagnosis that is carried through claims for a given beneficiary, we may be including beneficiaries in the GAD or insomnia populations that do not have GAD or insomnia during the analysis period.

Although GAD is a chronic condition, we use a one-year lookback period only to identify the presence of a prior GAD diagnosis in order to estimate condition prevalence in the total Medicare FFS population, without requiring lengthy continuous enrollment that would bias the overall Medicare FFS population to a healthier beneficiary mix.[24] This approach may further bias the GAD population towards a more severe, treated population. Additionally, 2020 saw a disruption in the healthcare system due to COVID-19, which may have led to fewer opportunities for diagnosis coding due to fewer healthcare services.[25,26] Certain racial/ethnic minorities experiencing symptoms of GAD or insomnia but disproportionately not seeking care may have led to the identification of relatively more severe GAD and insomnia minority populations, contributing to the observed racial/ethnic differences. These factors may change over time, and findings from different populations and time periods may differ from the estimates presented in this report for a variety of reasons.

As with any analysis, it is not possible to capture all factors that may be significant. No algorithms for identifying beneficiaries with GAD, insomnia, or other medical conditions are perfect, and we rely only on the information available in claims data, without reference to medical records. One of the authors, Harsha Mirchandani, is a member of the American Academy of Actuaries and meets its qualification standards for this work.

LANGUAGE USED TO DESCRIBE RACE

Consistent with the Associated Press (AP) style guide, we capitalize Black when used in a racial, ethnic, or cultural sense throughout this paper, while leaving white in lowercase in the same context.[27] When citing data from external references, we use the terms/race categories used in those sources for consistency. For example, our data source and external references use the term “Hispanic,” which may include those of Latin American and/or European-Spanish descent.[28] Additionally, some sources used the term “Asian,” which may include those of South Asian or Filipino descent. The race variable contained in the CMS 100% Innovator Research (IR) dataset is the Beneficiary Race Code. It contains the following values: non-Hispanic white; non-Hispanic Black; Asian, Asian American, or Pacific Islander; Hispanic; North American Native; Other; and Unknown. This code is populated by data from the Social Security Administration (SSA) master beneficiary record (MBR), which includes several definitions of race depending on the year in which a beneficiary was born. For those born between 1935 and 1980, the SSA only has three classifications of race: white, Black, and other (unknown is used for those who did not report race on the Social Security application form). In 1980, the SSA expanded the race categories to the options previously mentioned, but these definitions are not retroactively applied to all beneficiaries. Therefore, race data is not precise for races other than Black and white for the population studied, so we group all non-Black or white races into the single category “Other”.

Background

PREVALENCE OF MENTAL ILLNESS

Mental health disorders are prevalent in the United States (US) adult population, spanning a variety of conditions with a spectrum of severity levels. The National Institute of Mental Health estimates that, in 2020, nearly one in five adults in the US – over 50 million people – were living with a mental illness, including 14.5% of people over 50 years old.[29] The prevalence of mental illness among adults is 22.6% for non-Hispanic white people, 17.3% for non-Hispanic Black people, 18.4% for Hispanic people, 13.9% for Asian Americans, and 35.8% for adults who report more than one race.[29] Roughly 57% of those with mental illness in the US remain untreated with either psychotherapy or pharmacological treatment.[30] An even larger portion of racial and ethnic minority populations are not receiving care for their mental health disorders (73% of Asian American/Pacific Islanders, 69% of Black people, and 67% of Latinx/Hispanic people), due to factors such as access to mental health care, language barriers, cultural stigma, and others.[30–32] The most common mental illness is anxiety (which includes panic disorder, generalized anxiety disorder, and posttraumatic stress disorder), with an overall population prevalence of 19.1%.[33]

During the first year of the COVID-19 pandemic (March 2020 to March 2021), Americans experienced higher rates of anxiety compared to pre-pandemic levels due to uncertainty about the virus, job losses, additional childcare responsibilities, and other factors.[26] A large percentage of adults reported that they needed but were unable to access mental health services between March 2020 and March 2021 (e.g., 14% of people over aged 65 and 46% of mothers), with provider access, availability, and affordability being the biggest drivers of not receiving treatment.[26] A 2020 Kaiser Family Foundation (KFF) report found that people of color and people with lower socioeconomic status (SES) reported higher rates of mental illnesses compared to white people and people with higher SES, respectively, during the pandemic.[32] Notably, rates of anxiety or depression were higher in

low-income adults (37% for adults with household incomes less than $25,000) compared to higher-income adults (20% for adults with household incomes more than $100,000).[32] Additionally, specific subpopulations may be more vulnerable to negative pandemic-related effects on their mental health; a 2022 study of the mental health impact of COVID-19 on Medicare beneficiaries with disabilities found that 43.3% experienced symptoms of generalized anxiety disorder (GAD).[34]

Because anxiety is the most prevalent mental illness in the US and multiple studies report increased rates of anxiety during the COVID-19 pandemic, one focus of our analysis is understanding the pharmacological and non-pharmacological treatment patterns of the Medicare FFS population with GAD. Given that many individuals experience comorbid GAD and insomnia, we evaluate treatment patterns separately for the insomnia population.[35] Although depression is also highly correlated with GAD, we did not separately study depression. The drugs commonly used to treat depression do not have the same profile of adverse effects as some of the drugs typically used to treat GAD, where the risk is increased by use patterns that are not consistent with evidence-based clinical guidelines.[36] The remainder of this section discusses GAD and insomnia, as well as the current treatment options and care guidelines for these conditions.

INSOMNIA AND ASSOCIATED TREATMENT

Insomnia is defined as "dissatisfaction with sleep quantity or quality and is associated with difficulty initiating or maintaining sleep and early-morning waking with inability to return to sleep".[24] Poor sleep quality can contribute to the development and exacerbation of comorbidities, such as cardiovascular disease, Type II diabetes mellitus, hypertension, and obesity.[4,5] The prevalence of insomnia is difficult to determine because of the variations in definitions used in population classification. Various studies report that the prevalence of insomnia symptoms ranges from 10-30%, with rates up to 50% in those above the age of 65.[1,37–39] During the COVID-19 pandemic, Black people experienced greater increases in insomnia symptoms compared to white people, with symptom severity being linked to structural inequities that existed prior to the pandemic.[40]

Both the ACP and the AASM recommend cognitive behavioral therapy for insomnia (CBT-I) as first-line treatment, followed by consideration of pharmacologic treatment if CBT-I alone is unsuccessful.[7,8] Agents that can be considered for use include hypnotic benzodiazepines, nonbenzodiazepine hypnotics, suvorexant, ramelteon, doxepin, melatonin, and off-label drugs such as antidepressants, antihistamines, and antipsychotics.[7]

The ACP further recommends that pharmacologic insomnia management has many known risks that should be discussed with the patient prior to drug initiation and should not be used for longer than four to five weeks before being re-evaluated.[7] Adults over the age of 65 may be more sensitive to intended and adverse effects of medication use, should receive lower doses, and should be monitored more closely.[41] The AGS Beers Criteria® is a compendium of medications that should be prescribed with caution or avoided altogether because they often present an unfavorable balance of benefits and harms for older people. As part of the Beers Criteria, the American Geriatrics Society recommends against the general use of first-generation antihistamines, antidepressants, antipsychotics, barbiturates, benzodiazepines, and nonbenzodiazepine hypnotics because the risks outweigh the benefits in the elderly.[15,42]

Despite these recommendations, pharmacologic management of insomnia remains common. An analysis of Medicare administrative claims from the Part D inception in 2006 to2013 demonstrated an increase in the prevalence of insomnia medication prescribing from 21% in 2006 to 29.6% in 2013 (with hypnotic benzodiazepine increasing dramatically from 1.1% in 2006 to 17.6% in 2013).[3,43] However, after the 2013 FDA safety warnings about the risks of zolpidem, a hypnotic benzodiazepine, the use of this category of drugs started to decline.[44] The use of zolpidem to treat insomnia in adults with commercial insurance coverage decreased from 2011 (33.65%) to 2018 (22.60%).[45] However, the percentage of commercially-insured insomnia patients treated with trazodone, an off-label antidepressant used to treat insomnia, was 8.68% in 2011 and grew to 14.46% in 2018.[45]

GENERALIZED ANXIETY DISORDER AND ASSOCIATED TREATMENT

GAD is defined as "at least six months of persistent and excessive anxiety; recurring worry about common events; and physical symptoms, such as muscle tension, insomnia, and fatigue combined with significant distress or impairment in personal, occupational, or other areas of function."[24] The prevalence of anxiety disorders, including GAD, panic disorder, social phobia, and other anxiety disorders, in the Medicare FFS population has steadily increased from 15% in 2015 to 18.75% in 2019.[6]

Similar to the treatment for insomnia, the ACP recommends that CBT be utilized as first-line treatment for GAD, and pharmacologic interventions can be initiated if nonpharmacologic therapies are ineffective.[11] A meta-analysis from 2014 examining the treatment of adults with social anxiety disorder found that CBT was more effective than pharmacologic treatment.[46] Pharmacologic treatment for GAD includes SSRIs and SNRIs as first-line options.[11] Benzodiazepines, buspirone,

and pregabalin are recommended as second-line agents with benzodiazepine use recommended specifically as a short-term intervention (2-4 weeks).[11,47] Third-line agents include antipsychotics, hydroxyzine, and tricyclic antidepressants.[11]

GAD AND INSOMNIA: COGNITIVE BEHAVIORAL THERAPY

Multiple US and European clinical guidelines recommend the first-line use of CBT for the treatment of GAD and insomnia.[7,8,48] CBT is a structured psychotherapeutic treatment approach aimed at reducing the symptoms of certain mental health disorders.[49] CBT can be effectively provided both in-person and virtually, with several studies reporting that the treatment delivery format made no difference in treatment outcomes in people with insomnia, anxiety, and depression.[50,51] However, the use of CBT in the US is limited by a variety of factors: system barriers (demand for CBT providers exceeds supply), clinician barriers (lack of familiarity with CBT components, uncertainty about effectiveness, practitioner beliefs about patient acceptance of CBT), and patient barriers (lack of knowledge of nonpharmacological treatments, time constraints, degree of effort required for commitment to CBT).[52] To address mental health needs during the COVID-19 PHE, the FDA established an enforcement discretion policy for certain digital health devices that treat psychiatric conditions, including devices that furnish CBT.[53] At the time this white paper was published these products are still not widely covered or paid for by commercial payers, despite FDA action.[54] In addition, the Centers for Medicare and Medicaid Services (CMS) has not established separate payment for these devices under the Medicare program, which could make it harder for beneficiaries to gain access to the devices.[54]

GAD AND INSOMNIA: PHARMACOLOGICAL TREATMENT AND RISKS

Several drugs commonly used to treat GAD and insomnia pose a health risk, especially to beneficiaries 65+. These risks have been widely documented by the FDA, which has issued multiple communications and black box warnings related to certain drugs used to treat GAD and insomnia.[21,44,55–58] For example, in 2019 the FDA added a black box warning to three hypnotic z-drugs (eszopiclone, zaleplon, zolpidem), indicating a risk of serious injuries as a result of behaviors like sleep walking, sleep driving, and engaging in other activities while not being fully awake.[59] This black box warning came after three related FDA communications:

- January 2013: Risk of next-morning impairment with zolpidem.[58]
- May 2013: Approved lower recommended doses for zolpidem.[44]
- May 2014: Risk of next-morning impairment with eszopiclone; lowered recommended dose.[60]

Furthermore, the FDA updated the label in 2020 for all benzodiazepines (both hypnotic and non-hypnotic) to include a black box warning for dangers of abuse and physical dependence, among other risks.[21] The FDA label recommends using the lowest dose possible of alprazolam, the most commonly prescribed benzodiazepine in the US, and frequently reassessing the need to continue.[20] After an initial prescription for zolpidem, alprazolam, lorazepam, or diazepam, falls were found to be higher across users 65+ of all drugs.[12] A meta-analysis that included 33 studies evaluating hip fractures in people taking benzodiazepines found a 34% increase in fracture risk for users compared to non-users.[13] Another meta-analysis found that people using benzodiazepines were 25% more likely to experience a fracture of any kind compared to those not using benzodiazepines, with the risk of fracture further increased in those above 65 years of age.[14] Benzodiazepine use beyond one month is also associated with motor and cognitive impairment, as well as a risk of dependence.[10,11] Zolpidem is approved by the FDA for “short term” use and its FDA label says, “[...] Ambien has been shown to decrease sleep latency for up to 35 days in controlled clinical studies.”[61] Studies suggest that longer-term use in the elderly may lead to adverse events such as falls and cognitive impairment, as well as impact certain motor functions like grip strength.[62–64] However, for the under 65 population specifically, there have been some trials that have demonstrated efficacy for longer-term use of zolpidem and extended release zolpidem.[65]

Despite these known risks, benzodiazepine use remains common. Data from a 2015 retrospective analysis of benzodiazepine use found that 5.2% of adults aged 18-80 were using benzodiazepines, with higher use in the elderly (8.7% of adults aged 68-80).[66] Adults over the age of 65 were also more likely to be chronic users (31.4% of users 65-80 years old vs 14.7% of users 18-35 years old), and they notably were less likely to have their medication prescribed by a psychiatrist (5.7% of users 65-80 years old vs 15% of users 18-35 years old).[66] Another study found that 26.4% of older adults prescribed with benzodiazepines for the first time became long-term users in the subsequent year, with an average of 232.7 days prescribed. [67]

