RECOMBINANT ZOSTER VACCINE: UPTAKE AND SAFETY AMONG THE GENERAL POPULATION AND IMMUNOCOMPROMISED INDIVIDUALS

Jonathan Fix

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Approved by:

Sylvia Becker-Dreps

Michael G. Hudgens

Jennifer L. Lund

Jennifer S. Smith

Nadja Vielot

David J. Weber

ABSTRACT

Jonathan Fix: Recombinant Zoster Vaccine: Uptake and Safety Among the General Population and Immunocompromised Individuals
(Under the direction of Sylvia Becker-Dreps)

Herpes Zoster (HZ), also known as shingles, is a disease with cutaneous manifestations that results from the reactivation of the varicella zoster virus. The US Centers for Disease Control and Prevention (CDC) recommended the two-dose recombinant zoster vaccine (RZV) for immunocompetent adults aged ≥50 years old for prevention of HZ and sequelae in 2018, but did not expand its recommendation to include immunocompromised adults until 2022. The objectives of this dissertation were to identify groups with lower rates of RZV vaccination and improve our understanding of RZV safety.

Data from the IBM MarketScan® Commercial Claims and Encounters Database from 2017-2019 were used to identify vaccine-eligible adults, RZV vaccinations, and short- and long-term adverse events. Aim 1 characterized patterns of RZV initiation and completion by demographic, healthcare access, and clinical characteristics. Aim 2 evaluated short- and long-term safety using an age-adjusted self-controlled case series, with additional investigation of modification of safety by immune function.

From 2018-2019 there were 572,544 RZV administrations. The cumulative incidence of RZV series initiation was 10.0%. Initiation rates increased with age and number of medical office visits, and were higher among women, urban residents, high-deductible insurance

beneficiaries, and those who were immunocompromised compared to immunocompetent. Among immunocompromised adults, RZV initiation was highest among those with HIV and primary immunodeficiencies. Of those who initiated RZV, 89.5% received both doses. There were increased rates of both short- and long-term adverse events following RZV administration. Associations between RZV and short-term safety outcomes were attenuated among immunocompromised enrollees compared to immunocompetent enrollees; no differences by immune function were observed for long-term safety.

RZV uptake was low and differed by demographic, healthcare access, and clinical characteristics. Initiation rates were higher among immunocompromised compared to immunocompetent adults, despite no CDC recommendation for these groups during the study period. While there were slightly increased rates of autoimmune events following vaccination, these events were uncommon. Associations between RZV administration and short- and long-term adverse events were no higher among immunocompromised enrollees compared to immunocompetent. These findings should inform efforts to increase vaccination and provide additional evidence regarding the safety of RZV for policymakers and clinicians.

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LIST OF ABBREVIATIONS

ACIP	US Advisory Committee on Immunization Practices
AE(s)	Adverse Event(s)
AS01	Adjuvant System 01
BCG	bacilli Calmette-Guerin
CDC	US Centers for Disease Control and Prevention
GBS	Guillain-Barre syndrome
HIV	Human Immunodeficiency Virus
HPV	Human Papilloma Virus
HSCT	Hematopoietic Stem Cell Transplantation
HZ	Herpes Zoster
HZO	Herpes Zoster Ophthalmicus
ISR(s)	Injection Site Rection(s)
MMR	Measles, Mumps, and Rubella
PHN	Post-herpetic Neuralgia
pIMD(s)	potentially Immune Mediated Disease(s)
PY	Person Years
RZV	Recombinant Zoster Vaccine (Shingrix®)
SAE(s)	Severe Adverse Event(s)
SCCS	Self-Controlled Case Series
VRR	Vaccine Response Rate
VZV	Varicella Zoster Virus
ZVL	Live-Attenuated Zoster Vaccine (Zostavax®)

CHAPTER 1 - INTRODUCTION

Edward Jenner's cowpox experiments in 1796 were not the first use of inoculation in human history,[1] but they did play a pivotal role in expanding our understanding of immunization and in the development of vaccines in the future. Vaccines are arguably the most important scientific development in human history. It is estimated that vaccines against just 10 diseases prevented approximately 37 million deaths between 2000-2019.[2] Fortunately, the process of creating and clinically testing vaccines has evolved substantially since the uncontrolled inoculation of children and milkmaids with cowpox to protect against smallpox. New vaccines must now undergo multiple phases of clinical trials prior to licensure.[3]

The objectives and study populations of clinical trials change as new vaccines progress through the clinical development pipeline, reflecting the balance of producing scientifically valid evidence while prioritizing safety. Phase I clinical trials generally include healthy adults to establish safety, even if the primary target population for the vaccine may be children. As the vaccine progresses to phase II studies, the number of participants increases and the study population begins to more closely resemble the target population to provide stronger evidence regarding safety and immunogenicity. Assuming positive safety and immunogenicity results, the ensuing phase III trials include thousands of volunteers from the target population.[3] Despite this, specific groups are often excluded from participating in clinical trials, such as pregnant women and immunocompromised patients.[4,5] These exclusion criteria subsequently pose a problem when trying to determine the safety and efficacy of a vaccine for these groups, particularly if they are among key groups of interest for vaccination.

In the United States, after vaccine approval/authorization from the US Food and Drug Administration, vaccine policy is set by the CDC after reviewing recommendations made by the ACIP.[6] The impact of clinical trial exclusion criteria on recommendations for vaccination in the United States was demonstrated in the CDC's initial recommendations for RZV for the prevention of HZ and its sequelae. Although immunocompromised patients are at greatest need of protection due to higher rates of HZ and more severe outcomes in comparison to immunocompromised patients, the CDC's initial recommendations for RZV included only immunocompetent adults aged ≥50 years.[7] While the vaccine was not contraindicated in immunocompromised patients, their exclusion from the pivotal phase III clinical trials[8,9] meant that there was insufficient safety and efficacy evidence for this population. The CDC later expanded its recommendation in 2022 to include immunocompromised adults ≥19 years old[10] but, regardless, immunocompromised patients were receiving RZV in the period prior to the expanded recommendations. Herein lies an opportunity for assessing patterns of use, safety, and effectiveness. Even after completing phase I-III studies and achieving licensure, continued surveillance of vaccines via phase IV post-marketing safety studies is required and uses real world data to provide additional evidence to demonstrate safety and evaluate rare outcomes that are difficult to detect with the sample sizes provided by even the largest phase III trials.[11]

The motivation of this dissertation is to address gaps in knowledge about RZV safety that are naturally produced due to sample size limitations of clinical trials, and to characterize the use of the vaccine in the initial years following the CDC's recommendation. As RZV is being administered to immunocompromised patients, we ought to improve our understanding of the safety of the vaccine among this population. Enhancing public knowledge about the vaccine's

safety is critical to addressing vaccine hesitancy, improving vaccination rates, and reducing the burden of HZ and sequelae among older adults.

CHAPTER 2 - LITERATURE REVIEW

2.1 Overview

In early 2018, the CDC made a preferential recommendation of RZV for immunocompetent adults aged ≥50 years for the prevention of HZ and sequelae.[7] While this initial recommendation of RZV did not include immunocompromised patients due to their exclusion from the pivotal RZV clinical trials, immunocompromised patients were receiving the vaccine during this period.[12] RZV vaccination for immunocompromised patients is particularly important, as they are at higher risk of incident HZ and experience more severe outcomes of HZ and its sequelae.[13-16] Patterns of RZV use have been investigated generally,[17-19] but none of these studies have evaluated RZV use among immunocompromised patients, either overall or specifically within a type of immunocompromising condition. Assessing patterns of use of RZV will improve targeted efforts to increase vaccination rates among key populations of interest.

Given the initial lack of clinical trial data regarding RZV use among immunocompromised adults, questions remain concerning the safety of RZV for this population. Additional clinical trials of RZV among specific immunocompromised groups have been completed,[20-25] leading to the CDC expanding its recommendation in 2022 to include immunocompromised patients ≥19 years old;[10] however, the total number of participants in these trials was limited and subsequently constrains the ability to evaluate rare safety outcomes such as autoimmune events. Large database studies, such as those using insurance claims data, provide to opportunity to evaluate rare events among a large number of vaccinated persons. This information is critical to informing policy-making and clinical practice.

2.2 Herpes Zoster

Herpes Zoster (HZ) is a disease with prominent cutaneous manifestations that results from reactivation of the varicella zoster virus (VZV). The virus is most commonly acquired during childhood and causes chickenpox during primary infection.[26] The lifetime risk of HZ is estimated to be between 20%-30%, but may be as high as 50% among individuals who live to be 85 years or older.[27] HZ risk is markedly higher among persons of older age and those who are immunocompromised, as reactivation is a consequence of diminished cell-mediated immunity. Uncomplicated HZ, and sequelae such as post-herpetic neuralgia (PHN) and herpes zoster ophthalmicus (HZO) result in substantial morbidity and reduced quality of life among those affected.[28,29]

2.3 Herpes Zoster Biology and Pathogenesis

VZV is a neurotropic, double-stranded DNA virus, belonging to the herpesvirus family. The icosahedral nucleocapsid core is surrounded by an amorphous protein material and a lipid-rich envelope that is embedded with glycoproteins.[30] Other members of this family of viruses include HSV types 1 and 2, cytomegalovirus, Epstein-Barr virus, and human herpesvirus types 6, 7, and 8.[31] The similarities among these viruses has crucial implications for differential diagnoses, which will be discussed in a later section. Following VZV primary infection (chickenpox), the virus established latency via one of two possible routes: infiltration of the nerve endings of cutaneous sensory nerves and subsequent travel along these nerves to the dorsal root and cranial sensory ganglia to invade and establish latency in the sensory neurons; or, during viremia, whereby T-lymphocytes that have taken up VZV travel to and establish infection in neurons.[32,33]

Herpes zoster, and HZ-related diseases occur following the reactivation of latent VZV infection. Upon decline in VZV-specific cellular immunity beyond a critical threshold, whether due to aging or immunosuppression, the latent virus activates, replicates in keratinocytes and epithelial cells, and spreads along the affected nerve. Newly created virus-like particles are then transported to sensory neurons via central and distal axons, resulting in generalized necrosis and cell death in the skin, nerve, root, and ganglion.[34,35]

The decline in cell mediated immunity is a critical component to VZV reactivation. Although humoral immunity serves the central role in prevention of primary VZV, it is the cellular immune response that is necessary for HZ prevention and control. This can be more prominently observed in the increased risk among patients following hematopoietic stem cell transplantation, a population that experiences depleted cell mediated immunity, but maintains humoral immunity through intravenous γ-globulin.[33] Interestingly, despite immunosenescence of the cellular response, studies have found exogenous exposure to VZV, through exposure to a child with primary VZV infection, boosts cellular immunity. HZ incidence has been found to be lower among those with greater daily contact with children.[36]

2.4 Natural History of and Clinical Presentations of Herpes Zoster and Sequelae

2.4.1 Uncomplicated Herpes Zoster

Uncomplicated HZ presents initially as influenza-like-illness, with symptoms such as malaise, generalized headache, and photophobia. These may precede the rash by two or three days, as these symptoms occur soon after reactivation. Once the virus reaches the dermis and epidermis of the affected dermatome, the classic inflammation and rash occur.[31] HZ rash may present upon thoracic, cranial, lumbar, and cervical dermatomes - the thoracic being the most

common.[37] The rash typically does not cross the midline and lesions tend to form in clusters along the cutaneous sensory nerve. Pustulation is typically observed within a week of rash onset, followed by ulceration and crusting.[38] Pain resulting from HZ, either before or after rash presentation, may be described as burning, stabbing, throbbing or deep aching, tingling or stinking. Pain generally resolves within 2-4 weeks.[27,34]

Rare complications stemming from HZ include, but are not limited to, Bell's palsy, Ramsay-Hunt syndrome, transverse myelitis, transient ischemic attack, stroke, meningitis, meningoencephalitis, cerebellitis, isolated cranial nerve palsies, multiple cranial palsies, vasculopathy, myelitis, acute disseminated encephalomyelitis, Guillain-Barre syndrome (GBS), focal motor weakness, and various inflammatory disorders of eye.[16,37,39] Although rare, acute liver failure has been observed following HZ and has high mortality.[40] Differential diagnoses for HZ feature zosteriform herpes simplex (acute herpes simplex), contact dermatitis, impetigo, folliculitis, scabies, insect bites, drug-induced rash, and primary varicella infection.[37]

2.4.2 Post Herpetic Neuralgia and Herpes Zoster Ophthalmicus

HZ-related pain that does not resolve 2-4 weeks after rash onset can persist for months or years, and is referred to as PHN. Pain experienced during PHN is characterized as persistent (burning, aching, or throbbing), intermittent (stabbing or shooting), and/or mild stimulus-evoked pain (allodynia).[41] Definitions for PHN vary, ranging from any pain after rash healing to pain persisting >6 months after rash onset.[42] PHN interferes with sleep and activities of daily life among most patients, and can also result in anorexia, weight loss, fatigue, depression, withdrawal from societal activities and employment, and loss of independent living.[16,29]

HZO results from HZ reactivation with involvement of the ophthalmic division of the trigeminal nerve causing subsequent harmful complications of the eye. The ophthalmic division

can be further broken down into the nasociliary, frontal, and lacrimal branches, among which HZO most commonly results from HZ reactivation of the frontal nerves.[43] Ocular structures affected include the eyelid/conjunctiva, episcleral/sclera, cornea, anterior chamber, retina, and cranial nerves.[44]

HZO often begins with the same clinical features as uncomplicated HZ, with influenza-like-illness, accompanied by fever, myalgia, and malaise for about a week. Following this stage, macules form along the affected dermatome, which the quickly develop into papules and vesicles containing clear serous fluid and pustules over the next few days.[44] There are many severe effects of HZO resulting from damage to ocular structures, such as corneal anesthesia and ulceration, glaucoma, optic neuritis, eyelid scarring and retraction, visual impairment, and blindness among patients who do not receive antivirals.[27] Important differential diagnoses to consider for HZO include herpes simplex keratitis, other viral or bacterial conjunctivitis, uveitis, glaucoma, trauma, chemical exposure, vascular occlusion, migraine, cluster headache, trigeminal neuritis, optic neuritis, and vasculitis, among others.[45]

2.5 Epidemiology

2.5.1 Incidence and Lifetime Risk

It is widely cited, even in recent publications, that there are approximately 1 million cases of HZ each year in the United States. The research that produced this estimate utilized MarketScan commercial claims data from 2000-2001, and extrapolated from the incidence rates observed.[46] Recent publications citing this estimate fail to recognize changes in age distribution among the US population since 2000, increases in HZ incidence rates in recent years (Figure 4),[47,48] and the licensure of vaccines for HZ prevention. Despite lacking updated estimates, it

remains clear that the annual incidence of HZ in the U.S. presents a substantial burden on human health and the healthcare system.

Nearly all adults in the US are at risk of HZ, with estimations that over 95% of young adults are VZV-seropositive. Among the general U.S. population, the annual incidence rate of HZ is approximately 3.2/1,000 person-years; however, HZ incidence increases substantially with increased age. The incidence rate among adults ≥65 years old is estimated to be 10-14 cases per 1,000 person-years. Estimates of lifetime HZ incidence in the general population range between 20-30%, and rise to 50% among those living beyond 85 years.[27,34]

PHN is estimated to occur among 10%-20% of HZ cases. The risk also increases with age; the incidence among HZ cases ≥50 years old is estimated to be 18%, while it is 33% among cases ≥80 years old.[49] HZO occurs among between 10%-20% of HZ cases. The overall HZO incidence in the US is 30.9/100,000 person-years, while among adults ≥65 it is 104.6/100,000 person-years.[37]

2.5.2 HZ Risk by Immune Function

While the rate of HZ in the general population is 3.2/1,000 person-years, the rate among immunocompromised patients is considerably higher, ranging from 7.8 to 20 cases per 1000 person-years in studies using insurance claims data.[13-15] Populations considered immunocompromised include those with primary, acquired, or iatrogenic immunocompromising conditions, as well as those taking immunosuppressive therapies to treat autoimmune or inflammatory conditions. Among hematopoietic stem cell transplant, hematological malignancy, solid organ transplant, solid tumor malignancy, and HIV patient, the incidence rates of HZ range between 9 and 95 cases per 1,000 PY.[50] Only studies of hematopoietic stem cell transplant and hematological malignancy patients have reported incidence rates greater than 40/1,000 PY, while

the median incidence rate among the remaining studies was below 30/1,000 PY. The risk of PHN following HZ reactivation ranges from 6%-45%.[50] Elevated risk of HZ during use of immunosuppressing therapies, including disease modifying antirheumatic drugs (DMARDs), has been investigated through multiple studies, the findings of which were synthesized in a systematic review and meta-analysis. Use of biologics, corticosteroids, and nonbiological DMARDs were all shown to increase HZ risk after evaluating results from both clinical trials and observational studies.[51]

2.6 HZ Prevention

2.6.1 Recombinant Zoster Vaccine (RZV)

RZV is an $AS01_B$ adjuvanted recombinant VZV glycoprotein E vaccine, administered in two doses at least two months apart. RZV efficacy and safety were primarily established through two randomized clinical trials: Zoster Efficacy in Adults 50 Years of Age or Older (ZOE-50)[8] and Zoster Efficacy in Adults 70 Years of Age or Older (ZOE-70).[9] Both clinical trials excluded participants with disease- or treatment-related immunosuppression.

The primary endpoint in the ZOE-50/70 studies was vaccine efficacy against incident HZ. In ZOE-50, the estimated efficacy, with an average of 3.2 years of follow-up, was 97.2%, while estimated efficacy in ZOE-70 was 89.8%. Additionally, in the pooled ZOE-50/70 analysis, vaccine efficacy (VE) against PHN was 91.2%, and 88.8% among only adults ≥70 YOA. In the first 7 days post vaccination, solicited injection site reactions (ISRs) occurred among 81.5% of ZOE-50 RZV recipients and 74.1% in ZOE-70. The most common ISR among RZV recipients was pain in both studies (79.1% and 68.7%). Solicited general reactions were observed in 66.1% and 53.0% of RZV recipients in ZOE-50 and -70, respectively. Fatigue was most commonly

cited. Comparing vaccinated and placebo recipients in both studies, there were no statistical differences in the rates of severe adverse events (SAEs), pIMDs, or deaths between groups.

Four phase III studies of RZV have been conducted among immunocompromised patients. These included patients with solid tumors,[22] hematological malignancies,[20] renal transplants,[21] and hematopoietic stem cell transplantation (HSCT).[23] Vaccine efficacy against HZ, comparing RZV to placebo, was estimated among HSCT (68.2%) and HM (87.2%) populations. VE against incident HZ was lower among HSCT population compared to the nontransplant population; however, VE was only slightly lower between HM and non-HM populations from the other phase III trials. The primary endpoint in the ST and RT studies was the vaccine response rate (VRR), assessed separately for humoral and cell-mediated response. In the solid tumor clinical trial, only humoral VRR was assessed, estimated to be 93.8% among vaccinated patients. In the renal transplant clinical trial, vaccinated patients demonstrated humoral VRR of 80.2% and cellular VRR of 71.4%.

Risk of solicited ISRs in the first 7 days post vaccination ranged from 83.9% - 90%, while 7-day risk of systemic events ranged from 68.7% - 81.3%. The most commonly reported ISR was injection site pain among 79.5% - 87.0% of vaccinated patients. Fatigue was the most common solicited systemic reaction, reported by 45% - 69.6% of patients. The risk of unsolicited adverse events (AEs), SAEs, and pIMDs were similar between the RZV and control groups in all studies.

In October, 2017, the FDA approved RZV as a 2-dose vaccine administered to adults ≥50 between 2-6 months apart. The CDC recommended, in 2018, the use of RZV among immunocompetent adults ≥50 years old, with or without previous ZVL vaccination, and preferential use of RZV over ZVL. While the ACIP did not make a recommendation regarding

RZV use among the immunocompromised population, since this group was excluded from clinical trials, the only listed contraindication to RZV was having an allergy to any vaccine components.[52] Following additional research among immunocompromised patients, the CDC expanded its recommendation of RZV to include immunocompromised adults age ≥19 years in early 2022.[10]

2.6.2 Vaccine Adjuvants

Adjuvants are immune stimulating molecules that are added to vaccines in order to produce stronger innate immune responses, resulting in an enhanced adaptive response. Inclusion of adjuvants during vaccine administration increases cytokine production, leading mobilization of neutrophils, monocytes, and dendric cells that take up antigen to be subsequently presented to the adaptive immune system.[53] Adjuvant-prompted upregulation of molecules that are required for antigen presentation leads to more efficient antigen presentation to and uptake by the adaptive system.[54] For more than 50 years, aluminum salts (alum) were the only adjuvants used to improve vaccine response.[55] The desire for more robust and targeted immune responses following immunization lead to the development of adjuvant systems.

2.6.3 The AS01 Family

Adjuvant systems are combinations of two or more immunostimulatory molecules that function simultaneously. The two immunostimulatory molecules that are featured in AS01, MPL and QS-21, are believed to function synergistically to elicit a particularly effective immune response. MPL enhances innate immunity through activation of antigen presenting cells expressing TLR4 and subsequent cytokine and co-stimulatory molecule production, while QS-21 primarily increases antibody production.[53,56] In combination, MPL and QS-21 promote an

enhanced antigen-specific cytotoxic T-cell and TH-1 cell response through INF-γ induction as well as higher levels of antigen-specific antibody production.[55,57]

2.7 Vaccination and Autoimmunity

The theoretical biologic mechanisms contributing to vaccine-induced autoimmunity include, but are not limited to, molecular mimicry, epitope spreading, polyclonal/bystander activation.[54,58-60] Molecular mimicry is the most commonly described, and involves damage to tissue or organs by the immune system the due to structural similarity between the exogenous antigenic protein and self-peptides; epitope spreading describes the activation and polyclonal expansion of autoreactive T-cells with a range of specificities; and polyclonal/bystander activation involves the reactivation of T-cells at the site of inflammation.[58] Cytotoxic and Th1 cells are primarily responsible for autoimmunity, while humoral responses are generally protective.[61]

Vaccine-induced autoimmunity is noted in the literature to be rare, but has been described following mumps, measles, rubella (MMR); bacilli Calmette-Guerin (BCG); human papilloma virus(HPV); hepatitis B virus (HBV); and influenza vaccinations.[54,62] That being said, immune thrombocytopenic purpura risk after MMR immunization was 10-fold lower than the risk following natural infection,[59] and risk of autoimmune disorders following natural influenza infection is greater than following immunization.[54] Key considerations in the assessment of pIMDs following vaccination include theoretical risk periods,[63] systemic versus organ-specific diseases,[61] and the sample size required to detect a signal for rare events.[56]

2.8 Gaps in Knowledge

While a substantial amount of clinical and observation research has investigated RZV safety and efficacy, critical information is still missing. Characterization of RZV patterns of use is needed to identify groups at higher risk of being unvaccinated, particularly within strata of immune function. Immunocompromised patients were excluded from the pivotal RZV phase III clinical trials; additional trials were completed among this population, but only among specific immunocompromising conditions and with substantially smaller numbers of participants. More research is needed to understand the risk of adverse events following vaccination, in general and among immunocompromised patients, especially for rare outcomes such as pIMDs that require larger numbers of study participants to have adequate power for detection.

CHAPTER 3 - SPECIFIC AIMS

Herpes Zoster (HZ), commonly known as shingles, and sequelae including post herpetic neuralgic (PHN) and herpes zoster ophthalmicus (HZO) occur following the reactivation of latent varicella zoster infection.[64] HZ presents as a unilateral rash above the waist and pain described as aching, burning, stabbing, tingling, or itching.[64,65] Persistent pain months after acute HZ is characterized as PHN, and may feature constant, intermittent, or stimulus-evoked pain. HZO results from HZ that involves the ophthalmic division of the trigeminal nerve.

There are an estimated 1 million incident HZ cases in the US each year, although this figure is likely an underestimate. About one in three individuals in the U.S. will experience HZ in their lifetime. Among these, approximately 10% develop PHN[34] and 10-20% develop HZO.[30] The risk of HZ and related outcomes increases with older age,[13] and is markedly higher among immunocompromised patients.[66] Those affected by HZ and sequelae experience substantial morbidity and reduced quality of life.[28,29]

The two-dose recombinant subunit zoster vaccine (Shingrix, RZV), featuring a novel adjuvant ($AS01_B$), has high efficacy against HZ (97.2% in adults ≥50 years, 96.6%-97.9% for all age groups) and long duration of protection.[9] In 2018, the CDC made a preferential recommendation for RZV over the existing live-attenuated vaccine Zostavax (ZVL), but declined to recommend its use among immunocompromised patients, as they were excluded from clinical trials.[7] The CDC expanded its recommendation in 2022 to include immunocompromised adults aged ≥19 years in 2022.[10]

Important gaps in knowledge regarding RZV must be addressed. Although immunocompromised patients were not included in the CDC's initial recommendation, existing research reveals that these patients began receiving RZV soon after licensure. Investigating patterns of use of RZV, both generally and by immune function, can inform targeted programs to improve uptake among key populations. Recent phase III clinical trials of RZV in individuals with certain immunocompromising conditions indicate an acceptable safety profile, but have not featured the large sample sizes included in the landmark RZV efficacy trials. Further research is needed to demonstrate safety, particularly for rare adverse events, and in individuals with a broader spectrum of immunocompromising conditions.

The objectives of this study were to characterize RZV patterns of use (initiation and completion) by demographic, healthcare access, and clinical characteristics, and to evaluate post-vaccination safety using insurance claims data with the following specific aims:

Aim 1: Characterize the patterns of use of RZV between January 1, 2018 and December 31, 2019 among privately insured adults ages 50-64 years who are included in the MarketScan data**.**

- Investigate predictors of RZV series initiation (first dose) and completion (both doses) using demographic, healthcare access, and clinical characteristics.
- Among immunocompromised enrollees, stratify further by type of immunocompromising condition (HIV, malignancy, solid organ transplant, primary immunodeficiencies, and medication-induced immunosuppression).

Aim 2: Evaluate RZV safety using within-person comparisons of a post-vaccination risk period and a baseline control period among adults 50-64 years old.

- Estimate the relative incidence rates of short-term (7-day) and long-term (60-day) adverse events following RZV vaccination.

- Evaluate modification of RZV safety by immune function, comparing immunocompromised and immunocompetent adults.
- Contextualize RZV safety through evaluating the same short- and long-term safety events with incident HZ diagnosis as the index event.

This research characterized patterns of RZV administration in the first two years following licensure and provided insights into RZV safety among both immunocompromised and immunocompetent adults using real-world data.

CHAPTER 4 - METHODS

4.1 Overview

This research investigated RZV patterns of use (Aim 1) and safety (Aim 2) using insurance claims data captured in MarketScan. Analyses of patterns of use focused on available demographic (age, sex, region, urbanicity), healthcare access (type of insurance, medical office visits in the 6-months prior to study start), and clinical (immune function, type of immunocompromising condition) characteristics to identify subpopulations at higher risk of being unvaccinated or failing to complete the RZV series. These analyses were completed both for RZV initiation and completion, each separately an important clinical endpoint to ensure adequate protection against HZ and sequelae. Investigating RZV use among immunocompromised enrollees was a primary goal of the study and, therefore, patterns of use within strata of immune function and among the different types of immunocompromising conditions were additionally explored. The results generated provide essential information to targeting programs for increasing RZV initiation and completion among older adults.

After describing RZV uptake among the general population and within immunocompromised and immunocompetent enrollees, Aim 2 leveraged within-person comparisons using the self-controlled case series design to evaluate short- and long-term RZV safety. This study design implicitly controls for all time-invariant characteristics, which served as a major strength when investigating safety in MarketScan due to a lack of key demographic and clinical variables needed to control for potential confounding. This aim included numerous sensitivity analyses to test the impact of important assumptions in the study design, including the

method for characterizing time-varying immunosuppression and the length of the risk period for long-term safety, among others. Additionally, an analysis using incident diagnosis of HZ as the index event was completed to provide important context surrounding the safety of RZV. These results provide additional information regarding RZV safety, particularly among immunocompromised patients.

4.2 Data Sources

The IBM MarketScan® Commercial Claims and Encounters Database ("MarketScan")[67] includes nationwide healthcare encounter information for individuals receiving private insurance through selected employer-sponsored plans in the U.S. Data include privately insured individuals who work for employers that contribute to the MarketScan, and their families. Claims files utilized in this study include enrollment details, inpatient admissions, inpatient services, outpatient services, and outpatient pharmaceutical claims. Enrollees included in the data have unique identifiers, allowing for linkage between different files and tracking over time.

4.3 Study Populations

The study population for Aim 1 included all enrollees captured in MarketScan on January 1, 2018 with the following inclusion criteria:

- Aged 50-64 years old at study start
- Had a least 6-months of continuous insurance coverage prior to January 1, 2018
- Had prescription benefits

The lower bound on the age requirements for inclusion in Aim 1 was informed by the CDC recommendation for RZV (adults ≥50), and the upper bound was selected to avoid the

impact of dual coverage with Medicare on data quality. For this study aim, continuous coverage was defined as being continuously enrolled in insurance with lapses between coverage periods of no greater than 21 days. The 6-month lookback period prior to study start on 1/1/2018 was required for assessment of each enrollee's immune function. Prescription benefits were required as the analyses used pharmacy claims to identify RZV vaccinations and characterized immune function. Any enrollees who had received a dose of RZV prior to study start on January 1, 2018 were excluded from analysis.

Aim 2 featured similar inclusion criteria, with slight variations between the short- and long-term safety assessments. Both analyses included enrollees captured in MarketScan who had received at least one dose of RZV between October 1, 2017 – December 31, 2019. For the short-term safety analysis, RZV vaccinated enrollees were included if they:

- Were between 50-64 years old at the time of RZV initiation
- Had at least 6-months of continuous insurance coverage prior to RZV initiation for assessing immune function
- Had at least 42 days of observable time following RZV initiation
- Had at least 28 days between the two doses of RZV (among those who completed the series)
- Had at least 365 days of coverage prior to RZV initiation (only for assessment of cardiovascular and cerebrovascular events)

As with Aim 1, the same reasoning was employed when creating the requirements for age and 6-months of continuous coverage prior to RZV initiation. For this study aim, continuous coverage was defined as being continuously enrolled in insurance with lapses between coverage periods of no greater than 7 days. A shorter allowance for gaps in coverage was included in this

aim to reduce the chances of unobserved claims occurring during lapses in coverage. The requirements of 42-days of observable time after RZV initiation and, among those who completed the series, 28 days between RZV doses were included to ensure that each enrollee would have sufficient follow-up time during the control period. For safety analyses of short-term cardiovascular and cerebrovascular events, enrollees were required to have at least 365 days of coverage prior to RZV initiation so that those with a history of these events could be excluded from analysis to avoid classifying follow-up visits for prior events and new incident events.

For the long-term safety analysis, RZV vaccinated enrollees were included if they:

- Were between 50-64 years old at the time of RZV initiation
- Had at least 365 days of coverage prior to RZV initiation
- Had at least 162 days of observable time following RZV initiation
- Had at least 60 days between the two doses of RZV (among those who completed the series)

The requirement of 365 days prior to RZV initiation was included for all long-term safety assessments and accomplished both providing the necessary window for excluding enrollees with a history of events of interest and encompassed the 6-month period needed to characterize immune function. Enrollees were required to have had 162-days of observable time after RZV initiation to ensure that each enrollee would have sufficient follow-up time during the control period. Finally, the requirement of 60 days between RZV doses, among those who completed the series, was implemented to avoid overlapping risk periods between the two doses during analysis.[68] The same inclusion criteria were implemented for the short- and long-term safety analyses were implemented when using incident diagnosis of HZ as the index event.

4.4 Study Design and Follow-Up

In the first aim of this research, patterns of RZV use were characterized over the first two years following the CDC's recommendation. The study period research began on January 1, 2018 and ended December 31, 2019. Follow-up was completed in similar fashions for RZV initiation and completion. Regarding RZV initiation, follow-up began on January 1, 2018 and continued until the earliest occurrence of the following: time of vaccination; censoring due to loss of continuous coverage; aging out of the cohort when turning 65 years old; the end of follow-up on December 31, 2019. The assessment of RZV completion was completed only among initiators, began on the date of RZV initiation, and ended with the same criteria as noted for the series initiation analysis.

Aim 2 utilized a self-controlled case series design (a case-only analysis), and therefore included only enrollees who were both vaccinated and experienced the event of interest during follow-up. Although coverage prior to RZV initiation were required to characterizing immune function and excluding enrollees with a history of long-term events, only post-vaccination person-time was used for assessing relative incidence rates. For both short- and long-term events, the day of vaccination was defined as Day 1. For short-term safety (**Figure S2**) the risk period spanned the first 7-days after vaccination, inclusive of the vaccination day (i.e. days 1-7). This risk period was then followed by a 21 day washout period (days 8-21). The control period then followed (beginning day 29) and continued through the end of observation (loss of continuous coverage, aging out of the cohort, or end of observation). For long-term safety (**Figure S3**), the risk period spanned the first 60-days after vaccination, inclusive of the vaccination day (i.e. days 1-60), followed by a 60 day washout period (days 61-120). The control period then followed (beginning day 121) and continued through the end of observation.

4.5 Assessment of Measures

4.5.1 Aim 1 Measures

The primary endpoint for Aim 1 was RZV administration, which was captured in inpatient and outpatient services files using the CPT code 90750 and among pharmacy claims using NDCs: 58160-819-12, 58160-823-11, 58160-828-01, 58160-828-03, 58160-829-01, or 58160-829-03. Having two or more claims for RZV vaccination within a 21-day window was considered to reflect either duplicate records or administrative errors. In such a case, only the first claim was retained.

Patterns of use were explored by demographic, healthcare access, and clinical characteristics. These were abstracted from MarketScan enrollment, inpatient, outpatient, and pharmacy claims at study start for analyses of RZV initiation and at the time of initiation for analyses of RZV completion. Demographic variables included age (categorized into 5-year age groupings of 50-54, 55-59, 60-64), sex, region of residency, and urbanicity. Urbanicity was a derived variable, in which all enrollees with a recorded metropolitan statistical area (indicative of living in an urbanized area with a population of at least 50,000) were considered to be living in an urban area and all others in rural areas. Healthcare access variables included type of insurance plan (grouped into: comprehensive coverage, preferred provider, managed care, and high deductible plans), and the number of medical office visits in the 6-months prior to study-start. Clinical characteristics, immune function and type of immunocompromising conditions, were evaluated using the 6-month lookback period prior to study-start and utilizing claims for diagnosis codes, procedural codes, and prescription fills (see **Table S1-S5**).

4.5.2 Aim 2 Measures

Aim 2 considered only enrollees who had received at least 1 dose of RZV (identified via the methods noted in Section 4.5.1) or were diagnosed with HZ or its sequalae. For the analysis using incident HZ diagnosis as the index event, the timing of HZ diagnosis was defined as the first identified claim for HZ or sequelae via diagnosis code B02.X and all included subcodes. Demographic characteristics (age, sex, region of residency, urbanicity, and type of insurance plan) were captured at the time of RZV initiation or initial HZ diagnosis using the same methods as noted in Section 4.5.1. Characterization was completed using the 6-month lookback period and throughout the duration of follow-up using the same set of diagnosis codes, procedural codes, and prescription drug fills as in Aim 1. Continuous periods of immunosuppression were linked together using an assumed duration of immunosuppressive effect of medication (method described in **Figure S4**).

All safety events were identified via claims for diagnosis codes found in inpatient or outpatient settings. The set of codes used to identify short-term localized (cellulitis and pain), systemic (fever, anaphylaxis, myalgia, headache, fatigue, chills, nausea, and diarrhea), cardiovascular, and cerebrovascular events are featured in **Table S7**. The set of diagnosis codes used to identify long-term autoimmune, cardiovascular, and cerebrovascular events are presented in **Table S8**.

4.6 Aim 1 Analysis

The analyses of patterns of RZV initiation and completion in Aim 1 consisted of both descriptive and exploratory investigations. As an initial step, the monthly counts and rates of RZV administration among the study population were evaluated. Monthly rates were estimated

using monthly enrollment files to inform the denominators, and were presented as doses per 10,000 person-months. RZV initiation during the study period was evaluated over and stratified by demographic, healthcare access, and clinical characteristics. Enrollees contributed person-time to the denominator used for RZV initiation rates from the start of follow-up and until initiation, censoring, or the end of follow-up, whichever came first. Initiation rates were presented as RZV Dose-1 vaccinations per 1,000 person-years. The cumulative incidence of RZV initiation and completion were evaluated via the Kaplan-Meier method, accounting for censoring over time. Cumulative incidence of RZV initiation was calculated among all eligible enrollees, while the cumulative incidence of RZV series completion was only estimated among initiators. Both sets of analyses were completed overall and stratified by demographic, healthcare access, and clinical characteristics. Additionally, the cumulative incidence of completing the RZV series within the CDC's recommend 2-6 month window between doses was evaluated among RZV initiators (overall and by month of RZV initiation), and the time between doses (in months) among those who completed the series was characterized.

4.7 Aim 2 Analysis

The self-controlled case series[69] design was used to compare rates of short- and long-term safety events between prespecified risk and control periods. This approach allowed each individual to serve as their own control, addressing bias produced by non-temporally related confounding factors that would be difficult to control for if comparing vaccinated versus unvaccinated groups or recipients of different types of vaccines.[70] Associations between RZV administration and safety events were estimated using age-adjusted conditional Poisson regression, which produced incident rate ratios and corresponding 95% confidence intervals.

Person-time accrued during the washout periods was not included in the analysis. Modification of safety by immune function was then evaluated by including an interaction term between the risk period and immune function (dichotomized as immunocompromised or immunocompetent for continuous periods of time over follow-up).

To provide important context to considerations of RZV safety, the primary unmodified analyses were recreated with incident diagnosis of HZ as the index event. As those who received RZV and those who were diagnosed with HZ or sequelae reflect different populations, no direct comparisons were made between the findings of the SCCS using RZV versus HZ as the exposure.

For short-term safety, sensitivity analyses regarding the inclusion of safety events recorded during the encounter for vaccination, the need for a 21-day washout period, and the duration of immunosuppression following medication were explored. For long-term safety, the duration of the risk period, need for a washout period between risk and control, and duration of immunosuppression following medication were additionally explored.

CHAPTER 5 - MANUSCRIPT 1

5.1 Introduction

Herpes Zoster (HZ), also known as shingles, is a disease with prominent cutaneous manifestations that results from the reactivation of the varicella zoster virus, which causes chickenpox during primary infection.[26] The lifetime risk of HZ is estimated to be between 20%-30%, but may be as high as 50% among individuals aged 85 years or older.[27] The majority of HZ-related morbidity is due to HZ sequelae, including post herpetic neuralgia (PHN),[41] ocular complications of herpes zoster ophthalmicus (HZO),[43] and indirect effects such as insomnia and depression.[29] Each year in the United States (US), there are approximately 1 million HZ cases, of which 10% develop PHN and 10-20% develop HZO.[30]

Among the general U.S. population, the annual incidence rate of HZ is approximately 3.2/1,000 person-years. The risk of HZ among immunocompromised individuals is considerably higher than immunocompetent individuals, ranging from 7.8 to 20 cases per 1,000 person-years in studies using insurance claims data.[13-15] This is primarily a result of decreased T cell immunity leading to reactivation of the latent varicella zoster virus.[71] Immunocompromised populations include those with primary, acquired, or iatrogenic immunocompromising conditions, such as those receiving immunosuppressive therapies to treat cancer, autoimmune conditions, inflammatory conditions, or to prevent transplant rejection. Moreover, immunocompromised populations are more likely to have additional HZ-related complications and more severe outcomes in comparison to the immunocompetent.[16]

In June 2008, the US Centers for Disease Control and Prevention (CDC) recommended Zostavax, a live-attenuated vaccine, to prevent HZ.[65] As a live vaccine, it was contraindicated for immunocompromised individuals. In January 2018, the CDC recommended the preferential use of an adjuvanted recombinant subunit vaccine (RZV; Shingrix) among adults ≥50 years of age due to higher efficacy against HZ and its sequelae, and longer-lasting protection.[7] The Advisory Committee on Immunization Practices (ACIP) chose to not make a recommendation regarding RZV use among the immunocompromised population since this group was excluded from the two pivotal clinical trials of RZV.[8,9] However, RZV, as a recombinant protein subunit vaccine, is not contraindicated in immunocompromised individuals.[52] The limited findings from more recent randomized trials conducted among patients with solid tumors, hematological malignancies, renal transplants, and hematopoietic stem cell transplantation,[72] as well as real world evidence,[12] have demonstrated efficacy of RZV against HZ, albeit attenuated compared to effectiveness demonstrated among immunocompetent study participants. The CDC recommended RZV use among immunocompromised adults 19 years or older in January 2022[10] due to the high burden of HZ and an acceptable safety profile observed for RZV use in this population.

Even before the ACIP recommendation for RZV use in immunocompromised adults, the vaccine was starting to be administered to immunocompromised patients.[12] It is, therefore, imperative to accurately characterize the use of RZV administration among immunocompromised individuals, to identify groups with lower vaccination uptake for targeted interventions, and to continually assess vaccine safety in this high-risk group. Furthermore, as the existing RZV patterns of use research has primarily focused on series completion among those who received the first dose of the vaccine, there is limited information regarding patterns

of RZV series initiation. We aim here to characterize RZV administrations over time, including both vaccination initiation and completion, and the impact of immune function on RZV vaccination.

5.2 Methods

5.2.1 Data Sources

The IBM MarketScan® Commercial Claims and Encounters Database ("MarketScan")[67] includes nationwide healthcare encounter information for individuals receiving private insurance through selected employer-sponsored plans in the U.S. Data include privately insured individuals who work for employers that contribute to the IBM database, and their families. Claims files utilized in this study include enrollment details, inpatient admissions, inpatient services, outpatient services, and outpatient pharmaceutical claims. Enrollees included in the data have unique identifiers, allowing for linkage between different files and tracking over time.

5.2.2 Study Population and Follow-Up

This retrospective cohort study focused on RZV administrations captured in MarketScan between 1/1/2018 and 12/31/2019. While the CDC's initial recommendation for RZV among immunocompromised adults ages 50 years and older was made on January 26, 2018, the US Food and Drug Administration granted approval of RZV in October 2017. As such, we elected to begin our study on January 1, 2018 to capture any RZV vaccinations during that month.

To be included, enrollees must have been between the ages of 50-64 years at the beginning of follow-up (January 1, 2018), had prescription benefits, and have had at least 6-months of continuous coverage prior to study start (a 6-month "look-back period"). We ended observation at 65 years because of eligibility for Medicare coverage and reduced probability of

observing vaccination in MarketScan. We defined continuous coverage as continuous enrollment in their health insurance plan with lapses in coverage of no greater than 21 days. The 6-month look-back period was required to characterize baseline immune function and avoid misclassifying individuals as unvaccinated if they had been vaccinated prior to the start of follow-up. This look-back period was not included in the person-time of observation during follow-up. Any enrollees who received a dose of RZV prior to January 1, 2018 were excluded from analysis.

Enrollees were followed from 1/1/2018 through 12/31/2019 so long as they maintained continuous coverage during the study period. Observation continued until (1) the time of vaccination, (2) they were censored at lapse of coverage, (3) they aged out of the cohort when they turned 65 years, or (4) the end of follow-up.

5.2.3 Measures

Demographic variables

We extracted age, sex, region of residency, metropolitan statistical area, and insurance plan type from enrollment files. We categorized age into groupings of 50-54, 55-59, and 60-64-years using age at study start for all analyses regarding RZV Dose-1 vaccination (initiation) patterns of use, and age at first-dose vaccination for analyses of series completion of both RZV doses among those who had initiated RZV. We reported baseline characteristics for all other demographic variables extracted from the enrollment files. Enrollees were categorized as residing in an urban setting if their enrollment records indicated residence within a metropolitan statistical area (defined as an urbanized area with a population of at least 50,000 people). All other enrollees were categorized as rural. Types of insurance plans were categorized into groupings: Comprehensive Coverage; Preferred Provider; Managed Care (exclusive provider

organization, health maintenance organization, point-of-service, and point-of-service with capitation); and High Deductible Plans (consumer directed and high deductible health plans).

Engagement with Medical Offices

Medical office visits in the six months preceding the start of the study were identified via inpatient and outpatient services files; provider type and place of service were extracted for each RZV administration from the respective services and pharmacy files. We identified medical office visits during the look-back period using claims for any of the following Current Procedural Terminology (CPT) codes: 99201-99205, 99211-99215, and 99241-99245. The number of medical office visits was then categorized into zero, one, two or three, and four or more for each person.

RZV Administrations

We identified RZV vaccinations using CPT code 90750, or claims for prescription drug fills (vaccinations at pharmacies) using National Drug Codes (NDCs) 58160-819-12, 58160-823-11, 58160-828-01, 58160-828-03, 58160-829-01, or 58160-829-03. If two RZV vaccinations were identified within a 21-day window, only the first vaccination was retained to eliminate duplicate records and administrative errors.

Characterizing Immune Function

We characterized each enrollee as being immunocompromised if the enrollee's records included a claim with a diagnosis code, procedure code, or prescription drug fill indicative of any of the following during the 6-month lookback period: malignancy with or without immunosuppression, based on the presence of a bone marrow or hematological malignancy or administration of immunosuppressive cancer treatment**;** HIV infection**;** solid organ transplant; primary immunosuppression**;** or medication-induced immunosuppression (see **Table S1-S5**).

Immunosuppressive conditions were not recorded as exclusive categories, and an individual could be flagged for one or more immunosuppressive category. Enrollees without claims for any of the noted diagnosis codes, procedure codes, or prescription drug fills were categorized as immunocompetent.

Cancer treatments and other medications that result in immunosuppression were identified through a review of published literature[73-76] and the American Hospital Formulary Service online publication.[77] Enrollees were flagged as having medication-induced immunosuppression if their records featured a claim for a prescription drug fill for any of the identified immunosuppressive medications or for greater than 14 days of steroids (≥20 mg/day of prednisone or equivalent)[78] during the 6-month look-back period.

5.2.4 Data Analysis

To assess for potential selection bias in the analytic cohort, we evaluated demographic and healthcare access characteristics among the primary analytic cohort, as well as two populations of excluded enrollees (those who did not meet inclusion criteria for age and start date of insurance coverage; and those who were excluded for lacking sufficient continuous coverage during the look-back period).

We characterized monthly counts of RZV administrations and cumulative doses administered over time. We estimated rates of RZV initiation by calculating an individual's person-time contribution as the number of days between study start and either the date of vaccination, date of loss of continuous coverage, or the end of follow-up. Vaccination rates (RZV Dose-1 vaccinations per 1,000 person-years [PY]) were calculated and reported among the primary cohort: overall, and stratified by the presence and type of immunosuppression. Vaccination rates were further stratified by key demographic and healthcare access

characteristics. We compared vaccination rates both within and between strata of immune function and reported incidence rate ratios (IRRs) and corresponding 95% confidence intervals (95% CI). We calculated monthly rates of RZV initiation (per 10,000 person-months) as the number of Dose-1 RZV vaccinations divided by the number of unvaccinated enrollees meeting inclusion criteria during a given month. Monthly rates of RZV initiation were estimated and plotted by presence of immunosuppression, and type of immunosuppressive condition.

The cumulative incidence and corresponding 95% Cis of RZV initiation was estimated using the Kaplan-Meier method incorporating censoring of unvaccinated individuals at the time of lost continuous coverage or aging out of the cohort (i.e., on their 65th birthday), or administrative censoring at the end of follow-up. Cumulative incidence was estimated by age group, sex, region, urbanicity, insurance plan type, number of primary care visits in the first year of follow-up, presence of immunosuppression, and type of immunosuppressive condition.

We similarly estimated the cumulative incidence of receipt of both doses (series completion) among those who had initiated the RZV series. The reported cumulative incidence reflects the proportion fully vaccinated among initiators at any point prior to the end of follow-up. This analysis was completed overall and stratified by presence of immunosuppression. For analyses of RZV initiation, the look-back period spanned the 6 months that preceded study start on January 1, 2018. Among initiators, we measured the time between RZV doses using a 6-month look-back period that was anchored on the date of RZV initiation to assess immune function. This look-back period did not contribute to enrollee person-time in analysis.

We additionally investigated the cumulative incidence of series completion within the CDC's timing guidelines (two to six months between doses) overall and by the timing of initiation (month received). For this, we restricted analyses to those who received their first dose

of RZV by June 30, 2019 to ensure that all enrollees could be followed least 6 months after initiation. Finally, we characterized the timing between doses amongst those who had received both doses of RZV, and calculated the proportion of this subpopulation who received both doses in accordance with the CDC's recommended timing. All statistical analyses were completed using SAS® version 9.4 (SAS Institute, Cary, N.C.). The study was approved by the Institutional Review Board (IRB) of the University of North Carolina at Chapel Hill.

5.3 Results

5.3.1 Study Population

There were 4,678,729 enrollees who were between the ages of 50 to 64 years who had 6 months of continuous coverage prior to January 1, 2018. Compared to the final analytic cohort, those excluded due to insufficient coverage prior to study start tended to be younger and be more likely to have a managed care insurance plan. (**Figure S1**).

The primary analytic cohort was comprised of 52.8% women, 43.3% from the Southern region of the U.S., 86.0% who lived in urban settings, 54.0% who had a preferred provider insurance plan, and 51.9% who had one or less medical office visits during the six months preceding study start. We identified immunosuppression among 3.3% (n=156,097) of the study cohort. The most common types of immunosuppression were medication-induced (n=82,616), cancer with immunosuppression (n=57,344), solid organ transplant (n = 16,110), HIV (n=16,007), and primary immunodeficiency (n=8,197). Only 0.4% (n=63) of enrollees living with HIV with reported lab values could be confirmed to be immunosuppressed (had a CD4 count recorded below <200 cells/mm^3). Compared to the immunocompetent subgroup, immunosuppressed enrollees were more likely to be older, female, and have a greater number of medical office visits during the lookback period (**Table 1**).

