DEPARTMENT OF VETERANS AFFAIRS

OFFICE OF INSPECTOR GENERAL

Office of Healthcare Inspections

VETERANS HEALTH ADMINISTRATION

Drug Interactions Related to a Patient Death, Marion VA Medical Center in Illinois

HEALTHCARE INSPECTION | REPORT #20-03380-136 | MAY 20, 2021

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Executive Summary

Underlined terms are hyperlinks to a glossary.

The VA Office of Inspector General (OIG) conducted a healthcare inspection at the Marion VA Medical Center (facility) in Illinois, to assess an allegation that a patient died due to complications from high cholesterol. During the inspection, the OIG also reviewed the care provided by the primary care and behavioral health care staff and the facility's implementation of the fourth phase of a quality improvement program designed to improve the use of certain medications, the Psychotropic Drug Safety Initiative. Although the OIG identified some missed opportunities by providers, the OIG determined that the patient received adequate quality of care from the facility.

The patient was in their 30s with a history of hypothyroidism caused by Hashimoto's disease, tobacco use, and elevated cholesterol levels. The patient had multiple behavioral health diagnoses, including posttraumatic stress disorder (PTSD), major depressive disorder (depression), generalized anxiety disorder (anxiety), and cannabis use disorder. The patient received care at the facility for several years prior to their death at home in spring 2019. Facility providers prescribed various medications over the years to treat the patient's chronic illnesses, including thyroid replacement therapy, cholesterol-lowering agents, and antianxiety medications.

The OIG substantiated that high cholesterol contributed to the patient's death; however, the death certificate stated that the patient's primary cause of death was accidental acute multi-drug intoxication. Hypertensive cardiovascular disease and obesity were listed on the patient's death certificate as significant conditions contributing to the patient's death. The OIG determined that the patient's primary care provider addressed and monitored the patient's high cholesterol levels, blood pressure, and obesity recommending medication and lifestyle changes.

The OIG also found that during outpatient psychiatry appointments, the psychiatrist documented discussion about possible side effects and adverse drug-drug interactions. However, when medication changes occurred over the telephone, the OIG found no documented evidence that the psychiatrist or the behavioral health nurse discussed possible side effects or adverse drug-drug interactions.[1] The OIG concluded that the patient's prescribed medications, non-prescribed medications, and cannabis use created adverse drug-drug interaction that caused the patient's death.

The psychiatrist prescribed long-term benzodiazepine use for the patient, who had been diagnosed with PTSD. Both practices are contrary to clinical guidance.[2] In addition, the OIG

[1] VHA Directive 2011-012, *Medication Reconciliation*, March 9, 2011.

[2] VA/DoD *Clinical Practice Guidelines for the Management of Posttraumatic Stress Disorder and Acute Stress Disorder*, version 3.0, 2017.

noted that the psychiatrist failed to address the patient's report of improved concentration with the use of amphetamine/dextroamphetamine when two urine drug-screen results were negative for the medication. The OIG found that the patient's psychiatrist documented that the patient tested negative for amphetamine/dextroamphetamine; however, the OIG found no documented evidence that the psychiatrist communicated the negative urine drug screens to the patient or discussed that the patient appeared to not be taking the prescribed medication.

The patient's psychiatrist also failed to address a positive urine drug screen for cannabis as required by a Veterans Health Administration directive.[3] The patient's cannabis use may have contributed to the patient's anxiety, but the OIG found no documented evidence that the psychiatrist made or addressed this correlation with the patient.

In preparation for the launch of the Psychotropic Drug Safety Initiative Phase Four in March 2019, the facility selected to prioritize (1) reducing the use of benzodiazepine in patients diagnosed with PTSD, and (2) ensuring that Prescription Drug Monitoring Program checks were conducted on those patients prescribed benzodiazepines.[4] The facility developed a plan, but stated it was unable to implement it due to COVID-19. Although not implemented, the OIG noted that the facility's Phase Four metrics were trending in the right direction.

The OIG found that the patient's primary care provider did not comply with facility policy by failing to enter a return-to-clinic order following a June 2018 appointment.[5] Although primary care saw the patient twice in February 2019, both visits were unscheduled walk-in appointments. The OIG could not determine how the lack of future appointments may have affected the patient and the care and monitoring of their cholesterol level and weight.

The OIG determined that primary care staff did not comply with facility policy to telephone the patient, or if unable to reach the patient send a letter, after the patient missed appointments.[6] The

[3] VHA Directive 1088, *Communicating Test Results to Providers and Patients*, October 7, 2015.

[4] In 2013, VHA introduced the Psychotropic Drug Safety Initiative as a quality improvement strategy, focusing on improving the use of psychotropic medications to treat patients with mental health diagnoses. Phase Four focused on reducing benzodiazepine use in high-risk patients and improving psychopharmacological care in patients with substance use disorders.

[5] Facility Memorandum 11-11 GPM-16-552, *Clinic Scheduling, No-Shows and Cancellations,* November 8, 2016. This memorandum was in effect at the time of the events discussed in this report until it was rescinded and replaced by Facility Memorandum, 11-11 GPM-19-552, *Clinic Scheduling, No-Shows and Cancellations,* December 1, 2019. The revised policy states the clinic provider will enter a return-to-clinic order in the computerized patient record system (CPRS) orders tab before the patient leaves the treating provider.

[6] Facility Memorandum 11-11 GPM-16-552, *Clinic Scheduling, No-Shows and Cancellations,* November 8, 2016. This memorandum was in effect at the time of the events discussed in this report until it was rescinded and replaced by Facility Memorandum, 11-11 GPM-19-552, *Clinic Scheduling, No-Shows and Cancellations,* December 1, 2019. The revised policy states that established patients who miss an appointment must be contacted to determine if the appointment should be rescheduled. If unable to contact patient after two attempts, behavioral health requires three attempts, an *unable to contact* letter will be sent to request patient to contact clinic. An Administrative Contact Note will be documented in the patient's electronic health record.

patient's behavioral health team complied with calling the patient after the patient did not come or call to cancel appointments; however, when unable to reach the patient, the behavioral health team did not send a letter as required by policy.

The OIG made five recommendations to the Facility Director related to ensuring behavioral health staff provide and document patient education regarding possible side effects of medications and adverse drug-drug interactions; timely communicating test results to promote necessary clinical interventions; monitoring implementation of Phase Four of the Psychotropic Drug Safety Initiative; ensuring primary care staff comply with entering return-to-clinic orders; and ensuring primary care and behavioral health staff document contacts, attempted contacts, and letters sent when a patient misses an appointment.

Comments

The Veterans Integrated Service Network and System Directors concurred with the findings and recommendations and provided acceptable action plans (see appendixes A and B). The OIG will follow up on the planned actions until they are completed.

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Contents

Abbreviations

ADHD	attention-deficit/hyperactivity disorder
BMI	body mass index
DoD	Department of Defense
EHR	electronic health record
OIG	Office of Inspector General
PTSD	posttraumatic stress disorder
VHA	Veterans Health Administration
VISN	Veterans Integrated Service Network

Introduction

Underlined terms are hyperlinks to a glossary.

The VA Office of Inspector General (OIG) conducted a healthcare inspection to assess the allegation that a patient who received care at the Marion VA Medical Center (facility) in Illinois died due to complication from high cholesterol. The OIG identified additional concerns related to primary care and behavioral health care.

Background

The facility is part of Veterans Integrated Service Network (VISN) 15 and provides comprehensive health care through primary and specialty care, general medicine, surgery, and behavioral health. The facility offers residential rehabilitation treatment programs for patients with posttraumatic stress disorder (PTSD) and substance use disorders. From October 1, 2019, through September 30, 2020, the facility served 41,917 patients and had a total of 122 hospital operating beds, including 48 inpatient beds, 20 domiciliary beds, and 54 Community Living Center beds. The facility consists of the medical center, residential rehabilitation treatment program, the Community Living Center, and the Evansville Healthcare Center in Evansville, Indiana. In addition, the facility operates 10 community-based outpatient clinics located in Illinois, Indiana, and Kentucky.[1] The community-based outpatient clinics offer primary care and behavioral health services.

