U.S. Department of Health and Human Services
Centers for Medicare & Medicaid Services

Medicare Intravenous Immune Globulin (IVIG) Demonstration Evaluation

Final Report to Congress

September 2024

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LIST OF ACRONYMS

ASPE: Assistant Secretary for Planning and Evaluation
CMMI: Center for Medicare & Medicaid Innovation
CMS: Centers for Medicare & Medicaid Services
DME: Durable Medical Equipment
ER: Emergency Room
FDA: Food and Drug Administration
FFS: Fee-for-Service
HHS: Health and Human Services
IDF: Immune Deficiency Foundation
Ig: Immune globulin
IVIG: Intravenous Immune Globulin
LUPA: Low-Utilization Payment Adjustment
MAC: Medicare Administrative Contractor
PHE: Public Health Emergency
PIDD: Primary Immunodeficiency Disorders
RCT: Randomized Controlled Trials
SCIG: Subcutaneous Immune Globulin
SNF: Skilled Nursing Facility

Executive Summary

Primary immunodeficiency disorders (PIDD) are genetic conditions affecting antibody function, impairing the body's immune system. Immune globulin therapy, such as intravenous immune globulin (IVIG), is used to replace missing or dysfunctional antibodies, aiming to restore immune function. In 2003, Medicare Part B began covering IVIG therapy for PIDD patients in the home but did not include coverage for the items and services involved with the in-home administration of IVIG unless the individual was receiving Medicare home health services. The "Medicare IVIG Access and Strengthening Medicare and Repaying Taxpayers Act of 2012" mandated that Centers for Medicare & Medicaid Services (CMS) implement a three-year Medicare IVIG Demonstration (the Demonstration), which introduced a bundled payment for the items and services used for the in-home administration of IVIG for Medicare beneficiaries diagnosed with PIDD.

The Demonstration began in October 2014, was extended in both 2017 and 2021, and ended in December 2023. The Demonstration allowed for Medicare coverage of the items and services involved with the administration of the IVIG product in a beneficiary's home. This Final Report to Congress includes evaluation findings of the Demonstration from October 2014 to December 2023.

Eligibility for the Demonstration was contingent upon Medicare beneficiaries being enrolled in Part A and Part B, diagnosed with PIDD, and not currently under a home health episode. Over the course of the Demonstration, a total of 5,075 eligible Medicare beneficiaries enrolled, with 74.5 percent (3,783) receiving in-home IVIG therapy at least once.

Findings from the final analyses reveal significant implications of the Demonstration. CMS paid approximately $40M for in-home IVIG administration services under the Demonstration by the end of 2023. Medicare payments per beneficiary increased annually by $3,528, or $294 monthly. The initiative facilitated broader access to in-home IVIG for non-homebound beneficiaries with select PIDD, and active Demonstration participants received an average of half an additional IVIG infusion session across all care settings per year and an average of five additional in-home IVIG infusion sessions per year, when compared to non-participants. Services and IVIG administration in physician offices and outpatient settings, and usage of subcutaneous immunoglobulin (SCIG) all declined among Demonstration participants. The majority of active enrollees expressed high satisfaction with their in-home IVIG service and reported decreases in serious health issues in their survey responses.

While Medicare Part B uniformly covers IVIG product costs across care settings, payment for administration varies. Payment for the first hour of infusion of IVIG and for each additional hour of infusion varies between physicians' offices and hospital outpatient departments. Average IVIG administration payments were higher in the outpatient hospital than in the physician office setting. This is due largely to lower payment rates in physicians' offices, as the average length of the infusion is consistent between settings at approximately three hours. For example, in 2023, average payments for IVIG infusions were $93 in physicians' offices and $227 in outpatient hospitals. In contrast, the Demonstration's bundled payment was not dependent on infusion length, as it was a standardized per-visit payment based on an average of 4.5 hours. In 2023, the Demonstration's bundled per-visit payment for in-home IVIG administration was $408.23, while

the CY 2024 Home Health Prospective Payment System Final Rule set the payment rate at $420.48 based on an average of four hours in 2024.[1]

Between 2007 and 2018, there was significant growth in IVIG production and usage due to regulatory changes facilitating enhanced domestic production capacity. Nationwide shortages of immune globulin (Ig) began being reported in 2018, and supply disruptions persisted, especially during the COVID-19 pandemic, due to increased demand, manufacturing complexities, and the public health emergency's impacts. Since the COVID-19 pandemic, progress has been made in addressing supply, distribution, demand, and access challenges.

The Demonstration provided greater opportunity for non-homebound beneficiaries with select PIDD to receive in-home IVIG. On December 23, 2022, Congress passed legislation making IVIG in-home coverage a permanent Medicare benefit for those with PIDD, effective January 1, 2024. Medicare Part B now provides payment for the items and services involved with the in-home administration of IVIG for beneficiaries diagnosed with PIDD. Legislative actions, such as the provision of permanent Medicare coverage for in-home IVIG administration, emphasize ongoing efforts to enhance patient care and address the evolving landscape of IVIG therapy for PIDD beneficiaries.

[1] Centers for Medicare & Medicaid Services (CMS), Department of Health and Human Services (HHS). "Calendar Year (CY) 2024 Home Health (HH) Prospective Payment System Rate Update: Medicare Home Intravenous Immune Globulin (IVIG) Items and Services (Final Rule)." Federal Register 88:217 (August 13, 2023) p.77791-77797.

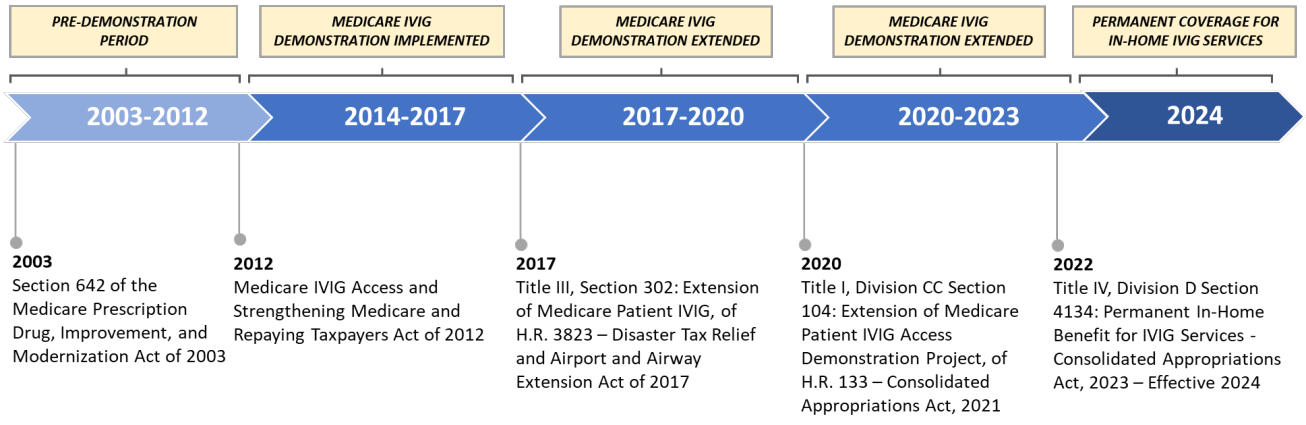
1. Legislative Summary

Section 101 of the Medicare IVIG Access and Strengthening Medicare and Repaying Taxpayers Act of 2012 (Medicare IVIG Access Act), Public Law 112-242, initially mandated the establishment, implementation, and evaluation of the three-year Medicare Intravenous Immune Globulin (IVIG) Demonstration (the Demonstration) under Part B of title XVIII of the Social Security Act, along with an Interim Report (completed in 2016) and a Final Report to Congress to be issued no later than one year after the completion of the Demonstration.

