REPORT TO CONGRESS

EVALUATION OF THE MEDICARE REPLACEMENT DRUG DEMONSTRATION

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Report to Congress—Evaluation of the Medicare Replacement Drug Demonstration

Executive Summary

This report summarizes findings of an evaluation of the Medicare Replacement Drug Demonstration (MRDD) that was mandated under the Medicare Prescription Drug, Improvement, and Modernization Act (MMA) of 2003. As stipulated by Congress, the evaluation examines the impact of the demonstration program on patient access to care and patient outcomes, and analyzes its impact on Medicare spending, specifically detailing any cost savings to the Medicare program due to reduced physicians' services and hospital outpatient department services for administration of replaced drugs.

Background

Section 641 of the Medicare Prescription Drug, Improvement, and Modernization Act (MMA) required the Secretary of Health and Human Services to implement a demonstration project for coverage of certain prescription drugs and biologicals. This demonstration project – known as the Medicare Replacement Drug Demonstration (MRDD) – spanned the period between September 2004 through December 2005 and provided Medicare beneficiaries with drug coverage for a limited set of drugs and biologicals that replace the need for drugs already covered under Medicare Part B and are described in section 1861(s)(2)(A)(B)(I)(J)(O)(Q) and (T) of the Social Security Act.

Before the introduction of this demonstration project, Medicare outpatient drug coverage was limited largely to those medications that were administered 'incident to' a physician's service. The demonstration aimed to improve beneficiary access to selected new oral anti-cancer drugs and other self-injected medications used to treat such conditions as multiple sclerosis and rheumatoid arthritis. By extending Medicare coverage to these self-administered medications, Medicare beneficiaries were expected to realize a wide array of benefits, including: added convenience through self administration; improved health outcomes; and reduced financial barriers. For beneficiaries without supplemental drug coverage, the cost of many of the self-administered medications covered under the demonstration may have posed a prohibitive barrier to their use, with costs often exceeding $20,000 per year.

The demonstration was structured to have similar patient cost-sharing arrangements as the Part D standard Medicare prescription drug benefit,

Evaluation Methods

The Centers for Medicare & Medicaid Services (CMS) designed and conducted the evaluation of the MRDD. To assist in the evaluation, CMS contracted with Mathematica Policy Research, Inc. (MPR) to conduct a survey of demonstration participants. CMS also requested that the Agency for Health Care Research and Quality (AHRQ) commission several technology assessments and an update of previous systematic reviews of the clinical literature. These reviews enabled CMS to examine the potential benefits of selected MRDD-covered drugs relative to replaceable Part B-covered drugs on patient outcomes, such as mortality and disease remission that would not easily have been studied within the constraints of the demonstration project. CMS supplemented these studies with analyses of enrollment data and drug spending using Part B and demonstration drug claims. Contractors' reports have been referenced and summarized in the attached Report to Congress prepared by CMS.

Outcomes examined included: access to demonstration drugs, perceived demonstration effects on financial burden and health care use, enrollee assessment of changes in health and symptoms, and net Medicare drug-related spending. The clinical reviews examined patient survival, disease remission, and adverse effects for selected demonstration drugs compared to substitute treatments covered under Part B. Although Congress directed CMS to examine the cost-effectiveness of the program to Medicare, as the demonstration unfolded we found the plurality of MRDD enrollees had been using demonstration-covered drugs before they enrolled in the demonstration. Those beneficiaries likely experienced little or no changes in health effects due to the demonstration as their drug regimen did not change. Other beneficiaries (new users of the demonstration-covered drugs) may have experienced improvements in outcomes, but it is difficult to assess the separate effects in this subgroup. For these reasons, costs and clinical outcomes are discussed separately. The component of this evaluation that focuses on costs examines the impact of the demonstration on *net Medicare spending*, taking into account drug spending under the demonstration less any savings attributable to reduced spending on Part B-replaced drugs and physicians' services and hospital outpatient departments' services for their administration, rather than a formal cost effectiveness analysis.

For the most part, the evaluation draws inferences about the demonstration program's impact using pre-post comparisons for a group of early enrollees. While a controlled study would have offered a stronger study design, for many reasons it was felt the selection of a control population was not appropriate. Two of these reasons include: 1) the lack of specificity of administrative data to enable the selection of patients with the demonstration conditions who would have been eligible for drug treatment; and 2) the high disease burden and mortality rate among selected demonstration conditions, which coupled with a lag in availability of administrative data would have resulted in a high loss of potential controls, or comparisons at different stages of the disease between enrollees and controls. As a result, this study design does not permit a cause and effect link between the demonstration enrollment and reported outcomes. Because of the different trajectories diseases take over time, without an appropriate control population of beneficiaries with similar conditions at similar stages of their disease who did not participate in the demonstration, the impact on outcomes and net spending should be viewed as suggestive of demonstration effects, rather than definitive.

Findings

Patient Access to Care. Over 42,000 Medicare beneficiaries enrolled in the MRDD, a number that approached the 50,000 enrollment limit mandated by Congress. The demonstration principally served vulnerable beneficiaries, many of whom were poor, lacked supplemental drug insurance, and suffered from chronic disease or terminal cancer. More than half of demonstration participants enrolled to receive drug coverage for self-administered biologics used to treat multiple sclerosis or rheumatoid arthritis. Another one-third enrolled to receive coverage for oral cancer medications.

The demonstration served a financially-vulnerable population and improved drug insurance coverage and reduced financial burden for a majority of participants. About 40 percent of participants qualified for federal subsidies under the program, with limited cost-sharing obligations.

Somewhat unexpectedly, the demonstration did not provide new access to drug therapy to most participants. Depending on the source (e.g., patient or physician report), estimates range from 62 to 76 percent of demonstration participants had been using MRDD-covered medications prior to enrollment. Our analysis suggests the demonstration program provided Medicare beneficiaries with new access to drugs in no more than one-third of the cases and possibly as low as one-tenth of cases. However, sampled enrollees who used no reported drugs in the pre-enrollment period generally described large and significant improvements in access problems related to their medications under this demonstration.

Patient Outcomes. Perceived improvements in health or symptoms were sometimes marked for beneficiaries who had been prior users of Part B replaceable drugs or who had been using some other nondemonstration covered drug to treat their condition prior to enrollment. The clinical reviews conducted for this evaluation also found the MRDD provided coverage for many life-extending or quality-enhancing advances in treatment relative to those covered under Part B, particularly in the area of cancer care. When improvements in survival were not found, MRDD-covered medications frequently caused fewer drug-related side effects than their Part B substitutes. MRDD-covered treatments for rheumatoid arthritis were for the most part equally as efficacious as the physician-administered Part B replaceable drugs, but offered added convenience to the patient, by allowing them to self-inject medications in the convenience of their own home. Sampled beneficiaries who used Part B drugs before enrolling in the demonstration traveled on average 44 minutes one-way to their doctor's office for drug administration, and the number of these sessions was nearly halved under the demonstration (reduced by about 2 sessions over a three month period). However, for the estimated 62-76 percent of early enrollees who had previously been using drugs covered under the demonstration, but not under Part B, the demonstration's probable impact on patient outcomes was likely modest

Medicare Spending. For the minority of participants for whom this demonstration enabled them to substitute MRDD for Part B drugs, the demonstration offered several economical alternatives for treatment, as intended. When factoring in the costs of physicians' services and hospital outpatient department services for administration of replaced drugs, our preliminary estimates showed weekly drug-related spending per enrollee was lower for demonstration-covered drugs versus the Part B replaced drugs for five of the seven conditions selected for the spending analysis.

Gross Medicare spending was estimated to have increased over the 16-month program by $248 million. Net spending—taking into account reduced spending on Part B drugs and associated administration costs that would have occurred in absence of the demonstration—was estimated to be $218 million. Savings due to reduced physicians' services and hospital outpatient department services for administration of replaceable drugs were predicted to be small as so few demonstration participants were estimated to have been Part B drug users in absence of the demonstration. Only nine percent of demonstration participants were using Part B drugs in the three months prior to the demonstration. Considering some newly-diagnosed participants may have used Part B drugs in absence of the demonstration – this estimate increases to 10 percent.[1] Analyzing the potential substitution effect among seven selected MRDD-covered conditions with adequate sample size, savings due to averted Part B drug use and associated administration spending accounted for no more than 12 percent of gross demonstration spending.

While not the central focus of the evaluation, a surprising finding of this study was that a high proportion of enrollees did not purchase MRDD-covered drugs under the demonstration. MRDD drug claims were submitted for only 61 percent of enrollees. Such low use of the benefit was unanticipated, as most demonstration participants suffered from chronic diseases that require ongoing pharmacologic treatment. Further analyses showed the most vulnerable enrollees – those receiving a subsidized benefit, minorities, and those originally qualifying for Medicare by reason of disability – were more likely than their counterparts to use the drug benefit.

[1] Our calculation methods are described on page I-21 in Appendix I.

Conclusion

The MRDD sought to improve beneficiary access to drugs prescribed as replacements for those already covered under Part B. Many of the demonstration drugs offered Medicare beneficiaries less toxic, and sometimes more effective, treatment alternatives than the Part B replaced drugs. Because the demonstration drugs are self-administered and do not require visits to physicians' offices for administration, the demonstration was also expected to reduce beneficiaries' time and travel burden, and potentially reduce their financial burden. The demonstration targeted chronically-ill beneficiaries who did not have comprehensive drug coverage and provided them with a drug benefit that was structured similarly to Medicare Part D.

Although the demonstration reached the targeted poor or near poor who lacked supplemental drug coverage, a surprising finding of this evaluation was that many participants already had access to MRDD drugs. As such, many of the expected benefits (e.g., improved outcomes, added convenience) accrued to a minority of participants who substituted Part B with MRDD drugs or who gained new access to drug treatment under the demonstration. For this subset of participants, however, the benefits were substantial, covering many medications that offered economical, life-extending or quality-enhancing clinical advances over those previously covered by Medicare. In addition, the demonstration appeared to offer at least some financial relief for nearly all participants. As a preliminary estimate, net spending will likely have increased by $218 million under the demonstration after taking into account potential substitution effects for reduced spending on Part B replaceable drugs.

While this evaluation, by necessity, reflects the experience of early enrollees, final enrollment reports show the composition of the demonstration participants did not change markedly from mid-year 2005 in terms of enrollment condition, qualifications for financial assistance, the likelihood of using the benefit, or reported prior use of demonstration drugs. The key findings – that under the demonstration poor or near poor beneficiaries gained financial assistance for many economical and quality-enhancing treatment alternatives to those previously covered by Medicare, are unlikely to be substantively altered once complete data are available.

Although the cost-sharing structure for the MRDD was similar to that of the Medicare prescription drug benefit (Part D), these two programs have some important and distinct differences. Part D targets all eligible beneficiaries, while the MRDD served a subset of beneficiaries with select chronic diseases who were taking high-cost prescription medications. The MRDD was also administered by one Medicare contractor and one pharmacy benefit management company who worked in partnership to process drug claims. In contrast, multiple private plans administer the Medicare prescription drug benefit for Medicare beneficiaries, with CMS oversight.

We did learn, in part through this demonstration, that reaching beneficiaries who were not already getting drug coverage was much more effective through extensive grassroots efforts - something that was not feasible in the short time frame and limited scope of the MRDD. Consequently, subsequent Medicare education and outreach efforts about new benefits like this one have been designed to be much more extensive, local, and personalized.

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I. Introduction

A. Report Requirements

This report summarizes findings of an evaluation of the Medicare Replacement Drug Demonstration (MRDD) that was mandated under the Medicare Prescription Drug, Improvement, and Modernization Act (MMA) of 2003. During the intervening period between the passage of the MMA and the implementation of a full-scale Medicare prescription drug benefit (Part D), the MRDD served as a bridge for many vulnerable Medicare beneficiaries with disabling or life threatening conditions. It provided coverage for selected oral or self-administered drugs and biologics that replaced drugs already covered under Medicare Part B. For this evaluation, Congress directed CMS to address the effects of the demonstration program on three key areas:

- patient access to care;
- patient outcomes; and
- the cost-effectiveness of the program to Medicare, specifically taking into account any cost savings attributable to reduced physicians' services and hospital outpatient departments' services for administration of the biological.

Congress also required that this report be submitted to it by July 1, 2006. Given lags in the availability of data and the time required to analyze it, this report largely reflects the experience of beneficiaries who enrolled within the first five months of the program and drug claims processed through mid-year 2005.

B. Organization of the Report

Including this introduction, this report is presented in five sections. Section 2 discusses the impetus for the demonstration program and its design, including beneficiary eligibility criteria, the structure of patient cost-sharing, and the selection of covered drugs. In Section 3, CMS' evaluation methods and data sources are described. Findings of the evaluation are presented in Section 4 under six major topic areas: enrollment trends and enrollment process; enrollee characteristics; use of the benefit; impact on patient access to care; impact on patient outcomes; and impact on Medicare spending. Finally, the insights gained through this evaluation are summarized in Section 5.

II. Background

Until recently, the Medicare program provided limited benefits for outpatient drugs described in sections 1861(s)(2)(A)(B)(I)(J)(O)(Q) and (T) of the Social Security Act. Under Part B, the program covers drugs that are furnished 'incident to a physician's service'. Part B does not cover drugs that are usually self-administered unless the statute provides for such coverage. The statute explicitly provides coverage for some self-administered agents, such as blood-clotting factors, drugs used in immunosuppressive therapy, erythropoietins for dialysis patients, and certain oral anti-cancer, if they contain the same active ingredients as physician-administered anti-cancer drugs already covered by Medicare, and certain anti-emetics if they are used as part of an anti-cancer regimen at or within 48 hours after chemotherapy as a full replacement for intravenous anti-emetics.