Allegations and Related Concerns

On May 22, 2020, the OIG received an allegation and subsequently identified concerns related to the patient's death:

1. Allegation: Complication of high cholesterol contributed to a patient's death
2. Concern: Medication Management by Psychiatrist
3. Concern: Incomplete implementation of the Psychotropic Drug Safety Initiative
4. Concern: Deficiencies in compliance with facility policy

Scope and Methodology

The OIG initiated the healthcare inspection on July 1, 2020, and conducted a virtual site visit August 17–25, 2020.

[1] The ten outpatient clinics are located in Carbondale, Illinois; Effingham, Illinois; Harrisburg, Illinois; Marion, Illinois; Mt Vernon, Illinois; Vincennes, Indiana; Madisonville, Kentucky; Mayfield, Kentucky; Owensboro, Kentucky; and Paducah, Kentucky.

The OIG team interviewed the complainant; the Facility Director; Chiefs of Staff, Primary Care, Behavioral Health, and Pharmacy; Quality Management and Pharmacy staff; facility nursing staff; and the patient's primary care provider, psychiatrist, and psychologist.

The OIG team reviewed the patient's electronic health record (EHR) as well as the care provided by Primary Care from early 2016 through spring 2019, and the care provided by behavioral health from early 2017 through spring 2019. The OIG team also reviewed relevant VA/Department of Defense (DoD) clinical guidelines, Veterans Health Administration (VHA) and facility policies related to primary care, behavioral health, pharmacy, and laboratory test results, and Behavioral Medicine Quality Assurance Committee (Committee) meeting minutes.

In the absence of current VA or VHA policy, the OIG considered previous guidance to be in effect until superseded by an updated or recertified directive, handbook, or other policy document on the same or similar issue(s).

The OIG substantiates an allegation when the available evidence indicates that the alleged event or action more likely than not took place. The OIG does not substantiate an allegation when the available evidence indicates that the alleged event or action more likely than not did not take place. The OIG is unable to determine whether an alleged event or action took place when there is insufficient evidence.

Oversight authority to review the programs and operations of VA medical facilities is authorized by the Inspector General Act of 1978, Pub. L. No. 95-452, 92 Stat 1105, as amended (codified at 5 U.S.C. App. 3). The OIG reviews available evidence to determine whether reported concerns or allegations are valid within a specified scope and methodology of a healthcare inspection and, if so, to make recommendations to VA leaders on patient care issues. Findings and recommendations do not define a standard of care or establish legal liability.

The OIG conducted the inspection in accordance with *Quality Standards for Inspection and Evaluation* published by the Council of the Inspectors General on Integrity and Efficiency.

Patient Case Summary

The patient, in their 30s, was followed by their primary care provider for multiple medical problems, including hypothyroidism caused by Hashimoto's disease, tobacco use, and elevated cholesterol levels. The patient was also under the care of clinical psychologists and a psychiatrist for multiple behavioral health disorders including PTSD, major depressive disorder (depression), generalized anxiety disorder (anxiety), and cannabis use disorder.

In spring 2016, the patient requested an endocrinology consult for further evaluation of their Hashimoto's disease. The primary care provider ordered thyroid laboratory tests, renewed the levothyroxine, and updated the patient's non-VA endocrinology consult request. Because the non-VA endocrinologist no longer accepted the patient's insurance, the primary care provider entered a VA endocrinology consult one month after the patient requested the consult.

Twelve days after the primary care provider entered the consult, the patient saw the endocrinologist for Hashimoto's disease. The endocrinologist ordered repeat laboratory tests and referred the patient back to primary care.

Approximately five weeks later, the patient saw the primary care provider for follow-up of their Hashimoto's disease consult. The patient's thyroid stimulating hormone laboratory result was within normal range.[2] The patient's primary care provider recommended the patient follow a low cholesterol diet and begin exercise. A dietician consult was entered; however, the patient declined meeting with the dietician when scheduling was attempted. The primary care provider ordered a cholesterol-lowering medication, atorvastatin, noting that the patient's previous cholesterol-lowering medication, rosuvastatin, was non-formulary. A smoking cessation referral was offered, but the patient declined. Because of the patient's complaint of snoring, the primary care provider ordered a sleep study, but the patient did not reply to repeated attempts to schedule an appointment.

Approximately three weeks later, the primary care clinic nurse notified the patient that the primary care provider recommended a decrease in the patient's atorvastatin due to an abnormal laboratory test.[3] The patient was instructed to contact the clinic if muscle pain developed. Four months later, the patient's atorvastatin was last filled.

The patient's fall 2016 laboratory tests results showed that the patient's cholesterol level was elevated at 251, and creatinine phosphokinase was elevated at 252.

In fall 2016, the patient saw the psychiatrist for medication management and supportive psychotherapy. The patient reported decreased irritability, improved depression and mood, and improved sleep on their current medications of diazepam, trazodone, venlafaxine, and zolpidem, but noted residual PTSD and panic symptoms. The patient reported a history since adolescence of difficulty with attention, focus, and completing tasks, although the patient was never diagnosed with or treated for attention-deficit/hyperactivity disorder (ADHD). The psychiatrist added a new medication, amphetamine/dextroamphetamine, for ADHD noting that the potential side effects were discussed, and the patient gave informed consent for the treatment with the medications.

Sixteen days later, the patient saw the psychologist for supportive psychotherapy to deal with issues related to PTSD and depression. The patient reported doing better because of the recent medication change and "coming out of a fog."

Approximately 10 weeks later (early 2017), the psychiatrist saw the patient for medication management and supportive psychotherapy. The patient complained of some depression, increased stress, PTSD symptoms, and panic symptoms. The patient noted the

[2] The patient's thyroid stimulating hormone level was 3.53 and a normal range is between 0.47 and 5.00.
[3] On August 16, the patient's creatinine phosphokinase was 225. A normal range is between 20 and 200.

amphetamine/dextroamphetamine helped with the ability to focus and stay on task, but there was continued distraction. The psychiatrist increased the dose of the amphetamine/dextroamphetamine to 15 milligrams (mg) three times a day. The psychiatrist noted the patient's occasional cannabis use and documented "encouraged continued abstinence from alcohol and/or drug use."

The following day, the primary care provider met with the patient and noted that the patient was in good spirits and had no complaints of chest pain or shortness of breath. With a weight of 222 pounds, the patient was advised to follow a low cholesterol diet, exercise, quit smoking, and follow up with the endocrinologist for Hashimoto's disease. Additional laboratory studies were ordered. The primary care clinic nurse contacted the patient four days later with the laboratory results and instructed the patient to take vitamin D because of low levels.

Eighteen days later, the behavioral health nurse called the patient for a condition report. The patient reported no side effects from the increased amphetamine/dextroamphetamine dose and was able to focus. The patient reported satisfaction with the medications.

Seventeen days later, the patient was seen by the behavioral health nurse for an unscheduled medication check and symptom and medication monitoring visit. The patient complained of a three-day history of violent nightmares, severe anxiety, chest tightness, palpitations, shortness of breath, and insomnia. The patient denied suicidal ideation. The nurse discussed the patient's complaints with the psychiatrist. The patient's psychiatrist recommended either diazepam or an over-the-counter antihistamine for sleep instead of the patient's prescribed zolpidem and trazadone. The patient was told to see the psychologist the following day but missed the appointment.

Eight days later, the patient called and spoke to the behavioral health nurse with complaints of worsening depression, insomnia, and nightmares. The patient reported thoughts of self-harm but denied having plans or intent. When questioned, the patient confirmed owning guns, but stated the guns were locked up at home and the patient did not know the combination. The patient assured the nurse that emergency care would be sought if thoughts of acting on ideas of self-harm developed. The psychiatrist, psychologist, and the Suicide Prevention Coordinator were alerted of the patient's condition by inclusion on the note. The psychiatrist ordered additional medications: bupropion, aripiprazole, and mirtazapine. The psychiatrist also recommended the patient resume taking zolpidem for sleep; continue venlafaxine, diazepam, and the amphetamine/dextroamphetamine at the current dose; and decrease the dose of divalproex. The clinic nurse informed the patient of the recommendations and explained the plan of care to the patient.