The Medicare IVIG Access Act established the Demonstration, which provided for a bundled payment for items and services involved with administering IVIG in the home for up to 4,000 Fee-for-Service (FFS) Medicare beneficiaries diagnosed with specific Primary Immunodeficiency Disorders (PIDD). Under the Demonstration, which began in October 2014, the IVIG product continued to be paid for separately under Medicare Part B. Section 302 of the Disaster Tax Relief and Airport and Airway Extension Act of 2017 (Pub. L. 115-63) extended the Demonstration for another three years, until December 2020, subject to the availability of funds.

Section 104, Division CC, of the Consolidated Appropriations Act, 2021 (Pub. L.116–260), further extended the Demonstration for another three years through December 2023, increased the enrollment limit from 4,000 to 6,500 FFS Medicare beneficiaries, and added requirements for an Updated Interim Report to Congress due no later than two years after enactment (December 2022) and for a Final Report to Congress to be issued no later than one year after the completion of the Demonstration (December 2024). Section 4134, Division D, of the Consolidated Appropriations Act, 2023 (Pub. L. 117-328), provided permanent Medicare Part B coverage and payment for the in-home administration of IVIG, including the items and services involved, effective January 1, 2024. The Demonstration legislative timeline is summarized in Figure 1, culminating with the permanent bundled payment for the items and services involved with administering the IVIG product in the home.

Figure 1: The Medicare IVIG Demonstration Legislative Timeline



The Medicare IVIG Access Act mandated the interim and final evaluation and reports. The Updated Interim Report to Congress was issued in October 2022. This Final Report to Congress

provides an update to the Interim Report, based on the full nine years of the Demonstration (2014 – 2023) and provides updated evaluation findings on the following matters:[2]

> (A) A final evaluation of the impact of the Demonstration project on access for Medicare beneficiaries to items and services needed for the in-home administration of intravenous immune globulin.
>
> (B) An analysis of the appropriateness of implementing a new methodology for payment for intravenous immune globulins in all care settings under Part B of Title XVIII of the Social Security Act (42 U.S.C. 1395k et seq.).
>
> (C) An update to the report entitled "Analysis of Supply, Distribution, Demand, and Access Issues Associated with immune Globulin Intravenous (IGIV)," issued in February 2007 by the Office of the Assistant Secretary for Planning and Evaluation (ASPE) of the Department of Health and Human Services (HHS).

This Final Report to Congress presents the evaluation findings from the Payment Methodology Report and the Beneficiary Experience Report, as well as the Update to the 2007 Report from ASPE. More information on the Beneficiary Experience Report, the Payment Methodology Report, and the Update to the 2007 Report from ASPE are available upon request to the Center for Medicare & Medicaid Innovation (CMMI).

2. Background

Primary Immunodeficiency Disorders (PIDD) are conditions triggered by genetic defects that cause a lack of and/or impairment in antibody function, resulting in the body's immune system not being able to function in a normal way. In most cases, individuals with PIDD are susceptible to acute, unusual, or recurrent infections, and face greater risks of complications if there is an infection.[3] Immune globulin (Ig) therapy is used to temporarily replace some of the antibodies (i.e., immunoglobulins) that are missing or not functioning properly in people with PIDD.[4] The goal of IVIG therapy is to use Ig obtained from normal donor plasma to maintain a sufficient level of antibodies in the blood of individuals with PIDD to fight off bacteria and viruses. Ig is formulated for both intravenous and subcutaneous administration. Clinicians can prescribe either product to the beneficiary with PIDD according to clinical need and preference, and beneficiaries can switch between intravenous and subcutaneous administration.

Section 642–of the Medicare Prescription Drug, Improvement, and Modernization Act of 2003 (Pub. L. 108-173), amended section 1861 of the Social Security Act (the Act) and allowed for Medicare Part B to cover the IVIG product for the treatment of PIDD in the home, but not the items and services involved with administering the IVIG product in the home.

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[2] This Final Report to Congress serves to update the Updated Interim Report to Congress in the following areas: Demonstration enrollment and claims information through December 2023, and revisions to the Medicare claims analysis methodology for determining the lookback period. Medicare claims analysis methodology details are provided in *Appendix B*.

[3] American Academy of Allergy, Asthma and Immunology (AAAI). (2011). *Eight Guiding Principles for Effective Use of IVIG for Patients with Primary Immunodeficiency*. https://www.aaaai.org/Aaaai/media/MediaLibrary/PDF%20Documents/Practice%20Resources/IVIG-guiding-principles.pdf.

[4] Perez EE, Orange JS, Bonilla F, et al. (2017) *Update on the use of immunoglobulin in human disease: A review of evidence;* Journal Allergy Clin Immunol. 139(3S): S1 – S46.

In 2006, the Federal Drug Administration (FDA) approved the subcutaneous immune globulin (SCIG) formulation for in-home self-administration. Medicare covers the SCIG product and the items (e.g., an infusion pump and supplies) involved with in-home use under the durable medical equipment (DME) benefit. After 2006, some beneficiaries elected to self-administer the Ig subcutaneously primarily because the pump used to administer SCIG in-home was covered under the Medicare DME benefit.[5]

In 2012, the Medicare IVIG Access Act mandated that the Centers for Medicare & Medicaid Services (CMS) conduct a three-year Demonstration in which Medicare would make a bundled payment for the items and services involved with in-home administration of the IVIG therapy for beneficiaries with specific PIDD diagnoses. Under typical Medicare FFS payment rules, the IVIG product for the treatment of PIDD is paid for in accordance with section 1847A of the Social Security Act (the Act). Items involved with administering the SCIG product in home, such as infusion pumps, are paid for under the Medicare DME benefit, but not for IVIG therapy in the home. Under the Demonstration, Medicare continued to pay for the IVIG product under Part B in accordance with the Act. However, a bundled payment for the items and services involved with the administration of IVIG in the home (infusion) was covered under the Demonstration – items may include infusion set and tubing, and services include nursing services to complete an infusion of IVIG lasting on average three to five hours.

Prior to the Demonstration, when Medicare Part B covered only the IVIG product for the treatment of PIDD in the home, approximately 200 Medicare beneficiaries with PIDD received their IVIG infusions in the home per year.[6] With the Demonstration's bundled payment that provided coverage for the items and services involved with IVIG administration in the home, approximately 1,900 beneficiaries with PIDD received in-home IVIG therapy per year, on average.[7] While beneficiaries enrolled in the Demonstration were able to receive their IVIG therapy in the home, these beneficiaries could have also chosen to receive their infusions in other care settings.

3. Demonstration Overview

Per the legislation, CMS implemented a bundled per-visit payment amount under the Demonstration, based on the national per-visit low-utilization payment adjustment (LUPA) for skilled nursing services used under the Medicare Home Health Prospective Payment System (Table 1). This payment amount was subject to coinsurance and deductibles, consistent with other Part B services.

[5] Immune Deficiency Foundation. (2013). *IDF Patient and Family Handbook for Primary Immunodeficiency Diseases Fifth Edition*. http://primaryimmune.org/idf-publications/patient-family-handbook/.
[6] Medicare claims data from a 100 percent sample of Medicare beneficiaries with PIDD for 2012-2014.
[7] Medicare claims data from a 100 percent sample of Medicare beneficiaries with PIDD for 2015-2022.