The MMA brought wide-sweeping change to the Medicare program, including a mandate to offer a standard prescription drug benefit to beneficiaries beginning in 2006. During the intervening years between the passage of the MMA and the start of the new drug benefit, Section 641 of the MMA required the Centers for Medicare and Medicaid Services (CMS) to conduct a demonstration program that would pay for drugs and biologicals prescribed as replacements for drugs covered under Medicare Part B. Congress limited the scope of this demonstration, known as the Medicare Replacement Drug Demonstration (MRDD), to 50,000 beneficiaries or $500 million in funding, whichever came first.

The demonstration aimed to improve beneficiary access to selected new oral anti-cancer drugs and other self-injected medications used to treat such conditions as multiple sclerosis (MS) and rheumatoid arthritis (RA). By extending Medicare coverage to these self-administered medications, Medicare beneficiaries were expected to realize a wide array of benefits, including:

- **Added convenience.** Medicare's prior policies of restricting drug coverage to medications administered incident to a physician's service were seen as posing a barrier to care, particularly for beneficiaries with disabling conditions, those without access to reliable transport, or those living in remote rural areas who found it difficult to travel regularly to the physician's office for treatment.
- **Better health outcomes.** The demonstration program opened beneficiary access to newer, sometimes more therapeutically-effective drugs and/or medications with fewer side effects than the Part B drugs. In addition, with more convenient administration, it was possible that patient adherence to medications might improve, which might lead to better outcomes.

- **Reduced financial barriers.** For beneficiaries without supplemental drug coverage, the cost of many of the self-administered medications may have posed a prohibitive barrier to their use prior to the demonstration, with costs often exceeding $20,000 per year.

Finally, despite the high cost of some of these self-administered medications, proponents of the demonstration noted that beneficiaries and Medicare would save on the costs related to administration of the Part B drug, which were sometimes substantial. Some Part B drugs expected to be replaced require monthly infusion sessions over long periods of time, for which Medicare pays for the costs of the pre- and post- infusion hydration fluids, injection, physician evaluation and management services, and other supplies in addition to the drug costs.

A. Structure of the Demonstration Program

Congress stipulated that the demonstration program start within three months of the passage of the MMA, or March 2004. However, due to the complexities of implementing such a major change in Medicare drug coverage policy, CMS did not begin accepting applications until July 6, 2004, and the flow of benefits did not start until six months later than anticipated -- in September 2004. Although the demonstration was national in scope, CMS selected through a competitive bidding process one Medicare contractor, TrailBlazer Health Enterprises, LLC, a subsidiary of Blue Cross and Blue Shield of South Carolina, to administer the drug plan and assist CMS in conducting beneficiary outreach and education. Caremark, a pharmacy benefit management firm, was selected to process the drug claims in partnership with Trailblazer. Demonstration participants were enrolled centrally by TrailBlazer through formal applications obtained by mail or fax.

Early CMS projections derived from advocacy group estimates and analyses of Medicare claims estimated about 200,000 beneficiaries might be eligible for enrollment[2]. As a result, the enrollment process allowed for a randomized selection of participants to ensure unbiased selection, giving everyone equal access to the drug program. Applicants were divided into those seeking coverage for an anti-cancer drug and all others, with the aim of ensuring 40 percent of the funding targeted oral cancer treatments. The randomized selection process was dropped at the outset of the program when it became clear that the number of applicants would be below the Congressionally-imposed cap.[3]

[2] These estimates were derived before drugs used to treat breast cancer, multiple myeloma, and psoriatic arthritis and ankylosing spondylitis were added to the benefit.

[3] Because early program enrollment fell below expectations, CMS funded a qualitative MRDD outreach and enrollment study that will be examining factors contributing to low enrollment and what outreach activities

Early in 2004, CMS held three Open Door Forums. The purpose of these forums was to assist the agency in making decisions about some of key design features of the demonstration, such as: how to define 'replacement drugs'; which drugs should be included in the demonstration and the criteria to be used for their selection; how to establish an effective outreach program; and how to select demonstration participants from among the qualified applicants. These design features of the MRDD are described below.

Eligibility. Beneficiaries were eligible for the demonstration if:

- they were entitled to Medicare Part A and enrolled in Medicare Part B;
- Medicare was their primary source of insurance;
- they were living in one of the 50 states or the District of Columbia;
- they would qualify for a physician's prescription for one of the medications to treat a condition allowed under the demonstration (as certified by a physician or a nurse practitioner); and
- they did not already have a comprehensive drug coverage plan.

The last criterion was added in order to target the demonstration to beneficiaries with the greatest need. Recent estimates show that sixty-five percent of Medicare beneficiaries have at least some supplemental drug coverage through a former employer, Medicaid, or other public or private sources (McCormack et al., 2005), and some more have assistance through manufacturer pharmacy assistance programs and other charitable organizations. The MRDD was intended to provide new access to beneficiaries with no or limited supplemental outpatient drug coverage. Comprehensive drug coverage plans were defined to include coverage through TriCARE, the PACE program, most Medicaid and SCHIP programs, and coverage under a comprehensive Medicare Advantage plan[4] or an employer- or union-sponsored retiree plan. Beneficiaries with these types of drug coverage were not directly turned away during the enrollment process, but were assisted by TrailBlazer staff during enrollment to compare current out-of-pocket obligations with what they would have to pay under the demonstration to ensure the program was financially beneficial to them.

Beneficiary cost sharing. Congress stipulated that cost-sharing arrangements under the MRDD were to be structured in the same manner as the standard prescription drug benefit under Medicare Part D. For the most part, the benefit

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the agency and other groups undertook. This study was not part of the original evaluation required by Congress, but should be available under separate cover before the end of 2007.

[4] Notably, most Medicare Advantage plans before 2006 had only limited coverage for specialty, brand name drugs.

structure was the same. In 2005, the standard benefit covered up to 75 percent of drug costs after beneficiaries met a $250 deductible up to $2,250 of drug spending (or total out-of-pocket spending was $750). After this limit was met, beneficiaries were responsible for paying 100 percent of drug costs until they met the annual out-of-pocket catastrophic cap of $3,600. Cost-sharing after this limit was reached was reduced to the greater of 5 percent of drug costs or a $5 co-payment for brand name drugs. (All but one of the demonstration drugs – tamoxifen—were brand name drugs.)

Beneficiaries with limited means were eligible for reduced cost-sharing arrangements. To qualify for reduced cost-sharing arrangements, beneficiaries had to attest their incomes were below 150 percent of the federal poverty level and they did not have assets worth more than $10,000 for an individual and $20,000 for a couple. Once they qualified for federal assistance, they were placed in one of four federal assistance benefit plans, depending on their income and assets (Table 1).

TABLE 1. COST SHARING UNDER THE MRDD, 2005

Benefit categories	Standard Benefit	Low-income Assistance			
	Benefit Level 1	Benefit Level 2	Benefit Level 3	Benefit Level 4	Benefit Level 5
Deductible	$250	$50	$0	$0	$0
Out-of-pocket Spending Ranges	**Co-insurance After Deductible**				
Under $750	25%	15%	$2/$5*	$1/$3	$0
$750-3,600	100%	15%	$2/$5*	$1/$3	$0
Above $3600	The greater of 5% or $2/$5*	$2/$5*	$0	$0	$0

*** The lower figure applies to generic drugs and the higher figure applies to brand name drugs.**

Because of the unique nature of the MRDD, there were some departures from the standard Part D drug benefit. As the benefit covered only a few selected drugs and was offered for a limited time period, beneficiaries were not required to pay a premium. Also, because the demonstration did not begin until late in 2004, beneficiary out-of-pocket obligations were pro-rated for the remaining months of that year.

Under the MRDD, six charitable organizations were authorized to provide beneficiaries with cost –sharing assistance. These included: HealthWell Foundation, National Organization for Rare Diseases, the Patient Advocate Foundation, the Patient Access Network Foundation, Patient Services, Inc, and the Caring Voice Coalition.[5] Only assistance received from these organizations counted toward a patient's true out-of-pocket expenses.

Drug prices under the demonstration were determined through Caremark's negotiations with suppliers and pharmacy chains, although prices were limited to 86 percent of average wholesale price plus a $1.50 dispensing fee for retail transactions and 82 percent of average wholesale price with no dispensing fee for mail order purchases. Reconciliation of Medicare payments would be made at the end of the demonstration taking into consideration the contractual limits on prices.

Selection of demonstration drugs. CMS established an intra-agency panel of clinicians from CMS, the Food and Drug Administration (FDA), and the National Institutes of Health (NIH) to lay out broad inclusion guidelines for the selection of drugs for the demonstration. Drugs were required to meet the following criteria:

- Must be a replacement by eliminating the concurrent need for a drug covered under Part B for the specific indication;
- Must be FDA-approved for the specific indication, or for FDA-approved drugs, new indications under consideration by the FDA were considered if the requestor provides documentation that no filing issues are pending;
- Must be of at least equal efficacy to the covered drug for which it is a replacement;
- Use of the drug represents an advantage in terms of access and/or convenience for beneficiaries compared with the currently covered drug; and
- Drugs are ineligible if they are replacing drugs not commonly provided incident to a physician's service (e.g., antihypertensives, antibiotics, oral hypoglycemics).

A panel of CMS clinicians also reviewed applications to add new drugs after the demonstration began. As neither the funding cap nor the limits on patient enrollment were reached, applications for new drugs remained open throughout the course of the demonstration. Most drugs covered under the demonstration

[5] Charitable organizations had to meet the following qualifications: an independent, non-profit, tax-exempt organization not subject to control by any donor; eligibility for assistance was open to all beneficiaries in the demonstration and not specific to any one drug (with the exception of condition-specific entitities); cost-sharing assistance does not vary by the drug the patient receives; selection of health care provider remains open to the applicant; the organization does not refer the patient to any donor or other provider.

were on the list at the outset of the program; however, some drugs, such as interferon alfacon-1 for treating Chronic Hepatitis C, were added as late as August 2005 – just four months before the conclusion of the demonstration program. A list of the drugs, their corresponding treatment indications, and the month in which they were added to the demonstration is shown in Table 2. One of the demonstration injection drugs – interferon beta-1a (Avonex) for treating MS—was already covered by Medicare if it was administered by a physician. Avonex was covered under the demonstration when it was self administered.

III. Evaluation Design

A. Overview of Methods and Data Sources

In order to meet the deadline for this Report to Congress, the evaluation of the MRDD was conducted while the demonstration was still ongoing. It relies on the collection and analysis of five different types of data, the timing of which varies by source. These include: 1) a survey of MRDD enrollees; 2) intake data from enrollment forms; 3) drug claims data under the demonstration; 4) Medicare Part B claims just prior to the start of the demonstration; and 5) clinical trials data for selected drugs included in the demonstration. For the most part, the impact of the demonstration on the three major domains: beneficiary access to care; beneficiary outcomes; and Medicare spending — is examined by making pre-post- comparisons for enrollees. Because of limitations in the timing and richness of available data sources, a case-control design was not considered appropriate for this evaluation.[6] The major evaluation domains, respective measures and data sources are shown in Table 3. Data sources are described in more detail below.

B. Beneficiary Access to Care

Data about changes in demonstration participants' access to care were collected through a survey designed and administered by Mathematica Policy Research, Inc (MPR). The survey targeted 3,962 demonstration enrollees who had been enrolled at least two months before the sample selection cut-off date of February 2004.[7] Those with less experience would likely not be able to tell whether their condition had changed since enrollment, and it was expected that the

[6] This issue is discussed in more depth in Appendix 1.
[7] Persons who had not filed a claim within 11 weeks of enrollment were omitted from the sample in order to target users of the benefit.

TABLE 2. LIST OF MRDD CONDITIONS AND DRUGS

Condition	Drugs	Date Added
Non-cancer		
Acromegaly	Pegvisomant (Somavert)	August 2004
Ankylosing Spondylitis	Etanercept (Enbrel)	February 2005
Chemotherapy-induced hemorraghic cystitis	Mesna (Mesnex)	August 2004
Chronic viral hepatitis C	Pegylated interferon alpha-2a (Pegasys)	Outset
	Pegylated interferon alpha 2b (Peg-Intron)	Outset
	Infergen (interferon alfacon-1)	August 2005
Cytomegalovirus retinitis in AIDS	Valcyte (valganciclovir)	Outset
Gaucher's disease	Miglustat (Zyvesca)	August 2005
Multiple sclerosis	Interferon beta 1a (Rebif)	Outset
	Glatiramer acetate (Copaxone)	Outset
	Interferon beta 1b (Betaseron)	Outset
	Interferon beta 1a (Avonex)	Outset
	H.P. Acthar gel	December 2004
Paget's disease	Alendronate (Fosamax)	Outset
	Risedronate (Actonel)	Outset
Psoriasis	Efalizumab (Raptiva)	December 2004
	Etanercept (Enbrel)	December 2004
Psoriatic arthritis	Etanercept (Enbrel)	October 2004
Pulmonary arterial hypertension	Bosentan (Tracleer)	Outset
Rheumatoid arthritis	Adalimumab (Humira)	Outset
	Anakinra (Kinaret)	Outset
	Etanercept (Enbrel)	Outset
Secondary hyperparathyroidism	Doxercalciferol (Hectoral)	Outset
Senile osteoporosis	Alendronate (Fosamax)	December 2004
	Calcitonin –nasal (Miacalcin)	Outset
	Raloxifene Hydrochloride (Evista)	November 2004
	Risedronate (Actonel)	August 2004
Cancer		
Breast cancer	Anastrazole (Arimedex)	Outset for stage 2-4 cancer with indications expanded in May 2005 to include recurrent breast cancer irrespective of stage
	Exemestane (Aromasin)	
	Letrazole (Femara)	
	Tamoxifen (Novaldex)	
	Toremifene (Fareston)	
Chronic myeloid leukemia	Imatinib mesylate (Gleevec)	Outset
Cutaneous t-cell lymphoma	Bexarotene (Targretin) – oral	Outset
GI stromal tumor	Imatinib mesylate (Gleevec)	Outset
Non small cell lung cancer (NSCLC) – primary	Gefitinib (Iressa)	Outset with restricted access beginning September 15, 2005*
	Erlotinib (Tarceva)	January 2005
Multiple myeloma	Thalidomide (Thalomid)	Outset
Epithelial ovarian cancer	Altretamine (Hexalen)	Outset

*After that date, all prescriptions for gefitinib had to be provided through a single pharmacy source and both beneficiaries and physicians had to complete new informed consent forms. New prescriptions were limited to those covered under a clinical trial or those who previously were on gefitinib and appeared to benefit from the drug. These restrictions were put in place due to an agreement reached between the manufacturer, Astra Zeneca, and the FDA, for the sale of gefitinib throughout the United States.