Table 1: Characteristics of privately insured adults, aged 50-64 years in MarketScan, stratified by immune function, 1/1/2018 - 12/31/2019

	Overall (n = 4,678,729)		Immunocompetent (n = 4,522,632)		Immunocompromised* (n = 156,097)	
	n	%	n	%	n	%
Age (years)						
50-54	1,573,725	33.6	1,528,255	33.8	45,470	29.1
55-59	1,648,657	35.2	1,594,154	35.2	54,503	34.9
60-64	1,456,347	31.1	1,400,223	31.0	56,124	36.0
Sex						
Female	2,471,838	52.8	2,385,796	52.8	86,042	55.1
Male	2,205,760	47.2	2,135,753	47.2	70,007	44.9
Geographic Region						
Northeast	920,147	19.7	888,524	19.7	31,623	20.3
North Central	1,005,720	21.5	972,529	21.5	33,191	21.3
South	2,022,852	43.3	1,953,253	43.3	69,599	44.7
West	720,049	15.4	698,709	15.5	21,340	13.7
Urbanicity†						
Urban	3,546,387	86.0	3,429,085	85.9	117,302	86.2
Rural	579,638	14.0	560,920	14.1	18,718	13.8
Insurance Plan Type‡						
Comprehensive	179,550	3.9	173,516	3.9	6,034	4.0
Preferred Provider	2,459,722	54.0	2,375,459	54.0	84,263	55.7
Managed Care	832,658	18.3	804,325	18.3	28,333	18.7
High Deductible	1,079,941	23.7	1,047,219	23.8	32,722	21.6
Medical Office Visits§						
0	1,422,648	30.4	1,416,877	31.3	5,771	3.7
1	1,005,917	21.5	991,796	21.9	14,121	9.0
2 or 3	1,212,001	25.9	1,174,841	26.0	37,160	23.8
4 or more	1,038,163	22.2	939,118	20.8	99,045	63.5

* Immunocompromised includes those identified as having any of the follow non-exclusive conditions: malignant cancer with immunosuppression, HIV, solid organ transplant, primary immunodeficiency, or medication-induced immunosuppression

† MSA – population size of least 50,000 considered urban

‡ Groupings include: Comprehensive Coverage; Preferred Provider; Managed Care (exclusive provider organization, health maintenance organization, point-of-service, and point-of-service with capitation); High Deductible Plans (consumer directed and high deductible health plans).

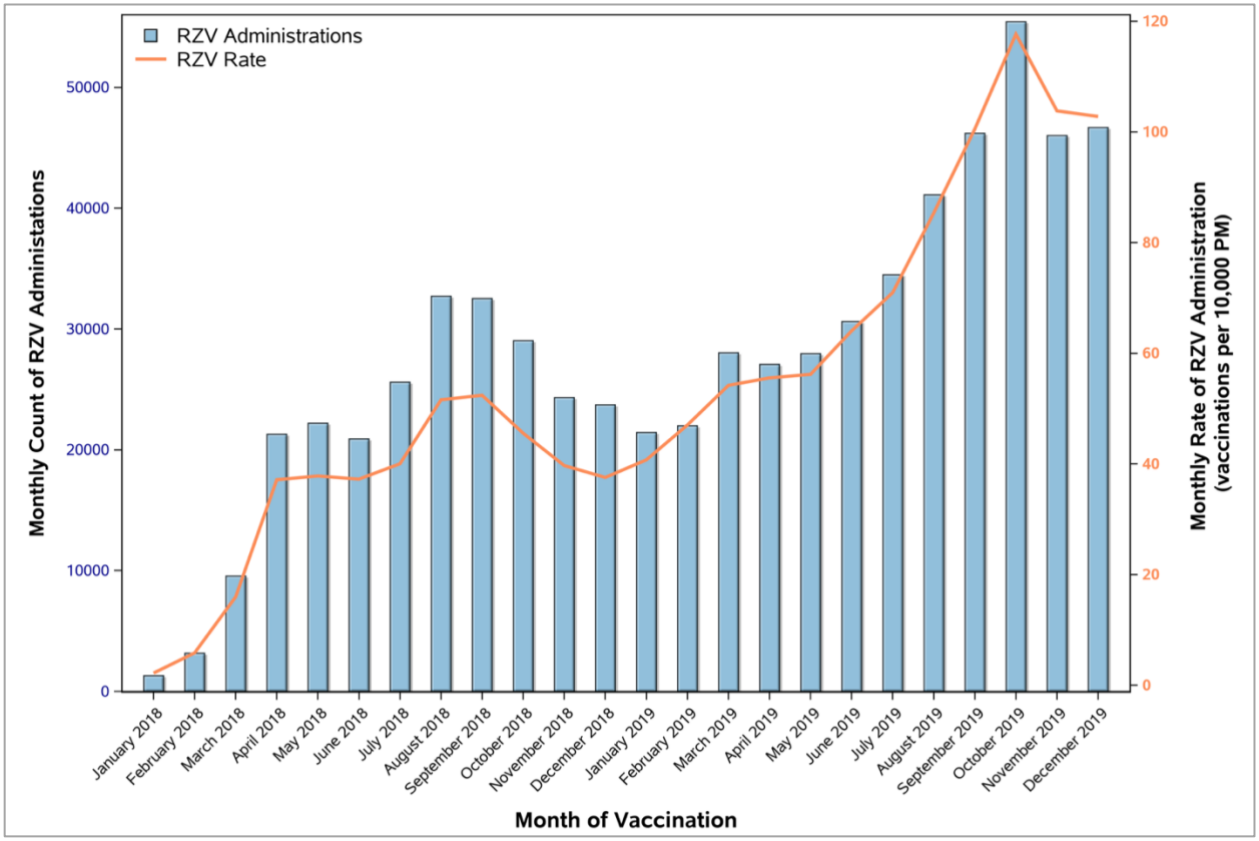
§ Number of medical office visits identified during the 6-month look back period.

5.3.2 RZV Administrations Over Time

Among our study cohort, there were 572,544 RZV administrations: 138,320 enrollees received only one dose, and 217,112 received two doses. The number of doses administered per month ranged from 1,343 in January 2018 (Rate: 2.2 doses per 10,000 person-months) to 45,476 in October 2019 (Rate: 117.7 doses per 10,000 person-months) (**Figure 1**). During this period,

there was a localized peak in the monthly rate of vaccination in August and September of 2018. Similar temporal patterns of monthly RZV vaccination counts and rates were observed among all enrollees in MarketScan, which included 830,766 total RZV administrations (224,842 enrollees who received only Dose-1 of the vaccine and 300,200 who received both doses).

Figure 1: Number of RZV doses per month and monthly rates of RZV vaccinations over time among adults 50-64 years old (doses per 10,000 person-months), MarketScan, 1/1/2018 - 12/31/2019



Abbreviations: RZV = recombinant zoster vaccine; PM = person-months
Monthly counts of RZV vaccinations (doses 1 and 2) range from 1,343 (January 2018) to 45,476 (October 2019).

5.3.3 Patterns and Correlates of RZV Vaccination Initiation

The overall rate of RZV initiation was 48.6 doses/1,000 PY (**Table 2**). Vaccination rates varied markedly by age group, ranging from 30.6 doses/1,000 PY for those 50-54 years old (95% CI: 30.4-30.9) to 71.0 doses/1,000 PY for those 60-64 years old (95% CI: 70.6-71.3). There was a higher rate of vaccination among women compared to men and among enrollees living in urban

versus rural areas. With respect to insurance plan types, those who had high deductible insurance had higher rates of vaccination (55.0 doses/1,000 PY [95% CI: 54.6-55.3]) compared to all other insurance types. Vaccination rates increased with higher numbers of medical office visits within the 6 months prior to study start, from 33.7 doses/1,000 PY (95% CI: 33.5-34.0) among those who had zero medical office visits, to 62.8 doses/1,000 PY (95% CI: 62.4-63.2) among those with four or more medical office visits in the first year of follow-up.

Stratification by immune function revealed substantially higher rates of initiation among the immunosuppressed group (63.9 doses/1,000 PY; 95% CI: 62.9-64.9), compared to the immunocompetent group (48.1 doses/1,000 PY; 95% CI: 47.9-48.2) (**Table 2**). Within each stratum of immunosuppression, we observed similar patterns of vaccination rates across the levels of age groups, region of residence, urbanicity, and type of insurance plan. Although both strata of immune function demonstrated increased vaccination rates with increased number of medical office visits, the differences in rates between strata become attenuated at higher numbers of medical office visits. Additionally, while women had a significantly higher rate of initiation compared with men among the immunocompetent (IRR=1.18; 95% CI: 1.17-1.19), there was no difference in rates among immunosuppressed enrollees by sex (IRR=0.99, 95% CI: 0.96-1.02).

The highest rate of RZV initiation was 87.9 doses/1,000 PY among those living with HIV (**Table 3**). Vaccination rates increased with age, and were higher among those living in urban versus rural settings within every type of immunosuppressive condition. Those living with HIV had higher rates of vaccination in the first 9 months of the time period studied (significantly higher in months 4 and 5) compared with all other types of immunosuppression, but there were no differences later on in the study period (**Figure 2**).

Table 2: Incidence rates (IR) of RZV initiation (per 1,000 person-years), overall and stratified by presence of any immunocompromising condition, among MarketScan enrollees 50-64 years old who had 6 months of continuous coverage prior to study start, 1/1/2018 - 12/31/2019

	Overall		Immunocompetent				Immunocompromised*				Between Strata Comparisons†	
	IR	95% CI	IR	95% CI	IRR	95% CI	IR	95% CI	IRR	95% CI	IRR	95% CI
Total Population	48.6	48.4, 48.7	48.1	47.9, 48.2	-	-	63.9	62.9, 64.9	-	-	1.33	1.31, 1.35
Age (years)												
50-54	30.6	30.4, 30.9	30.2	30.0, 30.4	-	-	45.1	43.6, 46.6	-	-	1.49	1.44, 1.54
55-59	49.6	49.4, 49.9	49.1	48.8, 49.4	1.63	1.61, 1.64	65.1	63.4, 66.8	1.44	1.38, 1.51	1.32	1.29, 1.36
60-64	71.0	70.6, 71.3	70.6	70.2, 70.9	2.33	2.31, 2.36	81.8	79.7, 83.9	1.81	1.74, 1.89	1.16	1.13, 1.19
Sex												
Female	52.1	51.9, 52.3	51.7	51.5, 52.0	1.18	1.17, 1.19	63.5	62.1, 64.9	0.99	0.96, 1.02	1.23	1.20, 1.25
Male	44.5	44.3, 44.7	43.9	43.7, 44.1	-	-	64.1	62.6, 65.7	-	-	1.46	1.43, 1.50
Region												
Northeast	41.7	41.4, 42.0	41.2	40.9, 41.5	0.89	0.88, 0.90	56.3	54.3, 58.5	0.94	0.90, 0.98	1.37	1.32, 1.42
North Central	54.2	53.9, 54.6	53.8	53.4, 54.1	1.16	1.15, 1.17	67.9	65.6, 70.2	1.13	1.08, 1.18	1.26	1.22, 1.31
South	46.7	46.5, 46.9	46.2	46.0, 46.5	-	-	60.1	58.6, 61.6	-	-	1.30	1.27, 1.33
West	54.9	54.4, 55.3	54.1	53.7, 54.6	1.17	1.16, 1.18	82.5	79.3, 85.9	1.37	1.31, 1.44	1.53	1.46, 1.59
Urbanicity												
Urban	49.3	49.1, 49.5	48.7	48.5, 48.9	-	-	65.9	64.7, 67.1	-	-	1.35	1.33, 1.38
Rural	40.2	39.8, 40.7	40.0	39.5, 40.4	0.82	0.81, 0.83	49.2	46.7, 51.9	0.75	0.72, 0.77	1.23	1.17, 1.30
Insurance Plan Type												
Comprehensive	38.6	37.9, 39.4	38.3	37.6, 39.0	0.83	0.81, 0.84	48.8	44.6, 53.5	0.79	0.72, 0.87	1.27	1.16, 1.40
Preferred Provider	46.9	46.7, 47.1	46.4	46.2, 46.6	-	-	61.8	60.5, 63.2	-	-	1.33	1.30, 1.36
Managed Care	47.7	47.3, 48.1	47.1	46.8, 47.5	1.02	1.01, 1.03	64.2	61.8, 66.6	1.04	0.99, 1.08	1.36	1.31, 1.41
High Deductible	55.0	54.6, 55.3	54.4	54.1, 54.8	1.17	1.16, 1.18	72.8	70.5, 75.2	1.18	1.13, 1.22	1.34	1.29, 1.38
Medical Office Visits												
0	33.7	33.5, 34.0	33.7	33.4, 33.9	-	-	52.0	47.4, 57.0	-	-	1.54	1.41, 1.69
1	48.0	47.7, 48.4	47.9	47.6, 48.2	1.42	1.41, 1.44	58.1	55.0, 61.4	1.12	1.00, 1.24	1.21	1.15, 1.28
2 or 3	54.9	54.6, 55.3	54.7	54.3, 55.0	1.62	1.61, 1.64	64.0	62.0, 66.1	1.23	1.12, 1.36	1.17	1.13, 1.21
4 or more	62.8	62.4, 63.2	62.5	62.1, 62.9	1.86	1.84, 1.88	65.5	64.2, 66.8	1.26	1.15, 1.38	1.05	1.03, 1.07

Abbreviations: RZV = recombinant zoster vaccine; IR = incidence rate; IRR = incidence rate ratio; 95% CI = 95% confidence interval

* Immunocompromised enrollees include all identified as having any of the following: malignant cancer with immunosuppression, HIV, solid organ transplant, primary immunodeficiency, or medication-induced immunosuppression.

† Comparing immunocompromised enrollees to immunocompetent, using immunocompetent enrollees as the referent category.

Table 3: Incidence rates of RZV Initiation (per 1,000 person-years) among immunocompromised enrollees, stratified by type of immunocompromising conditions, MarketScan, 1/1/2018 - 12/31/2019

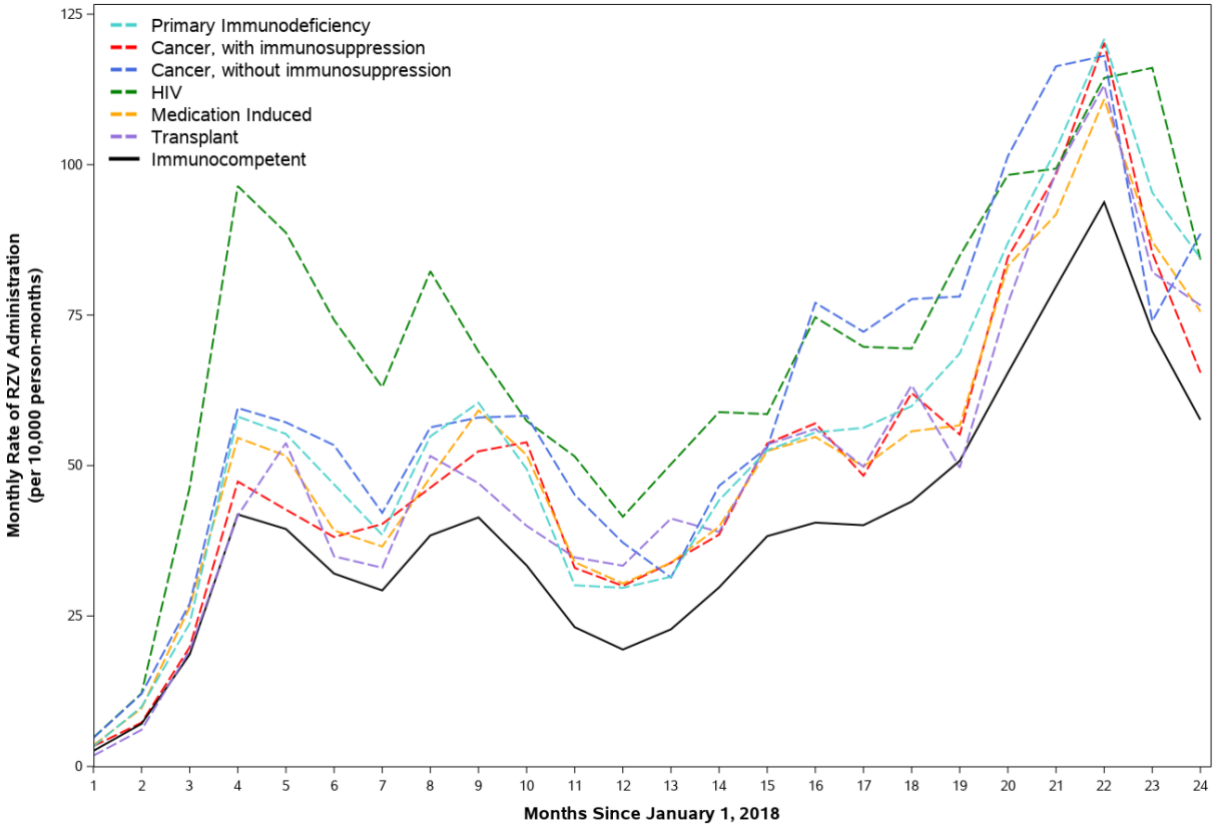
	HIV		Cancer, IC		Cancer, non-IC*		Solid Organ Transplant		Primary Immunodeficiency		Medication-Induced	
Number of Enrollees	16,007		57,344		180,510		16,110		8,197		82,616	
	IR	95% CI	IR	95% CI	IR	95% CI	IR	95% CI	IR	95% CI	IR	95% CI
Total Population	87.9	84.2, 91.7	59.3	57.7, 61.0	65.6	64.7, 66.6	59.1	56.1, 62.2	72.0	67.4, 76.9	61.7	60.3, 63.1
Age (years)												
50-54	71.2	66.3, 76.4	40.2	37.6, 42.9	39.4	38.0, 41.0	41.4	37.2, 46.2	48.2	41.7, 55.8	41.2	39.3, 43.2
55-59	92.1	86.0, 98.6	59.1	56.4, 61.9	64.0	62.5, 65.6	62.0	57.1, 67.3	70.1	62.7, 78.3	63.1	60.9, 65.4
60-64	116.6	107.4, 126.6	74.2	71.1, 77.4	84.6	82.8, 86.4	74.0	68.1, 80.4	96.9	87.6, 107.2	81.7	78.9, 84.6
Sex												
Female	53.9	47.8, 60.9	61.0	58.8, 63.2	67.6	66.4, 68.9	64.9	60.6, 69.5	72.0	66.4, 78.2	65.1	63.3, 66.9
Male	96.0	91.8, 100.4	56.7	54.2, 59.4	62.6	61.2, 64.1	52.4	48.4, 56.7	71.4	63.8, 80.	56.4	54.4, 58.5
Region												
Northeast	78.8	71.7, 86.5	54.7	51.4, 58.1	56.6	54.7, 58.5	43.0	37.3, 49.5	60.1	51.4, 70.2	53.4	50.6, 56.4
North Central	104.1	92.7, 116.9	62.7	58.9, 66.6	70.4	68.2, 72.6	73.1	66.5, 80.4	77.7	67.4, 89.6	65.5	62.7, 68.5
South	74.4	69.8, 79.4	57.1	54.7, 59.6	64.8	63.4, 66.2	52.7	48.5, 57.2	69.3	62.6, 76.7	58.5	56.6, 60.6
West	130.5	119.7, 142.2	70.3	65.2, 75.7	75.7	72.9, 78.6	74.7	66.0, 84.6	90.4	77.1, 106	78.1	73.8, 82.8
Urbanicity												
Urban	89.5	85.6, 93.7	61.0	59.1, 63	66.7	65.6, 67.8	61.2	57.7, 64.8	73.9	68.5, 79.6	63.0	61.4, 64.6
Rural	68.6	53.9, 87.3	45.3	41.1, 49.9	54.4	51.9, 57.1	50.1	42.7, 58.8	55.1	43.6, 69.8	50.2	46.9, 53.6
Insurance Plan Type												
Comprehensive	73.9	53.3, 102.4	53.3	45.9, 61.9	49.2	45.2, 53.5	45.6	34.1, 61.1	54.0	36.5, 80.0	44.6	39.4, 50.6
Preferred Provider	87.3	82.4, 92.6	56.6	54.5, 58.9	63.7	62.4, 65.0	54.4	50.5, 58.6	69.0	63.0, 75.6	60.2	58.4, 62.1
Managed Care	89.4	82.2, 97.2	56.8	53, 60.8	64.4	62.1, 66.7	54.3	47.9, 61.6	77.7	66.3, 91.2	60.8	57.6, 64.3
High Deductible	94.8	85.8, 104.7	70.4	66.6, 74.5	74.9	72.8, 77.1	76.6	69.6, 84.3	81.1	71.0, 92.8	69.8	66.7, 72.9
Medical Office Visits												
0	65.9	56.1, 77.3	49.8	39.5, 62.7	56.6	51.8, 61.9	35.3	26.0, 47.9	39.9	19.9, 79.7	46.8	40.7, 53.8
1	72.6	65.8, 80.0	50.8	45, 57.3	56.9	54.6, 59.3	55.5	46.9, 65.7	53.3	38.4, 73.9	52.2	47.8, 56.9
2-3	90.7	84.4, 97.4	63.9	60.1, 67.9	63.1	61.5, 64.8	58.0	52.3, 64.3	60.5	51.1, 71.7	57.2	54.6, 60.0
4 or more	101.3	94.7, 108.3	59.1	57.1, 61.1	70.6	69.1, 72.0	62.1	58.1, 66.2	76.9	71.4, 82.8	65.3	63.6, 67.1

Abbreviations: RZV = recombinant zoster vaccine; IR = incidence rate; 95% CI = 95% confidence interval; IC = immunocompromising

*Enrollees with diagnoses of non-immunosuppressive malignant cancers and who did not receive immunosuppressive treatment; these individuals were not included in the immunocompromised group.

Lists of ICD-10-CM diagnosis codes, CPT codes, and NDCs are presented separately for each: Cancer (Tables S1a-c; with and without immunosuppression), HIV (Tables S2a-b), Solid Organ Transplant (Table S3a-c), Primary Immunodeficiencies (Table S4), and medication-induced immunosuppression (Table S5a-b).

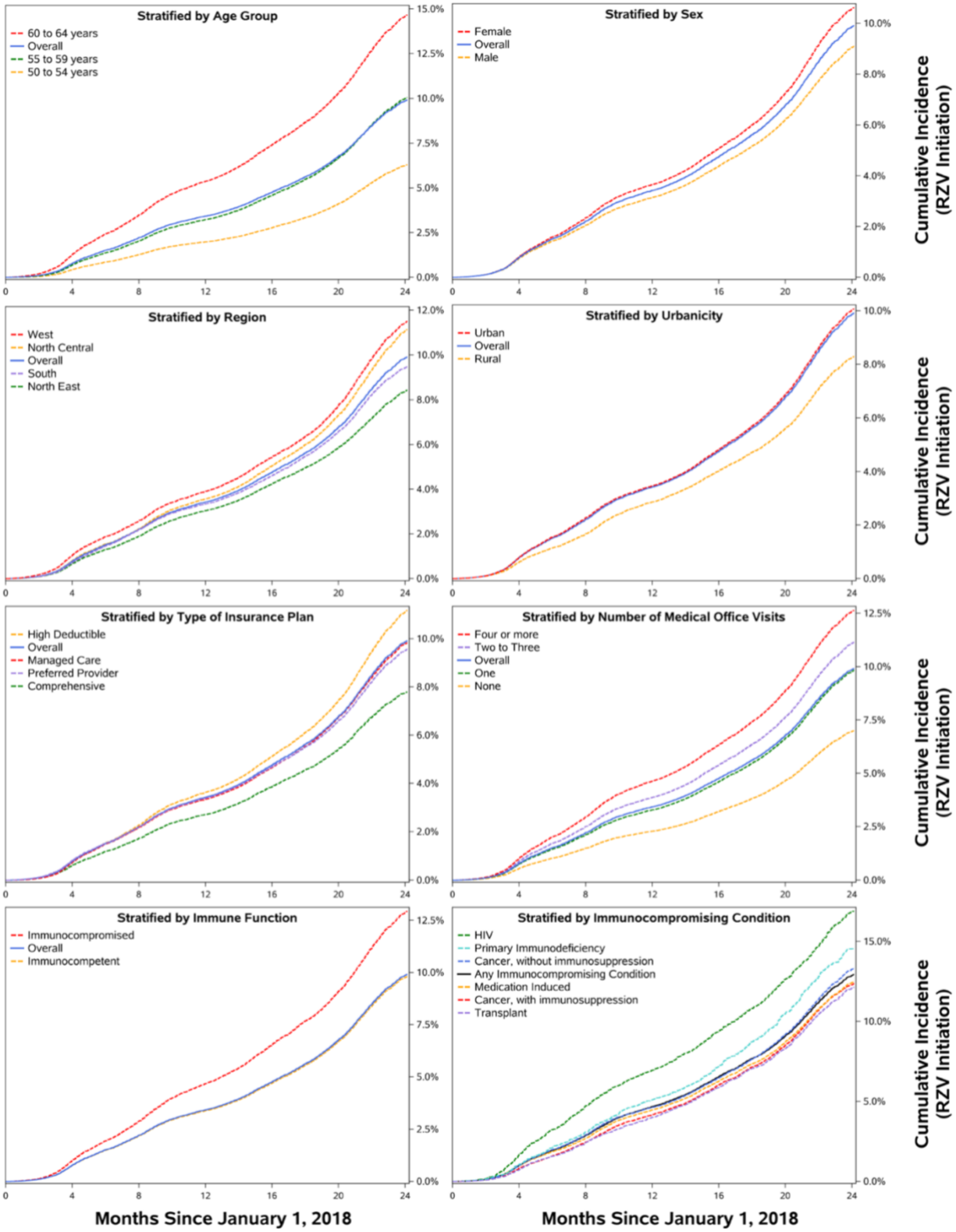
Figure 2: Monthly rates of RZV series initiation, immunocompetent versus types of immunocompromising conditions (doses per 10,000 person-months), MarketScan, 1/1/2018 - 12/31/2019



Abbreviations: RZV = recombinant zoster vaccine; HIV = Human Immunodeficiency Virus

The overall cumulative incidence of RZV initiation by the end of the study period was 10.0% (**Figure 3,** data in **Table S6**). The cumulative incidence of initiation increased with increasing age, and was greater among women, those living in urban settings, and those with high-deductible health insurance plans. The same patterns as those found among overall rates of RZV initiation were observed when stratifying the analysis by demographic and healthcare access variables, and immunosuppression.

Figure 3: Cumulative incidence of RZV initiation by key demographic, healthcare access, and clinical variables, MarketScan, 1/1/2018 - 12/31/2019



Abbreviations: RZV = recombinant zoster vaccine; HIV = Human Immunodeficiency Virus
The underlying data for each panel are presented in **Table S6.**

5.3.4 Patterns and Predictors of Receipt of Both Doses of RZV (Completion)

The cumulative incidence of RZV series completion was 89.5% among those who initiated the RZV series (**Table 4**). Completion rates were higher among those 60-64 years old compared to the other two age groups. Those who received their first dose of RZV at a pharmacy were most likely to complete the series (92.7%), followed by mobile units (90.1%) and mass immunization centers (88.1%), while those who initiated at an outpatient hospital demonstrated the lowest proportion of receiving both RZV doses (77.1%). RZV completion did not differ by immune status or immunocompromising condition.

Among those who received both doses, 88.6% (220,582/248,916) received the doses in accordance with the CDC's two to six month guideline, with an average of 3.7 months between doses (**Figure 4**)**.** The cumulative incidence of timely completion of the vaccination series was 70.2% (95% CI: 70.0, 70.4). This varied by the month in which Dose-1 was received, starting at 75.1% (95% CI: 72.7, 77.4) in January 2018, dropping to 59.9% (95% CI: 59.2, 60.6) in August 2018, and rising up to 78.2% (95% CI: 77.6, 78.8) by June 2019 (**Figure 5**).

Table 4: Cumulative Incidence of RZV series completion by December 31, 2019, among privately insured adults 50-64 years old who initiated RZV, MarketScan, 1/1/2018 - 12/31/2019

	Overall D-2 %	Immunocompetent			Immunocompromised		
		Total Dose-1	D-2 %	95% CI	Total Dose-1	D-2 %	95% CI
Overall	89.5	334,575	89.6	89.2, 90.0	16,134	88.6	87.6, 89.6
Age (years)							
50-54	87.3	55,709	87.3	85.9, 88.6	2,747	86.3	83.6, 88.8
55-59	89.0	109,494	89.0	88.4, 89.5	5,504	88.5	87.1, 89.8
60-64	90.7	169,372	90.8	90.2, 91.3	7,883	89.4	88.2, 90.5
Sex							
Female	89.6	190,982	89.7	89.2, 90.1	9,000	88.6	87.5, 89.6
Male	89.4	7,132	89.4	88.7, 90.0	7,132	88.5	86.9, 90.1
Geographic Region							
Northeast	89.6	2,994	89.7	88.9, 90.4	2,994	88.4	86.6, 90.1
North Central	91.4	3,464	91.3	90.5, 92.1	3,464	92.2	90.5, 93.8
South	88.5	6,981	88.6	87.9, 89.2	6,981	87.4	86.2, 88.6
West	89.6	2,652	89.7	88.3, 91.0	2,652	87.7	83.2, 91.4
Urbanicity							
Urban	89.3	259,138	89.3	88.8, 89.8	12,618	88.3	87.1, 89.5
Rural	90.2	34,733	90.2	88.9, 91.5	1,519	89.5	86.5, 92.0
Insurance Plan Type							
Comprehensive	89.1	9,677	89.1	87.9, 90.2	468	90.0	85.2, 93.7
Preferred Provider	89.6	166,303	90.2	89.4, 90.9	8,267	88.7	87.1, 90.3
Managed Care	88.8	67,930	88.8	86.8, 90.6	3,399	88.5	86.6, 90.3
High Deductible	90.1	83,453	89.7	89.2, 90.1	3,623	88.8	87.0, 90.3
Medical Office Visits							
0	88.9	70,472	88.9	87.9, 89.9	493	86.1	80.9, 90.5
1	89.4	73,466	89.4	88.6, 90.1	1,339	88.1	84.2, 91.3
2-3	90.0	100,020	90.0	89.1, 90.9	3,924	89.1	87.3, 90.7
4 or more	89.6	90,617	89.7	89.1, 90.2	10,378	88.3	87.4, 89.2
Place Received Dose-1							
Pharmacy	92.7	179,426	92.8	92.4, 93.1	8,699	91.0	90.1, 91.9
Medical Office	85.9	132,437	85.9	84.8, 86.9	6,056	86.1	84.0, 88.0
Mobile Unit	90.1	10,522	90.2	89.0, 91.3	506	87.5	83.3, 91.0
Outpatient Hospital	77.1	6,110	76.7	74.6, 78.8	615	79.4	74.4, 84.0
State/Local Public Health Clinic	87.3	1,011	87.0	83.6, 90.0	38	94.8	80.8, 99.5
Mass Immunization Center	88.1	1,518	88.6	83.4, 92.8	72	81.4	68.5, 91.3
Other/Unknown	86.0	3,551	86.2	82.9, 89.1	148	87.5	76.3, 95.0
Immunocompromising Condition							
HIV	-	-	-	-	2,155	87.6	84.2, 90.6
Cancer, with immunosuppression	-	-	-	-	5,090	89.2	87.7, 90.6
Cancer, without immunosuppression*	-	-	-	-	18,687	91.1	89.9, 92.2

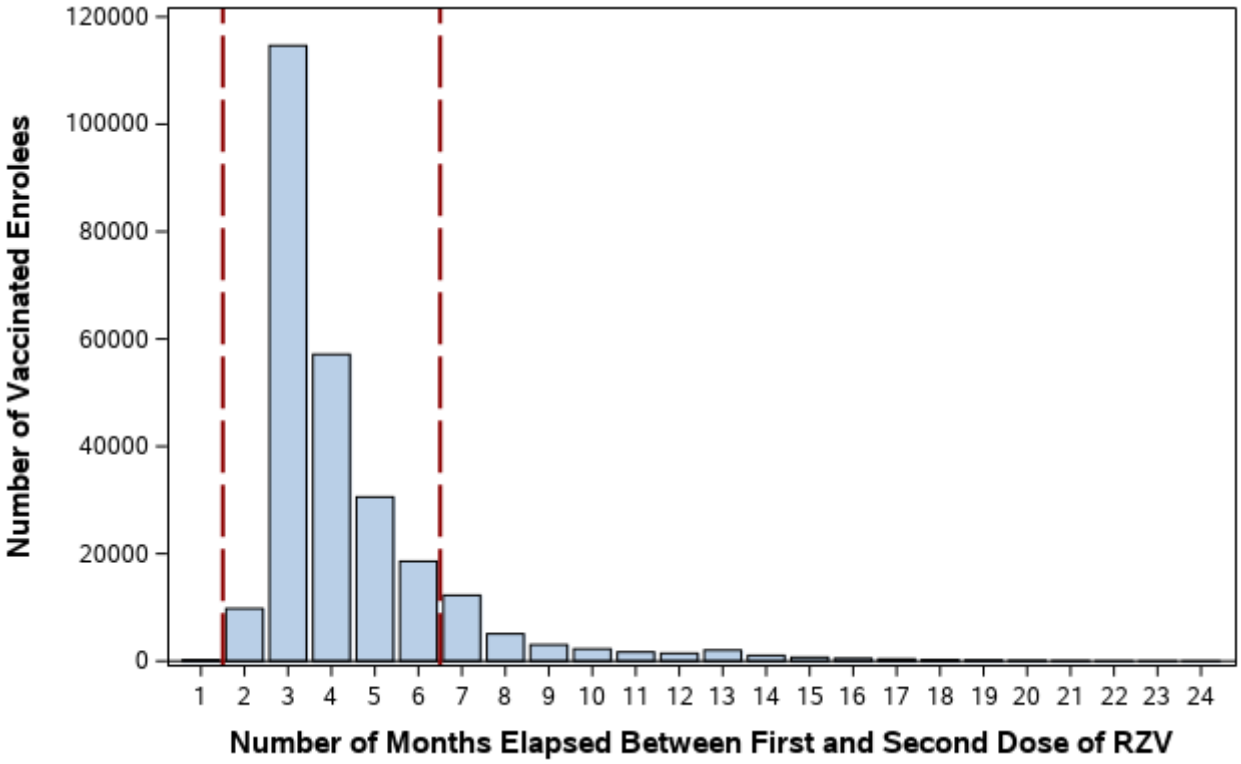
Transplant	-	-	-	-	1,558	90.8	88.0, 93.2
Primary Immunodeficiency	-	-	-	-	1,015	89.7	86.6, 92.4
Medication-Induced	-	-	-	-	8,590	87.9	86.9, 88.9

Abbreviations: RZV = recombinant zoster vaccine; D-2 = RZV completion; HIV = human immunodeficiency virus

* Enrollees who had cancer without immunosuppression are not included in the immunocompromised cohort.

Cumulative incidence was estimated with follow-up beginning at time of RZV initiation. Individuals were censored when they lost continuous coverage or turned 65.

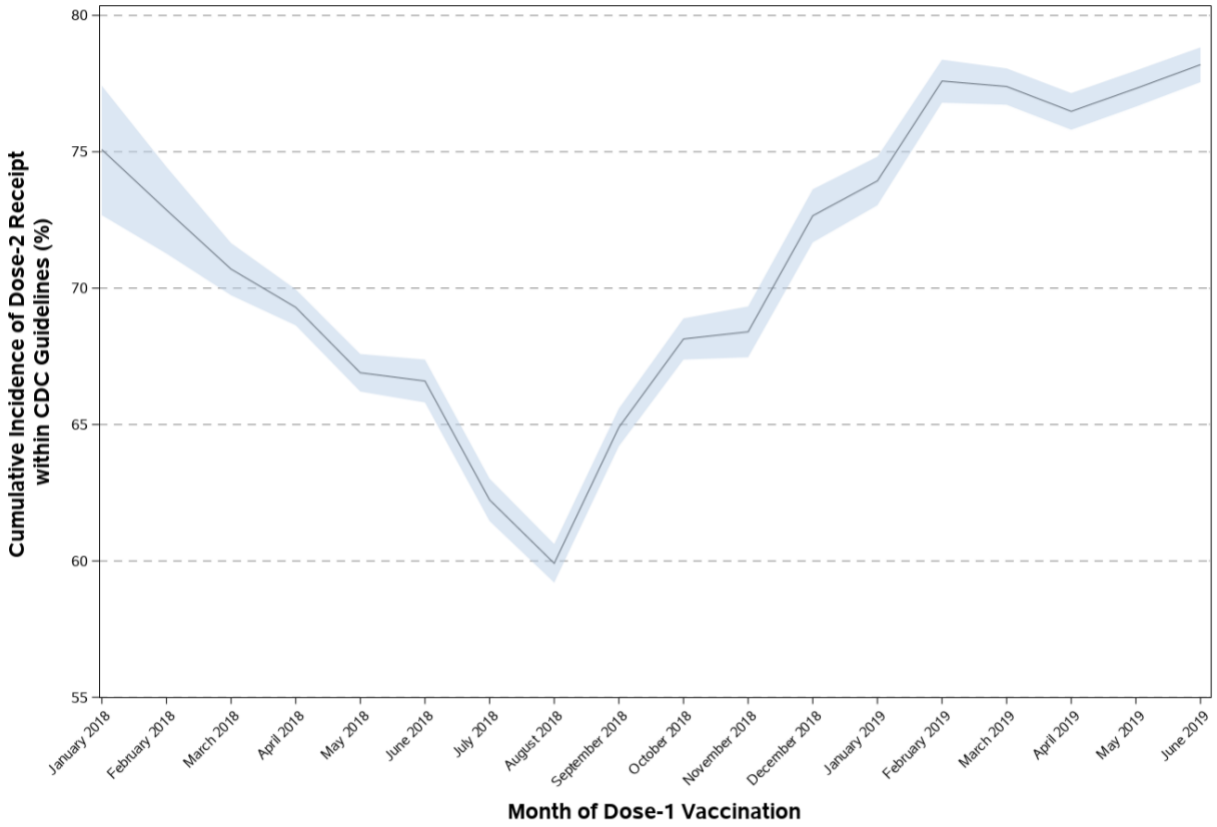
Figure 4: Time elapsed, in months, between the first and second dose of RZV vaccination, adults 50-64 years old, MarketScan, 1/1/2018 - 12/31/2019



Abbreviations: RZV = Recombinant Zoster Vaccine

The area of the graph between the dashed red bars reflects the CDC's recommending timing between the first and second dose of RZV. 88.6% (220,582/248,916) of second dose vaccinations occurred in accordance with the CDC guidelines.

Figure 5: Cumulative incidence of RZV series completion within CDC timing guidelines, by month of RZV initiation, among adults 50-64 years old who initiated the RZV series by the end of June 2019, MarketScan, 1/1/2018 - 12/31/2019



Abbreviations: RZV = recombinant zoster vaccine; CDC = Centers for Disease Control and Prevention
The blue shaded area represents the 95% confidence interval around proportions of timely completion of the RZV series.

5.4 Discussion

Herpes zoster produces substantial morbidity among US adults, and outcomes are more severe for immunocompromised patients. RZV provides the best method for reducing the burden of HZ and its sequelae. While the overall cumulative incidence of RZV initiation over the period studied was suboptimal (10.0%), a most of those who initiated the series completed it (cumulative incidence 89.5%) by the end of follow-up. We found higher rates of RZV initiation among immunocompromised adults, but RZV completion did not differ by immune status.

Furthermore, there was a higher proportion of series completion among vaccinated enrollees who received their first dose at a pharmacy compared to all other settings, including medical offices.

Overall, rates of RZV initiation increased with age and were higher among women compared to men, consistent with trends reported in recent publications.[18,79] While our study observed higher rates of series completion overall, we observed a similar incidence of RZV series completion within 6-months (70.2%) as estimated in the Kaiser (67.2%),[17] IQVIA (70.4%),[18] and Canadian (71.8%)[19] studies.

While immunocompromised populations were not included in the CDC's original recommendation for RZV vaccination, we found a higher rate of RZV initiation among immunocompromised enrollees compared to immunocompetent, suggesting that vaccine providers are using their judgment regarding risks and benefits of RZV to recommend it to their immunocompromised patients. Within strata of immune function, the patterns of use by demographic and healthcare access variables of interest were very similar. Comparing the different types of immunosuppressive conditions, those with HIV had the highest rates of initiation, while those with immunosuppressive cancer or a history of solid organ transplant had lower rates. Notably, it is likely that a small proportion of the population with HIV were immunosuppressed, as shown by the very low proportion with a CD4 count <200 cells/mm^3. Among the vaccinated, the cumulative incidence series completion did not differ by immune status or type of immunosuppressive condition. Given that the CDC has expanded their recommendations to include immunocompromised adults aged 19 years and older,[10] our findings could be used to target efforts to increase RZV uptake among this population.

We observed frequent missed opportunities for RZV initiation, as adults who had four or more medical office visits prior to study start had relatively low vaccination rates. Medical

providers should take advantage of opportunities to get patients to begin the RZV series, particularly given the high rates of series completion. Additionally, series completion rates were highest among those who got their first dose at a pharmacy. This setting for vaccinations likely serves as a convenient place for people to get vaccinated and could be leveraged to achieve higher vaccination rates. Implementation of automated reminders via electronic medical records, use of standing orders for vaccines, and co-administration of vaccines (such as RZV vaccination at the time of pneumococcal vaccination) are proven methods of increasing vaccination rates.[80]

The monthly counts and rates of vaccinations might reflect the impact of the RZV shortage reported in June 2018.[81] We observed decreases in the number of monthly RZV administrations in the months following announcement of the shortage. Furthermore, fewer enrollees who received their first dose just before or during the shortage received their second dose within the CDC's 2-6 month recommendation. Clinical trials have not evaluated RZV efficacy when the second dose is given outside of the 6-month window; however, real world evidence indicates that effectiveness is not significantly different between those who got within 6 months and those 6-12 months.[12] Additionally, the findings from a clinical trial of immunogenicity suggest that those who received a delayed second dose of RZV did not have an inferior immune response.[82]

This large, longitudinal study provided a unique opportunity to evaluate patterns of RZV vaccination over time, and enabled stratification by important variables of interest including immune status. Because we used insurance claims to identify vaccinations, we did not observe vaccinations for which enrollees paid out of pocket or through some other mechanism. However, given the cost of the vaccine ($140/dose)[83] and required vaccination coverage by commercial insurance plans, we likely observed most instances of vaccination. Our algorithm for

characterizing cancer with immunosuppression was conservative, and may have misclassified some of these individuals as immunocompetent. Additionally, the presence of a claim for an immunocompromising medication, such as high-dose steroids, does not guarantee that the medication was used as directed, and thus we might have misclassified some of these individuals as immunocompromised. Nonetheless, characterizing vaccination rates by immune status provides improved understanding of how RZV has been used in real-world settings among patients with different health status.

In conclusion, we found a relatively low initiation of RZV following the CDC recommendation, with lower uptake in men, those living in rural areas and in the Northeast and the South, and those of younger age. While initiation of RZV vaccination was low, overall RZV series completion was high. Also, RZV initiation rates were higher among immunosuppressed enrollees compared to immunocompetent, despite these groups not being included in the CDC's initial RZV recommendations during the study period. Due to their high burden of disease, public health messaging should promote higher RZV uptake in immunocompromised adults, including not missing opportunities to vaccinate during visits with clinicians or local pharmacies. The patterns of use identified here should be leveraged to promote awareness about and increase access to RZV among adults over 50 years in the US.

CHAPTER 6 - MANUSCRIPT 2

6.1 Introduction

An estimated 1 million cases of herpes zoster (HZ), commonly known as shingles, occur in the United States each year. In approximately 10% of HZ cases, patients will develop post-herpetic neuralgia and 10-20% herpes zoster ophthalmicus; these sequelae are responsible for most HZ-related morbidity.[41,43] The risk of HZ and sequalae increases with age and is higher among immunocompromised patients.[42] HZ and sequelae can be prevented via vaccination, boosting immunity to avoid reactivation of the dormant virus.

The US Centers for Disease Control and Prevention (CDC) recommended a live-attenuated vaccine against HZ in 2008, but only for immunocompetent populations.[65] An adjuvanted recombinant zoster vaccine (RZV) was later evaluated through two large phase III clinical trials and demonstrated robust protection against HZ and sequelae, an acceptable safety profile, and sustained immunogenicity over time.[8,9] The CDC subsequently provided a preferential recommendation for RZV in October 2017 for immunocompetent adults aged 50 years and older.[7]

The CDC's original recommendation for RZV did not include immunocompromised adults because they were excluded from the pivotal vaccine efficacy trials. In January 2022, the CDC expanded its RZV recommendation to include immunocompromised adults aged 19 years and older[10], following evaluation of safety and efficacy results from 6 clinical trials among immunocompromised populations.[20-25] However, while the CDC expanded its recommendation, among all clinical trials, fewer than 2,000 immunocompromised participants were vaccinated

with at least one dose of RZV, providing limited power to assess for rare outcomes post-vaccination.

We sought to investigate short- and long-term safety of RZV, overall and stratified by immune function. Key differences in underlying risk complicate direct comparisons of adverse events between vaccinated and unvaccinated populations, which are often are difficult to control.[84] Using a self-controlled design, we present here an assessment of adverse events associated with HZ diagnoses with an aim to provide important context regarding the benefits of the vaccine as compared to risk associated with HZ diagnosis.

6.2 Methods

6.2.1 Data Sources

The IBM MarketScan® Commercial Claims and Encounters Database ("MarketScan")[67] includes a variety of claims and encounter files of nationwide healthcare information. Individuals in the database either received private insurance in the U.S. through selected employer-sponsored plans or their covered family members. Claims and encounters files utilized in this analysis include enrollment details, inpatient admissions, inpatient services, outpatient services, and outpatient pharmaceutical claims. Enrollees included have unique identifiers, allowing for data linkage between different files and tracking over time.

6.2.2 Study Design and Cohort Development

We employed a self-controlled case series to estimate relative incidence rates of short- and long-term events between pre-specified risk and control periods **(Figure S1 and Figure S3)**.[85] This study design makes within-subject comparisons to implicitly account for all time-fixed confounders at the individual level. We conducted this retrospective analysis among adults

aged 50-64 years old who received at least one dose of RZV, were enrolled in private health insurance, and were included in MarketScan. We included all vaccinations administered between October 2017 (the month of FDA approval of RZV)[7] and December 2019, which were identified via a Current Procedural Terminology code 90750 and National Drug Codes 58160-819-12, 58160-823-11, 58160-828-01, 58160-828-03, 58160-829-01, or 58160-829-03. We identified all vaccinations that were recorded within 21 days of each other and excluded the later record under the assumption that the majority of these were administrative errors.

For each enrollee, we characterized periods of continuous insurance coverage, defined as having continuous enrollment in their insurance plan with gaps between coverage periods of no longer than 7 days. We then selected the continuous enrollment periods that included the first recorded dose of RZV (initiation) and continued until the first of the following: loss of continuous coverage, enrollee turned 65 years of age, or end of the observable study period (December 31, 2019). Once an enrollee turns 65, we may be missing some of their claims due to eligibility for Medicare coverage, so we chose to censor at this time. Enrollees who had claims for more than two doses of RZV were censored on the day before their third dose.

For assessments of short-term adverse events, we restricted the primary analyses of the RZV cohort to enrollees who maintained at least 6-months of continuous coverage prior to vaccination (for evaluation of immune function in the pre-vaccination period), had at least 42 days of observable time after the first dose of RZV, and, among those who completed the 2-dose vaccination series, had at least 28 days between the each dose. For analyses of cardiovascular and cerebrovascular adverse events, we additionally required that enrollees had 365 days of coverage prior to vaccination to allow for exclusion of those with a history of an event.

For long terms safety events, we included all enrollees who maintained at least 365 days of continuous coverage prior to vaccination, had at least 162 days of observable time after the first dose of RZV, and, among those who completed the series, had at least 60 days between the two doses **(Figure S1 and Figure S3)**.

To provide important context describing the safety of RZV relative to HZ, we constructed a second cohort to investigate rates of adverse events following a HZ diagnosis. We identified all enrollees who had a claim for HZ or its sequelae using ICD-10-CM diagnosis code B02 and included subcodes for sequelae. For this cohort, the index date was defined as the date of the first identifiable HZ-related code in either the inpatient or outpatient setting. The same design and analytic methods were used to assess safety outcomes for both the RZV and HZ cohorts.

6.2.3 Risk and Control Windows

We defined the day of RZV vaccination as day 1 for both short- and long-term safety analyses in the RZV cohort. For short-term safety, we employed a risk period spanning the first 7 days post vaccination, for either the first or second dose of RZV, inclusive of the day of vaccination (i.e. days 1-7). In our primary analysis, we implemented a 21-day washout period (days 8-28) to ensure that any events observed in the subsequent control period would not be vaccine-associated. The control period began on day 29 and continued through the end of observable period (loss of continuous coverage, turned 65 years of age, or end observation) for all enrollees (**Figure S2).**

For long-term safety, the risk period was 60 days long (spanning days 1-60). A recent self-controlled case series analysis of Guillain Barre following RZV administration used a 42-day risk period;[86] however, we employed a longer risk period under the assumption that additional time is needed for many autoimmune disorders to present, be clinically evaluated and

diagnosed, and then be observed via diagnosis codes in administrative data. The risk period was then followed by a washout period until 120 days post-vaccination (days 61-120). The control period for long-term safety analyses began on day 121 and continued through the end of observation (**Figure S3**).

6.2.4 Measures

Demographics

We used all inpatient, outpatient, and prescription data from 2017-2019 to characterize the demographic characteristics and immune function of all vaccinated enrollees. At the time of RZV initiation, we extracted patient age, region, metropolitan statistical area, type of insurance plan, and sex. We categorized age into groups of 50-54, 55-59, and 60-64 years. We categorized enrollees as living in an urban setting if they resided within a metropolitan statistical area (defined as an urbanized area with a population of at least 50,000 people), and all other enrollees were categorized as rural. We recategorized insurance plans into groupings: Comprehensive Coverage; Preferred Provider; Managed Care (exclusive provider organization, health maintenance organization, point-of-service, and point-of-service with capitation); and High Deductible Plans (consumer directed and high deductible health plans).

Immune status

Enrollees were classified as immunocompromised if they had: primary immunodeficiency, immunosuppressive malignancy, history of a solid organ transplant, or medication-induced immunosuppression based on diagnosis, procedural, or pharmacy claims. Enrollees with claims for diagnoses of bone marrow malignancy or blood cancers, solid organ transplants, or primary immunosuppression, or who had pharmacy claims or procedural codes

specific to any of these indications, were considered immunosuppressed from the time of the first relevant claim through the remainder of observation (see **Table S1-Table S5**).

We then accounted for temporary periods of immunosuppression induced by cancer therapeutics or other medications during follow-up for each enrollee to additionally analyze modification of associations between vaccination and adverse events by immune function. We characterized the duration of immunosuppression as a function of the date of the medication claim, the number of days prescribed, and an assumed duration of immunosuppressive effect following completion of the medication (**Figure S4**). For the period of immunosuppression following individual treatment periods, we recorded the start date as the day after the prescription was filled. We similarly defined immunosuppression following a claim for administration of chemotherapy (via procedural codes) as the date of the procedure plus the duration of immunosuppressive effects. For the primary analysis of modification of safety by immune function, we characterized the duration of immunosuppressive effects following treatment as 90 days. This duration was selected because the RZV clinical trials excluded potential participants who had used immunosuppressants or immune-modifying drugs within 6-months prior to enrollment.[8,9] Enrollees identified as living with HIV were not included in the immunocompromised sub-cohort, as only a small proportion (3.5%, 63/1,395) of those with had laboratory data available.