Table 1: Bundled Per-Visit Payment Amount for Items and Services Involved with In-home Administration of IVIG throughout the Demonstration Period (2014-2023)[8]

Demonstration Year	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023
Bundled Payment	$300.00	$319.23	$336.05	$354.60	$358.50	$366.25	$374.20	$381.57	$392.25	$408.23

Eligible suppliers who submitted claims to CMS for the IVIG product and its administration on a single claim form received the bundled payment for the services and items involved with the administration in the home under the Demonstration, in addition to a separate payment for the covered IVIG product.

CMS contracted a durable medical equipment (DME) Medicare administrative contractor (MAC) (the "Demonstration implementation contractor") to perform outreach to eligible beneficiaries with PIDD and enroll them into the Demonstration, as well as to educate suppliers concerning claims submission and the overall Demonstration. Suppliers submitted the claims for Demonstration services to the DME MAC for billing and processing.

The Medicare IVIG Demonstration provided coverage under Part B for items and services involved with in-home administration of IVIG to Medicare beneficiaries who are not homebound and receiving services under the Medicare home health benefit. The Demonstration benefit only applied to beneficiaries who chose to receive IVIG for the treatment of PIDD in the home.

Medicare FFS beneficiaries were eligible to voluntarily enroll in the Demonstration if they were:

- enrolled in Medicare Part B;
- had a select PIDD diagnosis[9] and were receiving either IVIG or SCIG treatment (and were interested in switching to in-home IVIG); and
- not currently receiving home health care services.

4. Evaluation Overview and Key Findings

In order to evaluate the impact of the Demonstration, the evaluation used a mixed-methods evaluation approach, which included a survey of Medicare FFS beneficiaries with PIDD, healthcare provider interviews, and an analysis of Medicare enrollment and claims data for beneficiaries who were eligible for the Demonstration. *Appendix A* provides a description of the populations of interest for each type of impact analysis, as well as the reference groups used throughout this report. The evaluation also included an examination of all beneficiaries receiving IVIG within the total Medicare FFS population, a comparison of the payment methodologies

[8] Prior to 2024, the Demonstration paid for the items and services with the in-home administration of IVIG. Effective 2024, Medicare Part B permanently provides payment for the items and services involved with the in-home IVIG administration of IVIG for beneficiaries diagnosed with PIDD. The CY 2024 Home Health Prospective Payment System Final Rule set the per-visit payment amount at $420.48 in 2024

[9] List of PIDD diagnoses: Congenital hypogammaglobulinemia (Bruton's agammaglobulinemia); Selective deficiency of immunoglobulin A Selective deficiency of immunoglobulin G; Selective deficiency of immunoglobulin M; Immune deficiency with increased IgM Antibody deficiency w/ near-normal immunoglobulin or w/ hyperimmunoglobulin; Transient hypogammaglobulinemia of infancy; Severe combined immune deficiencies; Purine nucleoside phosphorylase [PNP] deficiency; Major histocompatibility complex class I deficiency; Histocompatibility complex class II deficiency; Other combined immunodeficiencies; and Combined immunodeficiency, unspecified; Wiskott-Aldrich syndrome; Di George's syndrome; Hyperimmunoglobulin E [IgE] syndrome; Common variable immune deficiencies; Cerebellar ataxia with defective DNA repair.

currently used by CMS for administering IVIG in different care settings, and an analysis of the Ig market and other issues associated with IVIG products.

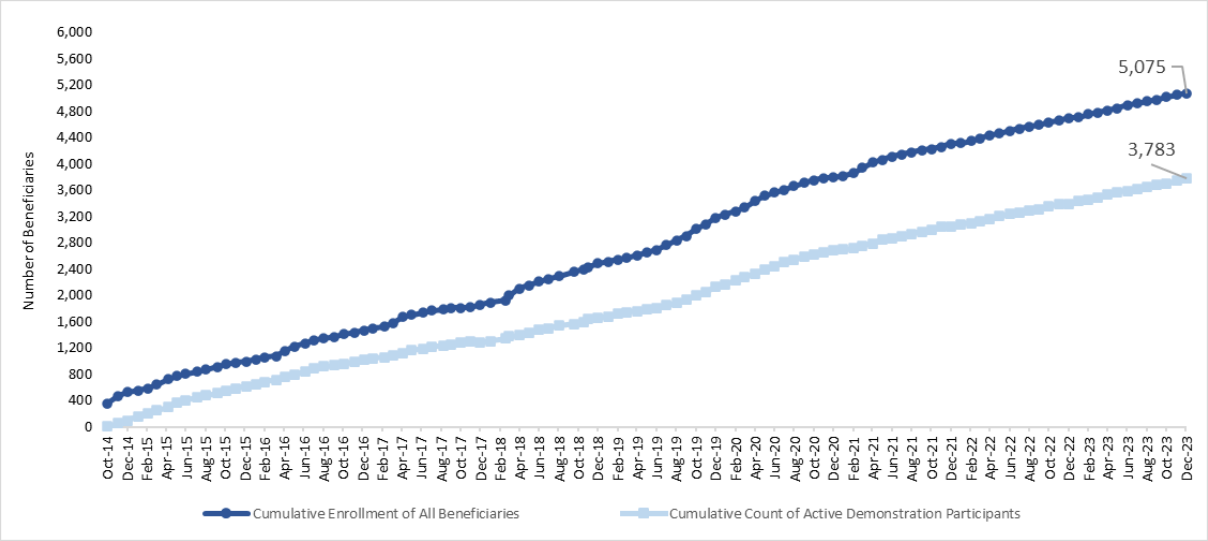
Summary of Key Evaluation Findings

(A) The total number of beneficiaries enrolled in the Demonstration project during the updated report period.

Between 2014 and 2023, the number of Medicare FFS beneficiaries with PIDD who received IVIG therapy and were eligible for the Demonstration increased from 9,473 to 11,994. The number of eligible Medicare FFS beneficiaries also include beneficiaries who received SCIG treatment and were interested in switching to in-home IVIG.

During this time, the number of FFS beneficiaries who enrolled in the Demonstration and those who actively participated in the Demonstration continually increased. Between October 2014 and December 2023, a total of 5,075 eligible Medicare FFS beneficiaries enrolled in the Demonstration. Of these, 74.5 percent (3,783) were active Demonstration participants, (i.e., Medicare beneficiaries who had at least one Demonstration Q2052 code in their claims data, meaning they received in-home IVIG therapy under the Demonstration at least once), as shown in Figure 2.

Figure 2: Cumulative Monthly Count of Medicare FFS beneficiaries enrolled in the Demonstration and Active Demonstration Participants during the Demonstration Period (2014 – 2023)



Source: Dobson | DaVanzo analysis of the IVIG Weekly Report January 8, 2024 – January 19, 2024 prepared by the Demonstration Implementation Contractor as of February 2024.