Increased health risk from polypharmacy is another concern when people are treated concurrently with combinations of psychoactive agents, including opioids.[17–19] For example, several studies have shown an increased risk of mortality when adults 65+ are prescribed a combination of opiates and benzodiazepines.[17,18] In 2016, the FDA required black box warnings for the concurrent use of opioids and central nervous system (CNS) depressants, such as benzodiazepines, due to the increased risk of respiratory depression, coma, and overdose-related deaths.[55,56] The AGS Beers Criteria® also cites an

increased risk of falls and fractures from concurrent use of several psychoactive agents and recommends against the combination of 3 or more CNS-active drugs (antidepressants, antipsychotics, benzodiazepines, nonbenzodiazepine receptor agonist hypnotics, antiepileptics, and opioids).[15] Despite these guidelines, a recent study older adults with dementia found that 13.9% of patients experienced CNS polypharmacy (i.e., 3 or more CNS-active agents), of which 57.8% were prescribed medication combinations for more than 180 days and 40.7% of polypharmacy days included a benzodiazepine.[68]

NEED FOR REAL-WORLD RESEARCH

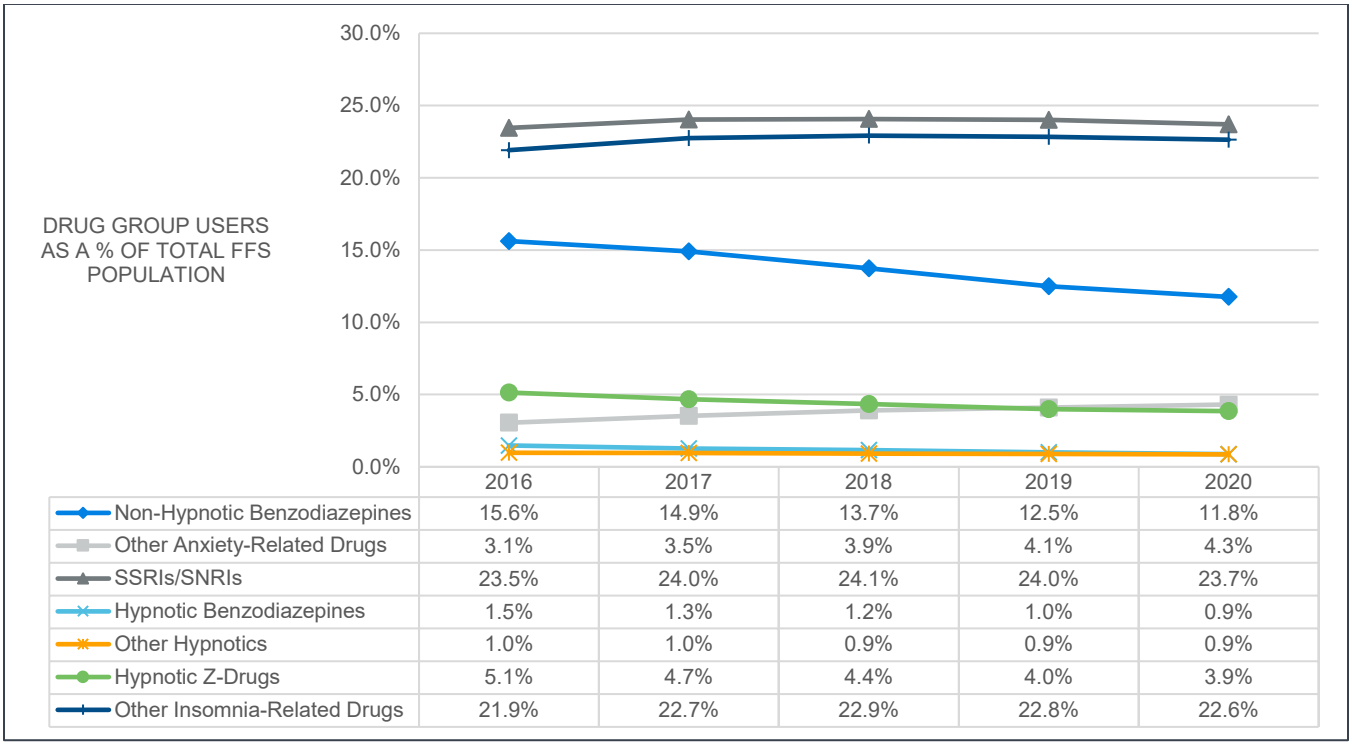
GAD and insomnia are significant, growing health conditions in the US, contributing to increased morbidity and healthcare expenditures, and negatively impacting quality of life. There is evidence that the prolonged social stressors associated with the COVID-19 pandemic is associated with higher levels of condition diagnosis and heightened symptomatology in individuals with existing disorders. At the same time, individuals may face additional barriers to mental health treatment. Although several studies have found that real-world treatment patterns are frequently not guideline-concordant for people with specific mental illnesses, few studies have evaluated patterns by specific mental health condition, age, race, and income status concurrently within a large, national insured population. In addition, studies have not generally examined treatment patterns at the level of granularity specified in clinical guidelines. Current care guidelines for GAD and insomnia recommend that CBT should be offered before initiating pharmacological treatment. GAD and insomnia patients above the age of 65 are at particularly high risk for harmful side effects resulting from pharmacological treatment for their conditions, and several clinical guidelines make specific duration and dosing recommendations regarding pharmacological treatment in older adults. This study aims to fill current knowledge gaps in analyzing the treatment patterns of Medicare FFS beneficiaries from 2016 to 2020 with GAD or insomnia by age, race, and income status, including comparing these patterns to the recommendations of clinical guidelines.

Findings

TOTAL UTILIZATION OF DRUG GROUPS THAT MAY BE USED TO TREAT GAD OR INSOMNIA

Up to 24.1% of the total Medicare FFS population (i.e., not limited to individuals with GAD or insomnia) fill a prescription for drug groups that may be used to treat GAD or insomnia in each year between 2016 and 2020. The use of benzodiazepines (hypnotic and non-hypnotic) and hypnotic z-drugs declines between 2016 and 2020, whereas use of other drug groups remains relatively stable. Figure 1 displays the trend in use for the seven drug groups between 2016 and 2020.

FIGURE 1: 2016-2020 UTILIZATION OF DRUG GROUPS THAT MAY BE USED TO TREAT GAD OR INSOMNIA



	2016	2017	2018	2019	2020
Non-Hypnotic Benzodiazepines	15.6%	14.9%	13.7%	12.5%	11.8%
Other Anxiety-Related Drugs	3.1%	3.5%	3.9%	4.1%	4.3%
SSRIs/SNRIs	23.5%	24.0%	24.1%	24.0%	23.7%
Hypnotic Benzodiazepines	1.5%	1.3%	1.2%	1.0%	0.9%
Other Hypnotics	1.0%	1.0%	0.9%	0.9%	0.9%
Hypnotic Z-Drugs	5.1%	4.7%	4.4%	4.0%	3.9%
Other Insomnia-Related Drugs	21.9%	22.7%	22.9%	22.8%	22.6%

A larger portion of beneficiaries taking non-hypnotic benzodiazepines (between 37% and 46% across the 5-year span, other anxiety-related drugs (between 55% and 63%), and other insomnia-related drugs (between 42% and 50%) are low-income compared to the total Medicare FFS population (between 30% and 35%). The percentage of beneficiaries taking hypnotic z-drugs (between 26% and 38%) and hypnotic benzodiazepines (between 30% and 42%) who are low-income is generally consistent with the total Medicare FFS population.

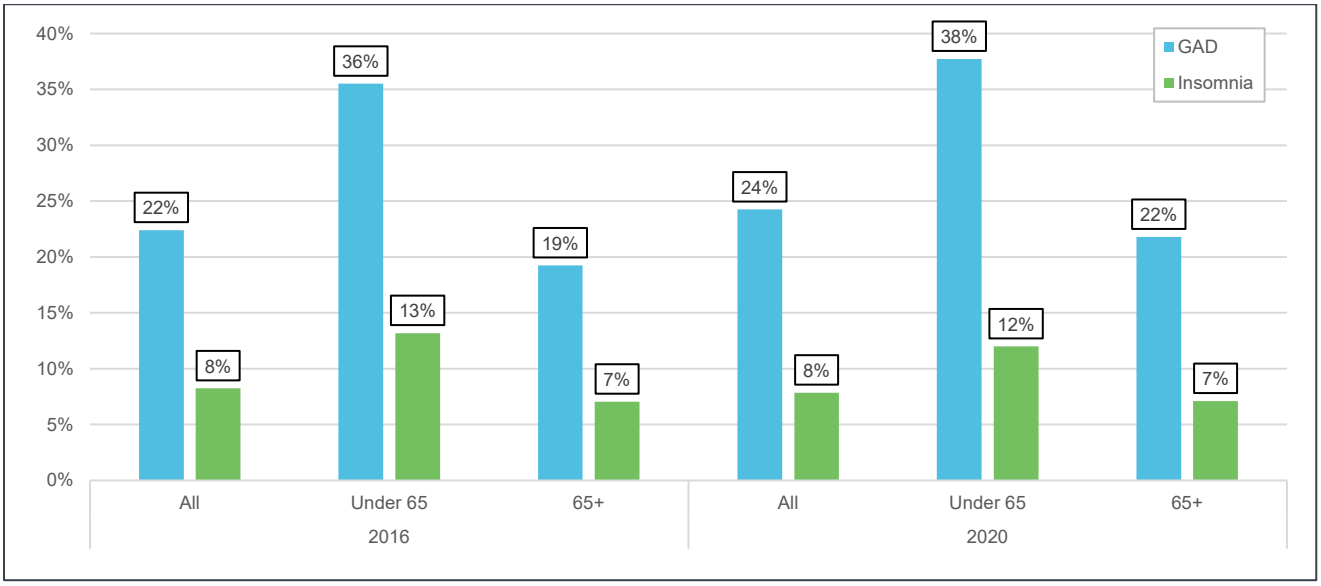
GAD AND INSOMNIA PREVALENCE AND DEMOGRAPHICS

Between 2016 and 2020, the prevalence of GAD in the Medicare FFS population ranges from 22% to 25%, with the highest prevalence in low-income non-Hispanic white beneficiaries (between 36% and 39%). A disproportionate number of beneficiaries with GAD are under 65 relative to the total Medicare FFS population (between 24% and 31% of beneficiaries with GAD versus 17% in the total FFS population). The GAD prevalence among those under 65 is higher (between 36% and 38%) than those 65+ (between 19% and 22%), with the highest prevalence again in low-income non-Hispanic white beneficiaries (between 42% and 45%). This pattern is also observed for those 65+. These rates are consistent with national estimates.[6,29,33]

Roughly 27% of beneficiaries with GAD have comorbid insomnia in a year. The prevalence of insomnia is about 8% in 2016-2020, with a prevalence of between 12% and 13% in those under 65. The insomnia population has a comparable proportion of beneficiaries under 65 as the GAD population – between 23% and 31% of beneficiaries with insomnia are under 65. The overall insomnia prevalence is consistent with national estimates.[1,37–39] The overall prevalence of insomnia decreases slightly over time from 2016 to 2020. This may be due to the decrease in utilization of hypnotic z-drugs and hypnotic benzodiazepines that contributes to identifying beneficiaries with insomnia (see Figure 2) or to fewer healthcare services being provided for insomnia symptoms in 2020 as a result of the COVID-19 pandemic.[69] We examine patterns of drug group use for GAD and insomnia later in this section.

Figure 2 displays 2016 and 2020 prevalence rates for GAD and insomnia. See Appendix Tables B1.1 through B1.3 for detailed prevalence rates for all segments of the GAD and insomnia populations.

FIGURE 2: 2016-2020 STUDY POPULATION COUNT (PREVALENCE) BY CONDITION (GAD AND INSOMNIA) AND AGE GROUP



For the GAD and insomnia populations, we report the co-occurrence of nine other medical conditions that are more prevalent in the GAD and insomnia populations relative to all Medicare FFS beneficiaries. For detailed results, see Figures B1.1 and B1.2 in Appendix B.

TREATMENT PATTERNS

Untreated Population

Approximately one in four beneficiaries with a diagnosis for GAD on administrative claims is untreated in 2019 and 2020, defined as no condition-specific drug use or outpatient psychotherapy encounters in the year. There may be other beneficiaries with undiagnosed GAD not captured by this analysis who also remain untreated because they do not have an

encounter with a provider, they do not seek care for complaints attributed by a provider to GAD or insomnia, or the provider does not report a relevant condition diagnosis code on a claim or prescribe an insomnia-identifying drug. For those 65+, the untreated rate is higher than those under 65, and substantially higher in racial minorities (36% of non-Hispanic Black beneficiaries and 31% of beneficiaries of other races compared to 23% of non-Hispanic white beneficiaries). Similar differences exist by race for the under 65 with GAD population. These racial differences likely result from multiple factors, such as patient distrust in the healthcare system which can lead to an avoidance of care, cultural stigma, or barriers to accessing quality care.[70] The findings regarding treatment for the GAD and insomnia populations are displayed in Table 2.

TABLE 2: 2019-2020 PERCENT OF GAD AND INSOMNIA POPULATIONS THAT IS UNTREATED BY AGE GROUP AND RACE/ETHNICITY

	GAD		*Insomnia*	
	2019	**2020**	**2019**	**2020**
Under 65	**19%**	**20%**	**15%**	**15%**
Non-Hispanic Black	29%	30%	17%	17%
Non-Hispanic White	17%	17%	14%	14%
Other	24%	23%	17%	17%
65+	**24%**	**24%**	**25%**	**24%**
Non-Hispanic Black	35%	36%	26%	25%
Non-Hispanic White	23%	23%	25%	24%
Other	31%	31%	26%	25%

Treated Population

Treatment Modalities

Most beneficiaries with GAD or insomnia are treated, but the type of treatment varies by population segment. We define treatment as an outpatient psychotherapy encounter or pharmacotherapy identified by a prescription fill for 1+ days supply of a drug included in one of the condition-specific drug groups listed below. See Appendix C.3.1 for a list of the generic drug names included in each drug group:

- **GAD**: non-hypnotic benzodiazepines; SSRIs/SNRIs; other-anxiety related drugs.
- **Insomnia**: hypnotic benzodiazepines; hypnotic z-drugs; other hypnotics; other insomnia-related drugs.