Approximately two weeks later, the patient saw the psychologist for therapy for PTSD and depression. Approximately three months later (summer 2017), after missing several behavioral health appointments, the psychologist instituted a Suicide Safety Plan, and the suicide prevention case manager added the patient to the facility high-risk for suicide list and a high-risk for suicide

flag was added to the patient's EHR. Based on a review of the patient's EHR, approximately six months later (late 2017), the patient's coping skills improved, they were emotionally stable, and denied suicidal ideation; the patient no longer met the criteria for placement on the high-risk list, and the patient record flag was inactivated. The patient missed or canceled many behavioral health appointments between late 2017 and spring 2018.

In spring 2018, the primary care provider noted the patient had missed their winter 2018 appointment. The urine drug screen was positive for cannabis. The provider noted cannabis use could be a cause of the patient's weight gain, lack of motivation, or behavioral health symptoms. One week later, the patient's urine drug screen was negative for the presence of amphetamine/dextroamphetamine.

The patient's urine drug screen in early 2019 did not report the detection of benzodiazepines or amphetamine/methamphetamine and was positive for cannabis. The following month, the primary care provider reviewed the patient's laboratory results noting that the patient's thyroid stimulating hormone level was normal, and no medication adjustments were needed.[4]

In spring 2019, the psychologist saw the patient for individual psychotherapy for PTSD and depression. The patient denied current suicidal or homicidal ideation. The patient stated that things have been going well for them and they were scheduled to transition from individual to group therapy the next month.

Five days later, the patient's thyroid stimulating hormone level of 3.913 was within the normal range.

The same day, the patient saw the psychiatrist for continued medication management and psychotherapy. The patient complained of continued nightmares once or twice a week, and sleep disturbance when their sleep was disrupted by staying up late. The patient reported their mood was good and that they felt their medications were effective. The patient noted ongoing anxiety from residual PTSD symptoms and noted some increased anxiety between doses of their medication. The patient denied suicidal ideation. The psychiatrist continued divalproex, zolpidem, melatonin and amphetamine/dextroamphetamine and increased the alprazolam to four times a day as needed for anxiety. Hydroxyzine was prescribed as needed for sleep at bedtime. The dose of venlafaxine was decreased to once a day due to possible sexual side effects and sildenafil was added. The psychiatrist documented the patient's occasional cannabis use, noted the diagnosis of cannabis use disorder and substance abuse and again "encouraged continued abstinence from alcohol and/or drug use."

Four days later, nursing staff were notified by the county coroner that the patient had died at home and the death was under review. An autopsy was performed by the medical examiner on the following day and completed approximately six weeks later. The medical examiner reported

[4] The patient's thyroid stimulating hormone level was 5.174. The normal range is between 0.47 and 5.00.

that the toxicology studies from blood demonstrated the presence of previously prescribed medications venlafaxine, alprazolam, and hydroxyzine.[5] Hydrocodone, an opioid pain medication not prescribed by the VA providers, and metabolites of cannabis were also detected.[6] The medical examiner noted that per the coroner report, the "patient traded [their] Adderall [amphetamine-dextroamphetamine] prescription for marijuana [cannabis]." No levels of amphetamine-dextroamphetamine were noted in the report.

Additional pertinent findings noted in the autopsy report included terminal aspiration of gastric contents and focal atherosclerosis of the proximal left circumflex artery. Moderate dilation of the right ventricle was noted. The left anterior descending and right coronary arteries did not have atherosclerosis.

The death certificate noted accidental "acute Multi-Drug Intoxication" as the immediate cause of death from substance abuse of hydrocodone, alprazolam, cannabis and metabolites, venlafaxine and metabolites, and hydroxyzine. The medical examiner opined that the death of the patient was attributed to "acute intoxication by the combined effects of hydrocodone, alprazolam, venlafaxine and hydroxyzine." Hypertensive cardiovascular disease and obesity were noted as significant conditions contributing to the death but not resulting in the underlying cause.

Inspection Results

1. Complications of High Cholesterol Contributed to a Patient's Death

The OIG substantiated that high cholesterol contributed to the patient's death; however, the patient's death certificate stated that the patient's primary cause of death was accidental acute multi-drug intoxication.

The postmortem toxicology report showed that the patient had prescribed medications, non-prescribed medications, and cannabis present in their system at the time of their death. The death certificate lists hypertensive cardiovascular disease and obesity as significant conditions contributing to the patient's death. Because of these contributing conditions, the OIG reviewed the care the patient received by their primary care provider related to the patient's cholesterol levels, blood pressure, and obesity.

[5] Alprazolam was noted to be 61.6 nanograms(ng)/milliliter (ml) that is above the therapeutic range of 10 to 40 ng/ml.

[6] Hydrocodone was noted to be 59.7 ng/ml that is above the therapeutic range of 10 to 40 ng/ml.

High Cholesterol

Cardiovascular disease is a "major cause of morbidity and mortality in the United States."[7] VA/DoD recommends screening and managing high cholesterol in men and women of a certain age; however, the guidelines also recognize that patients should be treated individually and variations in treatment may occur.[8] High cholesterol levels increase a patient's risk of cardiovascular disease, which may cause a heart attack, stroke, or other damage to the heart or brain. High cholesterol levels can be genetic or involve lifestyle factors such as excessive intake of dietary fats, sugars, and cholesterol. High cholesterol may also be associated with Hashimoto's disease due to the underactive thyroid gland.[9] In addition to lifestyle changes, some patients are prescribed medications to lower their cholesterol levels.

Between early 2016 and spring 2019, the primary care provider checked the patient's LDL-C at least annually. In summer 2016, the patient's LDL-C level was 170.1 mg/deciliter(dl). In response to the patient's high LDL-C level, the provider started the patient on atorvastatin and referred the patient to a dietician to discuss lifestyle changes. The patient's LDL-C decreased.[10] In summer 2017, the patient's atorvastatin was not renewed. The OIG found no documented evidence explaining why the medication was not renewed. The patient's primary care provider told the OIG that the patient's elevated cholesterol was being addressed with diet and exercise.

Hypertension

Hypertension (high blood pressure) "is clinically defined as a systolic blood pressure of ≥140 mm/Hg or a diastolic blood pressure of ≥90 mmHg."[11] Hypertension is diagnosed through routine blood pressure checks. The diagnosis of hypertension is based on at least two elevated readings on multiple visits one to four weeks apart.[12]

The patient's blood pressure was routinely checked between spring 2016 and spring 2019. The patient had three isolated high blood pressures in spring 2016, fall 2016, and spring 2018 with no

[7] VA/DoD *Clinical Practice Guideline for the Management of Dyslipidemia for Cardiovascular Risk Reduction*, version 3.0, December 2014, accessed July 23, 2020, https://www.healthquality.va.gov/guidelines/CD/lipids/VADoDDyslipidemiaCPG.pdf.

[8] VA/DoD *Clinical Practice Guideline for the Management of Dyslipidemia for Cardiovascular Risk Reduction*, version 3.0, December 2014, accessed July 23, 2020, https://www.healthquality.va.gov/guidelines/CD/lipids/VADoDDyslipidemiaCPG.pdf.

[9] Mayo Clinic, *Hashimoto's Disease,* accessed June 24, 2020, https://www.mayoclinic.org/diseases-conditions/hashimotos-disease/symptoms-causes/syc-20351855. The primary care provider treated the patient's Hashimoto's disease with medication, and the patient's thyroid levels were considered normal.

[10] The patient was 32 years old when the primary care provider started them on a cholesterol-lowering medication.

[11] *VA/DoD Clinical Practice Guideline for the Diagnosis and Management of Hypertension in the Primary Care Setting*, version 3.0, October 2014.

[12] *VA/DoD Clinical Practice Guideline for the Diagnosis and Management of Hypertension in the Primary Care Setting*, version 3.0, October 2014.

follow-up. One of the readings was taken in the Emergency Department, and according to the VA/DoD clinical guidelines, measurements when a patient is acutely ill or injured should not be used as a measurement for diagnosis.[13] The OIG determined that the patient's primary care provider did not treat the patient for hypertension because the criteria for diagnosis were not met.