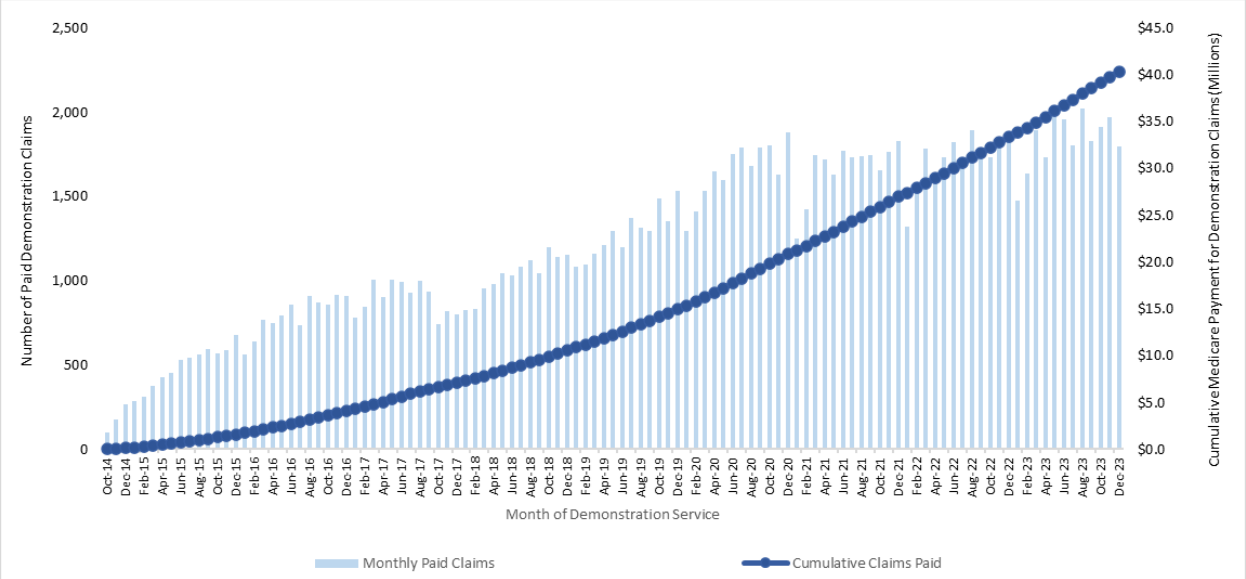
(B) The total number of claims submitted for services during the updated report period, disaggregated by month.

CMS processed and paid a total of 136,898 claims for items and services involved with the administration of IVIG in home under the Demonstration from October 1, 2014, through

December 31, 2023.[10] Figure 3 presents the number of claims paid monthly and cumulatively for items and services involved with administering in-home IVIG therapy.

Between October and December 2014, 543 claims were submitted for items and services under the Demonstration. The number of Demonstration claims continued to steadily increase from early 2015, up to 1,008 claims paid in the month of May 2017. The number of claims then decreased to 739 per month by October 2017, when the Demonstration was initially scheduled to end. Following the Demonstration's extension through 2020 as a result of the Disaster Tax Relief and Airport and Airway Extension Act of 2017, the trend of monthly Demonstration claims paid started to rise again. CMS paid 1,156 claims in the month of December 2018 and 1,529 claims in December 2019. Over 1,600 claims were paid for each month throughout 2020, concluding with 1,881 claims paid in December 2020. With the Demonstration's second extension through 2023 as a result of the Consolidated Appropriations Act of 2021, over 1,700 claims were paid for each month from 2021 to 2023, concluding with 1,795 claims paid in December 2023.[11]

Figure 3: Monthly Number of Claims Paid and Cumulative Medicare Payments for IVIG Services and Supplies during the Demonstration Period (2014 – 2023)



Source: Dobson | DaVanzo analysis of the IVIG Weekly Report March 18, 2024 – March 29, 2024 prepared by the Demonstration Implementation Contractor as of April 2024.

(C) An analysis of the impact of the Demonstration on beneficiary access to in-home administration of intravenous immune globulin, including the impact on beneficiary health.

The evaluation used a mixed methods evaluation approach, which included the Medicare claims analysis, the information from the healthcare provider interviews, and the results from the 2017

[10] The paid claims for services under the Demonstration were identified using the Demonstration code Q2052, which is the indicator for the bundled payment for items and services involved with the in-home administration of IVIG.

[11] In the IVIG Weekly Report December 25, 2023 - January 5, 2024 prepared by the Demonstration Implementation Contractor, 860 paid claims were identified in December 2023. The evaluation used the IVIG Weekly Report March 18 – March 29, 2024 to determine that there were 1,795 total paid Demonstration claims for December 2023, as this report accounts for the 3-month claims data lag.

and 2019 Beneficiary Surveys, to determine the impact of the Demonstration on beneficiary access to in-home administration of IVIG and beneficiary health. The evaluation analyzed the number of IVIG infusions from the claims and beneficiary responses to the survey related to Ig therapies to attempt to understand the impact of the Demonstration. The evaluation used the percentage of beneficiaries who had a physician visit for infection-related services and survey responses to questions concerning respondent health status as indicators of beneficiary health. The impact analysis used Medicare claims data from 2012-2023 for active Demonstration participants who received in–home IVIG services under the Demonstration (n=2,903)[12] and non-participants (i.e., beneficiaries who were eligible for the Demonstration but had no Demonstration claim code) as the comparison group (n=2,573).

Survey data were collected from active Demonstration enrollees (n=1,203) and non-enrollees (n=1,399) in both 2017 and 2019. Separately, interviews were conducted in 2017 with healthcare providers (e.g., physicians, nurses, and pharmacists) who treated patients with PIDD, and patient advocates from organizations supporting individuals with PIDD who were receiving IVIG or SCIG (n=84).

Beneficiary Access

Active Demonstration participants received an average of 7.2 IVIG infusions across all care settings per year. Claims analyses indicate that this was slightly more, or an average of half an additional IVIG infusion ($P<0.05$) across all care settings per year, when compared to non-participants, after adjusting for demographic factors, geographic location, and chronic illnesses.

Survey data indicate that 29.6 percent of Demonstration enrollees reported better access to IVIG therapy and less trouble obtaining their Ig treatments, compared to 10.3 percent of non-enrollees. Likewise, regression analysis suggests that surveyed non-enrollees with PIDD were 2.7 times more likely to have reported "more trouble overall" getting Ig treatments than Demonstration enrollees. In both interviews and surveys, healthcare providers and beneficiaries reported advantages of in-home IVIG therapy – including reduced transportation barriers, reduced risk of infection, increased treatment compliance, and improved monitoring of the infusion due to one-on-one nursing care.

Beneficiary Health

Surveyed Demonstration enrollees reported being in better health after enrolling in the Demonstration, as compared to surveyed non-enrollees. For example, regression analysis of the survey data indicates that non-enrollees were 5.9 times more likely to report suffering from infections and 2.6 times more likely to report having hospitalizations than active Demonstration enrollees (since enrollment). Likewise, similar analyses indicate that non-enrollees were 2.6 times more likely to report suffering from pneumonia, and 1.5 times more likely to report suffering from bronchitis than active Demonstration participants.

[12] From the 3,783 active Demonstration participants identified by the Demonstration Implementation Contractor, a total of 2,903 participants met the criteria to be considered for the evaluation's cost and utilization claims analyses, which required a "run-out" time period. These beneficiaries were required to have paid claims in both their pre-Demonstration and Demonstration periods and to have been entitled to Medicare FFS for a year by the end of 2023. A total of 210 beneficiaries enrolled into the Demonstration in 2023, and these were excluded from the claims analysis as they did not meet the Demonstration period restriction. Medicare claims analysis methodology details are provided in *Appendix B*.