Approximately three-fourths of beneficiaries with GAD or insomnia receive pharmacotherapy. While roughly 13% of beneficiaries 65+ with GAD receive both outpatient psychotherapy and pharmacotherapy, those under 65 receive both treatment types twice as often. Table 3 displays the percent of the GAD and insomnia populations receiving treatment by treatment type at any point in the year: outpatient psychotherapy, pharmacotherapy, or both.

TABLE 3: PERCENT OF GAD AND INSOMNIA POPULATIONS BY AGE GROUP AND TREATMENT MODALITY IN 2019 AND 2020

	GAD		*Insomnia*	
	2019	**2020**	**2019**	**2020**
Under 65				
Psychotherapy Only	5%	5%	4%	4%
Pharmacotherapy Only	68%	69%	71%	72%
Both	27%	26%	25%	24%
65+				
Psychotherapy Only	4%	3%	3%	3%
Pharmacotherapy Only	83%	84%	87%	88%
Both	14%	13%	10%	10%

Pharmacotherapy

Across all applicable drug groups for GAD or insomnia, beneficiaries using these drugs tend to skew younger and more female than the total FFS population. The main exception is beneficiaries with insomnia taking hypnotic benzodiazepines who have the same average age as the total FFS population. Table 4 displays the percent of beneficiaries with GAD and insomnia who are on condition-specific drugs in 2019 and 2020, with similar patterns in earlier study years. Refer to Appendix Tables B1.1 through 1.3 for relevant demographic characteristics for beneficiaries with GAD or insomnia. Tables 5A and 5B display the top three drugs by days supply in each drug group for each condition population in 2019 and 2020.

TABLE 4: PERCENT OF GAD AND INSOMNIA POPULATION ON CONDITION-SPECIFIC DRUGS IN 2019 AND 2020

	2019		2020	
	Member Count	% of Condition	Member Count	% of Condition
Medicare FFS Denominator Population	24,719,470	-	24,101,127	-
GAD				
Non-Hypnotic Benzodiazepines	965,790	16%	898,247	15%
SSRIs/ SNRIs	1,377,551	23%	1,350,431	22%
Other Anxiety-Related Drugs	436,726	7%	457,589	8%
Insomnia				
Hypnotic Benzodiazepines	244,637	12%	207,391	10%
Hypnotic Z-Drugs	970,390	47%	909,576	45%
Other Hypnotics	70,673	3%	67,974	3%
Other Insomnia-Related Drugs	925,264	45%	909,621	45%

TABLE 5A. GAD POPULATION - TOP DRUGS IN EACH DRUG GROUP (% OF ALL DAYS SUPPLY FOR THE DRUG GROUP) – 2019 AND 2020

Rank by Days Supply	Non-Hypnotic Benzodiazepines	SSRIs/ SNRIs	Other Anxiety-Related Drugs
2019			
Top 1	Alprazolam (36.1%)	Sertraline (22.7%)	Buspirone (60.8%)
Top 2	Clonazepam (28.1%)	Escitalopram (17.1%)	Hydroxyzine (39.2%)
Top 3	Lorazepam (25.7%)	Duloxetine (16.7%)	-
2020			
Top 1	Alprazolam (36.1%)	Sertraline (22.9%)	Buspirone (59.7%)
Top 2	Clonazepam (28.3%)	Escitalopram (17.8%)	Hydroxyzine (40.3%)
Top 3	Lorazepam (25.8%)	Duloxetine (16.9%)	-

TABLE 5B. INSOMNIA POPULATION – TOP DRUGS IN EACH DRUG GROUP (% OF ALL DAYS SUPPLY FOR THE DRUG GROUP) – 2019 AND 2020

Rank by Days supply	Hypnotic Benzodiazepines	Hypnotic Z -Drugs	Other Hypnotics	Other Insomnia-Related Drugs
2019				
Top 1	Temazepam (95.0%)	Zolpidem (87.3%)	Doxepin (54.0%)	Gabapentin (47.0%)
Top 2	Triazolam (4.0%)	Eszopiclone (7.0%)	Phenobarbital (30.1%)	Trazodone (21.1%)
Top 3	Estazolam (0.6%)	Zolpidem ER (3.5%)	Suvorexant (10.5%)	Quetiapine (13.0%)
2020				
Top 1	Temazepam (95.6%)	Zolpidem (86.9%)	Doxepin (54.7%)	Gabapentin (46.8%)
Top 2	Triazolam (3.6%)	Eszopiclone (7.3%)	Phenobarbital (28.6%)	Trazodone (21.7%)
Top 3	Estazolam (0.6%)	Zolpidem ER (3.6%)	Suvorexant (11.0%)	Quetiapine (12.9%)

Across all ages, the use of non-hypnotic benzodiazepines to treat beneficiaries with GAD decreases over time (Figure 3), with a similar level of decline in the under 65 and 65+ populations. The use of SSRIs/SNRIs in those 65+, as well as other anxiety-related drugs in the under 65 and 65+ populations, increases over the same period, whereas the use of SSRIs/SNRIs remains mostly stable in those under 65. Due to the potential for harmful side effects associated with benzodiazepine use, use of SSRIs/SNRIs to treat GAD is recommended as first-line pharmacological treatment instead of benzodiazepines.[11]

In 2016, most beneficiaries with insomnia are on hypnotic z-drugs (56% in those under age 65 and 65% in those 65+). This is partly because a prescription for hypnotic z-drugs qualifies a beneficiary for the insomnia population. From 2016-2020, the use of hypnotic benzodiazepines and hypnotic z-drugs declines across beneficiaries with insomnia (Figure 3), while the use of other insomnia-related drugs increases by 5% in those under age 65 and over 10% in those 65+. The increased utilization of other insomnia-related drugs is not driven by one drug; we observe a steady increase in most drugs included in this drug group, with the most common drivers being trazodone, gabapentin, and mirtazapine. These results for the Medicare FFS population with insomnia are consistent with decreased use of zolpidem and increased use of trazodone reported by a study on commercially-insured people with insomnia.[45] In general, the decline in use of hypnotic benzodiazepines and hypnotic z-drugs and increase in use of other insomnia-related drugs suggest a shift toward prescribing off-label drugs. A small portion of the insomnia population uses drugs in the other hypnotics drug group, which remains mostly stable between 2016 and 2020.

FIGURE 3: 2016-2020 PERCENT OF GAD AND INSOMNIA POPULATIONS USING RELEVANT DRUG GROUPS BY AGE GROUP

Prescribing Specialty for Initial Pharmacological Treatment

For new drug group users' initial prescription, we identify the prescribing physician specialty. New drug group users are defined as patients with GAD or insomnia who have a period of at least 60 days with no days supply of any drug in that drug group prior to their prescription fill for a drug in that drug group. Users can exit and reenter the new user cohort if they previously used a drug in a drug group, experience a period of at least 60 consecutive days with no days supply of any drug in that drug group, and then restart a drug in that drug group. Figures 4A and 4B display the provider specialty distribution for the prescribers of new users' initial prescriptions by condition-specific drug group for 2019 and 2020.

The majority of beneficiaries 65+ with GAD receive their initial prescriptions from a primary care physician (PCP), whereas about one-third of beneficiaries under 65 receive their initial prescriptions from a PCP. Across all GAD drug groups, beneficiaries under age 65 receive their first prescription from a psychiatrist nearly three times as often as those 65+. A similar pattern is observed for beneficiaries with insomnia. The majority of beneficiaries 65+ with insomnia receive their initial prescription from a PCP (between 58% and 65% in 2020), and the percentage of beneficiaries with insomnia under 65 who receive their initial prescription from a psychiatrist is nearly three times greater than those 65+.

FIGURE 4A: PRESCRIBING PHYSICIAN SPECIALTY OF NEW DRUG GROUP USERS' INITIAL PRESCRIPTION IN 2019 AND 2020 – GAD POPULATION

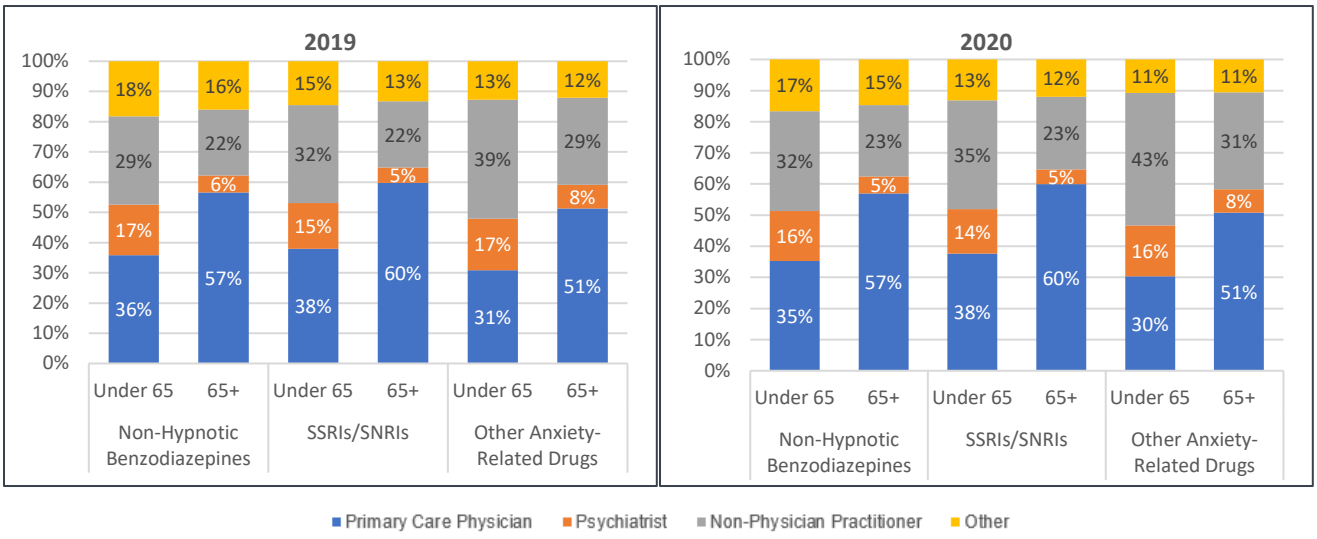
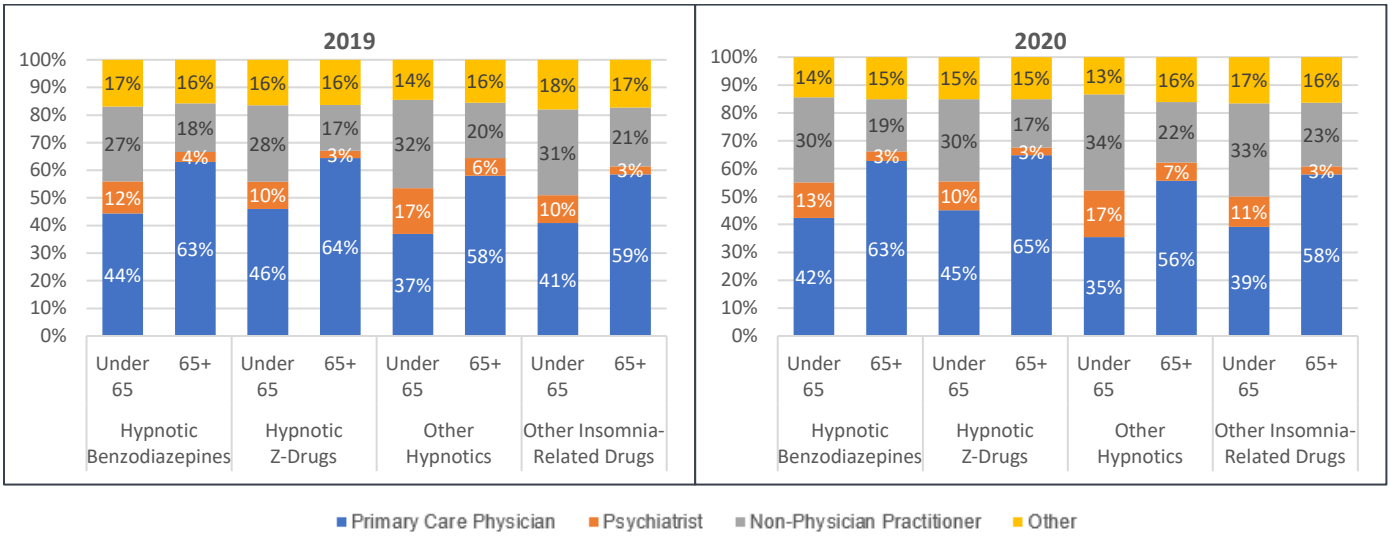


FIGURE 4B: PRESCRIBING PHYSICIAN SPECIALTY OF NEW DRUG GROUP USERS' INITIAL PRESCRIPTION IN 2019 AND 2020 – INSOMNIA POPULATION



GUIDELINE-CONCORDANT CARE

Outpatient Psychotherapy as a Proxy for CBT

ACP and AASM guidelines recommend the use of psychotherapy, specifically CBT, for the treatment of insomnia before proceeding to pharmacological treatment if CBT is unsuccessful.[7,8,11] Despite this, under 8% of the insomnia population receive outpatient psychotherapy in the 30 days prior to beginning pharmacologic treatment. For the 65+ population, only 3% of beneficiaries receive psychotherapy prior to initiating use of a hypnotic z-drug (the most used pharmacotherapy for beneficiaries with insomnia by a wide margin). ADAA guidelines recommend either psychotherapy or SSRI/SNRIs as first-line treatments for GAD, but we observe that only 8% of the 65+ GAD population receive psychotherapy before starting on a second-line non-hypnotic benzodiazepine.[9] There is also no meaningful difference in prior psychotherapy use in the GAD population between those receiving SSRIs/SNRIs, which would be considered guideline-concordant as first-line treatment, and those receiving non-hypnotic benzodiazepines or other anxiety-related drugs, both of which would not be considered guideline-concordant as first-line treatment. A higher portion of beneficiaries under 65 receive psychotherapy before initial drug treatment (15% of beneficiaries with GAD and 12% of beneficiaries with insomnia) compared to the 65+ population (Table 6). However, the vast majority in both groups do not receive psychotherapy before the first prescription fill. (Table 6).