TABLE 3. OUTCOME DOMAINS FOR THE EVALUATION OF THE MRDD

	Outcome Domains	Measures	Data Sources	Study Population
Access	Access to drug therapy	Whether previously using demonstration drug	Enrollee survey	2,649 respondents who had enrolled in the MRDD by February 2005 and had an MRDD claim by April 2005
			Intake form: Patient report Physician report	34,249 beneficiaries who had enrolled in the MRDD by July 15, 2005
		Prior insurance coverage for demonstration drug	Enrollee survey	2,649 respondents who had enrolled in the MRDD by February 2005 and had an MRDD claim by April 2005
			Intake form: Patient report	34,249 beneficiaries who had enrolled in the MRDD by July 15, 2005
		Beneficiary out of pocket spending on drugs and drug-administration-related services	Enrollee survey	2,649 respondents who had enrolled in the MRDD by February 2005 and had an MRDD claim by April 2005
			Drug claims under the MRDD	
		Self-reported financial burden, including effects on compliance with therapy, and rating of price of drug	Enrollee survey	2,649 respondents who had enrolled in the MRDD by February 2005 and had an MRDD claim by April 2005
Self-perceived Outcomes	Patient burden	Change in frequency of physician visits	Enrollee survey	122 respondents who were prior users of Part B replaceable drugs
		Major perceived benefits of demonstration drug over Part B replaceable drug (including ability to self-administer drug, reduced frequency of visits, and improved health)	Enrollee survey	148 respondents who were prior users of Part B replaceable drugs
	Health status	General health assessment and specific measures that vary by broad disease area, but include energy, fatigue, nausea, vomiting, and pain	Enrollee survey	651 respondents who were not prior users of the demonstration drug

TABLE 3. OUTCOME DOMAINS FOR THE EVALUATION OF THE MRDD

	Outcome Domains	Measures	Data Sources	Study Population
Clinical Outcomes	Survival	Varies by disease, but includes: disease-free survival, overall survival	Clinical literature	Population enrolled in clinical trials for demonstration drugs used to treat: chronic myeloid leukemia, gastrointestinal stromal tumor, multiple myeloma, non small cell lung cancer, multiple sclerosis, and rheumatoid arthritis.
	Disease remission	Varies by disease, but includes: tumor response, cytogenetic remission, and American College of Rheumatology (ACR) response		
	Adverse effects	Varies by disease, but includes: nausea, vomiting, rash, cardiac insufficiency, leucopenia, and neutropenia		
Medicare Spending	Net Medicare drug-related spending	Spending on demonstration drugs less spending on Part B replaceable drugs and associated administration costs, supplies and adjunct therapies	Drug claims data under the MRDD	16,238 beneficiaries who had enrolled in the demonstration by 02/15/2005 and had a demonstration drug claim by June 30, 2005
			Medicare Part B claims	15,467 beneficiaries who had enrolled in the demonstration by February 15, 2005 and had a claim in the 8 months preceding the demonstration start. To ensure an adequate claims experience for analysis the study population also was required in the 8-month study period to: be enrolled in both Medicare Part A and Part B, have Medicare as their primary source of insurance, not have been enrolled in Medicare managed care. The study cohort also could not have had end-stage renal disease and could not have been enrolled for multiple demonstration conditions. In addition, the study cohort was further limited to enrollees with seven conditions with sufficient sample size for analysis: breast cancer, multiple myeloma, non small cell lung cancer, cutaneous T-cell lymphoma, multiple sclerosis, pulmonary arterial hypertension, and rheumatoid arthritis.

demonstration would take more than two months to affect enrollees on the outcomes of interest. Early enrollees were targeted to allow enough time to complete a survey before the deadline for this Report to Congress. Altogether, 3,269 demonstration participants completed the survey, for an overall response rate of 86 percent. The survey was stratified into three disease groups: 1) cancer; 2) MS and other non-cancer related drugs; and 3) RA. The initial sample was modified to exclude non users of the benefit, resulting in a final analytic sample of 2,649 members. Participants served as their own controls and they were asked about their perspectives on changes in access to drug therapy that were brought about through the demonstration program and changes in beneficiary financial and travel burden. Respondents to this survey are referred to as sampled beneficiaries. Results can be generalized to the 9,613 enrollees who had enrolled by December 1, 2004 and had used the benefit by the start of the survey field period (sample universe) – referred to as the weighted survey population. Weighted survey population estimates are presented in the report.

Since the demonstration offered a new source of drug coverage, the potential benefits regarding access, outcomes and financial burden perceived by enrollees would depend greatly on prior access to drug therapy. Results for the survey generally group enrollees into one of four categories: 1) previous users of Part B replaceable drugs; 2) previous users of MRDD-covered drugs; 3) previous users of other non-demonstration or nonPart B replaceable drug to treat their condition; and 4) those who did not use any drugs to treat their condition before the demonstration.

The main indicators of access examined in the survey were sampled beneficiaries' pre-enrollment access to drug therapy, their prior access to drug insurance, and perceived effects of the demonstration on financial burden.

C. Beneficiary Outcomes

Data about participants' perceptions of the benefits of the demonstration were gathered in this same survey. Questions were asked about changes in perceived health status, satisfaction with medication costs and side effects, benefits intrinsic to the self-administration versus physician-administration of medications, and adherence to treatment regimen.

Many of the drugs included in the demonstration offer the possibility of improved clinical outcomes, such as disease remission, increased survival and enhanced patient quality of life over the treatments currently covered by Medicare. However, these outcomes are not easily captured within the constraints of the demonstration project. To examine the potential clinical benefits new Medicare coverage for these drugs might offer beneficiaries, CMS requested that AHRQ commission several technology assessments and updates of previous systematic reviews of the clinical literature for those conditions expected to account for the

bulk of spending under the demonstration. These include the noncancer conditions of RA and MS and the cancer conditions of chronic myeloid leukemia, multiple myeloma, non small cell lung cancer, and gastrointestinal stromal tumor. The MS review was not finalized in time for this Report to Congress so findings from that study have not been included. It was beyond the scope of the evaluation to conduct such reviews for all conditions and drugs included in the demonstration.

A systematic review uses explicit, methodical techniques to limit bias and reduce chance effects in a review of the clinical literature, which can provide more reliable results upon which to draw conclusions and make decisions. The reviews of cancer conditions were conducted by Duke University, one of the Evidence-based Practice Centers at the Agency for Health Care Research and Quality. The reviews of noncancer conditions were conducted by Sheffield University, one of the academic centers supporting the National Institute for Health and Clinical Excellence (NICE) in the United Kingdom. Both groups are poised to answer questions of relative efficacy in support of public sector coverage decisions on new drugs and devices. By conducting these reviews as part of this evaluation, the Report to Congress is able to address patient outcomes in a meaningful way other than simply reporting on what can be measured and observed under the demonstration project.[8]

D. Medicare Spending

Congress directed CMS to examine "*the cost-effectiveness of the program to Medicare, specifically taking into account any cost savings attributable to reduced physicians' services and hospital outpatient departments' services for administration of the biological*." Cost-effectiveness analysis is the structured comparison of two or more health care interventions. The analyses are designed to show the relationship between resources used (costs) and health benefits achieved (effects) for technologies or programs. Effects are measured in a common metric across health interventions, such as quality-adjusted life years, and both costs and effects are usually summarized in a series of cost-effectiveness ratios (Russell et al., 1996).

Because of the large number of drugs and conditions included in the demonstration, CMS felt it was beyond the scope of the evaluation to do a formal cost-effectiveness analysis for all of the demonstration-covered drug/condition combinations. Also, as the demonstration unfolded, we found the plurality of MRDD enrollees had been using demonstration-covered drugs before they enrolled in the demonstration. Those beneficiaries likely experienced little or no

[8] A detailed description of the methods used for the cancer condition reviews can be found at the following websites: http://www.ahrq.gov/clinic/ta/thalidomide/index.html; http://www.ahrq.gov/clinic/ta/nonsmall/index.html; http://www.ahrq.gov/clinic/ta/cml/index.html; http://www.ahrq.gov/clinic/ta/gist/index.html. Details of the RA review will be available in Nixon et al., a forthcoming publication in *Statistics and Medicine.* The MS study is currently under review and not yet published.

changes in health effects due to the demonstration as their drug regimen did not change. Other beneficiaries (new users of the demonstration-covered drugs) may have experienced improvements in outcomes, but it is difficult to assess the separate effects in this subgroup. For these reasons, we have interpreted the Congressional requirement to examine cost-effectiveness as an intent to ensure this report address both the impacts on health benefits and costs. Many of our evaluation studies have interpreted Congressional requirements to look at cost-effectiveness in this manner and do not combine the two elements into a formal cost-effectiveness ratio.

The component of this evaluation that focuses on costs examines the impact of the demonstration on *net Medicare spending*, taking into account drug spending under the demonstration less any savings attributable to reduced spending on Part B-replaced drugs and physicians' services and hospital outpatient departments' services for their administration.

Gross spending on covered drugs is reported based on an analysis of pharmacy benefit management claims under the demonstration through June 30, 2005. Net spending is estimated by subtracting the Medicare spending for Part B replaceable drugs and spending related to their administration from gross demonstration drug spending for those beneficiaries who were likely users of Part B drugs prior to the start of the demonstration. The Medicare costs for replaceable Part B drugs and their administration were derived from an analysis of Medicare claims for the 8-month period immediately prior to the start of the demonstration (January – August 2004 – referred to as the study period) for 14,060 enrollees who met the following criteria:

- were enrolled by February 15, 2005;
- had been using Part B drugs in the study period;
- were not enrolled for multiple demonstration conditions;
- did not have end stage renal disease;
- were enrolled for treatment of one of seven demonstration conditions with sufficiently large cohort with Part B claims experience during the study period for analysis (n > 20) (breast cancer, multiple myeloma, non small cell lung cancer, cutaneous T-cell lymphoma, MS, pulmonary arterial hypertension, and RA);
- were enrolled in both Medicare Part A and Part B during the study period;
- had Medicare as their primary payor for the study period; and
- were not enrolled in Medicare managed care in the study period.

Part B drug and administration service spending estimates for 2004 were inflated to 2005 by identifying the content of drug administration sessions and applying 2005 Medicare payments from the relevant Medicare fee schedule. Further details on the methods used for the claims analysis and the content of drug administration sessions are provided in Appendix I.