The survey findings are supported by claims analyses. As noted earlier, individuals with PIDD are susceptible to acute, unusual, or recurrent infections, and claims data indicate that Demonstration participants experienced less infections than comparable non-participants. For example, active Demonstration participants were 19.2 percent less likely to receive services (i.e., physician visits) for pneumonia relative to comparable non-participants, after adjusting for demographic factors, geographic location, and chronic illnesses ($P < 0.001$).[13] And, overall, they were 6.7 percent less likely to receive services for any infection relative to comparable non-participants, after adjusting for other factors ($P<0.01$).[14]

(D) An analysis of the impact of in-home administration of intravenous immune globulin on overall costs to Medicare, including the cost differential between in-home administration of intravenous immune globulin and administration of intravenous immune globulin in a healthcare facility.

Medicare Payments:

The impact analysis using Medicare claims data from 2012-2023 found that overall annual ***Medicare payments were greater*** by an average by $3,528 per beneficiary among active Demonstration participants, relative to the comparison group ($P<0.05$). The beneficiary's total cost of care includes all Medicare A/B expenses, encompassing Part B drug administration and all inpatient and outpatient utilization. To put this finding into context, average Medicare spending was $62,548 per active Demonstration participant per year during the Demonstration period. In contrast, average annual spending for the entire Medicare FFS population was $15,700 per Medicare beneficiary in 2022.[15] In other words, expenditures for health care among patients with PIDD who receive IVIG therapy can be substantial.[16]

The results from the impact analysis are shown in Table 2, along with the average Medicare spending among active Demonstration participants.

[13] For reference, the 19.2 percent reduction is a relative reduction equal to -0.97 percentage points divided by the 5.1 percent of Medicare beneficiaries with PIDD who received IVIG therapy and had physician visits to treat pneumonia in their baseline period.
[14] For reference, the 6.7 percent reduction is a relative reduction equal to -1.06 percentage points divided by the 15.8 percent of Medicare beneficiaries with PIDD who received IVIG therapy and had physician visits to treat any of the seven possible infections in their baseline period.
[15] Kaiser Family Foundation (KFF). (2023). *The Facts About Medicare Spending*. https://www.kff.org/interactive/the-facts-about-medicare-spending/
[16] Menzin, J., Sussman, M., Munsell, M., & Zbrozek, A. (2014). Economic Impact of Infections Among Patients with Primary Immunodeficiency Disease Receiving IVIG Therapy6. *ClinicoEconomics and Outcomes Research, 2014*(6), 297-302.

Table 2: Annualized Difference-in-Differences Regression Results for Medicare Payments[17] for Active Demonstration Participants versus Non-Participants Eligible for the Demonstration, and Average Annual Medicare Spending per Active Demonstration Participant (2014-2023)

	Annualized Difference-in-Differences Estimate	Average Medicare Spending (Demonstration Period), PMPY Active Demonstration Participants (*n=2,903*)
Total Medicare Payments	**$3,528 ***	**$62,548**
Physician's Office	-$4,876 ***	$9,279
Outpatient Hospital	-$7,821 ***	$6,142
Inpatient Hospital	$280	$7,564
Durable Medical Equipment (DME)	$13,399 *	$37,034
IVIG Drugs Provided At Home (DME Only)	$13,638 ***	$28,983
Other DME	-$826	$8,051
Skilled Nursing Facility (SNF)	$51	$942
Home Health	-$170	$1,311
Hospice	$135	$275
Infusion Payment	$961 ***	$2,983
Medicare Payment for SCIG Drugs	-$800 **	$270

*** = P<0.001, ** = P<0.01, * = P<0.05

Source: Dobson | DaVanzo analysis of claims from a 100 percent sample of Medicare claims data from 2012-2023.

The largest differences in Medicare costs were observed in the following areas:

- Medicare expenses for durable medical equipment (DME) were $13,399 greater among active Demonstration participants, when compared to non-participants.
- There was a relative decrease in Medicare expenditures for annual hospital outpatient department (-$7,821) and physician services (-$4,876) per beneficiary among active Demonstration participants. While there was no significant difference in inpatient hospital expenses (between participants and non-participants), it appears likely that the lower reported hospitalizations among participants are reflected in the outpatient hospital stays, for which average expenses were significantly lower for participants.
- There was a relative decrease in annual Medicare expenditures of $800 for SCIG products across all care settings per beneficiary among active Demonstration participants.

[17] Although total Medicare spending is the sum of spending across all the seven care settings (Physician, Outpatient, Inpatient, DME, SNF, Home Health and Hospice), the Difference-in-Differences estimates for each of the care settings cannot be added to obtain the estimate of total Medicare spending because the Difference-in-Differences model is non-linear and the model's error term is not normally distributed. The evaluation used a GLM (Generalized Linear Model) with log-link function and Gamma distribution for each of the Difference-in-Differences regression models. The impact analysis consisted of separate Difference-in-Differences regression models for each of the seven care settings. As each of the care setting estimates are computed separately using seven different samples with non-linear model assumptions, these seven samples are different in terms of the distribution of the covariates. Therefore, when adding the Difference-in-Differences estimates from these seven care setting files, the total estimate would not match with the Difference-in-Differences regression estimate that is derived from the seven care setting files together. The non-linear model was chosen for the evaluation given the distribution of the payment outcome variables.

- This decrease in Medicare expenditures for SCIG products may be due to some beneficiaries switching from SCIG to IVIG therapy in order to meet the Demonstration's eligibility requirements.

Cost Differential between In-home IVIG Administration and IVIG Administration in a Healthcare Facility

Computing a cost differential for the administration of IVIG infusion between in-home and in a health care facility is not straight forward, as payment methodologies differ across care settings.

- Payment methodologies for the administration of IVIG differ between in-home and in a healthcare facility, such as a physician's office or a hospital outpatient facility.
- Under the Demonstration, Medicare costs for the items and services involved with the in-home administration of IVIG were bundled into a single fixed payment, which was not dependent upon infusion length, whereas services for administering IVIG in a physician's office and a hospital outpatient facility are paid separately or on a per-unit basis (e.g., hours).
- In 2023, the average payment for the administration of IVIG was $83 in physicians' offices for an average of 3.05 hours infusion time, and $227 in hospital outpatient facilities for an average of 2.99 hours infusion time. For in-home administration of IVIG infusions, the average Medicare bundled payment under the Demonstration was $319 in 2023.

(E) To the extent practicable, a survey of providers and enrolled beneficiaries that participated in the Demonstration project that identifies barriers to accessing services, including reimbursement for items and services.

To identify barriers to accessing services prior to the Demonstration, the evaluation gathered information from the survey of Medicare beneficiaries eligible for the Demonstration and a series of semi-structured interviews with healthcare providers. Survey data were collected from active Demonstration enrollees (n=1,203) and non-enrollees (n=1,399) in 2017 and 2019. Interviews were conducted with healthcare providers (e.g., physicians, nurses, and pharmacists) who treated patients with PIDD, and patient advocates from organizations supporting individuals with PIDD who were receiving IVIG or SCIG (n=84) in 2017.

Surveyed beneficiaries who actively used the Demonstration's benefit identified the following reasons for applying to the IVIG Demonstration: transportation issues, concerns about risk of infection, out-of-pocket cost, and difficulties scheduling in-home IVIG therapy. In addition, the interviewed healthcare providers also indicated the following barriers to accessing IVIG services: transportation, risk of infection, difficulties scheduling in-home IVIG therapy, and staffing and supply issues.

- **Transportation:** Problems with transportation were identified by approximately half of the beneficiaries as a reason for wanting to participate in the Demonstration and receive services in the home. Respondent healthcare providers also identified transportation barriers for beneficiaries who receive IVIG therapy in healthcare settings.