TABLE 6: PERCENTAGE OF NEW DRUG GROUP USERS WITH AN OUTPATIENT PSYCHOTHERAPY ENCOUNTER IN THE 30 DAYS PRIOR TO FIRST PRESCRIPTION FILL – 2019 AND 2020

	2019		*2020*	
Drug Group	**Under 65**	**65+**	**Under 65**	**65+**
GAD				
Non-Hypnotic Benzodiazepines	15%	7%	17%	8%
Other Anxiety-Related Drugs	16%	10%	17%	10%
SSRIs/SNRIs	13%	7%	14%	8%
Insomnia				
Hypnotic Benzodiazepines	12%	3%	14%	4%
Hypnotic Z-Drugs	11%	3%	12%	3%
Other Hypnotics	15%	6%	18%	7%
Other Insomnia-Related Drugs	10%	4%	12%	5%

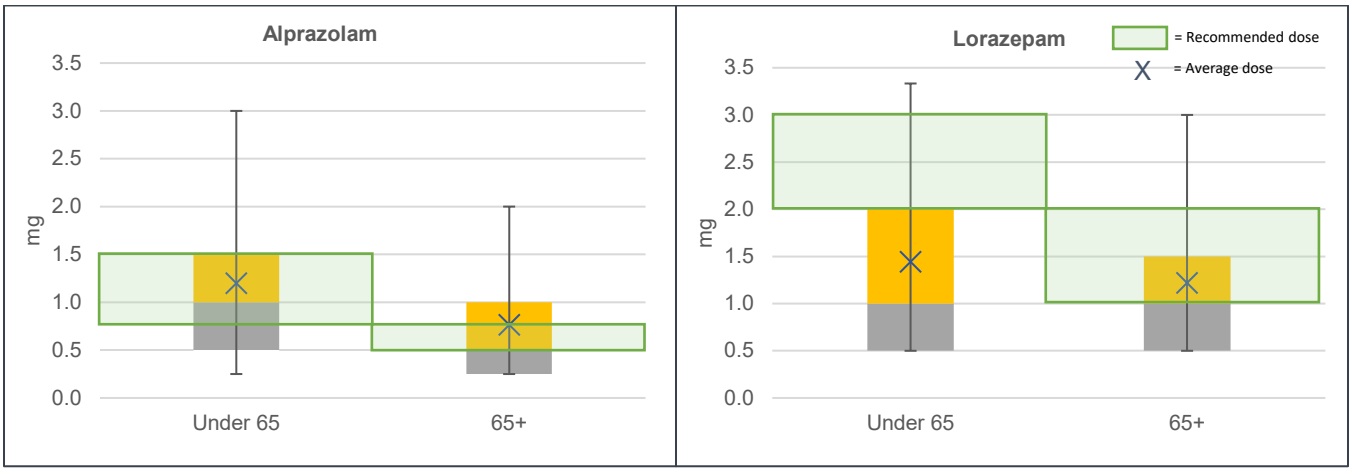
Initial Drug Dosing

The FDA label and/or clinical guidelines from professional organizations recommend lower doses for people 65+ for several drugs in the drug groups used to treat GAD and insomnia due to their association with harmful effects such as falls and fractures, risk of dependence, and cognitive decline.[10–14,20,21] Despite these recommendations, people 65+ with GAD and insomnia who are new to treatment with these drugs (i.e., a period of at least 60 days with no days supply of any drug in the drug group prior to their prescription fill) are not always receiving lower initial doses.

Figures 5A and 5B display the 2020 distributions of initial doses for select drugs from Tables 5A and 5B that have explicit lower-dose recommendations for people 65+ in the FDA label as well as a prescription count over 5,000 in the year. We note that beneficiaries under 65 are eligible for Medicare based on their disability status, ESRD, or amyotrophic lateral sclerosis (ALS). They may exhibit frailty characteristics similar to those 65+ and may be susceptible to similar health risks associated with the use of certain drugs in people 65+, such as falls and fractures.[37] Therefore, Medicare beneficiaries under 65 may be more likely than individuals under 65not covered by Medicare to receive lower than typical adult doses. However, we compare the initial drug doses for the under 65 and 65+ populations in this analysis because dosing guidelines distinguish the initial dose primarily based on age, not health status.

Consistent with dosing recommendations on the FDA labels, new users of alprazolam and lorazepam in the GAD population under age 65 are generally prescribed higher initial doses than those 65+.[20,71] While most new users of alprazolam who are 65+ receive lower doses than new users under 65, roughly one-third of the older population still receive higher initial doses than recommended by the FDA. Lorazepam dosing appears to be more consistent with the FDA's label compared to alprazolam dosing – most lorazepam users both under 65 and 65+ receive doses at or below the FDA's age-specific recommendations.

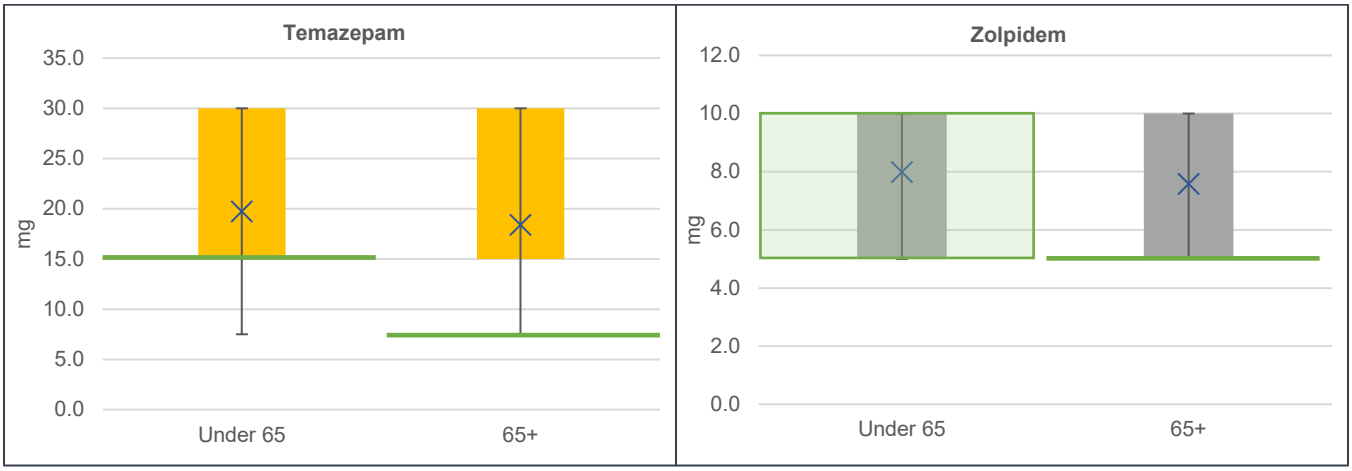
FIGURE 5A: DISTRIBUTION OF INITIAL DOSING FOR NEW USERS OF SELECT DRUGS – GAD POPULATION – 2020[1]



[1] The border between the orange and grey regions represents the median dose, the bottom of the grey region is the 25th percentile dose, the top of the orange region is the 75th percentile dose, and the 'X' is the mean dose. Charts with no grey or orange region imply that the median is the same as the 25th or 75th percentile, respectively. The bottom and top error bars represent the 5th and 95th percentile dose, respectively. The green boxes or lines represent the recommended range of initial starting doses or the initial starting dose, respectively, for each age group.

Among the 65+ insomnia population, new users of temazepam and zolpidem are generally prescribed higher initial doses than the FDA label recommendation, and there appears to be little to no difference in the dosing distributions by age group.[61,72] Only one quarter of new temazepam users under 65 are on the FDA-recommended dose of 15 mg per day, and even fewer new users 65+ are on the recommended reduced dose of 7.5 mg per day. While zolpidem dosing for beneficiaries under 65 is consistent with the recommended range for this age group, beneficiaries 65+ generally receive the same doses as those under 65 despite the lower dose recommendation for those 65+. A similar pattern is observed for extended-release zolpidem.

FIGURE 5B: DISTRIBUTION OF INITIAL DOSING FOR NEW DRUG GROUP USERS – INSOMNIA POPULATION – 2020[2]

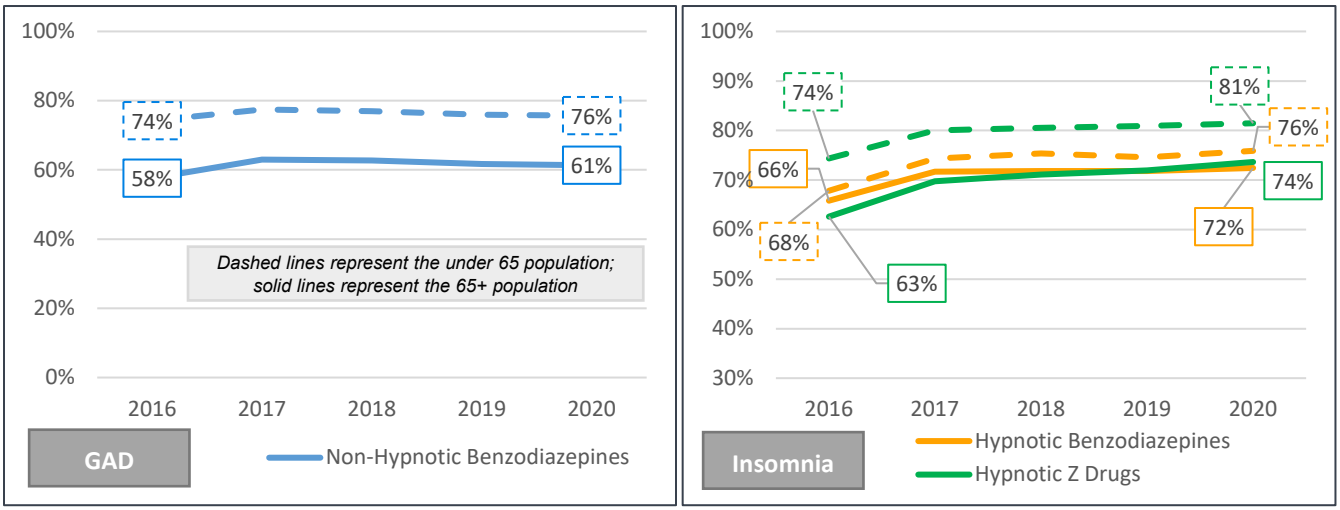


Drug Use Duration

In addition to recommending lower doses for people 65+, the FDA label and clinical guidelines from professional organizations for certain drugs recommend against prolonged drug use beyond 4 weeks because of concerns of abuse and dependence, as well as seizures when patients discontinue or decrease use.[20,21] We measure the percentage of users of benzodiazepines and hypnotic z-drugs with 31+ and 61+ continuous days supply, where continuous use is defined as an allowable gap of 20% of the days supply between prescriptions of any drug within the drug group. Figure 6 summarizes our findings for 31+ days supply for these drug groups with condition-specific recommendations for limited duration of use. While the percentage of drug group users with 61+ continuous days supply is lower by 5% to 15%, the pattern within a drug group is the same as those with 31+ continuous days supply. Overall, continuous drug treatment beyond 30 days is substantial for GAD (76% for under 65 and 61% for 65+ in 2020) and even greater for insomnia (between 76% and 81% for under 65 and between 72% and 74% for 65+ in 2020) populations, contrary to FDA labeling guidance for these drug groups. For 65+ beneficiaries with GAD who have continuous drug treatment beyond 30 days, the median number of continuous days of treatment of non-hypnotic benzodiazepines is 143. The median number of continuous days of treatment of hypnotic z-drugs for 65+ beneficiaries with insomnia who have continuous drug treatment beyond 30 days is 184.

[2] The border between the orange and grey regions represents the median dose, the bottom of the grey region is the 25th percentile dose, the top of the orange region is the 75th percentile dose, and the 'X' is the mean dose. Charts with no grey or orange region imply that the median is the same as the 25th or 75th percentile, respectively. The bottom and top error bars represent the 5th and 95th percentile dose, respectively. The green boxes or lines represent the recommended range of initial starting doses or the initial starting dose, respectively, for each age group.

