U.S. FOOD & DRUG ADMINISTRATION

Center for Biologics Evaluation and Research
Office of Biostatistics and Epidemiology

CBER Surveillance Program

Biologics Effectiveness and Safety (BEST) Initiative

Assessment of Immune Globulin Utilization in Commercially insured and Medicare Populations

Study Report

February 2022

Prepared By: Keran Moll, PhD, Kathryn Fingar, PhD, Jillian McCarty, MPH

Study Team:

FDA: Graça M. Dores, MD, MPH, Cindy Ke Zhou, PhD; Dorothy Scott, MD; Hui-Lee Wong, PhD; Joyce Obidi, PhD; Azadeh Shoaibi, PhD, MS, MPH

IBM: Keran Moll, PhD[1], Kathryn Fingar, PhD,[1] Timothy Burrell, MD, MBA,[1] Jillian McCarty[1], MPH, Molly Hensche[1] MS, Shayan Hobbi, MS, MBA[1]

Acumen: Yixin Jiao, MPP, Ellen Tworkoski, MS, Rowan McEvoy, BS, Ayushi Bhargava, MPH, BDS, Yuxin Ma, MS, Laurie Feinberg, MD, MPH, MS, Yoganand Chillarige, MPA, Thomas MaCurdy, PhD (Acumen/Stanford)

CMS: Jeffrey Kelman, MD, MMS

Table of Contents

List of Tables

List of Figures

1. ABBREVIATIONS AND TERMS

Abbreviation	Term
CBER	Center for Biologics Evaluation and Research
CMS	Centers for Medicare & Medicaid Services
COBRA	Consolidated Omnibus Budget Reconciliation Act
COVID-19	coronavirus disease 2019
CTD	connective tissue disease
ESRD	end-stage renal disease
FDA	U.S. Food and Drug Administration
FFS	fee-for-service
HCPCS	Healthcare Common Procedure Coding System
ICD-9-CM	International Classifications of Diseases, Ninth Revision, Clinical Modification
ICD-10-CM/PCS	International Classifications of Diseases, Tenth Revision, Clinical Modification/Procedure Coding System
IG	immune globulin
IgA	immune globulin A
IgG	immune globulin G
IgM	immune globulin M
IVIG	intravenous immune globulin
NDC	National Drug Code
SCIG	subcutaneous immune globulin

2. HISTORY OF AMENDMENTS TO THE FINAL REPORT

Version	Date	Amendments	Justification
1.0	September 10, 2021		
1.1	November 5, 2021		
2	December 20, 2021		Revised based on workgroup feedback
3	February 16, 2022		Final version for CBER clearance

3. INTRODUCTION AND BACKGROUND

Immune globulins (IGs) are gamma globulins purified from the plasma of human donors, containing primarily immune globulin G (IgG) as well as trace amounts of immune globulin A (IgA) and immune globulin M (IgM). IG products were first used in 1952 to treat immune deficiencies and later became an important treatment option in a variety of immune-related and inflammatory diseases.[1] Although IG therapy reduces morbidity and mortality in a wide array of conditions, as a plasma-based product, availability may be limited and use may be restricted to patients meeting predefined criteria.

Over the past decade, there has been an increase in IG use for a wide range of clinical conditions.[2] Although the use of IG therapy for some conditions is supported by evidence of clinical benefits or by evidence-based guidelines,[3,4,5,6] evidence is limited to support use for many other conditions.[7,8] The increase in the overall IG use, which may exceed supply, could affect access for patients with conditions that have limited alternative treatments. At the beginning of 2019, the U.S. Food and Drug Administration (FDA) Center for Biologics Evaluation and Research (CBER) was informed by physicians, pharmacists, and patients that they were unable to obtain IG to treat serious conditions.[9] This suggests that increased demand for IG products may have exceeded supply. Potential factors that could affect supply include uneven product distribution across different localities, logistics of contractual obligations, and production delays.[10]

In the United States and Canada, several studies examined IG utilization among a subset of the population (e.g., children) or at select care settings (e.g., hospital).[11] Longitudinal evaluation of IG utilization and conditions associated with IG use in large populations is limited. Understanding IG usage patterns at the national level is crucial to designing policies that effectively manage IG

product inventory and meet patient demand. This study used two large population-based claims databases to assess patterns and changes in IG utilization in the United States across different care settings from January 1, 2009, through December 31, 2019, overall and for individuals with select clinical conditions associated with IG use. The aim was to provide a better picture of the evolving IG use in the context of emerging scientific evidence and clinical trends.

4. OBJECTIVES

This descriptive study had two objectives. The primary objective was to summarize the overall IG utilization patterns and trends from 2009 through 2019 among individuals with private health insurance and on Medicare (section 5.3.1). A number of metrics are examined to better understand factors associated with IG utilization, including annual number of IG administrations and recipients, number of administrations per recipient, and dosage per recipient. The secondary objective was to assess how IG utilization patterns may have changed over time across condition categories (section 5.3.2) associated with IG use.

5. METHODS

5.1. Data sources

In this study, we evaluated data from the IBM® MarketScan® Commercial Database as well as Medicare enrollment and claims data from the Centers for Medicare & Medicaid Services (CMS).

5.1.1. IBM MarketScan Commercial Database

The MarketScan Commercial Database contains individual-level, deidentified healthcare claims information for inpatient and outpatient care and prescription drugs. The claims come from active employees, early retirees, Consolidated Omnibus Budget Reconciliation Act (COBRA) participants, and dependents insured by employer-sponsored plans.

5.1.2. CMS Medicare Parts A/B fee-for-service and Part D prescription drug data

Medicare provides federal health insurance coverage to individuals aged 65 years and older, those under age 65 years who are disabled as determined by the Social Security Administration, as well as those with end-stage renal disease (ESRD). This study used Medicare enrollment data and claims data for patients with Medicare fee-for-service (FFS) Part A (inpatient hospital care), Part B (outpatient care and physician services), and Part D (prescription drug) coverage.

5.2. Study period

The study period was January 1, 2009, through December 31, 2019. We ended the study period in 2019 prior to the start of the current COVID-19 pandemic. This was because the COVID-19 pandemic has affected healthcare utilization in the United States in 2020 and may have disrupted IG product supply, the availability of clinical professionals to administer IG, and the healthcare-seeking behavior of patients.

5.3. Study population

5.3.1. All enrollees (objective 1)

For the overall analysis of IG utilization patterns and trends (objective 1), the study population included all individuals enrolled with medical benefits (MarketScan data) or with FFS Part A and Part B (Medicare data) during the study period. Individuals enrolled for part of a month are considered enrolled for the entire month. Inclusion in the study did not require individuals to have pharmacy benefit (MarketScan data) or Medicare Part D enrollment (Medicare data) because most IG therapies are covered under medical benefits. (Of the observed IG administrations, 90% were on medical claims in the MarketScan data; 86% were on medical claims in Medicare data.)

For the Medicare FFS population, Medicare beneficiaries' health status may vary depending on their reason for entry. Thus, further analysis for the Medicare FFS population was conducted, stratifying by reason for entry (aged into Medicare or qualified due to disability or ESRD).

5.3.2. Enrollees with conditions associated with IG use (objective 2)

To identify enrollees with conditions associated with IG use, the work group adopted a combined data-driven and clinical review approach, because diagnoses recorded on claims data may not be directly attributed to reasons for medication use. Individuals' diagnoses on claims during the 3 months preceding through 1 month after an IG administration or dispensing were identified and ranked on the basis of their frequencies. A panel of five physicians reviewed the top 50 most common diagnoses among individuals receiving IG and selected the relevant ones, classifying them into the clinically meaningful condition categories listed below. Both clinical practice knowledge of the physicians and evidence collected from an extensive literature review guided this process. Conditions not categorized as relevant for IG use were considered implausible. This categorization was used to assess changes in conditions or diseases associated with IG use over time and to evaluate changes in IG therapies among patients within specific condition categories.

The following are condition categories relevant to IG use:

- Autoimmune/connective tissue disease (CTD)
- Hematologic
- Immunodeficiency
- Neurologic
- Oncologic

- Transplantation

Diagnosis codes in each condition category were identified in inpatient and outpatient claims, including both professional and institutional services.

This study spanned different coding system eras. Diagnosis codes classified into condition categories included both International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) diagnosis codes (for data prior to October 2015) and Tenth Revision (ICD-10-CM) diagnosis codes (for data from October 2015 forward). To harmonize the code sets between coding systems, the code list was expanded to include the approximate-equivalent codes from either system using the General Equivalence Mappings. The expanded code list was further reviewed and classified by the physician panel. The top 10 most common diagnoses within each condition category based on the count of IG recipients were also denoted (see Supplemental Table 1 in the Excel file, *IG Report_Supplementary_Materials.xlsx*).

5.4. IG products of interest

The study included the following IG products approved by FDA by the end of 2019.[12] For brand-specific analyses, we presented a subset of brands (brand names *italicized* below) because collectively they accounted for 93% and 95% of all IG administrations/dispensings with brand information in the commercially insured and Medicare populations, respectively.

- **Intravenous immune globulin (IVIG):** Asceniv, Bivigam, Carimune, *Flebogamma*, Gammagard S/D, Gammaplex, Gammar-P IV, Gamunex, *Octagam*, Panzyga, Panglobulin, Polygam, *Privigen*, Sandoglobulin
- **Subcutaneous immune globulin (SCIG):** Cutaquig, Cuvitru, *Hizentra*, Hyqvia, Vivaglobin, Xembify

- **Immune globulin that may be administered via either the IV or the SC route (IVIG or SCIG):** *Gammagard Liquid, Gammaked, Gamunex-C*

IG administrations/dispensings were identified via Healthcare Common Procedure Coding System (HCPCS) codes, National Drugs Codes (NDCs), and ICD-9-CM/ICD-10-Procedure Coding System (PCS) procedure codes observed in MarketScan or Medicare claims from institutional inpatient and outpatient care, professional services, and pharmacy settings. Complete lists of ICD-9-CM/ICD-10-PCS procedure codes, HCPCS codes, and NDCs used to identify IVIG and SCIG are given in Supplemental Tables 2 and 3 in the Excel file, *IG Report_Supplementary_Materials.xlsx*.

5.5. Statistical analyses

5.5.1. Population characteristics

First, demographic characteristics of IG recipients were described and compared with the enrolled populations by payer type (MarketScan or Medicare FFS). These characteristics included age, sex, census region of residence, metropolitan or nonmetropolitan residence, and reason for Medicare entry (Medicare only). For IG recipients, age and place of residence were measured at the time of the first observed IG use. For the overall enrolled population, these characteristics were captured when individuals were first enrolled.

5.5.2. Metrics

Nine metrics are presented throughout the report. Table 1 details how the nine metrics are computed at an annual level. For the assessment of the overall IG utilizations (objective 1), analyses are stratified by route (metrics 1–7) and by brand (metric 1).

For the condition-specific analyses (objective 2), metrics 1–5, 8, and 9 are reported. Except for metric 8, IG utilizations were classified into condition categories using method #1 described in section 5.5.5. Metrics 1 and 2 are presented in two ways:

1) By limiting the IG administrations (metric 1) and individuals receiving IG (metric 2) to those within a given condition category, while using total enrollee person-years or total enrollees as the denominator, respectively (by doing so, these condition-related metrics are standardized by the underlying population size)
2) By limiting both the numerators (IG administrations or IG recipients) and denominators (person-years or enrollees) to those in the condition category, consistent with metrics 3–5, which were computed within the specific populations with a given condition (i.e., the numerator and denominator are limited to individuals with the condition)

Based on condition classification of the IG administrations by method #2 described in section 5.5.5, we calculated the proportion of IG administrations associated with each of the six condition categories per year (metric 8). Metric 9 is presented to show the prevalence of the conditions in the overall population.

Table 1. Metric specifications

Metric	Denominator	Numerator
(1) Aggregate administrations*	Number of enrollee person-years in a year	Number of IG administrations received by individuals in the denominator of the same year
(2) Individuals receiving IG**	Number of enrollees in a year	Number of individuals who received IG in the denominator of the same year
(3) Annual average IG administration rate	Number of person-years enrolled for individuals receiving IG in a year	Number of IG administrations received by individuals in the denominator of the same year
(4) Annual average dose per recipient	Number of person-years enrolled for individuals receiving IG in a year who had complete dose information	Total dose received by individuals who were in the denominator of the same year
(5) Average dose per administration	Number of IG administrations with complete dose information in a year	Total dose of the administrations in the denominator of the same year
(6) Aggregate treatment episodes*	Number of enrollee person-years in a year	Number of treatment episodes for individuals in the denominator of the same year

Metric	Denominator	Numerator
(7) Average length of treatment episode	Number of treatment episodes	Total number of days of the episodes in the denominator of the same year
(8) Proportion of IG administrations classified into condition category	Number of administrations for individuals with continuous enrollment 3 months prior to 1 month after administration in a year	Number of administrations in the denominator classified into a condition category
(9) Prevalence of enrollees classified into condition category**	Number of enrollees in a year	Number of enrollees in the denominator classified into a condition category

Abbreviation: IG, immune globulin.

* Metrics are reported as per 100,000 person-years.

**Metrics are reported as per 100,000 individuals.

5.5.3. Unit of analysis

To summarize utilization trends, this study analyzed data using the four units of analysis described below:

1) **Administration of IG:** The definition of an IG administration differed by healthcare setting. Compared with IG administrations received in an outpatient setting, the number of infusions is not easily inferred on the basis of days' supply (pharmacy setting) or the presence of an ICD-9-CM/ICD-10-PCS procedure code during a hospitalization.
    a. In the outpatient setting, an administration was defined as the IG administration services received by an individual on a single service date.
    b. In a pharmacy setting, all IG products dispensed on a single fill date for an individual were defined as a single administration, regardless of the quantity and days' supply.
    c. In an inpatient setting, IG use identified on the basis of ICD-9-CM/ICD-10-PCS procedure codes during a single hospitalization was defined as a single administration.
2) **Individual:** To be included in an analysis, an individual must be enrolled with medical coverage in either the commercial or Medicare population for the year of evaluation.

3) **Dose administered:** For IG uses identified by HCPCS codes with specified units of service, dose of the administration was calculated as grams per unit multiplied by the number of units. For IG uses identified by NDCs, dose was calculated by multiplying the quantity dispensed by the strength and converting to grams as needed. Administrations identified through procedure codes with no dose information were excluded from the dose-related metrics. Administrations with extreme dose amount (<1 gram or >500 grams per administration) also were excluded from the dose-related analysis per clinical input (less than 1% in the Medicare data and 9% in the MarketScan data).
4) **Treatment episodes:** An IG treatment episode was defined as consecutive days of IG administration for an individual in an outpatient setting. The minimum length of an episode was 1 day (i.e., a single administration). A gap of 2 days was allowed within an episode to accommodate a potential treatment pause over a weekend or an unexpected intervening medical event. A new episode started when a subsequent IG administration was greater than 2 days after the previous administration. IG use in the inpatient and pharmacy settings was excluded from episode construction because the precise infusion dates and episode duration are not captured in the claims data. A small proportion (<1%) of treatment episodes involving multiple brands or routes were also excluded from the analysis because attributing portions of an episode to different brands or routes may be inaccurate and convolute the interpretation of the results.

The service date of the first administration in an episode was defined as the episode initiation. A treatment episode spanning months was only counted as a single episode in the month when the episode was initiated.

The length of an episode was calculated as the number of days an individual received an IG product during the episode. Gap days, if any, were not counted toward the length of an episode.

5.5.4. Classification of enrollees to relevant condition categories

We identified individuals in the study population (regardless of IG use) with each of the six IG-plausible conditions (section 5.3.2). Condition-specific episodes were constructed for each individual so that person-time was appropriated into condition categories. For chronic conditions, an individual's condition-specific episode started from the month of the first diagnosis in the condition category and extended 11 months afterward. At each subsequent diagnosis of the same condition, the episode extended further to cover the following 11 months. Episodes ended 11 months after the month of the last diagnosis if no subsequent diagnosis was present prior to the 12th month. Condition-specific episodes could restart when another qualifying diagnosis was present. For acute conditions, individuals were assigned to the condition category for the month of the diagnosis and 2 months after the diagnosis (except for Guillain-Barre syndrome, for which individuals were assigned to the neurologic category from the month of diagnosis through 3 months after diagnosis. Guillain-Barre syndrome persisting beyond 12 weeks meets criteria for chronic inflammatory demyelinating polyradiculoneuropathy, while other acute conditions of interest, such as Kawasaki disease, typically last less than two months). Individuals' person-time may be classified into multiple condition categories if they had multiple diagnoses indicating different conditions.

5.5.5. Classification of administrations to relevant condition categories

IG administrations were classified into relevant condition categories using two methods. Method #1: Administrations were classified into a condition category if the recipient was in a

condition-specific episode (as specified in section 5.5.4) at the time of the administration. Method #1 applies to metrics 1–5 (section 5.5.2) in the condition-specific analysis. Condition classification is based on diagnoses during the year prior to the IG use, as defined by individuals' condition-specific episodes. Method #2: We identified a subset of IG administrations from individuals with continuous enrollment during the adjacent time period around the administration (defined as 3 months before to 1 month after the administration date). IG administrations were classified to condition categories based on diagnoses during this adjacent time period. Method #2 applies to metric 8 (section 5.5.2) in the condition-specific analysis. Condition classification is based on diagnoses present during the adjacent time period around IG use. An IG administration may be classified into multiple conditions. If no diagnoses from the six condition categories were identified, IG administrations were categorized to the implausible condition category in the analysis related to metric 8.

5.5.6. Sensitivity analysis

Because we noticed unstable trends around the transition to the ICD-10-CM/PCS coding system in the commercially insured population, we conducted a sensitivity analysis for immunodeficiency. Certain immunodeficiency diagnoses (more common among certain ICD-10-CM codes) could be used as a "rule-out" or presumptive diagnosis with a laboratory test before a definitive diagnosis is made (e.g., a presumptive diagnosis for newborn screening of primary immunodeficiency).[13] Thus, we computed metrics 1–4 in three subsets of this group: (1) immunodeficiency, with a subsequent diagnosis at least 14 days after the initial diagnosis; (2) primary immunodeficiency (a subgroup of immunodeficiency); and (3) primary immunodeficiency, with a subsequent diagnosis at least 14 days after the initial diagnosis. For this analysis, individuals with primary immunodeficiency were identified on the basis of the

presence of primary immunodeficiency diagnosis codes (see Supplemental Table 4 in the Excel file, *IG Report_Supplementary_Materials.xlsx*).

6. RESULTS

6.1. Demographic characteristics

Table 2 summarizes demographic characteristics of individuals receiving IG and of all enrollees. Of the 161,023,704 commercially insured and 65,770,776 Medicare enrollees between 2009 and 2019, 80,361 (0.05%) commercially insured and 221,837 (0.34%) Medicare enrollees had at least one IG administration or prescription fill. In the commercially insured population, compared with the overall enrolled population, IG recipients had a higher mean age (38.7 vs. 31.2 years) and a higher proportion of females (57.2% vs. 51.0 %). Geographic distributions were similar.

In the Medicare population, a higher proportion of IG recipients qualified for Medicare due to ESRD or disability than the overall enrolled population (39.0% vs. 25.1%) and lived in metropolitan areas (80.4%vs. 74.2%). Medicare enrollees receiving IG had a similar sex and geographic distribution compared with all enrollees, and 30.7% of the IG recipients were under the age of 65 years upon their first documented use of IG.

6.2. IG utilization among all enrollees, overall and by route and brand

6.2.1. Overall

Figure 1 displays metrics 1–4, overall and by route, from 2009 through 2019. The number of IG administrations per 100,000 enrollee person-years was greater in the Medicare population than in the commercially insured population.