Outcomes

We identified patients with inpatient or outpatient claims for any localized reactions (arm pain and cellulitis), systemic events (anaphylaxis, headache, fatigue, chills, nausea/vomiting, diarrhea, and fever), cardiovascular events, cerebrovascular events, autoimmune disease, and falls (negative control event) using ICD-10-CM diagnosis codes (**Table S7 and Table S8**). The

codes used to identify outcomes of interest were selected following review of the literature and expert consultation.[87-90] For cerebrovascular events, we considered any type of stroke (hemorrhagic, ischemic, transient ischemic attacks) as a single outcome.[91] We analysed each of the localized reactions, and systemic, cardiovascular, cerebrovascular, and autoimmune events as independent outcomes. Autoimmune diseases were further subclassified into the following composite events: neuroinflammatory, skin, gastrointestinal, vasculidities, musculoskeletal, liver, and metabolic disorders. Then, we constructed compositive variables to capture the occurrence of any of the contributing outcomes. These composite variables allowed for different types of contributing outcomes to be recorded on the same day (i.e., co-presentation of fever and fatigue) and for each of those outcomes to be counted in the analysis. We included inpatient or outpatient visits for falls as a negative control, as it should not be associated with vaccination or HZ.

Enrollees could experience acute events multiple times throughout the study period. However, to avoid counting follow-up visits to an initial presentation as unique incident events, we linked together events that occurred within prespecified windows: 7 days for short-term localized and systemic events, and 35 days for all cardiovascular, cerebrovascular, pIMD, and control events (**Figure S5**). Although a prior study had linked together long-term events that occurred within 28 days of vaccination, we extended this to 35 days, to capture monthly follow-up visits.[92] Enrollees who had a history of any of the cardiovascular, cerebrovascular, or autoimmune events of interest in the 365 days prior to vaccination were excluded from analysis in order to avoid treating follow-up visits as unique incident events.

6.2.5 Statistical Analyses

We completed descriptive analyses of baseline characteristics (age group, sex, region, urbanicity, and insurance plan type) for all enrollees meeting inclusion/exclusion criteria for the

1) RZV vaccination and 2) HZ cohorts. We used conditional Poisson regression to calculate relative incidence rates (IRR) (and 95% confidence intervals) within the pre-specified risk and control intervals, using days since RZV vaccination or HZ presentation as the timescale. We controlled for age as a time-varying confounder in all analyses, characterized as whole number of years since the day of vaccination or HZ presentation, and treated as a categorical variable in the model to allow for non-uniform effect of each year of increased age. Results of the self-controlled case series are presented in forest plots for the RZV cohort overall and stratified by immunosuppression (using 90-day duration following treatment as the primary analysis). We included an interaction term between the risk period and immune competence in the model to estimate stratum-specific IRRs for each immunocompetent and immunocompromised person-time under observation.

Results from the RZV cohort and the HZ cohort are displayed side-by-side; these cohorts were developed independently and may not be directly comparable due to differences in demographics (age, sex, race/ethnicity) or comorbidities associated with increased risk of adverse events. We performed additional sensitivity analyses to evaluate potential impacts of assumptions that informed our study design. The design characteristics evaluated in sensitivity analyses include: the necessity of a washout period, exclusion of events that were recorded during the encounter for vaccination, duration of risk period for long-term events, and duration of immunosuppression following treatment. Descriptions and visualizations of these analyses are provided in **Figure S6-Figure S11**.

All analyses and figure development were completed in SAS 9.4 (Cary, N.C.) The study was approved by the Institutional Review Board (IRB) of the University of North Carolina at Chapel Hill.

6.3 Results

We identified 425,701 enrollees aged 50-64 years who initiated RZV and fulfilled all inclusion/exclusion criteria for short-term safety analyses, and 225,246 for the long-term safety analyses. For both the short- and long-term safety analyses, the RZV cohort was majority female, predominantly lived in urban settings, and most commonly were covered by preferred provider health insurance. Immunosuppression at any point during follow-up was identified among 7.8% of enrollees in the short-term safety analysis, and 8.3% in the long-term analysis (**Table 5**).

Table 5: Demographics of Recombinant Zoster Vaccine (RZV) recipients and Herpes Zoster (HZ) cases eligible for short-term and long-term safety analyses, adults 50-64 years old, 2017-2019, MarketScan

	Short Term Safety Outcomes				Long Term Safety Outcomes			
	RZV (n = 425,701)		HZ (n = 151,379)		RZV (N = 225,246)		HZ (N = 89,510)	
	n	%	n	%	n	%	n	%
Age (years)								
50-54	88,409	20.8	50,786	33.6	44,641	19.8	30,020	33.5
55-59	135,221	31.8	52,360	34.6	71,892	31.9	31,447	35.1
60-64	202,060	47.5	48,233	31.9	108,705	48.3	28,043	31.3
Sex								
Female	243,304	57.2	96,393	63.7	127,617	56.7	56,907	63.6
Male	182,386	42.8	54,986	36.3	97,621	43.3	32,603	36.4
Geographic Region of Residence								
Northeast	71,464	16.8	27,918	18.5	40,429	18.0	17,608	19.7
North Central	99,808	23.5	30,151	20.0	51,744	23.0	17,871	20.0
South	181,849	42.8	70,911	47.0	96,913	43.1	41,260	46.2
West	71,592	16.9	22,056	14.6	35,665	15.9	12,601	14.1
Urbanicity†								
Urban	332,304	88.5	116,194	85.5	173,623	88.4	66,285	85.1
Rural	43,407	11.6	19,731	14.5	22,815	11.6	11,568	14.9
Insurance Plan Type‡								
Comprehensive	11,383	2.7	5,160	3.5	6,856	3.1	3,355	3.8
Preferred Provider	211,009	50.7	82,003	55.2	113,852	51.8	47,934	54.5
Managed Care	88,855	21.3	30,113	20.3	42,285	19.2	16,726	19.0
High Deductible	105,180	25.3	31,372	21.1	56,981	25.9	19,871	22.6
Ever Immunocompromised	33,123	7.8	NE	NE	18,756	8.3	NE	NE

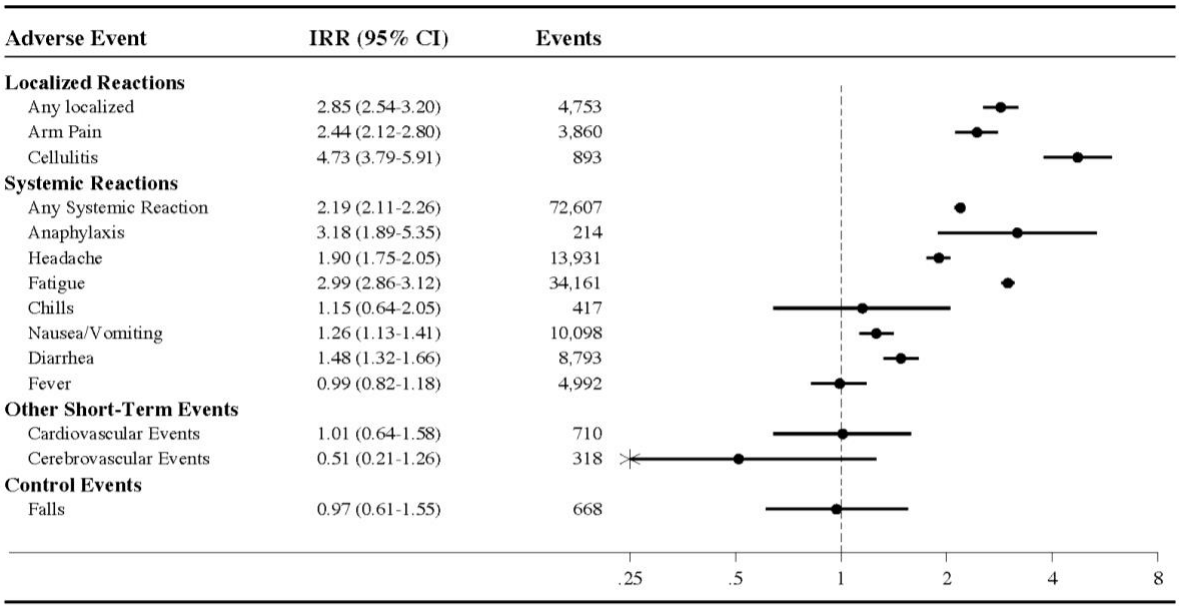
Abbreviations: RZV = Recombinant Zoster Vaccine; HZ = Herpes Zoster; NE = Not Evaluated
† MSA – population size of least 50,000 considered urban
‡ Groupings include: Comprehensive Coverage; Preferred Provider; Managed Care (exclusive provider organization, health maintenance organization, point-of-service, and point-of-service with capitation); High Deductible Plans (consumer directed and high deductible health plans).

6.3.1 Short-Term Adverse Events following vaccination

There were 4,753 claims for localized adverse events (median follow-up = 447 days; IQR: 275-562) and 72,607 for systemic adverse events (median follow-up = 218 days; IQR: 167-389) in the observable time following RZV administration (**Figure 6**). There were higher rates of claims for both localized (IRR 2.85; 95% CI: 2.54-3.20) and systemic (IRR: 2.19; 95% CI: 2.11-2.26) events in the 7 days following RZV administration compared to the control period.

Localized adverse events that were more common following vaccination included cellulitis (IRR: 4.73; 95% CI: 3.79-5.91) and arm pain (IRR: 2.44; 95% CI: 2.12-2.80). The associations for individual systemic events ranged from IRR=0.99 (95% CI: 0.82-1.18) for fever to IRR=3.18 (95% CI: 1.89-5.35) for anaphylaxis. Significant associations were only observed for anaphylaxis, headache, fatigue, nausea/vomiting, and diarrhea. Neither of the composite outcomes for cardiovascular or cerebrovascular events suggested increased rates of events in the risk compared to the control periods. The rates of falls, our negative control event, were nearly equivalent between the risk and control periods (IRR=0.97, 0.61-1.55).

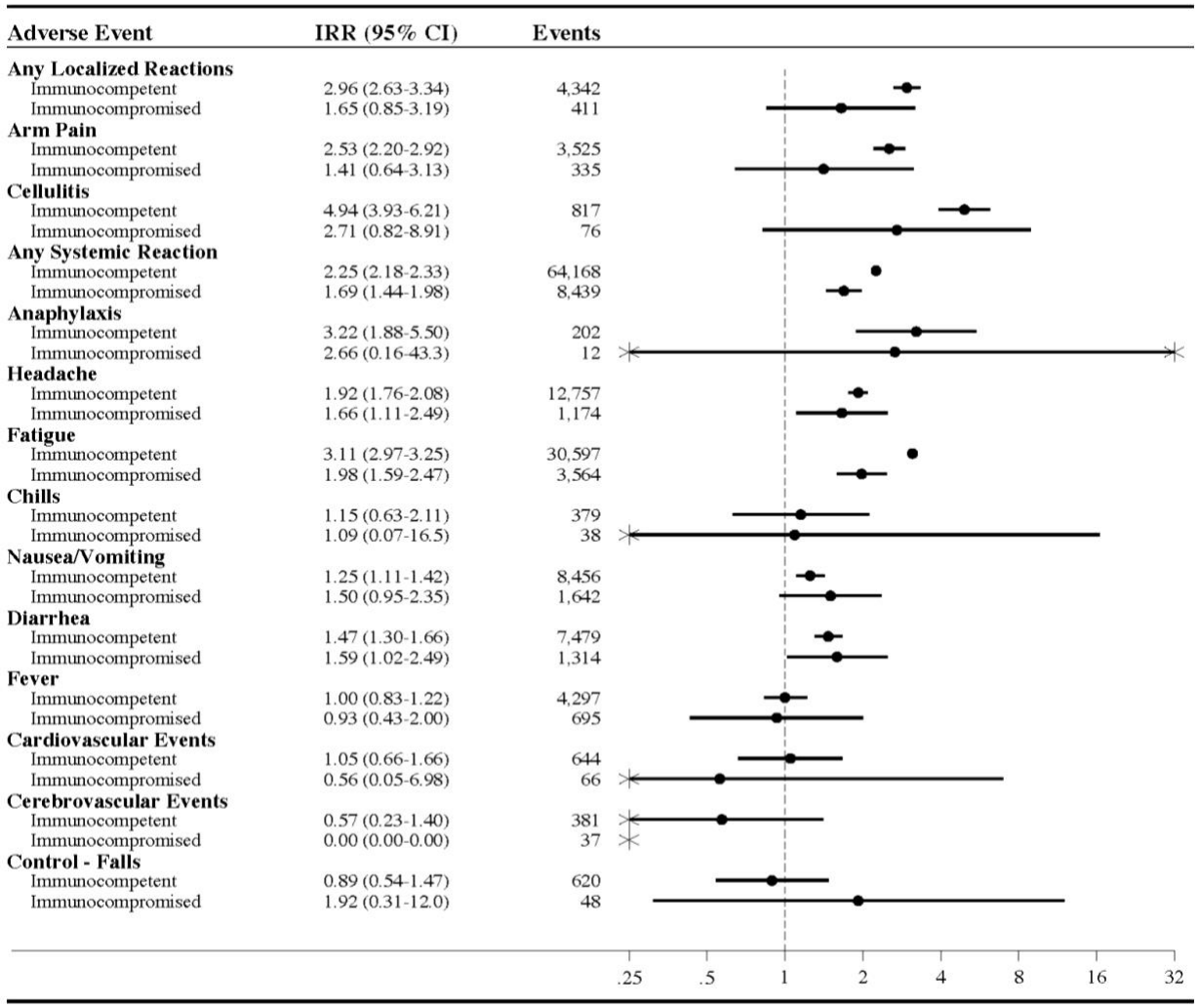
Figure 6: Relative incidence of short-term adverse events following receipt of Recombinant Zoster Vaccine (RZV), age-adjusted self-controlled case series, MarketScan



We observed median follow-up of 447 days (IQR: 275-562) for localized and 218 days (IQR: 167-389) for systemic events.

Differences in associations between immunocompetent and immunocompromised enrollees were only observed for "any systemic events" and fatigue, both of which demonstrated a less severe association between vaccination and rates of adverse events among immunocompromised enrollees (**Figure 7**).

Figure 7: Relative incidence of short-term adverse events following receipt of Recombinant Zoster Vaccine (RZV), stratified by immune function*, age-adjusted self-controlled case series, MarketScan



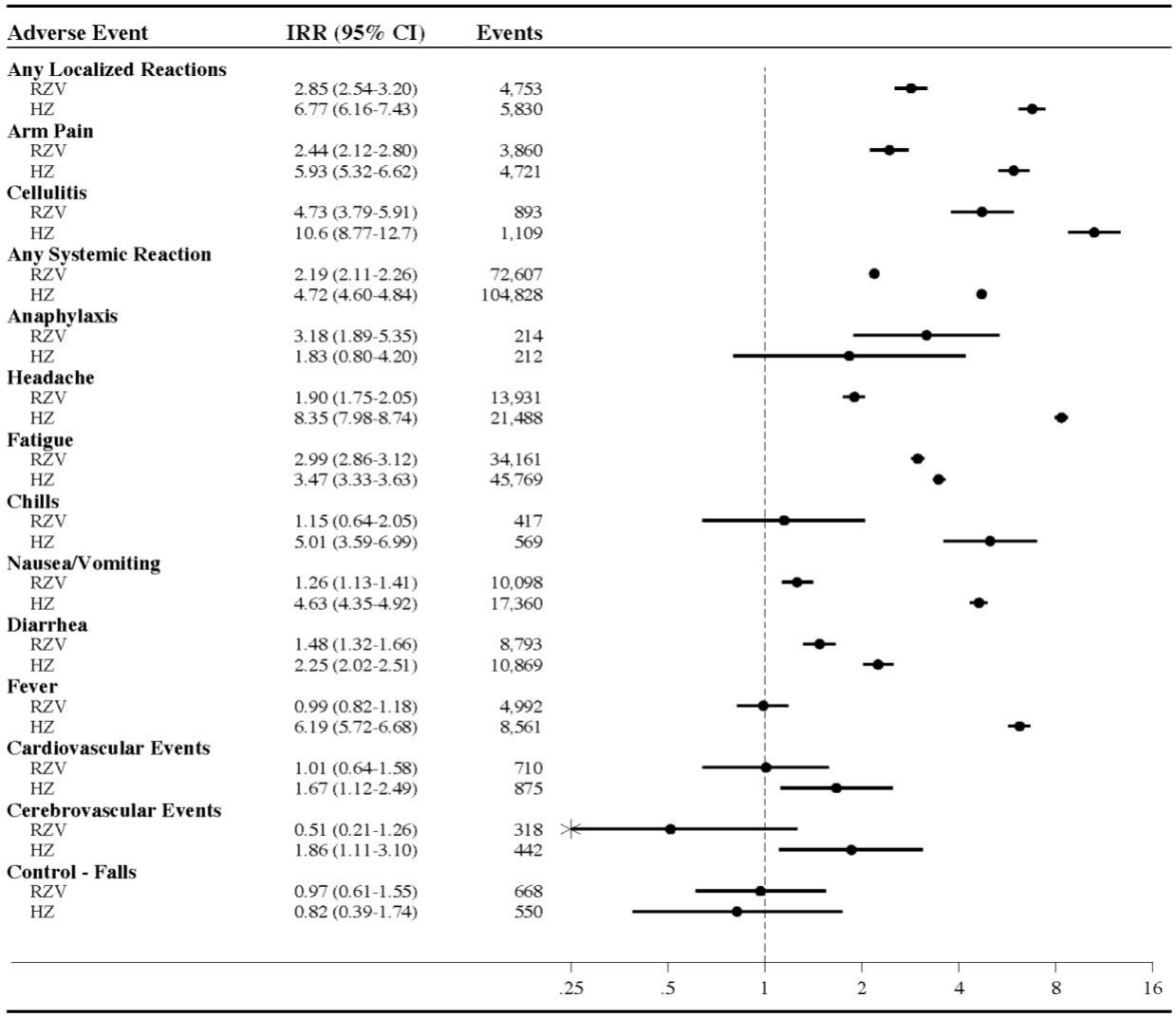
**Periods of continuous immunosuppression are linked together using an assumed 90-day duration of immunosuppressive effects following completion of treatment (method shown in supplemental figure 3).*

6.3.2 Short-Term Events following Herpes Zoster diagnosis

We identified 151,379 claims for HZ or sequelae during the study period that were eligible for analysis of short-term events. Statistically significant increases were observed for all short-term events, the highest observed for cellulitis (IRR: 10.6, 95% CI: 8.77-12.7) and headache (IRR: 8.35, 95% CI: 7.98-8.74) (**Figure 8**). Among the composite events, we observed a stronger age-adjusted association between HZ and diagnosed localized reactions IRR=6.77

(95% CI: 6.16-7.43) than for systemic reactions IRR=4.72 (95% CI: 4.60-4.84), cerebrovascular events IRR=1.86 (95% CI: 1.11-3.10), and cardiovascular events IRR=1.67 (95% CI: 1.12-2.49).

Figure 8: Associations between RZV administration and short-term adverse events, with contextualization using incident Herpes Zoster (HZ) diagnosis as the index event, age-adjusted self-controlled case series, MarketScan



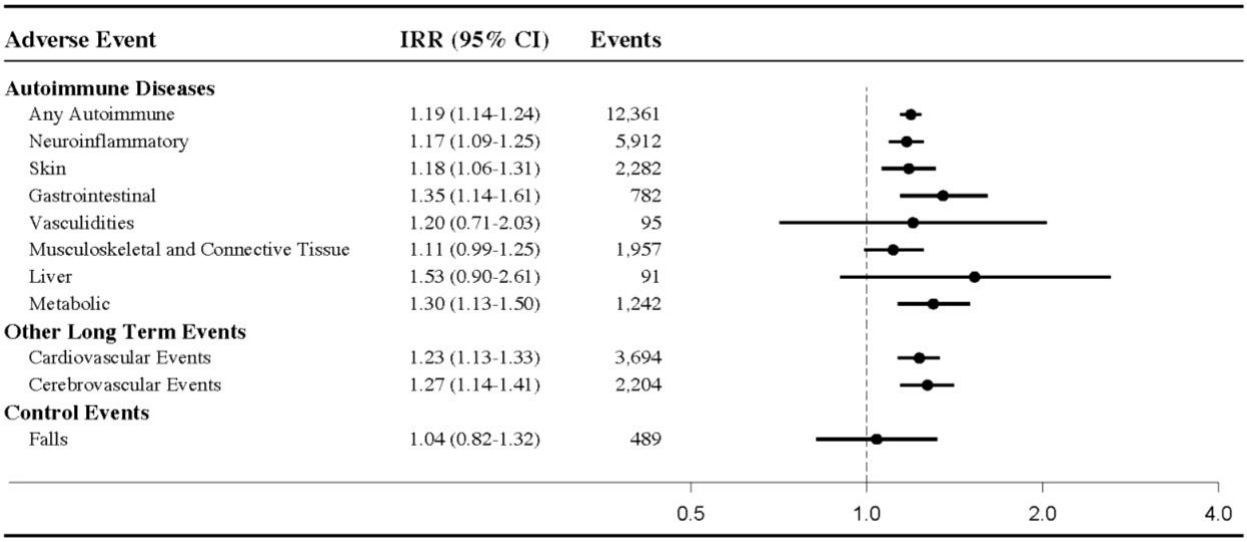
We are not making direct comparisons between the two scenarios here. The cohorts of enrollees who received RZV and those who had an incident HZ diagnosis reflect different populations. Instead, we are displaying both to provide important context regarding vaccine safety.

6.3.3 Long-Term Adverse Events following vaccination

There were 12,361 claims for any autoimmune disease (median follow-up = 380 days; IQR: 244-483), 3,694 for cardiovascular events (median follow-up = 381 days; IQR: 243-483),

and 2,204 for cerebrovascular events (median follow-up = 387 days; IQR: 235-490) in the observable time following RZV administration (**Figure 9**).

Figure 9: Relative incidence long-term adverse events following receipt of Recombinant Zoster Vaccine (RZV), age-adjusted self-controlled case series, MarketScan

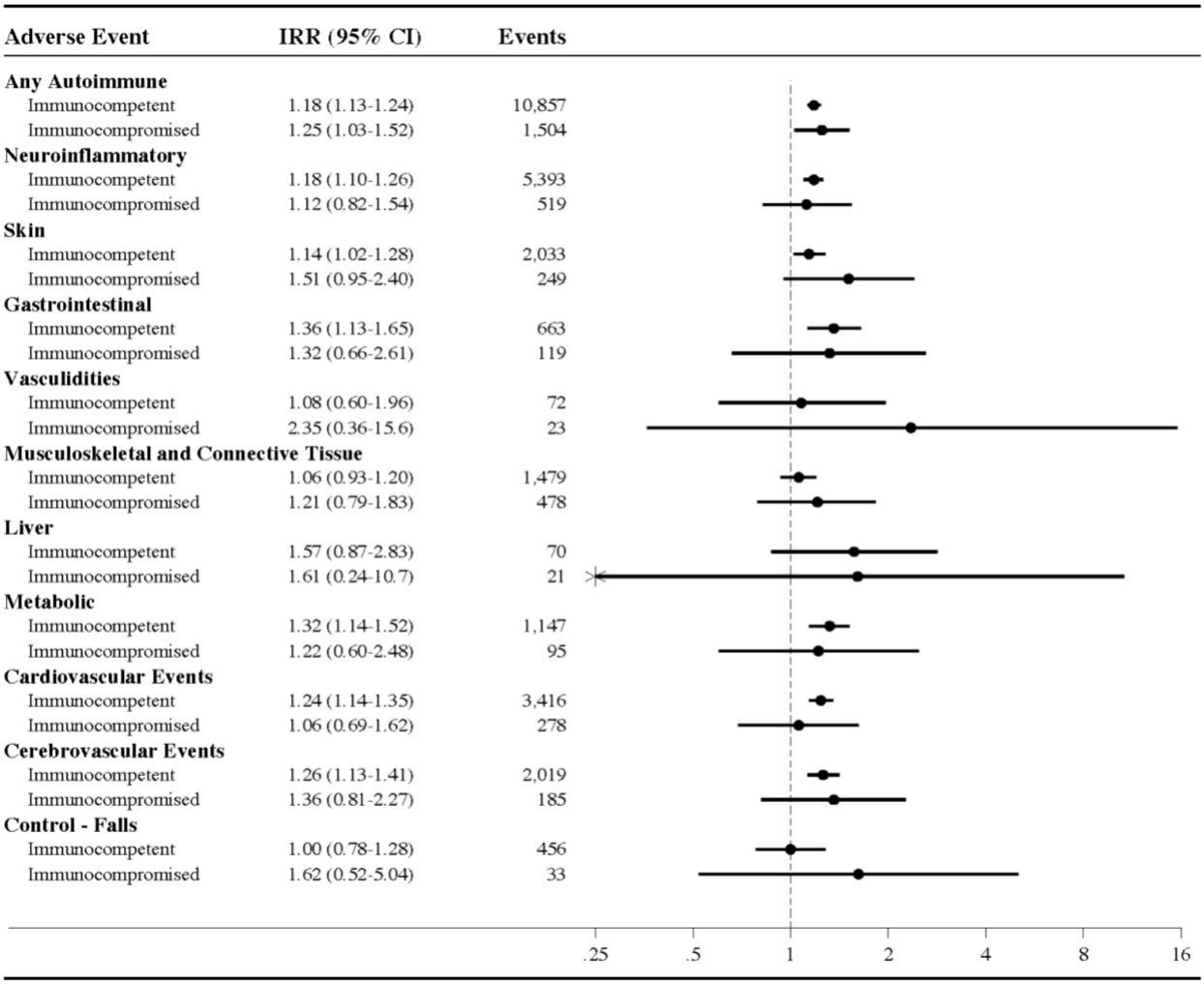


Among long-term safety, median follow-up observed was 380 days (IQR: 244-483) for autoimmune diseases, 381 days (IQR: 243-483) for cardiovascular events, and 387 days (IQR: 235-490) for cerebrovascular events.

There were slightly higher rates of diagnosis with autoimmune adverse events following vaccination in comparison to the control period (IRR=1.19; 95% CI: 1.14-1.24). Additionally, there were increased rates of cardiovascular (IRR=1.23; 95% CI: 1.13-1.33) and cerebrovascular (IRR=1.27; 95% CI: 1.14-1.41) events (**Figure 9**). Among the subgroups of autoimmune events, the rates of each neuroinflammatory, skin, gastrointestinal, and metabolic disorders were increased following vaccination. Individual autoimmune disorders that were associated with increased post-vaccination rates were neuritis, psoriasis, celiac, Sjogren's Syndrome, autoimmune thyroiditis, and Type I diabetes (**Figure S12**). There were also higher rates of incident diagnoses of chronic cardiovascular and cerebrovascular diseases in the post-vaccination risk period, but no differences in the rates of any of the acute cardiovascular and cerebrovascular events

Figure S13). We did not observe any differences in the associations between vaccination and any of the long-term outcomes when comparing immunocompetent and immunocompromised enrollees (**Figure 10**).

Figure 10: Associations between Recombinant Zoster Vaccine (RZV) administration and long-term adverse events, stratified by immune function*, age-adjusted self-controlled case series, MarketScan



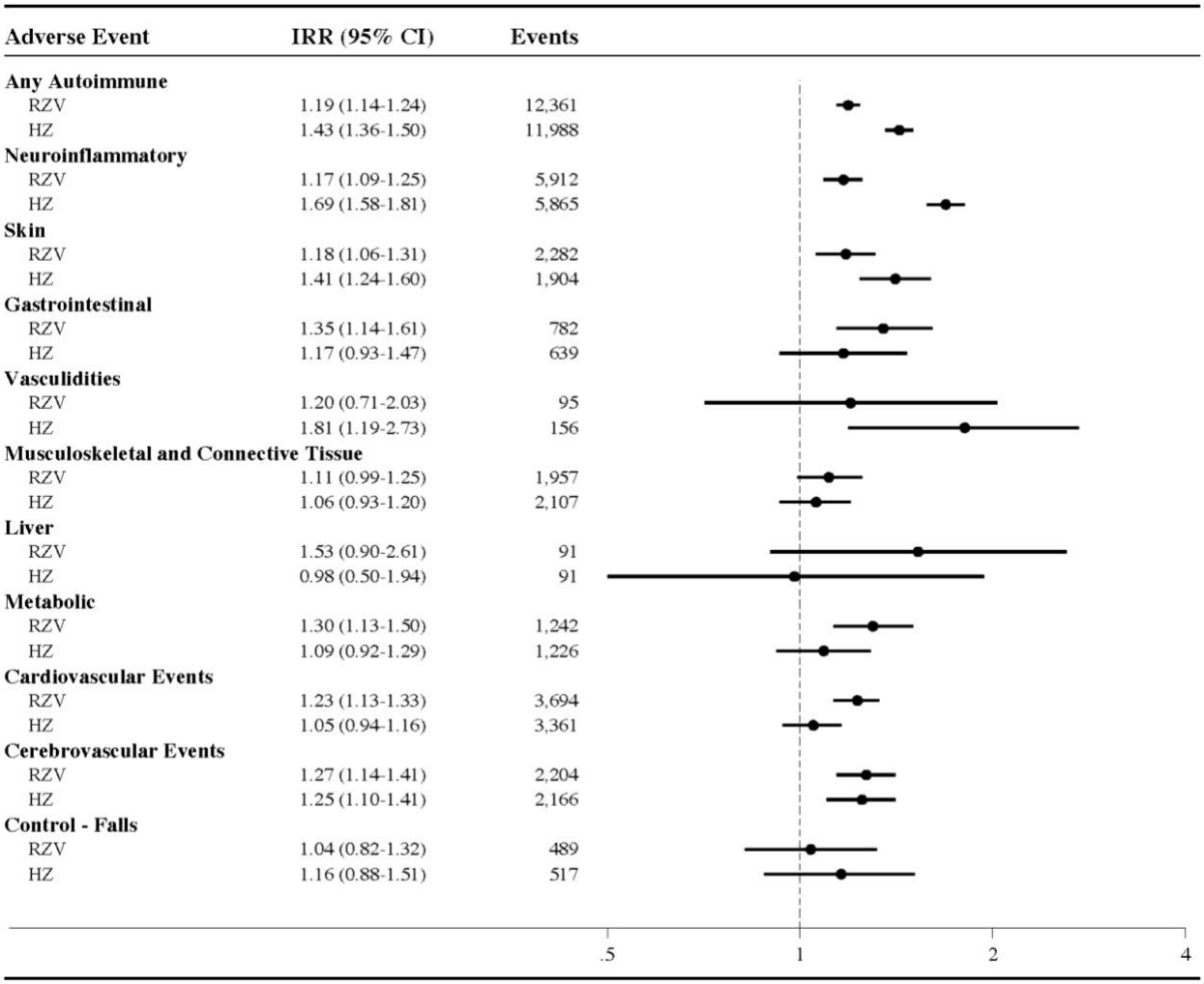
**Periods of continuous immunosuppression are linked together using an assumed 90-day duration of immunosuppressive effects following completion of treatment (method shown in supplemental figure 3).*

6.3.4 Long-Term Events following a Herpes Zoster Diagnosis

There were 89,510 cases of herpes zoster and its sequelae were included in the analysis (**Table 5**). There were higher rates of any incident diagnosed autoimmune disease following initial herpes zoster diagnosis (IRR=1.43; 95% CI: 1.36-1.50). Higher post-HZ diagnosis rates

were observed for autoimmune neuroinflammatory and skin disorders, vasculidities, and cerebrovascular events (**Figure 11**). No differences were observed for autoimmune gastrointestinal, musculoskeletal, liver, and metabolic disorders, nor for cardiovascular events.

Figure 11: Associations between RZV administration and long-term adverse events, with contextualization using incident Herpes Zoster (HZ) diagnosis as the index event, age-adjusted self-controlled case series, MarketScan



"Any Autoimmune" includes the composite of: neuroinflammatory, skin, gastrointestinal, vasculidities, musculoskeletal and connective tissue, liver, and metabolic disorders. Multiple events could have been experienced on the same day, and each would have been counted in analysis.

6.3.5 Sensitivity Analyses

There were attenuated associations between RZV and rates of short-term adverse events for "any systemic events," headache, and fatigue after excluding events that were diagnosed

during the encounter for RZV administration (**Figure S6**). Removal of the washout period for the short-term safety analyses resulted in higher associations for all events, although the changes to the estimates were only statistically significant for "any systemic events" and fatigue (**Figure S7**). For both the short-term (**Figure S8**) and long-term (**Figure S11**) analyses, there were minimal differences in the associations estimated among immunocompromised patients when changing the duration of immunosuppression following administration of chemotherapy or use of immunosuppressive medications.

We did not observe substantial changes to the associations between vaccination and long-term adverse events after extending the post-vaccination risk period from 60 days to 120 days (**Figure S9**). After removing the washout period from the long-term safety analysis, there was an attenuation of the associations; however, there were not statistically significant differences between these two scenarios (**Figure S10**).

6.4 Discussion

In a claims based analysis of privately insured adults aged 50-64 years, we observed increased rates of short-term and long-term adverse events following RZV administration. The associations between RZV and short-term safety outcomes were attenuated among immunocompromised enrollees compared to immunocompetent enrollees; no differences by immune function were observed in the long-term safety analysis. While there were increased rates of adverse events following vaccination, we similarly found increased rates of adverse events following incident HZ diagnoses, with larger effect sizes in most cases.

The increased rates of incident diagnoses of short-term adverse events following RZV observed in this study are consistent with the ZOE-50 clinical trials, in which high rates of short-

term localized adverse events were reported.[8] Interestingly, we did not find a difference in rates of diagnoses of fever or chills in the post vaccination period. This likely reflects the nature of the data used in this analysis, which captures incident diagnoses of events for billing purposes. While many people will not go to the doctor for fever or chills, more severe outcomes are likely to be better captured in claims – because they require a healthcare encounter. As such, our associations are attenuated estimates of relative post-vaccination risk in comparison to actual occurrence. The absence of an association between vaccination and short-term cardiovascular and cerebrovascular events is reassuring because these are severe events requiring medical attention.

Regarding long-term safety, there were slightly increased rates of diagnosis of any autoimmune disease, the majority of subgroupings of autoimmune disease, and long-term cardiovascular and cerebrovascular diseases following vaccination. While we did not observe an increased post-vaccination rate of Guillain-Barre Syndrome, as was found in a recent self-controlled case series evaluating RZV,[86] there was an increased post-vaccination rate for newly diagnosed neuroinflammatory disorders. A post-licensure safety study of RZV using GlaxoSmithKline's safety database, reported that the most common autoimmune disease was Bell's palsy/paresis, but that the number of events was below the expected number given background incidence.[93] Similarly, we did not find an increased rate of Bell's palsy following vaccination. Although we identified increased post-vaccination rates of neuritis, psoriasis, Sjogren's syndrome, celiac, autoimmune thyroiditis and Type I diabetes, prior clinical trials[94,95] and observational studies[93,96] of RZV have not found increased risk and additional research regarding these outcomes is needed.

The relative post-vaccination incidence rates of short-term safety events appeared attenuated among immunocompromised individuals in comparison to immunocompetent. One possible explanation for this trend is an attenuated immune response to the vaccine among this population and less subsequent reactogenicity. While still efficacious, prior research has demonstrated lower immune response and efficacy among immunocompromised patients compared to immunocompetent.[97,98] Another possible explanation is that higher baseline risk of localized and systemic reactions among immunocompromised patients. We did not observe differences in associations between vaccination and long-term events when comparing immunocompromised and immunocompetent enrollees.

We cannot make direct comparisons between the post-RZV safety results and post-HZ safety as these analyses feature different populations and we are only measuring rates in a case-only analysis. Nevertheless, the contextualization provided by the HZ analysis suggest that while there may be increased rates of events following RZV, there are similarly increased rates following HZ. Prior research has demonstrated increased rates of stroke and myocardial infarction within 3 months to a year following onset of herpes zoster.[99] When making recommendations and counseling patients about RZV vaccination, policy makers and clinicians should communicate that adverse events associated with vaccination also occur following HZ presentation, and that vaccination is likely safer than experiencing HZ. In addition, most of the adverse events that we observed are short-lived and manageable with minimal clinical intervention.

Although the self-controlled case series design is efficient for evaluating relative incident rates of events following transient exposures, the case-only design produces only relative measures between risk and control periods within an individual. As such, the results lack context

regarding the baseline incidence of safety events, particularly for rare events. For example, while we identified an increased rate of neuritis following vaccination, this was a relatively uncommon outcome (46 cases over two years) and we would not expect to observe many additional cases due to vaccination. Additionally, claims data are only able to capture cases in which an enrollee received medical care after vaccination, but do not reflect the true incidence of occurrence. This limitation is primarily of concern with respect to short term safety, as many individuals do not go to the doctor when experience reactogenicity following vaccination. The result is that our estimated associations are likely underestimates of the true relative post-vaccination rates; however, the fact that these individuals are not seeking medical attention suggests limited cause for concern.

Despite the limitations of using administrative data, the overall large number of enrollees included in this analysis provides the power required to evaluate rare outcomes, which is a major challenge of randomized control trials. The self-controlled case series design also provides substantial benefit when using claims data, as we lack sufficient information on potential confounders that would need to be accounted for and this design implicitly controls for all non-time-varying confounders. Future research should continue to evaluate risk of autoimmune diseases and other rare events following vaccination, in the context of risk of these outcomes from HZ disease. Inclusion of additional years of data in RZV safety studies using claims data will increase power to assess for the risk of rare events.

CHAPTER 7 - DISCUSSION

7.1 Summary of Findings

The global understanding about vaccines and policies for vaccination are constantly changing. When this research was initiated, the CDC's recommendation for RZV vaccination did not include immunocompromised adults due to a lack of important information regarding safety and efficacy.[7] Recently, the results of additional clinical trials demonstrated an acceptable safety profile of RZV among immunocompromised populations and the recommendations have been expanded to now include all immunocompromised adults.[10] Given the expanded recommendations and evidence of RZV use among immunocompromised patients in the preceding period, it is important to characterize patterns of RZV administration, overall and by immune function, to identify groups with lower levels of vaccination for targeted efforts to improve uptake. Additionally, continuous assessments of safety are required to assess rare safety events that are difficult to evaluate in pre-licensure clinical trials.

The aims of this dissertation were designed to address these needs for additional information. The assessment of patterns of use of RZV in Aim 1 revealed that the cumulative incidence of RZV initiation among privately insured adults was relatively low (10%). Furthermore, rates of initiation increased with older age and with greater number of medical office visits prior to the study, and were higher among females compared to males, those living urban versus rural areas, and among enrollees with high deductible insurance plans compared to other types of insurance. These patterns were similar to those observed in prior research,[18,79] but those existing studies did not investigate RZV administration by immune function. Despite not

being included in the CDC's RZV recommendation during the study period, immunocompromised enrollees had higher rates of RZV initiation (13%) compared to immunocompetent enrollees (9.8%). This may reflect that providers working with immunocompromised patients believed that the benefits of vaccination outweighed the potential risks. Among those who initiated the RZV series, the cumulative incidence of series completion was high (89.5%), and did not differ by immune function or with the same patterns as observed for RZV initiation. Interestingly, the largest differences in rates of RZV completion were observed by the place at which the first dose was received, highest among those who initiated the series at a pharmacy (92.7%) and lowest among those who initiated at an outpatient hospital (77.1%). The results of the Aim 1 analyses can be used to design strategies to improve RZV initiation and completion rates. Differences in RZV initiation by age and sex may reflect a need for more targeted programs to increase vaccination among those at the younger range of the CDC's recommendation and among men, while differences by urbanicity may reflect the need to improve access in rural areas. Furthermore, the lack of a difference in rates of series completion by immune function may be an initial indication that immunocompromised enrollees were not experiencing greater reactogenicity or adverse events following vaccination compared to immunocompetent enrollees. That hypothesis was further evaluated in the safety analysis completed in Aim 2.

Overall, the results of the self-controlled safety analyses indicated an association between RZV vaccination and short-term localized and systemic reaction and long-term autoimmune, cardiovascular and cerebrovascular events; however, providing additional context is critical to interpreting these results. Regarding short-term safety, there was increased post-vaccination risk was observed for both types localized events (arm pain and cellulitis) and all systemic events

evaluated with the exception of chills and fever. In a pooled assessment of the two main RZV clinical trials, solicited injection site and general symptoms were commonly reported by participants, at much higher frequencies than observed here. The start difference in occurrence of short-term events between the clinical trials and this study of real world data reflect a key aspect of the data used here. The first, is that the cases of short-term events in this study were derived from insurance claims from enrollees visiting a doctor's office, and many individuals will not go to a doctor's office when experiencing common side effects of vaccines. As such, the rates of post-vaccination short-term events presented here are certainly underestimates; however, the low levels of reporting adverse events may indicate that these reaction are generally not severe and may not pose a public health concern. There was a slightly higher risk of long-term autoimmune (IRR=1.19), cardiovascular (IRR=1.23), and cerebrovascular (IRR=1.27) events following RZV, which may be the result of a strong immune response elicited by the vaccine's adjuvant.[55,57] While increased risk of any of these events is concerning, it is important to note that these associations are relative measures and that the all of the long-term events were rare; relative measures may lead to overestimation of true risk, as a small relative increase in risk produces a small number of additional cases for rare events.[100]

A primary goal of this research was to investigate modification of RZV safety by immune function. In the analysis of short-term safety, there appeared to be an attenuation of the associations between RZV and short-term localized and systemic reactions among immunocompromised enrollees compared to immunocompetent. This may reflect reduced reactogenicity among immunocompromised enrollees due to an attenuated immune response to the vaccine, higher baseline rates of these events for immunocompromised enrollees, or a combination of the two. The investigation of long-term safety did not reveal any differences

between strata of immune function. Overall, the findings of both short- and long-term safety by immune function provides support for the CDC's expanded guidelines on the basis of safety. Furthermore, the assessments vaccine safety should not be limited to only events experienced following vaccination, but also consider potential events that could be experienced following natural disease. Influenza vaccination provides a good example of this contextualization, as lower risk of Guillain-Barre syndrome was observed following influenza vaccination compared with influenza infection.[101] In this study, there was increased risk of all short-term events and long-term autoimmune and cerebrovascular events following incident HZ diagnosis. As RZV has be demonstrated to be highly efficacious against HZ and sequelae, modeling vaccine safety should incorporate events following HZ in the overall assessment of risk and benefits.

7.2 Limitations

The limitations of this study are primarily a result of the data source. Insurance claims data provide a large number of enrollees to evaluate, but are initially collected for billing purposes. As such, analyses of these data are limited to only those diagnoses, procedures, and prescription fills that are recorded during healthcare encounters and visits to pharmacies.

The assessment of RZV patterns of use leveraged procedure codes from both inpatient and outpatient settings and pharmacy claims data. Any vaccinations that were paid for out of pocket would not be captured in MarketScan. It is unlikely that many vaccinations were missed due to the high cost of the vaccine and the requirement of insurance coverage for all CDC recommended vaccines. The data featured a limited set of patient identifiers in order to protect patient privacy and anonymity. As a result, RZV initiation and completion by demographic characteristics such as race/ethnicity and income could not be assessed. In both aims,

classification of immune function relief heavily on pharmacy claims and the assumption that enrollees adhered to their medication appropriately. In most cases, given the severe nature of the disease being treated, unlikely that filled prescriptions were not taken.

The safety analysis employed a self-controlled case series design to estimation relative incidence rates between post-vaccination risk and control period. While efficient, this case-only study design can only produce relative measures of effect. The limitations of these measures, as shown in the post-vaccination risk of autoimmune diseases, is that relative measures do not reflect underlying risk and therefore may indicate a safety problem when few additional cases of disease would be observed in reality. Further, the events in the safety analysis were identified via diagnosis codes and did not capture severity of disease. In clinical trials, solicited and unsolicited adverse events are evaluated using a grading scale to reflect the severity of reactions, which is critical to evaluating safety.[102]

7.3 Strengths

A major strength of using insurance claims data is the number of enrollees included. The patterns of use analyses included over 4.5 million adults meeting study inclusion criteria, enabling the evaluation of RZV series initiation and completion by key characteristics of interest, both overall and within strata of immune function. Characterizing immune function using diagnoses, procedures, and prescription filles allowed us to further stratify by immunocompromising conditions and investigate patterns of use among each of these populations.

The self-controlled case series design was particularly beneficial for the analysis of RZV safety, as the MarketScan data does not include many potential confounders. This study design

implicitly controls for all time-invariant confounders through use of within-person comparisons. As such, the analyses of short- and long-term safety only needed to control for age. The size of the MarketScan database provided sufficient power to assess rare safety events and stratify safety by immune function. Furthermore, repeating the analysis of safety with incident diagnosis of HZ as the index event providers policy makers, clinicians, and the general public with important context surrounding RZV safety.

7.4 Public Health Significance

This research provides important information for public health policy and practice. The assessment of RZV patterns of use in Aim 1 identified groups with generally lower rates of RZV initiation and completion. This information can be used in the design of targeted public health campaigns to improve vaccine update. Furthermore, these patterns were investigated within strata of immune function and by immunocompromising condition, which may assist specialists and pharmacists in increasing recommendations to groups with lower levels of vaccination.

The safety analyses presented here provide important information for policymakers, clinicians, and patients eligible for vaccination. The RZV clinical trials had limited ability to detect rare adverse events. Here, we demonstrate that, although RZV was associated with long-term autoimmune, cardiovascular, and cerebrovascular events, the risk of those events remained low and the number of cases attributable to the vaccine were rare. Associations between RZV and short- and long-term events were not higher among immunocompromised enrollees compared to immunocompetent. This should provide reassurance to clinicians and specialists who are considering recommending the vaccine to their immunocompromised patients.

7.5 Directions for Future Research

Additional research can expand on the methods used in and findings of this research to answer important questions that remain. Immunosuppression was defined using claims for diagnosis codes, procedural codes, and prescription fills, but employed a conservative approach when categorizing immunocompromising conditions – defaulting to immunosuppression via medication when obvious indications of the reason for immunosuppression were not present. Development of more intricate coding algorithms to classify immunocompromising conditions and validation of those methods using EHR-linked data would improve research activities within key subpopulations. Additionally, characterization of time-varying immunosuppression broadly assigned a uniform duration of immunosuppressive effect of medication; however, it is unlikely that all medications produce the same long-term effects on immunity. Medication-specific algorithms for characterizing time-varying immunosuppression would enhance research that seeks to assess biologic effects of immunosuppression on safety or other important outcomes.

We characterized vaccine safety using relative measures of association as produced via the self-controlled case series. Future research could evaluate safety on the absolute scale using alternate study designs such as the self-controlled risk interval. This was not used here, as the self-controlled risk interval design requires greater numbers of participants to achieve the same power as the self-controlled case series and limit our ability to investigate rare events; however, inclusion of additional years of claims data may overcome these sample size requirements in the future. Estimation of the number of additional cases of adverse events that are attributable to vaccination may further alleviate safety concerns.

After investigating RZV patterns of use and safety using insurance claims data, the next phase of this research would logically be to evaluate real-world effectiveness. Leveraging the

work completed here, effectiveness studies in MarketScan could be completed within strata of immune function and by immunocompromising condition. RZV effectiveness should be assessed with respect to HZ as well as important sequelae such as PHN and HZO. To ensure accuracy of effectiveness studies completed using claims data, validation of coding algorithms to identify HZ, PHN, and HZO using EHR-linked data should be completed.

7.6 Conclusion

While rates of RZV initiation were low, rates of series completion among initiators was relatively high. Immunocompromised patients were receiving RZV in the first couple years following the CDC's initial recommendation, despite not being specifically included in that recommendation, and had higher rates of series initiation in comparison to their immunocompetent peers. There was an increased risk of short-term events following vaccination, which was shown in the RZV clinical trials and is generally expected following vaccination. While there was an increased risk of long-term autoimmune, cardiovascular, and cerebrovascular events in the post-vaccination period, these events were rare. A central goal of this research was to evaluate risk among immunocompromised enrollees, as they were excluded from the pivotal clinical trials. Associations between RZV and short- and long-term events were not higher among immunocompromised enrollees. If anything, the relative incidence of reporting short-term events was attenuated among immunocompromised enrollees compared to immunocompetent. Real world data provide unique opportunities for evaluating vaccine patterns of use and safety after licensure, particularly for small subpopulations and rare events.