FIGURE 6: 2016-2020 GAD AND INSOMNIA PERCENTAGE OF DRUG USERS WITH CONTINUOUS DRUG USE FOR 31+ DAYS BY AGE



Discussion

GAD and insomnia are common behavioral health conditions in the Medicare FFS population associated with considerable morbidity and may be treated with psychotherapy and/or pharmacologic therapy. There is broad medical consensus that CBT should be used as first-line treatment for patients with insomnia and CBT or SSRIs/SNRIs should be used as first-line treatment for patients with GAD.[7–9] The AGS Beers Criteria® for Potentially Inappropriate Medication Use in Older Adults identifies benzodiazepines and hypnotic z-drugs as drugs to be avoided in older adults because they present an unfavorable balance of benefits and harms.[15] In addition, the labeling of certain benzodiazepines recommends caution in the use for those 65+.[20] For example, the FDA label for alprazolam indicates that patients over 65 may be more sensitive to the effects of benzodiazepines, should be prescribed the lowest effective dose, and should frequently be reassessed regarding the need for continued treatment.[20] Through our analysis of claims data, we identified several treatment patterns that indicate Medicare beneficiaries being treated for GAD and insomnia are not receiving care consistent with current guidelines:

- Roughly a quarter of beneficiaries with insomnia and GAD in 2019 and 2020 do not have any evidence of treatment (either pharmacotherapy or psychotherapy) in claims data, indicating a potential gap in care for these patients.
- Approximately 10% of beneficiaries with GAD and 5% of beneficiaries with insomnia receive psychotherapy within 30 days prior to initiating drugs like non-hypnotic benzodiazepines and hypnotic z-drugs in 2019 and 2020. These findings are in conflict with clinical guidelines for the treatment of insomnia and GAD.[7–9]
- In drug groups with indications for strictly short-term use (i.e., 30 days or less), most beneficiaries with GAD and insomnia in 2020 (GAD: 76% for under 65 and 61% for 65+; insomnia: between 76% and 81% for under 65 and between 72% and 74% for 65+) receive pharmacotherapy that extends for over 30 days.
- Many beneficiaries 65+ are treated with drug doses that are too high compared to the FDA label recommendations for a lower initial dose for people 65+, and are more appropriate for individuals under 65.

We note that some treatment patterns for drugs used to treat GAD and insomnia have evolved between 2016 and 2020 to reflect safer care that is more consistent with evidence-based best practices. For example, we found declines in the use of non-hypnotic benzodiazepines to treat beneficiaries with GAD (6% decline), as well as declines in the use of hypnotic benzodiazepines (7% decline) and hypnotic z-drugs to treat patients with insomnia (14% decline) during the 2016-2020 period. Nevertheless, the use of non-hypnotic benzodiazepines and hypnotic z-drugs for GAD and insomnia remains common in the Medicare FFS population. While the reduction in use of benzodiazepines and hypnotic z-drugs is a positive trend, very few beneficiaries receive first-line behavioral interventions (i.e., psychotherapy) before initiating these drugs. Moreover, the overall share of the Medicare FFS population with GAD and insomnia treated with psychotherapy is stable between 2019 and 2020 (see Figure 3). For the insomnia population where there is an overall decrease in use of hypnotic z-drugs over time, there is increased utilization (9% increase from 2016-2020) of other insomnia-related drugs, where use would be on-label for certain co-occurring conditions in the insomnia population but off-label for insomnia, including trazodone and gabapentin. The decline in hypnotic z-drugs and the uptick in trazodone use for the Medicare FFS population with insomnia are consistent with another study on commercially insured patients with insomnia.[45] We also note that the medical and pharmacy claims databases used

for this study do not capture use of OTC products, like melatonin, nor psychotherapy sessions with mental health practitioners who do not participate in the Medicare program and for which beneficiaries must pay out of pocket.

In addition, while we found that only a small percentage of beneficiaries with GAD or insomnia receive psychotherapy within 30 days prior to initiating drugs like non-hypnotic benzodiazepines and hypnotic z-drugs, our methodology for identifying psychotherapy services does not specifically identify the provision of CBT, which is the first-line non-pharmacologic treatment recommended for both conditions. Therefore, in identifying psychotherapy broadly, our findings may be overestimating the rates of CBT. For example, other research suggests that psychotherapy treatment for anxiety disorders commonly either does not include CBT or the CBT is inadequate (e.g., does not include three or more elements that would make it likely to be indicative of adequate quality CBT).[73,74]

Broadly, our findings indicate that people diagnosed with GAD or insomnia may not receive guideline-recommended care: a subset of the population is untreated, few patients receive clinically recommended psychotherapeutic interventions prior to initiating certain drug treatment, and drug treatment patterns do not reflect best practices. This all results in unnecessary health risks for Medicare beneficiaries. Factors contributing to treatment patterns that are not concordant with best practices include:

- **System issues**:
    - Drugs as first-line: Other than SSRIs/SNRIs which are considered first-line treatment for GAD, drugs that are recommended as later-line treatments for GAD and insomnia are being used as first-line.[7–9] Providers' lack of familiarity with CBT and beliefs about its utility, acceptability. or availability may be contributing to the initial prescription of pharmacotherapy instead of referral for behavioral health interventions.[52]
    - Limited access to CBT: PCPs and non-physician practitioners, many of whom practice in a primary care setting, are the predominant prescribers of initial insomnia and GAD-related prescriptions, especially in new drug users over 65 with GAD and insomnia. If a PCP's practice is not an integrated behavioral health model, for recommended first-line insomnia and non-pharmacologic GAD treatment the provider would need to refer patients out to a behavioral health provider trained in CBT. However, there are many barriers to successful referrals for timely behavioral health interventions for GAD and insomnia:
        - Limited supply of mental health professionals: Over one-third of the US population lives in a mental health professional shortage area, which is defined primarily as a region with a population to provider ratio to at least 30,000 to 1.[75,76] The proportion of Americans living in a mental health professional shortage area varies considerably by state, from 0% in Vermont to 96% in Wyoming.[75] While the increased availability of virtual care through telehealth encounters has expanded accessibility to the rural population, the supply of mental health professionals and the capacity required to provide needed care is limited.[77] We note that other countries have recognized digital therapeutics that furnish CBT, which may help mitigate some of the challenges associated with provider availability.[48,78] For example, in the United Kingdom digital therapeutics have been recommended for use by the National Institute for Health and Care Excellence (NICE) and are available nationally through Scotland's National Health Service.[48,78,79] However, US-based health insurers, including Medicare FFS, generally do not cover or do not pay separately for digital therapeutics, including those that furnish CBT.[54]
        - Comparatively low behavioral health provider Medicare participation: Limited participation of behavioral health providers in Medicare may prevent beneficiaries from accessing and affording this care. A 2022 study using data from CMS found that about 43% of providers who do not accept Medicare reimbursement practice in behavioral health specialties, which can be a significant barrier to accessing care.[80] Services provided by clinicians who do not participate in Medicare often involve higher patient cost-sharing compared to participating providers, which can be a considerable financial barrier. Additionally, fewer provider options may lead to delays in scheduling.
        - Inadequate diversity among mental health professionals: In 2019, the American Psychological Association (APA) reported that about 83% of psychologists in the US are white and only 3% of psychologists are Black.[81] Additionally, only 5% of psychologists have disabilities, whereas one in four Americans has a disability.[82] Lack of provider diversity of all types (racial/ethnic, ability, sexual orientation and gender, etc.) may lead to hesitance within minority populations to seek care due to a lack of trust in the healthcare system and lack of culturally competent providers.[31]

- **Patient barriers**:
    - Patient awareness: Patients may not be aware of the risks of pharmacological treatment or the effectiveness of non-pharmacological options available for the treatment of insomnia.[52]
    - Patient preference: Less than half of people with mental health conditions seek treatment for their condition, which suggests high barriers to patient-driven care.[23] While research indicates patients may prefer psychotherapy as a treatment modality, they may be unable or unwilling to seek care for a variety of reasons: self or social stigma, lack of time, cost, or the degree of effort and commitment required.[52,83,84]

Our analysis of key dimensions of care shows that common treatment patterns continue to pose unnecessary risks to the health of Medicare beneficiaries with GAD and insomnia. Claims analyses provide real-world evidence about the evolution of care for mental health conditions over time and can influence future initiatives and policy changes that seek to improve the quality of care and overall health of beneficiaries. Analyses of mental health conditions beyond GAD and insomnia, as well as populations covered by other types of health benefits coverage (e.g., Medicare Advantage, commercial, Medicaid, etc.), are necessary to identify gaps in care across other segments of the population.

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Appendix A: Data Sources and Methodology

DATA SOURCES

Medicare 100% Research Identifiable Files

The Medicare 100% Research Identifiable Files (RIFs) contain all Medicare Parts A, B, and D paid claims for 100% of Medicare FFS beneficiaries. Information includes county of residence, diagnosis codes, procedure codes, MS-DRG codes, site-of-service information, beneficiary age, eligibility status, race, and an indicator for HMO enrollment. Due to Milliman's data use agreement with CMS, data corresponding to member counts less than or equal to 10 must be redacted. We use 2015-2020 claims data in this analysis.

DETAILED METHODOLOGY

Denominator population identification

We identify the denominator population as beneficiaries enrolled in Medicare Part A, B, and D for at least one month between January 2016 and December 2020. Beneficiaries must not have HMO enrollment for all months of eligibility. Members who are enrolled in hospice are excluded beginning in their first month of hospice enrollment through the remainder of their Medicare enrollment during the analysis period, regardless of whether their hospice enrollment continues for this full time period. These members are included during their Medicare-enrolled months prior to their initial hospice enrollment.

Condition population identification

GAD population identification

We identify members of the denominator population with GAD based on the presence of an ICD-10-CM diagnosis code for GAD (Appendix C1: Condition Diagnosis Codes) in any diagnosis code position on any claim.

- We assign beneficiaries to the GAD population in a given year if they have a diagnosis code for GAD during that year or the year prior. For example, if a beneficiary has a diagnosis code for GAD in 2016, they are included in the GAD population for 2016 and 2017.

Insomnia population identification

We identify members of the denominator population with insomnia based on the presence of an ICD-10-CM diagnosis code for insomnia (Appendix C1: Condition Diagnosis Codes) in any diagnosis code position on any claim OR a prescription fill for hypnotic z-drugs or hypnotic benzodiazepines.

- We assign beneficiaries to the insomnia population from the date of the first claim or prescription that qualifies them into the insomnia population through the following 90 days. At that point, they are removed from the insomnia population. If they have another claim or prescription with an insomnia diagnosis code, they are reassigned to the insomnia population. Each claim with an insomnia diagnosis code or relevant prescription fill assigns the beneficiary to the insomnia population for the following 90 days.

Identification of other medical conditions

We also identify GAD and insomnia patients with the following medical conditions: cancer; chronic pain; conditions associated with spasticity (amyotrophic lateral sclerosis, cerebral palsy, multiple sclerosis, paralysis, spinal cord injury, traumatic brain injury); dementia/cognitive impairment; depression; epilepsy; hypertension; cardiovascular disease; and type 2 diabetes mellitus (T2DM). We identify these other conditions for one of several reasons: the other condition is commonly comorbid with GAD or insomnia; the other condition may be treated with a drug in a drug group that may also be used to treat GAD or insomnia and the expected drug treatment pattern for the other condition may be different; or the presence of the other condition may affect the GAD or insomnia treatment pattern.

- We identify beneficiaries with medical conditions in the list above other than hypertension, cardiovascular disease, and T2DM, as beneficiaries with a diagnosis code on any claim in any diagnosis code position for the other medical condition (Appendix C2: Related Condition Codes available upon request). This diagnosis code may precede, be the same as, or follow the date of assignment of the member to the GAD or insomnia population.
    - We assign depression, dementia, and/or epilepsy, as applicable, from the date of the first claim that qualifies the beneficiary into the depression, dementia, or epilepsy population and maintain them in the respective subgroup for all remaining years of the analysis period, regardless of whether or not the beneficiary has subsequent claims with a diagnosis code for depression, dementia, or epilepsy.

- We assign cancer, and conditions associated with spasticity, as applicable, from the date of the first claim that qualifies the beneficiary into the cancer, or conditions associated with spasticity population through the following 90 days. At that point, they are removed from the cancer, and/or conditions associated with spasticity subgroup. If they have another claim with a diagnosis code for cancer, or conditions associated with spasticity, then they are reassigned to the respective subgroup. Each claim with a cancer, and/or conditions associated with spasticity diagnosis code assigns the beneficiary to the respective subgroup for the following 90 days.
- We assign chronic pain from the date of the first claim that qualifies the beneficiary into the chronic pain population through the following six months. At that point, they are removed from the chronic pain population. If they have another claim with a chronic pain diagnosis code, they are reassigned to the chronic pain population. Each claim with a chronic pain diagnosis code assigns the beneficiary to the chronic pain population for the following six months.

- We identify beneficiaries with hypertension as beneficiaries with at least one claim with a relevant MS-DRG or diagnosis code in any diagnosis code position for hypertension on at least two outpatient claims on different dates of service or at least one acute inpatient, non-acute inpatient, emergency department (ED), or observation claim. We assign hypertension from the date of the first claim that qualifies the beneficiary into the population and maintain them in the hypertension population for all remaining years of the analysis period, regardless of whether or not they have subsequent claims with a diagnosis code for hypertension.
- We identify beneficiaries with cardiovascular disease as beneficiaries with at least one claim with a relevant HCPCS code, ICD-10-PCS procedure code, or MS-DRG, or a cardiovascular disease diagnosis code in any diagnosis code position on at least two outpatient claims on different dates of service or at least one acute inpatient, non-acute inpatient, ED, or observation claim. We assign cardiovascular disease from the date of the first claim that qualifies the beneficiary into the population and maintain them in the population for all remaining years of the analysis period, regardless of whether or not they have subsequent claims with a diagnosis code or other code signaling cardiovascular disease.
- We identify beneficiaries with T2DM as beneficiaries in the total diabetes population who do not meet the criteria for the type 1 diabetes mellitus (T1DM) population. We assign T2DM from the first year the beneficiary qualifies into the population and maintain them in the population for all remaining years of the analysis period unless they are assigned to the T1DM population in the given year.
    - We assign the total diabetes population based on the reporting of a diabetes diagnosis code in any diagnosis code position on at least two outpatient, observation, ED, or non-acute inpatient claims on different dates of service or at least one acute inpatient claim. Beneficiaries who fill prescriptions for hypoglycemic/antihyperglycemics/insulin and have at least one outpatient, observation, ED, or non-acute inpatient claim with a diagnosis of diabetes in any diagnosis code position are also included in the total diabetes population.
    - We assign the T1DM population as beneficiaries in the total diabetes population who fill a prescription for insulin, do not fill a prescription for T2DM-specific antihyperglycemics, and have a majority of diabetes diagnosis codes reported as type 1.