Overall, the total number of IG administrations and individuals receiving IG increased consistently during the study period among both commercially insured and Medicare enrollees

(Table 3). The number of administrations per 100,000 enrollee person-years (metric 1) increased by 120% for the commercially insured population (by 257 administrations, from 213 to 470) and by 145% for the Medicare population (by about 1,000 administrations, from 692 to 1,693). Similarly, from 2009 to 2019, the number of individuals per 100,000 enrollees receiving IG (metric 2) increased by 71% among the commercially insured population (from 24 to 42 individuals) and by 102% in Medicare (from 89 to 179 individuals). The average annual administrations per individual receiving IG (metric 3) increased by 28% for the commercially insured individuals (from 8 to 10) and by 19% among Medicare beneficiaries (from 8 to 9). The average annual dose per recipient (metric 4) increased by 29% for the commercially insured population (from 384 to 497 grams) and by 34% for the Medicare population (from 317 to 426 grams). The average dose per administration (metric 5) also increased but to a lesser extent, particularly for the commercially insured population (by 4%, from 43 to 45 grams) compared with the Medicare population (by 20%, from 38 to 46 grams).

Figure 2 displays episode-level statistics, including the average episode length and the number of treatment episodes per 100,000 enrollee person-years. The average episode length (metric 7) remained constant at 1.1 and 1.2 days for the commercially insured and Medicare populations, respectively (Table 3). Consistent with the metrics presented in Figure 1, the number of IG treatment episodes (metric 6) increased substantially between 2009 and 2019, by 91% for the commercially insured population (from 179 to 341 per 100,000 person-years) and by 130% for the Medicare population (from 526 to 1,207). Because most treatment episodes were about 1 day in length, the definition of an episode is operationally similar to an administration. Therefore, we focus the subsequent sections of this report on metrics related to administrations and dose.

Among the Medicare population, metrics 1–4 were evaluated separately by the reason for entry into Medicare (age or ESRD/disability). As shown in Figure 3, the number of IG administrations per 100,000 enrollee person-years (metric 1) and IG recipients per 100,000 enrollees (metric 2) were both higher among the beneficiaries who qualified for Medicare due to ESRD/disability than among those who aged into Medicare. The average dose per IG recipient (metric 4) was also consistently higher among Medicare enrollees with ESRD/disability than those who aged into Medicare. However, the average annual administrations per IG recipient (metric 3) were similar between enrollees who entered Medicare for either reason (Figure 3 and Table 4). Figure 4 and Table 4 also display the two episode-related metrics by the reason for entry into Medicare.

6.2.2. Route

In the commercially insured population, the number of IG administrations (metric 1) was highest for products that can be administered by either route (IV or SC) (Figure 1). For Medicare enrollees, utilization of products that can be administered by either route (IV or SC) or the IV-only route was similar. However, among both the commercially insured and Medicare enrollees, there appeared to be a plateau in the increasing trend in the number of recipients of IG products administered by the IV-only route after 2016, whereas use of products administered by either route continued to increase. SCIGs (SC-only route) were the least frequently used products among both the commercially insured and Medicare populations, but they became more widely used among commercially insured enrollees in the later years, reaching 144 administrations per 100,000 enrollee person-years in 2019 (Table 3).

6.2.3. Brand

Figure 5 displays the number of IG administrations per 100,000 enrollee person-years (metric 1) by brand. Gammagard Liquid and Gamunex-C/Gammaked were the most used IG brands in both the commercially insured and Medicare populations. Gammagard Liquid was the most common IG brand among both populations earlier during the study period, but its use was surpassed by Gamunex-C/Gammaked in the later years. From 2009 through 2019, Gamunex-C/Gammaked administrations increased from 43 to 119 per 100,000 enrollee person-years (a difference of 76, or 177%) in the commercially insured population, and from 130 to 488 per 100,000 enrollee person-years (a difference of 358, or 277%) in the Medicare population (Table 5). After its approval in 2010, Hizentra became the second most used IG brand in the commercially insured population by 2019, constituting 24% of all administrations. For both the commercially insured and Medicare enrollees, the use of Privigen increased substantially, from 11 to 49 commercial administrations (a difference of 38, or 361%) and from 49 to 435 Medicare administrations (a difference of 386, or 786%) per 100,000 enrollee person-years from 2009 to 2019. By 2019, Privigen constituted 10% of all commercial IG administrations and 26% of all Medicare IG administrations (compared with 5% and 7% in 2009, respectively).

6.3. Prevalence of conditions of interest among all enrollees

Compared with the commercially insured population, the Medicare population had a higher prevalence of each of the six condition categories (metric 9) (Figure 6). The most prevalent condition category was hematologic, followed by neurologic. In 2019, 3,579 (commercial) and 21,037 (Medicare) per 100,000 enrollees were classified in the hematologic condition category, and 1,205 (commercial) and 9,727 (Medicare) per 100,000 enrollees were classified in the neurologic condition category (Table 6). From 2009 to 2019, the prevalence of

all condition categories increased in the commercially insured population; in the Medicare population, all categories except hematologic and transplantation increased. The prevalence of immunodeficiency increased by 214% and 122% in the commercially insured and Medicare populations from 2009 to 2019, respectively. For the commercially insured population, autoimmune/CTD, neurologic, and hematologic disorders increased by 32%, 21%, and 16%, respectively. For the Medicare population, neurologic, autoimmune/CTD, and oncologic disorders increased by 23%, 16%, and 14%, respectively, whereas hematologic disorders and transplantation decreased by 13% and 14%, respectively (Table 6). Among the commercially insured, the prevalence of immunodeficiency requiring a subsequent confirmatory diagnosis, primary immune deficiency, and primary immune deficiency requiring a confirmatory diagnosis from the sensitivity analysis also showed an increase ranging from 120% to 325%.

Among the Medicare population, there were some notable differences in the prevalence of condition categories between enrollees who aged into Medicare or entered due to ESRD/disability (Figure 7 and Table 7). The prevalence of neurologic, transplantation, immunodeficiency, and autoimmune/CTD condition categories was higher among enrollees who entered Medicare due to disability/ESRD than those who aged into Medicare, whereas the prevalence of oncologic conditions was higher among those who aged into Medicare. In 2019, 13,406 (ESRD/disability) and 8,573 (aged in) per 100,000 enrollees were classified into the neurologic condition category, 6,149 (ESRD/disability) and 1,355 (aged in) per 100,000 enrollees were in the transplantation condition category, 3,849 (ESRD/disability) and 2,061 (aged in) per 100,000 enrollees were in the immunodeficiency condition category, and 2,380 (ESRD/disability) and 1,096 (aged in) per 100,000 enrollees were in the autoimmune/CTD condition category (Table 7). In contrast, the prevalence of oncologic conditions in 2019 was

2,684 per 100,000 enrollees among those who aged into Medicare versus 2,081 per 100,000 enrollees among those who entered due to ESRD/disability. The prevalence of hematologic conditions was similar between the two groups of Medicare enrollees. Like in the overall Medicare population, the prevalence of immunodeficiency showed the highest percentage increase from 2009 to 2019 in both the ESRD/disability and aged-in groups. However, the increase in prevalence was greater among the ESRD/disability group than the aged-in group (152% vs. 109%).

6.4. IG utilization among all enrollees, by condition category

To assess how IG use by individuals with diagnoses in each condition category contributes to overall trends in IG utilization, Figure 8 displays the number of IG administrations within each condition category per 100,000 total enrollee person-years (metric 1) and the number of individuals receiving IG within each condition category per 100,000 total enrollees (metric 2). As specified in section 5.5.2, the condition classification of the numerators is based on individuals' condition-specific episode, and the denominators include all enrollees and are not limited to individuals in each condition category (i.e., the metrics reflect total condition-related IG utilizations standardized by the underlying population size). Between 2009 and 2019, in both the commercial and Medicare populations, IG administrations associated with each condition category increased (Figure 8 and Table 8).

Administrations associated with immunodeficiency were the most common (Figure 8 and Table 8). By 2019, individuals with immunodeficiency received 68% of all IG administrations (compared with 60% in 2009) among commercially insured enrollees and 60% of all IG administrations (compared with 53% in 2009) among Medicare beneficiaries. Administrations associated with immunodeficiency also showed an increase from 127 to 321 administrations

among commercially insured enrollees (a 154% increase) and from 365 to 1,007 administrations among Medicare beneficiaries (by 642 administrations, or a 176% increase) per 100,000 enrollee person-years.

The neurologic and hematologic conditions were the second and third most common conditions among individuals receiving IG both in the number of administrations (with 35% in commercial and 51% in Medicare for neurologic conditions and 20% in commercial and 39% in Medicare for hematologic conditions in 2019) and in the number of recipients (with 34% in commercial and 45% in Medicare for neurologic conditions and 31% in commercial and 51% in Medicare for hematologic conditions in 2019) (Table 8). Although less common (fewer than 20 administrations per 100,000 person-years), IG administrations received by individuals with autoimmune and CTD had the largest percentage increase between 2009 and 2019 (220% and 226% in the commercially insured and Medicare populations, respectively).

Figure 9 displays the number of IG administrations within each condition category per 100,000 total enrollee person-years (metric 1) and the number of individuals receiving IG within each condition category per 100,000 total enrollees (metric 2) among the Medicare population by reason for entry into Medicare. For both groups, the number of IG administrations and number of IG recipients increased from 2009 to 2019 in each of the six condition categories. Overall, for both metrics, the ESRD/disability group had higher values than the aged-in group for most condition categories over time (Figure 9 and Table 9).

6.5. Proportion of IG administrations classified into condition categories

Figure 10 displays changes in the proportion of IG administrations classified into each of the six condition categories (metric 8) based on diagnoses during the adjacent time period around the administrations. Most of the IG administrations in this analysis were given to individuals

with at least one of these conditions recorded around the time of administration. IG administrations not classified into a plausible condition category were rare (3.9% of commercial administrations and 1.5% of Medicare administrations in 2019) (Table 10). In both populations, more than half of the administrations were received by individuals with an immunodeficiency diagnosis, followed by neurologic conditions. Hematologic and autoimmune/CTD condition categories were associated with more than 10% of administrations in the commercially insured population, whereas hematologic and oncologic conditions were associated with more than 25% of IG administrations among the Medicare population.

The proportion of IG administrations received by individuals with plausible condition categories shifted over time (Figure 10 and Table 10). In both populations, the share of autoimmune/CTD, immunodeficiencies, and transplantation administrations increased (all by more than 10%). In contrast, the proportion of administrations in the hematologic and oncologic categories decreased. The share of neurologic administrations remained stable in the commercially insured population but increased in the Medicare population by 14%.

6.6. IG utilization for individuals classified into the condition categories

Figure 11 displays metrics 1–4 among individuals classified into each of the six condition categories. In contrast to the analysis described in section 6.5, this set of analyses assessed changes in IG utilization patterns *within* patient populations of each condition category. As specified in section 5.5.2, the denominator in this analysis is limited to individuals with diagnoses for each of the condition categories. Among both commercially insured and Medicare populations, the number of administrations and recipients was the highest among individuals with immunodeficiency, followed by oncologic conditions, while it was lowest for individuals with hematologic conditions. Between 2009 and 2019, in both populations, the of number IG

administrations and IG recipients increased by at least 43% for all condition categories examined, except for immunodeficiency (Table 11).

Among commercially insured enrollees, individuals with immunodeficiency, neurologic, or autoimmune/CTD disorders had the highest annual average number of administrations per recipient (metric 3), and individuals with neurologic conditions or autoimmune/CTD disorders had the highest annual dose per recipient (metric 4) (Figure 11). Among Medicare beneficiaries receiving IG, those with neurologic and autoimmune/CTD disorders had the highest average annual number of administrations (metric 3) and the highest annual dose per recipient (metric 4). In both populations, across condition categories, average annual administrations per recipient (metric 3) increased by a range of 7% to 22%, and dose per recipient (metric 4) increased by 16% to 36% (Table 11). The average dose per administration (metric 5) also increased by a range of 2% to 25% across condition categories in both populations during the study period.

Figure 12 shows IG utilization patterns within each of the six condition categories, stratified by the reason for entry into Medicare. Across almost all condition categories, the number of administrations per 100,000 person-years (metric 1), IG recipients per 100,000 enrollees (metric 2), annual average number of administrations per recipient (metric 3), and annual dose per recipient (metric 4) increased among Medicare enrollees who aged into Medicare and those who entered due to ESRD/disability. Exceptions were metric 1 and metric 2 for the immunodeficiency condition category among those who entered Medicare due to ESRD/disability: a 4% decrease in administrations per 100,000 person-years and a 2% decrease in IG recipients per 100,000 enrollees (Figure 12 and Table 12). Among individuals classified into each condition category, although the average annual number of administrations per individual was similar between the aged-in and ESRD/disability groups, the ESRD/disability

group received higher average annual doses per individual and higher average doses per administration.

6.6.1. Sensitivity analysis among commercially insured individuals in the immunodeficiency condition category

We saw a marked decrease starting in 2015 in aggregate administrations and number of individuals treated among the immunodeficiency category in the commercially insured population but not in the Medicare population. A sensitivity analysis was performed in three subsets of this group: immunodeficiency, with a subsequent diagnosis ≥14 days after the initial diagnosis; primary immunodeficiency (a subgroup of immunodeficiency); and primary immunodeficiency, with a subsequent diagnosis ≥14 days after the initial diagnosis (Figure 13 and Table 13). In the subgroup of individuals with primary immunodeficiency and a subsequent confirmatory diagnosis, the metrics were largely stable over time despite a slight increase in administrations and recipients from 2017 to 2019. However, the overall immunodeficiency group still shows a sizable decrease in IG utilization with the requirement of a subsequent confirmatory diagnosis among the commercial population (e.g., a 31% decrease in the number of aggregate administrations per 100,000 person-years from 2009 to 2019).

7. DISCUSSION

Consistent with other studies,[14,15] this study found that IG utilization increased between 2009 and 2019 in both the commercially insured and Medicare populations, as evidenced by the consistent increase in the number of IG administrations. We found that both the number of enrollees receiving IG and the annual number of administrations per recipient increased, as did the average aggregate annual dose. Average dose per administration also increased but to a lesser extent. Although limited IG availability has been intermittently reported,[16] we did not observe an

apparent short-term reduction in IG usage during the study period. Data on IG supply in our study populations were not available; therefore, supply limitations could not be assessed.

The findings highlighted in this report allow readers to better interpret factors that may be associated with increases in IG utilization by providing a better understanding of the potentially associated clinical conditions that (1) are becoming more prevalent among enrollees, (2) are associated with the most IG administrations and growth over time, and (3) are associated with more administrations per year, potentially requiring a higher level of therapy.

First, the prevalence of immunodeficiencies more than tripled in the commercially insured population and more than doubled in the Medicare population; however, some of this increase may be due to coding changes, because the increase accelerated in 2016 around the time of the transition to the ICD-10-CM/PCS coding system. Additionally, in the commercially insured population, the prevalence of autoimmune/CTD, hematologic, and neurologic conditions also increased by more than 15%. In the Medicare population, the prevalence of autoimmune/CTD, neurologic, and oncologic conditions increased by more than 20%.

Second, in both the commercially insured and Medicare populations, individuals with immunodeficiency had the highest use of IG and contributed the most (in absolute terms) to the increase in IG administrations, followed by neurologic and hematologic conditions. This finding is consistent with IG utilization studies in the United States and Israel, which often found conditions such as immunodeficiency and immune-mediated conditions (e.g., hematologic and neurologic conditions) to be the most common indications of IG use.[17,18]

Third, the study found variations in the frequency of IG administrations per year depending on condition categories, with higher administration rates for some conditions noted above. The autoimmune/CTD and neurologic condition categories had the highest annual

average administrations (as well as immunodeficiency in the commercially insured population). Thus, not only did the number of enrollees with these conditions increase, but individuals with these conditions were also treated with more frequent IG administrations per year than those with other conditions.

Finally, we also evaluated the utilization patterns among two subpopulations of Medicare enrollees who either aged into Medicare or entered Medicare due to ESRD/disability. Overall IG utilization (the annual IG administrations per 100,000 person-years, the number of IG recipients, aggregate annual IG dose per recipient, and average dose per administration) was higher among those who entered Medicare due to ESRD/disability than those who aged into Medicare, reflecting a greater need and potentially a different treatment strategy for IG use among a population with ESRD/disability. However, the average annual number of administrations per recipient appeared similar between the two groups, indicating that the frequency of treatment did not differ between these two populations. There were differences in condition category prevalence between these populations. Oncologic conditions were more common among beneficiaries who qualified for Medicare due to age than those who qualified due to ESRD/disability. All other condition categories had a higher prevalence among those who entered Medicare due to ESRD/disability, with transplantation having the greatest difference. These differences in condition prevalence appeared to have contributed to the higher overall IG usage among the beneficiaries who entered due to ESRD/disability.

We also observed brand-specific utilization patterns that may be affected by such factors as regulatory actions, market forces, insurance policy, and patient or provider preference. Following the voluntary recall of Octagam due to concerns over its thromboembolic risks, use of the product subsequently dipped in 2011 in both databases.[19] Although the use of SCIG was

associated with a similar improvement in patient outcomes to use of IVIG and had the additional advantage of requiring no medical supervision during self-administration,[20,21] our results show it is more often used by commercially insured individuals than by the older Medicare population. These findings are consistent with those from Runken et al.'s study,[22] which found SCIG recipients to be significantly younger and to have fewer comorbidities than IVIG recipients and hypothesized that patient preference and greater autonomy in decision-making could have played a role in physician prescribing behavior.

Other findings can provide insight into IG use patterns and warrant further comment. IG utilization was more prevalent in the Medicare population than in the commercially insured population. This may reflect the higher prevalence of clinical conditions among older adults for whom IG could plausibly be used in this population. Additionally, we did not observe stretches of time with lower-dose treatments (average dose per administration) that may coincide with a potential lack of access to IG. IG dose per administration also increased over time, primarily in the Medicare population. IG dosing is based on an individual's body weight; a gradual increase in dose per administration may be partially related to the average body weight increase in the population.[23] We observed that the number of administrations per recipient per year increased, although the episode length remained stable, suggesting that the infusions generally were not clustered over several days (which might potentially indicate rationed dosage causing patients to return for infusions). Finally, we found an increase in IG use across all six condition categories studied without marked redistribution between conditions, suggesting it is unlikely certain condition categories diverted the IG utilizations from other conditions. We also observed very few IG administrations by individuals without any of these conditions. However, certain

conditions were associated with higher levels of use, growth over time, and/or dose (e.g., immunodeficiency, neurologic, hematologic, and autoimmune/CTD).