IV. Findings

A. Enrollment Trends and the Enrollment Process

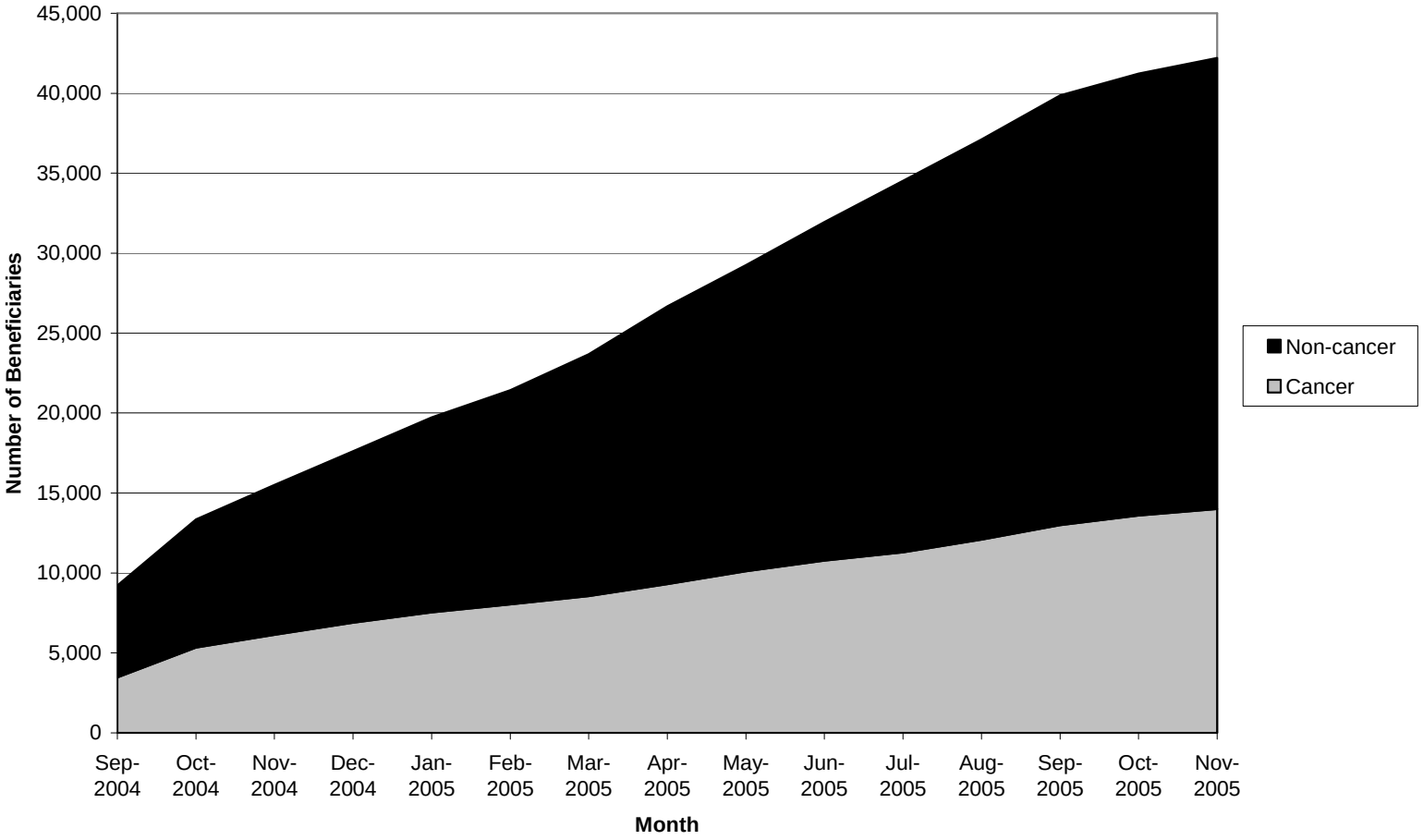
Overall, 42,220 Medicare beneficiaries enrolled in the MRDD – a number approaching the enrollment cap of 50,000 beneficiaries stipulated by Congress. Although fewer than 10,000 beneficiaries enrolled in the initial month of the program, enrollment continued at a steady pace over its duration (Figure 1), with the program adding around 3,000 new enrollees on average every month. Notably, beneficiaries continued to enroll in the demonstration up until the last month of the program. Close to 1,000 beneficiaries signed up for the program in November 2005, although at that time it would provide only one more month of drug coverage benefits. More than two-thirds of enrollees qualified for the program because they needed non-cancer medications covered by the MRDD to treat their condition. The remaining one-third enrolled to obtain access to cancer medications.

The overwhelming majority (78 percent) of those enrolling for noncancer conditions had either RA (14,649) or MS (7,682) (Figure 2). In fact, these two conditions accounted for more than half of total MRDD enrollment. Other noncancer conditions accounted for a relatively-small proportion of enrollees, with only four other noncancer conditions enrolling around 1,000 beneficiaries or more. These included pulmonary hypertension (1,878), psoriasis (1,387), hepatitis C (1,173), and psoriatic arthritis (992). Just under 7,000 demonstration participants enrolled for breast cancer medications, accounting for half of enrollees with cancer conditions (Figure 3). Cancer conditions with the next highest number of enrollees were multiple myeloma (2,778), chronic myeloid leukemia (CML) (1,974), and non small cell lung cancer (NSCLC) (1,304).

Initially, the number of applicants was expected to far surpass enrollment limits set by Congress, although it was difficult to predict the numbers of beneficiaries who might enroll. Ill-defined diagnoses for some demonstration conditions[9], uncertainty about the numbers of beneficiaries diagnosed with demonstration conditions who would be eligible for drug treatment, and uncertainty about the availability of supplemental drug coverage for persons needing these drugs were among the factors complicating these predictions. Subsequent analyses of claims data show in the three months prior to the start of the demonstration, at least two claims with one of the demonstration conditions had been filed for just over 980,000 beneficiaries. Of these, nearly 60,000 used the Part B drugs replaceable by the demonstration program within three months of the start of the demonstration. This provides upper and lower bounds for the numbers of beneficiaries that may have been eligible for the demonstration.

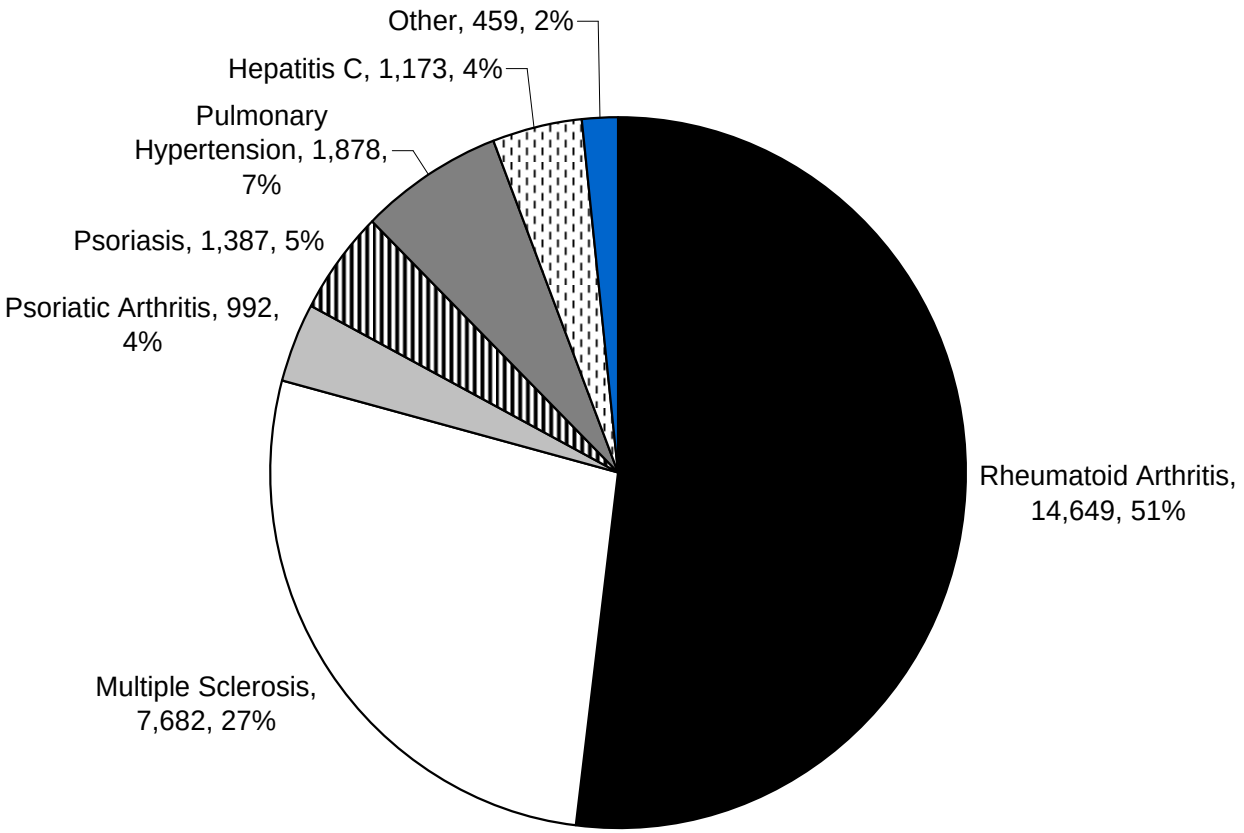
[9] For example, the diagnosis code that encompasses gastrointestinal stromal tumor is defined as “stomach neoplasm, pyloric antrim or unspecified”, and includes many soft tissue carcinomas.

FIGURE 1. CUMULATIVE MONTHLY ENROLLMENT BY MAJOR DISEASE CATEGORY



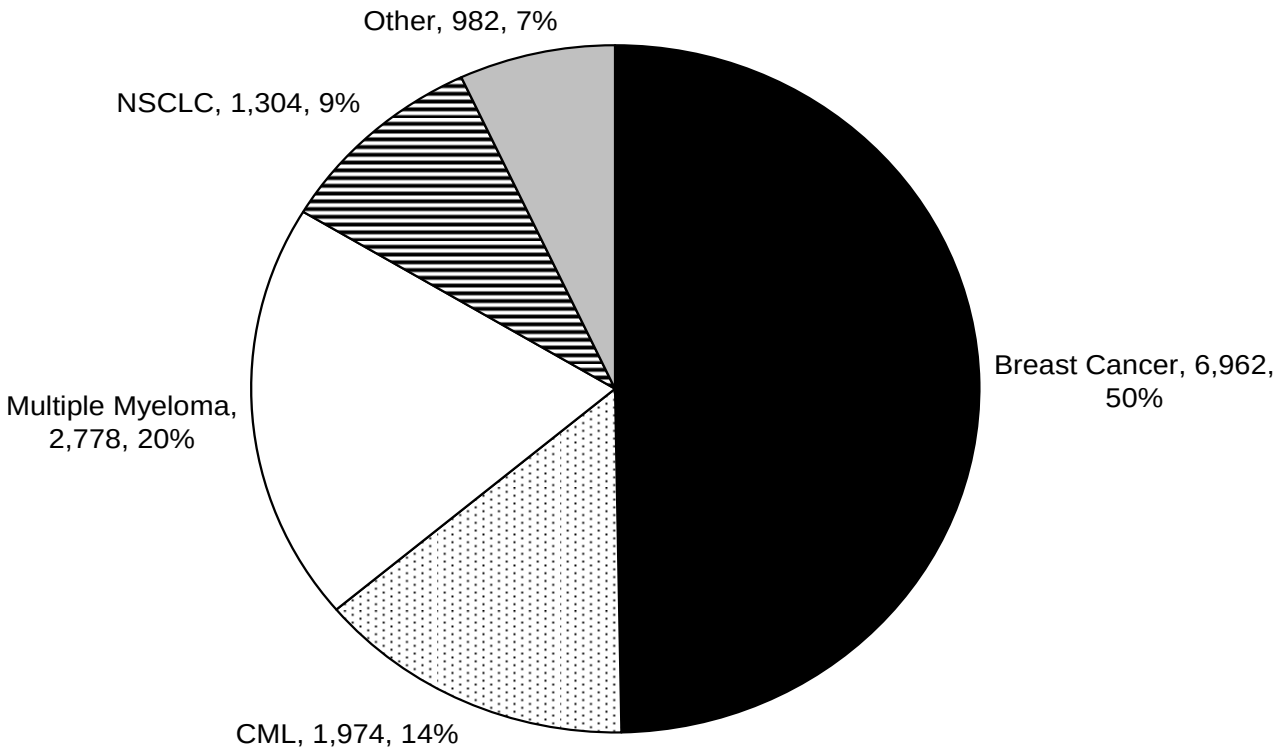
SOURCE: TrailBlazer's Weekly Reports, September 24, 2004 through December 2, 2005

FIGURE 2. ENROLLMENT BY NONCANCER CONDITION



SOURCE: TrailBlazer's Weekly Reports, September 24, 2004 through December 2, 2005

FIGURE 3. ENROLLMENT BY CANCER CONDITION



SOURCE: TrailBlazer's Weekly Reports, September 24, 2004 through December 2, 2005
Note: NSCLC – non small cell lung cancer; CML – chronic myeloid leukemia.

Once the demonstration program was formally announced, CMS began an aggressive campaign of beneficiary outreach to encourage enrollment. Assistance in enrolling and filling out the forms was provided by TrailBlazer through a 1-800 call center. TrailBlazer also hired a full-time outreach coordinator with responsibility for expanding beneficiary, physician, and pharmacist knowledge about the program. TrailBlazer's outreach campaign may have helped to spur the steady growth in enrollment over the course of the demonstration.

According to the enrollee survey conducted by Mathematica Policy Research, Inc., the most common sources for all sampled enrollees to have heard about the demonstration were their doctor's office or clinic (47 percent), broadcast or print media (13 percent), an advocacy organization (13 percent), and mailings (10 percent). Pharmaceutical companies and their affiliated drug assistance programs or foundations were also an important source of information for 8 to 10 percent of all sampled enrollees. Sample members with MS were more likely than members with other conditions to have heard about the demonstration through an advocacy group (28 percent) or through mailings (17 percent).

The primary reasons sampled beneficiaries cited for enrolling in the demonstration included drug affordability (56 percent), prior drug cost (30 percent), and a suggestion by a physician (12 percent). Sampled beneficiaries with cancer were more likely to report their drug was not affordable prior to entering the demonstration (60 percent, compared with 53-54 percent for enrollees with RA, MS, or other demonstration conditions). Sampled beneficiaries with RA were more likely to have a doctor suggest enrollment (19 percent, compared with 6-12 percent of enrollees in the other condition groups).

While there was some anecdotal evidence from Trailblazer suggesting that applicants were finding the demonstration application too difficult to complete, the majority of sampled enrollees (70 percent) did not report difficulty in completing the demonstration application form; only 5 percent said the paperwork was very difficult. Among those reporting difficulty, the top three mentioned problems were that the form was confusing, excessively long, and had a difficult income-reporting section. Less frequent, though still common, problems were challenges in reading and completing the form due to health problems (poor vision, arthritis, or in coordination, for example), the form's small print, and difficulty locating all of the information requested.