Demographic characteristic classification

Age, race, and low-income status are defined as follows:

- **Age**: age is determined as of December 31st of each year. Beneficiaries who turn 65 during the study period are included in the under 65 cohort up to and including the year in which they turn 65 and in the 65+ cohort for all subsequent years.
- **Race**: a beneficiary's race is defined as their race identified by the Beneficiary Race Code field in December of each year. We group races other than non-Hispanic Black and non- Hispanic white into the single category "Other" because of small sample sizes and/or imprecision in the data field for these races. Races included in the "Other" category are as follows:
    - Asian, Asian American, or Pacific Islander
    - Hispanic

    - North American Native
    - Other
    - Unknown
- **Low-income status**: a beneficiary is considered low-income if they qualify for at least one month of the Medicare low-income subsidy (LIS) prescription drug program in the year.

Treatment identification

Drug group users

We identify prescription fills for seven prescription drug groups of interest (Appendix C3: Drug Groups) across the GAD and insomnia populations. To increase our confidence that a prescription fill is related to the individual's GAD or insomnia, we require that the beneficiary have a claim reporting a diagnosis code of GAD or insomnia, respectively, within the 30 days prior to or 30 days following the first fill of a drug group other than hypnotic benzodiazepines and hypnotic z-drugs during the years of the analysis. Once a beneficiary with GAD or insomnia has been identified as a drug group user, future prescription fills for drugs in the same drug group in the same or later years are attributed to GAD or insomnia treatment (the proximate diagnosis code requirement does not apply). The drug groups are:

- **GAD**: Non-hypnotic benzodiazepines, SSRIs/SNRIs, and other anxiety-related drugs.
- **Insomnia**: Hypnotic benzodiazepines, hypnotic z-drugs, other hypnotics, and other insomnia-related drugs.

Each drug group is comprised of multiple generic drugs. To the extent that beneficiaries are taking multiple drugs within a drug group, they count once in the group. For some drug-specific sections, we analyzed the subset of drugs with the same generic name.

A beneficiary is considered a user of a drug group in a given year if they have at least one days supply of a drug in that drug group in that year, where the first fill for the drug group in all years of the analysis for the beneficiary meets the associated diagnosis code requirement (if applicable to the drug group). We use the reported days supply on pharmacy claims. To calculate continuous treatment, we allow a gap of 20% of the days supply for the drug group prescription. For example, if a patient fills a 10-day prescription, a 2-day gap is permitted before the next prescription fill for a patient to have a continuous days supply.

New Drug Group Users

Beneficiaries with no days supply of any drug in a drug group for at least 60 days prior to a prescription fill for that drug group are considered new drug group users. Beneficiaries can exit and reenter the new user cohort if they had previously used the drug, have a period of at least 60 days with no days supply of a drug in the drug group, and then restart the drug. We identify the prescribing physician specialty for new drug group users' initial prescriptions by drug group as the Medicare RIF-assigned prescriber ID to the primary taxonomy code for the Part D prescriber. We then map this code to a provider specialty code and assign specialty codes to specialty groups for purposes of reporting (Appendix C4).

Outpatient psychotherapy identification

We identify beneficiaries with psychotherapy treatment as those with an outpatient psychotherapy encounter (Appendix C5: Psychotherapy). Psychotherapy encounters are classified by provider specialty (Appendix C5.1: Psychiatrist Specialty Codes and Appendix C5.2: Other Specific Provider Specialties for Psychotherapy Encounters). We are using psychotherapy encounters as a proxy for CBT (Appendix C5.3: Outpatient Psychotherapy HCPCS Codes), but it is possible that techniques other than CBT are used during the encounter. We believe we define outpatient psychotherapy to comprehensively reflect what is most likely to include CBT, given the limitations on claims data in estimating CBT-specific encounters due to the lack of specificity of psychotherapy modality-specific codes.

Dosing

We calculate the average daily dose for the drug(s) prescribed in the first prescription for a drug in a group as follows:

1. Identify the unit value (e.g., 5 milligrams) present in one unit of the prescription filled. Identify the quantity of the NDC dispensed (e.g., 90 tablets) and the days supply (e.g., 30 days).
2. Calculate the total amount of drug dispensed as the unit value multiplied by quantity dispensed.
3. Divide the total amount of drug dispensed by the days supply to determine the daily dose.

Appendix B: Additional Detail

GAD and insomnia prevalence and demographics – additional detail

Tables B1.1-B1.3 contain additional beneficiary counts and prevalence rates for the GAD and insomnia populations by race and income status.

TABLE B1.1: GAD AND INSOMNIA POPULATION COUNTS (PREVALENCE) IN 2016-2020 BY AGE GROUP AND RACE – ALL

	2016	2017	2018	2019	2020
All Medicare FFS	**24,627,921 (100.0%)**	**24,806,224 (100.0%)**	**24,808,526 (100.0%)**	**24,719,470 (100.0%)**	**24,101,127 (100.0%)**
GAD or Insomnia	**6,038,287 (24.5%)**	**6,322,658 (25.5%)**	**6,447,513 (26.0%)**	**6,448,438 (26.1%)**	**6,136,464 (25.5%)**
GAD	**5,517,406 (22.4%)**	**5,830,601 (23.5%)**	**5,999,579 (24.2%)**	**6,064,633 (24.5%)**	**5,843,806 (24.2%)**
Non-Hispanic Black	*462,149 (18.0%)*	*475,678 (18.9%)*	*472,549 (19.5%)*	*457,548 (19.8%)*	*415,559 (19.6%)*
Non-Hispanic White	*4,733,981 (23.7%)*	*5,005,218 (24.9%)*	*5,156,804 (25.6%)*	*5,223,005 (26.0%)*	*5,048,189 (25.6%)*
Other	*321,276 (15.5%)*	*349,705 (16.1%)*	*370,226 (16.5%)*	*384,080 (16.7%)*	*380,058 (16.7%)*
Insomnia	**2,029,788 (8.2%)**	**2,069,668 (8.3%)**	**2,078,535 (8.4%)**	**2,043,154 (8.3%)**	**1,894,197 (7.9%)**
Non-Hispanic Black	*163,772 (6.4%)*	*163,890 (6.5%)*	*158,731 (6.5%)*	*149,872 (6.5%)*	*132,947 (6.3%)*
Non-Hispanic White	*1,729,408 (8.7%)*	*1,764,156 (8.8%)*	*1,775,810 (8.8%)*	*1,751,107 (8.7%)*	*1,626,348 (8.3%)*
Other	*136,608 (6.6%)*	*141,622 (6.5%)*	*143,994 (6.4%)*	*142,175 (6.2%)*	*134,902 (5.9%)*
GAD and Insomnia	**1,508,907 (6.1%)**	**1,577,611 (6.4%)**	**1,630,601 (6.6%)**	**1,659,349 (6.7%)**	**1,601,539 (6.6%)**
Under 65	**4,784,725 (100.0%)**	**4,639,174 (100.0%)**	**4,437,853 (100.0%)**	**4,130,277 (100.0%)**	**3,709,428 (100.0%)**
GAD or Insomnia	**1,817,406 (38.0%)**	**1,819,868 (39.2%)**	**1,768,103 (39.8%)**	**1,654,512 (40.1%)**	**1,453,180 (39.2%)**
GAD	***1,698,706 (35.5%)***	***1,713,059 (36.9%)***	***1,676,010 (37.8%)***	***1,580,995 (38.3%)***	***1,399,463 (37.7%)***
Non-Hispanic Black	*244,458 (23.8%)*	*246,532 (25.0%)*	*240,541 (25.7%)*	*225,681 (26.2%)*	*197,048 (26.0%)*
Non-Hispanic White	*1,327,529 (40.4%)*	*1,333,069 (42.0%)*	*1,298,777 (43.0%)*	*1,218,754 (43.5%)*	*1,073,026 (42.8%)*
Other	126,719 (26.7%)	133,458 (27.8%)	136,692 (28.5%)	136,560 (29.1%)	129,389 (29.0%)
Insomnia	**631,085 (13.2%)**	**610,581 (13.2%)**	**576,097 (13.0%)**	**522,275 (12.6%)**	**445,037 (12.0%)**
Non-Hispanic Black	*94,445 (9.2%)*	*91,513 (9.3%)*	*85,564 (9.1%)*	*76,768 (8.9%)*	*64,778 (8.6%)*
Non-Hispanic White	*487,192 (14.8%)*	*469,630 (14.8%)*	*442,339 (14.6%)*	*400,080 (14.3%)*	*339,097 (13.5%)*
Other	*49,448 (10.4%)*	*49,438 (10.3%)*	*48,194 (10.1%)*	*45,427 (9.7%)*	*41,162 (9.2%)*
GAD and Insomnia	**512,385 (10.7%)**	**503,772 (10.9%)**	**484,004 (10.9%)**	**448,758 (10.9%)**	**391,320 (10.5%)**
65+	**19,843,196 (100.0%)**	**20,167,050 (100.0%)**	**20,370,673 (100.0%)**	**20,589,193 (100.0%)**	**20,391,699 (100.0%)**
GAD or Insomnia	**4,220,881 (21.3%)**	**4,502,790 (22.3%)**	**4,679,410 (23.0%)**	**4,793,926 (23.3%)**	**4,683,284 (23.0%)**
GAD	**3,818,700 (19.2%)**	**4,117,542 (20.4%)**	**4,323,569 (21.2%)**	**4,483,638 (21.8%)**	**4,444,343 (21.8%)**
Non-Hispanic Black	*217,691 (14.1%)*	*229,146 (15.0%)*	*232,008 (15.6%)*	*231,867 (16.0%)*	*218,511 (16.0%)*
Non-Hispanic White	*3,406,452 (20.4%)*	*3,672,149 (21.7%)*	*3,858,027 (22.5%)*	*4,004,251 (23.1%)*	*3,975,163 (23.1%)*
Other	*194,557 (12.2%)*	*216,247 (12.7%)*	*233,534 (13.2%)*	*247,520 (13.5%)*	*250,669 (13.7%)*
Insomnia	**1,398,703 (7.0%)**	**1,459,087 (7.2%)**	**1,502,438 (7.4%)**	**1,520,879 (7.4%)**	**1,449,160 (7.1%)**
Non-Hispanic Black	*69,327 (4.5%)*	*72,377 (4.7%)*	*73,167 (4.9%)*	*73,104 (5.0%)*	*68,169 (5.0%)*
Non-Hispanic White	*1,242,216 (7.4%)*	*1,294,526 (7.6%)*	*1,333,471 (7.8%)*	*1,351,027 (7.8%)*	*1,287,251 (7.5%)*
Other	*87,160 (5.5%)*	*92,184 (5.4%)*	*95,800 (5.4%)*	*96,748 (5.3%)*	*93,740 (5.1%)*
GAD and Insomnia	**996,522 (5.0%)**	**1,073,839 (5.3%)**	**1,146,597 (5.6%)**	**1,210,591 (5.9%)**	**1,210,219 (5.9%)**

TABLE B1.2: GAD AND INSOMNIA POPULATION COUNTS (PREVALENCE) IN 2016-2020 BY AGE GROUP AND RACE – NON-LOW-INCOME

	2016	2017	2018	2019	2020
All Medicare FFS	**15,926,298 (100.0%)**	**16,224,220 (100.0%)**	**16,448,965 (100.0%)**	**16,760,266 (100.0%)**	**16,824,376 (100.0%)**
GAD or Insomnia	**3,216,122 (20.2%)**	**3,453,329 (21.3%)**	**3,616,327 (22.0%)**	**3,741,883 (22.3%)**	**3,705,074 (22.0%)**
GAD	**2,880,460 (18.1%)**	**3,136,599 (19.3%)**	**3,327,746 (20.2%)**	**3,493,435 (20.8%)**	**3,515,257 (20.9%)**
Non-Hispanic Black	*100,889 (11.8%)*	*105,268 (12.7%)*	*105,614 (13.2%)*	*107,648 (13.6%)*	*104,889 (13.6%)*
Non-Hispanic White	*2,694,939 (18.8%)*	*2,931,315 (20.1%)*	*3,108,213 (21.0%)*	*3,259,404 (21.7%)*	*3,276,930 (21.7%)*
Other	*84,632 (11.6%)*	*100,016 (12.4%)*	*113,919 (13.1%)*	*126,383 (13.5%)*	*133,438 (13.6%)*
Insomnia	**1,081,051 (6.8%)**	**1,124,092 (6.9%)**	**1,157,029 (7.0%)**	**1,171,912 (7.0%)**	**1,118,939 (6.7%)**
Non-Hispanic Black	*33,507 (3.9%)*	*33,490 (4.0%)*	*32,829 (4.1%)*	*32,338 (4.1%)*	*30,457 (4.0%)*
Non-Hispanic White	*1,012,199 (7.1%)*	*1,051,229 (7.2%)*	*1,081,467 (7.3%)*	*1,094,718 (7.3%)*	*1,043,569 (6.9%)*
Other	*35,345 (4.8%)*	*39,373 (4.9%)*	*42,733 (4.9%)*	*44,856 (4.8%)*	*44,913 (4.6%)*
GAD and Insomnia	**745,389 (4.7%)**	**807,362 (5.0%)**	**868,448 (5.3%)**	**923,464 (5.5%)**	**929,122 (5.5%)**
Under 65	**772,769 (100.0%)**	**728,237 (100.0%)**	**679,487 (100.0%)**	**633,840 (100.0%)**	**584,864 (100.0%)**
GAD or Insomnia	**273,193 (35.4%)**	**270,451 (37.1%)**	**260,814 (38.4%)**	**245,762 (38.8%)**	**221,643 (37.9%)**
GAD	**250,286 (32.4%)**	**250,220 (34.4%)**	**244,116 (35.9%)**	**232,707 (36.7%)**	**212,525 (36.3%)**