In the immunodeficiency category, we saw a marked decrease in the aggregate annual administrations and the number of individuals treated in the younger commercially insured population but not in the Medicare population. An abrupt increase in the prevalence of the immunodeficiency conditions among the commercially insured population (i.e., an increase in the denominator) appeared to drive the decrease noted. Upon further evaluation, we found that the increase in prevalence was most pronounced among infants with a primary immunodeficiency diagnosis and most notable around the time of the transition to the ICD-10-CM/PCS coding system in 2015 (data not shown). Our sensitivity analysis evaluated subgroups of individuals who had a subsequent diagnosis ≥14 days after the initial diagnosis. This requirement led to the exclusion of individuals with only a single immunodeficiency diagnosis for "rule-out" purposes and appeared to have stabilized the IG metrics among the individuals with primary immunodeficiency. Two factors may have led to the increased immunodeficiency prevalence we observed. First, newborn screening for primary immunodeficiency became increasingly common, with more than 90% of new cases detected by newborn screening around 2016,[24] and certain ICD-10-CM codes may have been used more often as a "rule-out" diagnosis than their ICD-9-CM counterparts (e.g., ICD-10-CM code D81.9 [*Combined immunodeficiency, unspecified*] vs. ICD-9-CM code 279.2 [*Combined immunity deficiency*]). Second, findings from our sensitivity analysis suggest that the coding system transition may have played a greater role in the coding practice for immunodeficiency conditions other than primary immunodeficiency. A decrease in healthcare encounters related to immune disorders has previously been reported after the implementation of the ICD-10-CM/PCS coding system.[25,26]

This study has a number of strengths. This retrospective descriptive study spanned the most recent decade in the United States and used two large administrative claims databases, one with commercially insured individuals and another with Medicare beneficiaries. IG utilization trends (administrations, dose, and specific health conditions) were summarized among more than 300,000 individuals treated with IG across all age groups. Our results are likely generalizable to adults aged 65 years and older because the Medicare FFS database includes most of this population. We used an approach combining data-driven and clinical expert review to provide insight into conditions potentially associated with changes in IG utilization. This may have mitigated some of the limitations of claims data (as noted below). We assessed condition categories associated with IG administrations using two methods, assigning condition category either based on an individual's diagnostic history during 1 year prior to the administration (after constructing condition-specific episodes, method #1) or based on diagnoses around the time of administration (3 months prior to 1 month after, method #2). Method #1 comprehensively identifies underlying chronic conditions that may not be recorded at the time of IG infusion if deemed unnecessary for billing, whereas method #2 likely captures the current manifestation of conditions that may more likely have led to the treatment. The two methods produced similar estimates of proportions of administrations associated with each of the six condition categories, suggesting robustness of the findings.

The study also has several limitations. First, claims data lack the level of clinical detail to determine whether IG utilization is attributable to a specific condition among several concurrent conditions coded on the same claim. Second, claims data have limitations in distinguishing clinical conditions (e.g., the use of nonspecific diagnoses). Therefore, we adopted a more inclusive approach and classified plausible diagnoses into large categories to obtain a stable

population. Additionally, condition-specific analyses, including both the utilization trends and the prevalence of conditions, may have been affected by the ICD-9-CM to ICD-10-CM/PCS coding transition. We evaluated the aberrant change in immunodeficiency trends among the commercially insured population by conducting a sensitivity analysis that required a subsequent diagnosis and examining the primary immunodeficiency subgroup. Finally, using claims data, we were unable to assess an IG shortage, which requires data on both demand and supply, or the causes of a shortage. Additionally, the lack of access to IG may be regional, which would not be reflected in our results.

8. CONCLUSION

In conclusion, this descriptive study of temporal trends in IG use during 2009–2019 in the U.S. population suggested a substantial increase in IG administrations overall, reflecting both an increase in individuals receiving IG and an increase in average annual administrations and dose per recipient. We found that most IG administrations were received by individuals with condition categories that were supported by emerging evidence and treatment guidelines. Although utilization associated with all six plausible condition categories increased, certain conditions, including immunodeficiency, neurologic, hematologic, and autoimmune/CTD disorders, should be assessed further in future studies. A better understanding of the extent to which specific diagnoses drive IG demand may aid efforts to ensure IG is provided to patients who depend on this treatment for their health and survival.

9. TABLES AND FIGURES

Table 2. Characteristics of the study population and individuals receiving IG, among commercially insured and Medicare populations, 2009–2019, in the United States

Characteristics	Commercial		Medicare	
	All enrollees	Individuals who received IG therapy	All enrollees	Individuals who received IG therapy
Total, N	161,023,704	80,361	65,770,776	221,837
Reason for entry into Medicare, N (%)				
Aged in	—*	—*	49,257,912 (74.9)	135,300 (61.0)
ESRD/disability	—*	—*	16,512,864 (25.1)	86,537 (39.0)
Age group (years), N (%)				
0–17	42,674,893 (26.5)	15,949 (19.8)	7,398 (0.0)	861 (0.4)
18–34	47,197,018 (29.3)	12,586 (15.7)	1,649,104 (2.5)	8,203 (3.7)
35–49	38,516,815 (23.9)	18,660 (23.2)	3,563,969 (5.4)	18,381 (8.3)
50–64	32,634,978 (20.3)	33,166 (41.3)	24,401,083 (37.1)	40,508 (18.3)
65–74	—†	—†	21,463,199 (32.6)	91,130 (41.1)
75–84	—†	—†	10,291,328 (15.6)	49,197 (22.2)
85+	—†	—†	4,394,695 (6.7)	13,557 (6.1)
Age, mean (STD)	31.19 (18.19)	38.72 (20.26)	66.6 (12.2)	66.5 (14.2)
Sex, N (%)				
Male	78,894,092 (49.0)	34,421 (42.8)	30,277,870 (46.0)	107,835 (48.6)
Female	82,129,612 (51.0)	45,940 (57.2)	35,492,869 (54.0)	114,002 (51.4)
Census region, N (%)				
Northeast	27,792,049 (17.3)	16,801 (20.9)	14,672,291 (22.3)	45,906 (20.7)
North Central	34,260,242 (21.3)	16,483 (20.5)	11,603,111 (17.6)	49,259 (22.2)
South	64,126,425 (39.8)	32,437 (40.4)	24,588,727 (37.4)	85,329 (38.5)
West	30,451,508 (18.9)	13,140 (16.4)	11,885,768 (18.1)	40,070 (18.1)
Unknown	4,393,480 (2.7)	1,500 (1.9)	3,020,879 (4.6)	1,273 (0.6)
Location of residence, N (%)				
Metropolitan	135,008,026 (83.8)	69,465 (86.4)	48,802,761 (74.2)	178,296 (80.4)
Nonmetropolitan	4,253,670 (2.6)	1,470 (1.8)	13,845,073 (21.1)	41,818 (18.9)
Missing	21,762,008 (13.5)	9,426 (11.7)	3,122,942 (4.7)	1,723 (0.8)

Abbreviations: ESRD, end-stage renal disease; IG, immune globulin; STD, standard deviation.

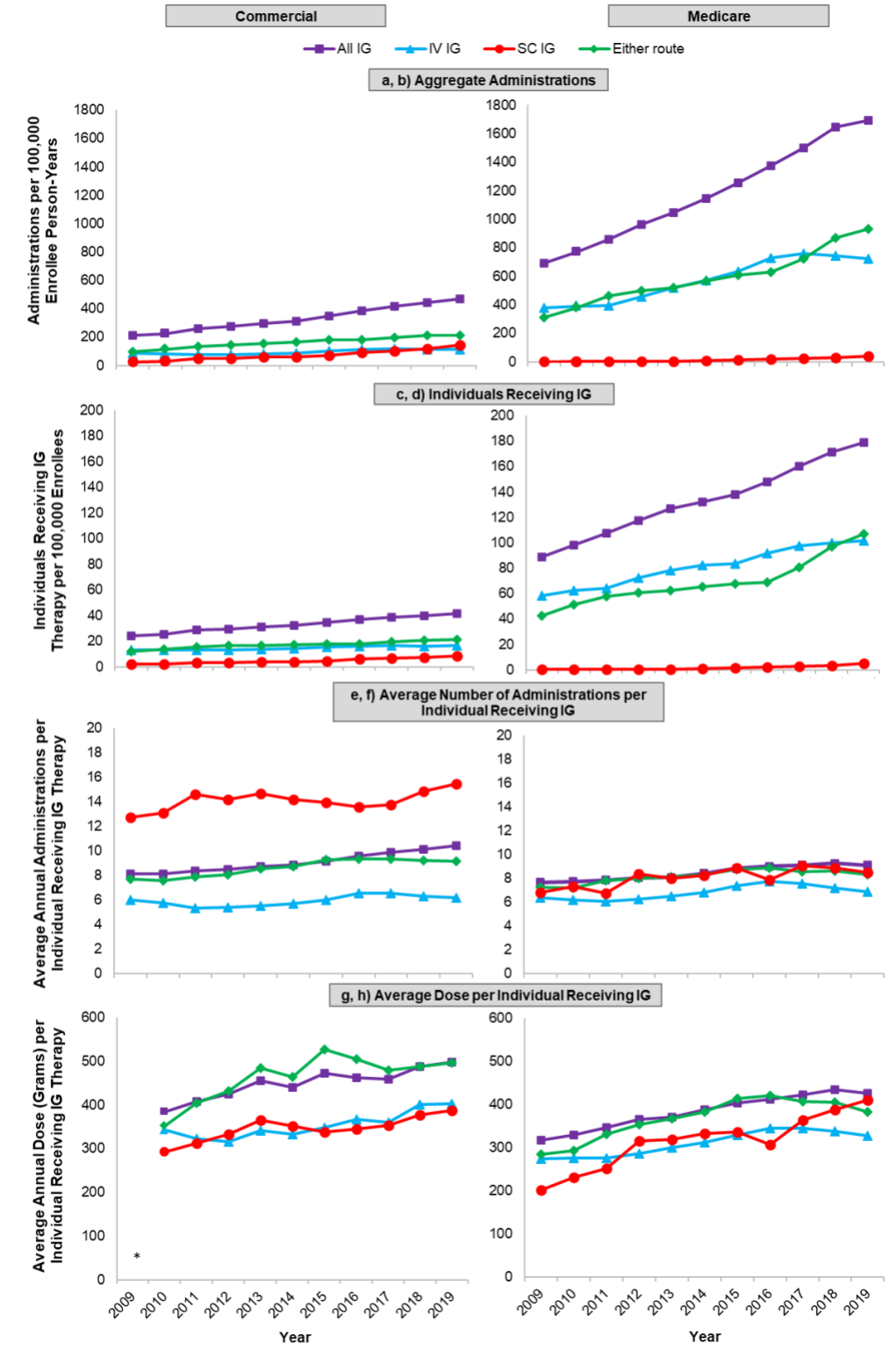
Notes: Location of residence is defined on the basis of core-based statistical areas specified by the Office of Management and Budget. Age is calculated as of the date of first enrollment. Region and location of residence are as of the first enrollment. Enrollee counts reflect all individuals enrolled with medical benefits (MarketScan) or Part A/Part B coverage (Medicare) for at least 1 day during 2009–2019. Individuals receiving IG therapy included individuals who received at least one administration of IG products of interest during 2009–2019.

* Characteristics are not applicable to the commercially insured population.

† Enrollees aged 65+ years were not included in the analysis of the commercially insured population.

Data sources: IBM MarketScan Commercial Database and Centers for Medicare & Medicaid Services Medicare Parts A/B fee-for-service and Part D prescription drug data, 2009–2019.

Figure 1. IG utilization, by route, among commercially insured and Medicare populations, 2009–2019



Abbreviations: IG, immune globulin; IV, intravenous; SC, subcutaneous.

Notes: "Either route" refers to IG products that may be administered either via the IV or SC route, including GAMMAGARD LIQUID, GAMMAKED, and GAMUNEX-C.

Panels a) and b): Administrations per 100,000 enrollee person-years was calculated by dividing the total IG administrations by the total person-years enrolled each year. The analysis was stratified by route of administration.

Panels c) and d): Individuals receiving IG therapy per 100,000 enrollees was calculated by dividing the number of individuals treated with IG by the total number of enrollees each year. The analysis was stratified by route of administration.

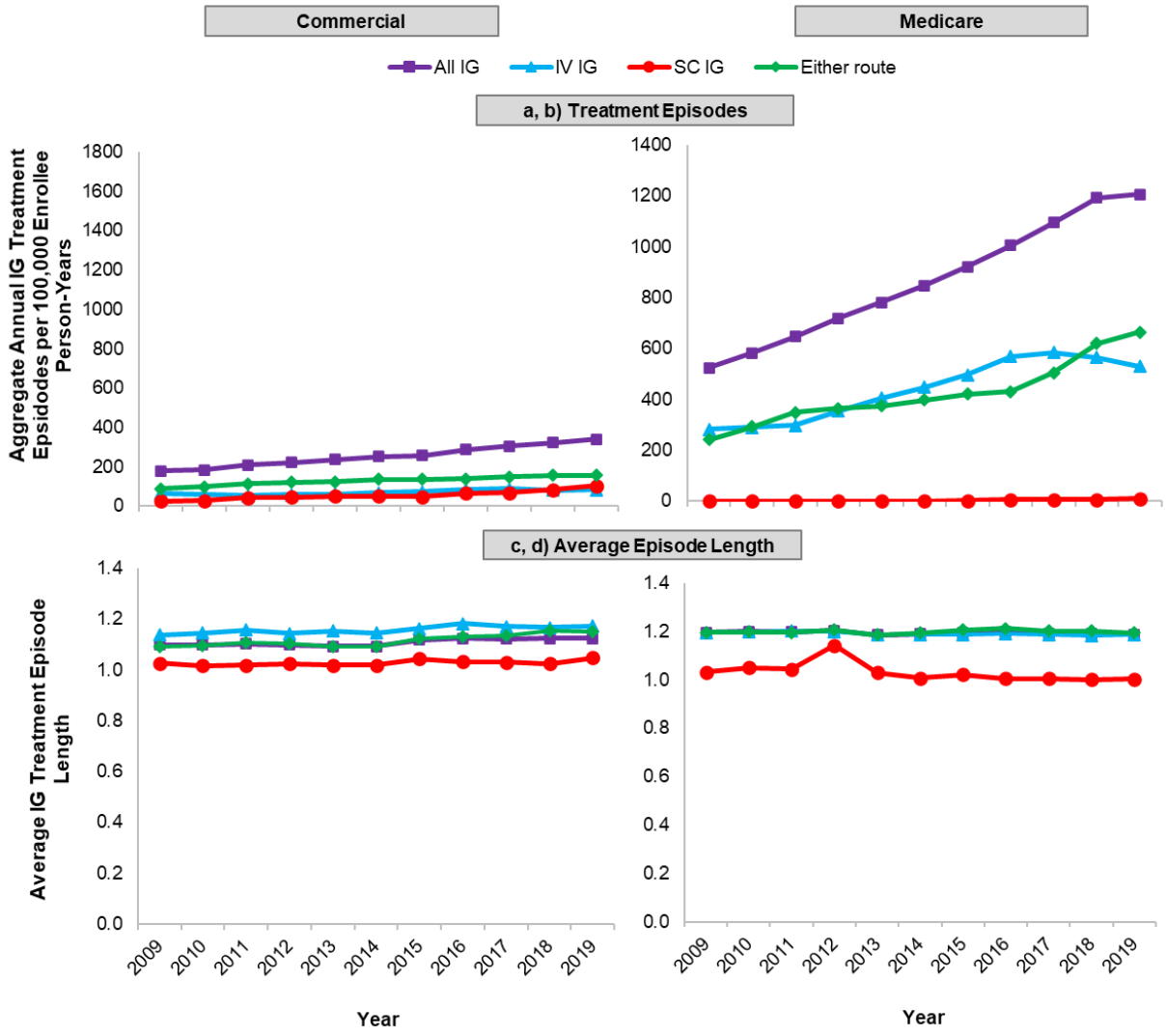
Panels e) and f): The individuals in this analysis were limited to those who had at least one IG administration in a given year. Average annual administrations per individual receiving IG therapy was calculated by dividing the number of IG administrations by the total person-years of IG-treated individuals each year. The analysis was stratified by route of administration.

Panels g) and h): The individuals in this analysis were limited to those who had complete dosage information in a given year. Average annual dose (grams) per individual receiving IG therapy was calculated by dividing the total grams infused or dispensed by the total person-years of IG-treated individuals each year. The analysis was stratified by route of administration.

* Dose information was not accurately collected in 2009 in the MarketScan data.

Data sources: IBM MarketScan Commercial Database and Centers for Medicare & Medicaid Services Medicare Parts A/B fee-for-service and Part D prescription drug data, 2009–2019.

Figure 2. IG utilization, at the episode level, among commercially insured and Medicare populations, 2009–2019



Abbreviations: IG, immune globulin; IV, intravenous; SC, subcutaneous.

Notes: "Either route" refers to IG products that may be administered via either the IV or SC route, including GAMMAGARD LIQUID, GAMMAKED, and GAMUNEX-C.

Panels a) and b): IG treatment episodes per 100,000 enrollee person-years was calculated by dividing the total IG treatment episodes by the total person-years enrolled each year. The analysis was stratified by route of administration.

Panels c) and d): Average treatment episode length was calculated by dividing the aggregate length of all treatment episodes (days) by the total number of treatment episodes each year. The analysis was stratified by route of administration.

Data sources: IBM MarketScan Commercial Database and Centers for Medicare & Medicaid Services Medicare Parts A/B fee-for-service and Part D prescription drug data, 2009–2019.

Table 3 (corresponding to Figures 1 and 2). IG utilization, by route, among commercially insured and Medicare populations, 2009 and 2019

Metric and route	Commercial							Medicare						
	2009*		2019		Absolute difference, 2009*–2019		Percentage difference, 2009*–2019	2009		2019		Absolute difference, 2009–2019		Percentage difference, 2009–2019
	N	%	N	%	N	%		N	%	N	%	N	%	
Administrations per 100,000 enrollee person-years[†]	**213.0**	**100.0**	**469.5**	**100.0**	**256.5**	**100.0**	**120.4**	**692.3**	**100.0**	**1,692.5**	**100.0**	**1,000.3**	**100.0**	**144.5**
IV	85.6	40.2	112.5	24.0	26.8	10.5	31.4	377.8	54.6	722.4	42.7	344.6	34.5	91.2
SC	28.2	13.2	143.8	30.6	115.6	45.1	409.6	2.1	0.3	43.3	2.6	41.2	4.1	1968.8
Either route	99.7	46.8	213.7	45.5	114.0	44.4	114.3	314.3	45.4	930.2	55.0	615.8	61.6	195.9
Individuals receiving IG therapy per 100,000 enrollees[‡]	**24.2**	**100.0**	**41.5**	**100.0**	**17.3**	**100.0**	**71.2**	**88.8**	**100.0**	**179.2**	**100.0**	**90.3**	**100.0**	**101.7**
IV	13.2	54.6	16.8	40.5	3.5	20.6	26.8	58.6	65.9	101.8	56.8	43.2	47.8	73.8
SC	2.0	8.3	8.6	20.6	6.5	37.9	324.9	0.3	0.3	4.9	2.7	4.6	5.1	1554.4
Either route	11.9	48.9	21.4	51.5	9.5	55.1	80.1	42.3	47.7	106.8	59.6	64.4	71.3	152.1
Average annual administrations per individual receiving IG therapy[§]	**8.1**	**N/A**	**10.4**	**N/A**	**2.3**	**N/A**	**28.4**	**7.7**	**N/A**	**9.1**	**N/A**	**1.4**	**N/A**	**18.9**
IV	6.0	N/A	6.2	N/A	0.2	N/A	3.3	6.3	N/A	6.8	N/A	0.5	N/A	7.9
SC	12.7	N/A	15.5	N/A	2.7	N/A	21.5	6.8	N/A	8.5	N/A	1.7	N/A	25.3
Either route	7.7	N/A	9.2	N/A	1.4	N/A	18.7	7.2	N/A	8.3	N/A	1.1	N/A	15.0
Average annual dose (grams) per individual receiving IG therapy*,‖	**384.3**	**N/A**	**497.2**	**N/A**	**113.0**	**N/A**	**29.4**	**317.2**	**N/A**	**426.1**	**N/A**	**108.9**	**N/A**	**34.3**
IV	342.9	N/A	402.8	N/A	59.9	N/A	17.5	273.7	N/A	328.1	N/A	54.4	N/A	19.9
SC	292.6	N/A	386.6	N/A	94.0	N/A	32.1	201.8	N/A	409.9	N/A	208.1	N/A	103.2
Either route	351.9	N/A	496.0	N/A	144.0	N/A	40.9	285.2	N/A	382.4	N/A	97.2	N/A	34.1
Average dose (grams) per IG administration*,‖	**43.4**	**N/A**	**45.3**	**N/A**	**1.9**	**N/A**	**4.3**	**37.8**	**N/A**	**45.5**	**N/A**	**7.7**	**N/A**	**20.3**
IV	45.2	N/A	51.8	N/A	6.6	N/A	14.7	36.3	N/A	43.4	N/A	7.1	N/A	19.7
SC	24.4	N/A	25.3	N/A	0.9	N/A	3.7	26.0	N/A	48.7	N/A	22.6	N/A	87.0
Either route	46.4	N/A	55.5	N/A	9.1	N/A	19.5	39.6	N/A	46.9	N/A	7.3	N/A	18.5

Metric and route	Commercial							Medicare						
	2009*		2019		Absolute difference, 2009*–2019		Percentage difference, 2009*–2019	2009		2019		Absolute difference, 2009–2019		Percentage difference, 2009–2019
	N	%	N	%	N	%		N	%	N	%	N	%	
Treatment episodes per 100,000 enrollee person-years**	**178.6**	**100.0**	**341.1**	**100.0**	**162.5**	**100.0**	**91.0**	**525.5**	**100.0**	**1,206.6**	**100.0**	**681.2**	**100.0**	**129.6**
IV	64.9	36.3	82.9	24.3	18.0	11.1	27.8	282.8	53.8	531.3	44.0	248.5	36.5	87.8
SC	25.4	14.2	102.9	30.2	77.5	47.7	304.8	0.4	0.1	10.8	0.9	10.4	1.5	2599.7
Either route	88.3	49.4	155.3	45.5	67.0	41.2	75.9	242.2	46.1	664.5	55.1	422.3	62.0	174.3
Average episode length††	**1.1**	**N/A**	**1.1**	**N/A**	**0.0**	**N/A**	**2.4**	**1.2**	**N/A**	**1.2**	**N/A**	**0.0**	**N/A**	**–0.6**
IV	1.1	N/A	1.2	N/A	0.0	N/A	3.1	1.2	N/A	1.2	N/A	0.0	N/A	–0.8
SC	1.0	N/A	1.0	N/A	0.0	N/A	2.2	1.0	N/A	1.0	N/A	0.0	N/A	–2.7
Either route	1.1	N/A	1.2	N/A	0.1	N/A	5.5	1.2	N/A	1.2	N/A	0.0	N/A	–0.2

Abbreviations: IG, immune globulin; IV, intravenous; N/A, not applicable; SC, subcutaneous.