Obesity

A significant problem facing the U.S. health care system today is the epidemic of the population being overweight or obese. A patient's body mass index (BMI) determines if a patient is of normal adult weight (18.5–24.9 kilograms/meter^2 (kg/m^2), overweight (25.0–29.9 kg/m^2), or obese (BMI ≥30 kg/m^2). VA/DoD recommends that "comprehensive lifestyle interventions for weight loss should be offered to all obese patients."[14]

Between spring 2016 and spring 2019, the patient's BMI ranged from 33 to 36 kg/m^2. In June 2016, the patient initially agreed to meet with a dietician to discuss high cholesterol. However, the patient canceled and then missed two scheduled appointments before notifying the primary care provider of not being interested in nutrition counseling at that time. During a primary care appointment in June 2018, the patient agreed to see a dietician to discuss high cholesterol and obesity. A few days later, the patient was seen by a dietician who helped develop an eating and exercise plan. During a follow-up appointment a month later, the patient reported weight loss, improved sleeping, and increased activity. The patient was encouraged to call or come to the clinic for follow-up as needed.

The OIG concluded that although the patient's cardiovascular risk factors of high cholesterol and obesity contributed to the patient's death, the patient's primary care provider addressed and monitored the patient's high cholesterol levels, blood pressure, and obesity recommending medication and lifestyle changes.

2. Medication Management by Psychiatrist

The patient had a complex mental health history that included PTSD, depression, anxiety, ADHD, cannabis use disorder, and sleep problems. For the treatment of PTSD and depression, the patient was followed by a psychiatrist for medication management and supportive psychotherapy, and by a psychologist for psychotherapy.

[13] *VA/DoD Clinical Practice Guideline for the Diagnosis and Management of Hypertension in the Primary Care Setting*, version 3.0, October 2014.

[14] *VA/DoD Clinical Practice Guideline for Screening and Management of Overweight and Obesity*, version 2.0, April 18, 2014.

Drug-Drug Interactions

According to the medical examiner's report, the combination of the patient's prescribed medications, non-prescribed medications, and cannabis created adverse drug-drug interactions that caused the patient's death.

VHA recommends educating patients when adverse drug-drug interactions may occur and documenting those discussions in patients' EHRs.[15]

Using Micromedex, the OIG reviewed possible drug-drug interactions for the patient's prescribed psychotropic medications from early 2017 through spring 2019.[16] Micromedex did not identify any contraindicated drug-drug interactions but did identify major drug-drug interactions.

The OIG found that the patient's psychiatrist documented discussion with the patient about possible side effects and potential adverse drug-drug interactions during the patient's in-person outpatient appointments. However, in three out of six telephone encounters, the OIG noted that neither the psychiatrist nor the behavioral health nurse documented discussion about possible side effects or potential adverse drug-drug interactions when discussing new medications and dosage changes to current medications. The OIG found no documented evidence that the patient reported adverse drug-drug interactions.

The OIG concluded based on the medical examiner's report that the patient's prescribed medications, non-prescribed medications, and cannabis created an adverse drug-drug interaction that caused the patient's death.

Anxiety, PTSD, and Benzodiazepines

The OIG found that the facility's psychiatrist prescribed benzodiazepines for over two years for the patient's anxiety.

VHA identifies that effective treatment of anxiety includes cognitive behavioral therapy and medication.[17] Cognitive behavioral therapy is used "to learn new ways of thinking, practice

[15] VHA Directive 2011-012, *Medication Reconciliation*, March 9, 2011.

[16] Micromedex is a drug information database that checks for and classifies drug-drug interactions into one of five severity categories: contraindicated, major, moderate, minor, and unknown. Micromedex recommends against using two medications that are contraindicated at the same time. Major drug-drug interactions may be life-threatening or require modifications to the therapy or both to minimize or prevent serious adverse events. Moderate interactions may worsen a patient's condition requiring change in therapy. Minor interactions have limited clinical effects that may not require any changes. Micromedex did not identify any moderate or minor drug interactions in the patient's medication profile. IBM Micromedex User Guide, February 2020. *Drug Interaction Checking (electronic version)*.

[17] "Anxiety: Treatment," VA Mental Health, accessed November 3, 2020, https://www.mentalhealth.va.gov/anxiety/treatment.asp.

positive behaviors, and take active steps beyond your symptoms."[18] Medications work to reduce symptoms of anxiety. Benzodiazepines are the most common medication used to treat anxiety. The National Institute of Mental Health recommends the short-term use of benzodiazepines for patients diagnosed with anxiety, but recommends using antidepressants for long-term treatment to avoid abuse and withdrawal symptoms.[19] Long-term use of benzodiazepines is not recommended because a patient may build a tolerance to the medication, become dependent on the medication, and may experience withdrawal symptoms if the medication is stopped suddenly. Providers must use their clinical judgment to determine what is appropriate for the patient and are required to discuss the expected benefits and known risks with the patient. The VA/DoD clinical guideline recommends against treating patients with PTSD with benzodiazepines because no strong evidence exists to support the effectiveness of treatment and the associated risk of tolerance, dependency, and withdrawal.[20]

The patient was diagnosed and treated for both anxiety and PTSD. The patient's psychiatrist provided supportive psychotherapy and medication management. For the treatment of anxiety, the patient's psychiatrist prescribed benzodiazepines. From early 2017 through spring 2018, the patient's psychiatrist prescribed diazepam.[21] In spring 2018, the patient complained of acute stress and requested a medication change for anxiety. The patient's psychiatrist discontinued the diazepam and started the patient on alprazolam, another benzodiazepine.[22] The patient noted feeling better approximately one month later. In spring 2019, the patient reported increased anxiety and in response, the psychiatrist increased the alprazolam dose.[23]

The increase in symptoms over time while being maintained on the same dose of the benzodiazepines suggests a developing tolerance. Despite the patient's reported possible tolerance, the patient's psychiatrist increased the dose.

The OIG concluded that the patient's psychiatrist continued the patient on long-term benzodiazepines for the treatment of anxiety and PTSD despite VA/DoD clinical guidance that long-term use of benzodiazepines is not recommended and benzodiazepines are not recommended for patients diagnosed with PTSD. While guidelines allow for the use of clinical

[18] "Anxiety: Treatment," VA Mental Health, accessed November 3, 2020, https://www.mentalhealth.va.gov/anxiety/treatment.asp.

[19] "Anxiety Disorders," National Institute of Mental Health, accessed September 4, 2020, https://www.nimh.nih.gov/health/topics/anxiety-disorders/index.shtml. The National Institute of Mental Health does not define short term versus long term. In the absence of a definition, the OIG defines short term as six months or less and long term as seven months or greater.

[20] VA/DoD *Clinical Practice Guideline for the Management of Posttraumatic Stress Disorder and Acute Stress Disorder*, version 3.0, June 2017.

[21] The patient was prescribed 5 mg of diazepam four times a day as needed.

[22] The patient was prescribed 1 mg of alprazolam three times a day as needed.

[23] The patient's provider increased the alprazolam from 1 mg three times a day to 1 mg four times a day as needed.

judgment when treating patients, the OIG did not find documentation of the provider's reasons for using long-term benzodiazepines for a patient diagnosed with anxiety and PTSD.

ADHD and Amphetamine/Dextroamphetamine

The OIG found that the psychiatrist continued to prescribe the patient amphetamine/dextroamphetamine despite negative urine screens that suggested the patient was not taking the medication.