- **Risk of infection:** Over half of beneficiaries identified their exposure to sick patients in healthcare settings as a barrier to accessing their IVIG services. Healthcare providers similarly described the increased risk of infection as an access barrier during their interviews, as a patient's fear of being exposed to infection can affect and/or delay their access to IVIG therapy in a healthcare setting.

- **Cost:** Some beneficiaries identified specific problems with affording their in-home IVIG infusion out-of-pocket costs without the Demonstration.

- **Scheduling in-home IVIG therapy:** Some beneficiaries reported specific difficulties with finding and/or scheduling an in-home IVIG therapy provider and maintaining consistent in-home IVIG therapy services. Some healthcare providers also reported that patients who live in rural locations are at a higher risk of not receiving their in-home IVIG therapy, as there may be limited availability of trained nurses who can travel long distances to administer their Ig.

- **Staffing and supply issues:** Healthcare providers described limited availability of trained and experienced nurses to administer in-home IVIG therapy, supply issues with certain concentrations or brands of IVIG, and potential unreliability of commercial shipping companies that deliver Ig products as barriers to accessing IVIG therapy.

(F) Recommendations to Congress on the appropriateness of establishing a permanent bundled services payment for the in-home administration of IVIG for Medicare beneficiaries.

The Consolidated Appropriations Act[18] provided permanent Medicare Part B coverage and payment for the items and services involved with the in-home administration of IVIG, effective January 1, 2024. Therefore, this report does not include legislative recommendations.

5. Discussion and Summary

This report provides an update of the evaluation findings of the Demonstration, including the impact on beneficiary access to in-home administration of IVIG, for the full Demonstration period from October 2014 through December 2023. The Demonstration led to a relative increase of $3,528 per beneficiary per year in Medicare payments, as compared to non-participants. Subcomponents of Medicare payments analyzed included hospital outpatient services, physician services, SCIG products, and in-home IVIG therapy. The Demonstration resulted in an increase in Medicare expenditures for DME (which includes IVIG drugs provided at home) and a decrease in Medicare expenditures for hospital outpatient services, physician services, SCIG products, and services for infections among active Demonstration participants.

Prior to the start of the Demonstration, Medicare FFS did not cover the items and services involved with administering IVIG therapy at home for patients that were not homebound and able to receive services under the Medicare home health benefit, and less than four percent of FFS Medicare IVIG recipients received IVIG therapy at home between 2012 and 2014. Nearly

[18] Section 4134, Division D of the Consolidated Appropriations Act of 2023 (Pub. L. 117-328).

all beneficiaries received IVIG therapy in a hospital outpatient department or a physician's office.

Results from the impact analysis indicate that active Demonstration participants received approximately half an additional IVIG therapy and an average of five additional in-home IVIG infusions per year, when compared to non-participants. The FDA guidance suggests that IVIG therapy is typically administered every three to four weeks, for approximately 15 infusions per year.[19] Given that active Demonstration participants received on average 7.2 IVIG infusions per year, it does not appear that active Demonstration participants are receiving extra therapies beyond recommended amounts.

Given that the 2014-2023 Demonstration period overlapped with the COVID-19 public health emergency (PHE), the evaluation assessed any potential impact of the PHE on the analysis by including the COVID-19 indicator variable as a flag in the regression model to control for the presence of the PHE. The analysis showed that the COVID-19 PHE did not significantly change the evaluation findings.

In summary, during the nine years of the Demonstration, there was an increase in the number of annual therapies received, a reduced likelihood of Demonstration enrollees missing or having to postpone their IVIG therapies, and a decrease in receipt of infection-related services (i.e., physician visits). Almost a decade after the Medicare IVIG Access Act established the IVIG Demonstration, new legislation making payment for the items and services involved with the in-home administration of IVIG for PIDD beneficiaries went into effect, and made a permanent Medicare benefit, in 2024.

[19] Food and Drug Administration (FDA). (2008). *Safety, Efficacy, and Pharmacokinetic Studies to Support Marketing of Immune Globulin Intravenous (Human) as Replacement Therapy for Primary Humoral Immunodeficiency.* https://www.fda.gov/regulatory-information/search-fda-guidance-documents/safety-efficacy-and-pharmacokinetic-studies-support-marketing-immune-globulin-intravenous-human

Appendix A: Data Sources

Table A-1 provides a description of the populations of interest for each type of impact analysis, as well as the reference groups used throughout this report.

Table A-1: Data Sources and Populations of Interest by Impact Analysis

Impact Analysis Method	Population of Interest	Description
Beneficiary Survey (2017 & 2019)	Active Demonstration Enrollees	Beneficiaries who self-reported that they were enrolled in the Demonstration and used the Demonstration's benefit at least once
	Non-enrollees with PIDD	Beneficiaries who were eligible for the Demonstration and self-reported that they did not enroll in the Demonstration
	Non-active Demonstration Enrollees	Beneficiaries who self-reported that they were enrolled in the Demonstration but had not received in-home IVIG under the Demonstration by the time the survey was fielded
Medicare Claims Analyses (2012-2023)	Active Demonstration Participants	Beneficiaries enrolled in the Demonstration who had at least one Demonstration claim code (i.e., Q2052), indicating that they had received items and services involved with the administration of IVIG in the home under the Demonstration
	Non-participants	Beneficiaries who were eligible for the Demonstration but had no Demonstration claim code
Reference Groups	Beneficiaries with PIDD who ever used IVIG or SCIG	This includes all Demonstration enrollees and participants, those eligible for the Demonstration who did not enroll, and beneficiaries with PIDD who received both SCIG and IVIG
	All Medicare beneficiaries	The overall population of Medicare FFS beneficiaries including all groups listed above

Appendix B: Medicare Claims Analysis Methodology

The evaluation analyzed changes in health care utilization and spending from the pre-Demonstration period to the Demonstration period to assess the impact of the Demonstration. The team explored the impact of receiving IVIG therapy at home under the Demonstration on Medicare expenditures by care setting, utilization of IVIG therapy-related services, emergency room (ER) use, and utilization of health services for infections.

The multivariate regression analysis, which compared Medicare beneficiaries who participated in the Demonstration relative to similar beneficiaries who did not participate, was conducted in several steps. These steps included episode creation, propensity score matching, and Difference-in-Differences regression analyses.

B.1 Episode Creation

Medicare beneficiaries with PIDD who received IVIG therapy were divided into study and comparison groups based upon their Demonstration enrollment status which is identified by the presence of the Q2052 code in their claims, indicating receipt of Demonstration services. The study group, referred to as "active Demonstration participants," comprised beneficiaries enrolled in the Demonstration and who had at least one claim using the Demonstration Q2052 code indictor. The comparison group comprised beneficiaries who had never used the Demonstration's benefits and services ("non-participants"), i.e., beneficiaries with no Q2052 code indicator in their claims.

Two multi-year episodes were created for each active Demonstration participant and non-participant using beneficiary-month level data. These multi-year episodes, which include all Medicare-covered health care services used by an eligible beneficiary with PIDD across all settings in chronological order, represent pre-Demonstration and Demonstration periods.

For active Demonstration participants, the reference date marking the transition from the pre-Demonstration period to the Demonstration period is the date of the beneficiary's first CMS paid Demonstration Q2052 claim. That is, the pre-Demonstration period is defined as only the 24 months (two years) prior to the date of the beneficiary's first paid Demonstration claim. The Demonstration period (or post-period) consists of at least 12 months (one year) of claims data starting from the date of the beneficiary's first paid Demonstration claim, and represents the patterns of care during the Demonstration. In summary, the database is designed so that active Demonstration participants have at least one year of post-period and only two years of pre-period information of claims data.