APPENDIX A: MANUSCRIPT 1 SUPPLEMENTAL TABLES AND FIGURES

Table S1a: Generic drugs associated with cancer, without or without immunosuppression

Generic Drug Name	Exclusively Cancer	Immunosuppressive
ABEMACICLIB	Yes	Yes
ACALABRUTINIB	Yes	Yes
ALDESLEUKIN	Yes	Yes
ARSENIC TRIOXIDE	Yes	Yes
ASPARAGINASE	Yes	Yes
ASPARAGINASE ERWINIA CHRYSANTHEMI	Yes	Yes
BELANTAMAB MAFODOTIN-BLMF	Yes	Yes
BELINOSTAT	Yes	Yes
BENDAMUSTINE HYDROCHLORIDE	Yes	Yes
BEXAROTENE	Yes	Yes
BLINATUMOMAB	Yes	Yes
BOSUTINIB	Yes	Yes
BRENTUXIMAB VEDOTIN	Yes	Yes
CABAZITAXEL	Yes	Yes
CALASPARGASE PEGOL-MKNL	Yes	Yes
CAPECITABINE	Yes	Yes
CARBOPLATIN	Yes	Yes
CARFILZOMIB	Yes	Yes
CISPLATIN	Yes	Yes
CLOFARABINE	Yes	Yes
CRIZOTINIB	Yes	Yes
CYTARABINE	Yes	Yes
CYTARABINE LIPOSOME/DAUNORUBICIN LIPOSOME	Yes	Yes
DACARBAZINE	Yes	Yes
DACOMITINIB	Yes	Yes
DACTINOMYCIN	Yes	Yes
DASATINIB	Yes	Yes
DAUNORUBICIN CITRATE LIPOSOME	Yes	Yes
DAUNORUBICIN HYDROCHLORIDE	Yes	Yes
DENILEUKIN DIFTITOX	Yes	Yes
DOCETAXEL	Yes	Yes
DOXORUBICIN HYDROCHLORIDE	Yes	Yes
DOXORUBICIN HYDROCHLORIDE LIPOSOME	Yes	Yes
DUVELISIB	Yes	Yes
ELOTUZUMAB	Yes	Yes
ENASIDENIB	Yes	Yes
EPIRUBICIN HYDROCHLORIDE	Yes	Yes

Generic Drug Name	Exclusively Cancer	Immunosuppressive
ETOPOSIDE	Yes	Yes
ETOPOSIDE PHOSPHATE	Yes	Yes
FEDRATINIB	Yes	Yes
FLOXURIDINE	Yes	Yes
FLUDARABINE PHOSPHATE	Yes	Yes
FLUOROURACIL	Yes	Yes
FLUTAMIDE	Yes	Yes
GEMCITABINE HYDROCHLORIDE	Yes	Yes
GEMCITABINE HYDROCHLORIDE/SODIUM CHLORIDE	Yes	Yes
GEMTUZUMAB OZOGAMICIN	Yes	Yes
GILTERITINIB	Yes	Yes
GLASDEGIB	Yes	Yes
HYALURONIDASE HUMAN, RECOMBINANT/RITUXIMAB	Yes	Yes
IDARUBICIN HYDROCHLORIDE	Yes	Yes
IDELALISIB	Yes	Yes
IFOSFAMIDE	Yes	Yes
IFOSFAMIDE/MESNA	Yes	Yes
IMATINIB MESYLATE	Yes	Yes
INOTUZUMAB OZOGAMICIN	Yes	Yes
IRINOTECAN HYDROCHLORIDE	Yes	Yes
IRINOTECAN LIPOSOME	Yes	Yes
ISATUXIMAB-IRFC	Yes	Yes
IVOSIDENIB	Yes	Yes
IXABEPILONE	Yes	Yes
IXAZOMIB	Yes	Yes
LENALIDOMIDE	Yes	Yes
LETROZOLE;RIBOCICLIB	Yes	Yes
LOMUSTINE	Yes	Yes
LOMUSTINE;LOMUSTINE;LOMUSTINE	Yes	Yes
LORLATINIB	Yes	Yes
LURBINECTEDIN	Yes	Yes
MECHLORETHAMINE HYDROCHLORIDE	Yes	Yes
MIDOSTAURIN	Yes	Yes
MITOMYCIN	Yes	Yes
MOGAMULIZUMAB-KPKC	Yes	Yes
MOXETUMOMAB PASUDOTOX-TDFK	Yes	Yes
NELARABINE	Yes	Yes
NILOTINIB HYDROCHLORIDE	Yes	Yes
NIRAPARIB	Yes	Yes

Generic Drug Name	Exclusively Cancer	Immunosuppressive
OBINUTUZUMAB	Yes	Yes
OFATUMUMAB	Yes	Yes
OLAPARIB	Yes	Yes
OMACETAXINE MEPESUCCINATE	Yes	Yes
PACLITAXEL	Yes	Yes
PACLITAXEL PROTEIN-BOUND	Yes	Yes
PALBOCICLIB	Yes	Yes
PANOBINOSTAT	Yes	Yes
PAZOPANIB HYDROCHLORIDE	Yes	Yes
PEGASPARGASE	Yes	Yes
PEMETREXED	Yes	Yes
PENTOSTATIN	Yes	Yes
POLATUZUMAB VEDOTIN-PIIQ	Yes	Yes
POMALIDOMIDE	Yes	Yes
PONATINIB HYDROCHLORIDE	Yes	Yes
PRALATREXATE	Yes	Yes
PROCARBAZINE HYDROCHLORIDE	Yes	Yes
REGORAFENIB	Yes	Yes
RIBOCICLIB	Yes	Yes
ROMIDEPSIN	Yes	Yes
SACITUZUMAB GOVITECAN-HZIY	Yes	Yes
SELINEXOR	Yes	Yes
SILTUXIMAB	Yes	Yes
TAFASITAMAB-CXIX	Yes	Yes
TAGRAXOFUSP-ERZS	Yes	Yes
TAZEMETOSTAT	Yes	Yes
TEMOZOLOMIDE	Yes	Yes
TEMSIROLIMUS	Yes	Yes
TENIPOSIDE	Yes	Yes
THIOGUANINE	Yes	Yes
TIPIRACIL/TRIFLURIDINE	Yes	Yes
TOPOTECAN HYDROCHLORIDE	Yes	Yes
TRABECTEDIN	Yes	Yes
TRASTUZUMAB	Yes	Yes
TRASTUZUMAB-ANNS	Yes	Yes
TRASTUZUMAB-DKST	Yes	Yes
TRASTUZUMAB-DTTB	Yes	Yes
TRASTUZUMAB-PKRB	Yes	Yes
TRASTUZUMAB-QYYP	Yes	Yes
TRETINOIN	Yes	Yes
VENETOCLAX	Yes	Yes

Generic Drug Name	Exclusively Cancer	Immunosuppressive
VENETOCLAX;VENETOCLAX;VENETOCLAX	Yes	Yes
VINBLASTINE SULFATE	Yes	Yes
VINCRISTINE SULFATE LIPOSOME	Yes	Yes
VINORELBINE TARTRATE	Yes	Yes
VORINOSTAT	Yes	Yes
ZANUBRUTINIB	Yes	Yes
ABIRATERONE ACETATE	Yes	No
ABIRATERONE ACETATE, MICRONIZED	Yes	No
ADO-TRASTUZUMAB EMTANSINE	Yes	No
AFATINIB DIMALEATE	Yes	No
ALECTINIB	Yes	No
ALPELISIB	Yes	No
ALPELISIB;ALPELISIB	Yes	No
ALTRETAMINE	Yes	No
AMIFOSTINE	Yes	No
APALUTAMIDE	Yes	No
ATEZOLIZUMAB	Yes	No
AVAPRITINIB	Yes	No
AVELUMAB	Yes	No
AXITINIB	Yes	No
BICALUTAMIDE	Yes	No
BINIMETINIB	Yes	No
BLEOMYCIN SULFATE	Yes	No
BRIGATINIB	Yes	No
BRIGATINIB;BRIGATINIB	Yes	No
CABOZANTINIB MALATE	Yes	No
CABOZANTINIB MALATE;CABOZANTINIB MALATE	Yes	No
CAPMATINIB	Yes	No
CEMIPLIMAB-RWLC	Yes	No
CERITINIB	Yes	No
CETUXIMAB	Yes	No
COBIMETINIB	Yes	No
DABRAFENIB MESYLATE	Yes	No
DAROLUTAMIDE	Yes	No
DINUTUXIMAB	Yes	No
DURVALUMAB	Yes	No
ENCORAFENIB	Yes	No
ENFORTUMAB VEDOTIN-EJFV	Yes	No
ENTRECTINIB	Yes	No
ENZALUTAMIDE	Yes	No

Generic Drug Name	Exclusively Cancer	Immunosuppressive
ERDAFITINIB	Yes	No
ERIBULIN MESYLATE	Yes	No
ERLOTINIB HYDROCHLORIDE	Yes	No
ESTRAMUSTINE PHOSPHATE SODIUM	Yes	No
FAM-TRASTUZUMAB DERUXTECAN-NXKI	Yes	No
GEFITINIB	Yes	No
HYALURONIDASE-OYSK/TRASTUZUMAB	Yes	No
HYALURONIDASE-ZZXF/PERTUZUMAB/TRASTUZUMAB	Yes	No
IOBENGUANE I 131	Yes	No
IOBENGUANE I 131 SULFATE	Yes	No
IPILIMUMAB	Yes	No
LAPATINIB DITOSYLATE	Yes	No
LAROTRECTINIB	Yes	No
LENVATINIB	Yes	No
LENVATINIB;LENVATINIB	Yes	No
LUTETIUM LU 177 DOTATATE	Yes	No
NECITUMUMAB	Yes	No
NERATINIB	Yes	No
NILUTAMIDE	Yes	No
NIVOLUMAB	Yes	No
OLARATUMAB	Yes	No
OSIMERTINIB	Yes	No
OXALIPLATIN	Yes	No
PANITUMUMAB	Yes	No
PEGINTERFERON ALFA-2B	Yes	No
PEMBROLIZUMAB	Yes	No
PEMIGATINIB	Yes	No
PERTUZUMAB	Yes	No
PLICAMYCIN	Yes	No
PORFIMER SODIUM	Yes	No
PRALSETINIB	Yes	No
RAMUCIRUMAB	Yes	No
RIPRETINIB	Yes	No
RUCAPARIB	Yes	No
SELPERCATINIB	Yes	No
SONIDEGIB	Yes	No
SORAFENIB TOSYLATE	Yes	No
STREPTOZOCIN	Yes	No
SUNITINIB MALATE	Yes	No
TALAZOPARIB	Yes	No

Generic Drug Name	Exclusively Cancer	Immunosuppressive
TALIMOGENE LAHERPAREPVEC	Yes	No
TRAMETINIB DIMETHYL SULFOXIDE	Yes	No
TUCATINIB	Yes	No
VANDETANIB	Yes	No
VEMURAFENIB	Yes	No
VINCRISTINE SULFATE	Yes	No
VISMODEGIB	Yes	No
ZIV-AFLIBERCEPT	Yes	No
ALEMTUZUMAB	No	Yes
BUSULFAN	No	Yes
CARMUSTINE	No	Yes
CEDAZURIDINE/DECITABINE	No	Yes
CHLORAMBUCIL	No	Yes
CLADRIBINE	No	Yes
CYCLOPHOSPHAMIDE	No	Yes
DARATUMUMAB	No	Yes
DARATUMUMAB/HYALURONIDASE-FIHJ	No	Yes
DECITABINE	No	Yes
DENOSUMAB	No	Yes
EVEROLIMUS	No	Yes
GOLIMUMAB	No	Yes
HYDROXYUREA	No	Yes
IBRITUMOMAB TIUXETAN	No	Yes
IBRUTINIB	No	Yes
INTERFERON ALFA-2B	No	Yes
MELPHALAN	No	Yes
MELPHALAN HYDROCHLORIDE	No	Yes
MERCAPTOPURINE	No	Yes
METHOTREXATE	No	Yes
METHOTREXATE SODIUM	No	Yes
MITOXANTRONE HYDROCHLORIDE	No	Yes
RITUXIMAB	No	Yes
RITUXIMAB-ABBS	No	Yes
RITUXIMAB-PVVR	No	Yes
RUXOLITINIB PHOSPHATE	No	Yes
THIOTEPA	No	Yes
BEVACIZUMAB	No	No
BEVACIZUMAB-AWWB	No	No
BEVACIZUMAB-BVZR	No	No
BORTEZOMIB	No	No
EXEMESTANE	No	No

Generic Drug Name	Exclusively Cancer	Immunosuppressive
MEGESTROL ACETATE	No	No
MITOTANE	No	No
PIPOBROMAN	No	No
AZACITIDINE	No	Yes

Table S1b: ICD-10-CM diagnosis codes associated with cancer, without or without immunosuppression

ICD-10-CM	Code Description	IC
C79.5	SECONDARY MALIGNANT NEOPLASM OF BONE AND BONE MARROW	Yes
C79.51	SECONDARY MALIGNANT NEOPLASM OF BONE	Yes
C79.52	SECONDARY MALIGNANT NEOPLASM OF BONE MARROW	Yes
C81	HODGKIN LYMPHOMA	Yes
C81.0	NODULAR LYMPHOCYTE PREDOMINANT HODGKIN LYMPHOMA	Yes
C81.00	NODULAR LYMPHOCYTE PREDOMINANT HODGKIN LYMPHOMA, UNSPECIFIED SITE	Yes
C81.01	NODULAR LYMPHOCYTE PREDOMINANT HODGKIN LYMPHOMA, LYMPH NODES OF HEAD, FACE, AND NECK	Yes
C81.02	NODULAR LYMPHOCYTE PREDOMINANT HODGKIN LYMPHOMA, INTRATHORACIC LYMPH NODES	Yes
C81.03	NODULAR LYMPHOCYTE PREDOMINANT HODGKIN LYMPHOMA, INTRA-ABDOMINAL LYMPH NODES	Yes
C81.04	NODULAR LYMPHOCYTE PREDOMINANT HODGKIN LYMPHOMA, LYMPH NODES OF AXILLA AND UPPER LIMB	Yes
C81.05	NODULAR LYMPHOCYTE PREDOMINANT HODGKIN LYMPHOMA, LYMPH NODES OF INGUINAL REGION AND LOWER LIMB	Yes
C81.06	NODULAR LYMPHOCYTE PREDOMINANT HODGKIN LYMPHOMA, INTRAPELVIC LYMPH NODES	Yes
C81.07	NODULAR LYMPHOCYTE PREDOMINANT HODGKIN LYMPHOMA, SPLEEN	Yes
C81.08	NODULAR LYMPHOCYTE PREDOMINANT HODGKIN LYMPHOMA, LYMPH NODES OF MULTIPLE SITES	Yes
C81.09	NODULAR LYMPHOCYTE PREDOMINANT HODGKIN LYMPHOMA, EXTRANODAL AND SOLID ORGAN SITES	Yes
C81.1	NODULAR SCLEROSIS HODGKIN LYMPHOMA	Yes
C81.10	NODULAR SCLEROSIS HODGKIN LYMPHOMA, UNSPECIFIED SITE	Yes
C81.11	NODULAR SCLEROSIS HODGKIN LYMPHOMA, LYMPH NODES OF HEAD, FACE, AND NECK	Yes
C81.12	NODULAR SCLEROSIS HODGKIN LYMPHOMA, INTRATHORACIC LYMPH NODES	Yes
C81.13	NODULAR SCLEROSIS HODGKIN LYMPHOMA, INTRA-ABDOMINAL LYMPH NODES	Yes
C81.14	NODULAR SCLEROSIS HODGKIN LYMPHOMA, LYMPH NODES OF AXILLA AND UPPER LIMB	Yes
C81.15	NODULAR SCLEROSIS HODGKIN LYMPHOMA, LYMPH NODES OF INGUINAL REGION AND LOWER LIMB	Yes
C81.16	NODULAR SCLEROSIS HODGKIN LYMPHOMA, INTRAPELVIC LYMPH NODES	Yes
C81.17	NODULAR SCLEROSIS HODGKIN LYMPHOMA, SPLEEN	Yes
C81.18	NODULAR SCLEROSIS HODGKIN LYMPHOMA, LYMPH NODES OF MULTIPLE SITES	Yes
C81.19	NODULAR SCLEROSIS HODGKIN LYMPHOMA, EXTRANODAL AND SOLID ORGAN SITES	Yes
C81.2	MIXED CELLULARITY HODGKIN LYMPHOMA	Yes
C81.20	MIXED CELLULARITY HODGKIN LYMPHOMA, UNSPECIFIED SITE	Yes

ICD-10-CM	Code Description	IC
C81.21	MIXED CELLULARITY HODGKIN LYMPHOMA, LYMPH NODES OF HEAD, FACE, AND NECK	Yes
C81.22	MIXED CELLULARITY HODGKIN LYMPHOMA, INTRATHORACIC LYMPH NODES	Yes
C81.23	MIXED CELLULARITY HODGKIN LYMPHOMA, INTRA-ABDOMINAL LYMPH NODES	Yes
C81.24	MIXED CELLULARITY HODGKIN LYMPHOMA, LYMPH NODES OF AXILLA AND UPPER LIMB	Yes
C81.25	MIXED CELLULARITY HODGKIN LYMPHOMA, LYMPH NODES OF INGUINAL REGION AND LOWER LIMB	Yes
C81.26	MIXED CELLULARITY HODGKIN LYMPHOMA, INTRAPELVIC LYMPH NODES	Yes
C81.27	MIXED CELLULARITY HODGKIN LYMPHOMA, SPLEEN	Yes
C81.28	MIXED CELLULARITY HODGKIN LYMPHOMA, LYMPH NODES OF MULTIPLE SITES	Yes
C81.29	MIXED CELLULARITY HODGKIN LYMPHOMA, EXTRANODAL AND SOLID ORGAN SITES	Yes
C81.3	LYMPHOCYTE DEPLETED HODGKIN LYMPHOMA	Yes
C81.30	LYMPHOCYTE DEPLETED HODGKIN LYMPHOMA, UNSPECIFIED SITE	Yes
C81.31	LYMPHOCYTE DEPLETED HODGKIN LYMPHOMA, LYMPH NODES OF HEAD, FACE, AND NECK	Yes
C81.32	LYMPHOCYTE DEPLETED HODGKIN LYMPHOMA, INTRATHORACIC LYMPH NODES	Yes
C81.33	LYMPHOCYTE DEPLETED HODGKIN LYMPHOMA, INTRA-ABDOMINAL LYMPH NODES	Yes
C81.34	LYMPHOCYTE DEPLETED HODGKIN LYMPHOMA, LYMPH NODES OF AXILLA AND UPPER LIMB	Yes
C81.35	LYMPHOCYTE DEPLETED HODGKIN LYMPHOMA, LYMPH NODES OF INGUINAL REGION AND LOWER LIMB	Yes
C81.36	LYMPHOCYTE DEPLETED HODGKIN LYMPHOMA, INTRAPELVIC LYMPH NODES	Yes
C81.37	LYMPHOCYTE DEPLETED HODGKIN LYMPHOMA, SPLEEN	Yes
C81.38	LYMPHOCYTE DEPLETED HODGKIN LYMPHOMA, LYMPH NODES OF MULTIPLE SITES	Yes
C81.39	LYMPHOCYTE DEPLETED HODGKIN LYMPHOMA, EXTRANODAL AND SOLID ORGAN SITES	Yes
C81.4	LYMPHOCYTE-RICH HODGKIN LYMPHOMA	Yes
C81.40	LYMPHOCYTE-RICH HODGKIN LYMPHOMA, UNSPECIFIED SITE	Yes
C81.41	LYMPHOCYTE-RICH HODGKIN LYMPHOMA, LYMPH NODES OF HEAD, FACE, AND NECK	Yes
C81.42	LYMPHOCYTE-RICH HODGKIN LYMPHOMA, INTRATHORACIC LYMPH NODES	Yes
C81.43	LYMPHOCYTE-RICH HODGKIN LYMPHOMA, INTRA-ABDOMINAL LYMPH NODES	Yes
C81.44	LYMPHOCYTE-RICH HODGKIN LYMPHOMA, LYMPH NODES OF AXILLA AND UPPER LIMB	Yes
C81.45	LYMPHOCYTE-RICH HODGKIN LYMPHOMA, LYMPH NODES OF INGUINAL REGION AND LOWER LIMB	Yes
C81.46	LYMPHOCYTE-RICH HODGKIN LYMPHOMA, INTRAPELVIC LYMPH NODES	Yes

ICD-10-CM	Code Description	IC
C81.47	LYMPHOCYTE-RICH HODGKIN LYMPHOMA, SPLEEN	Yes
C81.48	LYMPHOCYTE-RICH HODGKIN LYMPHOMA, LYMPH NODES OF MULTIPLE SITES	Yes
C81.49	LYMPHOCYTE-RICH HODGKIN LYMPHOMA, EXTRANODAL AND SOLID ORGAN SITES	Yes
C81.7	OTHER HODGKIN LYMPHOMA	Yes
C81.70	OTHER HODGKIN LYMPHOMA, UNSPECIFIED SITE	Yes
C81.71	OTHER HODGKIN LYMPHOMA, LYMPH NODES OF HEAD, FACE, AND NECK	Yes
C81.72	OTHER HODGKIN LYMPHOMA, INTRATHORACIC LYMPH NODES	Yes
C81.73	OTHER HODGKIN LYMPHOMA, INTRA-ABDOMINAL LYMPH NODES	Yes
C81.74	OTHER HODGKIN LYMPHOMA, LYMPH NODES OF AXILLA AND UPPER LIMB	Yes
C81.75	OTHER HODGKIN LYMPHOMA, LYMPH NODES OF INGUINAL REGION AND LOWER LIMB	Yes
C81.76	OTHER HODGKIN LYMPHOMA, INTRAPELVIC LYMPH NODES	Yes
C81.77	OTHER HODGKIN LYMPHOMA, SPLEEN	Yes
C81.78	OTHER HODGKIN LYMPHOMA, LYMPH NODES OF MULTIPLE SITES	Yes
C81.79	OTHER HODGKIN LYMPHOMA, EXTRANODAL AND SOLID ORGAN SITES	Yes
C81.9	HODGKIN LYMPHOMA, UNSPECIFIED	Yes
C81.90	HODGKIN LYMPHOMA, UNSPECIFIED, UNSPECIFIED SITE	Yes
C81.91	HODGKIN LYMPHOMA, UNSPECIFIED, LYMPH NODES OF HEAD, FACE, AND NECK	Yes
C81.92	HODGKIN LYMPHOMA, UNSPECIFIED, INTRATHORACIC LYMPH NODES	Yes
C81.93	HODGKIN LYMPHOMA, UNSPECIFIED, INTRA-ABDOMINAL LYMPH NODES	Yes
C81.94	HODGKIN LYMPHOMA, UNSPECIFIED, LYMPH NODES OF AXILLA AND UPPER LIMB	Yes
C81.95	HODGKIN LYMPHOMA, UNSPECIFIED, LYMPH NODES OF INGUINAL REGION AND LOWER LIMB	Yes
C81.96	HODGKIN LYMPHOMA, UNSPECIFIED, INTRAPELVIC LYMPH NODES	Yes
C81.97	HODGKIN LYMPHOMA, UNSPECIFIED, SPLEEN	Yes
C81.98	HODGKIN LYMPHOMA, UNSPECIFIED, LYMPH NODES OF MULTIPLE SITES	Yes
C81.99	HODGKIN LYMPHOMA, UNSPECIFIED, EXTRANODAL AND SOLID ORGAN SITES	Yes
C82	FOLLICULAR LYMPHOMA	Yes
C82.0	FOLLICULAR LYMPHOMA GRADE I	Yes
C82.00	FOLLICULAR LYMPHOMA GRADE I, UNSPECIFIED SITE	Yes
C82.01	FOLLICULAR LYMPHOMA GRADE I, LYMPH NODES OF HEAD, FACE, AND NECK	Yes
C82.02	FOLLICULAR LYMPHOMA GRADE I, INTRATHORACIC LYMPH NODES	Yes
C82.03	FOLLICULAR LYMPHOMA GRADE I, INTRA-ABDOMINAL LYMPH NODES	Yes
C82.04	FOLLICULAR LYMPHOMA GRADE I, LYMPH NODES OF AXILLA AND UPPER LIMB	Yes
C82.05	FOLLICULAR LYMPHOMA GRADE I, LYMPH NODES OF INGUINAL REGION AND LOWER LIMB	Yes
C82.06	FOLLICULAR LYMPHOMA GRADE I, INTRAPELVIC LYMPH NODES	Yes
C82.07	FOLLICULAR LYMPHOMA GRADE I, SPLEEN	Yes
C82.08	FOLLICULAR LYMPHOMA GRADE I, LYMPH NODES OF MULTIPLE SITES	Yes

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C82.09	FOLLICULAR LYMPHOMA GRADE I, EXTRANODAL AND SOLID ORGAN SITES	Yes
C82.1	FOLLICULAR LYMPHOMA GRADE II	Yes
C82.10	FOLLICULAR LYMPHOMA GRADE II, UNSPECIFIED SITE	Yes
C82.11	FOLLICULAR LYMPHOMA GRADE II, LYMPH NODES OF HEAD, FACE, AND NECK	Yes
C82.12	FOLLICULAR LYMPHOMA GRADE II, INTRATHORACIC LYMPH NODES	Yes
C82.13	FOLLICULAR LYMPHOMA GRADE II, INTRA-ABDOMINAL LYMPH NODES	Yes
C82.14	FOLLICULAR LYMPHOMA GRADE II, LYMPH NODES OF AXILLA AND UPPER LIMB	Yes
C82.15	FOLLICULAR LYMPHOMA GRADE II, LYMPH NODES OF INGUINAL REGION AND LOWER LIMB	Yes
C82.16	FOLLICULAR LYMPHOMA GRADE II, INTRAPELVIC LYMPH NODES	Yes
C82.17	FOLLICULAR LYMPHOMA GRADE II, SPLEEN	Yes
C82.18	FOLLICULAR LYMPHOMA GRADE II, LYMPH NODES OF MULTIPLE SITES	Yes
C82.19	FOLLICULAR LYMPHOMA GRADE II, EXTRANODAL AND SOLID ORGAN SITES	Yes
C82.2	FOLLICULAR LYMPHOMA GRADE III, UNSPECIFIED	Yes
C82.20	FOLLICULAR LYMPHOMA GRADE III, UNSPECIFIED, UNSPECIFIED SITE	Yes
C82.21	FOLLICULAR LYMPHOMA GRADE III, UNSPECIFIED, LYMPH NODES OF HEAD, FACE, AND NECK	Yes
C82.22	FOLLICULAR LYMPHOMA GRADE III, UNSPECIFIED, INTRATHORACIC LYMPH NODES	Yes
C82.23	FOLLICULAR LYMPHOMA GRADE III, UNSPECIFIED, INTRA-ABDOMINAL LYMPH NODES	Yes
C82.24	FOLLICULAR LYMPHOMA GRADE III, UNSPECIFIED, LYMPH NODES OF AXILLA AND UPPER LIMB	Yes
C82.25	FOLLICULAR LYMPHOMA GRADE III, UNSPECIFIED, LYMPH NODES OF INGUINAL REGION AND LOWER LIMB	Yes
C82.26	FOLLICULAR LYMPHOMA GRADE III, UNSPECIFIED, INTRAPELVIC LYMPH NODES	Yes
C82.27	FOLLICULAR LYMPHOMA GRADE III, UNSPECIFIED, SPLEEN	Yes
C82.28	FOLLICULAR LYMPHOMA GRADE III, UNSPECIFIED, LYMPH NODES OF MULTIPLE SITES	Yes
C82.29	FOLLICULAR LYMPHOMA GRADE III, UNSPECIFIED, EXTRANODAL AND SOLID ORGAN SITES	Yes
C82.3	FOLLICULAR LYMPHOMA GRADE IIIA	Yes
C82.30	FOLLICULAR LYMPHOMA GRADE IIIA, UNSPECIFIED SITE	Yes
C82.31	FOLLICULAR LYMPHOMA GRADE IIIA, LYMPH NODES OF HEAD, FACE, AND NECK	Yes
C82.32	FOLLICULAR LYMPHOMA GRADE IIIA, INTRATHORACIC LYMPH NODES	Yes
C82.33	FOLLICULAR LYMPHOMA GRADE IIIA, INTRA-ABDOMINAL LYMPH NODES	Yes
C82.34	FOLLICULAR LYMPHOMA GRADE IIIA, LYMPH NODES OF AXILLA AND UPPER LIMB	Yes
C82.35	FOLLICULAR LYMPHOMA GRADE IIIA, LYMPH NODES OF INGUINAL REGION AND LOWER LIMB	Yes
C82.36	FOLLICULAR LYMPHOMA GRADE IIIA, INTRAPELVIC LYMPH NODES	Yes

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C82.37	FOLLICULAR LYMPHOMA GRADE IIIA, SPLEEN	Yes
C82.38	FOLLICULAR LYMPHOMA GRADE IIIA, LYMPH NODES OF MULTIPLE SITES	Yes
C82.39	FOLLICULAR LYMPHOMA GRADE IIIA, EXTRANODAL AND SOLID ORGAN SITES	Yes
C82.4	FOLLICULAR LYMPHOMA GRADE IIIB	Yes
C82.40	FOLLICULAR LYMPHOMA GRADE IIIB, UNSPECIFIED SITE	Yes
C82.41	FOLLICULAR LYMPHOMA GRADE IIIB, LYMPH NODES OF HEAD, FACE, AND NECK	Yes
C82.42	FOLLICULAR LYMPHOMA GRADE IIIB, INTRATHORACIC LYMPH NODES	Yes
C82.43	FOLLICULAR LYMPHOMA GRADE IIIB, INTRA-ABDOMINAL LYMPH NODES	Yes
C82.44	FOLLICULAR LYMPHOMA GRADE IIIB, LYMPH NODES OF AXILLA AND UPPER LIMB	Yes
C82.45	FOLLICULAR LYMPHOMA GRADE IIIB, LYMPH NODES OF INGUINAL REGION AND LOWER LIMB	Yes
C82.46	FOLLICULAR LYMPHOMA GRADE IIIB, INTRAPELVIC LYMPH NODES	Yes
C82.47	FOLLICULAR LYMPHOMA GRADE IIIB, SPLEEN	Yes
C82.48	FOLLICULAR LYMPHOMA GRADE IIIB, LYMPH NODES OF MULTIPLE SITES	Yes
C82.49	FOLLICULAR LYMPHOMA GRADE IIIB, EXTRANODAL AND SOLID ORGAN SITES	Yes
C82.5	DIFFUSE FOLLICLE CENTER LYMPHOMA	Yes
C82.50	DIFFUSE FOLLICLE CENTER LYMPHOMA, UNSPECIFIED SITE	Yes
C82.51	DIFFUSE FOLLICLE CENTER LYMPHOMA, LYMPH NODES OF HEAD, FACE, AND NECK	Yes
C82.52	DIFFUSE FOLLICLE CENTER LYMPHOMA, INTRATHORACIC LYMPH NODES	Yes
C82.53	DIFFUSE FOLLICLE CENTER LYMPHOMA, INTRA-ABDOMINAL LYMPH NODES	Yes
C82.54	DIFFUSE FOLLICLE CENTER LYMPHOMA, LYMPH NODES OF AXILLA AND UPPER LIMB	Yes
C82.55	DIFFUSE FOLLICLE CENTER LYMPHOMA, LYMPH NODES OF INGUINAL REGION AND LOWER LIMB	Yes
C82.56	DIFFUSE FOLLICLE CENTER LYMPHOMA, INTRAPELVIC LYMPH NODES	Yes
C82.57	DIFFUSE FOLLICLE CENTER LYMPHOMA, SPLEEN	Yes
C82.58	DIFFUSE FOLLICLE CENTER LYMPHOMA, LYMPH NODES OF MULTIPLE SITES	Yes
C82.59	DIFFUSE FOLLICLE CENTER LYMPHOMA, EXTRANODAL AND SOLID ORGAN SITES	Yes
C82.6	CUTANEOUS FOLLICLE CENTER LYMPHOMA	Yes
C82.60	CUTANEOUS FOLLICLE CENTER LYMPHOMA, UNSPECIFIED SITE	Yes
C82.61	CUTANEOUS FOLLICLE CENTER LYMPHOMA, LYMPH NODES OF HEAD, FACE, AND NECK	Yes
C82.62	CUTANEOUS FOLLICLE CENTER LYMPHOMA, INTRATHORACIC LYMPH NODES	Yes
C82.63	CUTANEOUS FOLLICLE CENTER LYMPHOMA, INTRA-ABDOMINAL LYMPH NODES	Yes
C82.64	CUTANEOUS FOLLICLE CENTER LYMPHOMA, LYMPH NODES OF AXILLA AND UPPER LIMB	Yes
C82.65	CUTANEOUS FOLLICLE CENTER LYMPHOMA, LYMPH NODES OF INGUINAL REGION AND LOWER LIMB	Yes
C82.66	CUTANEOUS FOLLICLE CENTER LYMPHOMA, INTRAPELVIC LYMPH NODES	Yes

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C82.67	CUTANEOUS FOLLICLE CENTER LYMPHOMA, SPLEEN	Yes
C82.68	CUTANEOUS FOLLICLE CENTER LYMPHOMA, LYMPH NODES OF MULTIPLE SITES	Yes
C82.69	CUTANEOUS FOLLICLE CENTER LYMPHOMA, EXTRANODAL AND SOLID ORGAN SITES	Yes
C82.8	OTHER TYPES OF FOLLICULAR LYMPHOMA	Yes
C82.80	OTHER TYPES OF FOLLICULAR LYMPHOMA, UNSPECIFIED SITE	Yes
C82.81	OTHER TYPES OF FOLLICULAR LYMPHOMA, LYMPH NODES OF HEAD, FACE, AND NECK	Yes
C82.82	OTHER TYPES OF FOLLICULAR LYMPHOMA, INTRATHORACIC LYMPH NODES	Yes
C82.83	OTHER TYPES OF FOLLICULAR LYMPHOMA, INTRA-ABDOMINAL LYMPH NODES	Yes
C82.84	OTHER TYPES OF FOLLICULAR LYMPHOMA, LYMPH NODES OF AXILLA AND UPPER LIMB	Yes
C82.85	OTHER TYPES OF FOLLICULAR LYMPHOMA, LYMPH NODES OF INGUINAL REGION AND LOWER LIMB	Yes
C82.86	OTHER TYPES OF FOLLICULAR LYMPHOMA, INTRAPELVIC LYMPH NODES	Yes
C82.87	OTHER TYPES OF FOLLICULAR LYMPHOMA, SPLEEN	Yes
C82.88	OTHER TYPES OF FOLLICULAR LYMPHOMA, LYMPH NODES OF MULTIPLE SITES	Yes
C82.89	OTHER TYPES OF FOLLICULAR LYMPHOMA, EXTRANODAL AND SOLID ORGAN SITES	Yes
C82.9	FOLLICULAR LYMPHOMA, UNSPECIFIED	Yes
C82.90	FOLLICULAR LYMPHOMA, UNSPECIFIED, UNSPECIFIED SITE	Yes
C82.91	FOLLICULAR LYMPHOMA, UNSPECIFIED, LYMPH NODES OF HEAD, FACE, AND NECK	Yes
C82.92	FOLLICULAR LYMPHOMA, UNSPECIFIED, INTRATHORACIC LYMPH NODES	Yes
C82.93	FOLLICULAR LYMPHOMA, UNSPECIFIED, INTRA-ABDOMINAL LYMPH NODES	Yes
C82.94	FOLLICULAR LYMPHOMA, UNSPECIFIED, LYMPH NODES OF AXILLA AND UPPER LIMB	Yes
C82.95	FOLLICULAR LYMPHOMA, UNSPECIFIED, LYMPH NODES OF INGUINAL REGION AND LOWER LIMB	Yes
C82.96	FOLLICULAR LYMPHOMA, UNSPECIFIED, INTRAPELVIC LYMPH NODES	Yes
C82.97	FOLLICULAR LYMPHOMA, UNSPECIFIED, SPLEEN	Yes
C82.98	FOLLICULAR LYMPHOMA, UNSPECIFIED, LYMPH NODES OF MULTIPLE SITES	Yes
C82.99	FOLLICULAR LYMPHOMA, UNSPECIFIED, EXTRANODAL AND SOLID ORGAN SITES	Yes
C83	NON-FOLLICULAR LYMPHOMA	Yes
C83.0	SMALL CELL B-CELL LYMPHOMA	Yes
C83.00	SMALL CELL B-CELL LYMPHOMA, UNSPECIFIED SITE	Yes
C83.01	SMALL CELL B-CELL LYMPHOMA, LYMPH NODES OF HEAD, FACE, AND NECK	Yes
C83.02	SMALL CELL B-CELL LYMPHOMA, INTRATHORACIC LYMPH NODES	Yes
C83.03	SMALL CELL B-CELL LYMPHOMA, INTRA-ABDOMINAL LYMPH NODES	Yes
C83.04	SMALL CELL B-CELL LYMPHOMA, LYMPH NODES OF AXILLA AND UPPER LIMB	Yes

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C83.05	SMALL CELL B-CELL LYMPHOMA, LYMPH NODES OF INGUINAL REGION AND LOWER LIMB	Yes
C83.06	SMALL CELL B-CELL LYMPHOMA, INTRAPELVIC LYMPH NODES	Yes
C83.07	SMALL CELL B-CELL LYMPHOMA, SPLEEN	Yes
C83.08	SMALL CELL B-CELL LYMPHOMA, LYMPH NODES OF MULTIPLE SITES	Yes
C83.09	SMALL CELL B-CELL LYMPHOMA, EXTRANODAL AND SOLID ORGAN SITES	Yes
C83.1	MANTLE CELL LYMPHOMA	Yes
C83.10	MANTLE CELL LYMPHOMA, UNSPECIFIED SITE	Yes
C83.11	MANTLE CELL LYMPHOMA, LYMPH NODES OF HEAD, FACE, AND NECK	Yes
C83.12	MANTLE CELL LYMPHOMA, INTRATHORACIC LYMPH NODES	Yes
C83.13	MANTLE CELL LYMPHOMA, INTRA-ABDOMINAL LYMPH NODES	Yes
C83.14	MANTLE CELL LYMPHOMA, LYMPH NODES OF AXILLA AND UPPER LIMB	Yes
C83.15	MANTLE CELL LYMPHOMA, LYMPH NODES OF INGUINAL REGION AND LOWER LIMB	Yes
C83.16	MANTLE CELL LYMPHOMA, INTRAPELVIC LYMPH NODES	Yes
C83.17	MANTLE CELL LYMPHOMA, SPLEEN	Yes
C83.18	MANTLE CELL LYMPHOMA, LYMPH NODES OF MULTIPLE SITES	Yes
C83.19	MANTLE CELL LYMPHOMA, EXTRANODAL AND SOLID ORGAN SITES	Yes
C83.3	DIFFUSE LARGE B-CELL LYMPHOMA	Yes
C83.30	DIFFUSE LARGE B-CELL LYMPHOMA, UNSPECIFIED SITE	Yes
C83.31	DIFFUSE LARGE B-CELL LYMPHOMA, LYMPH NODES OF HEAD, FACE, AND NECK	Yes
C83.32	DIFFUSE LARGE B-CELL LYMPHOMA, INTRATHORACIC LYMPH NODES	Yes
C83.33	DIFFUSE LARGE B-CELL LYMPHOMA, INTRA-ABDOMINAL LYMPH NODES	Yes
C83.34	DIFFUSE LARGE B-CELL LYMPHOMA, LYMPH NODES OF AXILLA AND UPPER LIMB	Yes
C83.35	DIFFUSE LARGE B-CELL LYMPHOMA, LYMPH NODES OF INGUINAL REGION AND LOWER LIMB	Yes
C83.36	DIFFUSE LARGE B-CELL LYMPHOMA, INTRAPELVIC LYMPH NODES	Yes
C83.37	DIFFUSE LARGE B-CELL LYMPHOMA, SPLEEN	Yes
C83.38	DIFFUSE LARGE B-CELL LYMPHOMA, LYMPH NODES OF MULTIPLE SITES	Yes
C83.39	DIFFUSE LARGE B-CELL LYMPHOMA, EXTRANODAL AND SOLID ORGAN SITES	Yes
C83.5	LYMPHOBLASTIC (DIFFUSE) LYMPHOMA	Yes
C83.50	LYMPHOBLASTIC (DIFFUSE) LYMPHOMA, UNSPECIFIED SITE	Yes
C83.51	LYMPHOBLASTIC (DIFFUSE) LYMPHOMA, LYMPH NODES OF HEAD, FACE, AND NECK	Yes
C83.52	LYMPHOBLASTIC (DIFFUSE) LYMPHOMA, INTRATHORACIC LYMPH NODES	Yes
C83.53	LYMPHOBLASTIC (DIFFUSE) LYMPHOMA, INTRA-ABDOMINAL LYMPH NODES	Yes
C83.54	LYMPHOBLASTIC (DIFFUSE) LYMPHOMA, LYMPH NODES OF AXILLA AND UPPER LIMB	Yes
C83.55	LYMPHOBLASTIC (DIFFUSE) LYMPHOMA, LYMPH NODES OF INGUINAL REGION AND LOWER LIMB	Yes
C83.56	LYMPHOBLASTIC (DIFFUSE) LYMPHOMA, INTRAPELVIC LYMPH NODES	Yes

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C83.57	LYMPHOBLASTIC (DIFFUSE) LYMPHOMA, SPLEEN	Yes
C83.58	LYMPHOBLASTIC (DIFFUSE) LYMPHOMA, LYMPH NODES OF MULTIPLE SITES	Yes
C83.59	LYMPHOBLASTIC (DIFFUSE) LYMPHOMA, EXTRANODAL AND SOLID ORGAN SITES	Yes
C83.7	BURKITT LYMPHOMA	Yes
C83.70	BURKITT LYMPHOMA, UNSPECIFIED SITE	Yes
C83.71	BURKITT LYMPHOMA, LYMPH NODES OF HEAD, FACE, AND NECK	Yes
C83.72	BURKITT LYMPHOMA, INTRATHORACIC LYMPH NODES	Yes
C83.73	BURKITT LYMPHOMA, INTRA-ABDOMINAL LYMPH NODES	Yes
C83.74	BURKITT LYMPHOMA, LYMPH NODES OF AXILLA AND UPPER LIMB	Yes
C83.75	BURKITT LYMPHOMA, LYMPH NODES OF INGUINAL REGION AND LOWER LIMB	Yes
C83.76	BURKITT LYMPHOMA, INTRAPELVIC LYMPH NODES	Yes
C83.77	BURKITT LYMPHOMA, SPLEEN	Yes
C83.78	BURKITT LYMPHOMA, LYMPH NODES OF MULTIPLE SITES	Yes
C83.79	BURKITT LYMPHOMA, EXTRANODAL AND SOLID ORGAN SITES	Yes
C83.8	OTHER NON-FOLLICULAR LYMPHOMA	Yes
C83.80	OTHER NON-FOLLICULAR LYMPHOMA, UNSPECIFIED SITE	Yes
C83.81	OTHER NON-FOLLICULAR LYMPHOMA, LYMPH NODES OF HEAD, FACE, AND NECK	Yes
C83.82	OTHER NON-FOLLICULAR LYMPHOMA, INTRATHORACIC LYMPH NODES	Yes
C83.83	OTHER NON-FOLLICULAR LYMPHOMA, INTRA-ABDOMINAL LYMPH NODES	Yes
C83.84	OTHER NON-FOLLICULAR LYMPHOMA, LYMPH NODES OF AXILLA AND UPPER LIMB	Yes
C83.85	OTHER NON-FOLLICULAR LYMPHOMA, LYMPH NODES OF INGUINAL REGION AND LOWER LIMB	Yes
C83.86	OTHER NON-FOLLICULAR LYMPHOMA, INTRAPELVIC LYMPH NODES	Yes
C83.87	OTHER NON-FOLLICULAR LYMPHOMA, SPLEEN	Yes
C83.88	OTHER NON-FOLLICULAR LYMPHOMA, LYMPH NODES OF MULTIPLE SITES	Yes
C83.89	OTHER NON-FOLLICULAR LYMPHOMA, EXTRANODAL AND SOLID ORGAN SITES	Yes
C83.9	NON-FOLLICULAR (DIFFUSE) LYMPHOMA, UNSPECIFIED	Yes
C83.90	NON-FOLLICULAR (DIFFUSE) LYMPHOMA, UNSPECIFIED, UNSPECIFIED SITE	Yes
C83.91	NON-FOLLICULAR (DIFFUSE) LYMPHOMA, UNSPECIFIED, LYMPH NODES OF HEAD, FACE, AND NECK	Yes
C83.92	NON-FOLLICULAR (DIFFUSE) LYMPHOMA, UNSPECIFIED, INTRATHORACIC LYMPH NODES	Yes
C83.93	NON-FOLLICULAR (DIFFUSE) LYMPHOMA, UNSPECIFIED, INTRA-ABDOMINAL LYMPH NODES	Yes
C83.94	NON-FOLLICULAR (DIFFUSE) LYMPHOMA, UNSPECIFIED, LYMPH NODES OF AXILLA AND UPPER LIMB	Yes
C83.95	NON-FOLLICULAR (DIFFUSE) LYMPHOMA, UNSPECIFIED, LYMPH NODES OF INGUINAL REGION AND LOWER LIMB	Yes

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C83.96	NON-FOLLICULAR (DIFFUSE) LYMPHOMA, UNSPECIFIED, INTRAPELVIC LYMPH NODES	Yes
C83.97	NON-FOLLICULAR (DIFFUSE) LYMPHOMA, UNSPECIFIED, SPLEEN	Yes
C83.98	NON-FOLLICULAR (DIFFUSE) LYMPHOMA, UNSPECIFIED, LYMPH NODES OF MULTIPLE SITES	Yes
C83.99	NON-FOLLICULAR (DIFFUSE) LYMPHOMA, UNSPECIFIED, EXTRANODAL AND SOLID ORGAN SITES	Yes
C84	MATURE T/NK-CELL LYMPHOMAS	Yes
C84.0	MYCOSIS FUNGOIDES	Yes
C84.00	MYCOSIS FUNGOIDES, UNSPECIFIED SITE	Yes
C84.01	MYCOSIS FUNGOIDES, LYMPH NODES OF HEAD, FACE, AND NECK	Yes
C84.02	MYCOSIS FUNGOIDES, INTRATHORACIC LYMPH NODES	Yes
C84.03	MYCOSIS FUNGOIDES, INTRA-ABDOMINAL LYMPH NODES	Yes
C84.04	MYCOSIS FUNGOIDES, LYMPH NODES OF AXILLA AND UPPER LIMB	Yes
C84.05	MYCOSIS FUNGOIDES, LYMPH NODES OF INGUINAL REGION AND LOWER LIMB	Yes
C84.06	MYCOSIS FUNGOIDES, INTRAPELVIC LYMPH NODES	Yes
C84.07	MYCOSIS FUNGOIDES, SPLEEN	Yes
C84.08	MYCOSIS FUNGOIDES, LYMPH NODES OF MULTIPLE SITES	Yes
C84.09	MYCOSIS FUNGOIDES, EXTRANODAL AND SOLID ORGAN SITES	Yes
C84.1	SEZARY DISEASE	Yes
C84.10	SEZARY DISEASE, UNSPECIFIED SITE	Yes
C84.11	SEZARY DISEASE, LYMPH NODES OF HEAD, FACE, AND NECK	Yes
C84.12	SEZARY DISEASE, INTRATHORACIC LYMPH NODES	Yes
C84.13	SEZARY DISEASE, INTRA-ABDOMINAL LYMPH NODES	Yes
C84.14	SEZARY DISEASE, LYMPH NODES OF AXILLA AND UPPER LIMB	Yes
C84.15	SEZARY DISEASE, LYMPH NODES OF INGUINAL REGION AND LOWER LIMB	Yes
C84.16	SEZARY DISEASE, INTRAPELVIC LYMPH NODES	Yes
C84.17	SEZARY DISEASE, SPLEEN	Yes
C84.18	SEZARY DISEASE, LYMPH NODES OF MULTIPLE SITES	Yes
C84.19	SEZARY DISEASE, EXTRANODAL AND SOLID ORGAN SITES	Yes
C84.4	PERIPHERAL T-CELL LYMPHOMA, NOT CLASSIFIED	Yes
C84.40	PERIPHERAL T-CELL LYMPHOMA, NOT CLASSIFIED, UNSPECIFIED SITE	Yes
C84.41	PERIPHERAL T-CELL LYMPHOMA, NOT CLASSIFIED, LYMPH NODES OF HEAD, FACE, AND NECK	Yes
C84.42	PERIPHERAL T-CELL LYMPHOMA, NOT CLASSIFIED, INTRATHORACIC LYMPH NODES	Yes
C84.43	PERIPHERAL T-CELL LYMPHOMA, NOT CLASSIFIED, INTRA-ABDOMINAL LYMPH NODES	Yes
C84.44	PERIPHERAL T-CELL LYMPHOMA, NOT CLASSIFIED, LYMPH NODES OF AXILLA AND UPPER LIMB	Yes
C84.45	PERIPHERAL T-CELL LYMPHOMA, NOT CLASSIFIED, LYMPH NODES OF INGUINAL REGION AND LOWER LIMB	Yes

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C84.46	PERIPHERAL T-CELL LYMPHOMA, NOT CLASSIFIED, INTRAPELVIC LYMPH NODES	Yes
C84.47	PERIPHERAL T-CELL LYMPHOMA, NOT CLASSIFIED, SPLEEN	Yes
C84.48	PERIPHERAL T-CELL LYMPHOMA, NOT CLASSIFIED, LYMPH NODES OF MULTIPLE SITES	Yes
C84.49	PERIPHERAL T-CELL LYMPHOMA, NOT CLASSIFIED, EXTRANODAL AND SOLID ORGAN SITES	Yes
C84.6	ANAPLASTIC LARGE CELL LYMPHOMA, ALK-POSITIVE	Yes
C84.60	ANAPLASTIC LARGE CELL LYMPHOMA, ALK-POSITIVE, UNSPECIFIED SITE	Yes
C84.61	ANAPLASTIC LARGE CELL LYMPHOMA, ALK-POSITIVE, LYMPH NODES OF HEAD, FACE, AND NECK	Yes
C84.62	ANAPLASTIC LARGE CELL LYMPHOMA, ALK-POSITIVE, INTRATHORACIC LYMPH NODES	Yes
C84.63	ANAPLASTIC LARGE CELL LYMPHOMA, ALK-POSITIVE, INTRA-ABDOMINAL LYMPH NODES	Yes
C84.64	ANAPLASTIC LARGE CELL LYMPHOMA, ALK-POSITIVE, LYMPH NODES OF AXILLA AND UPPER LIMB	Yes
C84.65	ANAPLASTIC LARGE CELL LYMPHOMA, ALK-POSITIVE, LYMPH NODES OF INGUINAL REGION AND LOWER LIMB	Yes
C84.66	ANAPLASTIC LARGE CELL LYMPHOMA, ALK-POSITIVE, INTRAPELVIC LYMPH NODES	Yes
C84.67	ANAPLASTIC LARGE CELL LYMPHOMA, ALK-POSITIVE, SPLEEN	Yes
C84.68	ANAPLASTIC LARGE CELL LYMPHOMA, ALK-POSITIVE, LYMPH NODES OF MULTIPLE SITES	Yes
C84.69	ANAPLASTIC LARGE CELL LYMPHOMA, ALK-POSITIVE, EXTRANODAL AND SOLID ORGAN SITES	Yes
C84.7	ANAPLASTIC LARGE CELL LYMPHOMA, ALK-NEGATIVE	Yes
C84.70	ANAPLASTIC LARGE CELL LYMPHOMA, ALK-NEGATIVE, UNSPECIFIED SITE	Yes
C84.71	ANAPLASTIC LARGE CELL LYMPHOMA, ALK-NEGATIVE, LYMPH NODES OF HEAD, FACE, AND NECK	Yes
C84.72	ANAPLASTIC LARGE CELL LYMPHOMA, ALK-NEGATIVE, INTRATHORACIC LYMPH NODES	Yes
C84.73	ANAPLASTIC LARGE CELL LYMPHOMA, ALK-NEGATIVE, INTRA-ABDOMINAL LYMPH NODES	Yes
C84.74	ANAPLASTIC LARGE CELL LYMPHOMA, ALK-NEGATIVE, LYMPH NODES OF AXILLA AND UPPER LIMB	Yes
C84.75	ANAPLASTIC LARGE CELL LYMPHOMA, ALK-NEGATIVE, LYMPH NODES OF INGUINAL REGION AND LOWER LIMB	Yes
C84.76	ANAPLASTIC LARGE CELL LYMPHOMA, ALK-NEGATIVE, INTRAPELVIC LYMPH NODES	Yes
C84.77	ANAPLASTIC LARGE CELL LYMPHOMA, ALK-NEGATIVE, SPLEEN	Yes
C84.78	ANAPLASTIC LARGE CELL LYMPHOMA, ALK-NEGATIVE, LYMPH NODES OF MULTIPLE SITES	Yes
C84.79	ANAPLASTIC LARGE CELL LYMPHOMA, ALK-NEGATIVE, EXTRANODAL AND SOLID ORGAN SITES	Yes