Notes: "Either route" refers to IG products that may be administered either via the IV or SC route, including GAMMAGARD LIQUID, GAMMAKED, and GAMUNEX-C.

* Dose information was not accurately collected in 2009 in the MarketScan data; thus, for the commercially insured population, the average annual dose (grams) per individual receiving IG therapy is for 2010 instead of 2009.

† Administrations per 100,000 enrollee person-years was calculated by dividing the total IG administrations by the total person-years enrolled each year. The analysis was stratified by route of administration.

‡ Individuals receiving IG therapy per 100,000 enrollees was calculated by dividing the number of individuals treated with IG by the total number of enrollees each year. The analysis was stratified by route of administration.

§ The individuals in this analysis were limited to those who had at least one IG administration in a given year. Average annual administrations per individual receiving IG therapy was calculated by dividing the number of IG administrations by the total person-years of IG-treated individuals each year. The analysis was stratified by route of administration.

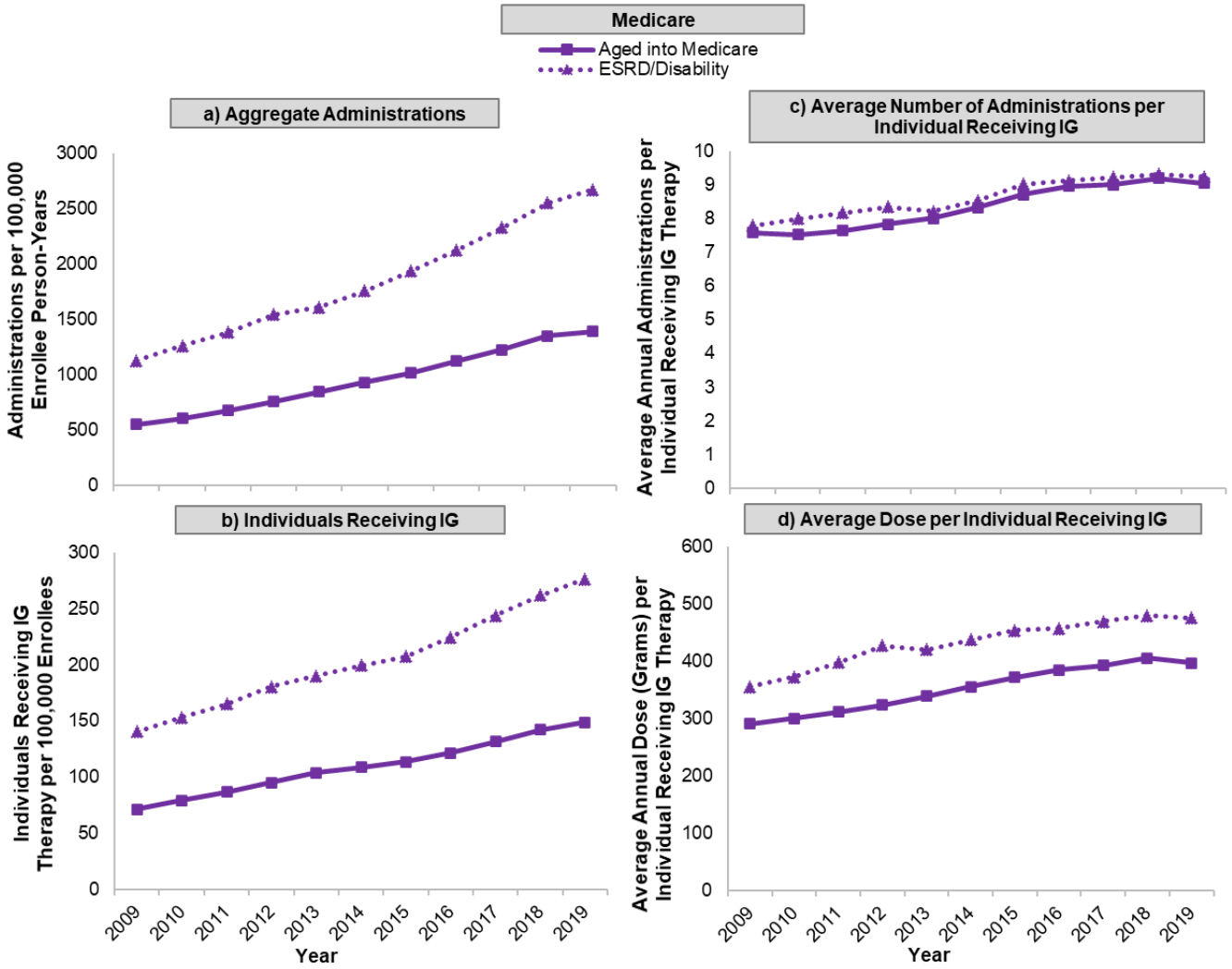
‖ The individuals in this analysis were limited to those who had complete dosage information in a given year. Average annual dose (grams) per individual receiving IG therapy was calculated by dividing the total grams infused or dispensed by the total person-years of IG-treated individuals each year. The analysis was stratified by route of administration. Average dose (grams) per administration was calculated by dividing the total grams infused or dispensed in the study population by the total number of IG administrations each year. The analysis was stratified by route of administration.

** IG treatment episodes per 100,000 enrollee person-years was calculated by dividing the total IG treatment episodes by the total person-years enrolled each year.

†† Average treatment episode length was calculated by dividing the aggregate length of all treatment episodes (days) by the total number of treatment episodes each year.

Data sources: IBM MarketScan Commercial Database and Centers for Medicare & Medicaid Services Medicare Parts A/B fee-for-service and Part D prescription drug data, 2009, 2010, 2019.

Figure 3. IG utilization, by reason for entry into Medicare, 2009–2019



Abbreviations: ESRD, end-stage renal disease; IG, immune globulin.

Panel a): Administrations per 100,000 enrollee person-years was calculated by dividing the total IG administrations by the total person-years enrolled each year.

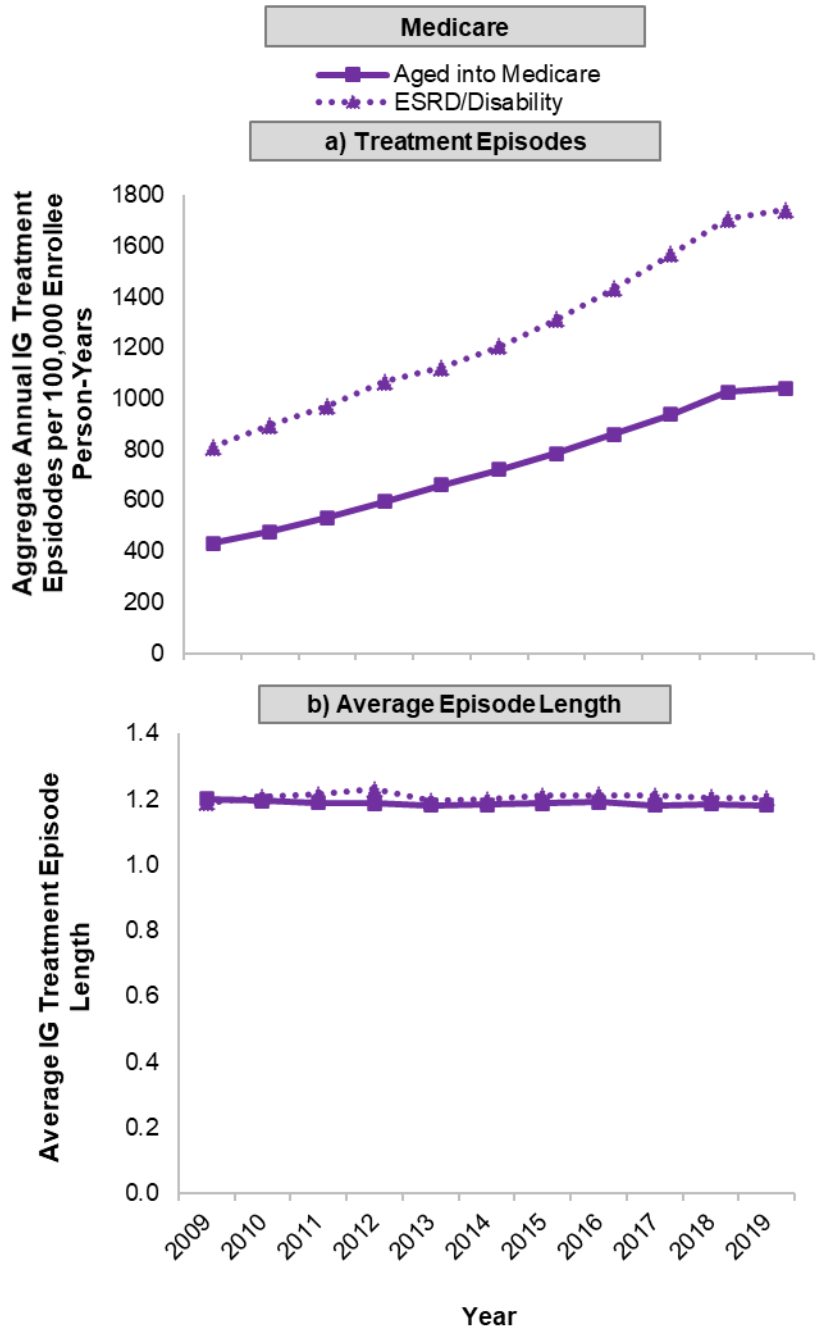
Panel b): Individuals receiving IG therapy per 100,000 enrollees was calculated by dividing the number of individuals treated with IG by the total number of enrollees each year.

Panel c): The individuals in this analysis were limited to those who had at least one IG administration in a given year. Average annual administrations per individual receiving IG therapy was calculated by dividing the number of IG administrations by the total person-years of IG-treated individuals each year.

Panel d): The individuals in this analysis were limited to those who had complete dosage information in a given year. Average annual dose (grams) per individual receiving IG therapy was calculated by dividing the total grams infused or dispensed by the total person-years of IG-treated individuals each year.

Data source: Centers for Medicare & Medicaid Services Medicare Parts A/B fee-for-service and Part D prescription drug data, 2009–2019.

Figure 4. IG utilization at the episode level, by reason for entry into Medicare, 2009–2019



Abbreviations: ESRD, end-stage renal disease; IG, immune globulin.

Panel a): IG treatment episodes per 100,000 enrollee person-years was calculated by dividing the total IG treatment episodes by the total person-years enrolled each year.

Panel b): Average treatment episode length was calculated by dividing the aggregate length of all treatment episodes (days) by the total number of treatment episodes each year.

Data source: Centers for Medicare & Medicaid Services Medicare Parts A/B fee-for-service and Part D prescription drug data, 2009–2019.

Table 4 (corresponding to Figures 3 and 4). IG utilization, by reason for entry into Medicare, 2009 and 2019

Metric and route	Aged into Medicare				ESRD/disability			
	2009	2019	Absolute difference, 2009–2019	Percentage difference, 2009–2019	2009	2019	Absolute difference, 2009–2019	Percentage difference, 2009–2019
Administrations per 100,000 enrollee person-years†	549.3	1,393.1	843.8	153.6	1,125.9	2,671.3	1,545.5	137.3
Individuals receiving IG therapy per 100,000 enrollees‡	71.4	148.7	77.3	108.2	140.7	276.4	135.7	96.5
Average annual administrations per individual receiving IG therapy§	7.6	9.0	1.5	19.2	7.8	9.2	1.4	18.6
Average annual dose (grams) per individual receiving IG therapy‖	291.9	398.0	106.1	36.4	356.6	476.1	119.5	33.5
Average dose (grams) per IG administration‖	35.4	43.1	7.7	21.7	41.5	49.7	8.3	20.0
Treatment episodes per 100,000 enrollee person-years**	431	1,042	611	141.6	811	1,744	933	115.1
Average episode length††	1.2	1.2	0.0	-1.6	1.2	1.2	0.0	1.1

Abbreviations: ESRD, end-stage renal disease; IG, immune globulin.

† Administrations per 100,000 enrollee person-years was calculated by dividing the total IG administrations by the total person-years enrolled each year. The analysis was stratified by route of administration.

‡ Individuals receiving IG therapy per 100,000 enrollees was calculated by dividing the number of individuals treated with IG by the total number of enrollees each year.

§ The individuals in this analysis were limited to those who had at least one IG administration in a given year. Average annual administrations per individual receiving IG therapy was calculated by dividing the number of IG administrations by the total person-years of IG-treated individuals each year.

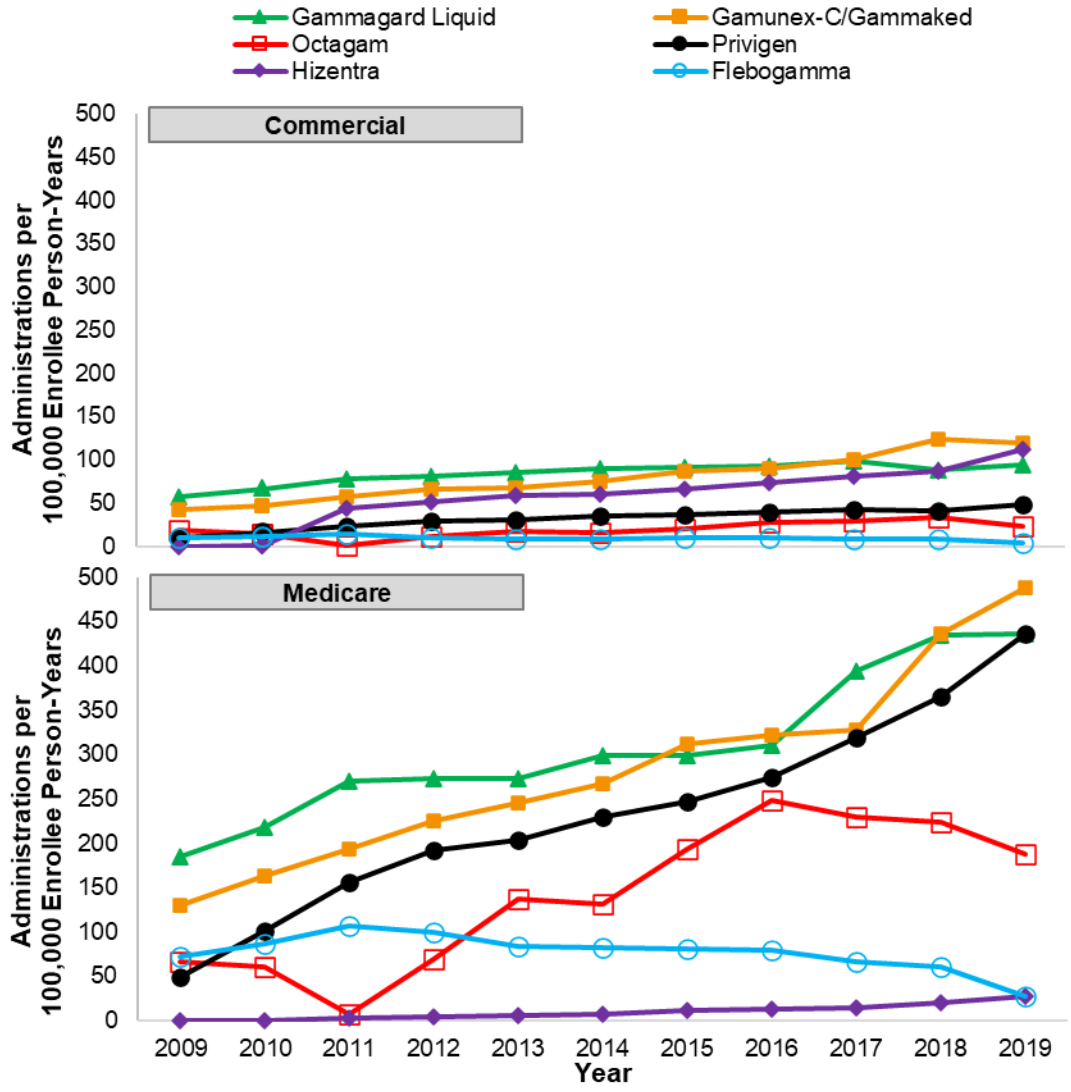
‖ The individuals in this analysis were limited to those who had complete dosage information in a given year. Average annual dose (grams) per individual receiving IG therapy was calculated by dividing the total grams infused or dispensed by the total person-years of IG-treated individuals each year. The analysis was stratified by route of administration. Average dose (grams) per administration was calculated by dividing the total grams infused or dispensed in the study population by the total number of IG administrations each year.

** IG treatment episodes per 100,000 enrollee person-years was calculated by dividing the total IG treatment episodes by the total person-years enrolled each year.

†† Average treatment episode length was calculated by dividing the aggregate length of all treatment episodes (days) by the total number of treatment episodes each year.

Data source: Centers for Medicare & Medicaid Services Medicare Parts A/B fee-for-service and Part D prescription drug data, 2009 and 2019.

Figure 5. IG utilization, by brand, among commercially insured and Medicare populations, 2009–2019



Abbreviation: IG, immune globulin.

Notes: Six brands (Gammagard Liquid, Gamunex C/Gammaked, Octogam, Privigen, Hizentra, Flebogamma) that covered 95% of usage were selected to report in this figure.

Administrations per 100,000 enrollee person-years was calculated by dividing the total IG administrations by the total person-years enrolled each year. The analysis was stratified by IG brands.

Data sources: IBM MarketScan Commercial Database and Centers for Medicare & Medicaid Services, Medicare Parts A/B fee-for-service and Part D prescription drug data, 2009–2019.