Patients with ADHD are often prescribed medication to help "reduce hyperactivity and impulsivity and improve their ability to focus, work, and learn."[24] Adult patients prescribed amphetamine/dextroamphetamine for the treatment of ADHD should be closely monitored by the prescribing provider.[25] Amphetamine/dextroamphetamine can increase anxiety and may lead to sleep problems.[26] VHA requires ordering providers to communicate test results (including urine drug screens), provide clinical intervention as needed, and document the communication in the patient's EHR.[27]

Between early 2017 and spring 2019, the patient was prescribed amphetamine/ dextroamphetamine monthly for ADHD. The patient repeatedly reported satisfaction with concentration on this medication. In reviewing the patient's EHR, the OIG noted that the patient tested negative for amphetamine/dextroamphetamine in spring 2018 and in early 2019. The OIG found that the patient's psychiatrist documented in fall 2018, early 2019, and spring2019, that the patient tested negative for amphetamine/dextroamphetamine; however, the OIG found no documented evidence that the psychiatrist communicated the negative urine drug screens to the patient nor did the psychiatrist provide the necessary clinical intervention. The psychiatrist documented continuing the patient on the amphetamine/dextroamphetamine medication. When the OIG asked about the negative test result, the psychiatrist stated that it was a "red flag that I missed."

Cannabis Use

The OIG found that the psychiatrist was aware of the patient's cannabis use but failed to discuss or document a discussion with the patient about substance use treatment and the possible interaction(s) with prescribed medications.

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[24] "Attention-Deficit/Hyperactivity Disorder," National Institute of Mental Health, accessed September 1, 2020, https://www.nimh.nih.gov/health/topics/attention-deficit-hyperactivity-disorder-adhd/index.shtml.

[25] "Attention-Deficit/Hyperactivity Disorder," National Institute of Mental Health, accessed September 1, 2020, https://www.nimh.nih.gov/health/topics/attention-deficit-hyperactivity-disorder-adhd/index.shtml.

[26] "Dextroamphetamine And Amphetamine," Mayo Clinic, accessed October 14, 2020, https://www.mayoclinic.org/drugs-supplements/dextroamphetamine-and-amphetamine-oral-route/description/drg-20071758.

[27] VHA Directive 1088, *Communicating Test Results to Providers and Patients*, October 7, 2015.

VHA requires all providers to work toward substance use treatment for patients with a substance use diagnosis, and document a treatment plan that includes interventions and how to monitor progress.[28] VHA recommends educating patients when adverse drug-drug interactions may occur and documenting those discussions in the patients' EHR.[29]

From early2017 through spring 2019, during outpatient psychiatry appointments, the patient reported either occasional or less frequent cannabis use. In September 2018, the patient reported decreased cannabis use. The psychiatrist documented that the patient believed that the "use of cannabis... had cognitive effects, and perhaps mood effects, with difficulty making decision." In spring 2018 and early 2019, the patient tested positive for cannabis on urine drug screens. The patient's psychiatrist documented in the patient's EHR the positive test results in fall 2018, and twice in the first quarter of 2019. However, in an interview with the OIG, the psychiatrist did not recall discussing the positive urine drug screens with the patient.

The OIG concluded that the psychiatrist failed to address that the patient's urine drug screen results were negative twice for amphetamine/dextroamphetamine despite the patient's reports of improved concentration with the use of the medication. The patient's cannabis use may have contributed to the patient's anxiety, but the OIG found no documented evidence that the psychiatrist addressed this correlation with the patient. The patient acknowledged occasional cannabis use and told the psychiatrist of decreasing use believing that the cannabis may have been affecting cognition, mood, and the ability to make decisions. The OIG concluded that the psychiatrist did not comply with VHA policy by failing to develop a treatment plan with the patient, monitor the patient's progress, or discuss the possible adverse drug-drug interactions between cannabis use and the patient's prescribed medications.

3. Incomplete Implementation of the Psychotropic Drug Safety Initiative

The OIG identified that the facility developed a plan to address and monitor the Phase Four metrics of the Psychotropic Drug Safety Initiative; however, the facility did not implement the plan.

In 2013, VHA introduced the Psychotropic Drug Safety Initiative as a quality improvement strategy, focusing on improving the use of psychotropic medications to treat patients with mental health diagnoses.[30] VHA required facilities to identify metrics in each of the four phases:

[28] VHA Handbook 1160.01, *Uniform Mental Health Services in VA Medical Centers and Clinics*, September 11, 2008, amended November 16, 2015.

[29] VHA Directive 2011-012, *Medication Reconciliation*, March 9, 2011.

[30] Oversight of the initiative is assigned to the Office of Mental Health and Suicide Prevention, which collaborated with Mental Health Service, Pharmacy Benefits Management, and Geriatric and Extended Care.

- Phase One, launched in December 2013, "broadly looked across multiple classes of medication and mental health diagnoses."[31]
- Phase Two, launched in October 2015, focused on the use of psychotropic medications in the treatment of geriatric patients.
- Phase Three, launched in March 2017, focused on access to medications in the treatment of patients with substance use disorders.
- Phase Four, launched in March 2019, focused on reducing benzodiazepine use in high-risk patients and improving psychopharmacological care in patients with substance use disorders.[32]

In preparation for implementation of Phase Four, the facility prioritized (1) reducing the use of benzodiazepines in patients diagnosed with PTSD, and (2) ensuring that Prescription Drug Monitoring Program checks were conducted for those patients prescribed benzodiazepines. During the May 31, 2019, Behavioral Medicine Quality Assurance Committee (Committee) meeting, the Committee discussed the Phase Four metrics and reviewed data related to the number of high-risk patients prescribed benzodiazepines.[33] VHA required the facility to submit their implementation plan by June 30, 2019.

The OIG reviewed the Committee meeting minutes from July 2019 through September 30, 2020, and found that the facility reported on the Phase Four metrics in three of the five committee meetings.[34]

VHA launched Phase Four approximately one month prior to the patient's death and had a start date of July 2019. The OIG acknowledges that Phase Four was initiated after the patient's death, but found that the relevance of Phase Four is important in the care of other patients. During OIG interviews, the Chief of Behavioral Health and a contributing staff member stated that they initially reviewed the data, but due to COVID-19, they had not been monitoring the Phase Four metrics.

The OIG concluded that the facility identified and developed a plan to address the Phase Four metrics. Based on interviews, the facility appeared to delay implementation of the Phase Four plan because of COVID-19. Although delayed, the facility's two identified metrics have been trending in the right direction.

[31] "About PDSI," Office of Mental Health and Suicide Prevention, access on July 21, 2020, https://spsites.cdw.va.gov/sites/OMHO_PsychPharm/PDSI_Resources/Pages/About-2.aspx.
[32] The facility defined high-risk patients as patients age 65 or older, with a PTSD diagnosis, actively using opioids, and with a substance use disorder.
[33] The Committee met quarterly.
[34] Reporting was deferred during two Committee meetings due to a change in personnel.

4. Deficiencies in Compliance with Two Facility Policies

Deficiencies with the Return-to-Clinic Policy

The OIG found that the primary care provider did not consistently enter return-to-clinic orders at the end of visits. Facility policy required that the provider determine when a patient should return for a follow-up appointment and enter a return-to-clinic order prior to the patient's departure.[35]

The OIG reviewed the patient's appointments from early 2016 through early 2019 and found that the patient's primary care provider documented that the patient should return to clinic in six months. The primary care provider entered a return-to-clinic order following all appointments except for the patient's summer 2018 appointment. Although documented in the patient's progress notes, the scheduling staff utilize the return-to-clinic order when scheduling appointments. Although primary care saw the patient twice in February 2019, both visits were unscheduled and were not established appointments based on a return-to-clinic order. The patient had no further scheduled appointments.

The OIG concluded that the primary care provider did not comply with facility policy by failing to enter a return-to-clinic order after the patient's summer 2018 appointment.

Deficiencies with No-Show Appointments Policy

The OIG determined that the primary care and behavioral health staff did not comply with the facility's no-show appointment policy.

Facility policy required that following a missed appointment, primary and specialty care staff must attempt to contact the patient once by telephone and if unsuccessful, a letter would be sent to the patient.[36]

The OIG found that following the patient's four missed primary care appointments, neither the primary care provider nor team called or sent a letter to the patient. The OIG found that the psychologist called or attempted to call the patient after 23 missed appointments; however, when the psychologist was unable to reach the patient in 10 instances, the psychologist did not send a

[35] Facility Memorandum 11-11 GPM-16-552, *Clinic Scheduling, No-Shows and Cancellations,* November 8, 2016. This memorandum was in effect at the time of the events discussed in this report until it was rescinded and replaced by Facility Memorandum, 11-11 GPM-19-552, *Clinic Scheduling, No-Shows and Cancellations,* December 1, 2019. The revised policy states the clinic provider will enter a return-to-clinic order in the computerized patient record system (CPRS) orders tab before the patient leaves the treating provider.