Non-Hispanic Black	*20,054 (19.0%)*	*18,885 (20.0%)*	*17,537 (20.8%)*	*16,647 (21.4%)*	*15,545 (21.3%)*
Non-Hispanic White	*219,034 (35.3%)*	*219,643 (37.4%)*	*214,679 (39.1%)*	*204,100 (40.0%)*	*185,239 (39.7%)*
Other	*11,198 (23.9%)*	*11,692 (25.0%)*	*11,900 (25.9%)*	*11,960 (26.2%)*	*11,741 (25.7%)*
Insomnia	**101,620 (13.2%)**	**97,237 (13.4%)**	**91,114 (13.4%)**	**83,090 (13.1%)**	**71,889 (12.3%)**
Non-Hispanic Black	*7,903 (7.5%)*	*7,145 (7.6%)*	*6,420 (7.6%)*	*5,785 (7.5%)*	*5,121 (7.0%)*
Non-Hispanic White	*89,167 (14.4%)*	*85,608 (14.6%)*	*80,292 (14.6%)*	*73,166 (14.3%)*	*62,855 (13.5%)*
Other	*4,550 (9.7%)*	*4,484 (9.6%)*	*4,402 (9.6%)*	*4,139 (9.1%)*	*3,913 (8.6%)*
GAD and Insomnia	**78,713 (10.2%)**	**77,006 (10.6%)**	**74,416 (11.0%)**	**70,035 (11.0%)**	**62,771 (10.7%)**
65+	**15,153,529 (100.0%)**	**15,495,983 (100.0%)**	**15,769,478 (100.0%)**	**16,126,426 (100.0%)**	**16,239,512 (100.0%)**
GAD or Insomnia	**2,942,929 (19.4%)**	**3,182,878 (20.5%)**	**3,355,513 (21.3%)**	**3,496,121 (21.7%)**	**3,483,431 (21.5%)**
GAD	**2,630,174 (17.4%)**	**2,886,379 (18.6%)**	**3,083,630 (19.6%)**	**3,260,728 (20.2%)**	**3,302,732 (20.3%)**
Non-Hispanic Black	*80,835 (10.8%)*	*86,383 (11.7%)*	*88,077 (12.3%)*	*91,001 (12.8%)*	*89,344 (12.8%)*
Non-Hispanic White	*2,475,905 (18.0%)*	*2,711,672 (19.4%)*	*2,893,534 (20.3%)*	*3,055,304 (21.0%)*	*3,091,691 (21.2%)*
Other	*73,434 (10.7%)*	*88,324 (11.6%)*	*102,019 (12.3%)*	*114,423 (12.9%)*	*121,697 (13.0%)*
Insomnia	**979,431 (6.5%)**	**1,026,855 (6.6%)**	**1,065,915 (6.8%)**	**1,088,822 (6.8%)**	**1,047,050 (6.4%)**
Non-Hispanic Black	*25,604 (3.4%)*	*26,345 (3.6%)*	*26,409 (3.7%)*	*26,553 (3.7%)*	*25,336 (3.6%)*
Non-Hispanic White	*923,032 (6.7%)*	*965,621 (6.9%)*	*1,001,175 (7.0%)*	*1,021,552 (7.0%)*	*980,714 (6.7%)*
Other	*30,795 (4.5%)*	*34,889 (4.6%)*	*38,331 (4.6%)*	*40,717 (4.6%)*	*41,000 (4.4%)*
GAD and Insomnia	**666,676 (4.4%)**	**730,356 (4.7%)**	**794,032 (5.0%)**	**853,429 (5.3%)**	**866,351 (5.3%)**

TABLE B1.3: GAD AND INSOMNIA POPULATION COUNTS (PREVALENCE) IN 2016-2020 BY AGE GROUP AND RACE – LOW-INCOME

	2016	2017	2018	2019	2020
All Medicare FFS	***8,701,623 (100.0%)***	***8,582,004 (100.0%)***	***8,359,561 (100.0%)***	***7,959,204 (100.0%)***	***7,276,751 (100.0%)***
GAD or Insomnia	**2,822,165 (32.4%)**	**2,869,329 (33.4%)**	**2,831,186 (33.9%)**	**2,706,555 (34.0%)**	**2,431,390 (33.4%)**
GAD	**2,636,946 (30.3%)**	**2,694,002 (31.4%)**	**2,671,833 (32.0%)**	**2,571,198 (32.3%)**	**2,328,549 (32.0%)**
Non-Hispanic Black	361,260 (21.0%)	370,410 (22.1%)	366,935 (22.6%)	349,900 (23.0%)	310,670 (22.9%)
Non-Hispanic White	2,039,042 (36.1%)	2,073,903 (37.5%)	2,048,591 (38.2%)	1,963,601 (38.7%)	1,771,259 (38.3%)
Other	236,644 (17.7%)	249,689 (18.3%)	256,307 (18.6%)	257,697 (18.9%)	246,620 (19.0%)
Insomnia	**948,737 (10.9%)**	**945,576 (11.0%)**	**921,506 (11.0%)**	**871,242 (10.9%)**	**775,258 (10.7%)**
Non-Hispanic Black	130,265 (7.6%)	130,400 (7.8%)	125,902 (7.8%)	117,534 (7.7%)	102,490 (7.6%)
Non-Hispanic White	717,209 (12.7%)	712,927 (12.9%)	694,343 (13.0%)	656,389 (12.9%)	582,779 (12.6%)
Other	101,263 (7.6%)	102,249 (7.5%)	101,261 (7.4%)	97,319 (7.1%)	89,989 (6.9%)
GAD and Insomnia	**763,518 (8.8%)**	**770,249 (9.0%)**	**762,153 (9.1%)**	**735,885 (9.2%)**	**672,417 (9.2%)**
Under 65	***4,011,956 (100.0%)***	***3,910,937 (100.0%)***	***3,758,366 (100.0%)***	***3,496,437 (100.0%)***	***3,124,564 (100.0%)***
GAD or Insomnia	**1,544,213 (38.5%)**	**1,549,417 (39.6%)**	**1,507,289 (40.1%)**	**1,408,750 (40.3%)**	**1,231,537 (39.4%)**
GAD	**1,448,420 (36.1%)**	**1,462,839 (37.4%)**	**1,431,894 (38.1%)**	**1,348,288 (38.6%)**	**1,186,938 (38.0%)**
Non-Hispanic Black	224,404 (24.4%)	227,647 (25.5%)	223,004 (26.1%)	209,034 (26.7%)	181,503 (26.5%)
Non-Hispanic White	1,108,495 (41.6%)	1,113,426 (43.1%)	1,084,098 (43.9%)	1,014,654 (44.3%)	887,787 (43.5%)
Other	115,521 (27.0%)	121,766 (28.1%)	124,792 (28.8%)	124,600 (29.5%)	117,648 (29.3%)
Insomnia	**529,465 (13.2%)**	**513,344 (13.1%)**	**484,983 (12.9%)**	**439,185 (12.6%)**	**373,148 (11.9%)**
Non-Hispanic Black	86,542 (9.4%)	84,368 (9.5%)	79,144 (9.3%)	70,983 (9.1%)	59,657 (8.7%)
Non-Hispanic White	398,025 (14.9%)	384,022 (14.9%)	362,047 (14.6%)	326,914 (14.3%)	276,242 (13.5%)
Other	44,898 (10.5%)	44,954 (10.4%)	43,792 (10.1%)	41,288 (9.8%)	37,249 (9.3%)
GAD and Insomnia	**433,672 (10.8%)**	**426,766 (10.9%)**	**409,588 (10.9%)**	**378,723 (10.8%)**	**328,549 (10.5%)**
65+	***4,689,667 (100.0%)***	***4,671,067 (100.0%)***	***4,601,195 (100.0%)***	***4,462,767 (100.0%)***	***4,152,187 (100.0%)***
GAD or Insomnia	**1,277,952 (27.3%)**	**1,319,912 (28.3%)**	**1,323,897 (28.8%)**	**1,297,805 (29.1%)**	**1,199,853 (28.9%)**
GAD	**1,188,526 (25.3%)**	**1,231,163 (26.4%)**	**1,239,939 (26.9%)**	**1,222,910 (27.4%)**	**1,141,611 (27.5%)**
Non-Hispanic Black	136,856 (17.2%)	142,763 (18.2%)	143,931 (18.7%)	140,866 (19.1%)	129,167 (19.3%)
Non-Hispanic White	930,547 (31.2%)	960,477 (32.6%)	964,493 (33.4%)	948,947 (34.1%)	883,472 (34.1%)
Other	121,123 (13.3%)	127,923 (13.7%)	131,515 (14.0%)	133,097 (14.2%)	128,972 (14.4%)
Insomnia	**419,272 (8.9%)**	**432,232 (9.3%)**	**436,523 (9.5%)**	**432,057 (9.7%)**	**402,110 (9.7%)**
Non-Hispanic Black	43,723 (5.5%)	46,032 (5.9%)	46,758 (6.1%)	46,551 (6.3%)	42,833 (6.4%)
Non-Hispanic White	319,184 (10.7%)	328,905 (11.1%)	332,296 (11.5%)	329,475 (11.8%)	306,537 (11.8%)
Other	56,365 (6.2%)	57,295 (6.1%)	57,469 (6.1%)	56,031 (6.0%)	52,740 (5.9%)
GAD and Insomnia	**329,846 (7.0%)**	**343,483 (7.4%)**	**352,565 (7.7%)**	**357,162 (8.0%)**	**343,868 (8.3%)**

Co-occurring conditions – additional detail

For the GAD and insomnia populations, we report the co-occurrence of nine other medical conditions. We selected these other conditions for one of several reasons: the other condition is common in the 65+ Medicare FFS population; the other condition is commonly comorbid with GAD or insomnia; the other condition may be treated with a drug in a drug group that may also be used to treat GAD or insomnia and the expected drug treatment pattern for the other condition may differ from GAD or insomnia treatment; or the presence of the other condition may affect the GAD or insomnia drug treatment pattern.

These other conditions are more prevalent in the GAD and insomnia populations relative to all Medicare FFS beneficiaries. The 2020 percentages of beneficiaries with GAD and insomnia diagnosed with the other medical conditions are displayed below in Figures B1.1 and B1.2, respectively. Similar prevalence rates of co-occurring conditions are observed in all study years. The other medical conditions are more common among beneficiaries with insomnia compared to beneficiaries with GAD. In beneficiaries 65+ with GAD, rates of most co-occurring conditions are consistently higher in non-Hispanic Black beneficiaries compared to non-Hispanic white beneficiaries (dementia: 38.2% vs. 26.8%; T2DM: 49.6% vs. 27.0%; cardiovascular disease: 63.4% vs. 49.1%; chronic pain: 85.1% vs. 80.6%; epilepsy: 16.0% vs 7.7%; conditions associated with spasticity: 13.6% vs. 6.4%; hypertension: 94.6% vs. 81.1%). The same general pattern is observed for the 65+ insomnia population (dementia: 43.9% vs. 30.4%; T2DM: 51.0% vs. 27.4%; cardiovascular disease: 67.1% vs. 52.6%; chronic pain: 88.7% vs. 85.8%; epilepsy: 18.2% vs 8.9%; conditions associated with spasticity: 15.7% vs. 7.6%; hypertension: 95.2% vs. 82.0%).