Table 5 (corresponding to Figure 5). IG utilization, by brand, among commercially insured and Medicare populations, 2009 and 2019

Metric and route	Commercial							Medicare						
	2009		2019		Absolute difference, 2009–2019		Percentage difference, 2009–2019	2009		2019		Absolute difference, 2009–2019		Percentage difference, 2009–2019
	N	%	N	%	N	%		N	%	N	%	N	%	
Administrations per 100,000 enrollee person-years*	**213**	**100.0**	**470**	**100.0**	**257**	**100.0**	**120.4**	**692**	**100.0**	**1,693**	**100.0**	**1,000**	**100.0**	**144.5**
Gammagard Liquid	57	26.7	95	20.2	38	14.8	66.7	185	26.8	436	25.7	250	25.0	135.1
Gamunex-C/Gammaked	43	20.1	119	25.3	76	29.6	177.4	130	18.7	488	28.8	358	35.8	276.6
Octagam	20	9.2	24	5.1	4	1.7	22.0	66	9.5	188	11.1	122	12.2	184.4
Privigen	11	4.9	49	10.3	38	14.8	361.4	49	7.1	435	25.7	386	38.6	785.7
Hizentra	0	0.0	112	23.8	112	43.5	—†	0	0.0	27	1.6	27	2.7	—†
Flebogamma	10	4.7	3	0.7	-7	-2.6	-66.6	73	10.5	28	1.7	-44	-4.4	-61.2

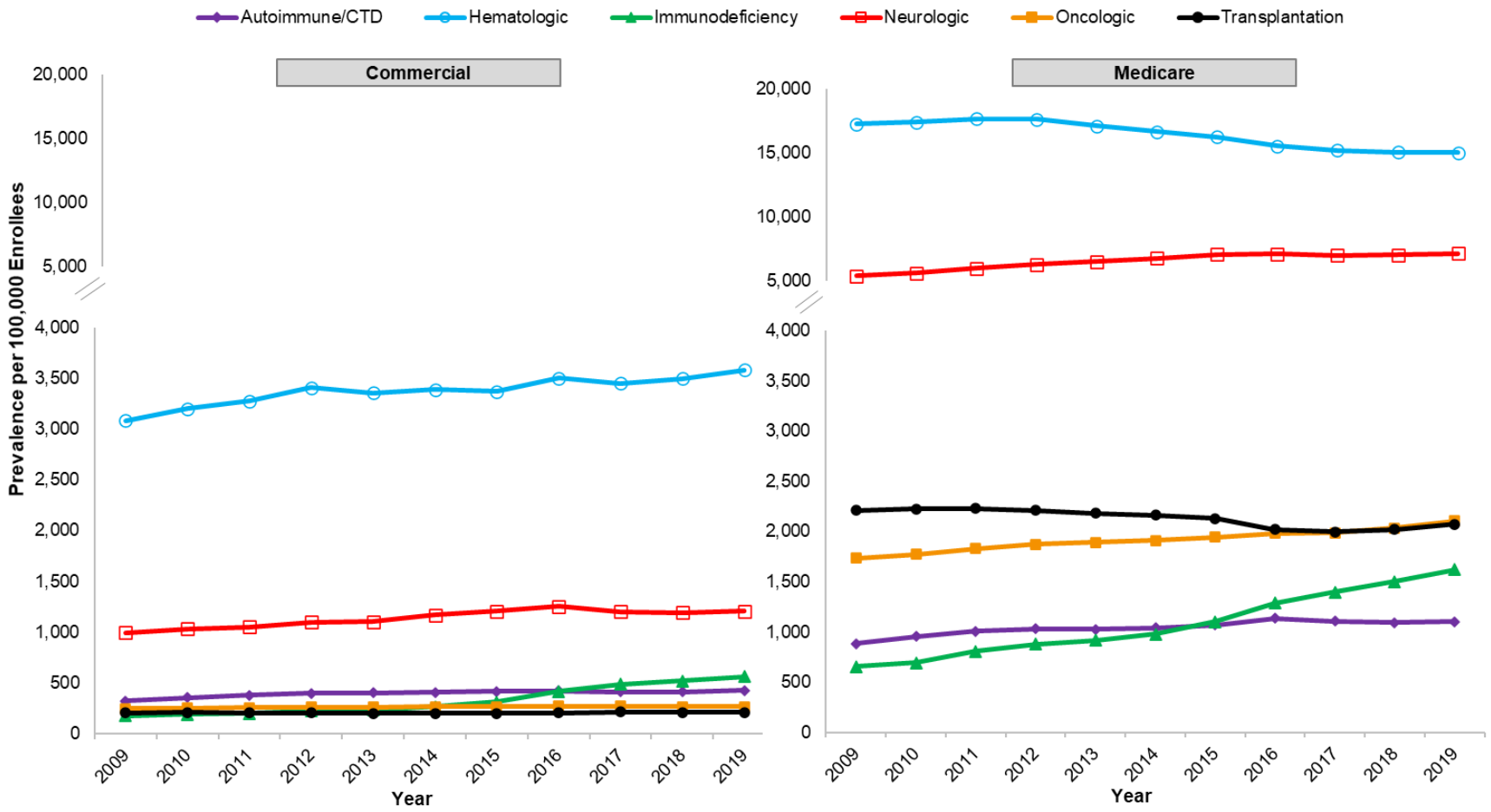
Abbreviation: IG, immune globulin.

* Administrations per 100,000 enrollee person-years was calculated by dividing the total IG administrations by the total person-years enrolled each year. The analysis was stratified by brand.

† Not calculated because there were zero administrations in 2009.

Data sources: IBM MarketScan Commercial Database and Centers for Medicare & Medicaid Services Medicare Parts A/B fee-for-service and Part D prescription drug data, 2009 and 2019.

Figure 6. Prevalence of condition categories per 100,000 enrollees in the commercially insured and Medicare populations, 2009–2019



Abbreviations: CTD, connective tissue disease; //, break in y-axis.

Data sources: IBM MarketScan Commercial Database and Centers for Medicare & Medicaid Services Medicare Parts A/B fee-for-service and Part D prescription drug data, 2009–2019.

Table 6 (corresponding to Figure 6). Prevalence of condition categories per 100,000 enrollees in the commercially insured and Medicare populations, 2009–2019

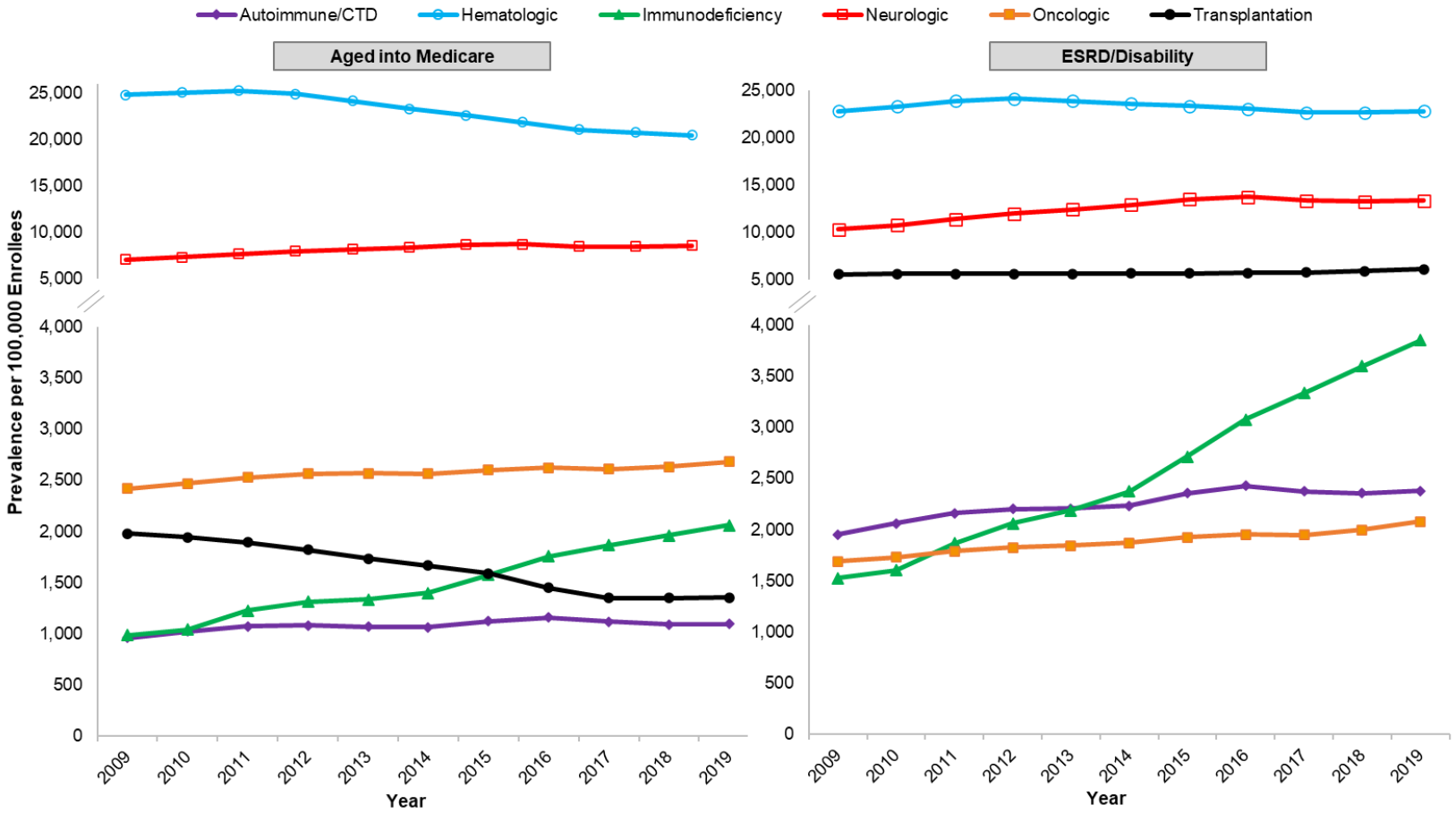
Condition	Commercial				Medicare			
	2009	2019	Absolute difference, 2009–2019	Percentage difference, 2009–2019	2009	2019	Absolute difference, 2009–2019	Percentage difference, 2009–2019
Prevalence per 100,000 enrollees								
Autoimmune/CTD	325	428	103	31.8	1,209	1,403	194	16.0
Hematologic	3,082	3,579	498	16.1	24,297	21,037	–3,260	–13.4
Immunodeficiency	180	565	386	214.3	1,122	2,488	1,366	121.8
Primary immune deficiency subset	20	85	65	325.4	56	133	77	136.8
Immunodeficiency (subsequent diagnosis)	72	249	177	245.2	—*	—*	—*	—*
Primary immune deficiency subset (subsequent diagnosis)	12	27	15	119.5	—*	—*	—*	—*
Neurologic	996	1,205	209	21.0	7,896	9,727	1,831	23.2
Oncologic	250	269	18	7.3	2,235	2,540	305	13.6
Transplantation	208	209	1	0.4	2,892	2,499	–393	–13.6

Abbreviation: CTD, connective tissue disease.

* Not calculated.

Data sources: IBM MarketScan Commercial Database and Centers for Medicare & Medicaid Services, Medicare Parts A/B fee-for-service and Part D prescription drug data, 2009 and 2019.

Figure 7. Prevalence of condition categories per 100,000 enrollees, by reason for entry into Medicare, 2009–2019



Abbreviations: CTD, connective tissue disease; ESRD, end-stage renal disease; //, break in y-axis.

Data source: Centers for Medicare & Medicaid Services Medicare Parts A/B fee-for-service and Part D prescription drug data, 2009–2019.

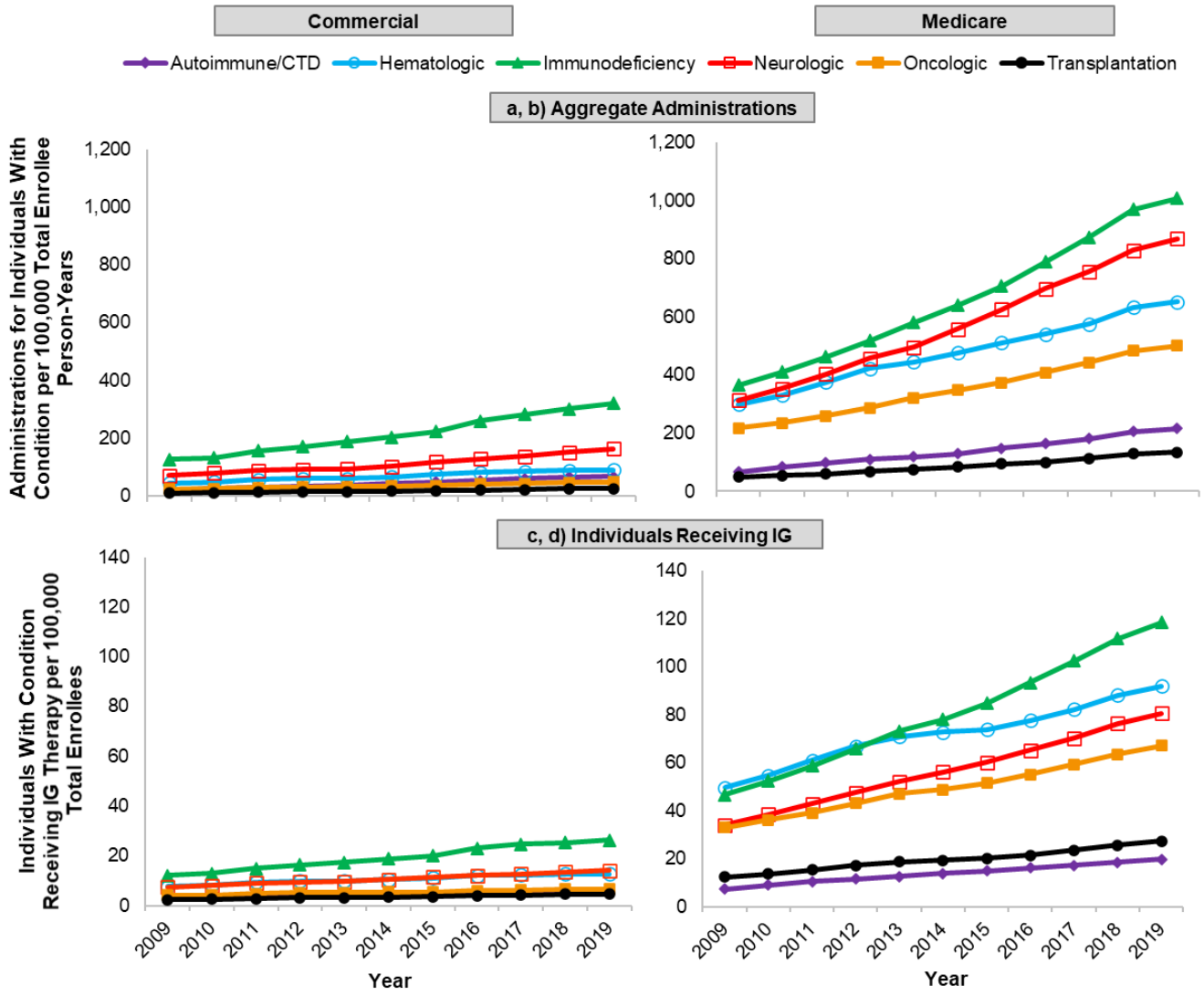
Table 7 (corresponding to Figure 7). Prevalence of condition categories per 100,000 enrollees by reason for entry into Medicare, 2009–2019

Condition	Aged into Medicare				ESRD/disability			
	2009	2019	Absolute difference, 2009–2019	Percentage difference, 2009–2019	2009	2019	Absolute difference, 2009–2019	Percentage difference, 2009–2019
Prevalence per 100,000 enrollees								
Autoimmune/CTD	958	1,096	138	14.4	1,954	2,380	426	21.8
Hematologic	24,781	20,466	–4,315	–17.4	22,855	22,857	2	0.0
Immunodeficiency	986	2,061	1,075	109.1	1,525	3,849	2,324	152.3
Primary immune deficiency subset	44	108	65	148.7	93	211	118	126.0
Neurologic	7,076	8,573	1,497	21.2	10,334	13,406	3,072	29.7
Oncologic	2,419	2,684	265	11.0	1,690	2,081	392	23.2
Transplantation	1,979	1,355	–624	–31.5	5,607	6,149	542	9.7

Abbreviations: CTD, connective tissue disease; ESRD, end-stage renal disease.

Data source: Centers for Medicare & Medicaid Services Medicare Parts A/B fee-for-service and Part D prescription drug data, 2009 and 2019.

Figure 8. IG utilization, by condition, among commercially insured and Medicare populations, 2009–2019



Abbreviations: IG, immune globulin; CTD, connective tissue disease.

Notes: Individuals were classified into condition categories of interest (autoimmune/CTD, hematologic, immunodeficiency, neurologic, oncologic, transplantation) based on diagnoses during the study period. Chronic conditions: A person's condition episode starts from the month of the first diagnosis in this condition category and extends 11 months afterward. At each subsequent diagnosis of the condition category, the episode will extend further to include the month of the diagnosis and the following 11 months. A condition episode would end 11 months after the month of a preceding diagnosis if no subsequent diagnosis was present during the 12th month after the preceding diagnosis. A condition may restart when another qualifying diagnosis was present. Acute conditions: Enrollees were assigned to the condition category for the month of diagnosis and 2 months after the diagnosis (except for Guillain-Barre syndrome, for which enrollees were assigned to the neurologic category from the month of diagnosis through 3 months after diagnosis). Individuals may be classified into more than one condition category.

Panels a) and b): Administrations per 100,000 enrollee person-years by condition was calculated by dividing the number of administrations received by individuals in each condition category by the total enrolled person-years in each year.

Panels c) and d): Individuals receiving IG therapy per 100,000 enrollee person-years by condition was calculated by dividing the number of individuals in each condition category treated with IG by the total enrolled individuals in each year.

Data sources: IBM MarketScan Commercial Database and Centers for Medicare & Medicaid Services Medicare Parts A/B fee-for-service and Part D prescription drug data, 2009–2019.

Table 8 (corresponding to Figure 8). IG utilization, by condition, among commercially insured and Medicare populations, 2009 and 2019

Metric and route	Commercial							Medicare						
	2009		2019		Absolute difference, 2009–2019		Percentage difference, 2009–2019	2009		2019		Absolute difference, 2009–2019		Percentage difference, 2009–2019
	N	%	N	%	N	%		N	%	N	%	N	%	
Administrations per 100,000 enrollee person-years*	**213**	**100.0**	**470**	**100.0**	**257**	**100.0**	**120.4**	**692**	**100.0**	**1,693**	**100.0**	**1,000**	**100.0**	**144.5**
Autoimmune/CTD	21	9.9	67	14.3	46	18.0	219.6	66	9.5	216	12.7	150	14.9	226.3
Hematologic	45	21.3	91	19.5	46	17.9	101.0	300	43.3	653	38.6	353	35.3	117.7
Immunodeficiency	127	59.5	321	68.4	195	75.9	153.5	365	52.8	1,007	59.5	642	64.2	175.8
Neurologic	72	33.9	163	34.8	91	35.6	126.6	313	45.2	868	51.3	555	55.5	177.4
Oncologic	25	11.7	49	10.4	24	9.4	96.9	217	31.4	501	29.6	284	28.4	130.6
Transplantation	11	5.2	26	5.5	15	5.8	134.3	50	7.3	135	8.0	85	8.5	168.5
Individuals receiving IG therapy per 100,000 enrollees†	**24**	**100.0**	**42**	**100.0**	**17**	**100.0**	**71.2**	**89**	**100.0**	**179**	**100.0**	**90**	**100.0**	**101.7**
Autoimmune/CTD	3	10.6	6	14.7	4	20.5	138.3	7	8.2	20	11.0	12	13.7	171.0
Hematologic	8	31.4	13	30.6	5	29.3	66.5	50	55.7	92	51.3	42	47.0	85.8
Immunodeficiency	12	50.4	26	63.6	14	82.1	116.0	47	52.6	118	66.1	72	79.3	153.5
Neurologic	7	30.9	14	34.3	7	39.2	90.4	34	38.4	81	45.0	47	51.5	136.3
Oncologic	4	17.3	7	16.2	3	14.6	60.5	33	37.0	67	37.5	34	37.9	104.0
Transplantation	2	10.2	5	11.2	2	12.6	88.2	12	13.9	27	15.2	15	16.5	120.5

Abbreviations: IG, immune globulin; CTD, connective tissue disease.