Following the construction of the multi-year episodes using beneficiary-month data for active Demonstration participants, the evaluation used the propensity score matching method to identify the comparison group of non-participants. The comparison group includes any beneficiaries with PIDD who received IVIG therapy, never enrolled in the Demonstration, and have at least three consecutive years of claims data. The transition from the pre-Demonstration period to the

Demonstration period is defined differently for active Demonstration participants and non-participants. The propensity score matching method is described in the following section.

For non-participants, the reference date marking the transition period from the pre-Demonstration period to the Demonstration period is the same as that of the active Demonstration participant to whom they matched (i.e., the date of the study group beneficiary's first paid Demonstration claim). While the Demonstration started in October 2014, only a few beneficiaries had begun to receive Demonstration services in 2014. Therefore, January 2015 is utilized as the start date for the Demonstration in the multivariate analysis. Similar to active Demonstration participants, the pre-Demonstration period consists of only two years prior to the reference date and the Demonstration period consists of at least one year following the reference date.

Following construction of the multi-year episodes using beneficiary-month level data, additional eligibility criteria were applied to the groups. Both active Demonstration participants and non-participants were required to have paid claims in both their pre-Demonstration and Demonstration periods, and to have been entitled to Medicare FFS Part A and B for at least one year by the end of 2023, to be included in the multivariate analyses.

B.2 Propensity Score Matching

To estimate the effect of the Demonstration project, the active Demonstration participants were compared to the comparison group. The comparison group was constructed using propensity score matching techniques of selected covariates in the pre-Demonstration period between the study and comparison groups. Propensity scores were estimated using the Logistic regression model to ensure that the distribution of observed baseline covariates is similar between active Demonstration participants and non-participants. Propensity scores are the probability of treatment assignment conditional on observed baseline covariates. In the study, it is the probability of participation in the Demonstration. Beneficiaries who have the same propensity score, regardless of their treatment status (i.e., Demonstration participation), also have the same distribution of the covariates at the baseline period. The covariates included patient demographic and clinical characteristics, and geographic location factors.

Participation in the Demonstration is not random, as it is voluntary. There is likely self-selection of individuals to participate in the Demonstration. This implies that there could be observed factors (e.g., health status or comorbidity) and unobserved factors (e.g., family background) that may result in some Medicare beneficiaries having greater Medicare spending or healthcare utilization, and choosing to engage in the Demonstration. Therefore, the effect of the Demonstration on Medicare expenditures or other healthcare utilization outcomes will be biased. To address this potential self-selection issue, the evaluation used the one-to-one optimal propensity score matching with replacement model.

Propensity score matching techniques are widely used in observational studies when randomized controlled trials (RCTs) are not possible or able to be generalized to the population or are unethical

or impractical to administer.[20] Literature suggests that applying these techniques to observational studies is sufficient to remove selection bias among treatment and control groups and can result in findings that approximate RCTs.[21, 22, 23, 24]

Matching variables, i.e., the selected covariates that were included as independent variables in the Logistic regression model, included:

- Age
- Gender
- Race
- Census Regions
- Dual eligibility
- History of SCIG utilization
- Presence of chronic conditions[25]

Once the sample of eligible beneficiaries was defined, the Logistic regression model was run. The propensity scores calculated through this Logistic regression were used to obtain a one-to-one optimal match with replacement between active Demonstration participants and non-participants in the pre-Demonstration period, defining the comparison group for the analysis. The matching was performed on the logit of the propensity score using calipers of width equal to 0.2 standard deviations. In order to include the matching variables in the model, the logit model was initially estimated to satisfy the condition that coefficients were significantly different from zero at the 25% level, with the final decision to remain included if, when added along with the other selected covariates, the coefficient retained significantly different from zero at the 35% level of significance.

A total of 2,903 active Demonstration participants who had claims in both the pre-Demonstration and Demonstration periods were matched to a comparison group of 2,573 non-participants, which was constructed using the one-to-one optimal propensity score matching with replacement model. For non-participants, the reference date marking their transition period from the pre-Demonstration period to the Demonstration period is the same as that of the active Demonstration participants to whom they matched (i.e., the date of the beneficiary's first paid Demonstration claim). The covariate distributions of the active Demonstration participants and non-participants were

[20] Trojano, M; Pellegrini, F; Paolicelli, D; Fuiani, A; Di Renzo, V. (2009) *Observational Studies Propensity Score analysis of Non-randomized Data;* The International MS Journal, 90-97.
[21] Austin, P.C. (2011) *An Introduction to Propensity Score Models for Reducing the Effects of Confounding in Observational Studies;* Multivariate Behavioral Research, 399-424.
[22] Kuss, O., Legler, T., Borgermann, J. (2011) *Treatment Effects from Randomized Trials and propensity Score Analyses Were Similar in Similar Populations in an Example from Cardiac Surgery*; Journal of Clinical Epidemiology, 1007-1084.
[23] Dehejia, R., Wahba, S. (2022) *Propensity score-matching methods for nonexperimental causal studies*; The Review of Economics and Statistics, 151-161.
[24] Rosenbaum, P.R., Rubin, D.B. (1983) *The central role of the propensity score in observational studies for causal effects;* Biometrika, 41-55.
[25] To prevent the dimensionality that may arise from including all of the comorbidities that are available in the chronic conditions warehouse, the evaluation selected 27 chronic conditions for inclusion in the model. The evaluation first systematically included 12 comorbidities, which included the 10 costliest as well as those believed to be related to either health care spending and/or the propensity to receive IVIG treatment at home. The evaluation then used stepwise selection to add 15 additional comorbidities to the model.

compared prior to matching, and again after matching for the selected comparison group using a standardized mean difference to ensure balance was achieved through matching (i.e., that the samples of active Demonstration participants and non-participants selected through propensity score matching were similar with respect to selected covariates). The sample extracted from the matching model is balanced such that the values of the standardized mean differences attached to all 42 included covariates are within the range of -0.10 and 0.10.

B.3 Difference-in-Differences Analyses

Following these matching procedures, the research team constructed a series of Difference-in-Differences regression models to determine the impact of the Demonstration project on several outcomes of interest, such as the number of IVIG infusion therapies, the receipt of infection-related services, healthcare utilization by type (e.g., inpatient, ER, physician), and Medicare spending among active participants compared to non-participants.[26] The outcome variables for which the team constructed regression models are listed in Table B-1.

Table B- 1: Outcome Variables for Difference-in-Differences Regression Models

Outcome Variables for Difference-in-Differences Regression Models, by Category
Medicare Payments Per Beneficiary Per Month
Total Medicare Payments
Physician Office
Outpatient Hospital
Inpatient Hospital
Skilled Nursing Facility (SNF)
Home Health
Hospice
Infusion Payment
Durable Medical Equipment (DME)
Medicare Payments for Ig Products (All Care Settings)
Medicare Payments for IVIG Drugs Products
Medicare Payments for SCIG Drugs Products
Medicare Payments for Ig Related Services (All Care Settings)
Total Payment for IVIG-related services for home – DME
Payment for other DME
Utilization Per Beneficiary Per Month
Total Number of IVIG Infusion Therapies
Physician Office
Outpatient Hospital
IVIG Products Delivered at Home
Number of Emergency Room Visits
Infection-Related Services per Month
Percent of Beneficiaries with Services for Infection
Percent of Beneficiaries with Services for Upper Respiratory Infection[27]
Percent of Beneficiaries with Services for Influenza Infection
Percent of Beneficiaries with Services for Pneumonia Infection
Percent of Beneficiaries with Services for Bronchitis Infection
Percent of Beneficiaries with Services for Septicemia Infection

[26] Months from the last quarter of 2014 were excluded from the Difference-in-Differences regression models, as the Demonstration started in October 2014 and only a few months of Demonstration-related data were available for the given year. Information from the Demonstration may not have been widespread during that period. Regressions were conducted which included and excluded the observations from the 189 beneficiaries who enrolled in the Demonstration during the last quarter of 2014. The evaluation determined that the results were slightly influenced by this quarter and chose to remove the observations from the regressions.