[36] Facility Memorandum 11-11 GPM-16-552, *Clinic Scheduling, No-Shows and Cancellations,* November 8, 2016. This memorandum was in effect at the time of the events discussed in this report until it was rescinded and replaced by Facility Memorandum, 11-11 GPM-19-552, *Clinic Scheduling, No-Shows and Cancellations,* December 1, 2019. The revised policy states that established patient's that miss an appointment must be contacted to determine if the appointment should be rescheduled. If unable to contact a patient after two attempts (behavioral health requires three attempts), an *unable to contact* letter will be sent to request the patient to contact the clinic. An Administrative Contact Note will be documented in the patient's EHR.

letter. The patient's psychologist told the OIG that the psychologist's practice was to call the patient following a missed appointment. Oftentimes, the patient would not answer the telephone call but would call into the clinic and reschedule appointments. The psychiatrist or behavioral health nurse called or attempted to call the patient after five of six missed appointments. A letter was sent in one instance when the psychiatrist or behavior health nurse was unable to reach the patient.

The OIG concluded that primary care staff did not comply with facility policy to telephone the patient, or if unable to reach the patient send a letter, after the patient missed appointments. The patient's behavioral health team complied with calling the patient after the patient missed appointments; however, when unable to reach the patient, the behavioral health team did not send the patient a letter.

Conclusion

The OIG substantiated that high cholesterol contributed to the patient's death; however, the patient's death certificate stated that the patient's primary cause of death was accidental acute multi-drug intoxication. The OIG found that the primary care provider addressed the patient's elevated cholesterol levels. The cholesterol levels were addressed with diet and activity recommendations.

Based on the medical examiner's report, the OIG concluded that the patient's prescribed medications, non-prescribed medications, and cannabis created adverse drug-drug interactions that caused the patient's death. While guidelines allow for the use of clinical judgment when treating patients, the OIG did not find documentation of the psychiatrist's reasons for using long-term benzodiazepines on a patient diagnosed with anxiety and PTSD. The deficiencies in compliance with addressing the patient's urine drug-screen results may have led to missed opportunities to address the patient's symptoms and decrease the patient's cannabis use. The failure to address the patient's cannabis use may have led to the psychiatric medications being less effective, causing the patient to take more medications.

The behavioral health nurse and the patient's psychiatrist failed to document in the EHR discussions about side effects or possible drug-drug interactions when discussing medication changes during three out of six telephone encounters.

The facility developed a plan to address and monitor the Phase Four metrics of the Psychotropic Drug Safety Initiative; however, the facility did not implement the plan due to COVID-19.

The primary care provider failed to enter a return-to-clinic order following the patient's summer 2018 appointment. The patient was seen as a walk-in twice in early 2019 but had no scheduled primary care appointments.

Primary care staff did not comply with facility policy to telephone the patient, or if unable to reach the patient send a letter, after the patient missed appointments. The patient's behavioral

health team complied with calling the patient after the patient missed appointments; however, when unable to reach the patient, the behavioral health team did not send the patient a letter.

Recommendations 1–5

1. The Marion VA Medical Center Director ensures that behavioral health staff provide, and document patient education including discussion of side effects and possible adverse drug-drug interactions during telephone encounters when medications are added or adjusted and monitors compliance.

2. The Marion VA Medical Center Director confirms that behavioral health providers are communicating test results to patients and providing necessary clinical interventions as required by policy.

3. The Marion VA Medical Center Director monitors implementation of Phase Four of the Psychotropic Drug Safety Initiative.

4. The Marion VA Medical Center Director ensures that primary care providers enter return-to-clinic orders and monitors compliance.

5. The Marion VA Medical Center Director verifies primary care and behavioral health staff document contacts, attempted contacts, and letters sent when patients missed their appointments and monitors compliance.

Appendix A: VISN Director Memorandum

Department of Veterans Affairs Memorandum

Date: April 16, 2021

From: Director, VA Heartland Network (10N15)

Subj: **VAOIG Hotline – Marion IL (54HL08) – Draft Report**

To: Office of Inspector General, Operations Division (53B)

Attached is the facility's comments to the Draft Healthcare Inspection Report: DRUG INTERACTIONS RELATED TO A PATIENT DEATH AT THE MARION VA MEDICAL CENTER.

I reviewed and concur with the facility's comments.

For additional questions, please feel free to contact Michelle Boylan, VISN 15 Quality Management Officer.

(*Original signed by*:)

William P. Patterson, M.D., MSS
Network Director
VA Heartland Network (VISN 15)

Appendix B: Facility Director Memorandum

Department of Veterans Affairs Memorandum

Date: April 14, 2021

From: Director, Marion VA Medical Center (657A5/00)

Subj: Healthcare Inspection—Drug Interactions Related to a Patient Death, Marion VA Medical Center in Illinois

To: Director, VA Heartland Network (10N15)

I have reviewed the findings within the report of the Healthcare Inspection – Drug Interactions Related to a Patient Death, Marion VA Medical Center in Illinois. I concur with all the findings of the review.

Corrective action plans have been established with planned completion dates outlined in this report.

(*Original signed by*:)

Jo-Ann Ginsberg, RN, MSN
Medical Center Director

Facility Director Response

Recommendation 1

The Marion VA Medical Center Director ensures that behavioral health staff provide, and document patient education including discussions of side effects and possible adverse drug-drug interactions during telephone encounters when medications are added or adjusted and monitors for compliance.

Concur.

Target date for completion: March 31, 2022

Director Comments

The Chief of Behavioral Health (BH) in collaboration with the Associate Chief Nurse of Extended Care and Behavioral Health will create a standardized template titled, BH New Medication Counseling-MA. The use of this template will ensure documentation of patient education including discussions of side effects and possible adverse drug-drug interactions during telephone encounters when medications are added or adjusted. All BH providers and nursing staff will be educated on the utilization of the new template.

The Behavioral Health Nurse Manager will ensure compliance by conducting monthly chart audits reviewing thirty medication telephone encounters for use of the newly developed standardized template with compliance goal of 90% for six months or two consecutive quarters. The compliance data will be reported to the Executive Leadership Council.

Recommendation 2

The Marion VA Medical Center Director confirms that behavioral health providers are communicating test results with patients and necessary clinical interventions as required by policy.

Concur.

Target date for completion: March 31, 2022

Director Comments

The Chief of Behavioral Health (BH) in collaboration with the Associate Chief Nurse of Extended Care and Behavioral Health will create a standardized template for behavioral health test results notifications titled, BH Test Results Letter-MA to ensure test results and necessary clinical interventions are communicated to the patient. The template will be used by all behavioral health providers and nursing staff when relaying test results and clinical interventions

if indicated. Education on the utilization of the new template will be provided to the behavioral health provider and nursing staff.

The Behavioral Health Nurse Manager will ensure compliance by conducting thirty monthly chart audits reviewing communication of test results with patients and providing necessary clinical interventions with use of the newly developed standardized template with compliance goal of 90% for six months or two consecutive quarters. The compliance data will be reported to the Executive Leadership Council.

Recommendation 3

The Marion VA Medical Center Director monitors implementation with Phase Four of the Psychotropic Drug Safety Initiative.

Concur.

Target date for completion: December 31, 2021

Director Comments

The Chief of Behavioral Health Service conducted a comprehensive review of the Phase Four of the Psychotropic Drug Safety initiative and found that implementation was partially completed. Two quality improvement priorities, including staff education and prescribing monitoring were not consistently addressed. The Chief of Pharmacy will resume providing monthly data on patients receiving benzodiazepine to the identified providers.

Psychotropic Drug Safety Initiative education was provided by the Chief of Behavioral Health during the monthly medical staff meeting on April 08, 2021 and a follow up email was sent to all medical staff. A status update on Phase Four of the Psychotropic Drug Safety Initiative implementation will be reported to the Behavioral Health Quality Committee (BQAC) monthly as a standing agenda item to include staff education and prescribing monitoring. The implementation status will be reported monthly to the Executive Leadership Council for six months.