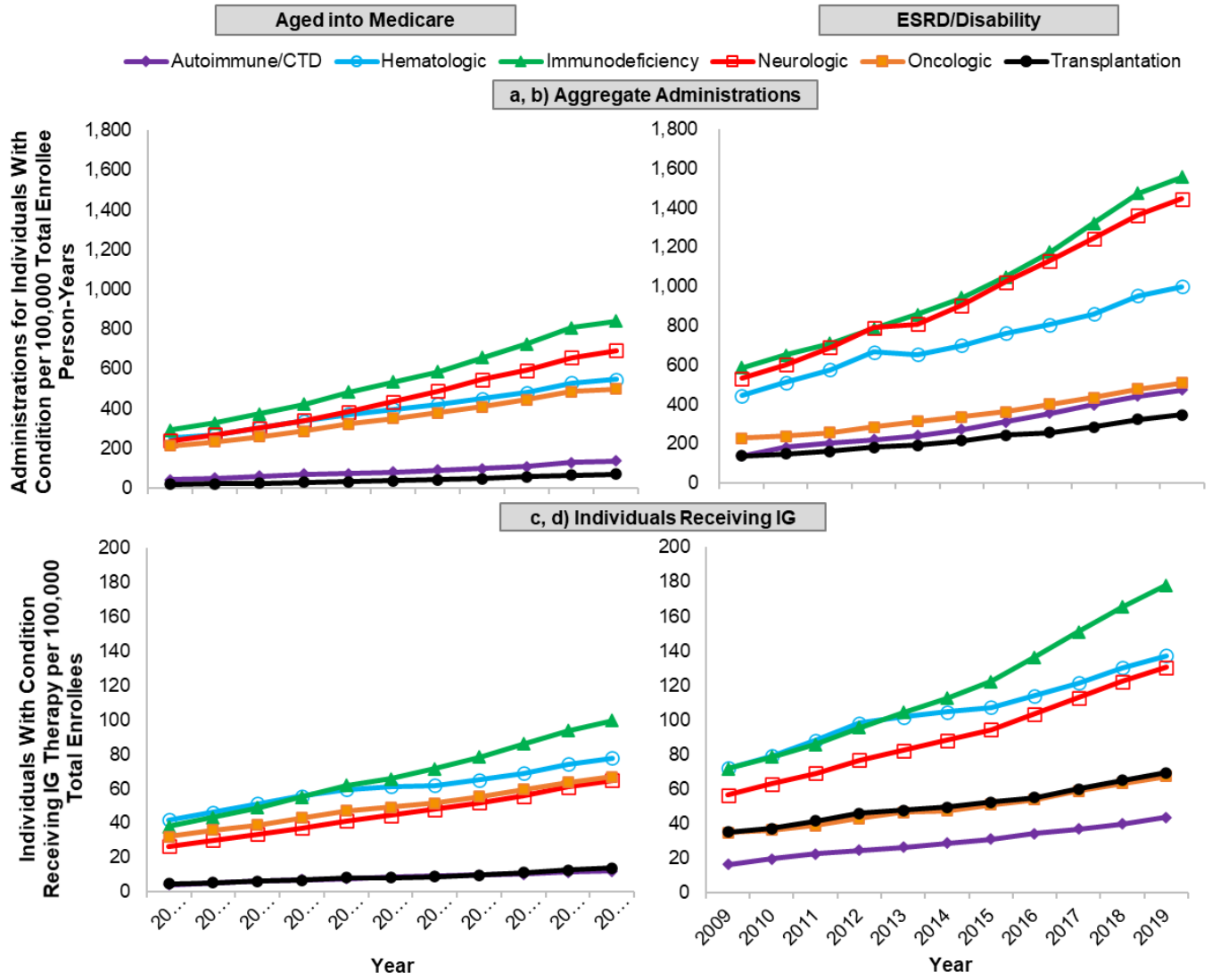
Notes: Individuals were classified into condition categories of interest (autoimmune/CTD, hematologic, immunodeficiency, neurologic, oncologic, transplantation) based on diagnoses during the study period. Chronic conditions: A person's condition episode starts from the month of the first diagnosis in this condition category and extends 11 months afterward. At each subsequent diagnosis of the condition category, the episode will extend further to include the month of the diagnosis and the following 11 months. A condition episode would end 11 months after the month of a preceding diagnosis if no subsequent diagnosis was present during the 12th month after the preceding diagnosis. A condition may restart when another qualifying diagnosis was present. Acute conditions: Enrollees were assigned to the condition category for the month of diagnosis and 2 months after the diagnosis (except for Guillain-Barre syndrome, for which enrollees were assigned to the neurologic category from the month of diagnosis through 3 months after diagnosis). Individuals may be classified into more than one condition category.

* Administrations per 100,000 enrollee person-years by condition was calculated by dividing the number of administrations received by individuals in each condition category by the total enrolled person-years in each year.

† Individuals receiving IG therapy per 100,000 enrollee person-years by condition was calculated by dividing the number of individuals in each condition category treated with IG by the total enrolled individuals in each year.

Data sources: IBM MarketScan Commercial Database and Centers for Medicare & Medicaid Services Medicare Parts A/B fee-for-service and Part D prescription drug data, 2009 and 2019.

Figure 9. IG utilization, by condition and reason for entry into Medicare, 2009–2019



Abbreviations: CTD, connective tissue disease; ESRD, end-stage renal disease; IG, immune globulin.

Notes: Individuals were classified into condition categories of interest (autoimmune/CTD, hematologic, immunodeficiency, neurologic, oncologic, transplantation) based on diagnoses during the study period. Chronic conditions: A person's condition episode starts from the month of the first diagnosis in this condition category and extends 11 months afterward. At each subsequent diagnosis of the condition category, the episode will extend further to include the month of the diagnosis and the following 11 months. A condition episode would end 11 months after the month of a preceding diagnosis if no subsequent diagnosis was present during the 12th month after the preceding diagnosis. A condition may restart when another qualifying diagnosis was present. Acute conditions: Enrollees were assigned to the condition category for the month of diagnosis and 2 months after the diagnosis (except for Guillain-Barre syndrome, for which enrollees were assigned to the neurologic category from the month of diagnosis through 3 months after diagnosis). Individuals may be classified into more than one condition category.

Panels a) and b): Administrations per 100,000 enrollee person-years by condition was calculated by dividing the number of administrations received by individuals in each condition category by the total enrolled person-years in each year.

Panels c) and d): Individuals receiving IG therapy per 100,000 enrollee person-years by condition was calculated by dividing the number of individuals in each condition category treated with IG by the total enrolled individuals in each year.

Data source: Centers for Medicare & Medicaid Services Medicare Parts A/B fee-for-service and Part D prescription drug data, 2009–2019.

Table 9 (corresponding to Figure 9). IG utilization, by condition and reason for entry into the Medicare population, 2009 and 2019

Metric and route	Aged into Medicare							ESRD/disability						
	2009		2019		Absolute difference, 2009–2019		Percentage difference, 2009–2019	2009		2019		Absolute difference, 2009–2019		Percentage difference, 2009–2019
	N	%	N	%	N	%		N	%	N	%	N	%	
Administrations per 100,000 enrollee person-years*	**549.3**	**100.0**	**1,393.1**	**100.0**	**843.8**	**100.0**	**153.6**	**1,125.9**	**100.0**	**2,671.3**	**100.0**	**1,545.5**	**100.0**	**137.3**
Autoimmune/CTD	42.5	7.7	136.8	9.8	94.3	11.2	222.0	137.7	12.2	473.3	17.7	335.7	21.7	243.9
Hematologic	252.0	45.9	546.3	39.2	294.4	34.9	116.8	444.8	39.5	1,000.4	37.4	555.6	36.0	124.9
Immunodeficiency	291.7	53.1	839.5	60.3	547.8	64.9	187.8	588.1	52.2	1,555.6	58.2	967.6	62.6	164.5
Neurologic	240.1	43.7	691.7	49.7	451.6	53.5	188.1	533.5	47.4	1,444.2	54.1	910.8	58.9	170.7
Oncologic	213.9	38.9	498.8	35.8	285.0	33.8	133.2	228.3	20.3	509.6	19.1	281.4	18.2	123.3
Transplantation	21.0	3.8	70.4	5.1	49.3	5.8	234.7	139.0	12.3	346.3	13.0	207.3	13.4	149.2
Individuals receiving IG therapy per 100,000 enrollees†	**71.4**	**100.0**	**148.7**	**100.0**	**77.3**	**100.0**	**108.2**	**140.7**	**100.0**	**276.4**	**100.0**	**135.7**	**100.0**	**96.5**
Autoimmune/CTD	4.2	5.9	12.1	8.2	7.9	10.2	187.6	16.3	11.6	43.6	15.8	27.3	20.1	168.1
Hematologic	41.9	58.7	77.8	52.4	36.0	46.5	85.9	72.3	51.4	137.2	49.6	64.9	47.8	89.9
Immunodeficiency	38.2	53.5	99.6	67.0	61.4	79.5	160.9	72.0	51.2	178.2	64.5	106.2	78.2	147.5
Neurologic	26.6	37.2	65.0	43.7	38.5	49.8	144.7	56.6	40.3	130.6	47.2	73.9	54.5	130.6
Oncologic	32.2	45.1	67.0	45.1	34.8	45.0	108.1	34.9	24.8	67.5	24.4	32.5	24.0	93.0
Transplantation	4.6	6.5	14.0	9.4	9.3	12.1	200.9	35.2	25.0	69.4	25.1	34.1	25.2	96.9

Abbreviations: CTD, connective tissue disease; ESRD, end-stage renal disease; IG, immune globulin.

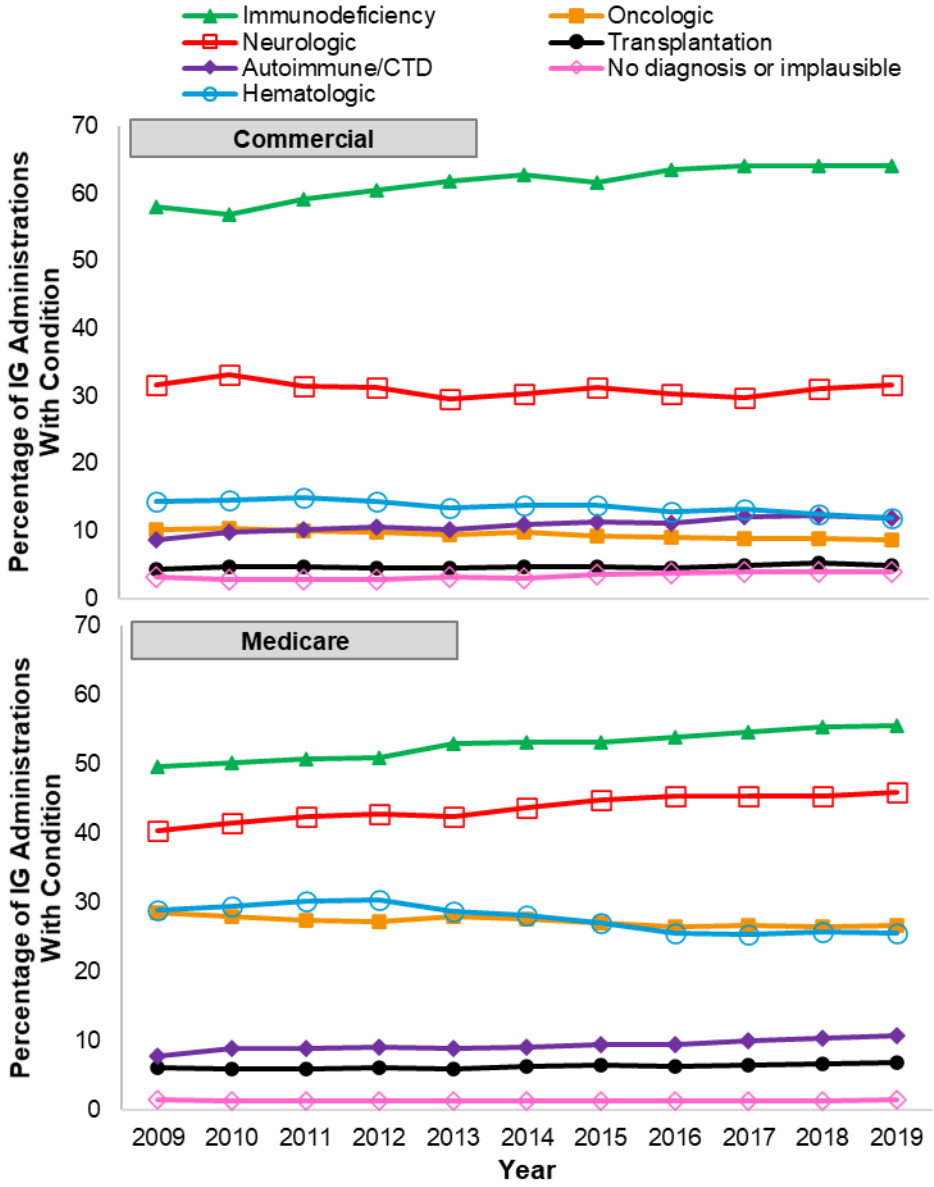
Notes: Individuals were classified into condition categories of interest (autoimmune/CTD, hematologic, immunodeficiency, neurologic, oncologic, transplantation) based on diagnoses during the study period. Chronic conditions: A person's condition episode starts from the month of the first diagnosis in this condition category and extends 11 months afterward. At each subsequent diagnosis of the condition category, the episode will extend further to include the month of the diagnosis and the following 11 months. A condition episode would end 11 months after the month of a preceding diagnosis if no subsequent diagnosis was present during the 12th month after the preceding diagnosis. A condition may restart when another qualifying diagnosis was present. Acute conditions: Enrollees were assigned to the condition category for the month of diagnosis and 2 months after the diagnosis (except for Guillain-Barre syndrome, for which enrollees were assigned to the neurologic category from the month of diagnosis through 3 months after diagnosis). Individuals may be classified into more than one condition category.

* Administrations per 100,000 enrollee person-years by condition was calculated by dividing the number of administrations received by individuals in each condition category by the total enrolled person-years in each year.

† Individuals receiving IG therapy per 100,000 enrollee person-years by condition was calculated by dividing the number of individuals in each condition category treated with IG by the total enrolled individuals in each year.

Data source: Centers for Medicare & Medicaid Services Medicare Parts A/B fee-for-service and Part D prescription drug data, 2009 and 2019.

Figure 10. Proportion of IG administrations received by individuals with plausible condition categories for commercially insured and Medicare populations, 2009–2019



Abbreviations: CTD, connective tissue disease; IG, immune globulin.

The proportion of administrations classified into each condition category of interest (autoimmune/CTD, hematologic, immunodeficiency, neurologic, oncologic, transplantation) is reported, among commercially insured (a) and Medicare fee-for-service (b) populations. Administrations of individuals who had continuous enrollment from –90 days to +30 days around the administrations were included for each calendar year. The administrations were classified into six condition categories based on the presence of diagnoses of the individuals during the –90 to +30 days around the administrations. A single administration may be cross-classified into more than one of the condition categories. If no diagnoses were present or none of the diagnoses fell into the condition categories of interest during the range of –90 to +30 days around the administrations, administrations were classified into the "no diagnosis or implausible" category.

Data sources: IBM MarketScan Commercial Database and Centers for Medicare & Medicaid Services Medicare Parts A/B fee-for-service and Part D prescription drug data, 2009–2019.

Table 10 (corresponding to Figure 10). Proportion of IG administrations with select health conditions, among commercially insured and Medicare populations, 2009 and 2019

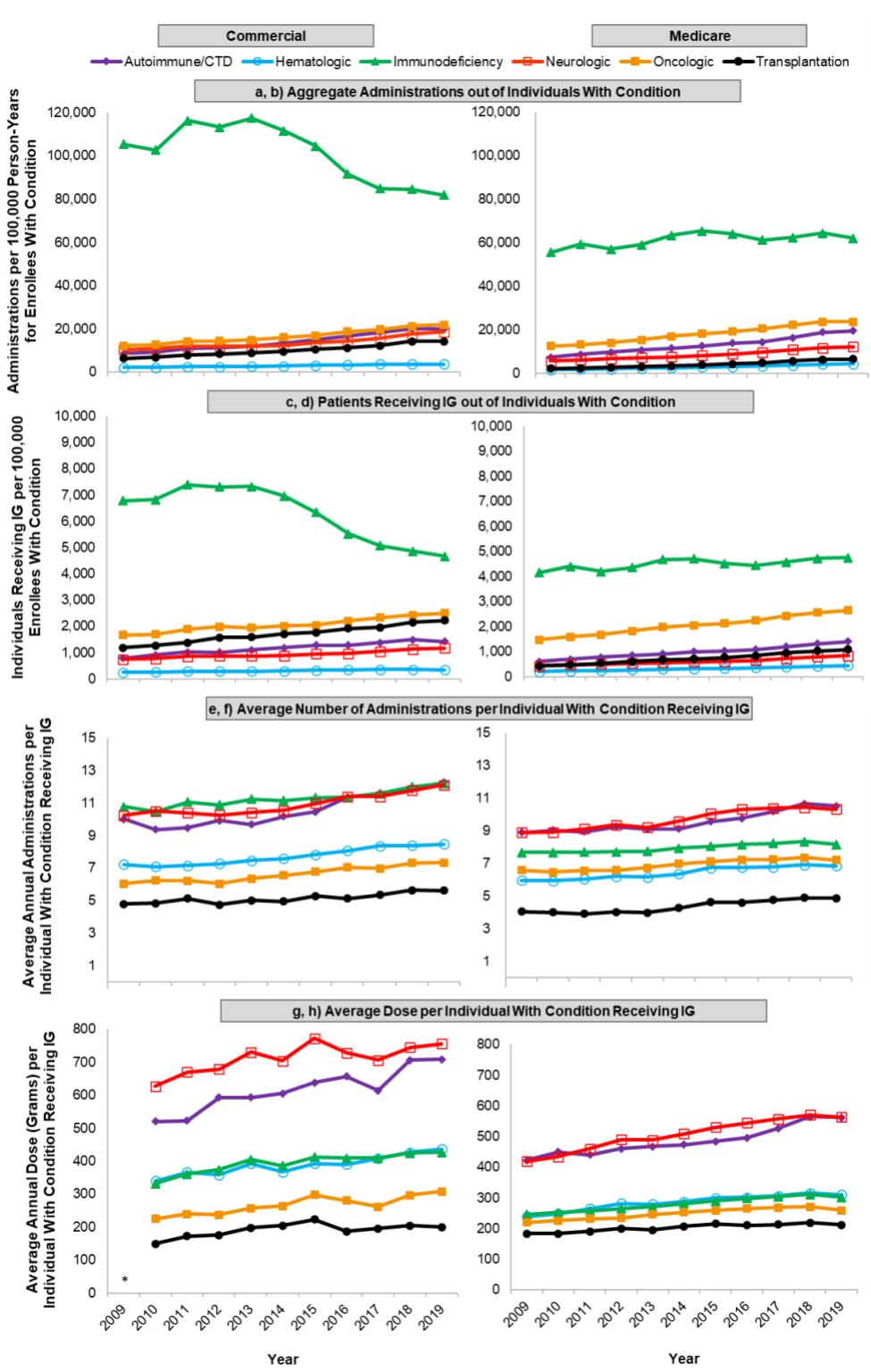
Condition category	Commercial				Medicare			
	Administrations classified into condition category, %		Increase in share, pp	Increase in share, %	Administrations classified into condition category, %		Increase in share, pp	Increase in share, %
	2009	2019			2009	2019		
Autoimmune/CTD	8.6	11.9	3.2	37.4	7.7	10.6	2.9	37.8
Hematologic	14.4	11.9	–2.5	–17.2	28.8	25.6	–3.2	–11.1
Immunodeficiency	58.0	64.0	6.0	10.3	49.6	55.4	5.8	11.7
Neurologic	31.6	31.7	0.1	0.4	40.4	45.9	5.5	13.6
Oncologic	10.2	8.6	–1.5	–15.0	28.5	26.7	–1.8	–6.3
Transplantation	4.4	4.8	0.5	10.4	6.0	6.7	0.7	11.9
No diagnosis or implausible	3.2	3.9	0.7	22.6	1.4	1.5	0.1	6.7

Abbreviations: CTD, connective tissue disease; IG, immune globulin; pp, percentage points.