[27] Diagnoses for upper respiratory infections included acute nasopharyngitis, acute sinusitis, acute pharyngitis, acute tonsillitis, acute laryngitis & tracheitis, and other upper respiratory infection, unspecified.

Outcome Variables for Difference-in-Differences Regression Models, by Category
Percent of Beneficiaries with Services for Conjunctivitis Infection
Percent of Beneficiaries with Services for Otitis Media Infection

To obtain an unbiased and consistent estimate of the effect of the Demonstration on utilization and spending, the team estimated the following Difference-in-Differences regression model using data at the beneficiary-month level for all relevant categories. The database was constructed such that each beneficiary had separate records for each month of Medicare claims that the beneficiary was entitled to Medicare Parts A and B.[28] Active Demonstration participants were attributed to the Demonstration group; beneficiaries were not attributed to the Demonstration study group if they had not participated in the Demonstration. As described in Section B.1 Episode Creation, the database was also designed for the pre-Demonstration period to consist of only two years of claims data prior to the reference date, and for the demonstration period to consist of at least one year of claims data following the reference date.

The regression model was applied separately to each outcome variable listed in Table B-1:

$$g(E(Y_{it})) = \beta_0 + \beta_1 * Demo_{it} + \beta_2 * Post_{it} + \beta_3 * Demo_{it} * Post_{it} + \beta_4 * Z_{it} + \varepsilon_{it}$$

Where i = patient and t = month.

Following a generalized linear model approach, the evaluation assumed that a transformation of the conditional expectation $E(Y_{it})$ is a linear function of the dependent variable. On the right-hand side of the equation is a set of exploratory variables that are included in the model, including Demonstration enrollment, time, beneficiaries' health and demographic characteristics, geographic location factors, and COVID-19 indicator. The variable *Demo* is a dummy variable to indicate whether a beneficiary participated in the Demonstration; it is equal to 1 for all months if beneficiaries were active Demonstration participants, i.e., enrolled in the Demonstration and used its benefits to receive in-home IVIG. Otherwise, it is equal to 0 to signal that the beneficiaries are in the comparison group, i.e., they did not enroll and/or participate in the Demonstration. The dummy variable *Post* indicates the Demonstration time period: it is equal to 1 for the Active Demonstration participants' first paid Q2052 claim and at least 12 months following this reference date for both groups, i.e., the time period after the policy intervention. Otherwise, it is equal to zero for the 24 months preceding the first paid Q2052 claim for Demonstration participants and for the months preceding the reference date for the comparison group. The variable Z_{it} is a vector of all beneficiary level demographic and other risk adjustment variables. These variables included gender, age, race, geographic location factors (census regions), COVID-19 indicator,[29] Medicare

[28] Months in which a beneficiary was not entitled to Medicare Parts A and B were excluded from the database. Overall, 99.7 percent of person-months included both Part A and Part B entitlement for active Demonstration participants, and 99.6 percent of person-months included both Part A and Part B entitlement for non-participants.

[29] In 2021, under the previous evaluation contract, the evaluation conducted a sensitivity analysis using claims data from 2010-2020 to examine whether the impact of the Demonstration on Medicare costs and services was influenced by the COVID-19 public health emergency (PHE). The sensitivity analysis evaluated the impact of the COVID-19 indicator and once the flag was added to the outcome model, there were very minor changes in the Difference-in-Differences estimates for Medicare spending and health care utilization, when compared to the results excluding the COVID-19 flag from the model. The evaluation concluded that there were no major COVID-19 related trends in the data, and included the COVID-19 indicator variable as a flag in the Difference-in-Differences regression model to control for the presence of the PHE.

dual eligibility, history of SCIG utilization, and various chronic conditions.[30] The team built this regression model separately for each outcome measure of interest (with the appropriate distribution and link function in generalized linear modeling).

The evaluation used generalized linear models in order to appropriately account for distribution of each outcome variable while estimating the Difference-in-Differences average treatment effect. The appropriate link function and variance structure for each outcome variable were selected using Box-Cox and modified Park tests, respectively. Moreover, two-part models were used to account for the significant proportion of zero values in the data for all outcome variables with the exception of total Medicare payments and infection-related outcomes. In these two-part models, Logistic regression was first used for modeling the probability of positive values, while generalized linear models selected based on the Box-Cox and modified Park tests were used for the second part which estimated positive outcomes where zero values rarely exist. The treatment effect reflects the combined results of both parts of the two-part models.

Given this framework, the main coefficient of interest was β_3, the estimated coefficient of the interaction between the dummy variables *Demo* and *Post* – also commonly referred to as the Difference-in-Differences estimator in linear models. This coefficient shows the difference in outcomes between active Demonstration participants and non-participants from the pre-Demonstration period to the Demonstration intervention period. More specifically, it will show the changes in average spending among the active Demonstration participants relative to the comparison group due to the intervention of the Demonstration. In a linear model, the Difference-in-Differences effect can be interpreted directly from the coefficient of interest (β_3) which is the incremental effect of the interaction term between *Demo* and *Post*. However, given non-linearity of the relationship between the outcome variable and the independent variables in these analyses, the coefficient β_3 cannot be interpreted as the estimated average effect of the treated. The evaluation has therefore calculated the marginal effects[31] related to the interaction term to calculate the average effects of the treated from the Difference-in-Differences estimated model.[32] Specifically, the treatment effect was derived as the average predicted value of the outcome variables for the active Demonstration participants during the Demonstration period.

A statistically significant Difference-in-Differences estimator indicates that estimated changes are due in part to the Demonstration project. For example, if the outcome measure is total spending for IVIG products, a statistically significant positive coefficient (β_3) would indicate an increase in spending among active Demonstration participants due to their use of the Demonstration benefit. If the outcome measure were the number of IVIG infusions, a statistically significant positive coefficient (β_3) would indicate an increase in the number of IVIG infusions among active

[30] The evaluation included the 27 chronic conditions utilized in the propensity score model into the regression model.
[31] "Marginal effects" for any dichotomous outcome variable is interpreted as the percentage point difference in the likelihood of treatment group beneficiaries receiving a particular service (e.g., infection related services) compared to the comparison group. For a continuous outcome variable (e.g., spending), marginal effect is the change in spending per member per month for the treatment group compared to the comparison group.
[32] Puhani, P.A. (2012) *The treatment effect, the cross difference, and the interaction term in nonlinear "difference-in-differences" models;* Economics Letters, 85-87.

Demonstration participants due to their use of the Demonstration's benefit. A statistically significant negative coefficient (β_3) would indicate a decrease in the number of IVIG infusions among active Demonstration participants due to their use of the Demonstration's benefit.