Recommendation 4

The Marion VA Medical Center ensures that primary care providers enter return-to-clinic orders and monitors compliance.

Concur.

Target date for completion: March 31, 2022

Director Comments

The Chief of Primary Care reviewed the requirements of the facility policy MCP [Medical Center Policy] 552, Clinic Scheduling, No Show and Cancellation and determined it there was inconsistent compliance. The facility policy requires that clinic providers enter a return to clinic order before the patient leaves the clinic. Reeducation was provided to all Primary Care providers by email on April 9, 2021 and will be discussed again in the Primary Care monthly staff meeting on April 22, 2021 to reinforce the policy requirements.

The Administrative Officer of Primary Care will conduct ten monthly chart audits to validate the return to clinic orders are being entered by Primary Care providers. Results of the audit will be reported to the Executive Leadership Council with a goal of 90% compliance for six months or two consecutive quarters.

Recommendation 5

The Marion VA Medical Center verifies that primary care and behavioral health staff document contacts, attempted contacts, and letters sent when a patient missed their appointments and monitors compliance.

Concur.

Target date for completion: March 31, 2022

Director Comments

The Service Chiefs for Primary Care and Behavioral Health (BH) reviewed the requirements of the facility policy MCP 552, Clinic Scheduling, No Show and Cancellation and determined that the policy was not consistently followed.

Primary Care actions to attempt contact for a missed appointment will be documented in the note title, Administrative Contact Note MA. Primary Care and Behavioral Health staff will be provided a copy of the MCP 552, Clinic Scheduling, No Show and Cancellation and reeducated on the requirements by June 30, 2021.

Behavioral Health will develop a SOP [standard operating procedure] and educate staff on their process for utilizing the BH Missed Appointment note and BH Missed Appointment Letter.

The Lead Advanced Medical Support Assistants for Behavioral Health and Primary Care will conduct monthly chart audits reviewing ten missed appointments per service (Behavioral Health and Primary Care) to validate that the appointments were addressed according to MCP 552 Clinic Scheduling, No Show and Cancellation. Audit results will be reported to the Executive Leadership Council with a goal of 90% compliance for six months or two consecutive quarters.

Glossary

To go back, press "alt" and "left arrow" keys.

adverse drug-drug interaction. Unintended injury or harm caused by administration of a medication due to drug-drug interactions.[1]

alprazolam. Classified as a benzodiazepine, used to treat anxiety and panic disorder.[2]

amphetamine/dextroamphetamine. "This drug combination is used to treat attention-deficit disorder (ADHD) and works to increase attention and decrease restlessness in patients who are overactive, cannot concentrate or are easily distracted."[3]

anticonvulsant. A classification of drugs used to treat or prevent seizures.[4]

antihistamine. "A group of medications that work to prevent the effects of a substance called histamine, which is produced in the body. Also, may be used to help people go to sleep since a side effect is drowsiness."[5]

aripiprazole. Classified as an antipsychotic, used as add-on therapy for the treatment of major depressive disorder.[6]

atherosclerosis. "Refers to the buildup of fats, cholesterol and other substances in and on your artery walls (plaque), which can restrict blood flow."[7]

atorvastatin. When utilized with a "proper diet, this medication can help to lower cholesterol and triglyceride (fats) levels in the blood."[8]

attention-deficit/hyperactivity disorder (ADHD). "A mental health disorder that includes a combination of persistent problems, such as difficulty paying attention, hyperactivity and

[1] VHA Directive 1070, *Adverse Drug Event Reporting and Monitoring*, September 14, 2014.

[2] Mayo Clinic, *Alprazolam*, accessed June 29, 2020, https://www.mayoclinic.org/drugs-supplements/alprazolam-oral-route/description/drg-20061040.

[3] Mayo Clinic, *Dextroamphetamine and Amphetamine,* accessed June 29, 2020, https://www.mayoclinic.org/drugs-supplements/dextroamphetamine-and-amphetamine-oral-route/description/drg-20071758.

[4] Merriam-Webster. *Anticonvulsant*, accessed September 30, 2020, https://www.merriam-webster.com/dictionary/anticonvulsant.

[5] Mayo Clinic, *Antihistamine,* accessed November 9, 2020, https://www.mayoclinic.org/drugs-supplements/antihistamine-oral-route-parenteral-route-rectal-route/description/drg-20070373.

[6] Mayo Clinic, *Aripiprazole*, accessed February 2, 2021, https://www.mayoclinic.org/drugs-supplements/aripiprazole-oral-route/description/drg-20066890.

[7] Mayo Clinic, *Arteriosclerosis,* accessed November 9, 2020, https://www.mayoclinic.org/diseases-conditions/arteriosclerosis-atherosclerosis/symptoms-causes/syc-20350569.

[8] Mayo Clinic, *Atorvastatin*, accessed June 24, 2020, https://www.mayoclinic.org/drugs-supplements/atorvastatin-oral-route/description/drg-20067003.

impulsive behavior. Adult ADHD can lead to unstable relationships, poor work or school performance, low self-esteem, and other problems."[9]

benzodiazepine. "A medication that produces sedation, induces sleep, relieves anxiety and prevents seizures."[10]

blood pressure. Pressure that is exerted by the blood upon the walls of the blood vessels and especially arteries, and that varies with the muscular efficiency of the heart, the blood volume and viscosity, the age and health of the individual, and the state of the vascular wall.[11]

body mass index (BMI). "A formula that uses weight and height to estimate body fat. A high BMI is associated with an increased risk for chronic diseases such as heart disease, high blood pressure and type 2 diabetes in adults."[12]

bupropion. Classified as an antidepressant, used for the treatment of major depressive disorder.[13]

cannabis. A marijuana plant that contains components of tetrahydrocannabinol (THC), cannabidiol, and cannabinol.[14]

cannabis use disorder. A disease that "affects a person's brain and behavior" and leads to an inability to control the use of cannabis. Symptoms can include difficulty concentrating, anxiety, paranoid thoughts, not meeting responsibilities, and urges to continue to use cannabis.[15]

cardiovascular disease. "The term "heart disease" is often used interchangeably with the term "cardiovascular disease." Cardiovascular disease generally refers to conditions that involve narrowed or blocked blood vessels that can lead to a heart attack, chest pain (angina) or stroke."[16]

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[9] Mayo Clinic, *ADHD,* accessed June 24, 2020, *https://www.mayoclinic.org/diseases-conditions/adult-adhd/symptoms-causes/syc-20350878*.
[10] U.S. Drug Enforcement Administration, *Benzodiazepines,* accessed September 24, 2020, https://www.dea.gov/factsheets/benzodiazepines.
[11] Merriam-Webster, *Blood pressure,* accessed November 2, 2020, https://www.merriam-webster.com/dictionary/blood%20pressure.
[12] Mayo Clinic, *Body Mass Index*, accessed November 2, 2020, https://www.mayoclinic.org/diseases-conditions/obesity/in-depth/bmi-calculator/itt-20084938.
[13] Mayo Clinic, *Bupropion*, accessed February 2, 2021, https://www.mayoclinic.org/drugs-supplements/bupropion-oral-route/description/drg-20062478.
[14] Merriam-Webster, *Cannabis*, accessed February 2, 2021, https://www.merriam-webster.com/dictionary/cannabis.
[15] Mayo Clinic, *Drug Addiction*, accessed October 14, 2020, https://www.mayoclinic.org/diseases-conditions/drug-addiction/symptoms-causes/syc-20365112.
[16] Mayo Clinic, *Heart Disease,* accessed November 2, 2020, https://www.mayoclinic.org/diseases-conditions/heart-disease/symptoms-causes/syc-20353118.

cholesterol. "A waxy substance found in blood. The body needs cholesterol to build healthy cells, but high cholesterol can increase risk for heart disease."[17]

cognitive behavioral therapy. A structured, talk therapy technique that works toward responding to difficult situations more clearly and rationally. Cognitive behavioral therapy is often used with major depressive disorder, posttraumatic stress disorder, anxiety disorders, substance use disorders, and phobias.[18]

contraindicated. Combination that is not to be used together.[19]

creatinine phosphokinase. "A protein that helps to elicit chemical changes in the body and is found in the heart, brain and skeletal muscle tissue. When muscle tissue is damaged, creatinine phosphokinase leaks into the blood and indicates stress or injury to the muscle."[20]

diazepam. Classified as a benzodiazepine, used to treat anxiety.[21]

divalproex. An anticonvulsant used primarily to treat seizure disorders, but can also be used to stabilize mood.[22]

drug-drug interaction. Unexpected side effects as a result of two or more medications reacting with each other.[23]

endocrinologist. A medical doctor "who evaluates and treats people for endocrine and metabolic disorders."[24]

endocrinology. A branch of medicine concerned with the structure, function, and disorders of the endocrine glands.[25]

generalized anxiety disorder . An anxiety disorder marked by chronic excessive anxiety and worry that is difficult to control, causes distress or impairment in daily functioning, and is

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[17] Mayo Clinic, *High Cholesterol,* accessed June 29, 2020, https://www.mayoclinic.org/diseases-conditions/high-blood-cholesterol/symptoms-causes/syc-20350800.