The proportion of administrations classified into each condition category of interest (autoimmune/CTD, hematologic, immunodeficiency, neurologic, oncologic, transplantation) is reported, among commercially insured (a) and Medicare fee-for-service (b) populations. Administrations of individuals who had continuous enrollment from –90 days to +30 days around the administrations were included for each calendar year. The administrations were classified into six condition categories based on the presence of diagnoses of the individuals during the –90 to +30 days around the administrations. A single administration may be cross-classified into more than one of the condition categories. If no diagnoses were present or none of the diagnoses fell into the condition categories of interest during the range of –90 to +30 days around the administrations, administrations were classified into the "no diagnosis or implausible" category.

Data sources: IBM MarketScan Commercial Database and Centers for Medicare & Medicaid Services Medicare Parts A/B fee-for-service and Part D prescription drug data, 2009 and 2019.

Figure 11. IG utilization among individuals with plausible conditions in commercially insured and Medicare populations, 2009–2019



Abbreviations: CTD, connective tissue disease; IG, immune globulin.

Notes: Individuals were classified into condition categories of interest (autoimmune/CTD, hematologic, immunodeficiency, neurologic, oncologic, transplantation) based on diagnoses during the study period. Chronic conditions: A person's condition

episode starts from the month of the first diagnosis in this condition category and extends 11 months afterward. At each subsequent diagnosis of the condition category, the episode will extend further to include the month of the diagnosis and the following 11 months. A condition episode would end 11 months after the month of a preceding diagnosis if no subsequent diagnosis was present during the 12th month after the preceding diagnosis. A condition may restart when another qualifying diagnosis was present. Acute conditions: Enrollees were assigned to the condition category for the month of diagnosis and 2 months after the diagnosis (except for Guillain-Barre syndrome, for which enrollees were assigned to the neurologic category from the month of diagnosis through 3 months after diagnosis). Individuals may be classified into more than one condition category.

Panels a) and b): Administrations per 100,000 person-years for enrollees with condition was calculated by dividing the number of administrations received by individuals in each condition category by the total person-years of individuals in the same condition category in each year.

Panels c) and d): Individuals receiving IG therapy per 100,000 enrollees with condition was calculated by dividing the number of individuals in each condition category treated with IG by the total enrolled individuals in the same condition category in each year.

Panels e) and f): The individuals in this analysis were limited to those who had at least one IG administration in a given year. Average annual administrations per individual receiving IG therapy was calculated by dividing the number of IG administrations received among individuals in a condition category by the total person-years of IG-treated individuals in the same condition category in each year.

Panels g) and h): The individuals in this analysis were limited to those who had full dosage information in a given year. Average annual dose (grams) per individual receiving IG therapy was calculated by dividing the total grams infused or dispensed to individuals in a condition category by the total person-years of IG-treated individuals in the same condition category in each year.

* Dose information was not accurately collected in 2009 in the MarketScan data.

Data sources: IBM MarketScan Commercial Database and Centers for Medicare & Medicaid Services Medicare Parts A/B fee-for-service and Part D prescription drug data, 2009–2019.

Table 11 (corresponding to Figure 11). IG utilization among individuals with plausible IG conditions in commercially insured and Medicare populations, 2009–2019

Metric and condition	Commercial				Medicare			
	2009*	2019	Absolute difference, 2009*–2019	Percentage difference, 2009*–2019	2009	2019	Absolute difference, 2009–2019	Percentage difference, 2009–2019
Administrations per 100,000 person-years for enrollees with condition†								
Autoimmune/CTD	8,545	20,013	11,468	134.2	7,468	19,561	12,093	161.9
Hematologic	2,225	3,771	1,546	69.5	1,738	4,349	2,611	150.3
Immunodeficiency	105,400	81,832	–23,568	–22.4	55,569	62,056	6,487	11.7
Neurologic	10,387	18,606	8,218	79.1	5,826	12,201	6,375	109.4
Oncologic	12,337	22,025	9,688	78.5	12,519	23,784	11,265	90.0
Transplantation	6,407	14,394	7,987	124.7	2,273	6,510	4,237	186.5
Individuals receiving IG per 100,000 enrollees with condition‡								
Autoimmune/CTD	789	1,428	638	80.9	600	1,401	801	133.5
Hematologic	247	354	107	43.3	204	437	234	114.6
Immunodeficiency	6,794	4,670	–2,125	–31.3	4,162	4,757	595	14.3
Neurologic	751	1,182	431	57.4	432	829	397	91.9
Oncologic	1,671	2,499	827	49.5	1,472	2,643	1,171	79.6
Transplantation	1,185	2,221	1,036	87.5	427	1,089	662	155.1
Average annual administrations per individual with condition receiving IG§								
Autoimmune/CTD	10.0	12.3	2.2	22.3	8.9	10.5	1.6	18.2
Hematologic	7.2	8.5	1.3	17.4	6.0	6.8	0.9	14.8
Immunodeficiency	10.8	12.2	1.4	13.2	7.7	8.2	0.5	6.6
Neurologic	10.2	12.1	1.9	18.4	8.9	10.3	1.4	16.0
Oncologic	6.1	7.3	1.3	21.1	6.6	7.2	0.6	9.5
Transplantation	4.8	5.6	0.8	17.1	4.0	4.9	0.8	20.3
Average annual dose (grams) per individual with condition receiving IG *,‖								
Autoimmune/CTD	520.1	709.3	189.1	36.4	422.6	562.4	139.8	33.1
Hematologic	339.4	436.4	97.1	28.6	239.3	310.4	71.1	29.7
Immunodeficiency	332.1	426.5	94.4	28.4	246.0	301.7	55.8	22.7
Neurologic	627.7	756.4	128.7	20.5	418.7	563.8	145.2	34.7
Oncologic	225.7	307.9	82.2	36.4	220.0	259.1	39.1	17.8
Transplantation	149.6	200.3	50.7	33.9	183.1	211.9	28.8	15.7

Metric and condition	Commercial				Medicare			
	2009*	2019	Absolute difference, 2009*–2019	Percentage difference, 2009*–2019	2009	2019	Absolute difference, 2009–2019	Percentage difference, 2009–2019
Average dose (grams) per IG administration*,‖								
Autoimmune/CTD	54.6	56.7	2.1	3.8	44.4	53.1	8.7	19.6
Hematologic	43.7	47.4	3.6	8.3	36.6	43.5	6.9	18.9
Immunodeficiency	32.3	34.9	2.6	8.1	31.5	37.0	5.5	17.4
Neurologic	58.1	63.4	5.2	9.0	43.2	53.8	10.6	24.5
Oncologic	35.7	40.4	4.7	13.1	32.5	35.9	3.4	10.5
Transplantation	29.3	35.4	6.1	20.8	39.0	39.7	0.7	1.8

Abbreviations: CTD, connective tissue disease; IG, immune globulin.

Notes: Individuals were classified into condition categories of interest (autoimmune/CTD, hematologic, immunodeficiency, neurologic, oncologic, transplantation) based on diagnoses during the study period. Chronic conditions: A person's condition episode starts from the month of the first diagnosis in this condition category and extends 11 months afterward. At each subsequent diagnosis of the condition category, the episode will extend further to include the month of the diagnosis and the following 11 months. A condition episode would end 11 months after the month of a preceding diagnosis if no subsequent diagnosis was present during the 12th month after the preceding diagnosis. A condition may restart when another qualifying diagnosis was present. Acute conditions: Enrollees were assigned to the condition category for the month of diagnosis and 2 months after the diagnosis (except for Guillain-Barre syndrome, for which enrollees were assigned to the neurologic category from the month of diagnosis through 3 months after diagnosis). Individuals may be classified into more than one condition category.

* Dose information was not accurately collected in 2009 in the MarketScan data; thus, for the commercially insured population, the average annual dose (grams) per individual receiving IG therapy is for 2010 instead of 2009.

† Administrations per 100,000 person-years for enrollees with condition was calculated by dividing the number of administrations received by individuals in each condition category by the total person-years of individuals in the same condition category in each year.

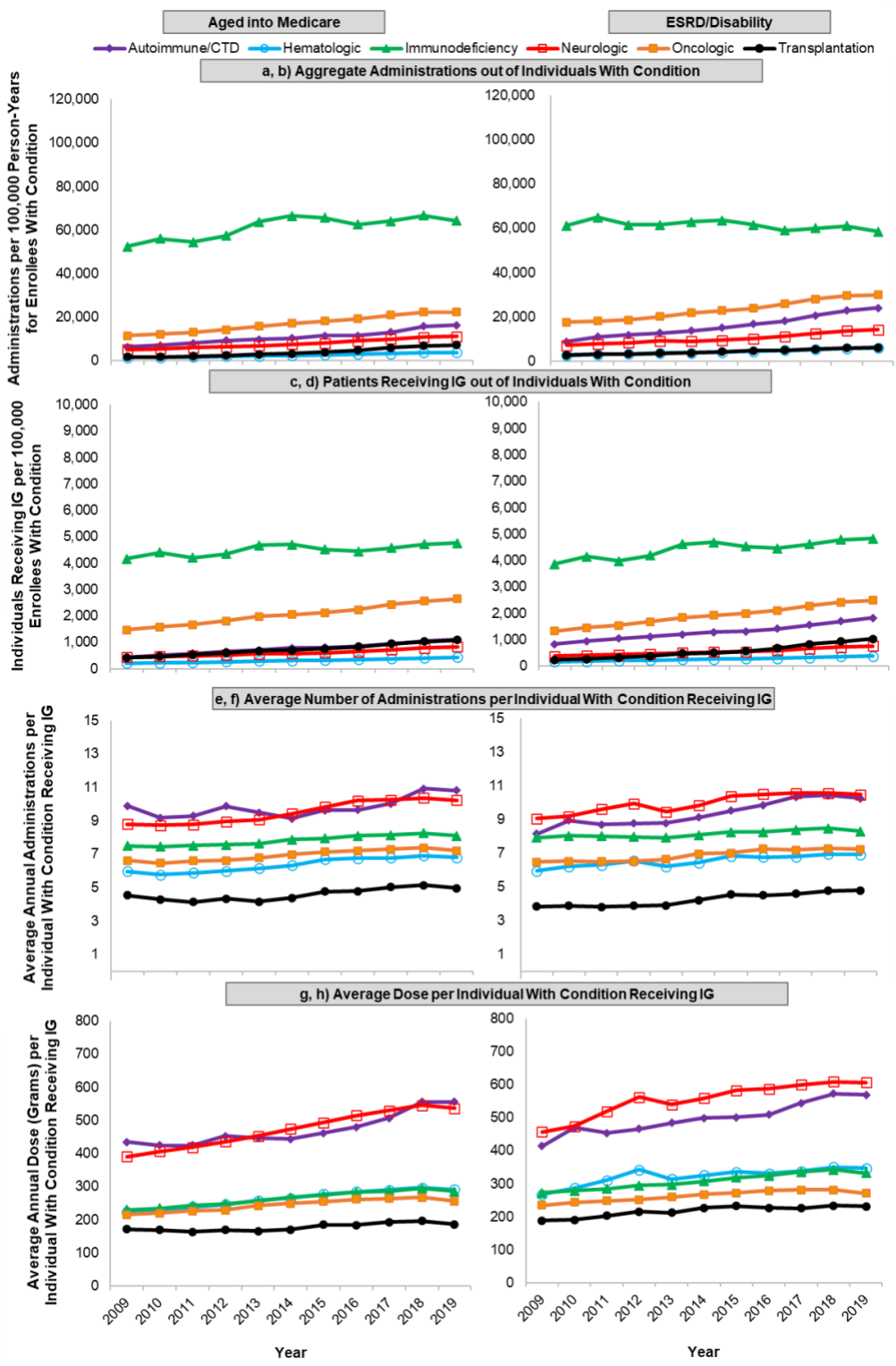
‡ Individuals receiving IG therapy per 100,000 enrollees with condition was calculated by dividing the number of individuals in each condition category treated with IG by the total enrolled individuals in the same condition category in each year.

§ The individuals in this analysis were limited to those who had at least one IG administration in a given year. Average annual administrations per individual receiving IG therapy was calculated by dividing the number of IG administrations received among individuals in a condition category by the total person-years of IG-treated individuals in the same condition category in each year.

‖ The individuals in this analysis were limited to those who had full dosage information in a given year. Average annual dose (grams) per individual receiving IG therapy was calculated by dividing the total grams infused or dispensed to individuals in a condition category by the total person-years of IG-treated individuals in the same condition category in each year. Average dose (grams) per administration was calculated by dividing the total grams infused or dispensed in the study population by the total number of IG administrations each year. The analysis was stratified by route of administration.

Data sources: IBM MarketScan Commercial Database and Centers for Medicare & Medicaid Services Medicare Parts A/B fee-for-service and Part D prescription drug data, 2009–2019.

Figure 12. IG utilization among individuals with plausible IG conditions, by reason for entry into Medicare, 2009–2019



Abbreviations: CTD, connective tissue disease; ESRD, end-stage renal disease; IG, immune globulin.

Notes: Individuals were classified into condition categories of interest (autoimmune/CTD, hematologic, immunodeficiency, neurologic, oncologic, transplantation) based on diagnoses during the study period. Chronic conditions: A person's condition

episode starts from the month of the first diagnosis in this condition category and extends 11 months afterward. At each subsequent diagnosis of the condition category, the episode will extend further to include the month of the diagnosis and the following 11 months. A condition episode would end 11 months after the month of a preceding diagnosis if no subsequent diagnosis was present during the 12th month after the preceding diagnosis. A condition may restart when another qualifying diagnosis was present. Acute conditions: Enrollees were assigned to the condition category for the month of diagnosis and 2 months after the diagnosis (except for Guillain-Barre syndrome, for which enrollees were assigned to the neurologic category from the month of diagnosis through 3 months after diagnosis). Individuals may be classified into more than one condition category.

Panels a) and b): Administrations per 100,000 person-years for enrollees with condition was calculated by dividing the number of administrations received by individuals in each condition category by the total person-years of individuals in the same condition category in each year.

Panels c) and d): Individuals receiving IG therapy per 100,000 enrollees with condition was calculated by dividing the number of individuals in each condition category treated with IG by the total enrolled individuals in the same condition category in each year.

Panels e) and f): The individuals in this analysis were limited to those who had at least one IG administration in a given year. Average annual administrations per individual receiving IG therapy was calculated by dividing the number of IG administrations received among individuals in a condition category by the total person-years of IG-treated individuals in the same condition category in each year.

Panels g) and h): The individuals in this analysis were limited to those who had full dosage information in a given year. Average annual dose (grams) per individual receiving IG therapy was calculated by dividing the total grams infused or dispensed to individuals in a condition category by the total person-years of IG-treated individuals in the same condition category in each year.

Data source: Centers for Medicare & Medicaid Services, Medicare Parts A/B fee-for-service and Part D prescription drug data, 2009–2019.

Table 12 (corresponding to Figure 12). IG utilization among individuals with plausible IG conditions, by reason for entry into Medicare, 2009–2019

Metric and condition	Aged into Medicare				ESRD/disability			
	2009	2019	Absolute difference, 2009–2019	Percentage difference, 2009–2019	2009	2019	Absolute difference, 2009–2019	Percentage difference, 2009–2019
Administrations per 100,000 person-years for enrollees with condition[†]								
Autoimmune/CTD	6,358.9	16,324.5	9,965.5	156.7	8,924.5	24,067.	15,142.9	169.7
Hematologic	1,436.6	3,752.0	2,315.4	161.2	2,714.4	6,073.0	3,358.6	123.7
Immunodeficiency	52,337.3	64,232.8	11,895.5	22.7	61,259.8	58,554.	–2,705.0	–4.4
Neurologic	5,095.0	11,146.6	6,051.6	118.8	7,244.2	14,320.	7,076.7	97.7
Oncologic	11,356.8	22,322.7	10,965.8	96.6	17,650.0	30,087.	12,437.6	70.5
Transplantation	1,556.5	7,128.2	5,571.7	358.0	2,880.3	6,155.1	3,274.9	113.7
Individuals receiving IG per 100,000 enrollees with condition[‡]								
Autoimmune/CTD	440.5	1,107.2	666.7	151.4	831.9	1,831.5	999.6	120.2
Hematologic	169.0	380.4	211.4	125.1	316.1	600.1	284.0	89.8
Immunodeficiency	3,872.8	4,832.4	959.6	24.8	4,718.1	4,628.7	–89.3	–1.9
Neurologic	375.5	758.5	383.0	102.0	547.9	973.9	425.9	77.7
Oncologic	1,331.5	2,496.9	1,165.4	87.5	2,068.3	3,241.5	1,173.2	56.7
Transplantation	234.9	1,032.4	797.5	339.5	628.2	1,128.3	500.0	79.6
Average annual administrations per individual with condition receiving IG[§]								
Autoimmune/CTD	9.9	10.8	0.9	9.3	8.1	10.3	2.1	26.0
Hematologic	6.0	6.8	0.8	13.8	5.9	6.9	1.0	16.5
Immunodeficiency	7.5	8.1	0.6	8.0	7.9	8.3	0.4	4.6
Neurologic	8.8	10.2	1.4	16.4	9.0	10.5	1.4	15.8
Oncologic	6.6	7.2	0.6	8.8	6.5	7.2	0.7	11.5
Transplantation	4.5	5.0	0.4	9.3	3.9	4.8	0.9	24.6
Average annual dose (grams) per individual with condition receiving IG [‖]								
Autoimmune/CTD	434.0	555.2	121.2	27.9	413.7	568.9	155.2	37.5
Hematologic	223.6	291.0	67.4	30.1	267.4	346.9	79.5	29.7
Immunodeficiency	229.5	285.3	55.8	24.3	272.7	332.4	59.7	21.9
Neurologic	390.7	536.4	145.7	37.3	457.3	607.1	149.9	32.8
Oncologic	214.7	255.4	40.8	19.0	234.7	271.1	36.4	15.5
Transplantation	171.2	185.6	14.4	8.4	188.5	231.1	42.6	22.6

Metric and condition	Aged into Medicare				ESRD/disability			
	2009	2019	Absolute difference, 2009–2019	Percentage difference, 2009–2019	2009	2019	Absolute difference, 2009–2019	Percentage difference, 2009–2019
Average dose (grams) per IG administration[‖]								
Autoimmune/CTD	42.0	51.1	9.1	21.6	46.7	55.1	8.4	17.9
Hematologic	34.4	41.3	6.9	20.2	40.4	47.4	7.0	17.2
Immunodeficiency	30.1	35.4	5.3	17.5	33.6	39.8	6.2	18.5
Neurologic	40.5	51.3	10.8	26.7	46.9	57.7	10.8	22.9
Oncologic	31.5	35.3	3.8	12.1	35.1	37.5	2.4	6.9
Transplantation	34.5	35.5	1.0	3.0	41.2	42.5	1.3	3.3

Abbreviations: CTD, connective tissue disease; ESRD, end-stage renal disease; IG, immune globulin.