B. Characteristics of Enrollees

In many ways, MRDD enrollees differed from the general Medicare population (Table 4). Based on enrollment data through July 15, 2005, enrollees were more likely to be under 65 (39 percent versus 15 percent), originally entitled for Medicare due to disability (48 percent versus 14 percent), and female (74 percent versus 56 percent) than Medicare beneficiaries overall. Ninety-two

TABLE 4. CHARACTERISTICS OF MRDD ENROLLEES, JULY 15, 2005

Characteristic	Total	Cancer	Rheumatoid Arthritis	Multiple Sclerosis	Other	Medicare Population (2004)
All	34,249	11,872	11,772	6,488	4,117	41,760,380
Age*						
Mean	65.2	73.5	64.8	51.8	63.8	---
Younger than 65	38.5%	8.5%	40.7%	87.0%	42.3%	15.3%
65-74	36.2%	45.5%	39.7%	11.8%	38.1%	43.2%
75 or older	25.3%	46.0%	19.6%	1.2%	19.6%	41.4%
Gender						
Female	73.9%	73.7%	77.5%	76.9%	59.4%	56.2%
Male	26.1%	26.3%	22.5%	23.1%	40.6%	43.5%
Race						
White	86.4%	87.1%	86.3%	85.2%	86.5%	84.2%
Black	9.7%	10.0%	8.9%	11.0%	9.3%	9.8%
Other/Unknown	3.9%	2.9%	4.9%	3.6%	4.2%	6.1%
Original Reason for Medicare						
Disabled	47.9%	16.8%	92.3%	54.4%	49.0%	14.3%
Resides in an Urban Location	75.5%	75.0%	73.7%	78.3%	77.5%	77.0%
Region						
Northeast	12.8%	12.0%	11.3%	15.6%	15.2%	19.8%
North central	22.2%	25.0%	20.3%	21.9%	19.7%	22.8%
South	47.0%	46.3%	50.2%	41.6%	48.0%	35.7%
West	18.1%	16.7%	18.2%	21.0%	17.2%	19.5%
Outlying Areas						2.3%
Benefit Level						
Benefit Level 1 ($250)	61.5%	63.0%	61.0%	56.7%	65.9%	NA
Benefit Level 2 ($50)	6.8%	6.8%	7.0%	6.6%	6.3%	NA
Benefit Level 3 ($0)	28.4%	27.6%	28.4%	32.7%	23.4%	NA
Benefit Level 4 ($0)	3.4%	2.5%	3.6%	3.9%	4.3%	NA
Benefit Level 5 ($0)	0.1%	0.0%	0.0%	0.1%	0.1%	NA
Income (from survey): N	2,649	802	887	833	127	16,315
Less than $20,000	70.5%	63.2%	75.6%	74.5%	53.4%	50%
$20,000 - $30,000	14.1%	15.7%	12.3%	14.3%	14.6%	20%
More than $30,000	15.4%	21.1%	12.2%	11.2%	32%	30%

SOURCE: CMS analysis of MRDD enrollment data through July 15, 2005 linked with the Medicare EDB and 2003 Area Resource File and MPR analysis of survey of demonstration participants. Data for Medicare population from unpublished 2005 Annual Statistical Report and the 2002 Medicare Current Beneficiary Survey (for income). * Age at the start of the demonstration. Percentages may not sum due to 100 percent. -- Data not available. NA Data not applicable.

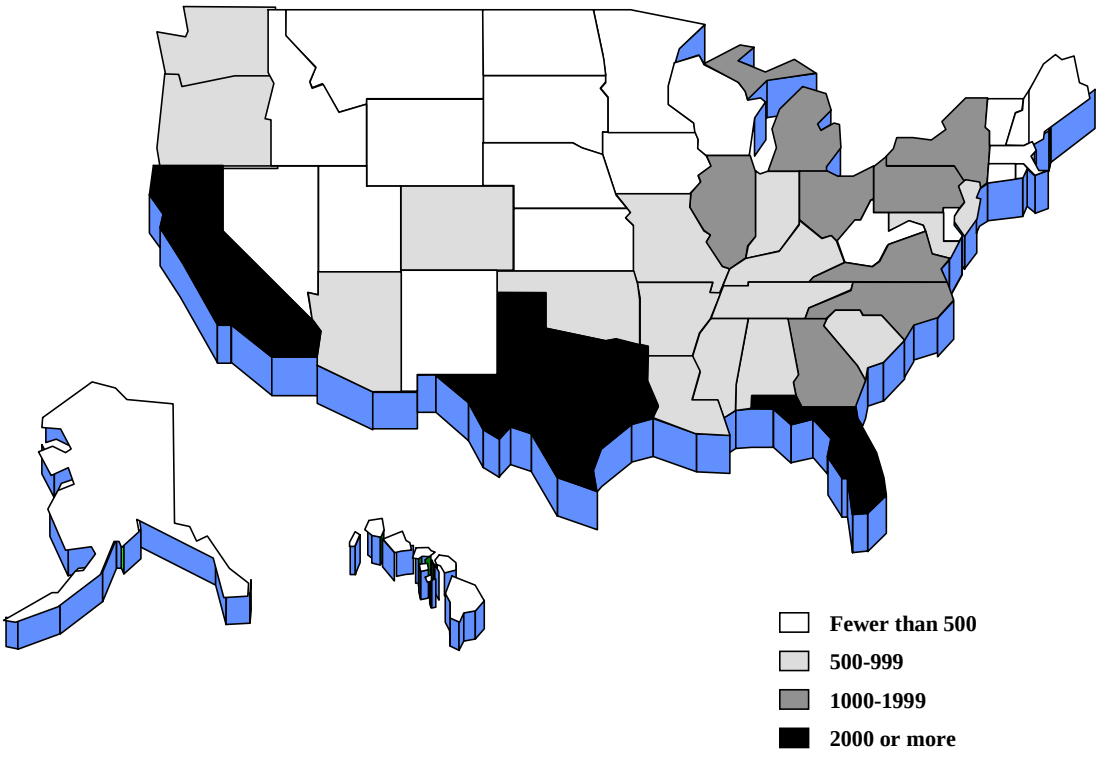
percent of enrollees with RA and more than half of enrollees with MS qualified for Medicare by reason of disability, which is reflected in the relatively young age of demonstration participants as well. High female participation is consistent with the high proportion of enrollees with breast cancer, RA and MS – all of which affect women in disproportionately high numbers.

As intended, the demonstration program attracted those with lower incomes. Seventy-one percent of surveyed demonstration participants reported annual income below $20,000 – corresponding to less than twice the federal poverty level. Fifty percent of the general Medicare population reported income below $20,000 in 2002. Sampled enrollees with RA and MS were more likely than other disease groups to report incomes below $20,000. Thirty-nine percent of enrollees through July 15, 2005 qualified for some level of federal cost sharing for their drugs. The majority of those enrollees (74 percent) qualified for a zero deductible benefit with low co-payments ($2 for generic and $5 for brand name drugs – Benefit Level 3). Relatively few qualified for the plan with no patient cost sharing (Benefit Level 5). It should be noted that the demonstration program was not designed to attract beneficiaries with Medicaid –which often provides a relatively rich drug benefit—or those who were institutionalized (as the program had no nursing home pharmacy contracts). Beneficiaries dually-eligible for Medicare and Medicaid and those in a nursing home would most likely qualify for the highest level of Federal subsidies.

Relative to the geographic distribution of Medicare beneficiaries in general, MRDD enrollment was disproportionately high in the South and disproportionately low in the Northeast. However, the demonstration touched every state in the nation, with no state enrolling fewer than 30 beneficiaries by July 15, 2005, and the states of California, Florida, and Texas each enrolling more than 2,000 beneficiaries (Figure 4).

MRDD enrollees were similar to the general Medicare population in their racial characteristics, and urbanicity.

FIGURE 4. MRDD ENROLLMENT BY STATE, JULY 15, 2005



C. Use of the Benefit

As of July 15, 2005, MRDD enrollees had on average 6 months experience with the program (Table 5). Length of experience with the drug benefit varied by disease category with persons enrolled for noncancer conditions other than RA and MS having the lowest amount of experience. (Many drugs in this category were added several months into the program.) By mid-summer only 53 percent of enrollees had used the benefit under the demonstration. Such low use of the benefit was unanticipated, as most demonstration participants suffered from chronic diseases that require ongoing pharmacologic treatment.

TABLE 5. MRDD PLAN EXPERIENCE, AS OF JULY 15, 2005

Characteristic	Total	Cancer	Rheumatoid Arthritis	Multiple Sclerosis	Other
All	34,249	11,872	11,772	6,488	4,117
Duration of enrollment					
mean (months)	5.8	6.2	5.6	6.8	3.6
less than 3 months	30.9%	26.0%	34.1%	20.2%	52.3%
3-6 months	18.7%	16.9%	19.3%	13.7%	30.2%
more than 6 months	50.4%	57.1%	46.6%	66.1%	17.5%
Used Benefit by July 15, 2005	52.9%	47.9%	50.5%	69.0%	49.1%

SOURCE: CMS analysis of MRDD enrollment data through July 15, 2005.

Results of a logistic regression of characteristics influencing the likelihood of drug benefit use are presented in Table 6. This analysis shows the most vulnerable enrollees – those receiving a subsidized benefit, minorities, and those originally qualifying for Medicare by reason of disability – were more likely than their counterparts to use the drug benefit. Notably, enrollees receiving a subsidized benefit were more than three times more likely than those with a standard drug benefit to have a claim under the demonstration. As expected, the longer an enrollee had been in the demonstration, the greater the likelihood that they would have used the benefit. However, utilization was still lower than anticipated among beneficiaries who had been enrolled for several months. For those who had enrolled by July 15, and had been in the program at least six months, 59 percent used the benefit.

TABLE 6. ENROLLEE CHARACTERISTICS INFLUENCING THE PROBABILITY OF DRUG BENEFIT USE

Prognostic variable	Parameter Estimate	Wald Chi-Square	p-value	Odds Ratio
Intercept	0.0606	0.5228	0.0105	
Received subsidized benefit	1.2276	2319.8442	<.0001	3.413
Duration of enrollment	0.1110	1035.1829	<.0001	1.117
Died during demonstration	-1.0131	371.1889	<.0001	0.363
Disabled as original reason for entitlement	0.2327	42.0370	<.0001	1.253
Age	-0.0164	141.9514	<.0001	0.984
Enrolled for cancer condition	-0.1720	35.9871	<.0001	0.842
White	-0.1589	15.2803	<.0001	0.853
Resides in Urban Area	0.0718	4.1212	0.0084	1.074

SOURCE: CMS analysis of MRDD enrollment data linked with EDB and 2003 Area Resource File.

Because the MRDD provided drug treatment coverage for many conditions with poor long term prognosis, it is not surprising that some beneficiaries died before they had a chance to use the benefit. Overall, six percent (2,138) of the 34,249 beneficiaries who had enrolled by July 15, 2005 were no longer living on September 8, 2005. Of these, nearly 70 percent (1,479) had not used the benefit before they had died. Mortality was highest among enrollees with non small cell lung cancer (50 percent), epithelial ovarian cancer (46 percent), secondary hyperparathyroidism (39 percent), and multiple myeloma (20 percent). As shown in the logistic regression in Table 6, death during the demonstration was inversely related to the use of the drug benefit.

Other factors influencing the use of the drug benefit include beneficiary age [with the younger (and disabled) more likely to use the benefit], enrollment for a cancer condition (positive association), and whether the beneficiary resided in an urban area (positive association).

CMS and TrailBlazer were interested in finding out more about why enrollees were not using the benefit. CMS funded a qualitative outreach and enrollment study that was not required for this evaluation by Congress. Results of this study are expected to be available by the end of 2007. In an independent survey fielded by TrailBlazer of 3,500 beneficiaries who had enrolled by December

2005, but had not used the benefit by March 2006, the top three reasons cited by beneficiaries for not using the benefit were:

- still obtaining free medications from a charitable source (30 percent);
- could not afford the co-payments (19 percent); and
- not taking the prescribed medication (9 percent).

Normal delays associated with claims processing were not a factor in the low use of the benefit. While inpatient claims may not be complete before 3-6 months after the inpatient stay, drug claims processing is highly automated and claims are often processed in two week billing cycles. According to representatives from TrailBlazer, nearly all claims were paid within one billing cycle after the service date. The data presented in Tables 5 and 6 represent experience under the demonstration through mid-Summer 2005. However, by the close of the demonstration only 61 percent of enrollees had used the benefit.

D. Impact on Patient Access to Care

An estimated 62-76 percent of MRDD enrollees were using MRDD covered drugs prior to their participation in the demonstration program, depending on the source of information. The latter estimate is derived using a hierarchy of responses from three sources that were generally consistent, including patient report at the time of enrollment, physician report at the time of enrollment and the survey of MRDD enrollees (Table 7). Clinical information supplied by beneficiaries' physicians at intake was viewed to be more accurate than beneficiary-supplied information. Similarly, information supplied on the written application form about prior drug use was viewed to be more accurate than beneficiary report in the survey, as beneficiaries were more likely to have had the relevant paper work or written information in hand when filling out the application form, and many received help from family members, physician office staff, or advocacy organization staff. Survey information about whether the patient needed to go to the doctor's office or clinic for injection or infusion was used to distinguish Part B-covered drugs for MS from demonstration-covered drugs.

Notably, an estimated 17 percent of beneficiaries were newly diagnosed or were not previously using either a Part B drug or a demonstration drug to treat their condition and some of them may have used MRDD-covered drugs even in the absence of the demonstration program.