[18] Mayo Clinic, *Cognitive Behavioral Therapy*, accessed October 14, 2020, https://www.mayoclinic.org/tests-procedures/cognitive-behavioral-therapy/about/pac-20384610.

[19] Merriam-Webster, *Contraindicated*, accessed February 2, 2021, https://www.merriam-webster.com/dictionary/contraindicated.

[20] Johns Hopkins Lupus Center, *Creatine Phosphokinase,* accessed October 5, 2020, https://www.hopkinslupus.org/lupus-tests/clinical-tests/creatine-phosphokinase-cpk/.

[21] Mayo Clinic, *Diazepam*, accessed October 7, 2020, https://www.mayoclinic.org/drugs-supplements/diazepam-rectal-route/description/drg-20072190.

[22] Mayo Clinic, *Divalproex*, accessed February 2, 2021, https://www.mayoclinic.org/drugs-supplements/divalproex-sodium-oral-route/description/drg-20072886.

[23] Council on Family Health, *Drug Interactions: What you should know,* March 2004.

[24] Mayo Clinic, *Endocrinology*, accessed February 2, 2021, https://www.mayoclinic.org/departments-centers/endocrinology/sections/overview/ovc-20392506.

[25] Merriam Webster, *Endocrinology,* accessed November 9, 2020, https://www.merriam-webster.com/dictionary/endocrinologist.

accompanied by three or more associated symptoms (such as restlessness, irritability, poor concentration, and sleep disturbances).[26]

Hashimoto's Disease. A thyroid condition caused by the immune system attacking the thyroid gland at the base of the neck. It leads to hypothyroidism (underactive thyroid gland).[27]

high cholesterol. Low density lipoprotein cholesterol (LDL-C) >130 milligram per deciliter (mg/dL), high density lipoprotein cholesterol (HDL-C) <40 mg/dL, or triglyceride (TG) >200 mg/dL.[28]

hydroxyzine. An antihistamine medication used to treat anxiety.[29]

hypothyroidism. An underactive condition of the thyroid gland which causes the body to produce lower amounts of thyroid hormone, leading to problems such as obesity, joint pain, infertility, and heart disease.[30]

insomnia. A disorder in which individuals are discontent with the quality, timing, and amount of sleep resulting in daytime impairment.[31]

levothyroxine. A medication that is used to treat patients that do not produce enough thyroid hormone.[32]

major depressive disorder (depression). A disorder that affects the mood with persistent feelings of sadness and emptiness impacting an individual's ability to function normally.[33]

melatonin. An over-the-counter herbal supplement used for sleep disorders.[34]

mirtazapine. A tetracyclic antidepressant used to treat major depressive disorder.[35]

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[26] Merriam-Webster, *Generalized Anxiety Disorder,* accessed August 27, 2020, https://www.merriam-webster.com/dictionary/generalized%20anxiety%20disorder.

[27] Mayo Clinic, *Hashimoto's Disease,* accessed June 24, 2020, https://www.mayoclinic.org/diseases-conditions/hashimotos-disease/symptoms-causes/syc-20351855.

[28] VA/DoD *Clinical Practice Guidelines for the Management of Dyslipidemia for Cardiovascular Risk Reduction*, Version 3.0, December 2014, accessed July 23, 2020, https://www.healthquality.va.gov/guidelines/CD/lipids/VADoDDyslipidemiaCPG.pdf.

[29] Mayo Clinic, *Hydroxyzine*, accessed August 6, 2020, https://www.mayoclinic.org/drugs-supplements/hydroxyzine-oral-route/description/drg-20311434.

[30] Mayo Clinic, *Hyperthyroidism,* accessed August 6, 2020, https://www.mayoclinic.org/diseases-conditions/hypothyroidism/symptoms-causes/syc-20350284.

[31] Diagnostic and Statistical Manual of Mental Disorders, Fifth Ed. *Sleep-Wake Disorders.*

[32] Mayo Clinic, *Levothyroxine,* accessed August 10, 2020, https://www.mayoclinic.org/drugs-supplements/levothyroxine-oral-route/description/drg-20072133.

[33] Diagnostic and Statistical Manual of Mental Disorders, Fifth Ed. *Depressive Disorders.*

[34] Mayo Clinic. *Melatonin,* accessed August 6, 2020, https://www.mayoclinic.org/drugs-supplements-melatonin/art-20363071?p=1.

[35] Mayo Clinic, *Mirtazapine*, accessed February 2, 2021, https://www.mayoclinic.org/drugs-supplements/mirtazapine-oral-route/description/drg-20067334.

mm/Hg. A unit of pressure equal to the pressure exerted by a column of mercury 1 millimeter high at 0 degree C and under the acceleration of gravity and nearly equivalent to 1 torr.[36]

non-formulary. A list of generic and name brand pharmaceutical drugs not covered by a health insurance provider or the VA.[37]

obesity. "A complex disease involving an excessive amount of body fat. It increases risk of heart disease, diabetes, high blood pressure and certain cancers."[38]

postmortem. Done, occurring, or collected after death.[39]

posttraumatic stress disorder (PTSD). "A mental health condition that's triggered by a terrifying event—either experiencing it or witnessing it. Symptoms may include flashbacks, nightmares and severe anxiety, as well as uncontrollable thoughts about the event."[40]

Prescription Drug Monitoring Program. "An electronic database that tracks controlled substance prescriptions. [Prescription Drug Monitoring Programs] can help identify patients who may be misusing prescription opioids or other prescription drugs and who may be at risk for overdose."[41]

psychotherapy. Talk therapy with a licensed mental health provider that is used to treat a variety of mental health disorders.[42]

psychotropic drugs. Include antianxiety, antidepressant, and antipsychotic medication.[43]

rosuvastatin. When utilized with a "proper diet, this medication can help to lower bad cholesterol (LDL) and triglyceride (fats) levels in the blood and can increase your good cholesterol (HDL)."[44]

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serotonin norepinephrine reuptake inhibitors. Antidepressant medications used to treat depression and anxiety.[45]

sildenafil. A medication "used to treat men with erectile dysfunction."[46]

substance use disorder. "A disease that affects a person's brain and behavior and leads to an inability to control the use of a legal or illegal drug or medication.[47]

thyroid stimulating hormone. A hormone produced in the pituitary gland.[48]

trazodone. An antidepressant medication used to treat major depressive disorder.[49]

venlafaxine. An antidepressant, classified as serotonin norepinephrine reuptake inhibitors, used to treat general anxiety disorder and major depressive disorder.[50]

ventricle. A chamber of the heart which receives blood from a corresponding atrium and from which blood is forced into the arteries.[51]

vitamin D. A critical substance in the body that is necessary for strong bones and teeth.[52]

zolpidem. A medication that is used to treat insomnia.[53]

[45] Mayo Clinic. *Serotonin Norepinephrine Reuptake Inhibitor,* accessed October 1, 2020, https://www.mayoclinic.org/diseases-conditions/depression/in-depth/antidepressants/art-20044970.

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