Notes: Individuals were classified into condition categories of interest (autoimmune/CTD, hematologic, immunodeficiency, neurologic, oncologic, transplantation) based on diagnoses during the study period. Chronic conditions: A person's condition episode starts from the month of the first diagnosis in this condition category and extends 11 months afterward. At each subsequent diagnosis of the condition category, the episode will extend further to include the month of the diagnosis and the following 11 months. A condition episode would end 11 months after the month of a preceding diagnosis if no subsequent diagnosis was present during the 12th month after the preceding diagnosis. A condition may restart when another qualifying diagnosis was present. Acute conditions: Enrollees were assigned to the condition category for the month of diagnosis and 2 months after the diagnosis (except for Guillain-Barre syndrome, for which enrollees were assigned to the neurologic category from the month of diagnosis through 3 months after diagnosis). Individuals may be classified into more than one condition category.

[†] Administrations per 100,000 person-years for enrollees with condition was calculated by dividing the number of administrations received by individuals in each condition category by the total person-years of individuals in the same condition category in each year.

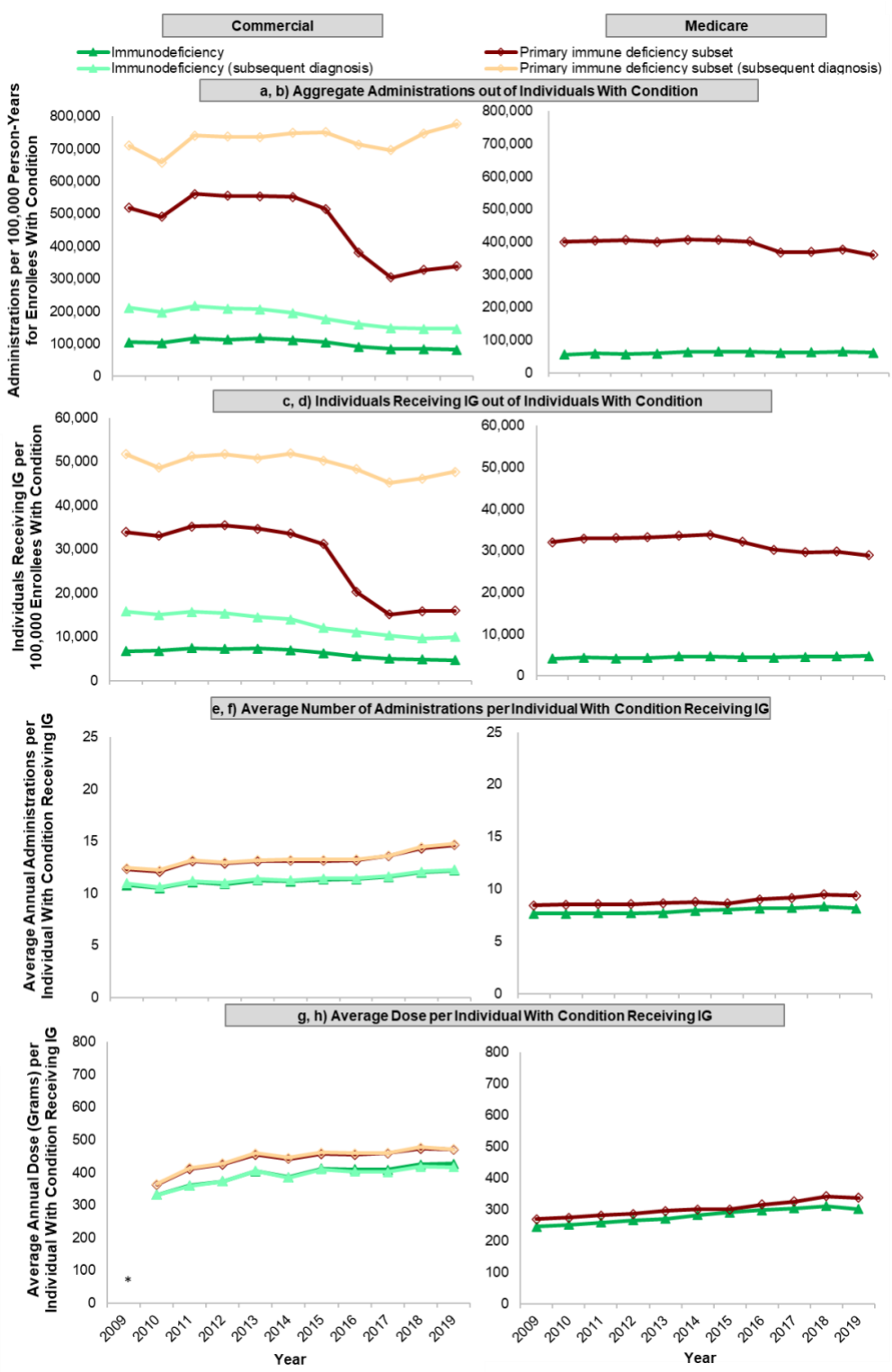
[‡] Individuals receiving IG therapy per 100,000 enrollees with condition was calculated by dividing the number of individuals in each condition category treated with IG by the total enrolled individuals in the same condition category in each year.

[§] The individuals in this analysis were limited to those who had at least one IG administration in a given year. Average annual administrations per individual receiving IG therapy was calculated by dividing the number of IG administrations received among individuals in a condition category by the total person-years of IG-treated individuals in the same condition category in each year.

[‖] The individuals in this analysis were limited to those who had full dosage information in a given year. Average annual dose (grams) per individual receiving IG therapy was calculated by dividing the total grams infused or dispensed to individuals in a condition category by the total person-years of IG-treated individuals in the same condition category in each year. Average dose (grams) per administration was calculated by dividing the total grams infused or dispensed in the study population by the total number of IG administrations each year.

Data source: Centers for Medicare & Medicaid Services, Medicare Parts A/B fee-for-service and Part D prescription drug data, 2009–2019.

Figure 13. IG utilization among individuals with immunodeficiency and primary immunodeficiency in commercially insured and Medicare populations, 2009–2019



Abbreviation: IG, immune globulin.

Notes: Individuals were classified into condition categories of interest (autoimmune/CTD, hematologic, immunodeficiency, neurologic, oncologic, transplantation) based on diagnoses during the study period. Chronic conditions: A person's condition

episode starts from the month of the first diagnosis in this condition category and extends 11 months afterward. At each subsequent diagnosis of the condition category, the episode will extend further to include the month of the diagnosis and the following 11 months. A condition episode would end 11 months after the month of a preceding diagnosis if no subsequent diagnosis was present during the 12th month after the preceding diagnosis. A condition may restart when another qualifying diagnosis was present. Acute conditions: Enrollees were assigned to the condition category for the month of diagnosis and 2 months after the diagnosis (except for Guillain-Barre syndrome, for which enrollees were assigned to the neurologic category from the month of diagnosis through 3 months after diagnosis). Individuals may be classified into more than one condition category.

Panels a) and b): Administrations per 100,000 person-years for enrollees with condition was calculated by dividing the number of administrations received by individuals in each condition category by the total person-years of individuals in the same condition category in each year. In the commercially insured population (panel a), additional analyses were conducted by limiting the person-years of enrollees with primary immunodeficiency (yellow line) and immunodeficiency (light green line) conditions to those with a subsequent diagnosis of the condition at least 14 days after the initial diagnosis.

Panels c) and d): Individuals receiving IG therapy per 100,000 enrollees with condition was calculated by dividing the number of individuals in each condition category treated with IG by the total enrolled individuals in the same condition category in each year. In the commercially insured population (panel c), additional analyses were conducted by limiting the enrollees with primary immunodeficiency (yellow line) and immunodeficiency (light green line) conditions to those with a subsequent diagnosis of the condition at least 14 days after the initial diagnosis.

Panels e) and f): The individuals in this analysis were limited to those who had at least one IG administration in a given year. Average annual administrations per individual receiving IG therapy was calculated by dividing the number of IG administrations received among individuals in a condition category by the total person-years of IG-treated individuals in the same condition category in each year. In the commercially insured population (panel e), additional analyses were conducted by further limiting the IG-treated individuals with primary immunodeficiency (yellow line) and immunodeficiency (light green line) conditions to those with a subsequent diagnosis of the condition at least 14 days after the initial diagnosis.

Panels g) and h): The individuals in this analysis were limited to those who had full dosage information in a given year. Average annual dose (grams) per individual receiving IG therapy was calculated by dividing the total grams infused or dispensed to individuals in a condition category by the total person-years of IG-treated individuals in the same condition category in each year. In the commercially insured population (panel g), additional analyses were conducted by further limiting the IG-treated individuals with primary immunodeficiency (yellow line) and immunodeficiency (light green line) conditions to those with a subsequent diagnosis of the condition at least 14 days after the initial diagnosis.

* Dose information was not accurately collected in 2009 in the MarketScan data.

Data sources: IBM MarketScan Commercial Database and Centers for Medicare & Medicaid Services Medicare Parts A/B fee-for-service and Part D prescription drug data, 2009–2019.

Table 13 (corresponding to Figure 13). IG utilization among individuals with immunodeficiency and primary immunodeficiency in commercially insured and Medicare populations, 2009 and 2019

Metric and condition	Commercial				Medicare			
	2009*	2019	Absolute difference, 2009*–2019	Percentage difference, 2009*–2019	2009	2019	Absolute difference, 2009–2019	Percentage difference, 2009–2019
Administrations per 100,000 person-years for enrollees with condition[†]								
Immunodeficiency	105,400	81,832	–23,568	–22.4	55,569	62,056	6,487	11.7
Primary immune deficiency subset	518,747	338,732	–180,015	–34.7	400,673	360,302	–40,372	–10.1
Immunodeficiency (subsequent diagnosis)	211,222	146,866	–64,356	–30.5	—**	—**	—**	—**
Primary immune deficiency subset (subsequent diagnosis)	709,808	776,669	66,861	9.4	—**	—**	—**	—**
Individuals receiving IG per 100,000 enrollees with condition[‡]								
Immunodeficiency	6,794	4,670	–2,125	–31.3	4,162	4,757	595	14.3
Primary immune deficiency subset	33,929	15,979	–17,950	–52.9	32,043	28,963	–3,080	–9.6
Immunodeficiency (subsequent diagnosis)	15,825	10,003	–5,822	–36.8	—**	—**	—**	—**
Primary immune deficiency subset (subsequent diagnosis)	51,734	47,742	–3,992	–7.7	—**	—**	—**	—**
Average annual administrations per individual with condition receiving IG[§]								
Immunodeficiency	10.8	12.2	1.4	13.2	7.7	8.2	0.5	6.6
Primary immune deficiency subset	12.3	14.6	2.3	18.7	8.5	9.4	0.9	10.9
Immunodeficiency (subsequent diagnosis)	11.0	12.3	1.3	11.9	—**	—**	—**	—**
Primary immune deficiency subset (subsequent diagnosis)	12.5	14.7	2.3	18.3	—**	—**	—**	—**
Average annual dose (grams) per individual with condition receiving IG*,‖								
Immunodeficiency	332	426	94	28.4	246	302	56	22.7
Primary immune deficiency subset	362	471	108	29.8	269	337	67	25.0
Immunodeficiency (subsequent diagnosis)	332	417	84	25.4	—**	—**	—**	—**
Primary immune deficiency subset (subsequent diagnosis)	365	472	107	29.4	—**	—**	—**	—**

Abbreviation: IG, immune globulin.

Notes: Individuals were classified into condition categories of interest (autoimmune/CTD, hematologic, immunodeficiency, neurologic, oncologic, transplantation) based on diagnoses during the study period. Chronic conditions: A person's condition episode starts from the month of the first diagnosis in this condition category and extends 11 months afterward. At each subsequent diagnosis of the condition category, the episode will extend further to include the month of the diagnosis and the following 11 months. A condition episode would end 11 months after the month of a preceding diagnosis if no subsequent diagnosis was present during the 12th month after the preceding diagnosis. A condition may restart when another qualifying diagnosis was present. Acute conditions: Enrollees were assigned to the condition category for the month of diagnosis and 2 months after the diagnosis (except for Guillain-Barre syndrome, for which enrollees were assigned to the neurologic category from the month of diagnosis through 3 months after diagnosis). Individuals may be classified into more than one condition category.

* Dose information was not accurately collected in 2009 in the MarketScan data; thus, for the commercially insured population, the average annual dose (grams) per individual receiving IG therapy is for 2010 instead of 2009.

† Administrations per 100,000 person-years for enrollees with condition was calculated by dividing the number of administrations received by individuals in each condition category by the total person-years of individuals in the same condition category in each year. In the commercially insured population, additional analyses were conducted by limiting the person-years of enrollees with primary immunodeficiency and immunodeficiency conditions to those with a subsequent diagnosis of the condition at least 14 days after the initial diagnosis.

‡ Individuals receiving IG therapy per 100,000 enrollees with condition was calculated by dividing the number of individuals in each condition category treated with IG by the total enrolled individuals in the same condition category in each year. In the commercially insured population, additional analyses were conducted by limiting the enrollees with primary immunodeficiency and immunodeficiency conditions to those with a subsequent diagnosis of the condition at least 14 days after the initial diagnosis.

§ The individuals in this analysis were limited to those who had at least one IG administration in a given year. Average annual administrations per individual receiving IG therapy was calculated by dividing the number of IG administrations received among individuals in a condition category by the total person-years of IG-treated individuals in the same condition category in each year. In the commercially insured population, additional analyses were conducted by further limiting the IG-treated individuals with primary immunodeficiency and immunodeficiency conditions to those with a subsequent diagnosis of the condition at least 14 days after the initial diagnosis.

‖ The individuals in this analysis were limited to those who had full dosage information in a given year. Average annual dose (grams) per individual receiving IG therapy was calculated by dividing the total grams infused or dispensed to individuals in a condition category by the total person-years of IG-treated individuals in the same condition category in each year. In the commercially insured population, additional analyses were conducted by further limiting the IG-treated individuals with primary immunodeficiency and immunodeficiency conditions to those with a subsequent diagnosis of the condition at least 14 days after the initial diagnosis. The individuals in this analysis were limited to those who had complete dosage information in a given year. Average dose (grams) per administration was calculated by dividing the total grams infused or dispensed in the study population by the total number of IG administrations each year.

** Not calculated.

Data sources: IBM MarketScan Commercial Database and Centers for Medicare & Medicaid Services Medicare Parts A/B fee-for-service and Part D prescription drug data, 2009, 2010 and 2019

10. REFERENCES

1. Kivity S, Agmon-Levin N, Blank M, Shoenfeld Y. Infections and autoimmunity—friends or foes? Trends Immunol 2009;30(8):409-14.

2. Sutton D, Visintini S. Off-Label Use of Intravenous IG for Neurological Conditions: A Review of Clinical Effectiveness. Canadian Agency for Drugs and Technologies in Health; 2018.

3. Lünemann JD, Nimmerjahn F, Dalakas MC. Intravenous IG in neurology—mode of action and clinical efficacy. Neurology 2015;11(2):80-9.

4. Patwa HS, Chaudhry V, Katzberg H, Rae-Grant AD, So YT. Evidence-based guideline: intravenous IG in the treatment of neuromuscular disorders: report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. Neurology 2012;78(13):1009-15.

5. Perez EE, Orange JS, Bonilla F, et al. Update on the use of IG in human disease: a review of evidence. J Allergy Clin Immunol 2017;139(3S):S1-46.

6. Yong PL, Boyle J, Ballow M, et al. Use of intravenous IG and adjunctive therapies in the treatment of primary immunodeficiencies: a working group report of and study by the Primary Immunodeficiency Committee of the American Academy of Allergy Asthma and Immunology. Clin Immunol 2010;135(2):255-63.

7. Perez et al. 2017. Op. cit.

8. Balch A, Wilkes J, Thorell E, Pavia A, Sherwin CMT, Enioutina EY. Changing trends in IVIG use in pediatric patients: a retrospective review of practices in a network of major USA pediatric hospitals. Int Immunopharmacol 2019;76:105868.

9. Food and Drug Administration. Information About Immune Globulin (Human) Product Shortage. August 12, 2019. (Accessed February 10, 2022, at https://www.fda.gov/vaccines-blood-biologics/safety-availability-biologics/information-about-immune-globulin-human-product-shortage.)

10. American Society of Health-System Pharmacists. Immune Globulin, Intravenous or Subcutaneous (Human). November 23, 2021. (Accessed February 10, 2022, at https://www.ashp.org/drug-shortages/current-shortages/drug-shortage-detail.aspx?id=527&loginreturnUrl=SSOCheckOnly.)

11. Murphy MSQ, Tinmouth A, Goldman M, et al. Trends in IVIG use at a tertiary care Canadian center and impact of provincial use mitigation strategies: 10-year retrospective study with interrupted time series analysis. Transfusion 2019;59(6):1988-96.

12. Food and Drug Administration. Immune Globulins. July 1, 2020. (Accessed February 10, 2022, at https://www.fda.gov/vaccines-blood-biologics/approved-blood-products/immune-globulins.)

13. Quinn J, Orange JS, Modell V, Modell F. The case for severe combined immunodeficiency (SCID) and T cell lymphopenia newborn screening: saving lives…one at a time. Immunol Res 2020;68(1):48-53.

14. Balch et al. 2019. Op. cit.

15. Murphy et al. 2019. Op. cit.

16. Food and Drug Administration 2019. Op. cit.

17. Huang F, Feuille E, Cunningham-Rundles C. Home care use of intravenous and subcutaneous immunoglobulin for primary immunodeficiency in the United States. J Clin Immunol 2013;33(1):49-54.

18. Shemer A, Kivity S, Shoenfeld Y. Clinical indications for intravenous immunoglobulin utilization in a tertiary medical center: a 9-year retrospective study. Transfusion 2018;58(2):430-8.

19. Lowes R. Octagam Withdrawn From Market Over Unresolved Blood Clots, Embolisms. Medscape. September 24, 2010. (Accessed February 10, 2022, at https://www.medscape.com/viewarticle/729411).

20. Anterasian C, Duong R, Gruenemeier P, Ernst C, Kitsen J, Geng B. Quality of life differences for primary immunodeficiency patients on home SCIG versus IVIG. J Clin Immunol 2019;39(8):814-22.

21. Chapel HM, Spickett GP, Ericson D, Engl W, Eibl MM, Bjorkander J. The comparison of the efficacy and safety of intravenous versus subcutaneous immunoglobulin replacement therapy. J Clin Immunol 2000;20(2):94-100.

22. Runken MC, Noone JM, Blanchette CM, Zacherle E, Howden R. Differences in patient demographics and healthcare costs of patients with PIDD receiving intravenous or subcutaneous immunoglobulin therapies in the United States. Am Health Drug Benefits 2019;12(6):294-304.

23. Centers for Disease Control and Prevention. Prevalence of Obesity and Severe Obesity Among Adults: United States, 2017–2018. NCHS Data Brief No. 360. February 2020.

(Accessed February 10, 2022, at https://www.cdc.gov/nchs/products/databriefs/db360.htm.)

24. Puck JM, Gennery AR. Establishing newborn screening for SCID in the USA; experience in California. Int J Neonatal Screen 2021;7(4):72.

25. Moore BJ, McDermott KW, Elixhauser A. ICD-10-CM Diagnosis Coding in HCUP Data: Comparisons With ICD-9-CM and Precautions for Trend Analyses. Agency for Healthcare Research and Quality. November 28, 2017. (Accessed February 10, 2022, at https://www.hcup-us.ahrq.gov/datainnovations/ICD-10_DXCCS_Trends112817.pdf.)

26. Food and Drug Administration 2019. Op. cit.