TABLE 7. ENROLLEE DRUG USE AND PATIENT DIAGNOSIS PRIOR TO THE DEMONSTRATION

Characteristic	Source	Total		Cancer		Multiple Sclerosis		Rheumatoid Arthritis		Other Conditions	
		N****	Percent	N****	Percent	N****	Percent	N****	Percent	N****	Percent
Already Using MRDD Drug Before Enrollment	Enrollment Form Physician Report	34,157	62%	11,834	71%	6,477	73%	11,745	56%	4,101	34%
	Enrollment Form Patient Report	34,195	65%	11,850	78%	6,481	70%	11,752	60%	4,112	33%
	Enrollee Survey Best Estimate	9,613	76%	3,028	82%	3,013	83%	3,110	68%	462	40%
Proportion With New Diagnosis*	Medicare Claims**	4,839	17%	1,394	16%	863	19%	2,164	11%	418	52%
Use of Part B Drug											
Within Three Months Before Demonstration	Medicare Claims**	15,467	9%	6,183	9%	3,469	13%	5,087	7%	726	3%
Within Eight Months Before Demonstration	Medicare Claims**	15,467	12%	6,183	13%	3,469	15%	5,087	11%	726	3%
At Enrollment	Enrollment Form***	34,249	13%	11,872	5%	6,488	19%	11,772	22%	4,117	22%
Just Prior to Enrollment	Enrollee Survey	9,613	5.5%	3,028	2.5%	3,013	7.1%	3,110	7.4%	462	3.1%

* Proportion of beneficiaries in the claims analysis who were not using the MRDD drug before the start of the demonstration and had no diagnoses for their MRDD condition in 8 months prior to the start of the demonstration. **Excludes conditions with small numbers of enrollees by February 15, 2005, including: acromegaly, ankylosing spondylitis, epithelian ovarian cancer, Paget's disease, psoriasis, and secondary hyperparathyroidism. Beneficiaries with multiple conditions have also been excluded. ***Assessment of physician-reported data; some drugs reported are considered to be earlier step therapy or combination therapy rather than strict replacements of the MRDD medication (e.g., methotrexate for RA). ****N represents the number of people within a data source responding to a particular question or meeting selection criteria. They are weighted population counts for the survey.

Considering this, our analysis suggests the demonstration program provided Medicare beneficiaries with new access to drugs from no more than 38 percent of the cases, and possibly as low as 11 percent of the cases, with the best estimate likely toward the lower bound.[10] However, sampled enrollees who used no reported drugs in the pre-enrollment period generally described large and significant improvements in access problems related to their medications (MPR, 2006).

The demonstration program had a variable impact on beneficiary access by disease category. Enrollees diagnosed with cancer conditions had relatively high prior access to their MRDD medication – with an estimated 71-82 percent having used the drugs before enrollment. Among this group, beneficiaries with breast cancer (91 percent), beneficiaries with chronic myeloid leukemia (95 percent) and beneficiaries with gastrointestinal stromal tumor (95 percent) had particularly high prior use of MRDD medications. By contrast, enrollees diagnosed with noncancer conditions other than MS and RA had low prior access to their MRDD medications (33 to 40 percent had prior access). The latter is due to the fact that several of the medications received FDA approval for treating demonstration indications about the time that the demonstration began, including drugs used to treat ankylosing spondylitis, psoriasis and psoriatic arthritis.

Prior Use of Medicare-covered Replaceable Drugs. Largely because so many beneficiaries were already using MRDD covered drugs before the start of the demonstration, the MRDD apparently did not serve as a major vehicle to allow beneficiaries to substitute away from physician-administered injectables or infusion drugs already covered under Part B. In fact, the claims analysis of beneficiaries who had enrolled by February 15, 2005 revealed that only 9 percent were using Part B replacement drugs in the three months before the demonstration began, although 12 percent had been using these drugs within the 8 months prior to the start of the demonstration (Table 7). Patient report at enrollment reflects the latter estimate with 13 percent stating they would replace a Part B drug they were currently using once they enrolled. An analysis of drugs surveyed enrollees were using prior to the demonstration showed many reported Part B drugs were over the counter medications (e.g., nonsteroidal anti-inflammatory drugs) or oral drugs that were not covered under Part B (e.g., tamoxifen). After extensive data cleaning on the basis of drug name, only 6 percent of sampled beneficiaries were classified as having been a Part B drug user before enrollment.

[10] The upper bound assumes all persons not previously using MRDD drugs before enrollment, may have gained new access to these treatments, using the lowest estimate of prior MRDD drug use (62%). The low range assumes beneficiaries with no prior history of MRDD or replaced drug use for their condition would have had access to MRDD medications in the same proportions as those who had not been newly diagnosed, assuming the highest estimate of prior MRDD drug use (76%) Given the high proportion of prior MRDD drug users, the best estimate is most likely near the lower bound.

Drug Insurance Coverage. For many enrollees, the demonstration program did improve insurance coverage for MRDD drugs, resulting in reduced patient cost sharing. More than two-thirds (70 percent) of sampled beneficiaries said they did not have any drug insurance coverage before they enrolled in the demonstration. This is in contrast to the levels of supplemental drug coverage for the Medicare population in general, where 65 percent reported having drug coverage through a supplemental insurance plan in 2003 (McCormack et al., 2005), again suggesting the demonstration targeted those without comprehensive drug insurance. Notably on the intake form for beneficiaries who had enrolled by July 15, 2005, 16 percent of demonstration participants who had been previously using demonstration drugs before enrollment reported they bore the entire cost of the drug out of pocket – costs that could be higher than $30,000 per year for treating pulmonary arterial hypertension, as an illustration.

Out of Pocket Spending and Self-Reported Financial Burden. Under the demonstration, on average, beneficiaries had spent $1,440 out of pocket on demonstration drugs by June 30, 2005 (Table 8). Beneficiaries in the standard benefit package spent about $3,000 on average since enrollment. Out-of-pocket spending for those receiving Federal cost-sharing assistance ranged from $666 for beneficiaries in Benefit Level 2 to no cost sharing for beneficiaries in Benefit Level 5. Just over 40 percent of enrollees filing claims by mid-summer 2005 had spent $20 or less out of pocket since they had enrolled. Just over three-quarters of beneficiaries in the standard benefit had met the catastrophic spending limit in 2004, and about half had met that limit mid-year through 2005.

The MRDD beneficiary survey asked respondents who said they paid for at least part of their drug costs to report both before and after enrollment several indicators of the financial burden of drug treatment, including the frequency of skipping medications to make them last longer, whether they took less medications to make them last longer, or whether they needed help from friends or family to pay for medications, and spending less on basic needs to pay for medications (MPR, 2006). Although there were some differences by condition category, in general there were improvements in these indicators of financial burden for beneficiaries who reported being treated by either a demonstration drug or a Part B replaceable drug before the demonstration for their condition (highlighted in Table 9). Results for sampled beneficiaries with MS who had been using Part B-covered drugs before they enrolled were an exception. Those beneficiaries were more likely to skip or take less of a medication to make it last longer after the demonstration began than before.

TABLE 8. ENROLLEE OUT-OF-POCKET SPENDING BY YEAR, as of JUNE 30, 2005

	2004		2005		Both Years	
Mean Out-of-Pocket Spending	N	Mean or proportion	N	Mean or proportion	N	Mean or proportion
All	6,245	$510	15,425	$1,316	16,238	$1,440
Standard Benefit	2,837	$1,140	7,358	$2,673	7,848	$2,889
Benefit Level 2	235	$244	890	$621	916	$666
Benefit Level 3	2,833	$6	6,444	$12	6,704	$14
Benefit Level 4	333	$4	722	$7	759	$8
Benefit Level 5	7	$0	11	$0	11	$0
Proportion in Standard Benefit Meeting Catastrophic Spending Limit in Year	2,837	76.7%	7,358	52.2%	---	---

SOURCE: CMS analysis of MRDD drug claims filed through June 30, 2005. -- not applicable, catastrophic limits begin anew each year. Ns represent totals in category (e.g., total in 2004 with standard benefit).

Overall and for persons with RA, improvements were more marked for beneficiaries who had been prior users of demonstration drugs than for prior users of Part B medications. As an illustration, before the demonstration began both groups were equally likely to spend less on basic needs to afford their medications. After the demonstration began, prior users of MRDD drugs were a third less likely than prior Part B drug users to say they spent less on basic needs to pay for their medications.

Survey respondents were also asked about their satisfaction with medication cost and with their current financial condition compared to before enrollment. Over half of sampled enrollees (62 percent) rated the cost of the MRDD medication under the demonstration as excellent or very good, although this varied by benefit level (not shown in table) and condition group. While 45 percent of sampled enrollees in the standard benefit rated the cost of their MRDD medication as excellent or very good under the demonstration, this increased to 76 percent for sampled enrollees in intermediate benefit levels (levels 2 and 3), and 86 percent for beneficiaries in the most generous benefit levels (levels 3 and 4).

Sampled beneficiaries with MS were most likely to be satisfied with the cost of their MRDD medication compared to respondents in other condition groups (70 percent); sampled beneficiaries with cancer were the least likely to be satisfied with the cost of their medication (53 percent). More of those taking demonstration drugs prior to enrollment rated the cost of their demonstration drug as excellent or very good (63 percent) compared to those previously taking a Part-B replaceable drug (54 percent giving excellent and very good ratings) (MPR, 2006).

While not implying causation, roughly one-third of sampled enrollees felt their current financial situation had improved compared to before enrollment, while 13 percent felt it had worsened. This broad question captures the entire financial health of the respondent, not just that related to the change in insurance for the demonstration drug, and may reflect progression of the disease and its overall impact as well as other factors external to the demonstration affecting financial health. Sampled enrollees who lacked drug insurance before the demonstration, or who received low income subsidies from the demonstration, were less likely to say their financial health had worsened than other respondents.

TABLE 9. SELF-REPORTED FINANCIAL BURDEN BEFORE (B) AND AFTER (A) THE DEMONSTRATION FOR SAMPLED BENEFICIARIES REPORTING USE OF PART B-REPLACEABLE VERSUS DEMONSTRATION-COVERED DRUGS

Characteristic	All				Cancer				Rheumatoid Arthritis				Multiple Sclerosis			
	Prior Drug Use				Prior Drug Use				Prior Drug Use				Prior Drug Use			
	Part B		MRDD		Part B		MRDD		Part B		MRDD		Part B		MRDD	
	B	A	B	A	B	A	B	A	B	A	B	A	B	A	B	A
All	(N=531)		(N=7,262)		(N= 75)		(N= 2,479)		(N=229)		(N=2,111)		(N=213)		(N=2,486)	
Ever Skipped or Took Less of Medication Because of Cost To Make It Last Longer	3%	3%	7%	2%	0%	0%	7%	1%	9%	5%	8%	4%	0%	3%	0%	0%
	(N=217)		(N=1,485)		(N=12)		(N=1,019)		(N=75)		(N=376)		(N=123)		(N=40)	
Needed Someone to Help Pay for Medications	35%	16%	26%	11%	---	---	23%	11%	30%	20%	35%	10%	42%	17%	25%	25%
	(N=134)		(N=1,322)		(N=4)		(N=1,000)		(N=35)		(N=243)		(N=87)		(N=29)	
Spent Less on Basic Needs to Pay for Medication	28%	17%	28%	11%	---	---	24%	10%	30%	10%	50%	14%	26%	17%	22%	22%
	(N=130)		(N=1,312)		(N=4)		(N=996)		(N=35)		(N=232)		(N=83)		(N=33)	

SOURCE: MPR analysis of MRDD Beneficiary Survey, 2006. NOTES: B: Before demonstration enrollment; A: After demonstration enrollment. Surveyed beneficiaries with conditions other than those listed are not reported due to small sample sizes of Part B replaceable drug users. – Data not reported due to small cell sizes. Ns represent weighted population counts for survey.

Use of Mail Order Supply. Another potential advantage of the demonstration program was that it offered beneficiaries the option of mail order supply of their medications. For beneficiaries with chronic conditions, like those participating in the demonstration, mail order is convenient and may provide lower drug prices. The convenience of ordering by mail can be particularly helpful to beneficiaries without a regular means of transportation or those who live far from a pharmacy.

While we do not know how many demonstration participants used mail order before the demonstration began, the mail order option was commonly used under the demonstration. Through June 30, 2005, mail order prescribing accounted for 54 percent of filed claims and 71 percent of total claims payments. The typical mail order prescription covered twice the time period (days supply) of a typical prescription from a retail pharmacy. Table 10 presents data on the percentage savings in billed charges per days supply by using mail order versus retail prescribing for the most commonly prescribed medications under the demonstration. For purposes of comparability, the most commonly prescribed dose and packaging (as described by a National Drug Code (NDC) were selected for each of these medications. Savings range from 2 percent for gleevec (indicated for chronic myeloid leukemia and gastrointestinal stromal tumor) to 13 percent for adalimumab (indicated for RA). For a drug such as adalimumab that can cost nearly $20,000 for a year's supply these savings can be substantial, both to Medicare and to beneficiaries.