ICD-10-CM	Code Description	IC
C84.9	MATURE T/NK-CELL LYMPHOMAS, UNSPECIFIED	Yes
C84.90	MATURE T/NK-CELL LYMPHOMAS, UNSPECIFIED, UNSPECIFIED SITE	Yes
C84.91	MATURE T/NK-CELL LYMPHOMAS, UNSPECIFIED, LYMPH NODES OF HEAD, FACE, AND NECK	Yes
C84.92	MATURE T/NK-CELL LYMPHOMAS, UNSPECIFIED, INTRATHORACIC LYMPH NODES	Yes
C84.93	MATURE T/NK-CELL LYMPHOMAS, UNSPECIFIED, INTRA-ABDOMINAL LYMPH NODES	Yes
C84.94	MATURE T/NK-CELL LYMPHOMAS, UNSPECIFIED, LYMPH NODES OF AXILLA AND UPPER LIMB	Yes
C84.95	MATURE T/NK-CELL LYMPHOMAS, UNSPECIFIED, LYMPH NODES OF INGUINAL REGION AND LOWER LIMB	Yes
C84.96	MATURE T/NK-CELL LYMPHOMAS, UNSPECIFIED, INTRAPELVIC LYMPH NODES	Yes
C84.97	MATURE T/NK-CELL LYMPHOMAS, UNSPECIFIED, SPLEEN	Yes
C84.98	MATURE T/NK-CELL LYMPHOMAS, UNSPECIFIED, LYMPH NODES OF MULTIPLE SITES	Yes
C84.99	MATURE T/NK-CELL LYMPHOMAS, UNSPECIFIED, EXTRANODAL AND SOLID ORGAN SITES	Yes
C84.A	CUTANEOUS T-CELL LYMPHOMA, UNSPECIFIED	Yes
C84.A0	CUTANEOUS T-CELL LYMPHOMA, UNSPECIFIED, UNSPECIFIED SITE	Yes
C84.A1	CUTANEOUS T-CELL LYMPHOMA, UNSPECIFIED LYMPH NODES OF HEAD, FACE, AND NECK	Yes
C84.A2	CUTANEOUS T-CELL LYMPHOMA, UNSPECIFIED, INTRATHORACIC LYMPH NODES	Yes
C84.A3	CUTANEOUS T-CELL LYMPHOMA, UNSPECIFIED, INTRA-ABDOMINAL LYMPH NODES	Yes
C84.A4	CUTANEOUS T-CELL LYMPHOMA, UNSPECIFIED, LYMPH NODES OF AXILLA AND UPPER LIMB	Yes
C84.A5	CUTANEOUS T-CELL LYMPHOMA, UNSPECIFIED, LYMPH NODES OF INGUINAL REGION AND LOWER LIMB	Yes
C84.A6	CUTANEOUS T-CELL LYMPHOMA, UNSPECIFIED, INTRAPELVIC LYMPH NODES	Yes
C84.A7	CUTANEOUS T-CELL LYMPHOMA, UNSPECIFIED, SPLEEN	Yes
C84.A8	CUTANEOUS T-CELL LYMPHOMA, UNSPECIFIED, LYMPH NODES OF MULTIPLE SITES	Yes
C84.A9	CUTANEOUS T-CELL LYMPHOMA, UNSPECIFIED, EXTRANODAL AND SOLID ORGAN SITES	Yes
C84.Z	OTHER MATURE T/NK-CELL LYMPHOMAS	Yes
C84.Z0	OTHER MATURE T/NK-CELL LYMPHOMAS, UNSPECIFIED SITE	Yes
C84.Z1	OTHER MATURE T/NK-CELL LYMPHOMAS, LYMPH NODES OF HEAD, FACE, AND NECK	Yes
C84.Z2	OTHER MATURE T/NK-CELL LYMPHOMAS, INTRATHORACIC LYMPH NODES	Yes
C84.Z3	OTHER MATURE T/NK-CELL LYMPHOMAS, INTRA-ABDOMINAL LYMPH NODES	Yes
C84.Z4	OTHER MATURE T/NK-CELL LYMPHOMAS, LYMPH NODES OF AXILLA AND UPPER LIMB	Yes

ICD-10-CM	Code Description	IC
C84.Z5	OTHER MATURE T/NK-CELL LYMPHOMAS, LYMPH NODES OF INGUINAL REGION AND LOWER LIMB	Yes
C84.Z6	OTHER MATURE T/NK-CELL LYMPHOMAS, INTRAPELVIC LYMPH NODES	Yes
C84.Z7	OTHER MATURE T/NK-CELL LYMPHOMAS, SPLEEN	Yes
C84.Z8	OTHER MATURE T/NK-CELL LYMPHOMAS, LYMPH NODES OF MULTIPLE SITES	Yes
C84.Z9	OTHER MATURE T/NK-CELL LYMPHOMAS, EXTRANODAL AND SOLID ORGAN SITES	Yes
C85	OTHER SPECIFIED AND UNSPECIFIED TYPES OF NON-HODGKIN LYMPHOMA	Yes
C85.1	UNSPECIFIED B-CELL LYMPHOMA	Yes
C85.10	UNSPECIFIED B-CELL LYMPHOMA, UNSPECIFIED SITE	Yes
C85.11	UNSPECIFIED B-CELL LYMPHOMA, LYMPH NODES OF HEAD, FACE, AND NECK	Yes
C85.12	UNSPECIFIED B-CELL LYMPHOMA, INTRATHORACIC LYMPH NODES	Yes
C85.13	UNSPECIFIED B-CELL LYMPHOMA, INTRA-ABDOMINAL LYMPH NODES	Yes
C85.14	UNSPECIFIED B-CELL LYMPHOMA, LYMPH NODES OF AXILLA AND UPPER LIMB	Yes
C85.15	UNSPECIFIED B-CELL LYMPHOMA, LYMPH NODES OF INGUINAL REGION AND LOWER LIMB	Yes
C85.16	UNSPECIFIED B-CELL LYMPHOMA, INTRAPELVIC LYMPH NODES	Yes
C85.17	UNSPECIFIED B-CELL LYMPHOMA, SPLEEN	Yes
C85.18	UNSPECIFIED B-CELL LYMPHOMA, LYMPH NODES OF MULTIPLE SITES	Yes
C85.19	UNSPECIFIED B-CELL LYMPHOMA, EXTRANODAL AND SOLID ORGAN SITES	Yes
C85.2	MEDIASTINAL (THYMIC) LARGE B-CELL LYMPHOMA	Yes
C85.20	MEDIASTINAL (THYMIC) LARGE B-CELL LYMPHOMA, UNSPECIFIED SITE	Yes
C85.21	MEDIASTINAL (THYMIC) LARGE B-CELL LYMPHOMA, LYMPH NODES OF HEAD, FACE, AND NECK	Yes
C85.22	MEDIASTINAL (THYMIC) LARGE B-CELL LYMPHOMA, INTRATHORACIC LYMPH NODES	Yes
C85.23	MEDIASTINAL (THYMIC) LARGE B-CELL LYMPHOMA, INTRA-ABDOMINAL LYMPH NODES	Yes
C85.24	MEDIASTINAL (THYMIC) LARGE B-CELL LYMPHOMA, LYMPH NODES OF AXILLA AND UPPER LIMB	Yes
C85.25	MEDIASTINAL (THYMIC) LARGE B-CELL LYMPHOMA, LYMPH NODES OF INGUINAL REGION AND LOWER LIMB	Yes
C85.26	MEDIASTINAL (THYMIC) LARGE B-CELL LYMPHOMA, INTRAPELVIC LYMPH NODES	Yes
C85.27	MEDIASTINAL (THYMIC) LARGE B-CELL LYMPHOMA, SPLEEN	Yes
C85.28	MEDIASTINAL (THYMIC) LARGE B-CELL LYMPHOMA, LYMPH NODES OF MULTIPLE SITES	Yes
C85.29	MEDIASTINAL (THYMIC) LARGE B-CELL LYMPHOMA, EXTRANODAL AND SOLID ORGAN SITES	Yes
C85.8	OTHER SPECIFIED TYPES OF NON-HODGKIN LYMPHOMA	Yes
C85.80	OTHER SPECIFIED TYPES OF NON-HODGKIN LYMPHOMA, UNSPECIFIED SITE	Yes
C85.81	OTHER SPECIFIED TYPES OF NON-HODGKIN LYMPHOMA, LYMPH NODES OF HEAD, FACE, AND NECK	Yes

ICD-10-CM	Code Description	IC
C85.82	OTHER SPECIFIED TYPES OF NON-HODGKIN LYMPHOMA, INTRATHORACIC LYMPH NODES	Yes
C85.83	OTHER SPECIFIED TYPES OF NON-HODGKIN LYMPHOMA, INTRA-ABDOMINAL LYMPH NODES	Yes
C85.84	OTHER SPECIFIED TYPES OF NON-HODGKIN LYMPHOMA, LYMPH NODES OF AXILLA AND UPPER LIMB	Yes
C85.85	OTHER SPECIFIED TYPES OF NON-HODGKIN LYMPHOMA, LYMPH NODES OF INGUINAL REGION AND LOWER LIMB	Yes
C85.86	OTHER SPECIFIED TYPES OF NON-HODGKIN LYMPHOMA, INTRAPELVIC LYMPH NODES	Yes
C85.87	OTHER SPECIFIED TYPES OF NON-HODGKIN LYMPHOMA, SPLEEN	Yes
C85.88	OTHER SPECIFIED TYPES OF NON-HODGKIN LYMPHOMA, LYMPH NODES OF MULTIPLE SITES	Yes
C85.89	OTHER SPECIFIED TYPES OF NON-HODGKIN LYMPHOMA, EXTRANODAL AND SOLID ORGAN SITES	Yes
C85.9	NON-HODGKIN LYMPHOMA, UNSPECIFIED	Yes
C85.90	NON-HODGKIN LYMPHOMA, UNSPECIFIED, UNSPECIFIED SITE	Yes
C85.91	NON-HODGKIN LYMPHOMA, UNSPECIFIED, LYMPH NODES OF HEAD, FACE, AND NECK	Yes
C85.92	NON-HODGKIN LYMPHOMA, UNSPECIFIED, INTRATHORACIC LYMPH NODES	Yes
C85.93	NON-HODGKIN LYMPHOMA, UNSPECIFIED, INTRA-ABDOMINAL LYMPH NODES	Yes
C85.94	NON-HODGKIN LYMPHOMA, UNSPECIFIED, LYMPH NODES OF AXILLA AND UPPER LIMB	Yes
C85.95	NON-HODGKIN LYMPHOMA, UNSPECIFIED, LYMPH NODES OF INGUINAL REGION AND LOWER LIMB	Yes
C85.96	NON-HODGKIN LYMPHOMA, UNSPECIFIED, INTRAPELVIC LYMPH NODES	Yes
C85.97	NON-HODGKIN LYMPHOMA, UNSPECIFIED, SPLEEN	Yes
C85.98	NON-HODGKIN LYMPHOMA, UNSPECIFIED, LYMPH NODES OF MULTIPLE SITES	Yes
C85.99	NON-HODGKIN LYMPHOMA, UNSPECIFIED, EXTRANODAL AND SOLID ORGAN SITES	Yes
C86	OTHER SPECIFIED TYPES OF T/NK-CELL LYMPHOMA	Yes
C86.0	EXTRANODAL NK/T-CELL LYMPHOMA, NASAL TYPE	Yes
C86.1	HEPATOSPLENIC T-CELL LYMPHOMA	Yes
C86.2	ENTEROPATHY-TYPE (INTESTINAL) T-CELL LYMPHOMA	Yes
C86.3	SUBCUTANEOUS PANNICULITIS-LIKE T-CELL LYMPHOMA	Yes
C86.4	BLASTIC NK-CELL LYMPHOMA	Yes
C86.5	ANGIOIMMUNOBLASTIC T-CELL LYMPHOMA	Yes
C86.6	PRIMARY CUTANEOUS CD30-POSITIVE T-CELL PROLIFERATIONS	Yes
C88	MALIGNANT IMMUNOPROLIFERATIVE DISEASES AND CERTAIN OTHER B-CELL LYMPHOMAS	Yes
C88.0	WALDENSTROM MACROGLOBULINEMIA	Yes
C88.2	HEAVY CHAIN DISEASE	Yes

ICD-10-CM	Code Description	IC
C88.3	IMMUNOPROLIFERATIVE SMALL INTESTINAL DISEASE	Yes
C88.4	EXTRANODAL MARGINAL ZONE B-CELL LYMPHOMA OF MUCOSA-ASSOCIATED LYMPHOID TISSUE [MALT-LYMPHOMA]	Yes
C88.8	OTHER MALIGNANT IMMUNOPROLIFERATIVE DISEASES	Yes
C88.9	MALIGNANT IMMUNOPROLIFERATIVE DISEASE, UNSPECIFIED	Yes
C90	MULTIPLE MYELOMA AND MALIGNANT PLASMA CELL NEOPLASMS	Yes
C90.0	MULTIPLE MYELOMA	Yes
C90.00	MULTIPLE MYELOMA NOT HAVING ACHIEVED REMISSION	Yes
C90.01	MULTIPLE MYELOMA IN REMISSION	Yes
C90.02	MULTIPLE MYELOMA IN RELAPSE	Yes
C90.2	EXTRAMEDULLARY PLASMACYTOMA	Yes
C90.20	EXTRAMEDULLARY PLASMACYTOMA NOT HAVING ACHIEVED REMISSION	Yes
C90.21	EXTRAMEDULLARY PLASMACYTOMA IN REMISSION	Yes
C90.22	EXTRAMEDULLARY PLASMACYTOMA IN RELAPSE	Yes
C90.3	SOLITARY PLASMACYTOMA	Yes
C90.30	SOLITARY PLASMACYTOMA NOT HAVING ACHIEVED REMISSION	Yes
C90.31	SOLITARY PLASMACYTOMA IN REMISSION	Yes
C90.32	SOLITARY PLASMACYTOMA IN RELAPSE	Yes
C91	LYMPHOID LEUKEMIA	Yes
C91.0	ACUTE LYMPHOBLASTIC LEUKEMIA [ALL]	Yes
C91.00	ACUTE LYMPHOBLASTIC LEUKEMIA NOT HAVING ACHIEVED REMISSION	Yes
C91.01	ACUTE LYMPHOBLASTIC LEUKEMIA, IN REMISSION	Yes
C91.02	ACUTE LYMPHOBLASTIC LEUKEMIA, IN RELAPSE	Yes
C91.3	PROLYMPHOCYTIC LEUKEMIA OF B-CELL TYPE	Yes
C91.30	PROLYMPHOCYTIC LEUKEMIA OF B-CELL TYPE NOT HAVING ACHIEVED REMISSION	Yes
C91.31	PROLYMPHOCYTIC LEUKEMIA OF B-CELL TYPE, IN REMISSION	Yes
C91.32	PROLYMPHOCYTIC LEUKEMIA OF B-CELL TYPE, IN RELAPSE	Yes
C91.4	HAIRY CELL LEUKEMIA	Yes
C91.40	HAIRY CELL LEUKEMIA NOT HAVING ACHIEVED REMISSION	Yes
C91.41	HAIRY CELL LEUKEMIA, IN REMISSION	Yes
C91.42	HAIRY CELL LEUKEMIA, IN RELAPSE	Yes
C91.5	ADULT T-CELL LYMPHOMA/LEUKEMIA (HTLV-1-ASSOCIATED)	Yes
C91.50	ADULT T-CELL LYMPHOMA/LEUKEMIA (HTLV-1-ASSOCIATED) NOT HAVING ACHIEVED REMISSION	Yes
C91.51	ADULT T-CELL LYMPHOMA/LEUKEMIA (HTLV-1-ASSOCIATED), IN REMISSION	Yes
C91.52	ADULT T-CELL LYMPHOMA/LEUKEMIA (HTLV-1-ASSOCIATED), IN RELAPSE	Yes
C91.6	PROLYMPHOCYTIC LEUKEMIA OF T-CELL TYPE	Yes
C91.60	PROLYMPHOCYTIC LEUKEMIA OF T-CELL TYPE NOT HAVING ACHIEVED REMISSION	Yes
C91.61	PROLYMPHOCYTIC LEUKEMIA OF T-CELL TYPE, IN REMISSION	Yes
C91.62	PROLYMPHOCYTIC LEUKEMIA OF T-CELL TYPE, IN RELAPSE	Yes

ICD-10-CM	Code Description	IC
C91.9	LYMPHOID LEUKEMIA, UNSPECIFIED	Yes
C91.90	LYMPHOID LEUKEMIA, UNSPECIFIED NOT HAVING ACHIEVED REMISSION	Yes
C91.91	LYMPHOID LEUKEMIA, UNSPECIFIED, IN REMISSION	Yes
C91.92	LYMPHOID LEUKEMIA, UNSPECIFIED, IN RELAPSE	Yes
C91.A	MATURE B-CELL LEUKEMIA BURKITT-TYPE	Yes
C91.A0	MATURE B-CELL LEUKEMIA BURKITT-TYPE NOT HAVING ACHIEVED REMISSION	Yes
C91.A1	MATURE B-CELL LEUKEMIA BURKITT-TYPE, IN REMISSION	Yes
C91.A2	MATURE B-CELL LEUKEMIA BURKITT-TYPE, IN RELAPSE	Yes
C91.Z	OTHER LYMPHOID LEUKEMIA	Yes
C91.Z0	OTHER LYMPHOID LEUKEMIA NOT HAVING ACHIEVED REMISSION	Yes
C91.Z1	OTHER LYMPHOID LEUKEMIA, IN REMISSION	Yes
C91.Z2	OTHER LYMPHOID LEUKEMIA, IN RELAPSE	Yes
C92	MYELOID LEUKEMIA	Yes
C92.0	ACUTE MYELOBLASTIC LEUKEMIA	Yes
C92.00	ACUTE MYELOBLASTIC LEUKEMIA, NOT HAVING ACHIEVED REMISSION	Yes
C92.01	ACUTE MYELOBLASTIC LEUKEMIA, IN REMISSION	Yes
C92.02	ACUTE MYELOBLASTIC LEUKEMIA, IN RELAPSE	Yes
C92.2	ATYPICAL CHRONIC MYELOID LEUKEMIA, BCR/ABL-NEGATIVE	Yes
C92.20	ATYPICAL CHRONIC MYELOID LEUKEMIA, BCR/ABL-NEGATIVE, NOT HAVING ACHIEVED REMISSION	Yes
C92.21	ATYPICAL CHRONIC MYELOID LEUKEMIA, BCR/ABL-NEGATIVE, IN REMISSION	Yes
C92.22	ATYPICAL CHRONIC MYELOID LEUKEMIA, BCR/ABL-NEGATIVE, IN RELAPSE	Yes
C92.3	MYELOID SARCOMA	Yes
C92.30	MYELOID SARCOMA, NOT HAVING ACHIEVED REMISSION	Yes
C92.31	MYELOID SARCOMA, IN REMISSION	Yes
C92.32	MYELOID SARCOMA, IN RELAPSE	Yes
C92.4	ACUTE PROMYELOCYTIC LEUKEMIA	Yes
C92.40	ACUTE PROMYELOCYTIC LEUKEMIA, NOT HAVING ACHIEVED REMISSION	Yes
C92.41	ACUTE PROMYELOCYTIC LEUKEMIA, IN REMISSION	Yes
C92.42	ACUTE PROMYELOCYTIC LEUKEMIA, IN RELAPSE	Yes
C92.5	ACUTE MYELOMONOCYTIC LEUKEMIA	Yes
C92.50	ACUTE MYELOMONOCYTIC LEUKEMIA, NOT HAVING ACHIEVED REMISSION	Yes
C92.51	ACUTE MYELOMONOCYTIC LEUKEMIA, IN REMISSION	Yes
C92.52	ACUTE MYELOMONOCYTIC LEUKEMIA, IN RELAPSE	Yes
C92.6	ACUTE MYELOID LEUKEMIA WITH 11Q23-ABNORMALITY	Yes
C92.60	ACUTE MYELOID LEUKEMIA WITH 11Q23-ABNORMALITY NOT HAVING ACHIEVED REMISSION	Yes
C92.61	ACUTE MYELOID LEUKEMIA WITH 11Q23-ABNORMALITY IN REMISSION	Yes
C92.62	ACUTE MYELOID LEUKEMIA WITH 11Q23-ABNORMALITY IN RELAPSE	Yes
C92.9	MYELOID LEUKEMIA, UNSPECIFIED	Yes
C92.90	MYELOID LEUKEMIA, UNSPECIFIED, NOT HAVING ACHIEVED REMISSION	Yes

ICD-10-CM	Code Description	IC
C92.91	MYELOID LEUKEMIA, UNSPECIFIED IN REMISSION	Yes
C92.92	MYELOID LEUKEMIA, UNSPECIFIED IN RELAPSE	Yes
C92.A	ACUTE MYELOID LEUKEMIA WITH MULTILINEAGE DYSPLASIA	Yes
C92.A0	ACUTE MYELOID LEUKEMIA WITH MULTILINEAGE DYSPLASIA, NOT HAVING ACHIEVED REMISSION	Yes
C92.A1	ACUTE MYELOID LEUKEMIA WITH MULTILINEAGE DYSPLASIA, IN REMISSION	Yes
C92.A2	ACUTE MYELOID LEUKEMIA WITH MULTILINEAGE DYSPLASIA, IN RELAPSE	Yes
C92.Z	OTHER MYELOID LEUKEMIA	Yes
C92.Z0	OTHER MYELOID LEUKEMIA NOT HAVING ACHIEVED REMISSION	Yes
C92.Z1	OTHER MYELOID LEUKEMIA, IN REMISSION	Yes
C92.Z2	OTHER MYELOID LEUKEMIA, IN RELAPSE	Yes
C93	MONOCYTIC LEUKEMIA	Yes
C93.0	ACUTE MONOBLASTIC/MONOCYTIC LEUKEMIA	Yes
C93.00	ACUTE MONOBLASTIC/MONOCYTIC LEUKEMIA, NOT HAVING ACHIEVED REMISSION	Yes
C93.01	ACUTE MONOBLASTIC/MONOCYTIC LEUKEMIA, IN REMISSION	Yes
C93.02	ACUTE MONOBLASTIC/MONOCYTIC LEUKEMIA, IN RELAPSE	Yes
C93.3	JUVENILE MYELOMONOCYTIC LEUKEMIA	Yes
C93.30	JUVENILE MYELOMONOCYTIC LEUKEMIA, NOT HAVING ACHIEVED REMISSION	Yes
C93.31	JUVENILE MYELOMONOCYTIC LEUKEMIA, IN REMISSION	Yes
C93.32	JUVENILE MYELOMONOCYTIC LEUKEMIA, IN RELAPSE	Yes
C93.9	MONOCYTIC LEUKEMIA, UNSPECIFIED	Yes
C93.90	MONOCYTIC LEUKEMIA, UNSPECIFIED, NOT HAVING ACHIEVED REMISSION	Yes
C93.91	MONOCYTIC LEUKEMIA, UNSPECIFIED IN REMISSION	Yes
C93.92	MONOCYTIC LEUKEMIA, UNSPECIFIED IN RELAPSE	Yes
C93.Z	OTHER MONOCYTIC LEUKEMIA	Yes
C93.Z0	OTHER MONOCYTIC LEUKEMIA, NOT HAVING ACHIEVED REMISSION	Yes
C93.Z1	OTHER MONOCYTIC LEUKEMIA, IN REMISSION	Yes
C93.Z2	OTHER MONOCYTIC LEUKEMIA, IN RELAPSE	Yes
C94	OTHER LEUKEMIAS OF SPECIFIED CELL TYPE	Yes
C94.0	ACUTE ERYTHROID LEUKEMIA	Yes
C94.00	ACUTE ERYTHROID LEUKEMIA, NOT HAVING ACHIEVED REMISSION	Yes
C94.01	ACUTE ERYTHROID LEUKEMIA, IN REMISSION	Yes
C94.02	ACUTE ERYTHROID LEUKEMIA, IN RELAPSE	Yes
C94.2	ACUTE MEGAKARYOBLASTIC LEUKEMIA	Yes
C94.20	ACUTE MEGAKARYOBLASTIC LEUKEMIA NOT HAVING ACHIEVED REMISSION	Yes
C94.21	ACUTE MEGAKARYOBLASTIC LEUKEMIA, IN REMISSION	Yes
C94.22	ACUTE MEGAKARYOBLASTIC LEUKEMIA, IN RELAPSE	Yes
C94.3	MAST CELL LEUKEMIA	Yes
C94.30	MAST CELL LEUKEMIA NOT HAVING ACHIEVED REMISSION	Yes
C94.31	MAST CELL LEUKEMIA, IN REMISSION	Yes
C94.32	MAST CELL LEUKEMIA, IN RELAPSE	Yes

ICD-10-CM	Code Description	IC
C94.4	ACUTE PANMYELOSIS WITH MYELOFIBROSIS	Yes
C94.40	ACUTE PANMYELOSIS WITH MYELOFIBROSIS NOT HAVING ACHIEVED REMISSION	Yes
C94.41	ACUTE PANMYELOSIS WITH MYELOFIBROSIS, IN REMISSION	Yes
C94.42	ACUTE PANMYELOSIS WITH MYELOFIBROSIS, IN RELAPSE	Yes
C94.6	MYELODYSPLASTIC DISEASE, NOT CLASSIFIED	Yes
C94.8	OTHER SPECIFIED LEUKEMIAS	Yes
C94.80	OTHER SPECIFIED LEUKEMIAS NOT HAVING ACHIEVED REMISSION	Yes
C94.81	OTHER SPECIFIED LEUKEMIAS, IN REMISSION	Yes
C94.82	OTHER SPECIFIED LEUKEMIAS, IN RELAPSE	Yes
C95	LEUKEMIA OF UNSPECIFIED CELL TYPE	Yes
C95.0	ACUTE LEUKEMIA OF UNSPECIFIED CELL TYPE	Yes
C95.00	ACUTE LEUKEMIA OF UNSPECIFIED CELL TYPE NOT HAVING ACHIEVED REMISSION	Yes
C95.01	ACUTE LEUKEMIA OF UNSPECIFIED CELL TYPE, IN REMISSION	Yes
C95.02	ACUTE LEUKEMIA OF UNSPECIFIED CELL TYPE, IN RELAPSE	Yes
C95.9	LEUKEMIA, UNSPECIFIED	Yes
C95.90	LEUKEMIA, UNSPECIFIED NOT HAVING ACHIEVED REMISSION	Yes
C95.91	LEUKEMIA, UNSPECIFIED, IN REMISSION	Yes
C95.92	LEUKEMIA, UNSPECIFIED, IN RELAPSE	Yes
C96	OTHER AND UNSPECIFIED MALIGNANT NEOPLASMS OF LYMPHOID, HEMATOPOIETIC AND RELATED TISSUE	Yes
C96.0	MULTIFOCAL AND MULTISYSTEMIC (DISSEMINATED) LANGERHANS-CELL HISTIOCYTOSIS	Yes
C96.2	MALIGNANT MAST CELL NEOPLASM	Yes
C96.20	Malignant mast cell neoplasm, unspecified	Yes
C96.21	Aggressive systemic mastocytosis	Yes
C96.22	Mast cell sarcoma	Yes
C96.29	Other malignant mast cell neoplasm	Yes
C96.4	SARCOMA OF DENDRITIC CELLS (ACCESSORY CELLS)	Yes
C96.5	MULTIFOCAL AND UNISYSTEMIC LANGERHANS-CELL HISTIOCYTOSIS	Yes
C96.6	UNIFOCAL LANGERHANS-CELL HISTIOCYTOSIS	Yes
C96.9	MALIGNANT NEOPLASM OF LYMPHOID, HEMATOPOIETIC AND RELATED TISSUE, UNSPECIFIED	Yes
C96.A	HISTIOCYTIC SARCOMA	Yes
C96.Z	OTHER SPECIFIED MALIGNANT NEOPLASMS OF LYMPHOID, HEMATOPOIETIC AND RELATED TISSUE	Yes
C00	MALIGNANT NEOPLASM OF LIP	No
C00.0	MALIGNANT NEOPLASM OF EXTERNAL UPPER LIP	No
C00.1	MALIGNANT NEOPLASM OF EXTERNAL LOWER LIP	No
C00.2	MALIGNANT NEOPLASM OF EXTERNAL LIP, UNSPECIFIED	No
C00.3	MALIGNANT NEOPLASM OF UPPER LIP, INNER ASPECT	No
C00.4	MALIGNANT NEOPLASM OF LOWER LIP, INNER ASPECT	No

ICD-10-CM	Code Description	IC
C00.5	MALIGNANT NEOPLASM OF LIP, UNSPECIFIED, INNER ASPECT	No
C00.6	MALIGNANT NEOPLASM OF COMMISSURE OF LIP, UNSPECIFIED	No
C00.8	MALIGNANT NEOPLASM OF OVERLAPPING SITES OF LIP	No
C00.9	MALIGNANT NEOPLASM OF LIP, UNSPECIFIED	No
C01	MALIGNANT NEOPLASM OF BASE OF TONGUE	No
C02	MALIGNANT NEOPLASM OF OTHER AND UNSPECIFIED PARTS OF TONGUE	No
C02.0	MALIGNANT NEOPLASM OF DORSAL SURFACE OF TONGUE	No
C02.1	MALIGNANT NEOPLASM OF BORDER OF TONGUE	No
C02.2	MALIGNANT NEOPLASM OF VENTRAL SURFACE OF TONGUE	No
C02.3	MALIGNANT NEOPLASM OF ANTERIOR TWO-THIRDS OF TONGUE, PART UNSPECIFIED	No
C02.4	MALIGNANT NEOPLASM OF LINGUAL TONSIL	No
C02.8	MALIGNANT NEOPLASM OF OVERLAPPING SITES OF TONGUE	No
C02.9	MALIGNANT NEOPLASM OF TONGUE, UNSPECIFIED	No
C03	MALIGNANT NEOPLASM OF GUM	No
C03.0	MALIGNANT NEOPLASM OF UPPER GUM	No
C03.1	MALIGNANT NEOPLASM OF LOWER GUM	No
C03.9	MALIGNANT NEOPLASM OF GUM, UNSPECIFIED	No
C04	MALIGNANT NEOPLASM OF FLOOR OF MOUTH	No
C04.0	MALIGNANT NEOPLASM OF ANTERIOR FLOOR OF MOUTH	No
C04.1	MALIGNANT NEOPLASM OF LATERAL FLOOR OF MOUTH	No
C04.8	MALIGNANT NEOPLASM OF OVERLAPPING SITES OF FLOOR OF MOUTH	No
C04.9	MALIGNANT NEOPLASM OF FLOOR OF MOUTH, UNSPECIFIED	No
C05	MALIGNANT NEOPLASM OF PALATE	No
C05.0	MALIGNANT NEOPLASM OF HARD PALATE	No
C05.1	MALIGNANT NEOPLASM OF SOFT PALATE	No
C05.2	MALIGNANT NEOPLASM OF UVULA	No
C05.8	MALIGNANT NEOPLASM OF OVERLAPPING SITES OF PALATE	No
C05.9	MALIGNANT NEOPLASM OF PALATE, UNSPECIFIED	No
C06	MALIGNANT NEOPLASM OF OTHER AND UNSPECIFIED PARTS OF MOUTH	No
C06.0	MALIGNANT NEOPLASM OF CHEEK MUCOSA	No
C06.1	MALIGNANT NEOPLASM OF VESTIBULE OF MOUTH	No
C06.2	MALIGNANT NEOPLASM OF RETROMOLAR AREA	No
C06.8	MALIGNANT NEOPLASM OF OVERLAPPING SITES OF OTHER AND UNSPECIFIED PARTS OF MOUTH	No
C06.80	MALIGNANT NEOPLASM OF OVERLAPPING SITES OF UNSPECIFIED PARTS OF MOUTH	No
C06.89	MALIGNANT NEOPLASM OF OVERLAPPING SITES OF OTHER PARTS OF MOUTH	No
C06.9	MALIGNANT NEOPLASM OF MOUTH, UNSPECIFIED	No
C07	MALIGNANT NEOPLASM OF PAROTID GLAND	No
C08	MALIGNANT NEOPLASM OF OTHER AND UNSPECIFIED MAJOR SALIVARY GLANDS	No

ICD-10-CM	Code Description	IC
C08.0	MALIGNANT NEOPLASM OF SUBMANDIBULAR GLAND	No
C08.1	MALIGNANT NEOPLASM OF SUBLINGUAL GLAND	No
C08.9	MALIGNANT NEOPLASM OF MAJOR SALIVARY GLAND, UNSPECIFIED	No
C09	MALIGNANT NEOPLASM OF TONSIL	No
C09.0	MALIGNANT NEOPLASM OF TONSILLAR FOSSA	No
C09.1	MALIGNANT NEOPLASM OF TONSILLAR PILLAR (ANTERIOR) (POSTERIOR)	No
C09.8	MALIGNANT NEOPLASM OF OVERLAPPING SITES OF TONSIL	No
C09.9	MALIGNANT NEOPLASM OF TONSIL, UNSPECIFIED	No
C10	MALIGNANT NEOPLASM OF OROPHARYNX	No
C10.0	MALIGNANT NEOPLASM OF VALLECULA	No
C10.1	MALIGNANT NEOPLASM OF ANTERIOR SURFACE OF EPIGLOTTIS	No
C10.2	MALIGNANT NEOPLASM OF LATERAL WALL OF OROPHARYNX	No
C10.3	MALIGNANT NEOPLASM OF POSTERIOR WALL OF OROPHARYNX	No
C10.4	MALIGNANT NEOPLASM OF BRANCHIAL CLEFT	No
C10.8	MALIGNANT NEOPLASM OF OVERLAPPING SITES OF OROPHARYNX	No
C10.9	MALIGNANT NEOPLASM OF OROPHARYNX, UNSPECIFIED	No
C11	MALIGNANT NEOPLASM OF NASOPHARYNX	No
C11.0	MALIGNANT NEOPLASM OF SUPERIOR WALL OF NASOPHARYNX	No
C11.1	MALIGNANT NEOPLASM OF POSTERIOR WALL OF NASOPHARYNX	No
C11.2	MALIGNANT NEOPLASM OF LATERAL WALL OF NASOPHARYNX	No
C11.3	MALIGNANT NEOPLASM OF ANTERIOR WALL OF NASOPHARYNX	No
C11.8	MALIGNANT NEOPLASM OF OVERLAPPING SITES OF NASOPHARYNX	No
C11.9	MALIGNANT NEOPLASM OF NASOPHARYNX, UNSPECIFIED	No
C12	MALIGNANT NEOPLASM OF PYRIFORM SINUS	No
C13	MALIGNANT NEOPLASM OF HYPOPHARYNX	No
C13.0	MALIGNANT NEOPLASM OF POSTCRICOID REGION	No
C13.1	MALIGNANT NEOPLASM OF ARYEPIGLOTTIC FOLD, HYPOPHARYNGEAL ASPECT	No
C13.2	MALIGNANT NEOPLASM OF POSTERIOR WALL OF HYPOPHARYNX	No
C13.8	MALIGNANT NEOPLASM OF OVERLAPPING SITES OF HYPOPHARYNX	No
C13.9	MALIGNANT NEOPLASM OF HYPOPHARYNX, UNSPECIFIED	No
C14	MALIGNANT NEOPLASM OF OTHER AND ILL-DEFINED SITES IN THE LIP, ORAL CAVITY AND PHARYNX	No
C14.0	MALIGNANT NEOPLASM OF PHARYNX, UNSPECIFIED	No
C14.2	MALIGNANT NEOPLASM OF WALDEYER'S RING	No
C14.8	MALIGNANT NEOPLASM OF OVERLAPPING SITES OF LIP, ORAL CAVITY AND PHARYNX	No
C15	MALIGNANT NEOPLASM OF ESOPHAGUS	No
C15.3	MALIGNANT NEOPLASM OF UPPER THIRD OF ESOPHAGUS	No
C15.4	MALIGNANT NEOPLASM OF MIDDLE THIRD OF ESOPHAGUS	No
C15.5	MALIGNANT NEOPLASM OF LOWER THIRD OF ESOPHAGUS	No
C15.8	MALIGNANT NEOPLASM OF OVERLAPPING SITES OF ESOPHAGUS	No

ICD-10-CM	Code Description	IC
C15.9	MALIGNANT NEOPLASM OF ESOPHAGUS, UNSPECIFIED	No
C16	MALIGNANT NEOPLASM OF STOMACH	No
C16.0	MALIGNANT NEOPLASM OF CARDIA	No
C16.1	MALIGNANT NEOPLASM OF FUNDUS OF STOMACH	No
C16.2	MALIGNANT NEOPLASM OF BODY OF STOMACH	No
C16.3	MALIGNANT NEOPLASM OF PYLORIC ANTRUM	No
C16.4	MALIGNANT NEOPLASM OF PYLORUS	No
C16.5	MALIGNANT NEOPLASM OF LESSER CURVATURE OF STOMACH, UNSPECIFIED	No
C16.6	MALIGNANT NEOPLASM OF GREATER CURVATURE OF STOMACH, UNSPECIFIED	No
C16.8	MALIGNANT NEOPLASM OF OVERLAPPING SITES OF STOMACH	No
C16.9	MALIGNANT NEOPLASM OF STOMACH, UNSPECIFIED	No
C17	MALIGNANT NEOPLASM OF SMALL INTESTINE	No
C17.0	MALIGNANT NEOPLASM OF DUODENUM	No
C17.1	MALIGNANT NEOPLASM OF JEJUNUM	No
C17.2	MALIGNANT NEOPLASM OF ILEUM	No
C17.3	MECKEL'S DIVERTICULUM, MALIGNANT	No
C17.8	MALIGNANT NEOPLASM OF OVERLAPPING SITES OF SMALL INTESTINE	No
C17.9	MALIGNANT NEOPLASM OF SMALL INTESTINE, UNSPECIFIED	No
C18	MALIGNANT NEOPLASM OF COLON	No
C18.0	MALIGNANT NEOPLASM OF CECUM	No
C18.1	MALIGNANT NEOPLASM OF APPENDIX	No
C18.2	MALIGNANT NEOPLASM OF ASCENDING COLON	No
C18.3	MALIGNANT NEOPLASM OF HEPATIC FLEXURE	No
C18.4	MALIGNANT NEOPLASM OF TRANSVERSE COLON	No
C18.5	MALIGNANT NEOPLASM OF SPLENIC FLEXURE	No
C18.6	MALIGNANT NEOPLASM OF DESCENDING COLON	No
C18.7	MALIGNANT NEOPLASM OF SIGMOID COLON	No
C18.8	MALIGNANT NEOPLASM OF OVERLAPPING SITES OF COLON	No
C18.9	MALIGNANT NEOPLASM OF COLON, UNSPECIFIED	No
C19	MALIGNANT NEOPLASM OF RECTOSIGMOID JUNCTION	No
C20	MALIGNANT NEOPLASM OF RECTUM	No
C21	MALIGNANT NEOPLASM OF ANUS AND ANAL CANAL	No
C21.0	MALIGNANT NEOPLASM OF ANUS, UNSPECIFIED	No
C21.1	MALIGNANT NEOPLASM OF ANAL CANAL	No
C21.2	MALIGNANT NEOPLASM OF CLOACOGENIC ZONE	No
C21.8	MALIGNANT NEOPLASM OF OVERLAPPING SITES OF RECTUM, ANUS AND ANAL CANAL	No
C22	MALIGNANT NEOPLASM OF LIVER AND INTRAHEPATIC BILE DUCTS	No
C22.0	LIVER CELL CARCINOMA	No
C22.1	INTRAHEPATIC BILE DUCT CARCINOMA	No
C22.2	HEPATOBLASTOMA	No

ICD-10-CM	Code Description	IC
C22.3	ANGIOSARCOMA OF LIVER	No
C22.4	OTHER SARCOMAS OF LIVER	No
C22.7	OTHER SPECIFIED CARCINOMAS OF LIVER	No
C22.8	MALIGNANT NEOPLASM OF LIVER, PRIMARY, UNSPECIFIED AS TO TYPE	No
C22.9	MALIGNANT NEOPLASM OF LIVER, NOT SPECIFIED AS PRIMARY OR SECONDARY	No
C23	MALIGNANT NEOPLASM OF GALLBLADDER	No
C24	MALIGNANT NEOPLASM OF OTHER AND UNSPECIFIED PARTS OF BILIARY TRACT	No
C24.0	MALIGNANT NEOPLASM OF EXTRAHEPATIC BILE DUCT	No
C24.1	MALIGNANT NEOPLASM OF AMPULLA OF VATER	No
C24.8	MALIGNANT NEOPLASM OF OVERLAPPING SITES OF BILIARY TRACT	No
C24.9	MALIGNANT NEOPLASM OF BILIARY TRACT, UNSPECIFIED	No
C25	MALIGNANT NEOPLASM OF PANCREAS	No
C25.0	MALIGNANT NEOPLASM OF HEAD OF PANCREAS	No
C25.1	MALIGNANT NEOPLASM OF BODY OF PANCREAS	No
C25.2	MALIGNANT NEOPLASM OF TAIL OF PANCREAS	No
C25.3	MALIGNANT NEOPLASM OF PANCREATIC DUCT	No
C25.4	MALIGNANT NEOPLASM OF ENDOCRINE PANCREAS	No
C25.7	MALIGNANT NEOPLASM OF OTHER PARTS OF PANCREAS	No
C25.8	MALIGNANT NEOPLASM OF OVERLAPPING SITES OF PANCREAS	No
C25.9	MALIGNANT NEOPLASM OF PANCREAS, UNSPECIFIED	No
C26	MALIGNANT NEOPLASM OF OTHER AND ILL-DEFINED DIGESTIVE ORGANS	No
C26.0	MALIGNANT NEOPLASM OF INTESTINAL TRACT, PART UNSPECIFIED	No
C26.1	MALIGNANT NEOPLASM OF SPLEEN	No
C26.9	MALIGNANT NEOPLASM OF ILL-DEFINED SITES WITHIN THE DIGESTIVE SYSTEM	No
C30	MALIGNANT NEOPLASM OF NASAL CAVITY AND MIDDLE EAR	No
C30.0	MALIGNANT NEOPLASM OF NASAL CAVITY	No
C30.1	MALIGNANT NEOPLASM OF MIDDLE EAR	No
C31	MALIGNANT NEOPLASM OF ACCESSORY SINUSES	No
C31.0	MALIGNANT NEOPLASM OF MAXILLARY SINUS	No
C31.1	MALIGNANT NEOPLASM OF ETHMOIDAL SINUS	No
C31.2	MALIGNANT NEOPLASM OF FRONTAL SINUS	No
C31.3	MALIGNANT NEOPLASM OF SPHENOID SINUS	No
C31.8	MALIGNANT NEOPLASM OF OVERLAPPING SITES OF ACCESSORY SINUSES	No
C31.9	MALIGNANT NEOPLASM OF ACCESSORY SINUS, UNSPECIFIED	No
C32	MALIGNANT NEOPLASM OF LARYNX	No
C32.0	MALIGNANT NEOPLASM OF GLOTTIS	No
C32.1	MALIGNANT NEOPLASM OF SUPRAGLOTTIS	No
C32.2	MALIGNANT NEOPLASM OF SUBGLOTTIS	No
C32.3	MALIGNANT NEOPLASM OF LARYNGEAL CARTILAGE	No

ICD-10-CM	Code Description	IC
C32.8	MALIGNANT NEOPLASM OF OVERLAPPING SITES OF LARYNX	No
C32.9	MALIGNANT NEOPLASM OF LARYNX, UNSPECIFIED	No
C33	MALIGNANT NEOPLASM OF TRACHEA	No
C34	MALIGNANT NEOPLASM OF BRONCHUS AND LUNG	No
C34.0	MALIGNANT NEOPLASM OF MAIN BRONCHUS	No
C34.00	MALIGNANT NEOPLASM OF UNSPECIFIED MAIN BRONCHUS	No
C34.01	MALIGNANT NEOPLASM OF RIGHT MAIN BRONCHUS	No
C34.02	MALIGNANT NEOPLASM OF LEFT MAIN BRONCHUS	No
C34.1	MALIGNANT NEOPLASM OF UPPER LOBE, BRONCHUS OR LUNG	No
C34.10	MALIGNANT NEOPLASM OF UPPER LOBE, UNSPECIFIED BRONCHUS OR LUNG	No
C34.11	MALIGNANT NEOPLASM OF UPPER LOBE, RIGHT BRONCHUS OR LUNG	No
C34.12	MALIGNANT NEOPLASM OF UPPER LOBE, LEFT BRONCHUS OR LUNG	No
C34.2	MALIGNANT NEOPLASM OF MIDDLE LOBE, BRONCHUS OR LUNG	No
C34.3	MALIGNANT NEOPLASM OF LOWER LOBE, BRONCHUS OR LUNG	No
C34.30	MALIGNANT NEOPLASM OF LOWER LOBE, UNSPECIFIED BRONCHUS OR LUNG	No
C34.31	MALIGNANT NEOPLASM OF LOWER LOBE, RIGHT BRONCHUS OR LUNG	No
C34.32	MALIGNANT NEOPLASM OF LOWER LOBE, LEFT BRONCHUS OR LUNG	No
C34.8	MALIGNANT NEOPLASM OF OVERLAPPING SITES OF BRONCHUS AND LUNG	No
C34.80	MALIGNANT NEOPLASM OF OVERLAPPING SITES OF UNSPECIFIED BRONCHUS AND LUNG	No
C34.81	MALIGNANT NEOPLASM OF OVERLAPPING SITES OF RIGHT BRONCHUS AND LUNG	No
C34.82	MALIGNANT NEOPLASM OF OVERLAPPING SITES OF LEFT BRONCHUS AND LUNG	No
C34.9	MALIGNANT NEOPLASM OF UNSPECIFIED PART OF BRONCHUS OR LUNG	No
C34.90	MALIGNANT NEOPLASM OF UNSPECIFIED PART OF UNSPECIFIED BRONCHUS OR LUNG	No
C34.91	MALIGNANT NEOPLASM OF UNSPECIFIED PART OF RIGHT BRONCHUS OR LUNG	No
C34.92	MALIGNANT NEOPLASM OF UNSPECIFIED PART OF LEFT BRONCHUS OR LUNG	No
C37	MALIGNANT NEOPLASM OF THYMUS	No
C38	MALIGNANT NEOPLASM OF HEART, MEDIASTINUM AND PLEURA	No
C38.0	MALIGNANT NEOPLASM OF HEART	No
C38.1	MALIGNANT NEOPLASM OF ANTERIOR MEDIASTINUM	No
C38.2	MALIGNANT NEOPLASM OF POSTERIOR MEDIASTINUM	No
C38.3	MALIGNANT NEOPLASM OF MEDIASTINUM, PART UNSPECIFIED	No
C38.4	MALIGNANT NEOPLASM OF PLEURA	No
C38.8	MALIGNANT NEOPLASM OF OVERLAPPING SITES OF HEART, MEDIASTINUM AND PLEURA	No
C39	MALIGNANT NEOPLASM OF OTHER AND ILL-DEFINED SITES IN THE RESPIRATORY SYSTEM AND INTRATHORACIC ORGANS	No
C39.0	MALIGNANT NEOPLASM OF UPPER RESPIRATORY TRACT, PART UNSPECIFIED	No
C39.9	MALIGNANT NEOPLASM OF LOWER RESPIRATORY TRACT, PART UNSPECIFIED	No

ICD-10-CM	Code Description	IC
C40	MALIGNANT NEOPLASM OF BONE AND ARTICULAR CARTILAGE OF LIMBS	No
C40.0	MALIGNANT NEOPLASM OF SCAPULA AND LONG BONES OF UPPER LIMB	No
C40.00	MALIGNANT NEOPLASM OF SCAPULA AND LONG BONES OF UNSPECIFIED UPPER LIMB	No
C40.01	MALIGNANT NEOPLASM OF SCAPULA AND LONG BONES OF RIGHT UPPER LIMB	No
C40.02	MALIGNANT NEOPLASM OF SCAPULA AND LONG BONES OF LEFT UPPER LIMB	No
C40.1	MALIGNANT NEOPLASM OF SHORT BONES OF UPPER LIMB	No
C40.10	MALIGNANT NEOPLASM OF SHORT BONES OF UNSPECIFIED UPPER LIMB	No
C40.11	MALIGNANT NEOPLASM OF SHORT BONES OF RIGHT UPPER LIMB	No
C40.12	MALIGNANT NEOPLASM OF SHORT BONES OF LEFT UPPER LIMB	No
C40.2	MALIGNANT NEOPLASM OF LONG BONES OF LOWER LIMB	No
C40.20	MALIGNANT NEOPLASM OF LONG BONES OF UNSPECIFIED LOWER LIMB	No
C40.21	MALIGNANT NEOPLASM OF LONG BONES OF RIGHT LOWER LIMB	No
C40.22	MALIGNANT NEOPLASM OF LONG BONES OF LEFT LOWER LIMB	No
C40.3	MALIGNANT NEOPLASM OF SHORT BONES OF LOWER LIMB	No
C40.30	MALIGNANT NEOPLASM OF SHORT BONES OF UNSPECIFIED LOWER LIMB	No
C40.31	MALIGNANT NEOPLASM OF SHORT BONES OF RIGHT LOWER LIMB	No
C40.32	MALIGNANT NEOPLASM OF SHORT BONES OF LEFT LOWER LIMB	No
C40.8	MALIGNANT NEOPLASM OF OVERLAPPING SITES OF BONE AND ARTICULAR CARTILAGE OF LIMB	No
C40.80	MALIGNANT NEOPLASM OF OVERLAPPING SITES OF BONE AND ARTICULAR CARTILAGE OF UNSPECIFIED LIMB	No
C40.81	MALIGNANT NEOPLASM OF OVERLAPPING SITES OF BONE AND ARTICULAR CARTILAGE OF RIGHT LIMB	No
C40.82	MALIGNANT NEOPLASM OF OVERLAPPING SITES OF BONE AND ARTICULAR CARTILAGE OF LEFT LIMB	No
C40.9	MALIGNANT NEOPLASM OF UNSPECIFIED BONES AND ARTICULAR CARTILAGE OF LIMB	No
C40.90	MALIGNANT NEOPLASM OF UNSPECIFIED BONES AND ARTICULAR CARTILAGE OF UNSPECIFIED LIMB	No
C40.91	MALIGNANT NEOPLASM OF UNSPECIFIED BONES AND ARTICULAR CARTILAGE OF RIGHT LIMB	No
C40.92	MALIGNANT NEOPLASM OF UNSPECIFIED BONES AND ARTICULAR CARTILAGE OF LEFT LIMB	No
C41	MALIGNANT NEOPLASM OF BONE AND ARTICULAR CARTILAGE OF OTHER AND UNSPECIFIED SITES	No
C41.0	MALIGNANT NEOPLASM OF BONES OF SKULL AND FACE	No
C41.1	MALIGNANT NEOPLASM OF MANDIBLE	No
C41.2	MALIGNANT NEOPLASM OF VERTEBRAL COLUMN	No
C41.3	MALIGNANT NEOPLASM OF RIBS, STERNUM AND CLAVICLE	No
C41.4	MALIGNANT NEOPLASM OF PELVIC BONES, SACRUM AND COCCYX	No
C41.9	MALIGNANT NEOPLASM OF BONE AND ARTICULAR CARTILAGE, UNSPECIFIED	No
C44	OTHER AND UNSPECIFIED MALIGNANT NEOPLASM OF SKIN	No