FIGURE B1.1: PERCENT OF GAD POPULATION WITH CO-OCCURRING CONDITIONS – 2020

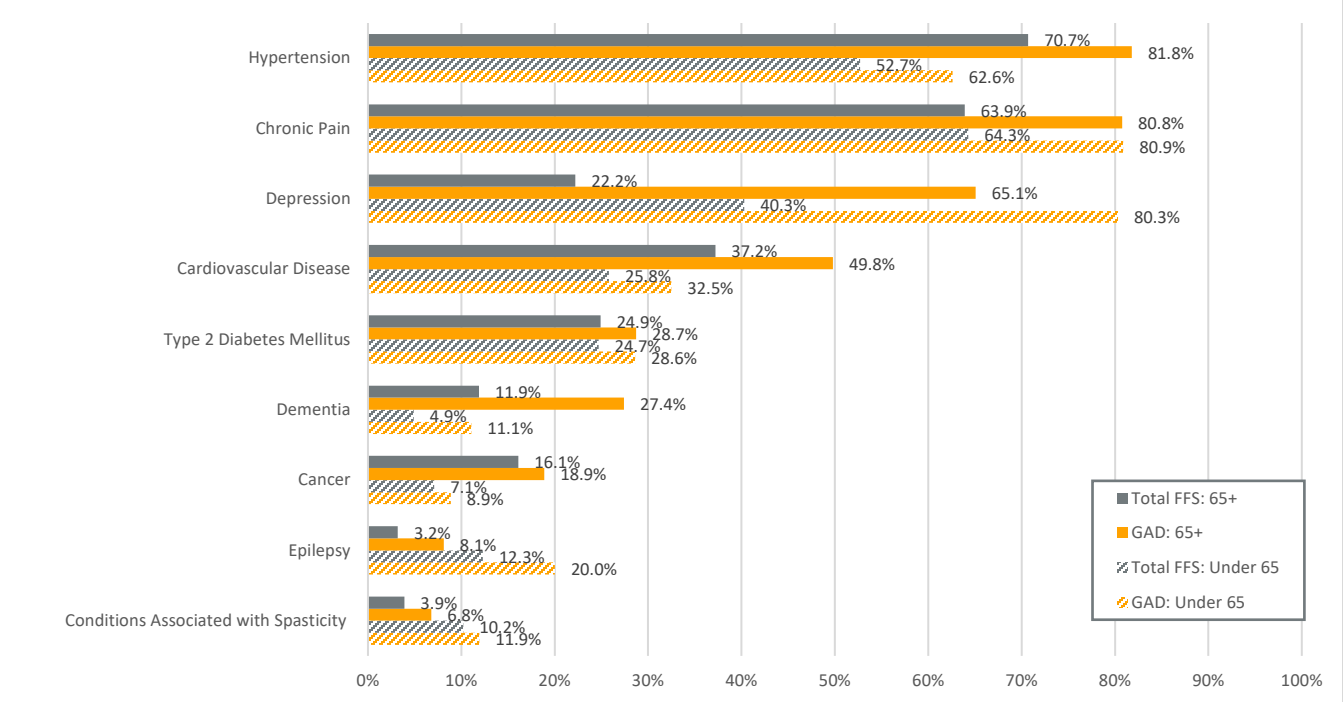
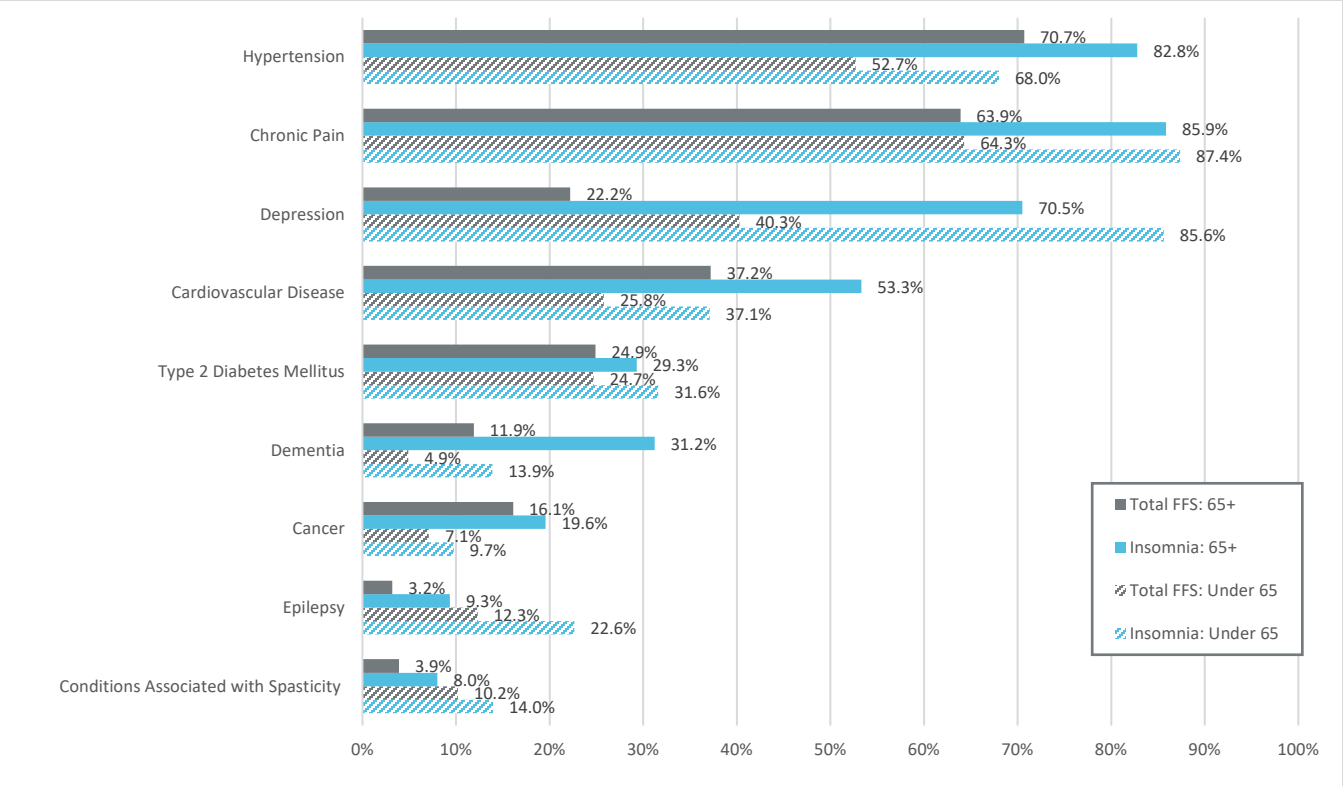


FIGURE B1.2: PERCENT OF INSOMNIA POPULATION WITH CO-OCCURRING CONDITIONS – 2020



Pharmacotherapy – additional detail

Table B2 displays the relevant demographic information for GAD and insomnia beneficiaries taking condition-specific drugs.

TABLE B2: DEMOGRAPHIC CHARACTERISTICS OF DRUG GROUP USERS WITH GAD AND INSOMNIA IN 2019 AND 2020

		GAD			Insomnia			
Demographics as of latest enrollment month the year	**Medicare FFS Denominator Population**	**Non-Hypnotic Benzodiazepines**	**SSRIs/ SNRIs**	**Other Anxiety-Related Drugs**	**Hypnotic Benzodiazepines**	**Hypnotic Z-Drugs**	**Other Hypnotics**	**Other Insomnia-Related Drugs**
2019								
Member Count	*24,719,470*	965,790	1,377,551	436,726	244,637	970,390	70,673	925,264
% of Condition	-	16%	23%	7%	12%	47%	3%	45%
% Female	*57%*	70%	70%	70%	61%	61%	64%	63%
Average Age	*70.8*	66.7	66.6	63.1	70.8	68.2	65.5	68.1
% Under 65	*17%*	31%	31%	44%	19%	22%	37%	28%
% 65+	*83%*	69%	69%	56%	81%	78%	63%	72%
% Low-income	*32%*	45%	44%	59%	33%	30%	52%	43%
2020								
Member Count	*24,101,127*	898,247	1,350,431	457,589	207,391	909,576	67,974	909,621
% of Condition	-	15%	22%	8%	10%	45%	3%	45%
% Female	*57%*	69%	69%	70%	60%	61%	63%	62%
Average Age	*71.1*	67.0	66.7	63.4	71.0	68.7	66.0	68.3
% Under 65	*15%*	29%	28%	42%	18%	20%	34%	25%
% 65+	*85%*	71%	72%	58%	82%	80%	66%	75%
% Low-income	*30%*	42%	41%	56%	30%	26%	49%	40%

Outpatient Psychotherapy as a proxy for CBT – additional detail

Table B3 displays the distribution of psychotherapy provider specialties for beneficiaries who have an outpatient psychotherapy encounter prior to initial drug treatment. The provider specialties in the 'Other' group are addiction medicine providers, opioid treatment programs, psychiatric/mental health facilities, and alcohol/drug abuse treatment facilities.

TABLE B3: DISTRIBUTION OF OUTPATIENT PSYCHOTHERAPY PROVIDER SPECIALTIES IN 30 DAYS PRIOR TO FIRST PRESCRIPTION FILL – 2019 AND 2020

Provider Specialty Distribution for OP Psychotherapy Encounters in 30 days Prior to First Rx Fill

	GAD				Insomnia			
	2019		2020		2019		2020	
Provider Specialty	Under 65	65+	Under 65	65+	Under 65	65+	Under 65	65+
Psychologist	20%	33%	19%	33%	20%	32%	20%	32%
Psychiatrist	23%	25%	22%	25%	27%	30%	26%	29%
Licensed Clinical Social Worker	36%	32%	38%	33%	34%	29%	35%	30%
Other	35%	20%	34%	20%	34%	20%	33%	19%

Drug use duration – additional detail for beneficiaries with co-occurring conditions

For beneficiaries 65+ with GAD and co-occurring dementia, prolonged use of non-hypnotic benzodiazepines for 31+ days is more common than in those without dementia (in 2020: 67% compared to 59%). The difference in prolonged use for beneficiaries with insomnia with dementia and without dementia is small (in 2020: 74% versus 74% for users of hypnotic benzodiazepines and 76% versus 74% for users of hypnotic z-drugs). The rate of prolonged non-hypnotic benzodiazepine use in beneficiaries with GAD under 65 is the same for populations with and without co-occurring conditions related to spasticity, even though these drugs may sometimes be used to treat spasticity on an ongoing basis. The rate of prolonged non-hypnotic benzodiazepine use in beneficiaries 65+ is slightly higher in those with conditions related to spasticity compared to those without (65% versus 61%). A similar pattern is observed by age group for the GAD population with and without epilepsy, where non-hypnotic benzodiazepines may be used as a long-term treatment for epilepsy. These findings demonstrate that the presence of co-occurring conditions does not account for the high rates of long-term use of those GAD and insomnia drugs that are recommended for short-term use.

Appendix C: Code Sets

APPENDIX C1: GAD AND INSOMNIA DIAGNOSIS CODES

ICD-10-CM Diagnosis Code	Description	Condition
F064	Anxiety disorder due to known physiological condition	GAD
F4000	Agoraphobia, unspecified	GAD
F4001	Agoraphobia with panic disorder	GAD
F4002	Agoraphobia without panic disorder	GAD
F4010	Social phobia, unspecified	GAD
F4011	Social phobia, generalized	GAD
F40240	Claustrophobia	GAD
F410	Panic disorder [episodic paroxysmal anxiety]	GAD
F411	Generalized anxiety disorder	GAD
F413	Other mixed anxiety disorders	GAD
F418	Other specified anxiety disorders	GAD
F419	Anxiety disorder, unspecified	GAD
F4322	Adjustment disorder with anxiety	GAD
F4323	Adjustment disorder with mixed anxiety and depressed mood	GAD
F5101	Primary insomnia	Insomnia
F5102	Adjustment insomnia	Insomnia
F5103	Paradoxical insomnia	Insomnia
F5104	Psychophysiologic insomnia	Insomnia
F5105	Insomnia due to other mental disorder	Insomnia
F5109	Other insomnia not due to a substance or known physiological condition	Insomnia
F5112	Insufficient sleep syndrome	Insomnia
G4700	Insomnia, unspecified	Insomnia
G4701	Insomnia due to medical condition	Insomnia
G4709	Other insomnia	Insomnia

APPENDIX C2: OTHER MEDICAL CONDITION DIAGNOSIS CODES

These code lists are available upon request.

APPENDIX C3: DRUG GROUPS

Appendix C3.1: Drug Group Generic Names

Non-Hypnotic Benzodiazepines	SSRIs/SNRIs	Other Anxiety-Related Drugs	Hypnotic Benzodiazepines	Hypnotic Z-Drugs	Other Hypnotics	Other Insomnia-Related Drugs
Alprazolam	Citalopram	Buspirone	Estazolam	Eszopiclone	Butobarbital	Amitriptyline
Chlordiazepoxide	Desvenlafaxine	Hydroxyzine	Flurazepam	Zaleplon	Doxepin	Gabapentin
Clonazepam	Duloxetine		Quazepam	Zolpidem	Lemborexant	Mirtazapine
Clorazepate	Escitalopram		Temazepam	Eszopiclone	Mephobarbital	Nortriptyline
Diazepam	Fluoxetine		Triazolam		Phenobarbital	Quetiapine
Lorazepam	Fluvoxamine				Ramelteon	Trazodone
Oxazepam	Levomilnacipran				Secobarbital	
	Paroxetine				Suvorexant	
	Sertraline				Tasimelteon	
	Venlafaxine					

Appendix C3.2: Drug Group NDCs

These code lists are available upon request.

APPENDIX C4: SPECIALTY CODE MAPPING TO SPECIALTY GROUP

Specialty Code	Specialty Code Description	Specialty Group
89	Certified clinical nurse specialist	Non-physician practitioner
42	Certified nurse midwife	Non-physician practitioner
50	Nurse practitioner	Non-physician practitioner
97	Physician assistant	Non-physician practitioner
08	Family practice	Primary Care Physician
11	Internal medicine	Primary Care Physician
86	Neuropsychiatry	Psychiatrist
26	Psychiatry	Psychiatrist
All Others	-	Other

Taxonomy code to specialty code mapping is available upon request.

APPENDIX C5: OUTPATIENT PSYCHOTHERAPY

Appendix C5.1: Psychiatrist Specialty Codes

Specialty Code	Description
26	Psychiatry
27	Geriatric psychiatry
86	Neuropsychiatry

Appendix C5.2: Other Outpatient Psychotherapy Provider Specialties

Specialty Code	Description	Specialty Group
62	Psychologist (billing independently)	Psychologist
68	Clinical psychologist	Psychologist
79	Addiction medicine	Other
80	Licensed clinical social worker	Other
D5	Opioid Treatment Program	Other
Y2	Psych/Mental Health Facility	Other
Y4	Alcohol/Drug Abuse Treatment Facility	Other

Appendix C5.3: Outpatient Psychotherapy HCPCS Codes

HCPCS Code
90832-90834
90836-90840
90849
90853
90875-90876
G0469-G0470

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