TABLE 10. MAIL ORDER SAVINGS FOR COMMONLY PRESCRIBED DRUGS

Drug	Number of Prescriptions	NDC	Percent savings over retail pharmacy*
Copaxone	6,711	88115330	9.2%
Enbrel	5,481	58406043504	4.0%
Gleevec	1,972	78040105	1.7%
Humira	6,942	74379902	13.7%
Thalomid	2,405	59572020594	2.7%
Total number of MRDD prescriptions	51,401		

SOURCE: CMS Analysis of MRDD Claims Filed Through June 30, 2005* Observations for billed charges per days supply that were outside three times the standard deviation of the mean for an NDC were eliminated (0.6 percent of claims). Comparisons were based on drug charges at the point of sale for beneficiaries under the demonstration. Medicare payments plus beneficiary obligations equal total charges.

There was not a significant difference in the use of mail order between beneficiaries enrolled under the standard benefit and those qualifying for additional Federal subsidies (p-value = .1695).

Demonstration participants appeared to be satisfied with their mail order service. Sixty-two percent of survey respondents using the mail order service rated it as excellent or very good. One additional benefit of mail order over retail purchases was that Caremark helped to coordinate benefits with charitable organizations assisting with co-payments. Beneficiaries enrolled in these assistance programs would face no co-payments with mail order, but would have been required to be reimbursed by the charitable organization for their out-of-pocket expenses for retail purchases. There were some down sides to mail order purchases, however. TrailBlazer reported there were some delivery-related problems, with enrollees not being home at the time of the delivery or not being able to make it to the door for one reason or another. As a result, there were numerous requests for redelivery – leading to added drug expense for Medicare and the beneficiary.

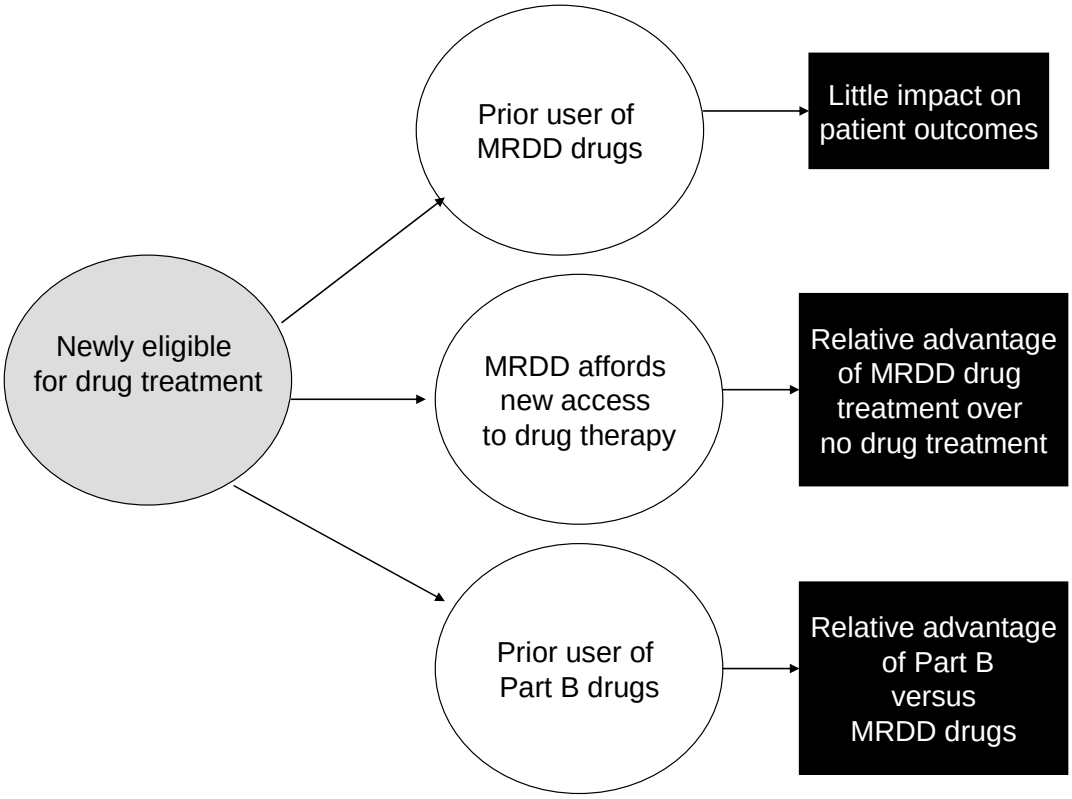
E. Impact on Patient Outcomes

The MRDD was anticipated to have varying effects on patient outcomes because of the wide variety of drugs and conditions it covered. As found in the syntheses of clinical literature completed for this evaluation and reported below, some drugs covered under the demonstration, such as imatinib mesylate for treating gastrointestinal stromal tumor, offered a life-extending advance in treatment over existing Medicare-covered treatment options. Other drugs covered under the demonstration, such as the biologics used for treating RA (e.g., etanercept and adalimumab), provide comparable clinical outcomes to the Medicare Part B drug (infliximab), but can be self-administered at home – allowing the patient to avoid three-hour infusions every month or every other month at the clinic.

Demonstration participants' prior access to the demonstration drugs also would have affected the impact of the demonstration on patient outcomes, as shown conceptually in Figure 5. For those demonstration enrollees who had prior access to MRDD drugs, the demonstration may have had only a modest impact, if any, on patient outcomes.[11] For beneficiaries who replaced their previous Part B drug use with the demonstration drug, outcomes would reflect the relative advantages of the demonstration drugs over the Medicare Part B drugs. For beneficiaries, who either because of cost or other reasons did not use any medication to treat their illness, outcomes would reflect the advantages of

[11] However, even beneficiaries who had prior access to the demonstration drugs may have experienced some clinical benefits, if they improved their compliance with therapy as a result of reduced cost-sharing burden under the demonstration.

FIGURE 5. CONCEPTUAL FRAMEWORK FOR THE IMPACT OF THE MRDD ON PATIENT OUTCOMES



using the demonstration drug versus receiving no treatment at all. Some demonstration participants became newly eligible for drug treatment during the time of the demonstration. These beneficiaries, presumably, would have fallen into one of the three groups (MRDD drug users, Part B drug users, no drug use) if the demonstration had not occurred.[12]

1. Self-perceived Outcomes of Demonstration Participants

Beneficiaries who did not switch drug treatment upon enrollment in the demonstration were not asked about changes in self-perceived outcomes of treatment in the survey. As shown in Table 11, for sampled enrollees who switched drug treatment, the perceived effects of the demonstration on health and symptoms were modest with some notable exceptions that are discussed

[12] It should be noted that the demonstration also allowed some beneficiaries to substitute away from one demonstration-covered drug to another demonstration-covered drug (e.g., from tamoxifen to anastrazole for breast cancer treatment), but this was not further analyzed for this evaluation.

TABLE 11. PERCEIVED EFFECTS ON HEALTH AND SYMPTOMS FOR BENEFICIARIES REPORTING NO PRIOR USE OF MRDD DRUGS

Characteristic	ALL	Prior Drug Use for Beneficiaries Who Had Not Previously Been Using Demonstration Drugs		
		Part B Replaceable Drug	No Reported Drug	Other Drug
All Conditions	**(N=3,586)**	**(N=313)**	**(N=684)**	**(N=743)**
General Health				
Much or somewhat better	23.4	40.4	41.1	58.3
The same	25.7	48.1	45.8	32.8
Much or somewhat worse	50.9	11.5	13.1	8.9
Feeling Ill				
Much or somewhat better	43.5	52.0	32.9	49.4
The same	45.4	36.4	52.0	41.2
Much or somewhat worse	11.1	11.6	15.1	9.4
Feeling Sad or Depressed				
Much or somewhat better	32.9	27.6	25.5	38.0
The same	53.6	59.7	57.8	51.8
Much or somewhat worse	13.5	12.7	16.7	10.2
Lack of Energy				
Much or somewhat better	44.1	48.4	35.7	50.2
The same	38.9	39.0	43.3	36.5
Much or somewhat worse	17.0	12.6	21.0	13.3
Feeling Able to Meet the Needs of the Family				
Much or somewhat better	34.4	39.3	23.8	44.4
The same	53.5	49.2	61.6	46.0
Much or somewhat worse	12.1	11.5	14.6	9.6

SOURCE: MPR analysis of MRDD Beneficiary Survey, 2006.
NOTES: Ns represent weighted population counts for survey.
Sampled beneficiaries were eligible for these questions if they were not using demonstration drugs prior to the demonstration and had been using the demonstration drug for at least three months.

TABLE 11. PERCEIVED EFFECTS ON HEALTH AND SYMPTOMS FOR BENEFICIARIES REPORTING NO PRIOR USE OF MRDD DRUGS

Characteristic	ALL	Prior Drug Use for Beneficiaries Who Had Not Previously Been Using Demonstration Drugs		
		Part B Replaceable Drug	No Reported Drug	Other Drug
Cancer	**(N=953)**	**(N=57)**	**(N=218)**	**(N=75)**
Shortness of Breath				
Much or somewhat better	22.9	40.1	15.3	24.5
The same	64.9	53.5	74.6	65.4
Much or somewhat worse	12.2	6.4	10.1	10.1
Pain				
Much or somewhat better	27.8	53.7	13.8	30.3
The same	55.9	39.9	62.1	64.6
Much or somewhat worse	16.3	6.4	24.1	5.1
Amount of Time Spent in Bed				
Much or somewhat better	28.2	39.5	19.9	34.4
The same	61.1	60.5	64.6	55.0
Much or somewhat worse	10.7	0.0	15.5	10.6
Lack of Energy				
Much or somewhat better	33.3	40.1	21.3	29.5
The same	42.6	40.5	47.9	35.0
Much or somewhat worse	24.1	19.4	30.8	35.5
Side Effects of Treatment				
Much or somewhat better	28.7	13.2	N/A	40.4
The same	51.6	47.9		49.8
Much or somewhat worse	19.7	38.9		9.8

SOURCE: MPR analysis of MRDD Beneficiary Survey, 2006.
NOTES: N/A Side effects of treatment were compared only for those respondents reporting prior drug use.
Ns represent weighted population counts for survey.
Sampled beneficiaries were eligible for these questions if they were not using demonstration drugs prior to the demonstration and had been using the demonstration drug for at least three months.

TABLE 11. PERCEIVED EFFECTS ON HEALTH AND SYMPTOMS FOR BENEFICIARIES REPORTING NO PRIOR USE OF MRDD DRUGS

Characteristic	ALL	Prior Drug Use for Beneficiaries Who Had Not Previously Been Using Demonstration Drugs		
		Part B Replaceable Drug	No Reported Drug	Other Drug
Rheumatoid Arthritis	**(N=1,702)**	**(N=202)**	**(N=153)**	**(N=525)**
Feeling Ill				
Much or somewhat better	52.1	51.4	48.4	51.6
The same	40,2	34.4	46.7	40.9
Much or somewhat worse	7.7	14.2	4.9	7.5
Feeling Able to Meet Needs of Family				
Much or somewhat better	45.7	40.9	39.1	50.1
The same	46.1	46.7	58.6	40.0
Much or somewhat worse	7.2	12.4	2.3	7.9
Lack of Energy				
Much or somewhat better	54.5	49.5	51.2	53.5
The same	34.8	38.3	39.8	36.6
Much or somewhat worse	10.7	12.2	9.0	9.9
Shortness of Breath				
Much or somewhat better	25.4	19.3	20.9	24.6
The same	61.3	73.6	60.5	63.1
Much or somewhat worse	13.3	7.1	18.6	12.3
Side Effects of Treatment				
Much or somewhat better	43.5	34.9	N/A	42.3
The same	49.0	57.2		47.4
Much or somewhat worse	7.5	7.9		10.3

SOURCE: MPR analysis of MRDD Beneficiary Survey, 2006. NOTES: N/A Side effects of treatment were compared only for those respondents reporting prior drug use. Sampled beneficiaries were eligible for these questions if they were not using demonstration drugs prior to the demonstration and had been using the demonstration drug for at least three months. Ns represent weighted population counts for survey.

TABLE 11. PERCEIVED EFFECTS ON HEALTH AND SYMPTOMS FOR BENEFICIARIES REPORTING NO PRIOR USE OF MRDD DRUGS

Characteristic	ALL	Prior Drug Use for Beneficiaries Who Had Not Previously Been Using Demonstration Drugs		
		Part B Replaceable Drug	No Reported Drug	Other Drug
Multiple Sclerosis	**(N=658)**	**(N=40)**	**(N=212)**	**(N=26)**
Feeling Ill				
Much or somewhat better	36.6	63.5	29.3	28.0
The same	49.0	27.3	58.7	57.5
Much or somewhat worse	14.4	9.2	12.0	14.5
Feeling Sad or Depressed				
Much or somewhat better	25.8	36.5	13.9	43.4
The same	56.5	45.2	69.1	56.6
Much or somewhat worse	17.7	18.3	17.0	0.0
Feeling Able to Meet Needs of Family				
Much or somewhat better	25.0	54.4	20.8	28.9
The same	54.0	36.4	63.7	56.2
Much or somewhat worse	21.0	9.2	15.5	14.9
Shortness of Breath				
Much or somewhat better	15.8	9.2	8.7	28.9
The same	73.6	72.5	82.6	71.1
Much or somewhat worse	10.6	18.3	8.7	0.0
Side Effects of Treatment				
Much or somewhat better	34.4	72.6	N/A	56.9
The same	52.3	9.1		43.1
Much or somewhat worse	13.3	18.3		0.0

SOURCE: MPR analysis of MRDD Beneficiary Survey, 2006.
NOTES: N/A Side effects of treatment were compared only for those respondents reporting prior drug use. Sampled beneficiaries were eligible for these questions if they were not using demonstration drugs prior to the demonstration and had been using the demonstration drug for at least three months.
Ns represent weighted population counts for survey.