ICD-10-CM	Code Description	IC
C44.0	OTHER AND UNSPECIFIED MALIGNANT NEOPLASM OF SKIN OF LIP	No
C44.00	UNSPECIFIED MALIGNANT NEOPLASM OF SKIN OF LIP	No
C44.01	BASAL CELL CARCINOMA OF SKIN OF LIP	No
C44.02	SQUAMOUS CELL CARCINOMA OF SKIN OF LIP	No
C44.09	OTHER SPECIFIED MALIGNANT NEOPLASM OF SKIN OF LIP	No
C44.1	OTHER AND UNSPECIFIED MALIGNANT NEOPLASM OF SKIN OF EYELID, INCLUDING CANTHUS	No
C44.10	UNSPECIFIED MALIGNANT NEOPLASM OF SKIN OF EYELID, INCLUDING CANTHUS	No
C44.101	UNSPECIFIED MALIGNANT NEOPLASM OF SKIN OF UNSPECIFIED EYELID, INCLUDING CANTHUS	No
C44.102	UNSPECIFIED MALIGNANT NEOPLASM OF SKIN OF RIGHT EYELID, INCLUDING CANTHUS	No
C44.1021	Unspecified malignant neoplasm of skin of right upper eyelid, including canthus	No
C44.1022	Unspecified malignant neoplasm of skin of right lower eyelid, including canthus	No
C44.109	UNSPECIFIED MALIGNANT NEOPLASM OF SKIN OF LEFT EYELID, INCLUDING CANTHUS	No
C44.1091	Unspecified malignant neoplasm of skin of left upper eyelid, including canthus	No
C44.1092	Unspecified malignant neoplasm of skin of left lower eyelid, including canthus	No
C44.11	BASAL CELL CARCINOMA OF SKIN OF EYELID, INCLUDING CANTHUS	No
C44.111	BASAL CELL CARCINOMA OF SKIN OF UNSPECIFIED EYELID, INCLUDING CANTHUS	No
C44.112	BASAL CELL CARCINOMA OF SKIN OF RIGHT EYELID, INCLUDING CANTHUS	No
C44.1121	Basal cell carcinoma of skin of right upper eyelid, including canthus	No
C44.1122	Basal cell carcinoma of skin of right lower eyelid, including canthus	No
C44.119	BASAL CELL CARCINOMA OF SKIN OF LEFT EYELID, INCLUDING CANTHUS	No
C44.1191	Basal cell carcinoma of skin of left upper eyelid, including canthus	No
C44.1192	Basal cell carcinoma of skin of left lower eyelid, including canthus	No
C44.12	SQUAMOUS CELL CARCINOMA OF SKIN OF EYELID, INCLUDING CANTHUS	No
C44.121	SQUAMOUS CELL CARCINOMA OF SKIN OF UNSPECIFIED EYELID, INCLUDING CANTHUS	No
C44.122	SQUAMOUS CELL CARCINOMA OF SKIN OF RIGHT EYELID, INCLUDING CANTHUS	No
C44.1221	Squamous cell carcinoma of skin of right upper eyelid, including canthus	No
C44.1222	Squamous cell carcinoma of skin of right lower eyelid, including canthus	No
C44.129	SQUAMOUS CELL CARCINOMA OF SKIN OF LEFT EYELID, INCLUDING CANTHUS	No
C44.1291	Squamous cell carcinoma of skin of left upper eyelid, including canthus	No
C44.1292	Squamous cell carcinoma of skin of left lower eyelid, including canthus	No
C44.13	Sebaceous cell carcinoma of skin of eyelid, including canthus	No
C44.131	Sebaceous cell carcinoma of skin of unspecified eyelid, including canthus	No
C44.132	Sebaceous cell carcinoma of skin of right eyelid, including canthus	No
C44.1321	Sebaceous cell carcinoma of skin of right upper eyelid, including canthus	No

ICD-10-CM	Code Description	IC
C44.1322	Sebaceous cell carcinoma of skin of right lower eyelid, including canthus	No
C44.139	Sebaceous cell carcinoma of skin of left eyelid, including canthus	No
C44.1391	Sebaceous cell carcinoma of skin of left upper eyelid, including canthus	No
C44.1392	Sebaceous cell carcinoma of skin of left lower eyelid, including canthus	No
C44.19	OTHER SPECIFIED MALIGNANT NEOPLASM OF SKIN OF EYELID, INCLUDING CANTHUS	No
C44.191	OTHER SPECIFIED MALIGNANT NEOPLASM OF SKIN OF UNSPECIFIED EYELID, INCLUDING CANTHUS	No
C44.192	OTHER SPECIFIED MALIGNANT NEOPLASM OF SKIN OF RIGHT EYELID, INCLUDING CANTHUS	No
C44.1921	Other specified malignant neoplasm of skin of right upper eyelid, including canthus	No
C44.1922	Other specified malignant neoplasm of skin of right lower eyelid, including canthus	No
C44.199	OTHER SPECIFIED MALIGNANT NEOPLASM OF SKIN OF LEFT EYELID, INCLUDING CANTHUS	No
C44.1991	Other specified malignant neoplasm of skin of left upper eyelid, including canthus	No
C44.1992	Other specified malignant neoplasm of skin of left lower eyelid, including canthus	No
C44.2	OTHER AND UNSPECIFIED MALIGNANT NEOPLASM OF SKIN OF EAR AND EXTERNAL AURICULAR CANAL	No
C44.20	UNSPECIFIED MALIGNANT NEOPLASM OF SKIN OF EAR AND EXTERNAL AURICULAR CANAL	No
C44.201	UNSPECIFIED MALIGNANT NEOPLASM OF SKIN OF UNSPECIFIED EAR AND EXTERNAL AURICULAR CANAL	No
C44.202	UNSPECIFIED MALIGNANT NEOPLASM OF SKIN OF RIGHT EAR AND EXTERNAL AURICULAR CANAL	No
C44.209	UNSPECIFIED MALIGNANT NEOPLASM OF SKIN OF LEFT EAR AND EXTERNAL AURICULAR CANAL	No
C44.21	BASAL CELL CARCINOMA OF SKIN OF EAR AND EXTERNAL AURICULAR CANAL	No
C44.211	BASAL CELL CARCINOMA OF SKIN OF UNSPECIFIED EAR AND EXTERNAL AURICULAR CANAL	No
C44.212	BASAL CELL CARCINOMA OF SKIN OF RIGHT EAR AND EXTERNAL AURICULAR CANAL	No
C44.219	BASAL CELL CARCINOMA OF SKIN OF LEFT EAR AND EXTERNAL AURICULAR CANAL	No
C44.22	SQUAMOUS CELL CARCINOMA OF SKIN OF EAR AND EXTERNAL AURICULAR CANAL	No
C44.221	SQUAMOUS CELL CARCINOMA OF SKIN OF UNSPECIFIED EAR AND EXTERNAL AURICULAR CANAL	No
C44.222	SQUAMOUS CELL CARCINOMA OF SKIN OF RIGHT EAR AND EXTERNAL AURICULAR CANAL	No
C44.229	SQUAMOUS CELL CARCINOMA OF SKIN OF LEFT EAR AND EXTERNAL AURICULAR CANAL	No

ICD-10-CM	Code Description	IC
C44.29	OTHER SPECIFIED MALIGNANT NEOPLASM OF SKIN OF EAR AND EXTERNAL AURICULAR CANAL	No
C44.291	OTHER SPECIFIED MALIGNANT NEOPLASM OF SKIN OF UNSPECIFIED EAR AND EXTERNAL AURICULAR CANAL	No
C44.292	OTHER SPECIFIED MALIGNANT NEOPLASM OF SKIN OF RIGHT EAR AND EXTERNAL AURICULAR CANAL	No
C44.299	OTHER SPECIFIED MALIGNANT NEOPLASM OF SKIN OF LEFT EAR AND EXTERNAL AURICULAR CANAL	No
C44.3	OTHER AND UNSPECIFIED MALIGNANT NEOPLASM OF SKIN OF OTHER AND UNSPECIFIED PARTS OF FACE	No
C44.30	UNSPECIFIED MALIGNANT NEOPLASM OF SKIN OF OTHER AND UNSPECIFIED PARTS OF FACE	No
C44.300	UNSPECIFIED MALIGNANT NEOPLASM OF SKIN OF UNSPECIFIED PART OF FACE	No
C44.301	UNSPECIFIED MALIGNANT NEOPLASM OF SKIN OF NOSE	No
C44.309	UNSPECIFIED MALIGNANT NEOPLASM OF SKIN OF OTHER PARTS OF FACE	No
C44.31	BASAL CELL CARCINOMA OF SKIN OF OTHER AND UNSPECIFIED PARTS OF FACE	No
C44.310	BASAL CELL CARCINOMA OF SKIN OF UNSPECIFIED PARTS OF FACE	No
C44.311	BASAL CELL CARCINOMA OF SKIN OF NOSE	No
C44.319	BASAL CELL CARCINOMA OF SKIN OF OTHER PARTS OF FACE	No
C44.32	SQUAMOUS CELL CARCINOMA OF SKIN OF OTHER AND UNSPECIFIED PARTS OF FACE	No
C44.320	SQUAMOUS CELL CARCINOMA OF SKIN OF UNSPECIFIED PARTS OF FACE	No
C44.321	SQUAMOUS CELL CARCINOMA OF SKIN OF NOSE	No
C44.329	SQUAMOUS CELL CARCINOMA OF SKIN OF OTHER PARTS OF FACE	No
C44.39	OTHER SPECIFIED MALIGNANT NEOPLASM OF SKIN OF OTHER AND UNSPECIFIED PARTS OF FACE	No
C44.390	OTHER SPECIFIED MALIGNANT NEOPLASM OF SKIN OF UNSPECIFIED PARTS OF FACE	No
C44.391	OTHER SPECIFIED MALIGNANT NEOPLASM OF SKIN OF NOSE	No
C44.399	OTHER SPECIFIED MALIGNANT NEOPLASM OF SKIN OF OTHER PARTS OF FACE	No
C44.4	OTHER AND UNSPECIFIED MALIGNANT NEOPLASM OF SKIN OF SCALP AND NECK	No
C44.40	UNSPECIFIED MALIGNANT NEOPLASM OF SKIN OF SCALP AND NECK	No
C44.41	BASAL CELL CARCINOMA OF SKIN OF SCALP AND NECK	No
C44.42	SQUAMOUS CELL CARCINOMA OF SKIN OF SCALP AND NECK	No
C44.49	OTHER SPECIFIED MALIGNANT NEOPLASM OF SKIN OF SCALP AND NECK	No
C44.5	OTHER AND UNSPECIFIED MALIGNANT NEOPLASM OF SKIN OF TRUNK	No
C44.50	UNSPECIFIED MALIGNANT NEOPLASM OF SKIN OF TRUNK	No
C44.500	UNSPECIFIED MALIGNANT NEOPLASM OF ANAL SKIN	No
C44.501	UNSPECIFIED MALIGNANT NEOPLASM OF SKIN OF BREAST	No
C44.509	UNSPECIFIED MALIGNANT NEOPLASM OF SKIN OF OTHER PART OF TRUNK	No
C44.51	BASAL CELL CARCINOMA OF SKIN OF TRUNK	No

ICD-10-CM	Code Description	IC
C44.510	BASAL CELL CARCINOMA OF ANAL SKIN	No
C44.511	BASAL CELL CARCINOMA OF SKIN OF BREAST	No
C44.519	BASAL CELL CARCINOMA OF SKIN OF OTHER PART OF TRUNK	No
C44.52	SQUAMOUS CELL CARCINOMA OF SKIN OF TRUNK	No
C44.520	SQUAMOUS CELL CARCINOMA OF ANAL SKIN	No
C44.521	SQUAMOUS CELL CARCINOMA OF SKIN OF BREAST	No
C44.529	SQUAMOUS CELL CARCINOMA OF SKIN OF OTHER PART OF TRUNK	No
C44.59	OTHER SPECIFIED MALIGNANT NEOPLASM OF SKIN OF TRUNK	No
C44.590	OTHER SPECIFIED MALIGNANT NEOPLASM OF ANAL SKIN	No
C44.591	OTHER SPECIFIED MALIGNANT NEOPLASM OF SKIN OF BREAST	No
C44.599	OTHER SPECIFIED MALIGNANT NEOPLASM OF SKIN OF OTHER PART OF TRUNK	No
C44.6	OTHER AND UNSPECIFIED MALIGNANT NEOPLASM OF SKIN OF UPPER LIMB, INCLUDING SHOULDER	No
C44.60	UNSPECIFIED MALIGNANT NEOPLASM OF SKIN OF UPPER LIMB, INCLUDING SHOULDER	No
C44.601	UNSPECIFIED MALIGNANT NEOPLASM OF SKIN OF UNSPECIFIED UPPER LIMB, INCLUDING SHOULDER	No
C44.602	UNSPECIFIED MALIGNANT NEOPLASM OF SKIN OF RIGHT UPPER LIMB, INCLUDING SHOULDER	No
C44.609	UNSPECIFIED MALIGNANT NEOPLASM OF SKIN OF LEFT UPPER LIMB, INCLUDING SHOULDER	No
C44.61	BASAL CELL CARCINOMA OF SKIN OF UPPER LIMB, INCLUDING SHOULDER	No
C44.611	BASAL CELL CARCINOMA OF SKIN OF UNSPECIFIED UPPER LIMB, INCLUDING SHOULDER	No
C44.612	BASAL CELL CARCINOMA OF SKIN OF RIGHT UPPER LIMB, INCLUDING SHOULDER	No
C44.619	BASAL CELL CARCINOMA OF SKIN OF LEFT UPPER LIMB, INCLUDING SHOULDER	No
C44.62	SQUAMOUS CELL CARCINOMA OF SKIN OF UPPER LIMB, INCLUDING SHOULDER	No
C44.621	SQUAMOUS CELL CARCINOMA OF SKIN OF UNSPECIFIED UPPER LIMB, INCLUDING SHOULDER	No
C44.622	SQUAMOUS CELL CARCINOMA OF SKIN OF RIGHT UPPER LIMB, INCLUDING SHOULDER	No
C44.629	SQUAMOUS CELL CARCINOMA OF SKIN OF LEFT UPPER LIMB, INCLUDING SHOULDER	No
C44.69	OTHER SPECIFIED MALIGNANT NEOPLASM OF SKIN OF UPPER LIMB, INCLUDING SHOULDER	No
C44.691	OTHER SPECIFIED MALIGNANT NEOPLASM OF SKIN OF UNSPECIFIED UPPER LIMB, INCLUDING SHOULDER	No
C44.692	OTHER SPECIFIED MALIGNANT NEOPLASM OF SKIN OF RIGHT UPPER LIMB, INCLUDING SHOULDER	No
C44.699	OTHER SPECIFIED MALIGNANT NEOPLASM OF SKIN OF LEFT UPPER LIMB, INCLUDING SHOULDER	No

ICD-10-CM	Code Description	IC
C44.7	OTHER AND UNSPECIFIED MALIGNANT NEOPLASM OF SKIN OF LOWER LIMB, INCLUDING HIP	No
C44.70	UNSPECIFIED MALIGNANT NEOPLASM OF SKIN OF LOWER LIMB, INCLUDING HIP	No
C44.701	UNSPECIFIED MALIGNANT NEOPLASM OF SKIN OF UNSPECIFIED LOWER LIMB, INCLUDING HIP	No
C44.702	UNSPECIFIED MALIGNANT NEOPLASM OF SKIN OF RIGHT LOWER LIMB, INCLUDING HIP	No
C44.709	UNSPECIFIED MALIGNANT NEOPLASM OF SKIN OF LEFT LOWER LIMB, INCLUDING HIP	No
C44.71	BASAL CELL CARCINOMA OF SKIN OF LOWER LIMB, INCLUDING HIP	No
C44.711	BASAL CELL CARCINOMA OF SKIN OF UNSPECIFIED LOWER LIMB, INCLUDING HIP	No
C44.712	BASAL CELL CARCINOMA OF SKIN OF RIGHT LOWER LIMB, INCLUDING HIP	No
C44.719	BASAL CELL CARCINOMA OF SKIN OF LEFT LOWER LIMB, INCLUDING HIP	No
C44.72	SQUAMOUS CELL CARCINOMA OF SKIN OF LOWER LIMB, INCLUDING HIP	No
C44.721	SQUAMOUS CELL CARCINOMA OF SKIN OF UNSPECIFIED LOWER LIMB, INCLUDING HIP	No
C44.722	SQUAMOUS CELL CARCINOMA OF SKIN OF RIGHT LOWER LIMB, INCLUDING HIP	No
C44.729	SQUAMOUS CELL CARCINOMA OF SKIN OF LEFT LOWER LIMB, INCLUDING HIP	No
C44.79	OTHER SPECIFIED MALIGNANT NEOPLASM OF SKIN OF LOWER LIMB, INCLUDING HIP	No
C44.791	OTHER SPECIFIED MALIGNANT NEOPLASM OF SKIN OF UNSPECIFIED LOWER LIMB, INCLUDING HIP	No
C44.792	OTHER SPECIFIED MALIGNANT NEOPLASM OF SKIN OF RIGHT LOWER LIMB, INCLUDING HIP	No
C44.799	OTHER SPECIFIED MALIGNANT NEOPLASM OF SKIN OF LEFT LOWER LIMB, INCLUDING HIP	No
C44.8	OTHER AND UNSPECIFIED MALIGNANT NEOPLASM OF OVERLAPPING SITES OF SKIN	No
C44.80	UNSPECIFIED MALIGNANT NEOPLASM OF OVERLAPPING SITES OF SKIN	No
C44.81	BASAL CELL CARCINOMA OF OVERLAPPING SITES OF SKIN	No
C44.82	SQUAMOUS CELL CARCINOMA OF OVERLAPPING SITES OF SKIN	No
C44.89	OTHER SPECIFIED MALIGNANT NEOPLASM OF OVERLAPPING SITES OF SKIN	No
C44.9	OTHER AND UNSPECIFIED MALIGNANT NEOPLASM OF SKIN, UNSPECIFIED	No
C44.90	UNSPECIFIED MALIGNANT NEOPLASM OF SKIN, UNSPECIFIED	No
C44.91	BASAL CELL CARCINOMA OF SKIN, UNSPECIFIED	No
C44.92	SQUAMOUS CELL CARCINOMA OF SKIN, UNSPECIFIED	No
C44.99	OTHER SPECIFIED MALIGNANT NEOPLASM OF SKIN, UNSPECIFIED	No
C48	MALIGNANT NEOPLASM OF RETROPERITONEUM AND PERITONEUM	No
C48.0	MALIGNANT NEOPLASM OF RETROPERITONEUM	No
C48.1	MALIGNANT NEOPLASM OF SPECIFIED PARTS OF PERITONEUM	No
C48.2	MALIGNANT NEOPLASM OF PERITONEUM, UNSPECIFIED	No

ICD-10-CM	Code Description	IC
C48.8	MALIGNANT NEOPLASM OF OVERLAPPING SITES OF RETROPERITONEUM AND PERITONEUM	No
C49	MALIGNANT NEOPLASM OF OTHER CONNECTIVE AND SOFT TISSUE	No
C49.0	MALIGNANT NEOPLASM OF CONNECTIVE AND SOFT TISSUE OF HEAD, FACE AND NECK	No
C49.1	MALIGNANT NEOPLASM OF CONNECTIVE AND SOFT TISSUE OF UPPER LIMB, INCLUDING SHOULDER	No
C49.10	MALIGNANT NEOPLASM OF CONNECTIVE AND SOFT TISSUE OF UNSPECIFIED UPPER LIMB, INCLUDING SHOULDER	No
C49.11	MALIGNANT NEOPLASM OF CONNECTIVE AND SOFT TISSUE OF RIGHT UPPER LIMB, INCLUDING SHOULDER	No
C49.12	MALIGNANT NEOPLASM OF CONNECTIVE AND SOFT TISSUE OF LEFT UPPER LIMB, INCLUDING SHOULDER	No
C49.2	MALIGNANT NEOPLASM OF CONNECTIVE AND SOFT TISSUE OF LOWER LIMB, INCLUDING HIP	No
C49.20	MALIGNANT NEOPLASM OF CONNECTIVE AND SOFT TISSUE OF UNSPECIFIED LOWER LIMB, INCLUDING HIP	No
C49.21	MALIGNANT NEOPLASM OF CONNECTIVE AND SOFT TISSUE OF RIGHT LOWER LIMB, INCLUDING HIP	No
C49.22	MALIGNANT NEOPLASM OF CONNECTIVE AND SOFT TISSUE OF LEFT LOWER LIMB, INCLUDING HIP	No
C49.3	MALIGNANT NEOPLASM OF CONNECTIVE AND SOFT TISSUE OF THORAX	No
C49.4	MALIGNANT NEOPLASM OF CONNECTIVE AND SOFT TISSUE OF ABDOMEN	No
C49.5	MALIGNANT NEOPLASM OF CONNECTIVE AND SOFT TISSUE OF PELVIS	No
C49.6	MALIGNANT NEOPLASM OF CONNECTIVE AND SOFT TISSUE OF TRUNK, UNSPECIFIED	No
C49.8	MALIGNANT NEOPLASM OF OVERLAPPING SITES OF CONNECTIVE AND SOFT TISSUE	No
C49.9	MALIGNANT NEOPLASM OF CONNECTIVE AND SOFT TISSUE, UNSPECIFIED	No
C49.A	Gastrointestinal stromal tumor	No
C49.A0	GASTROINTESTINAL STROMAL TUMOR, UNSPECIFIED SITE	No
C49.A1	GASTROINTESTINAL STROMAL TUMOR OF ESOPHAGUS	No
C49.A2	GASTROINTESTINAL STROMAL TUMOR OF STOMACH	No
C49.A3	GASTROINTESTINAL STROMAL TUMOR OF SMALL INTESTINE	No
C49.A4	GASTROINTESTINAL STROMAL TUMOR OF LARGE INTESTINE	No
C49.A5	GASTROINTESTINAL STROMAL TUMOR OF RECTUM	No
C49.A9	GASTROINTESTINAL STROMAL TUMOR OF OTHER SITES	No
C4A	MERKEL CELL CARCINOMA	No
C4A.0	MERKEL CELL CARCINOMA OF LIP	No
C4A.1	MERKEL CELL CARCINOMA OF EYELID, INCLUDING CANTHUS	No
C4A.10	MERKEL CELL CARCINOMA OF UNSPECIFIED EYELID, INCLUDING CANTHUS	No
C4A.11	MERKEL CELL CARCINOMA OF RIGHT EYELID, INCLUDING CANTHUS	No
C4A.111	Merkel cell carcinoma of right upper eyelid, including canthus	No
C4A.112	Merkel cell carcinoma of right lower eyelid, including canthus	No

ICD-10-CM	Code Description	IC
C4A.12	MERKEL CELL CARCINOMA OF LEFT EYELID, INCLUDING CANTHUS	No
C4A.121	Merkel cell carcinoma of left upper eyelid, including canthus	No
C4A.122	Merkel cell carcinoma of left lower eyelid, including canthus	No
C4A.2	MERKEL CELL CARCINOMA OF EAR AND EXTERNAL AURICULAR CANAL	No
C4A.20	MERKEL CELL CARCINOMA OF UNSPECIFIED EAR AND EXTERNAL AURICULAR CANAL	No
C4A.21	MERKEL CELL CARCINOMA OF RIGHT EAR AND EXTERNAL AURICULAR CANAL	No
C4A.22	MERKEL CELL CARCINOMA OF LEFT EAR AND EXTERNAL AURICULAR CANAL	No
C4A.3	MERKEL CELL CARCINOMA OF OTHER AND UNSPECIFIED PARTS OF FACE	No
C4A.30	MERKEL CELL CARCINOMA OF UNSPECIFIED PART OF FACE	No
C4A.31	MERKEL CELL CARCINOMA OF NOSE	No
C4A.39	MERKEL CELL CARCINOMA OF OTHER PARTS OF FACE	No
C4A.4	MERKEL CELL CARCINOMA OF SCALP AND NECK	No
C4A.5	MERKEL CELL CARCINOMA OF TRUNK	No
C4A.51	MERKEL CELL CARCINOMA OF ANAL SKIN	No
C4A.52	MERKEL CELL CARCINOMA OF SKIN OF BREAST	No
C4A.59	MERKEL CELL CARCINOMA OF OTHER PART OF TRUNK	No
C4A.6	MERKEL CELL CARCINOMA OF UPPER LIMB, INCLUDING SHOULDER	No
C4A.60	MERKEL CELL CARCINOMA OF UNSPECIFIED UPPER LIMB, INCLUDING SHOULDER	No
C4A.61	MERKEL CELL CARCINOMA OF RIGHT UPPER LIMB, INCLUDING SHOULDER	No
C4A.62	MERKEL CELL CARCINOMA OF LEFT UPPER LIMB, INCLUDING SHOULDER	No
C4A.7	MERKEL CELL CARCINOMA OF LOWER LIMB, INCLUDING HIP	No
C4A.70	MERKEL CELL CARCINOMA OF UNSPECIFIED LOWER LIMB, INCLUDING HIP	No
C4A.71	MERKEL CELL CARCINOMA OF RIGHT LOWER LIMB, INCLUDING HIP	No
C4A.72	MERKEL CELL CARCINOMA OF LEFT LOWER LIMB, INCLUDING HIP	No
C4A.8	MERKEL CELL CARCINOMA OF OVERLAPPING SITES	No
C4A.9	MERKEL CELL CARCINOMA, UNSPECIFIED	No
C50	MALIGNANT NEOPLASM OF BREAST	No
C50.0	MALIGNANT NEOPLASM OF NIPPLE AND AREOLA	No
C50.01	MALIGNANT NEOPLASM OF NIPPLE AND AREOLA, FEMALE	No
C50.011	MALIGNANT NEOPLASM OF NIPPLE AND AREOLA, RIGHT FEMALE BREAST	No
C50.012	MALIGNANT NEOPLASM OF NIPPLE AND AREOLA, LEFT FEMALE BREAST	No
C50.019	MALIGNANT NEOPLASM OF NIPPLE AND AREOLA, UNSPECIFIED FEMALE BREAST	No
C50.02	MALIGNANT NEOPLASM OF NIPPLE AND AREOLA, MALE	No
C50.021	MALIGNANT NEOPLASM OF NIPPLE AND AREOLA, RIGHT MALE BREAST	No
C50.022	MALIGNANT NEOPLASM OF NIPPLE AND AREOLA, LEFT MALE BREAST	No
C50.029	MALIGNANT NEOPLASM OF NIPPLE AND AREOLA, UNSPECIFIED MALE BREAST	No
C50.1	MALIGNANT NEOPLASM OF CENTRAL PORTION OF BREAST	No
C50.11	MALIGNANT NEOPLASM OF CENTRAL PORTION OF BREAST, FEMALE	No
C50.111	MALIGNANT NEOPLASM OF CENTRAL PORTION OF RIGHT FEMALE BREAST	No

ICD-10-CM	Code Description	IC
C50.112	MALIGNANT NEOPLASM OF CENTRAL PORTION OF LEFT FEMALE BREAST	No
C50.119	MALIGNANT NEOPLASM OF CENTRAL PORTION OF UNSPECIFIED FEMALE BREAST	No
C50.12	MALIGNANT NEOPLASM OF CENTRAL PORTION OF BREAST, MALE	No
C50.121	MALIGNANT NEOPLASM OF CENTRAL PORTION OF RIGHT MALE BREAST	No
C50.122	MALIGNANT NEOPLASM OF CENTRAL PORTION OF LEFT MALE BREAST	No
C50.129	MALIGNANT NEOPLASM OF CENTRAL PORTION OF UNSPECIFIED MALE BREAST	No
C50.2	MALIGNANT NEOPLASM OF UPPER-INNER QUADRANT OF BREAST	No
C50.21	MALIGNANT NEOPLASM OF UPPER-INNER QUADRANT OF BREAST, FEMALE	No
C50.211	MALIGNANT NEOPLASM OF UPPER-INNER QUADRANT OF RIGHT FEMALE BREAST	No
C50.212	MALIGNANT NEOPLASM OF UPPER-INNER QUADRANT OF LEFT FEMALE BREAST	No
C50.219	MALIGNANT NEOPLASM OF UPPER-INNER QUADRANT OF UNSPECIFIED FEMALE BREAST	No
C50.22	MALIGNANT NEOPLASM OF UPPER-INNER QUADRANT OF BREAST, MALE	No
C50.221	MALIGNANT NEOPLASM OF UPPER-INNER QUADRANT OF RIGHT MALE BREAST	No
C50.222	MALIGNANT NEOPLASM OF UPPER-INNER QUADRANT OF LEFT MALE BREAST	No
C50.229	MALIGNANT NEOPLASM OF UPPER-INNER QUADRANT OF UNSPECIFIED MALE BREAST	No
C50.3	MALIGNANT NEOPLASM OF LOWER-INNER QUADRANT OF BREAST	No
C50.31	MALIGNANT NEOPLASM OF LOWER-INNER QUADRANT OF BREAST, FEMALE	No
C50.311	MALIGNANT NEOPLASM OF LOWER-INNER QUADRANT OF RIGHT FEMALE BREAST	No
C50.312	MALIGNANT NEOPLASM OF LOWER-INNER QUADRANT OF LEFT FEMALE BREAST	No
C50.319	MALIGNANT NEOPLASM OF LOWER-INNER QUADRANT OF UNSPECIFIED FEMALE BREAST	No
C50.32	MALIGNANT NEOPLASM OF LOWER-INNER QUADRANT OF BREAST, MALE	No
C50.321	MALIGNANT NEOPLASM OF LOWER-INNER QUADRANT OF RIGHT MALE BREAST	No
C50.322	MALIGNANT NEOPLASM OF LOWER-INNER QUADRANT OF LEFT MALE BREAST	No
C50.329	MALIGNANT NEOPLASM OF LOWER-INNER QUADRANT OF UNSPECIFIED MALE BREAST	No
C50.4	MALIGNANT NEOPLASM OF UPPER-OUTER QUADRANT OF BREAST	No
C50.41	MALIGNANT NEOPLASM OF UPPER-OUTER QUADRANT OF BREAST, FEMALE	No
C50.411	MALIGNANT NEOPLASM OF UPPER-OUTER QUADRANT OF RIGHT FEMALE BREAST	No
C50.412	MALIGNANT NEOPLASM OF UPPER-OUTER QUADRANT OF LEFT FEMALE BREAST	No
C50.419	MALIGNANT NEOPLASM OF UPPER-OUTER QUADRANT OF UNSPECIFIED FEMALE BREAST	No
C50.42	MALIGNANT NEOPLASM OF UPPER-OUTER QUADRANT OF BREAST, MALE	No

ICD-10-CM	Code Description	IC
C50.421	MALIGNANT NEOPLASM OF UPPER-OUTER QUADRANT OF RIGHT MALE BREAST	No
C50.422	MALIGNANT NEOPLASM OF UPPER-OUTER QUADRANT OF LEFT MALE BREAST	No
C50.429	MALIGNANT NEOPLASM OF UPPER-OUTER QUADRANT OF UNSPECIFIED MALE BREAST	No
C50.5	MALIGNANT NEOPLASM OF LOWER-OUTER QUADRANT OF BREAST	No
C50.51	MALIGNANT NEOPLASM OF LOWER-OUTER QUADRANT OF BREAST, FEMALE	No
C50.511	MALIGNANT NEOPLASM OF LOWER-OUTER QUADRANT OF RIGHT FEMALE BREAST	No
C50.512	MALIGNANT NEOPLASM OF LOWER-OUTER QUADRANT OF LEFT FEMALE BREAST	No
C50.519	MALIGNANT NEOPLASM OF LOWER-OUTER QUADRANT OF UNSPECIFIED FEMALE BREAST	No
C50.52	MALIGNANT NEOPLASM OF LOWER-OUTER QUADRANT OF BREAST, MALE	No
C50.521	MALIGNANT NEOPLASM OF LOWER-OUTER QUADRANT OF RIGHT MALE BREAST	No
C50.522	MALIGNANT NEOPLASM OF LOWER-OUTER QUADRANT OF LEFT MALE BREAST	No
C50.529	MALIGNANT NEOPLASM OF LOWER-OUTER QUADRANT OF UNSPECIFIED MALE BREAST	No
C50.6	MALIGNANT NEOPLASM OF AXILLARY TAIL OF BREAST	No
C50.61	MALIGNANT NEOPLASM OF AXILLARY TAIL OF BREAST, FEMALE	No
C50.611	MALIGNANT NEOPLASM OF AXILLARY TAIL OF RIGHT FEMALE BREAST	No
C50.612	MALIGNANT NEOPLASM OF AXILLARY TAIL OF LEFT FEMALE BREAST	No
C50.619	MALIGNANT NEOPLASM OF AXILLARY TAIL OF UNSPECIFIED FEMALE BREAST	No
C50.62	MALIGNANT NEOPLASM OF AXILLARY TAIL OF BREAST, MALE	No
C50.621	MALIGNANT NEOPLASM OF AXILLARY TAIL OF RIGHT MALE BREAST	No
C50.622	MALIGNANT NEOPLASM OF AXILLARY TAIL OF LEFT MALE BREAST	No
C50.629	MALIGNANT NEOPLASM OF AXILLARY TAIL OF UNSPECIFIED MALE BREAST	No
C50.8	MALIGNANT NEOPLASM OF OVERLAPPING SITES OF BREAST	No
C50.81	MALIGNANT NEOPLASM OF OVERLAPPING SITES OF BREAST, FEMALE	No
C50.811	MALIGNANT NEOPLASM OF OVERLAPPING SITES OF RIGHT FEMALE BREAST	No
C50.812	MALIGNANT NEOPLASM OF OVERLAPPING SITES OF LEFT FEMALE BREAST	No
C50.819	MALIGNANT NEOPLASM OF OVERLAPPING SITES OF UNSPECIFIED FEMALE BREAST	No
C50.82	MALIGNANT NEOPLASM OF OVERLAPPING SITES OF BREAST, MALE	No
C50.821	MALIGNANT NEOPLASM OF OVERLAPPING SITES OF RIGHT MALE BREAST	No
C50.822	MALIGNANT NEOPLASM OF OVERLAPPING SITES OF LEFT MALE BREAST	No
C50.829	MALIGNANT NEOPLASM OF OVERLAPPING SITES OF UNSPECIFIED MALE BREAST	No
C50.9	MALIGNANT NEOPLASM OF BREAST OF UNSPECIFIED SITE	No
C50.91	MALIGNANT NEOPLASM OF BREAST OF UNSPECIFIED SITE, FEMALE	No
C50.911	MALIGNANT NEOPLASM OF UNSPECIFIED SITE OF RIGHT FEMALE BREAST	No
C50.912	MALIGNANT NEOPLASM OF UNSPECIFIED SITE OF LEFT FEMALE BREAST	No

ICD-10-CM	Code Description	IC
C50.919	MALIGNANT NEOPLASM OF UNSPECIFIED SITE OF UNSPECIFIED FEMALE BREAST	No
C50.92	MALIGNANT NEOPLASM OF BREAST OF UNSPECIFIED SITE, MALE	No
C50.921	MALIGNANT NEOPLASM OF UNSPECIFIED SITE OF RIGHT MALE BREAST	No
C50.922	MALIGNANT NEOPLASM OF UNSPECIFIED SITE OF LEFT MALE BREAST	No
C50.929	MALIGNANT NEOPLASM OF UNSPECIFIED SITE OF UNSPECIFIED MALE BREAST	No
C51	MALIGNANT NEOPLASM OF VULVA	No
C51.0	MALIGNANT NEOPLASM OF LABIUM MAJUS	No
C51.1	MALIGNANT NEOPLASM OF LABIUM MINUS	No
C51.2	MALIGNANT NEOPLASM OF CLITORIS	No
C51.8	MALIGNANT NEOPLASM OF OVERLAPPING SITES OF VULVA	No
C51.9	MALIGNANT NEOPLASM OF VULVA, UNSPECIFIED	No
C52	MALIGNANT NEOPLASM OF VAGINA	No
C53	MALIGNANT NEOPLASM OF CERVIX UTERI	No
C53.0	MALIGNANT NEOPLASM OF ENDOCERVIX	No
C53.1	MALIGNANT NEOPLASM OF EXOCERVIX	No
C53.8	MALIGNANT NEOPLASM OF OVERLAPPING SITES OF CERVIX UTERI	No
C53.9	MALIGNANT NEOPLASM OF CERVIX UTERI, UNSPECIFIED	No
C54	MALIGNANT NEOPLASM OF CORPUS UTERI	No
C54.0	MALIGNANT NEOPLASM OF ISTHMUS UTERI	No
C54.1	MALIGNANT NEOPLASM OF ENDOMETRIUM	No
C54.2	MALIGNANT NEOPLASM OF MYOMETRIUM	No
C54.3	MALIGNANT NEOPLASM OF FUNDUS UTERI	No
C54.8	MALIGNANT NEOPLASM OF OVERLAPPING SITES OF CORPUS UTERI	No
C54.9	MALIGNANT NEOPLASM OF CORPUS UTERI, UNSPECIFIED	No
C55	MALIGNANT NEOPLASM OF UTERUS, PART UNSPECIFIED	No
C56	MALIGNANT NEOPLASM OF OVARY	No
C56.1	MALIGNANT NEOPLASM OF RIGHT OVARY	No
C56.2	MALIGNANT NEOPLASM OF LEFT OVARY	No
C56.9	MALIGNANT NEOPLASM OF UNSPECIFIED OVARY	No
C57	MALIGNANT NEOPLASM OF OTHER AND UNSPECIFIED FEMALE GENITAL ORGANS	No
C57.0	MALIGNANT NEOPLASM OF FALLOPIAN TUBE	No
C57.00	MALIGNANT NEOPLASM OF UNSPECIFIED FALLOPIAN TUBE	No
C57.01	MALIGNANT NEOPLASM OF RIGHT FALLOPIAN TUBE	No
C57.02	MALIGNANT NEOPLASM OF LEFT FALLOPIAN TUBE	No
C57.1	MALIGNANT NEOPLASM OF BROAD LIGAMENT	No
C57.10	MALIGNANT NEOPLASM OF UNSPECIFIED BROAD LIGAMENT	No
C57.11	MALIGNANT NEOPLASM OF RIGHT BROAD LIGAMENT	No
C57.12	MALIGNANT NEOPLASM OF LEFT BROAD LIGAMENT	No
C57.2	MALIGNANT NEOPLASM OF ROUND LIGAMENT	No
C57.20	MALIGNANT NEOPLASM OF UNSPECIFIED ROUND LIGAMENT	No

ICD-10-CM	Code Description	IC
C57.21	MALIGNANT NEOPLASM OF RIGHT ROUND LIGAMENT	No
C57.22	MALIGNANT NEOPLASM OF LEFT ROUND LIGAMENT	No
C57.3	MALIGNANT NEOPLASM OF PARAMETRIUM	No
C57.4	MALIGNANT NEOPLASM OF UTERINE ADNEXA, UNSPECIFIED	No
C57.7	MALIGNANT NEOPLASM OF OTHER SPECIFIED FEMALE GENITAL ORGANS	No
C57.8	MALIGNANT NEOPLASM OF OVERLAPPING SITES OF FEMALE GENITAL ORGANS	No
C57.9	MALIGNANT NEOPLASM OF FEMALE GENITAL ORGAN, UNSPECIFIED	No
C58	MALIGNANT NEOPLASM OF PLACENTA	No
C60	MALIGNANT NEOPLASM OF PENIS	No
C60.0	MALIGNANT NEOPLASM OF PREPUCE	No
C60.1	MALIGNANT NEOPLASM OF GLANS PENIS	No
C60.2	MALIGNANT NEOPLASM OF BODY OF PENIS	No
C60.8	MALIGNANT NEOPLASM OF OVERLAPPING SITES OF PENIS	No
C60.9	MALIGNANT NEOPLASM OF PENIS, UNSPECIFIED	No
C61	MALIGNANT NEOPLASM OF PROSTATE	No
C62	MALIGNANT NEOPLASM OF TESTIS	No
C62.0	MALIGNANT NEOPLASM OF UNDESCENDED TESTIS	No
C62.00	MALIGNANT NEOPLASM OF UNSPECIFIED UNDESCENDED TESTIS	No
C62.01	MALIGNANT NEOPLASM OF UNDESCENDED RIGHT TESTIS	No
C62.02	MALIGNANT NEOPLASM OF UNDESCENDED LEFT TESTIS	No
C62.1	MALIGNANT NEOPLASM OF DESCENDED TESTIS	No
C62.10	MALIGNANT NEOPLASM OF UNSPECIFIED DESCENDED TESTIS	No
C62.11	MALIGNANT NEOPLASM OF DESCENDED RIGHT TESTIS	No
C62.12	MALIGNANT NEOPLASM OF DESCENDED LEFT TESTIS	No
C62.9	MALIGNANT NEOPLASM OF TESTIS, UNSPECIFIED WHETHER DESCENDED OR UNDESCENDED	No
C62.90	MALIGNANT NEOPLASM OF UNSPECIFIED TESTIS, UNSPECIFIED WHETHER DESCENDED OR UNDESCENDED	No
C62.91	MALIGNANT NEOPLASM OF RIGHT TESTIS, UNSPECIFIED WHETHER DESCENDED OR UNDESCENDED	No
C62.92	MALIGNANT NEOPLASM OF LEFT TESTIS, UNSPECIFIED WHETHER DESCENDED OR UNDESCENDED	No
C63	MALIGNANT NEOPLASM OF OTHER AND UNSPECIFIED MALE GENITAL ORGANS	No
C63.0	MALIGNANT NEOPLASM OF EPIDIDYMIS	No
C63.00	MALIGNANT NEOPLASM OF UNSPECIFIED EPIDIDYMIS	No
C63.01	MALIGNANT NEOPLASM OF RIGHT EPIDIDYMIS	No
C63.02	MALIGNANT NEOPLASM OF LEFT EPIDIDYMIS	No
C63.1	MALIGNANT NEOPLASM OF SPERMATIC CORD	No
C63.10	MALIGNANT NEOPLASM OF UNSPECIFIED SPERMATIC CORD	No
C63.11	MALIGNANT NEOPLASM OF RIGHT SPERMATIC CORD	No
C63.12	MALIGNANT NEOPLASM OF LEFT SPERMATIC CORD	No

ICD-10-CM	Code Description	IC
C63.2	MALIGNANT NEOPLASM OF SCROTUM	No
C63.7	MALIGNANT NEOPLASM OF OTHER SPECIFIED MALE GENITAL ORGANS	No
C63.8	MALIGNANT NEOPLASM OF OVERLAPPING SITES OF MALE GENITAL ORGANS	No
C63.9	MALIGNANT NEOPLASM OF MALE GENITAL ORGAN, UNSPECIFIED	No
C64	MALIGNANT NEOPLASM OF KIDNEY, EXCEPT RENAL PELVIS	No
C64.1	MALIGNANT NEOPLASM OF RIGHT KIDNEY, EXCEPT RENAL PELVIS	No
C64.2	MALIGNANT NEOPLASM OF LEFT KIDNEY, EXCEPT RENAL PELVIS	No
C64.9	MALIGNANT NEOPLASM OF UNSPECIFIED KIDNEY, EXCEPT RENAL PELVIS	No
C65	MALIGNANT NEOPLASM OF RENAL PELVIS	No
C65.1	MALIGNANT NEOPLASM OF RIGHT RENAL PELVIS	No
C65.2	MALIGNANT NEOPLASM OF LEFT RENAL PELVIS	No
C65.9	MALIGNANT NEOPLASM OF UNSPECIFIED RENAL PELVIS	No
C66	MALIGNANT NEOPLASM OF URETER	No
C66.1	MALIGNANT NEOPLASM OF RIGHT URETER	No
C66.2	MALIGNANT NEOPLASM OF LEFT URETER	No
C66.9	MALIGNANT NEOPLASM OF UNSPECIFIED URETER	No
C67	MALIGNANT NEOPLASM OF BLADDER	No
C67.0	MALIGNANT NEOPLASM OF TRIGONE OF BLADDER	No
C67.1	MALIGNANT NEOPLASM OF DOME OF BLADDER	No
C67.2	MALIGNANT NEOPLASM OF LATERAL WALL OF BLADDER	No
C67.3	MALIGNANT NEOPLASM OF ANTERIOR WALL OF BLADDER	No
C67.4	MALIGNANT NEOPLASM OF POSTERIOR WALL OF BLADDER	No
C67.5	MALIGNANT NEOPLASM OF BLADDER NECK	No
C67.6	MALIGNANT NEOPLASM OF URETERIC ORIFICE	No
C67.7	MALIGNANT NEOPLASM OF URACHUS	No
C67.8	MALIGNANT NEOPLASM OF OVERLAPPING SITES OF BLADDER	No
C67.9	MALIGNANT NEOPLASM OF BLADDER, UNSPECIFIED	No
C68	MALIGNANT NEOPLASM OF OTHER AND UNSPECIFIED URINARY ORGANS	No
C68.0	MALIGNANT NEOPLASM OF URETHRA	No
C68.1	MALIGNANT NEOPLASM OF PARAURETHRAL GLANDS	No
C68.8	MALIGNANT NEOPLASM OF OVERLAPPING SITES OF URINARY ORGANS	No
C68.9	MALIGNANT NEOPLASM OF URINARY ORGAN, UNSPECIFIED	No
C69	MALIGNANT NEOPLASM OF EYE AND ADNEXA	No
C69.0	MALIGNANT NEOPLASM OF CONJUNCTIVA	No
C69.00	MALIGNANT NEOPLASM OF UNSPECIFIED CONJUNCTIVA	No
C69.01	MALIGNANT NEOPLASM OF RIGHT CONJUNCTIVA	No
C69.02	MALIGNANT NEOPLASM OF LEFT CONJUNCTIVA	No
C69.1	MALIGNANT NEOPLASM OF CORNEA	No
C69.10	MALIGNANT NEOPLASM OF UNSPECIFIED CORNEA	No
C69.11	MALIGNANT NEOPLASM OF RIGHT CORNEA	No
C69.12	MALIGNANT NEOPLASM OF LEFT CORNEA	No

ICD-10-CM	Code Description	IC
C69.2	MALIGNANT NEOPLASM OF RETINA	No
C69.20	MALIGNANT NEOPLASM OF UNSPECIFIED RETINA	No
C69.21	MALIGNANT NEOPLASM OF RIGHT RETINA	No
C69.22	MALIGNANT NEOPLASM OF LEFT RETINA	No
C69.3	MALIGNANT NEOPLASM OF CHOROID	No
C69.30	MALIGNANT NEOPLASM OF UNSPECIFIED CHOROID	No
C69.31	MALIGNANT NEOPLASM OF RIGHT CHOROID	No
C69.32	MALIGNANT NEOPLASM OF LEFT CHOROID	No
C69.4	MALIGNANT NEOPLASM OF CILIARY BODY	No
C69.40	MALIGNANT NEOPLASM OF UNSPECIFIED CILIARY BODY	No
C69.41	MALIGNANT NEOPLASM OF RIGHT CILIARY BODY	No
C69.42	MALIGNANT NEOPLASM OF LEFT CILIARY BODY	No
C69.5	MALIGNANT NEOPLASM OF LACRIMAL GLAND AND DUCT	No
C69.50	MALIGNANT NEOPLASM OF UNSPECIFIED LACRIMAL GLAND AND DUCT	No
C69.51	MALIGNANT NEOPLASM OF RIGHT LACRIMAL GLAND AND DUCT	No
C69.52	MALIGNANT NEOPLASM OF LEFT LACRIMAL GLAND AND DUCT	No
C69.6	MALIGNANT NEOPLASM OF ORBIT	No
C69.60	MALIGNANT NEOPLASM OF UNSPECIFIED ORBIT	No
C69.61	MALIGNANT NEOPLASM OF RIGHT ORBIT	No
C69.62	MALIGNANT NEOPLASM OF LEFT ORBIT	No
C69.8	MALIGNANT NEOPLASM OF OVERLAPPING SITES OF EYE AND ADNEXA	No
C69.80	MALIGNANT NEOPLASM OF OVERLAPPING SITES OF UNSPECIFIED EYE AND ADNEXA	No
C69.81	MALIGNANT NEOPLASM OF OVERLAPPING SITES OF RIGHT EYE AND ADNEXA	No
C69.82	MALIGNANT NEOPLASM OF OVERLAPPING SITES OF LEFT EYE AND ADNEXA	No
C69.9	MALIGNANT NEOPLASM OF UNSPECIFIED SITE OF EYE	No
C69.90	MALIGNANT NEOPLASM OF UNSPECIFIED SITE OF UNSPECIFIED EYE	No
C69.91	MALIGNANT NEOPLASM OF UNSPECIFIED SITE OF RIGHT EYE	No
C69.92	MALIGNANT NEOPLASM OF UNSPECIFIED SITE OF LEFT EYE	No
C70	MALIGNANT NEOPLASM OF MENINGES	No
C70.0	MALIGNANT NEOPLASM OF CEREBRAL MENINGES	No
C70.1	MALIGNANT NEOPLASM OF SPINAL MENINGES	No
C70.9	MALIGNANT NEOPLASM OF MENINGES, UNSPECIFIED	No
C71	MALIGNANT NEOPLASM OF BRAIN	No
C71.0	MALIGNANT NEOPLASM OF CEREBRUM, EXCEPT LOBES AND VENTRICLES	No
C71.1	MALIGNANT NEOPLASM OF FRONTAL LOBE	No
C71.2	MALIGNANT NEOPLASM OF TEMPORAL LOBE	No
C71.3	MALIGNANT NEOPLASM OF PARIETAL LOBE	No
C71.4	MALIGNANT NEOPLASM OF OCCIPITAL LOBE	No
C71.5	MALIGNANT NEOPLASM OF CEREBRAL VENTRICLE	No
C71.6	MALIGNANT NEOPLASM OF CEREBELLUM	No
C71.7	MALIGNANT NEOPLASM OF BRAIN STEM	No

ICD-10-CM	Code Description	IC
C71.8	MALIGNANT NEOPLASM OF OVERLAPPING SITES OF BRAIN	No
C71.9	MALIGNANT NEOPLASM OF BRAIN, UNSPECIFIED	No
C72	MALIGNANT NEOPLASM OF SPINAL CORD, CRANIAL NERVES AND OTHER PARTS OF CENTRAL NERVOUS SYSTEM	No
C72.0	MALIGNANT NEOPLASM OF SPINAL CORD	No
C72.1	MALIGNANT NEOPLASM OF CAUDA EQUINA	No
C72.2	MALIGNANT NEOPLASM OF OLFACTORY NERVE	No
C72.20	MALIGNANT NEOPLASM OF UNSPECIFIED OLFACTORY NERVE	No
C72.21	MALIGNANT NEOPLASM OF RIGHT OLFACTORY NERVE	No
C72.22	MALIGNANT NEOPLASM OF LEFT OLFACTORY NERVE	No
C72.3	MALIGNANT NEOPLASM OF OPTIC NERVE	No
C72.30	MALIGNANT NEOPLASM OF UNSPECIFIED OPTIC NERVE	No
C72.31	MALIGNANT NEOPLASM OF RIGHT OPTIC NERVE	No
C72.32	MALIGNANT NEOPLASM OF LEFT OPTIC NERVE	No
C72.4	MALIGNANT NEOPLASM OF ACOUSTIC NERVE	No
C72.40	MALIGNANT NEOPLASM OF UNSPECIFIED ACOUSTIC NERVE	No
C72.41	MALIGNANT NEOPLASM OF RIGHT ACOUSTIC NERVE	No
C72.42	MALIGNANT NEOPLASM OF LEFT ACOUSTIC NERVE	No
C72.5	MALIGNANT NEOPLASM OF OTHER AND UNSPECIFIED CRANIAL NERVES	No
C72.50	MALIGNANT NEOPLASM OF UNSPECIFIED CRANIAL NERVE	No
C72.59	MALIGNANT NEOPLASM OF OTHER CRANIAL NERVES	No
C72.9	MALIGNANT NEOPLASM OF CENTRAL NERVOUS SYSTEM, UNSPECIFIED	No
C73	MALIGNANT NEOPLASM OF THYROID GLAND	No
C74	MALIGNANT NEOPLASM OF ADRENAL GLAND	No
C74.0	MALIGNANT NEOPLASM OF CORTEX OF ADRENAL GLAND	No
C74.00	MALIGNANT NEOPLASM OF CORTEX OF UNSPECIFIED ADRENAL GLAND	No
C74.01	MALIGNANT NEOPLASM OF CORTEX OF RIGHT ADRENAL GLAND	No
C74.02	MALIGNANT NEOPLASM OF CORTEX OF LEFT ADRENAL GLAND	No
C74.1	MALIGNANT NEOPLASM OF MEDULLA OF ADRENAL GLAND	No
C74.10	MALIGNANT NEOPLASM OF MEDULLA OF UNSPECIFIED ADRENAL GLAND	No
C74.11	MALIGNANT NEOPLASM OF MEDULLA OF RIGHT ADRENAL GLAND	No
C74.12	MALIGNANT NEOPLASM OF MEDULLA OF LEFT ADRENAL GLAND	No
C74.9	MALIGNANT NEOPLASM OF UNSPECIFIED PART OF ADRENAL GLAND	No
C74.90	MALIGNANT NEOPLASM OF UNSPECIFIED PART OF UNSPECIFIED ADRENAL GLAND	No
C74.91	MALIGNANT NEOPLASM OF UNSPECIFIED PART OF RIGHT ADRENAL GLAND	No
C74.92	MALIGNANT NEOPLASM OF UNSPECIFIED PART OF LEFT ADRENAL GLAND	No
C75	MALIGNANT NEOPLASM OF OTHER ENDOCRINE GLANDS AND RELATED STRUCTURES	No
C75.0	MALIGNANT NEOPLASM OF PARATHYROID GLAND	No
C75.1	MALIGNANT NEOPLASM OF PITUITARY GLAND	No
C75.2	MALIGNANT NEOPLASM OF CRANIOPHARYNGEAL DUCT	No

ICD-10-CM	Code Description	IC
C75.3	MALIGNANT NEOPLASM OF PINEAL GLAND	No
C75.4	MALIGNANT NEOPLASM OF CAROTID BODY	No
C75.5	MALIGNANT NEOPLASM OF AORTIC BODY AND OTHER PARAGANGLIA	No
C75.8	MALIGNANT NEOPLASM WITH PLURIGLANDULAR INVOLVEMENT, UNSPECIFIED	No
C75.9	MALIGNANT NEOPLASM OF ENDOCRINE GLAND, UNSPECIFIED	No
C76	MALIGNANT NEOPLASM OF OTHER AND ILL-DEFINED SITES	No
C76.0	MALIGNANT NEOPLASM OF HEAD, FACE AND NECK	No
C76.1	MALIGNANT NEOPLASM OF THORAX	No
C76.2	MALIGNANT NEOPLASM OF ABDOMEN	No
C76.3	MALIGNANT NEOPLASM OF PELVIS	No
C76.4	MALIGNANT NEOPLASM OF UPPER LIMB	No
C76.40	MALIGNANT NEOPLASM OF UNSPECIFIED UPPER LIMB	No
C76.41	MALIGNANT NEOPLASM OF RIGHT UPPER LIMB	No
C76.42	MALIGNANT NEOPLASM OF LEFT UPPER LIMB	No
C76.5	MALIGNANT NEOPLASM OF LOWER LIMB	No
C76.50	MALIGNANT NEOPLASM OF UNSPECIFIED LOWER LIMB	No
C76.51	MALIGNANT NEOPLASM OF RIGHT LOWER LIMB	No
C76.52	MALIGNANT NEOPLASM OF LEFT LOWER LIMB	No
C76.8	MALIGNANT NEOPLASM OF OTHER SPECIFIED ILL-DEFINED SITES	No
C77	SECONDARY AND UNSPECIFIED MALIGNANT NEOPLASM OF LYMPH NODES	No
C77.0	SECONDARY AND UNSPECIFIED MALIGNANT NEOPLASM OF LYMPH NODES OF HEAD, FACE AND NECK	No
C77.1	SECONDARY AND UNSPECIFIED MALIGNANT NEOPLASM OF INTRATHORACIC LYMPH NODES	No
C77.2	SECONDARY AND UNSPECIFIED MALIGNANT NEOPLASM OF INTRA-ABDOMINAL LYMPH NODES	No
C77.3	SECONDARY AND UNSPECIFIED MALIGNANT NEOPLASM OF AXILLA AND UPPER LIMB LYMPH NODES	No
C77.4	SECONDARY AND UNSPECIFIED MALIGNANT NEOPLASM OF INGUINAL AND LOWER LIMB LYMPH NODES	No
C77.5	SECONDARY AND UNSPECIFIED MALIGNANT NEOPLASM OF INTRAPELVIC LYMPH NODES	No
C77.8	SECONDARY AND UNSPECIFIED MALIGNANT NEOPLASM OF LYMPH NODES OF MULTIPLE REGIONS	No
C77.9	SECONDARY AND UNSPECIFIED MALIGNANT NEOPLASM OF LYMPH NODE, UNSPECIFIED	No
C78	SECONDARY MALIGNANT NEOPLASM OF RESPIRATORY AND DIGESTIVE ORGANS	No
C78.0	SECONDARY MALIGNANT NEOPLASM OF LUNG	No
C78.00	SECONDARY MALIGNANT NEOPLASM OF UNSPECIFIED LUNG	No
C78.01	SECONDARY MALIGNANT NEOPLASM OF RIGHT LUNG	No
C78.02	SECONDARY MALIGNANT NEOPLASM OF LEFT LUNG	No
C78.1	SECONDARY MALIGNANT NEOPLASM OF MEDIASTINUM	No

ICD-10-CM	Code Description	IC
C78.2	SECONDARY MALIGNANT NEOPLASM OF PLEURA	No
C78.3	SECONDARY MALIGNANT NEOPLASM OF OTHER AND UNSPECIFIED RESPIRATORY ORGANS	No
C78.30	SECONDARY MALIGNANT NEOPLASM OF UNSPECIFIED RESPIRATORY ORGAN	No
C78.39	SECONDARY MALIGNANT NEOPLASM OF OTHER RESPIRATORY ORGANS	No
C78.4	SECONDARY MALIGNANT NEOPLASM OF SMALL INTESTINE	No
C78.5	SECONDARY MALIGNANT NEOPLASM OF LARGE INTESTINE AND RECTUM	No
C78.6	SECONDARY MALIGNANT NEOPLASM OF RETROPERITONEUM AND PERITONEUM	No
C78.7	SECONDARY MALIGNANT NEOPLASM OF LIVER AND INTRAHEPATIC BILE DUCT	No
C78.8	SECONDARY MALIGNANT NEOPLASM OF OTHER AND UNSPECIFIED DIGESTIVE ORGANS	No
C78.80	SECONDARY MALIGNANT NEOPLASM OF UNSPECIFIED DIGESTIVE ORGAN	No
C78.89	SECONDARY MALIGNANT NEOPLASM OF OTHER DIGESTIVE ORGANS	No
C79	SECONDARY MALIGNANT NEOPLASM OF OTHER AND UNSPECIFIED SITES	No
C79.0	SECONDARY MALIGNANT NEOPLASM OF KIDNEY AND RENAL PELVIS	No
C79.00	SECONDARY MALIGNANT NEOPLASM OF UNSPECIFIED KIDNEY AND RENAL PELVIS	No
C79.01	SECONDARY MALIGNANT NEOPLASM OF RIGHT KIDNEY AND RENAL PELVIS	No
C79.02	SECONDARY MALIGNANT NEOPLASM OF LEFT KIDNEY AND RENAL PELVIS	No
C79.1	SECONDARY MALIGNANT NEOPLASM OF BLADDER AND OTHER AND UNSPECIFIED URINARY ORGANS	No
C79.10	SECONDARY MALIGNANT NEOPLASM OF UNSPECIFIED URINARY ORGANS	No
C79.11	SECONDARY MALIGNANT NEOPLASM OF BLADDER	No
C79.19	SECONDARY MALIGNANT NEOPLASM OF OTHER URINARY ORGANS	No
C79.2	SECONDARY MALIGNANT NEOPLASM OF SKIN	No
C79.3	SECONDARY MALIGNANT NEOPLASM OF BRAIN AND CEREBRAL MENINGES	No
C79.31	SECONDARY MALIGNANT NEOPLASM OF BRAIN	No
C79.32	SECONDARY MALIGNANT NEOPLASM OF CEREBRAL MENINGES	No
C79.4	SECONDARY MALIGNANT NEOPLASM OF OTHER AND UNSPECIFIED PARTS OF NERVOUS SYSTEM	No
C79.40	SECONDARY MALIGNANT NEOPLASM OF UNSPECIFIED PART OF NERVOUS SYSTEM	No
C79.49	SECONDARY MALIGNANT NEOPLASM OF OTHER PARTS OF NERVOUS SYSTEM	No
C79.6	SECONDARY MALIGNANT NEOPLASM OF OVARY	No
C79.60	SECONDARY MALIGNANT NEOPLASM OF UNSPECIFIED OVARY	No
C79.61	SECONDARY MALIGNANT NEOPLASM OF RIGHT OVARY	No
C79.62	SECONDARY MALIGNANT NEOPLASM OF LEFT OVARY	No
C79.7	SECONDARY MALIGNANT NEOPLASM OF ADRENAL GLAND	No
C79.70	SECONDARY MALIGNANT NEOPLASM OF UNSPECIFIED ADRENAL GLAND	No
C79.71	SECONDARY MALIGNANT NEOPLASM OF RIGHT ADRENAL GLAND	No
C79.72	SECONDARY MALIGNANT NEOPLASM OF LEFT ADRENAL GLAND	No
C79.8	SECONDARY MALIGNANT NEOPLASM OF OTHER SPECIFIED SITES	No

ICD-10-CM	Code Description	IC
C79.81	SECONDARY MALIGNANT NEOPLASM OF BREAST	No
C79.82	SECONDARY MALIGNANT NEOPLASM OF GENITAL ORGANS	No
C79.89	SECONDARY MALIGNANT NEOPLASM OF OTHER SPECIFIED SITES	No
C79.9	SECONDARY MALIGNANT NEOPLASM OF UNSPECIFIED SITE	No
C7A	MALIGNANT NEUROENDOCRINE TUMORS	No
C7A.0	MALIGNANT CARCINOID TUMORS	No
C7A.00	MALIGNANT CARCINOID TUMOR OF UNSPECIFIED SITE	No
C7A.01	MALIGNANT CARCINOID TUMORS OF THE SMALL INTESTINE	No
C7A.010	MALIGNANT CARCINOID TUMOR OF THE DUODENUM	No
C7A.011	MALIGNANT CARCINOID TUMOR OF THE JEJUNUM	No
C7A.012	MALIGNANT CARCINOID TUMOR OF THE ILEUM	No
C7A.019	MALIGNANT CARCINOID TUMOR OF THE SMALL INTESTINE, UNSPECIFIED PORTION	No
C7A.02	MALIGNANT CARCINOID TUMORS OF THE APPENDIX, LARGE INTESTINE, AND RECTUM	No
C7A.020	MALIGNANT CARCINOID TUMOR OF THE APPENDIX	No
C7A.021	MALIGNANT CARCINOID TUMOR OF THE CECUM	No
C7A.022	MALIGNANT CARCINOID TUMOR OF THE ASCENDING COLON	No
C7A.023	MALIGNANT CARCINOID TUMOR OF THE TRANSVERSE COLON	No
C7A.024	MALIGNANT CARCINOID TUMOR OF THE DESCENDING COLON	No
C7A.025	MALIGNANT CARCINOID TUMOR OF THE SIGMOID COLON	No
C7A.026	MALIGNANT CARCINOID TUMOR OF THE RECTUM	No
C7A.029	MALIGNANT CARCINOID TUMOR OF THE LARGE INTESTINE, UNSPECIFIED PORTION	No
C7A.09	MALIGNANT CARCINOID TUMORS OF OTHER SITES	No
C7A.090	MALIGNANT CARCINOID TUMOR OF THE BRONCHUS AND LUNG	No
C7A.091	MALIGNANT CARCINOID TUMOR OF THE THYMUS	No
C7A.092	MALIGNANT CARCINOID TUMOR OF THE STOMACH	No
C7A.093	MALIGNANT CARCINOID TUMOR OF THE KIDNEY	No
C7A.094	MALIGNANT CARCINOID TUMOR OF THE FOREGUT, UNSPECIFIED	No
C7A.095	MALIGNANT CARCINOID TUMOR OF THE MIDGUT, UNSPECIFIED	No
C7A.096	MALIGNANT CARCINOID TUMOR OF THE HINDGUT, UNSPECIFIED	No
C7A.098	MALIGNANT CARCINOID TUMORS OF OTHER SITES	No
C7A.1	MALIGNANT POORLY DIFFERENTIATED NEUROENDOCRINE TUMORS	No
C7A.8	OTHER MALIGNANT NEUROENDOCRINE TUMORS	No
C7B	SECONDARY NEUROENDOCRINE TUMORS	No
C7B.0	SECONDARY CARCINOID TUMORS	No
C7B.00	SECONDARY CARCINOID TUMORS, UNSPECIFIED SITE	No
C7B.01	SECONDARY CARCINOID TUMORS OF DISTANT LYMPH NODES	No
C7B.02	SECONDARY CARCINOID TUMORS OF LIVER	No
C7B.03	SECONDARY CARCINOID TUMORS OF BONE	No
C7B.04	SECONDARY CARCINOID TUMORS OF PERITONEUM	No

ICD-10-CM	Code Description	IC
C7B.09	SECONDARY CARCINOID TUMORS OF OTHER SITES	No
C7B.1	SECONDARY MERKEL CELL CARCINOMA	No
C7B.8	OTHER SECONDARY NEUROENDOCRINE TUMORS	No
C80	MALIGNANT NEOPLASM WITHOUT SPECIFICATION OF SITE	No
C80.0	DISSEMINATED MALIGNANT NEOPLASM, UNSPECIFIED	No
C80.1	MALIGNANT (PRIMARY) NEOPLASM, UNSPECIFIED	No
C80.2	MALIGNANT NEOPLASM ASSOCIATED WITH TRANSPLANTED ORGAN	No

Abbreviations: IC = Immunocompromising

Table S1c: Current Procedural Terminology (CPT) codes associated with cancer

CPT Code	Code Description
96401	Chemotherapy administration, subcutaneous or intramuscular; non-hormonal anti-neoplastic
96402	Chemotherapy administration, subcutaneous or intramuscular; hormonal anti-neoplastic
96405	Chemotherapy administration, intralesional, up to and including 7 lesion
96406	Chemotherapy administration, intralesional, more than 7 lesions
96409	Chemotherapy administration, intravenous push technique, single or initial substance/drug
96411	Chemotherapy administration, intravenous push technique, each additional substance/drug
96413	Chemotherapy administration, intravenous infusion technique; up to 1 hour, single or initial substance/drug
96415	Chemotherapy administration, intravenous infusion technique; each additional hour, single or initial substance/drug
96416	Chemotherapy administration, intravenous infusion technique; initiation of prolonged chemotherapy infusion (up to 8 hours), requiring use of a portable or implantable pump
96417	Chemotherapy administration, intravenous infusion technique; each additional sequential infusion (different substance/drug), up to 1 hour
96420	Chemotherapy administration, intra-arterial; push technique
96422	Chemotherapy administration, intra-arterial; infusion technique, up to 1 hour
96423	Chemotherapy administration, intra-arterial; infusion technique, each additional hour
96425	Chemotherapy administration, intra-arterial; infusion technique, initiation of prolonged infusion (more than 8 hours), requiring the use of a portable or implantable pump
96440	Chemotherapy administration into pleural cavity, requiring and including thoracentesis
96446	Chemotherapy administration into the peritoneal cavity via indwelling port or catheter
96450	Chemotherapy administration, in CNS (e.g. intrathecal), requiring and including spinal puncture
96521	Refilling and maintenance of portable pump
96522	Refilling and maintenance of implantable pump or reservoir for drug delivery, systemic (e.g. intravenous, intra-arterial)
96523	Irrigation of implanted venous access device for drug delivery systems
96542	Chemotherapy injection, subarachnoid or intraventricular via subcutaneous reservoir, single or multiple agents
96549	Unlisted chemotherapy procedure

Table S1d: Methodology for classifying cancer with versus without immunosuppression

Diagnosis	Procedure	Cancer-Related Drugs	IC Classification
Leukemia, lymphoma, or malignancy of bone marrow	None recorded	None recorded	Cancer, with immunosuppression
None recorded	Chemotherapy administration	None recorded	Cancer, with immunosuppression
None recorded	None recorded	Exclusively cancer AND Immunosuppressive	Cancer, with immunosuppression
Any other malignancy diagnosis	None recorded	Exclusively cancer AND Immunosuppressive	Cancer, with immunosuppression
None recorded	None recorded	Exclusively cancer AND NOT Immunosuppressive	Cancer, without immunosuppression
Any other malignancy diagnosis	None recorded	None recorded	Cancer, without immunosuppression
None recorded	None recorded	NOT exclusively cancer AND Immunosuppressive	Medication-induced immunosuppression
None recorded	None recorded	NOT exclusively cancer AND NOT Immunosuppressive	Immunocompetent

Table S2a: Generic drugs associated with HIV

Generic Drug Name
Abacavir
Atazanavir
Atravirine
Cabotegravir
Cobicistat
Darunavir
Dolutegravir
Doravirine
Efavirenz
Emtricitabine
Enfuvirtide
Fosemprenavir
Fostemsavir
Ibalizumab-uiyk
Lamivudine
Maraviroc
Nevirapine
Raltegravir
Rilpivirine
Ritonavir
Saquinavir
Tenofovir disoproxil fumarate
Tipranivir
Zidovudine
Abacavir and lamivudine (*Epzicom*)
Dolutegravir + abacavir + lamivudine (*Triumeq*)
Abacavir + lamivudine + zidovudine (*Trizivir*)
Atazanavir + cobicistat (*Evotaz*)
Bictegravir + emtricitabine + tenofovir alafenamide (*Biktarvy*)
Cabotegravir + rilpivirine (*Cabenuva*)
Darunavir + cobicistat (*Prezcobix*)
Darunavir + cobicistat + emtricitabine + tenofovir alafenamide (*Symtuza*)
Dolutegravir + lamivudine (*Dovato*)
Dolutegravir + rilpivirine (*Juluca*)
Doravirine + lamivudine + tenofovir disoproxil fumarate (*Delstrigo*)
Efavirenz + emtricitabine + tenofovir disoproxil fumarate (*Atripla*)
Efavirenz + lamivudine + tenofovir disoproxil fumarate (*Symfi*)
Elvitegravir + cobicistat + emtricitabine + tenofovir alafenamide (*Genvoya*)

Generic Drug Name
Elvitegravir + cobicistat + emtricitabine + tenofovir disoproxil fumarate (*Stribild*)
Rilpivirine + emtricitabine + tenofovir alafenamide (*Odefsey*)
Rilpivirine + emtricitabine + tenofovir disoproxil fumarate (*Complera*)
Lamivudine + tenofovir disoproxil fumarate (*Cimduo*)
Zidovudine + lamivudine (*Combivir*)
Lopinavir + ritonavir (*Kaletra*)

Table S2b: Diagnosis codes associated with HIV

ICD-10-CM	Code Description
B97.35	HUMAN IMMUNODEFICIENCY VIRUS, TYPE 2 [HIV 2] AS THE CAUSE OF DISEASES CLASSIFIED ELSEWHERE
B20	HUMAN IMMUNODEFICIENCY VIRUS [HIV] DISEASE
Z21	Asymptomatic human immunodeficiency virus [HIV] infection status

Table S3a: Generic drugs associated with solid organ transplant, without or without immunosuppression

Generic Drug Name
ANTITHYMOCYTE GLOBULIN EQUINE
ANTITHYMOCYTE GLOBULIN RABBIT
AZATHIOPRINE
AZATHIOPRINE SODIUM
BASILIXIMAB
BELATACEPT
DACLIZUMAB
MUROMONAB-CD3
MYCOPHENOLATE MOFETIL
PALIFERMIN
SIROLIMUS
TACROLIMUS

Table S3b: Diagnosis codes associated with solid organ transplant

ICD-10-CM	Code Description
D47.Z1	POST-TRANSPLANT LYMPHOPROLIFERATIVE DISORDER (PTLD)
I25.75	ATHEROSCLEROSIS OF NATIVE CORONARY ARTERY OF TRANSPLANTED HEART WITH ANGINA PECTORIS
I25.750	ATHEROSCLEROSIS OF NATIVE CORONARY ARTERY OF TRANSPLANTED HEART WITH UNSTABLE ANGINA
I25.751	ATHEROSCLEROSIS OF NATIVE CORONARY ARTERY OF TRANSPLANTED HEART WITH ANGINA PECTORIS WITH DOCUMENTED SPASM
I25.758	ATHEROSCLEROSIS OF NATIVE CORONARY ARTERY OF TRANSPLANTED HEART WITH OTHER FORMS OF ANGINA PECTORIS
I25.759	ATHEROSCLEROSIS OF NATIVE CORONARY ARTERY OF TRANSPLANTED HEART WITH UNSPECIFIED ANGINA PECTORIS
I25.76	ATHEROSCLEROSIS OF BYPASS GRAFT OF CORONARY ARTERY OF TRANSPLANTED HEART WITH ANGINA PECTORIS
I25.760	ATHEROSCLEROSIS OF BYPASS GRAFT OF CORONARY ARTERY OF TRANSPLANTED HEART WITH UNSTABLE ANGINA
I25.761	ATHEROSCLEROSIS OF BYPASS GRAFT OF CORONARY ARTERY OF TRANSPLANTED HEART WITH ANGINA PECTORIS WITH DOCUMENTED SPASM
I25.768	ATHEROSCLEROSIS OF BYPASS GRAFT OF CORONARY ARTERY OF TRANSPLANTED HEART WITH OTHER FORMS OF ANGINA PECTORIS
I25.769	ATHEROSCLEROSIS OF BYPASS GRAFT OF CORONARY ARTERY OF TRANSPLANTED HEART WITH UNSPECIFIED ANGINA PECTORIS
I25.811	ATHEROSCLEROSIS OF NATIVE CORONARY ARTERY OF TRANSPLANTED HEART WITHOUT ANGINA PECTORIS
I25.812	ATHEROSCLEROSIS OF BYPASS GRAFT OF CORONARY ARTERY OF TRANSPLANTED HEART WITHOUT ANGINA PECTORIS
T86.1	COMPLICATIONS OF KIDNEY TRANSPLANT
T86.10	UNSPECIFIED COMPLICATION OF KIDNEY TRANSPLANT
T86.11	KIDNEY TRANSPLANT REJECTION
T86.12	KIDNEY TRANSPLANT FAILURE
T86.13	KIDNEY TRANSPLANT INFECTION
T86.19	OTHER COMPLICATION OF KIDNEY TRANSPLANT
T86.2	COMPLICATIONS OF HEART TRANSPLANT
T86.20	UNSPECIFIED COMPLICATION OF HEART TRANSPLANT
T86.21	HEART TRANSPLANT REJECTION
T86.22	HEART TRANSPLANT FAILURE
T86.23	HEART TRANSPLANT INFECTION
T86.29	OTHER COMPLICATIONS OF HEART TRANSPLANT
T86.290	CARDIAC ALLOGRAFT VASCULOPATHY
T86.298	OTHER COMPLICATIONS OF HEART TRANSPLANT
T86.3	COMPLICATIONS OF HEART-LUNG TRANSPLANT
T86.30	UNSPECIFIED COMPLICATION OF HEART-LUNG TRANSPLANT
T86.31	HEART-LUNG TRANSPLANT REJECTION
T86.32	HEART-LUNG TRANSPLANT FAILURE

ICD-10-CM	Code Description
T86.33	HEART-LUNG TRANSPLANT INFECTION
T86.39	OTHER COMPLICATIONS OF HEART-LUNG TRANSPLANT
T86.4	COMPLICATIONS OF LIVER TRANSPLANT
T86.40	UNSPECIFIED COMPLICATION OF LIVER TRANSPLANT
T86.41	LIVER TRANSPLANT REJECTION
T86.42	LIVER TRANSPLANT FAILURE
T86.43	LIVER TRANSPLANT INFECTION
T86.49	OTHER COMPLICATIONS OF LIVER TRANSPLANT
T86.81	COMPLICATIONS OF LUNG TRANSPLANT
T86.810	LUNG TRANSPLANT REJECTION
T86.811	LUNG TRANSPLANT FAILURE
T86.812	LUNG TRANSPLANT INFECTION
T86.818	OTHER COMPLICATIONS OF LUNG TRANSPLANT
T86.819	UNSPECIFIED COMPLICATION OF LUNG TRANSPLANT
Z48.2	ENCOUNTER FOR AFTERCARE FOLLOWING ORGAN TRANSPLANT
Z94.0	KIDNEY TRANSPLANT STATUS
Z94.1	HEART TRANSPLANT STATUS
Z94.2	LUNG TRANSPLANT STATUS
Z94.3	HEART AND LUNGS TRANSPLANT STATUS
Z94.4	LIVER TRANSPLANT STATUS
Z94.8	OTHER TRANSPLANTED ORGAN AND TISSUE STATUS

Table S3c: Current Procedural Terminology (CPT) codes associated with solid organ transplant

CPT Code	Code Description
32581	Lung transplant, single
32582	Lung transplant with bypass
32583	Lung transplant, double
32584	Lung transplant with bypass
33935	Transplantation, heart/lung
33945	Transplantation of heart
44136	Intestine transplant, live
47135	Transplantation of liver
47136	Transplantation of liver
48554	Transplant allograft pancreas
50360	Transplantation of kidney
50365	Transplantation of kidney
50370	Remove transplanted kidney
38240	Bone marrow/stem transplant
38241	Bone marrow or blood-derived peripheral stem cell transplantation; autologous
38242	Bone marrow or blood-derived peripheral stem cell transplantation; allogeneic donor lymphocyte infusions

Table S4: Diagnosis codes associated with primary immunodeficiencies

ICD-10-CM	Code Description
D80	IMMUNODEFICIENCY WITH PREDOMINANTLY ANTIBODY DEFECTS
D80.0	HEREDITARY HYPOGAMMAGLOBULINEMIA
D80.1	NONFAMILIAL HYPOGAMMAGLOBULINEMIA
D80.2	SELECTIVE DEFICIENCY OF IMMUNOGLOBULIN A [IGA]
D80.3	SELECTIVE DEFICIENCY OF IMMUNOGLOBULIN G [IGG] SUBCLASSES
D80.4	SELECTIVE DEFICIENCY OF IMMUNOGLOBULIN M [IGM]
D80.5	IMMUNODEFICIENCY WITH INCREASED IMMUNOGLOBULIN M [IGM]
D80.6	ANTIBODY DEFICIENCY WITH NEAR-NORMAL IMMUNOGLOBULINS OR WITH HYPERIMMUNOGLOBULINEMIA
D80.7	TRANSIENT HYPOGAMMAGLOBULINEMIA OF INFANCY
D80.8	OTHER IMMUNODEFICIENCIES WITH PREDOMINANTLY ANTIBODY DEFECTS
D80.9	IMMUNODEFICIENCY WITH PREDOMINANTLY ANTIBODY DEFECTS, UNSPECIFIED
D81	COMBINED IMMUNODEFICIENCIES
D81.0	SEVERE COMBINED IMMUNODEFICIENCY [SCID] WITH RETICULAR DYSGENESIS
D81.1	SEVERE COMBINED IMMUNODEFICIENCY [SCID] WITH LOW T- AND B-CELL NUMBERS
D81.2	SEVERE COMBINED IMMUNODEFICIENCY [SCID] WITH LOW OR NORMAL B-CELL NUMBERS
D81.3	ADENOSINE DEAMINASE [ADA] DEFICIENCY
D81.30	Adenosine deaminase deficiency, unspecified
D81.31	Severe combined immunodeficiency due to adenosine deaminase deficiency
D81.32	Adenosine deaminase 2 deficiency
D81.39	Other adenosine deaminase deficiency
D81.4	NEZELOF'S SYNDROME
D81.5	PURINE NUCLEOSIDE PHOSPHORYLASE [PNP] DEFICIENCY
D81.6	MAJOR HISTOCOMPATIBILITY COMPLEX CLASS I DEFICIENCY
D81.7	MAJOR HISTOCOMPATIBILITY COMPLEX CLASS II DEFICIENCY
D81.8	OTHER COMBINED IMMUNODEFICIENCIES
D81.81	BIOTIN-DEPENDENT CARBOXYLASE DEFICIENCY
D81.810	BIOTINIDASE DEFICIENCY
D81.818	OTHER BIOTIN-DEPENDENT CARBOXYLASE DEFICIENCY
D81.819	BIOTIN-DEPENDENT CARBOXYLASE DEFICIENCY, UNSPECIFIED
D81.89	OTHER COMBINED IMMUNODEFICIENCIES
D81.9	COMBINED IMMUNODEFICIENCY, UNSPECIFIED
D82	IMMUNODEFICIENCY ASSOCIATED WITH OTHER MAJOR DEFECTS
D82.0	WISKOTT-ALDRICH SYNDROME
D82.1	DI GEORGE'S SYNDROME
D82.2	IMMUNODEFICIENCY WITH SHORT-LIMBED STATURE
D82.3	IMMUNODEFICIENCY FOLLOWING HEREDITARY DEFECTIVE RESPONSE TO EPSTEIN-BARR VIRUS
D82.4	HYPERIMMUNOGLOBULIN E [IGE] SYNDROME
D82.8	IMMUNODEFICIENCY ASSOCIATED WITH OTHER SPECIFIED MAJOR DEFECTS

D82.9	IMMUNODEFICIENCY ASSOCIATED WITH MAJOR DEFECT, UNSPECIFIED
D83	COMMON VARIABLE IMMUNODEFICIENCY
D83.0	COMMON VARIABLE IMMUNODEFICIENCY WITH PREDOMINANT ABNORMALITIES OF B-CELL NUMBERS AND FUNCTION
D83.1	COMMON VARIABLE IMMUNODEFICIENCY WITH PREDOMINANT IMMUNOREGULATORY T-CELL DISORDERS
D83.2	COMMON VARIABLE IMMUNODEFICIENCY WITH AUTOANTIBODIES TO B- OR T-CELLS
D83.8	OTHER COMMON VARIABLE IMMUNODEFICIENCIES
D83.9	COMMON VARIABLE IMMUNODEFICIENCY, UNSPECIFIED
D84	OTHER IMMUNODEFICIENCIES
D84.0	LYMPHOCYTE FUNCTION ANTIGEN-1 [LFA-1] DEFECT
D84.1	DEFECTS IN THE COMPLEMENT SYSTEM
D84.8	OTHER SPECIFIED IMMUNODEFICIENCIES
D84.9	IMMUNODEFICIENCY, UNSPECIFIED

Table S5a: Generic drugs associated with medication-induced immunosuppression

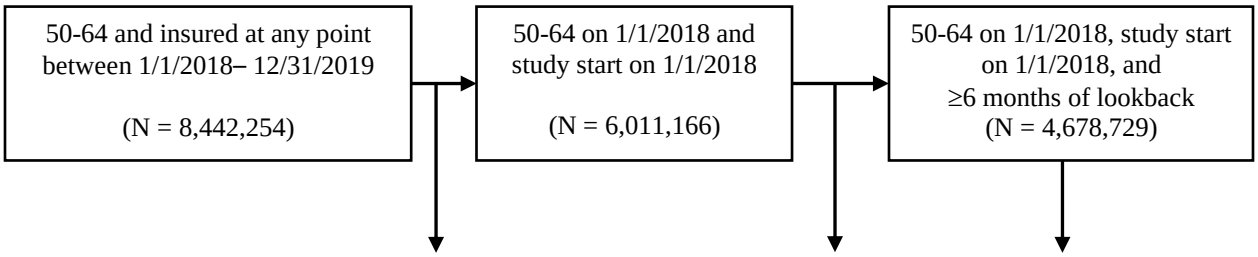
Generic Drug Name
RISANKIZUMAB-RZAA
TOFACITINIB CITRATE
ABATACEPT
ADALIMUMAB
ADALIMUMAB;ADALIMUMAB
ALEFACEPT
ANAKINRA
BARICITINIB
BELIMUMAB
BISMUTH SUBGALLATE/HYDROCORTISONE ACETATE
BRODALUMAB
BUDESONIDE
BUDESONIDE, MICRONIZED
CANAKINUMAB
CERTOLIZUMAB PEGOL
CORTISONE ACETATE
CORTISONE ACETICUM/PULSATILLA/SULFUR
CYCLOSPORINE
CYCLOSPORINE, MODIFIED
DEXAMETHASONE
DEXAMETHASONE ACETATE
DEXAMETHASONE SODIUM PHOSPHATE
DEXAMETHASONE SODIUM PHOSPHATE/DEXTROSE
DEXAMETHASONE SODIUM PHOSPHATE/SODIUM CHLORIDE
DIPHENHYDRAMINE HYDROCHLORIDE;PREDNISONE
ECULIZUMAB
EFALIZUMAB
ETANERCEPT
GUSELKUMAB
HYDROCORTISONE
HYDROCORTISONE ACETATE
HYDROCORTISONE ACETATE/LIDOCAINE HYDROCHLORIDE
HYDROCORTISONE ACETATE/PRAMOXINE HYDROCHLORIDE
HYDROCORTISONE CYPIONATE
HYDROCORTISONE SODIUM PHOSPHATE
HYDROCORTISONE SODIUM SUCCINATE
INFLIXIMAB
INFLIXIMAB-ABDA
INFLIXIMAB-AXXQ
INFLIXIMAB-DYYB
IXEKIZUMAB

Generic Drug Name
LEFLUNOMIDE
LIDOCAINE HYDROCHLORIDE/TRIAMCINOLONE ACETONIDE
MESNA
METHYLPREDNISOLONE
METHYLPREDNISOLONE ACETATE
METHYLPREDNISOLONE SODIUM SUCCINATE
MYCOPHENOLATE MOFETIL HYDROCHLORIDE
MYCOPHENOLATE SODIUM
NALTREXONE/TRIAMCINOLONE
NATALIZUMAB
PREDNISOLONE
PREDNISOLONE ACETATE
PREDNISOLONE ACETATE/PREDNISOLONE SODIUM PHOSPHATE
PREDNISOLONE SODIUM PHOSPHATE
PREDNISOLONE TEBUTATE
PREDNISONE
RILONACEPT
SARILUMAB
SECUKINUMAB
TOCILIZUMAB
TRIAMCINOLONE
TRIAMCINOLONE ACETONIDE
TRIAMCINOLONE DIACETATE
TRIAMCINOLONE HEXACETONIDE
UPADACITINIB
USTEKINUMAB

Table S5b: Immunosuppressive threshold and maximum daily dose for steroids

Steroid	**Dose Equivalent** (mg/day)	**Maximum Daily Dose** (mg/day)
Prednisone	20	250
Prednisolone	20	250
Methylprednisolone	16	200
Triamcinolone	16	200
Dexamethasone	3.0	37.5
Hydrocortisone	80	1000
Cortisone	100	1250

Figure S1: Inclusion flowchart and cohort characteristics for Aim 1



	Excluded due to Age or Start Date (N = 2,431,088)		Excluded due to <6mo Lookback (N = 1,332,437)		Final Analytic Cohort (N = 4,678,729)	
Rate of RZV Initiation (95% CI)*	**22.1 (22.0, 22.3)**		**42.9 (42.6, 43.2)**		**48.6 (48.4, 48.7)**	
	n	**%**	**n**	**%**	**n**	**%**
Age (years)						
50-54	1515110	62.3	490438	36.8	1573725	33.6
55-59	523183	21.5	476629	35.8	1648657	35.2
60-64	392795	16.2	365370	27.4	1456347	31.1
Sex						
Female	1194936	52.0	686680	51.5	2471838	52.8
Male	1101440	48.0	645600	48.5	2205760	47.2
Geographic Region						
Northeast	402552	17.6	235030	17.7	920147	19.7
North Central	417310	18.3	272015	20.5	1005720	21.5
South	1050643	46.0	582044	43.9	2022852	43.3
West	412388	18.1	236593	17.8	720049	15.4
Urbanicity						
Urban	1856063	87.8	1119400	87.9	3546387	86.0
Rural	257494	12.2	154550	12.1	579638	14.0
Insurance Plan Type						
Comprehensive	29491	1.3	12409	0.9	179550	3.9
Preferred Provider	1113764	50.0	546189	41.7	2459722	54.0
Managed Care	644176	28.9	586188	44.8	832658	18.3
High Deductible	441672	19.8	164754	12.6	1079941	23.7

Abbreviations: RZV = Recombinant Zoster Vaccine; 95% CI = 95% Confidence Interval
*Rate is the number of RZV Dose-1 vaccinations per 1,000 person-years.

Table S6: Cumulative incidence of RZV initiation by demographic, and healthcare access, and clinical characteristics, MarketScan, 1/1/2018 - 12/31/2019

	Cumulative Incidence	95% CI
Overall	10.0	9.9, 10.0
Age (years)		
50-54	6.3	6.3, 6.4
55-59	10.1	10.0, 10.1
60-64	14.7	14.6, 14.8
Sex		
Female	10.6	10.6, 10.7
Male	9.1	9.1, 9.2
Geographic Region		
Northeast	8.4	8.4, 8.5
North Central	11.1	11.1, 11.2
South	9.5	9.4, 9.5
West	11.5	11.4, 11.6
Urbanicity		
Urban	10.1	10.0, 10.1
Rural	8.3	8.2, 8.4
Insurance Plan Type		
Comprehensive	7.8	7.7, 7.9
Preferred Provider	9.6	9.5, 9.6
Managed Care	9.8	9.8, 9.9
High Deductible	11.2	11.1, 11.3
Medical Office Visits		
0	7.0	7.0, 7.1
1	9.8	9.8, 9.9
2-3	11.2	11.1, 11.2
4 or more	12.7	12.6, 12.7
Immunocompromised		
Yes	13.0	12.8, 13.2
No	9.8	9.8, 9.9
Immunocompromising Condition		
HIV	16.9	16.3, 17.6
Cancer, with immunosuppression	12.4	12.1, 12.7
Cancer, without immunosuppression*	13.3	13.2, 13.5
Transplant	12.2	11.6, 12.8
Primary Immunodeficiency	14.6	13.7, 15.5
Medication-Induced	12.5	12.3, 12.8

Abbreviations: RZV = recombinant zoster vaccine; 95% CI = 95% Confidence Interval; HIV = Human Immunodeficiency Virus

*Those with cancer without immunosuppression are not included in the immunocompromised group.

APPENDIX B: MANUSCRIPT 2 SUPPLEMENTAL TABLES AND FIGURES

Table S7: ICD-10-CM codes used to identify short-term adverse events

Adverse Event	ICD-10-CM Code	Code Description	Key Details
Localized Reactions			
Cellulitis	L03.113-4	Cellulitis of the upper limb	
Pain	M79.601-3	Pain in arm	
	M89.62	Pain in upper arm	
Systemic Events			
Anaphylaxis	T78.2	Anaphylactic shock	
	T80.52	Anaphylactic reaction due to vaccination	
Headache	G44.1	Vascular headache, not elsewhere classified	
	G44.4	Drug-induced headache, not elsewhere classified	
	R51	Headache	
Fatigue	R53	Malaise and fatigue	
Chills	R68.83	Chills (without fever)	
Nausea/Vomiting	R11	Nausea and vomiting	
Diarrhea	R19.7	Diarrhea, unspecified	
Fever	R50	Fever	
Cardiovascular Events			
Acute Myocardial Infarction	I21	ST elevation and non-ST elevation myocardial infarction	Only inpatient files
	I22	Subsequent ST elevation and non-ST elevation myocardial infarction	
Myocarditis	I40	Acute myocarditis	
Endocarditis	I33	Acute and subacute endocarditis	
Pericarditis	I30	Acute pericarditis	

Other acute and subacute forms of Ischemic Heart Disease	I24	Other acute ischemic heart diseases	
Cerebrovascular Events			
Stroke	I60	Nontraumatic subarachnoid hemorrhage	Only inpatient files
	I62	Other and unspecified nontraumatic intercranial hemorrhage	
	I61	Nontraumatic intracerebral hemorrhage	
	I63	Cerebral infarction	
	G45	Transient cerebral ischemic attacks and related syndromes	
Control Event			
Falls	W10	Fall on and from stairs and steps	
	W18	Other slipping, tripping and stumbling and falls	

Table S8: ICD-10-CM codes used to identify long-term adverse events

Adverse Event	ICD-10-CM Code	Code Description	Acute or Chronic
Neuroinflammatory Disorders			
Cranial nerve disorders, including paralyses/paresis and optic neuritis	G50	Disorders of the trigeminal nerve	Chronic
	G51*	Facial nerve disorders	
	G52	Disorders of other cranial nerves	
Bell's Palsy	G51.0	Bell's Palsy	Acute
Multiple sclerosis (including variants)	G35	Multiple Sclerosis	Chronic
Transverse myelitis	G37.3	Acute transverse myelitis in demyelinating disease of central nervous system	Chronic
Guillain-Barré syndrome	G61.0	Guillain-Barre syndrome	Acute
Myasthenia gravis (including Lambert-Eaton myasthenic syndrome)	G70.XX	Myasthenia gravis and other myoneural disorders	Chronic
Non-infectious encephalitis/ encephalomyelitis	G04.81	Other encephalitis and encephalomyelitis (encephalomyelitis acute disseminated noninfectious)	Chronic
Narcolepsy	G47.41	Narcolepsy	Chronic
	G47.42	Narcolepsy in conditions classified elsewhere	
Neuritis (including peripheral neuropathies)	G54	Nerve root and plexus disorders	Chronic
	G56	Mononeuropathies of upper limb	
	G57	Mononeuropathies of lower limb	
	G58	Other mononeuropathies	
	G60.2	Idiopathic progressive neuropathy	
	G62.9	Polyneuropathy, unspecified	
	G64	Other disorders of the peripheral nervous system	
Other demyelinating diseases (including acute disseminated encephalomyelitis (ADEM))	G04.0	Acute disseminated encephalitis and encephalomyelitis (ADEM)	Chronic
	G36	Other acute disseminated demyelination	
	G37	Other demyelinating diseases of central nervous system	
Skin Disorders			
Psoriasis	L40	Psoriasis	Chronic

Vitiligo	L80	Vitiligo	Chronic
	H02.73	Vitiligo of eyelid and periocular area	
Raynaud's phenomenon	I73.0	Raynaud's Syndrome	Chronic
	M34.1	CR(E)ST syndrome	
Erythema nodosum	L52	Erythema nodosum	Acute
Autoimmune bullous skin diseases (including pemphigus, pemphigoid and dermatitis herpetiformis)	L10	Pemphigus	Chronic
	L12.0	Bullous pemphigoid	
	L12.1	Cicatricial pemphigoid	
	L12.3	Acquired epidermolysis bullosa	
	L12.8	Other pemphigoid	
	L12.9	Pemphigoid, unspecified	
	L13.0	Dermatitis herpetiformis	
Cutaneous lupus erythematosus	L93	Lupus erythematosus	Chronic
Alopecia areata	L63		Chronic
Lichen planus	L43	Lichen Planus	Chronic
	L66.1	Lichen planopilaris (Lichen planus follicular)	Chronic
Sweet's syndrome	L98.2	Febrile Neutrophilic Dermatosis (Sweet)	
Gastrointestinal Disorders			
Crohn's disease	K50	Crohn's disease	Chronic
Ulcerative colitis and ulcerative proctitis	K51	Ulcerative colitis	Chronic
Celiac disease	K90.0	Celiac disease	Chronic
Vasculidities			
Large vessel vasculitis	M31.4	Aortic arch syndrome (Takayasu)	Chronic
	M31.5	Giant cell arteritis with polymyalgia rheumatica	
	M31.6	Other giant cell arteritis	
Medium and small vessel vasculitis	M30.0	Polyarteritis nodosa	Chronic
	M30.8	Other conditions related to polyarteritis nodosa	
	M30.3	Mucocutaneous lymph node syndrome [Kawasaki]	
	M31.7	Microscopic polyangiitis	

	M31.3	Wegener's granulomatosis	
	M30.1	Polyarteritis with lung involvement (Churg-Strauss)	
	I73.1	Thromboangiitis obliterans [Buerger's disease]	
	M31.0	Hypersensitivity angiitis (Goodpasture's syndrome)	
	M31.1	Thrombotic microangiopathy	
	M31.2	Lethal midline granuloma	
	M31.8	Other specified necrotizing vasculopathies	
	M31.9	Necrotizing vasculopathy, unspecified	
	D69.0	Allergic purpura	
	M31.8	Other specified necrotizing vasculopathies	
	M35.2	Bechet's disease	
	L95	Vasculitis limited to skin, not elsewhere classified	
Musculoskeletal and Connective Tissue Disorders			
Systemic lupus erythematosus	M32	Systemic lupus erythematosus (SLE)	Chronic
Scleroderma (including CREST syndrome and morphea)	L94.0	Localized scleroderma (morphea)	Chronic
	L94.1	Linear scleroderma	
	M34	Systemic sclerosis (scleroderma)	
Systemic sclerosis	M34	Systemic sclerosis (scleroderma)	Chronic
Dermatomyositis	M33.1	Other dermatopolymyositis	Chronic
Polymyositis	M33.2	Polymyositis	Chronic
Antisynthetase syndrome	M35.8	Other specified systemic involvement of connective tissue	Chronic
Rheumatoid arthritis	M05	Rheumatoid arthritis with rheumatoid factor	Chronic
	M06	Other rheumatoid arthritis	
Still’s Disease	M06.1	Adult-onset Still's Disease	Chronic
Polymyalgia rheumatica	M35.3	Polymyalgia rheumatica	Chronic
Reactive arthritis	M02.3XX	Reiter's disease (reactive arthritis)	Chronic
Psoriatic arthropathy	L40.5X	Arthropathic psoriasis	Chronic
Ankylosing spondylitis	M45.X	Ankylosing spondylitis	Chronic
Relapsing polychondritis	M94.1	Relapsing polychondritis	Chronic

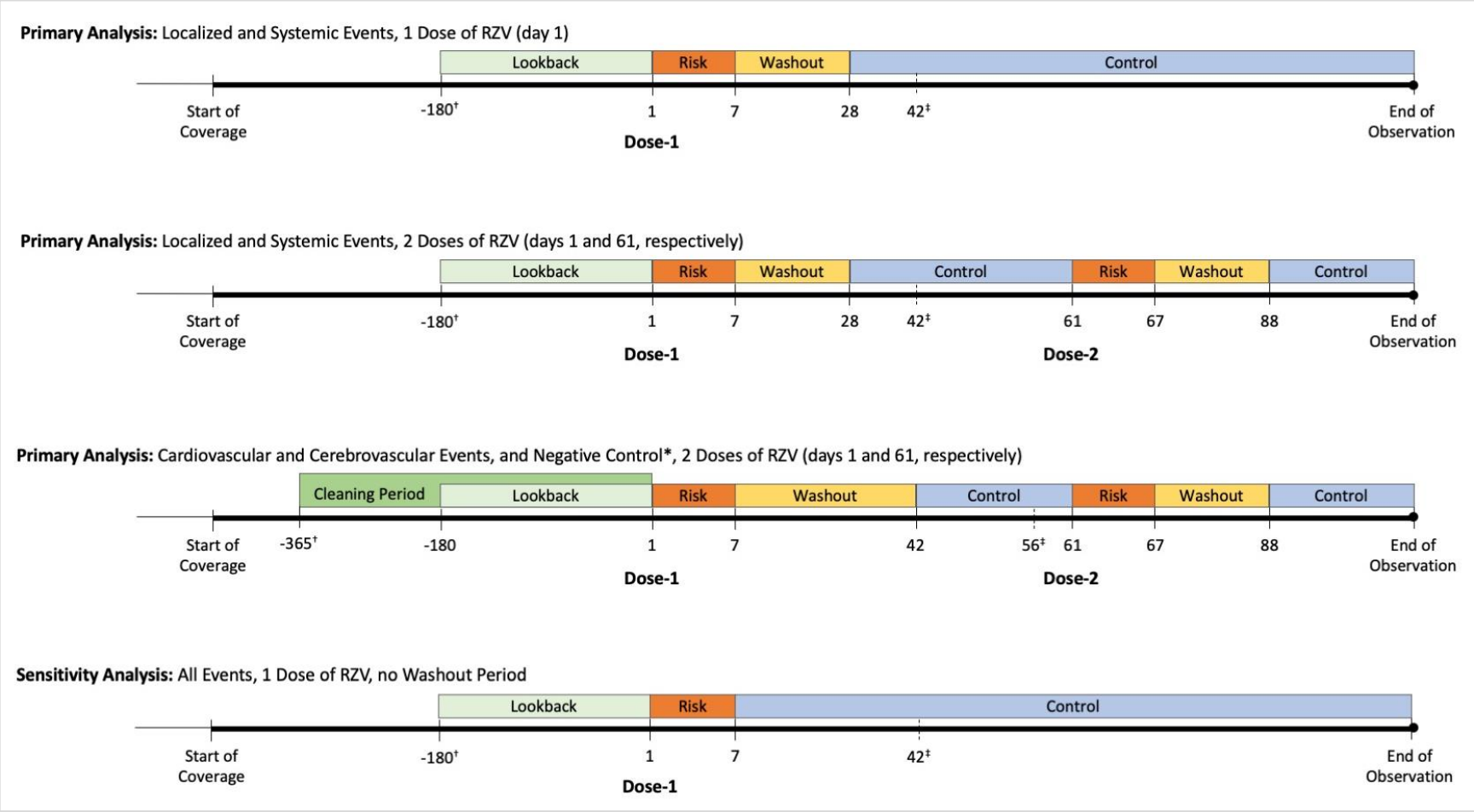
Sjogren’s syndrome	M35.0	Sicca syndrome [Sjogren's]	Chronic
Mixed connective tissue disorder	M35.1	Other overlap syndromes (mixed connective tissue disease)	Chronic
Liver Disorders			
Autoimmune hepatitis	K75.4	Autoimmune hepatitis	Chronic
Primary biliary cirrhosis	K74.3	Primary biliary cirrhosis	Chronic
Autoimmune Cholangitis	K83.0	Cholangitis (primary cholangitis, sclerosing cholangitis)	Chronic
Metabolic Disorders			
Autoimmune thyroiditis (including Hashimoto thyroiditis)	E06.3	Autoimmune thyroiditis	Chronic
Graves' or Basedow’s disease	E05.0X	Thyrotoxicosis with diffuse goiter (Graves' disease, Syndrome Basedow)	Chronic
Diabetes mellitus type I	E10.XXX	Type 1 diabetes mellitus	Chronic
Addison’s disease	E27.1	Primary adrenocortical insufficiency (Addison's disease)	Chronic
Cardiovascular Events			
Acute Myocardial Infarction+	I21	ST elevation and non-ST elevation myocardial infarction	Acute
	I22	Subsequent ST elevation and non-ST elevation myocardial infarction	
Myocarditis	I40	Acute myocarditis	Acute
Endocarditis	I33	Acute and subacute endocarditis	Acute
Pericarditis	I30	Acute pericarditis	Acute
Other acute and subacute forms of Ischemic Heart Disease	I24	Other acute ischemic heart diseases	Acute
Other forms of chronic heart disease	I25	Chronic ischemic heart disease	Chronic
Other Autoimmune Disorders			
Stevens-Johnson Syndrome	L51.1	Stevens-Johnson syndrome	Chronic
	L51.3	Stevens-Johnson syndrome-toxic epidermal necrolysis overlap syndrome	
Autoimmune Thrombosis	D69.3	Immune thrombocytopenic purpura	Chronic

Autoimmune Hemolytic Anemia	D59.1	Other autoimmune hemolytic anemias	Chronic
Sarcoidosis	D86	Sarcoidosis	Chronic
Uveitis	H20	Iridocyclitis	Chronic
	H30	Chorioretinal inflammation	
	H44.11	Panuveitis	
	H35.02	Exudative retinopathy	
	H35.06	Retinal vasculitis	
Cerebrovascular Events			
Stroke	I60	Nontraumatic subarachnoid hemorrhage	Acute
	I62	Other and unspecified nontraumatic intercranial hemorrhage	
	I61	Nontraumatic intracerebral hemorrhage	
	I63	Cerebral infarction	
	G45	Transient cerebral ischemic attacks and related syndromes	
Other and ill-define cerebrovascular disease	I65	Occlusion and stenosis of precerebral arteries, not resulting in cerebral infarction	Chronic
	I66	Occlusion and stenosis of cerebral arteries, not resulting in cerebral infarction	
	I67	Other cerebrovascular disease	
Control Event			
Falls	W10	Fall on and from stairs and steps	Acute
	W18	Other slipping, tripping and stumbling and falls	

***** Excludes Bell's Palsy (G51.0)

+ Only includes hospitalized (inpatient) myocardial infarctions

Figure S2: Design of the self-controlled case series study to evaluate short-term adverse events



Abbreviations: RZV = Recombinant Zoster Vaccine

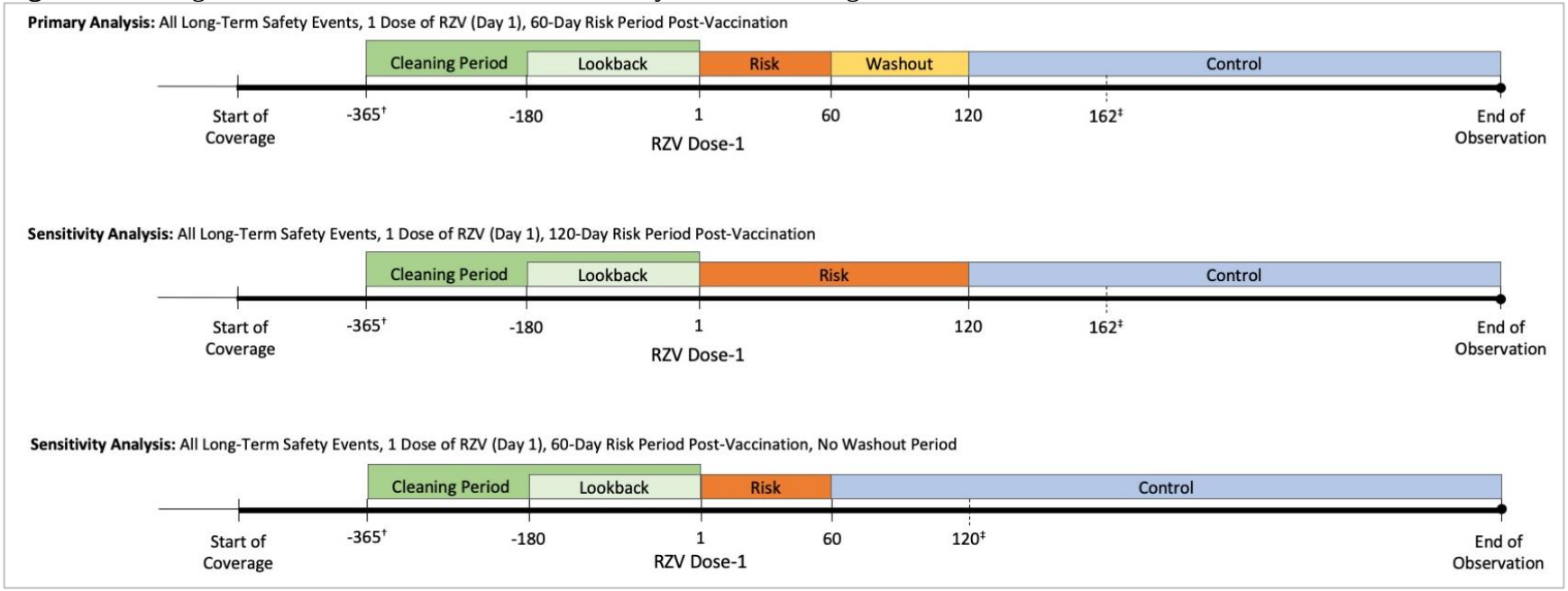
* The algorithm for identifying falls, the negative control event, does not feature a restriction based on history of occurrence (cleaning).

† Minimum amount of coverage (in days) prior to first dose of RZV required for inclusion

‡ Minimum amount of coverage (in days) following first dose of RZV required for inclusion.

Enrollees begin contributing person-time on the day of RZV dose-1 administration (day 1). For study designs that feature a washout the period of time is not included in rate estimation.

Figure S3: Design of the self-controlled case series study to evaluate long-term adverse events



Abbreviations: RZV = Recombinant Zoster Vaccine

† Minimum amount of coverage (in days) prior to first dose of RZV required for inclusion

‡ Minimum amount of coverage (in days) following first dose of RZV required for inclusion.

Enrollees begin contributing person-time on the day of RZV dose-1 administration (day 1). For study designs that feature a washout the period of time is not included in rate estimation.

Table S9: Short-term events, counts and risk of events post-vaccination

Short-Term Adverse Event	Events During Risk Period	Post-Vaccination Risk (events/100,000 doses)
Localized AEs	525	75.3
Cellulitis	164	23.5
Arm Pain	361	51.8
Systemic Events	6375	914.6
Anaphylaxis	22	3.2
Headache	1110	159.3
Fatigue	3640	522.2
Chills	34	4.9
Nausea/Vomiting	606	86.9
Diarrhea	608	87.2
Fever	355	50.9
Cardiovascular Events	36	5.2
Acute Myocardial Infarction	21	3.0
Myocarditis	0	0.0
Endocarditis	1	0.1
Pericarditis	8	1.1
Other acute and subacute forms of ischemic heart disease	6	0.9
Cerebrovascular Events	11	1.6

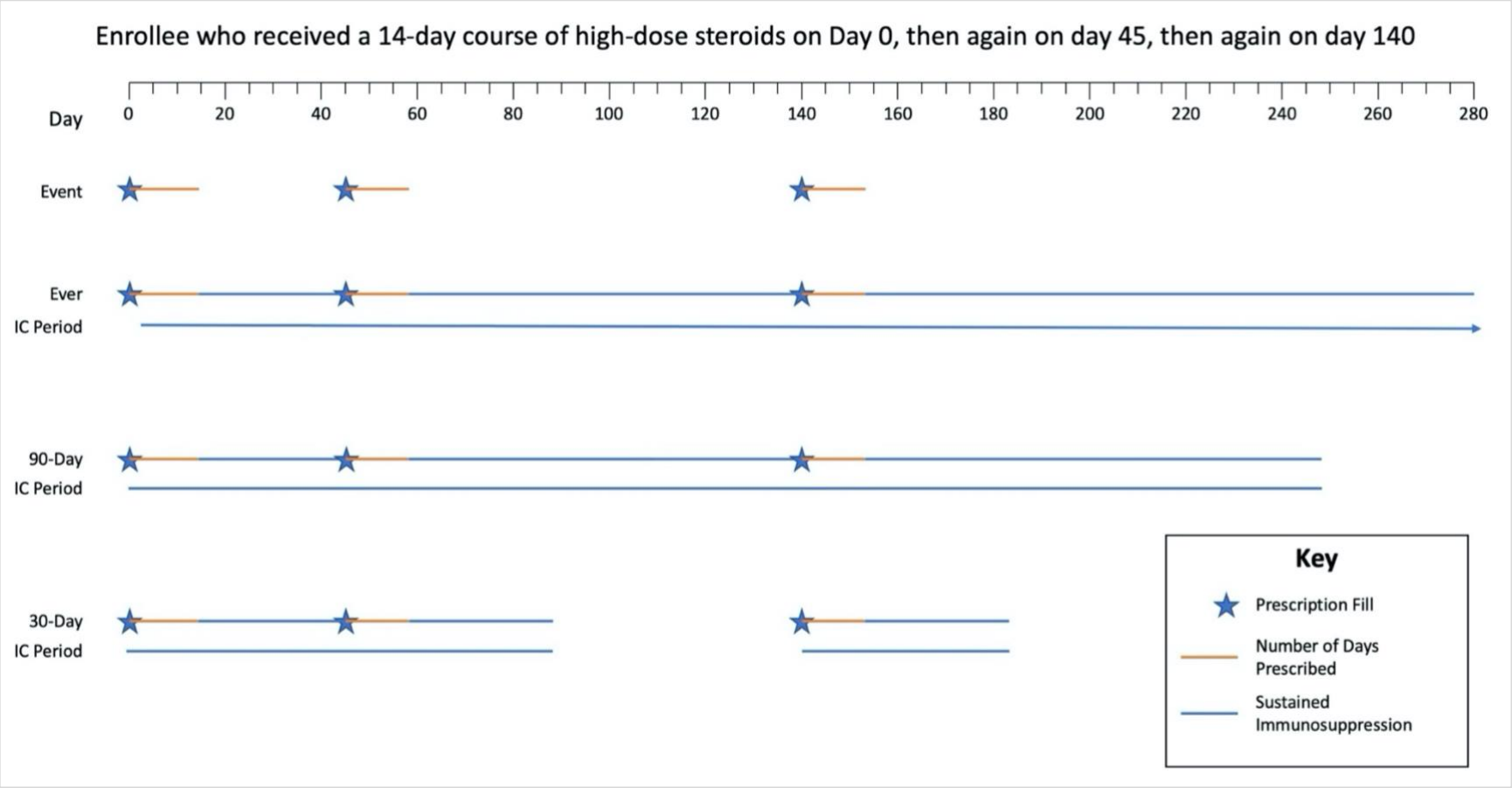
Risk determined using 697,001 total doses as the denominator

Table S10: Long-term events, counts and risk of events post-vaccination

Long-Term Adverse Event	Events During Risk Period	Eligible Doses	Proportion Reported (%)
Any Autoimmune Disorder	4,485	411,862	1.0890%
Neuroinflammatory Disorders	2,307	411,863	0.5601%
Cranial nerve disorders, including paralyses/paresis and optic neuritis	162	411,781	0.0393%
Bell's Palsy	37	411,863	0.0090%
Multiple sclerosis (including variants)	27	411,842	0.0066%
Transverse myelitis	2	411,862	0.0005%
Guillain-Barré syndrome	0	411,863	0.0000%
Myasthenia gravis (including Lambert-Eaton myasthenic syndrome)	18	411,853	0.0044%
Non-infectious encephalitis/ encephalomyelitis	2	411,862	0.0005%
Narcolepsy	12	411,858	0.0029%
Neuritis (including peripheral neuropathies)	1,868	410,703	0.4548%
Other demyelinating diseases (including acute disseminated encephalomyelitis (ADEM))	17	411,850	0.0041%
Skin Disorders	830	411,863	0.2015%
Psoriasis	433	411,609	0.1052%
Vitiligo	58	411,828	0.0141%
Raynaud's phenomenon	114	411,796	0.0277%
Erythema nodosum	3	411,863	0.0007%
Autoimmune bullous skin diseases (including pemphigus, pemphigoid and dermatitis herpetiformis)	18	411,853	0.0044%
Cutaneous lupus erythematosus	34	411,835	0.0083%
Alopecia areata	56	411,834	0.0136%
Lichen planus	112	411,788	0.0272%
Sweet's syndrome	2	411,863	0.0005%
Gastrointestinal Disorders	303	411,863	0.0736%
Crohn's disease	72	411,819	0.0175%
Ulcerative colitis and ulcerative proctitis	167	411,757	0.0406%
Celiac disease	64	411,820	0.0155%
Vasculidities	29	411,863	0.0070%
Large vessel vasculitis	11	411,856	0.0027%
Medium and small vessel vasculitis	18	411,849	0.0044%
Musculoskeletal and Connective Tissue Disorders	673	411,863	0.1634%
Systemic lupus erythematosus	55	411,834	0.0134%
Scleroderma (including CREST syndrome and morphea)	25	411,852	0.0061%
Dermatomyositis	2	411,861	0.0005%

Polymyositis	3	411,861	0.0007%
Antisynthetase syndrome	4	411,860	0.0010%
Rheumatoid arthritis	264	411,695	0.0641%
Polymyalgia rheumatica	24	411,845	0.0058%
Reactive arthritis	4	411,860	0.0010%
Psoriatic arthropathy	74	411,817	0.0180%
Ankylosing spondylitis	38	411,842	0.0092%
Relapsing polychondritis	1	411,863	0.0002%
Sjogren's syndrome	122	411,786	0.0296%
Mixed connective tissue disorder	10	411,856	0.0024%
Liver Disorders	30	411,863	0.0073%
Autoimmune hepatitis	13	411,863	0.0032%
Primary biliary cirrhosis	7	411,863	0.0017%
Autoimmune Cholangitis	10	411,863	0.0024%
Metabolic Disorders	475	411,863	0.1153%
Autoimmune thyroiditis (including Hashimoto thyroiditis)	248	411,707	0.0602%
Graves' or Basedow's disease	63	411,821	0.0153%
Diabetes mellitus type I	155	411,769	0.0376%
Addison's disease	9	411,858	0.0022%
Other Autoimmune Disorders			
Stevens-Johnson Syndrome	2	411,862	0.0005%
Autoimmune Thrombosis	24	411,851	0.0058%
Autoimmune Hemolytic Anemia	3	411,860	0.0007%
Sarcoidosis	33	411,842	0.0080%
Uveitis	99	411,797	0.0240%
Cardiovascular Events	1,432	411,863	0.3477%
Acute Myocardial Infarction	109	411,863	0.0265%
Myocarditis	3	411,863	0.0007%
Endocarditis	6	411,863	0.0015%
Pericarditis	21	411,863	0.0051%
Other acute and subacute forms of Ischemic Heart Disease	43	411,863	0.0104%
Other forms of chronic heart disease	1,250	411,089	0.3041%
Cerebrovascular Events	788	411,863	0.1913%
Stroke	95	411,863	0.0231%
Other and ill-define cerebrovascular disease	693	411,413	0.1684%

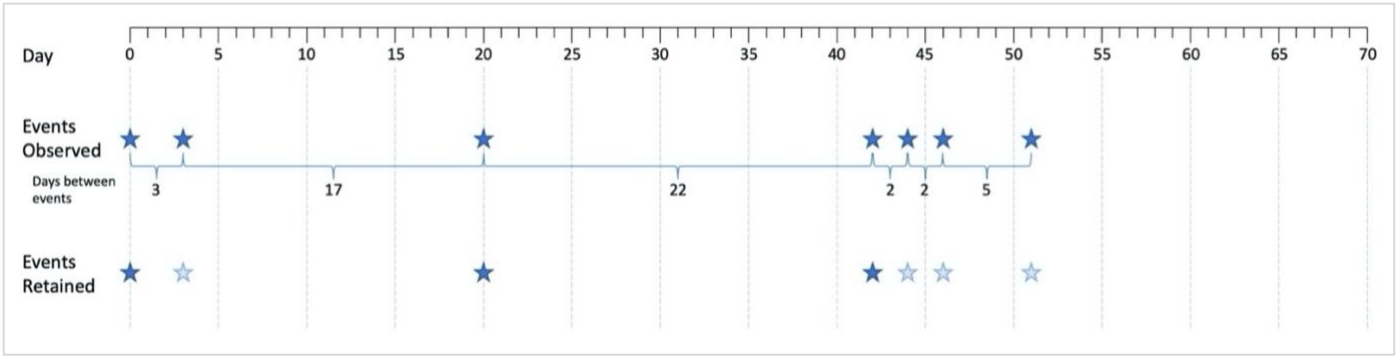
Figure S4: Methods for characterizing temporary periods of immunosuppression following receipt of immunocompromising cancer therapeutics or other immunocompromising medication



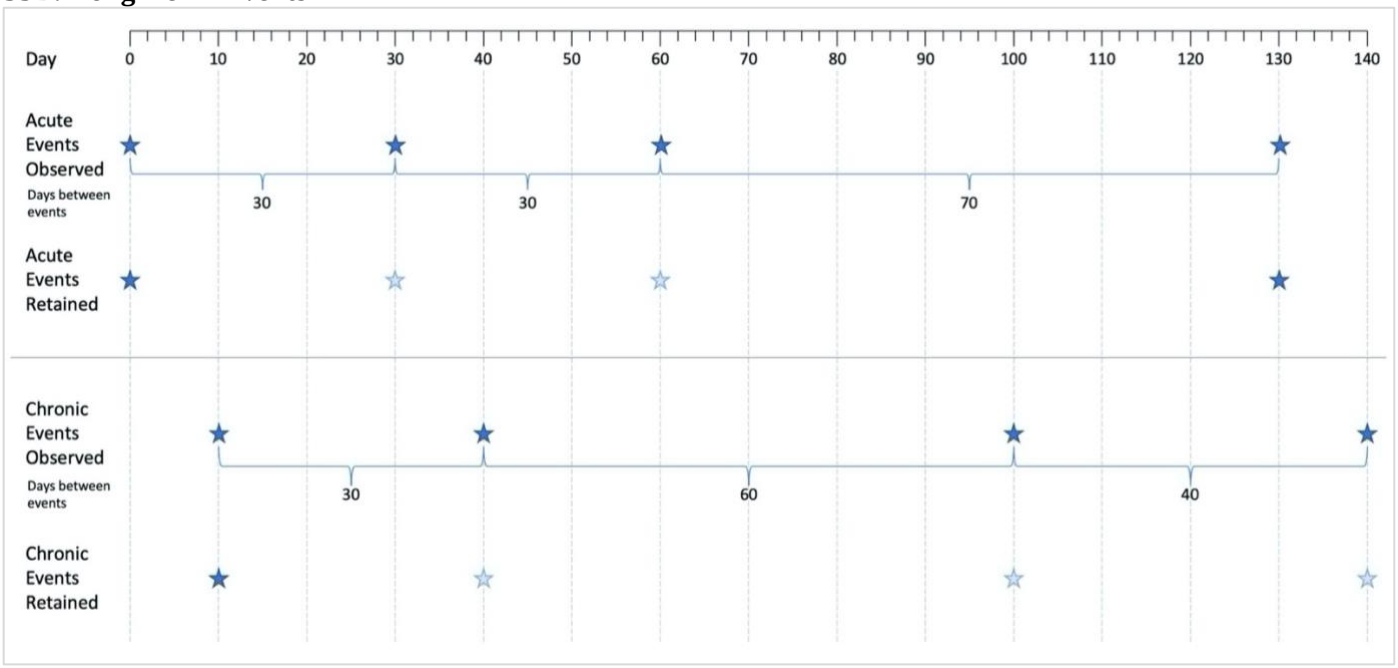
Abbreviations: IC = Immunocompromised

Figure S5: Methods for linking together initial and subsequent diagnoses of short-term (S4A) and long-term (S4B) adverse events to isolate only incident events in analysis

S5A: Short-Term Events

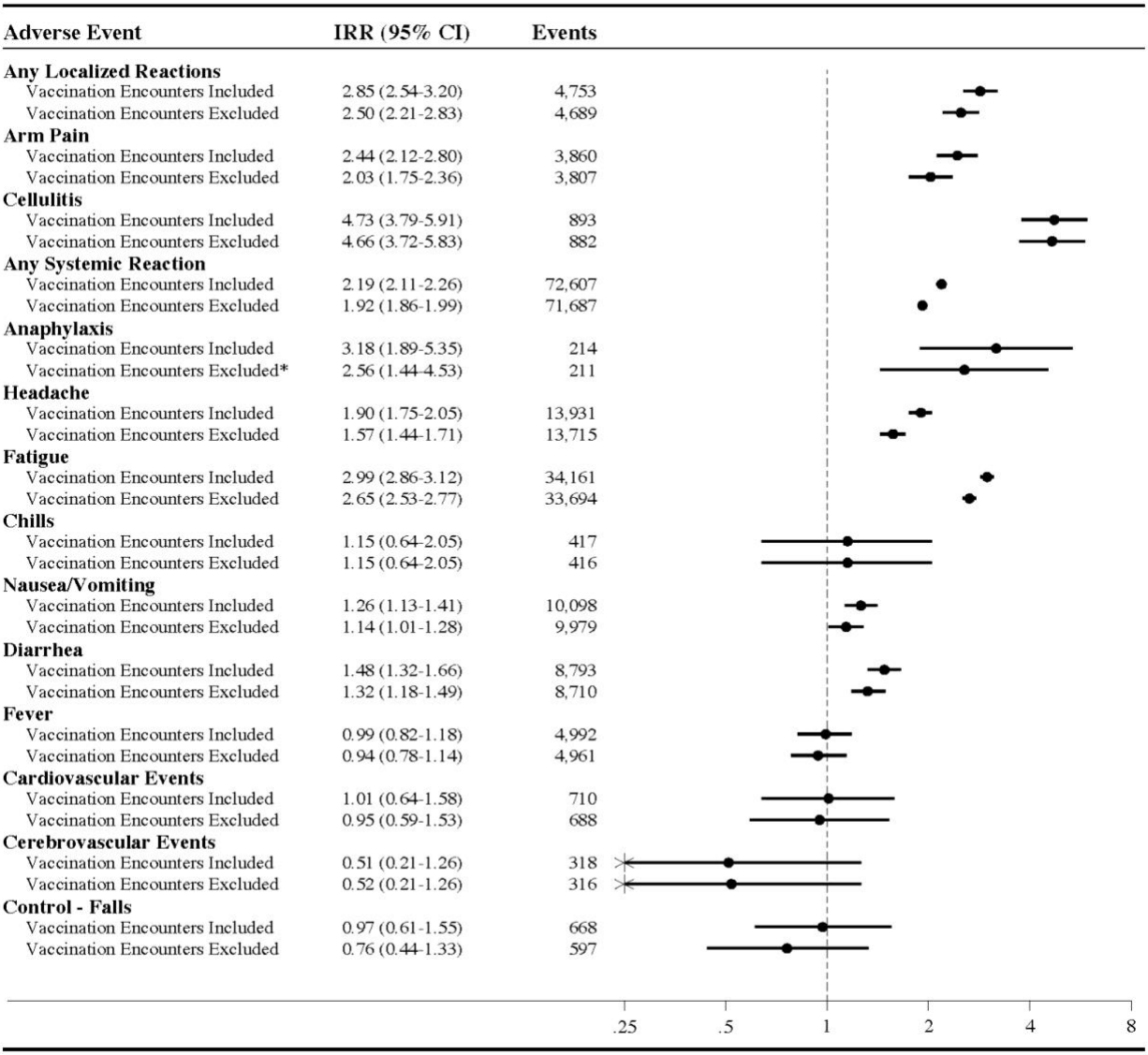


S5B: Long-Term Events



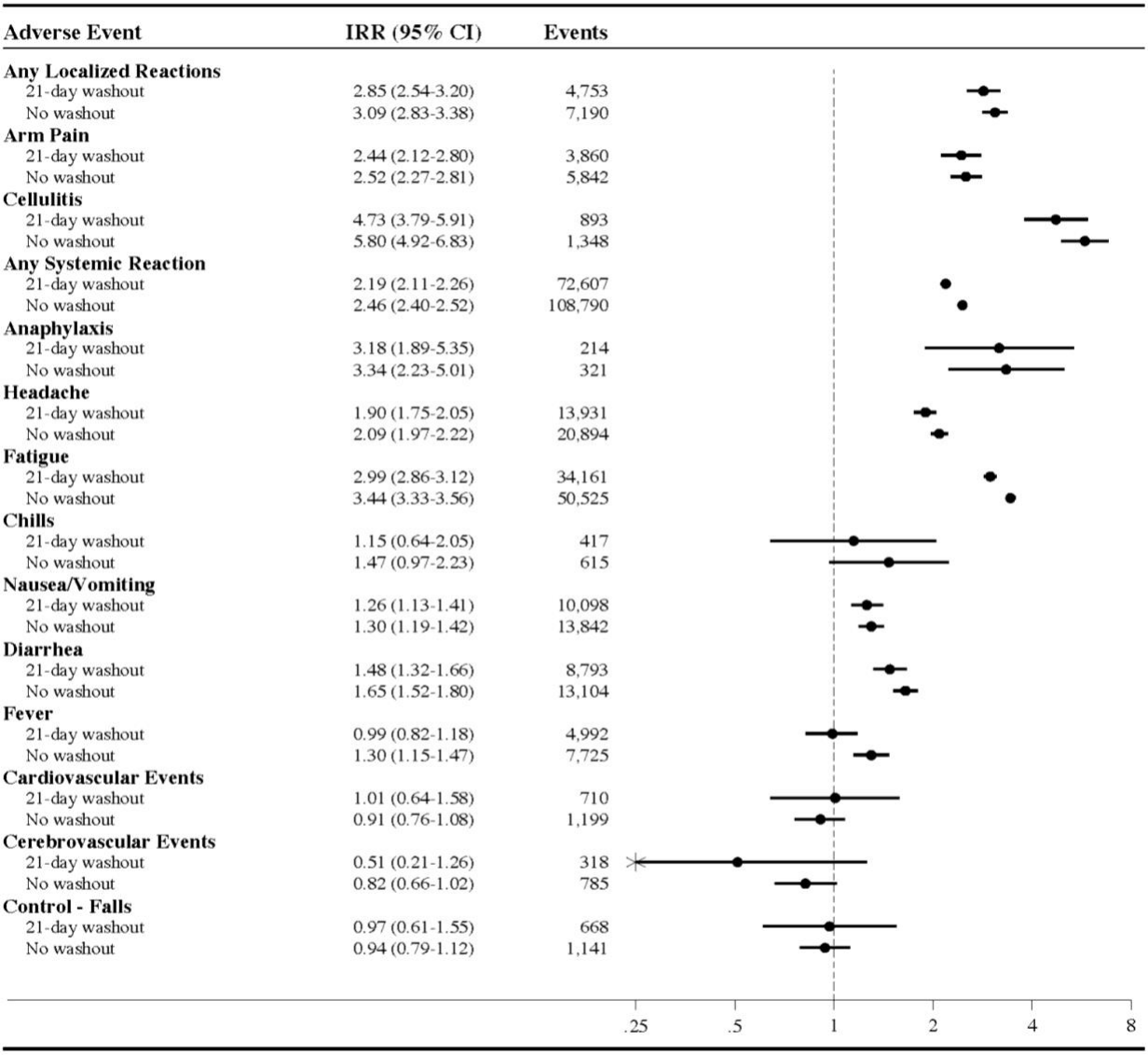
Faded stars indicate that the event is not counted after linkage process.

Figure S6: Sensitivity analysis of short-term safety in which outcomes that occurred during encounters for RZV administration are excluded



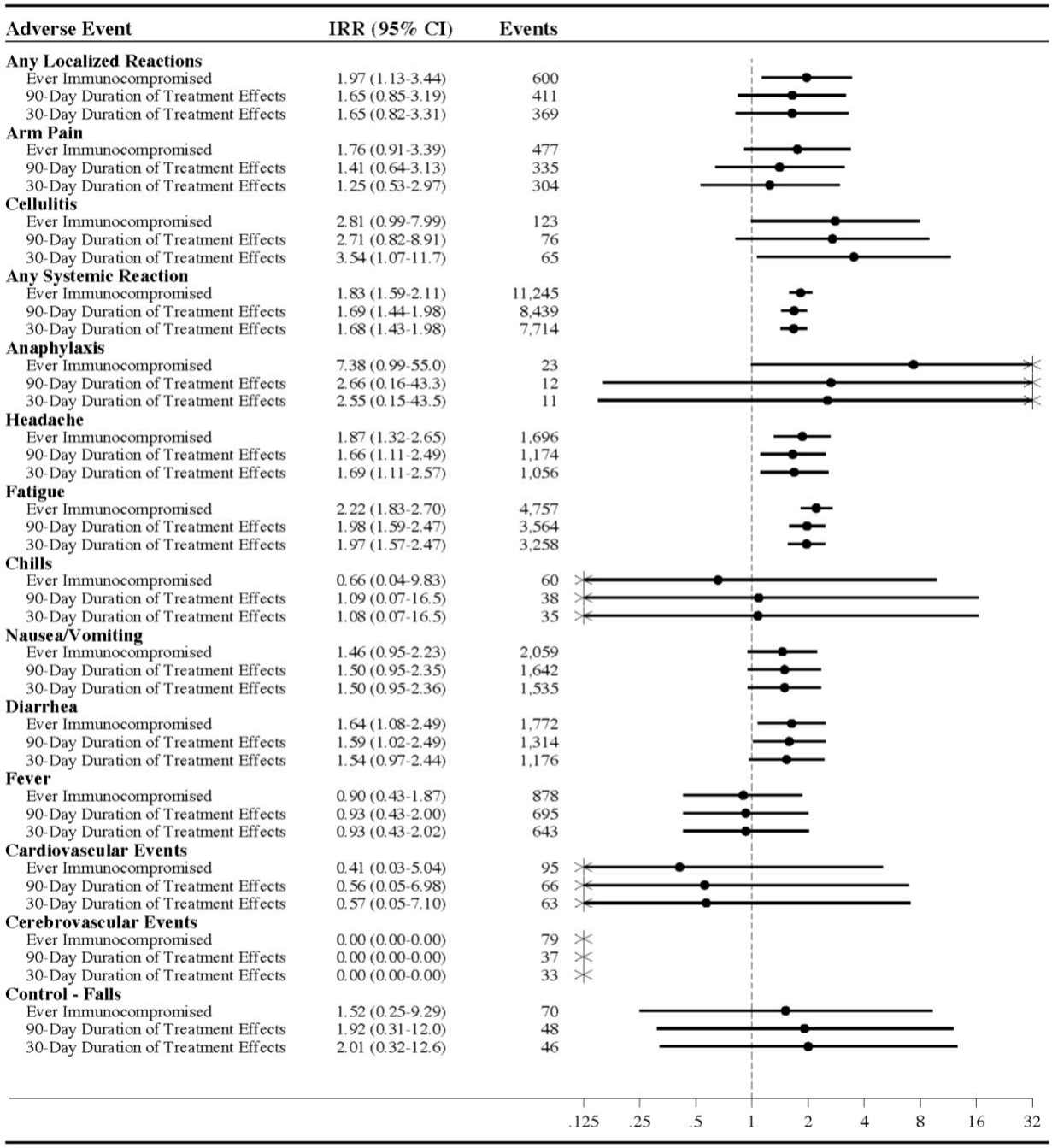
As an initial sensitivity analysis, we excluded events that occurred during the same visit during which RZV was administered. This was achieved via use of a unique visit number featured in the services file. We completed this with the assumption that these events preceded vaccination, and not a result of it.

Figure S7: Sensitivity analysis of short-term safety, comparing use of a 21-day washout period between the risk and control periods to use of no washout period



Sensitivity analysis completed for short-term event by removing the 21 day washout period between the risk and control periods.

Figure S8: Sensitivity analysis short-term safety, using differing periods of assuming effects of immunosuppressive medications



Sensitivity analysis assessing the impact of differential periods of sustained immunosuppression following treatment. Three scenarios are considered: life-long effect, 90-day treatment effect (base case), and 30 day treatment effect.

Figure S9: Sensitivity analysis of long-term safety comparing different risk periods (60 vs 120 days)

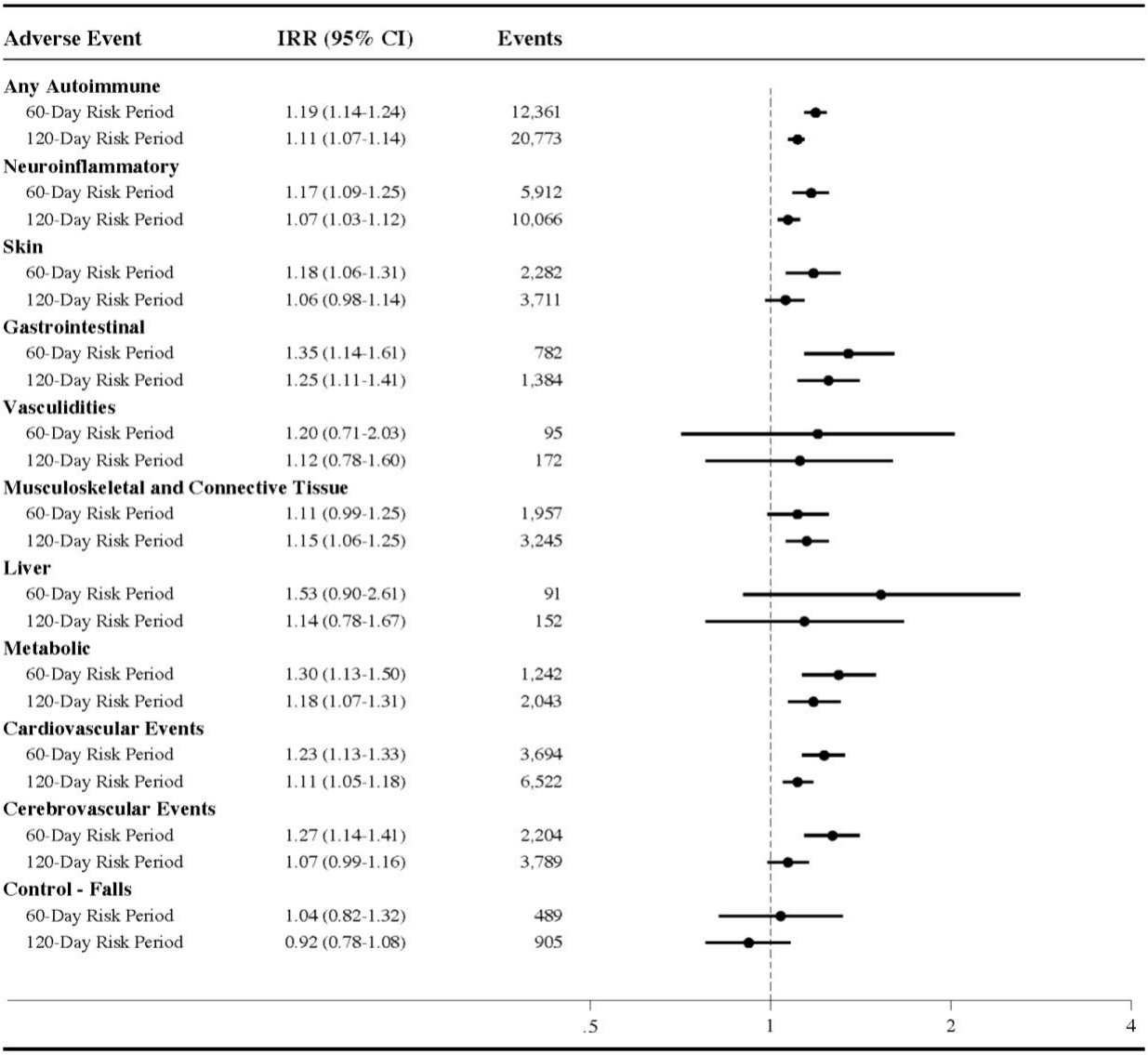


Figure S10: Sensitivity analysis of long-term safety, comparing use of a 60-day washout period between the risk and control periods to use of no washout period

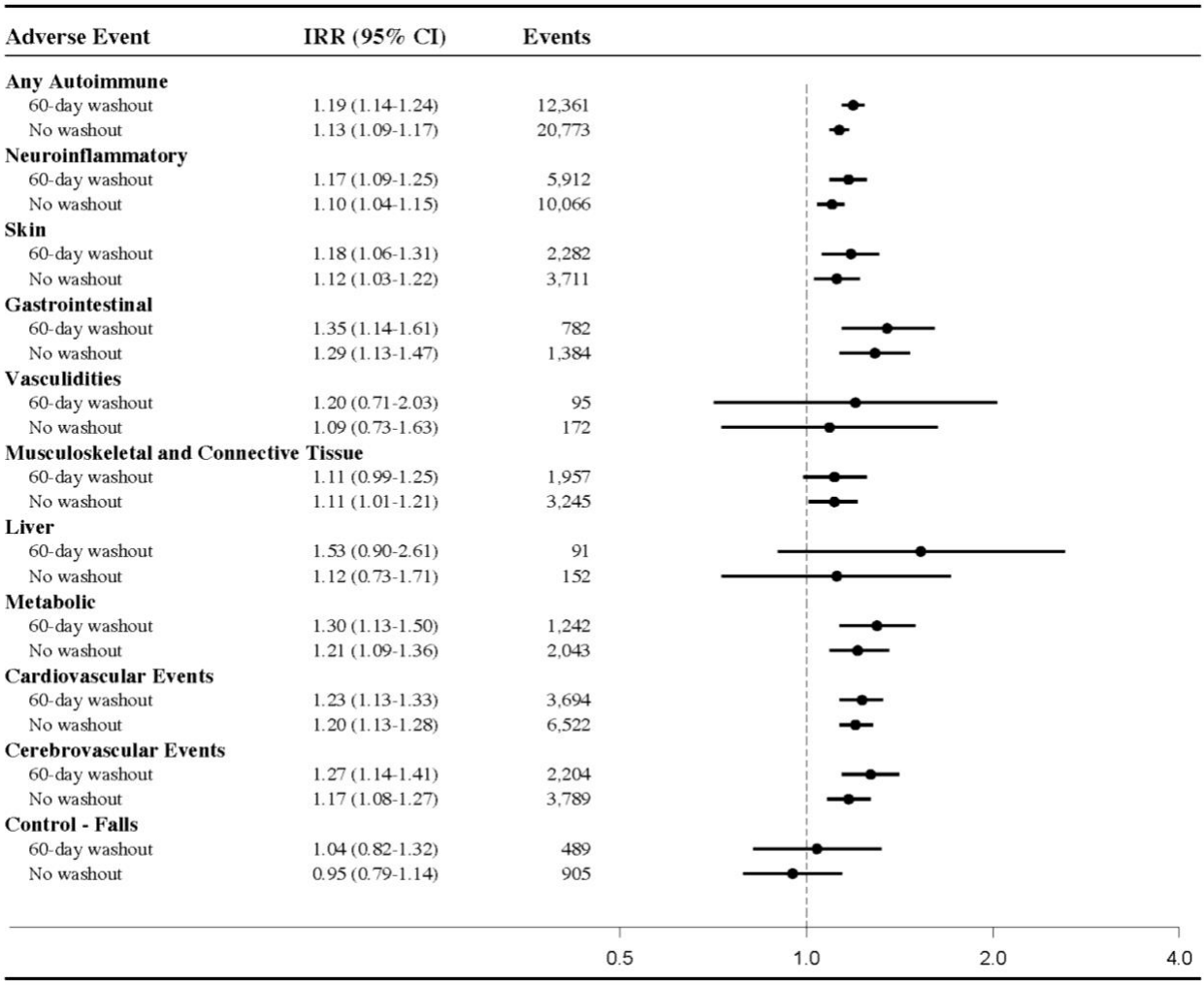


Figure S11: Sensitivity analysis long-term safety, using differing periods of assuming effects of immunosuppressive medications

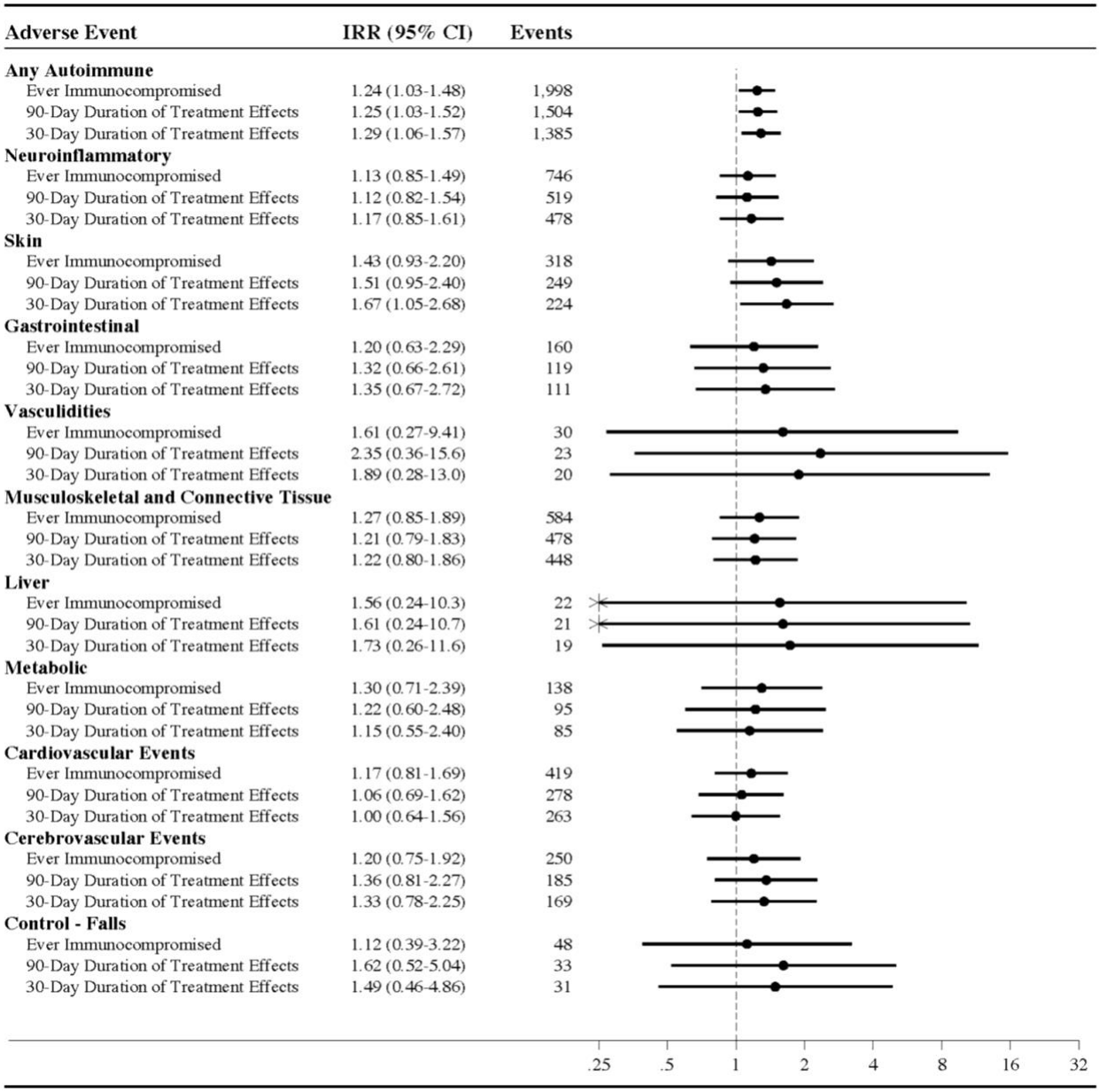
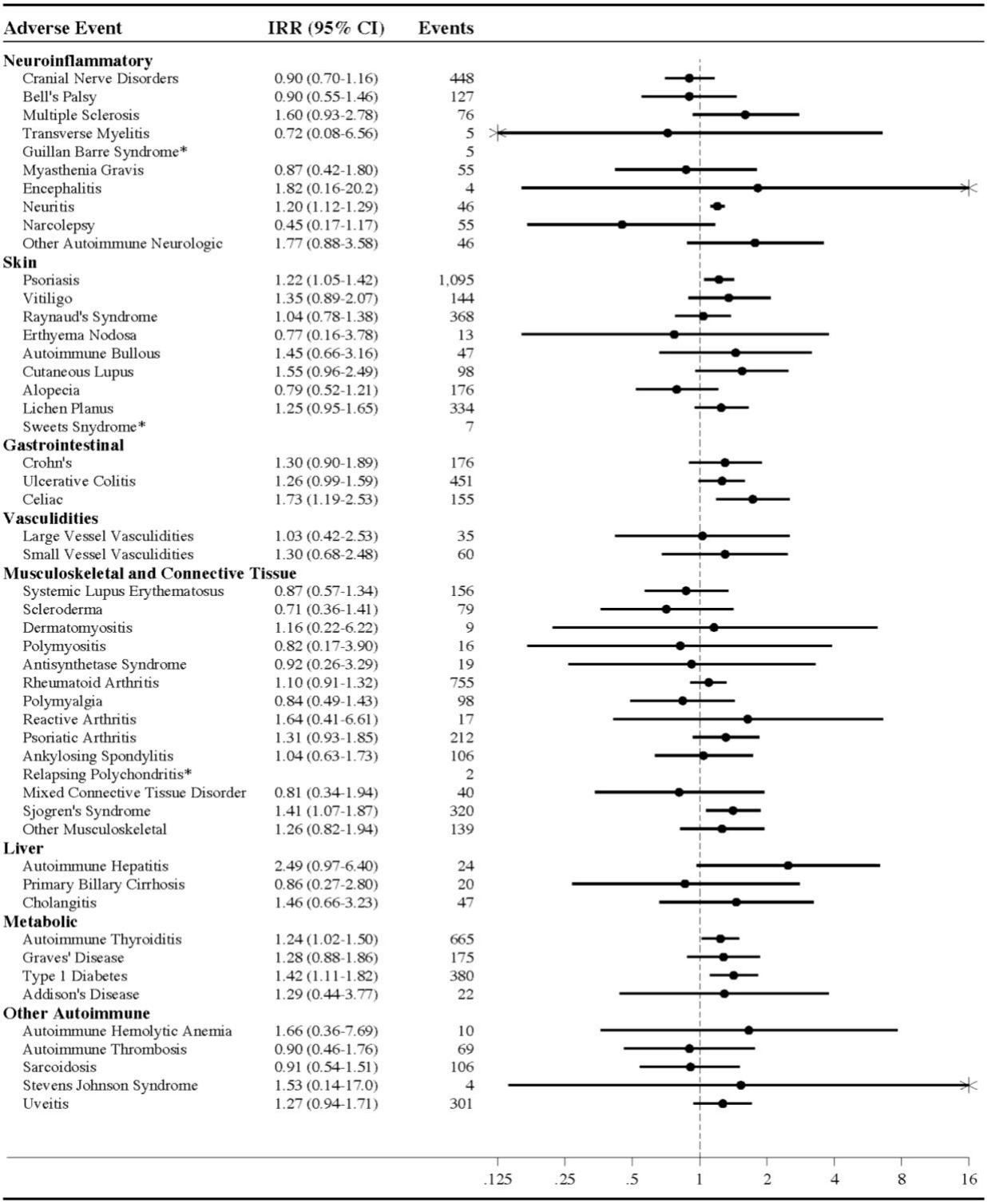
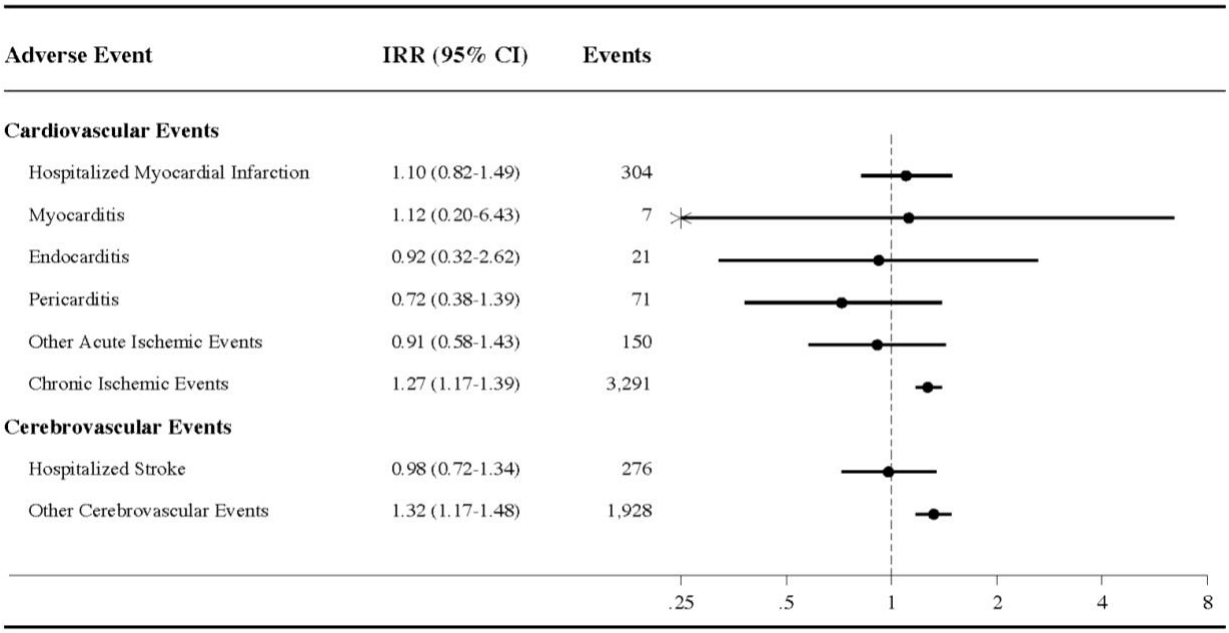


Figure S12: Associations between RZV administration and individual long-term autoimmune events



**No events were observed during the risk period.*

Figure S13: Associations between RZV administration and individual long-term cardiovascular and cerebrovascular events



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