TABLE 11. PERCEIVED EFFECTS ON HEALTH AND SYMPTOMS FOR BENEFICIARIES REPORTING NO PRIOR USE OF MRDD DRUGS

Characteristic	ALL	Prior Drug Use for Beneficiaries Who Had Not Previously Been Using Demonstration Drugs		
		Part B Replaceable Drug	No Reported Drug	Other Drug
Other Demonstration Conditions	**(N=273)**	**(N=14)**	**(N=102)**	**(N=117)**
Feeling Ill				
Much or somewhat better	50.9	75.5	49.8	50.4
The same	30.2	24.5	21.5	37.0
Much or somewhat worse	18.9	0.0	28.7	12.6
Shortness of Breath				
Much or somewhat better	25.7	75.5	21.0	29.4
The same	56.9	24.5	53.7	55.0
Much or somewhat worse	17.4	0.0	25.3	15.6
Lack of Energy				
Much or somewhat better	50.5	100.0	45.8	50.3
The same	30.6	0.0	25.0	37.1
Much or somewhat worse	18.9	0.0	29.2	12.6
Able to Walk or Climb Stairs				
Much or somewhat better	35.0	75.5	28.5	38.1
The same	46.3	24.5	50.0	46.1
Much or somewhat worse	18.7	0.0	21.5	15.8
Side Effects of Treatment				
Much or somewhat better	32.3	49.8	N/A	35.3
The same	47.8	50.2		40.1
Much or somewhat worse	19.9	0.0		24.6

SOURCE: MPR analysis of MRDD Beneficiary Survey, 2006. NOTES: N/A Side effects of treatment were compared only for those respondents reporting prior drug use. Sampled beneficiaries were eligible for these questions if they were not using demonstration drugs prior to the demonstration and had been using the demonstration drug for at least three months. Ns represent weighted population counts for survey

later in this section. The majority of these sampled beneficiaries reporting their health and symptoms were the same or worse than they had been before they had enrolled in the demonstration for many health symptoms. This finding must be tempered by the fact that many enrollees suffered from chronic diseases or terminal cancer where their condition was likely to worsen over time. Overall, 50 percent of survey respondents with cancer, 65 percent of those with RA, 61 percent of those with MS, and 59 percent of those with other demonstration conditions said they were in fair or poor health at the time of the survey.

Comparing across prior drug use categories, some pronounced improvements in health and symptoms can be seen for sampled beneficiaries who had been using Part B replaceable drugs or other non-demonstration drugs before enrollment. As an illustration, 54 percent of beneficiaries with cancer who had been using Part B replaceable drugs stated the pain they experienced was much or somewhat better than before their enrollment; around 50 percent of patients with RA who had substituted the Part B replaceable drug under the demonstration felt much or somewhat better along the dimensions of “feeling ill” or “lack of energy”.

Among patients who had been using a drug other than a demonstration-covered drug or a Part B replaceable drug, about half of respondents with RA reported feeling much or somewhat better along the dimensions of “feeling ill” or “lack of energy.” Most often methotrexate was the other drug that had been used by these respondents. Monotherapy with methotrexate is typically used to treat symptoms of RA before a course of treatment with the demonstration-covered biologics is considered. These respondents may have newly failed methotrexate monotherapy or may have been using methotrexate alone because they could not afford treatment with a biologic. Notably, about half of respondents in this subgroup said they felt much or somewhat better about their ability to meet the needs of their family under the demonstration than before.

Compared with the Part B-replaceable drugs, side effects of treatment associated with the demonstration-covered drugs were largely the same or diminished (reported as better) for persons with RA (35 percent better; 57 percent the same), MS (73 percent better; 9 percent the same) and other demonstration conditions (50 percent better; 50 percent the same). By contrast, side effects of treatment were much or somewhat worse for 39 percent of sampled cancer beneficiaries who had previously been using Part B drugs. This is somewhat surprising as the review of medical literature reported in the next section found many demonstration-covered cancer drugs had lower drug-related side effects than their substitute Part-B covered drugs.

Although many of the expected benefits of the demonstration on reductions in travel to the doctor’s office or clinic, reduced frequency of physician visits, and lowered burden of drug delivery (e.g., self-administered versus infusion) accrued to only a minority of demonstration participants who replaced Part B drugs with

demonstration drugs, some of these reported benefits appear to be substantial. Responses to these questions in the beneficiary survey reported in Table 12 highlight this subgroup that the demonstration intended to target.[13] Results should be interpreted with some caution, however, as many were on complex treatment regimens and there may have been some confusion among beneficiaries about which prior drug for their treatment was being compared during the interview.

Of sampled beneficiaries with cancer, the main reported benefit of the demonstration drug over prior Part B drug treatment was improved health (31 percent), this was followed by not having to go to the doctor for drug administration (11 percent), and fewer side effects (10 percent).[14] The average frequency of visits to the physician's office or clinic for these beneficiaries fell from 8.8 to 4.4 over a three-month period. With a reported average one-way travel time to the physician's office of 50 minutes, cancer beneficiaries substituting from Part B to demonstration drugs saved an average of seven hours in travel time alone over the three months. For many of the cancer conditions, beneficiaries would also have saved time in the physicians' office or clinic for the chemotherapy infusion.

For sampled beneficiaries with RA, nearly 40 percent said the main benefit of their demonstration-covered biologics over the Part B-covered infliximab was either self-administration or not having to visit the doctor's office or clinic for drug administration.[15] On average, sampled beneficiaries with RA took 42 minutes traveling one way to their doctor's office or clinic. The average number of doctor or clinic visits over a three-month period fell by just over one visit, from 3.2 to 1.7.

Sampled beneficiaries with MS who previously used the Part B replaceable drug saved, on average, more than eight trips to the doctor over a three-month period by substituting to a self-administered medication under the demonstration. With an average 26 minute one-way trip to their treating physician, this amounts to seven hours over that period of time. MS treatments covered under Part B are administered on a weekly basis. Notably, 37 percent of these respondents stated the main benefit of the demonstration was either not having to go to the doctor or being able to self-administer the medication.

[13] These questions were only asked of persons identified in the survey as having been prior users of Part B replaceable drugs.
[14] This should be qualified by the finding that 39 percent of sampled enrollees with cancer who previously used Part B replaceable drugs stated that their side effects had worsened under the demonstration (Table 11).
[15] These were reported as separate choices on the survey.

TABLE 12. INDICATORS OF DEMONSTRATION BENEFITS FOR SAMPLED BENEFICIARIES REPORTING PRIOR USE OF PART B-REPLACEABLE DRUGS

Characteristic	ALL		Cancer		Rheumatoid Arthritis		Multiple Sclerosis	
All	(N=531)		(N=75)		(N=229)		(N=213)	
Average Reported Travel Time to Treat Demonstration-Covered Condition in Minutes – one way (95 percent confidence interval)	39 (33 ,45) N=478		50 (21, 79) N=57		42 (35,50) N=194		26 (22, 30) N=213	
	Before	**After**	**Before**	**After**	**Before**	**After**	**Before**	**After**
Mean Number of Doctor's Visits in Three Month Period	7.3	2.1	8.8	4.4	3.2	1.7	10.9	2.1
	(N=438)		(N=38)		(N=176)		(N=209)	
Main Benefit of Demonstration versus Part B Drug								
Improved health, feel better	23.1%		30.5%		22.7%		9.1%	
Don't have to go to the doctor	15.3%		10.9%		19.0%		9.2%	
Self administer	19.4%		0.0%		19.1%		27.3%	
No benefit	18.9%		29.0%		20.6%		9.2%	
Fewer side effects	13.9%		10.0%		8.4%		45.4%	
Other	9.4%		19.6%		10.2%		0.0%	
	(N=261)		(N=37)		(N=169)		(N=40)	

SOURCE: MPR analysis of MRDD Beneficiary Survey, 2006. NOTES: Sample sizes for these questions for beneficiaries with other conditions were too small to report. Results for these groups have been omitted from the table. Results for this group are included in the "all" column. Ns represent weighted population counts for survey.

Of the sampled members with RA, few reported trouble with self-injection. For sampled members with MS, 70 percent said self-injection was not at all difficult.

2. Outcomes Reported in the Clinical Literature

As mentioned in the methods section, CMS solicited several systematic reviews of the clinical literature from Duke and Sheffield Universities. These reviews compare the efficacy of the demonstration drugs and biologicals relative to replaceable drugs covered under Medicare Part B. Because a systematic review is time and resource intensive, reviews of all drugs included in the demonstration were beyond the scope of this evaluation. These reviews targeted only those drugs and conditions that were expected to account for the majority of spending under the demonstration. These include:

- imatinib compared with interferon alpha or best supportive care for the treatment of chronic myeloid leukemia (CML);
- imatinib versus single-agent doxorubicin or ifosfamide or these agents combined with conventional chemotherapy for the treatment of gastrointestinal stromal tumor;
- monotherapy with gefitinib or erlotinib for treating locally advanced or metastatic non-small cell lung cancer compared to docetaxel or best supportive care;
- thalidomide versus combination chemotherapy programs such as VBCMP (vincristine, carmustine, cyclophosphamide, melphalan, and prednisone) and VAD (vincristine, doxorubicin, and dexamethasone) for the treatment of multiple myeloma;
- etanercept, adalimumab, and anakinra compared with infliximab with and without combination methotrexate therapy for the treatment of RA; and
- glatiramer acetate, interferon beta-1b, and interferon beta-1a (Rebif) compared with interferon beta-1a (Avonex) or conventional drug therapy for MS[16].

Together, these drugs and conditions accounted for 88 percent of spending under the demonstration through June 30, 2005. Clearly, the improved clinical outcomes (relative to best supportive care or Part B-covered drugs) reported below would largely pertain to that fraction of enrollees for whom the demonstration afforded new access to these therapies. The outcome domains reviewed include survival, remission rates, adverse effects and treatment tolerability, compliance with therapy, and quality of life.

[16] The report on MS clinical outcomes was available only in draft form at the time this Report to Congress was due, so findings from that report have not been discussed.

In general, the demonstration did provide a new source of insurance for some major life-extending advances in treatment. Where survival benefits were not found, many of the reviewed anticancer drugs offered fewer drug-related side effects than conventional chemotherapy. The major findings under each outcome domain are presented below. Evidence reports for the cancer drugs have been posted on the web.[17] Unless otherwise cited, findings below are drawn directly from the commissioned evidence reports (Abernethy and McCrory, 2005 (a-c); Nixon RM, Bansback N, Brennan A., publication pending; Kelly and McCrory, 2005).

In interpreting these results, it is important to bear in mind several limitations pertinent to any syntheses of the clinical literature. First, medical therapies and our knowledge of their efficacy are rapidly evolving. Syntheses of the medical literature are by necessity retrospective – they summarize reported findings in the literature that meet prospectively-defined study inclusion criteria, and neither reflect a review of other literature nor current clinical practice. Clinical practice evolves so quickly that such a review may quickly become outdated and regular updates are important. The reviews, which were conducted in a staggered fashion, had publication cut-off dates for study inclusion varying from January to August 2005.

Second, for many of the conditions, head to head trials comparing the demonstration drug to the Part B replaced drug do not exist, and likely would be unethical to conduct for some of the demonstration drugs, such as imatinib for GIST, given the great improvements in efficacy witnessed in the Phase II and III clinical trials. In cases where head-to-head trials have not been conducted, comparative efficacy is inferred based on indirect comparisons of placebo controlled trials. The clinical review of drugs used for treating rheumatoid arthritis achieves this by using mixed treatment comparison models (Lu and Ades, 2004). This is an extension of meta-analysis that allows the synthesis of evidence where control arms are not equivalent and/or multiple treatment arms are included that use different doses or timing regimes. Results control for differences in trial and patient characteristics, such as baseline disease duration and severity of disease. Such models are complex, and assumptions are made in the modeling, although the findings for the RA review are robust under varying assumptions.

Also, there is ample evidence that studies showing significant clinical improvements are more likely to be published than studies that fail to show a clinical benefit – leading to an overestimate of clinical benefits or underestimate of treatment risks (Song et al., 2000). This phenomenon, known as publication bias, can be countered by locating unpublished studies and incorporating the results in the review. This approach is rarely practical, and was beyond the scope of this evaluation. Finally, findings from clinical trials may not be realized

[17] See the following web sites: http://www.ahrq.gov/clinic/ta/thalidomide/index.html; http://www.ahrq.gov/clinic/ta/nonsmall/index.html; http://www.ahrq.gov/clinic/ta/cml/index.html; http://www.ahrq.gov/clinic/ta/gist/index.html.

in practice, where the characteristics of patients often differ from the stringent criteria required for trial enrollment or compliance with therapy is poor. Findings from these clinical reviews are suggestive of the potential benefits and risks of these demonstration drugs for demonstration participants who replaced Part B drugs or who gained new access, but may not represent their actual experience under the program. These limitations apply to all of these clinical reviews. There are also unique limitations that pertain to the individual reviews summarized below. A more detailed discussion can be found in each of the published reports.

Survival

- There is convincing evidence that the use of imatinib for treating gastrointestinal stromal tumor (GIST) provides survival benefits over chemotherapeutic regimens traditionally covered by Medicare. Data from one of the most complete studies on survival using imatinib estimate two-year survival at 72 percent (Verweij et al., 2004), which can be compared with 25-30 percent for combination therapy including doxorubicin and ifosfamide (Antman et al., 1993). Importantly, the latter study was done in an era when it was hard to differentiate GIST from other soft tissue sarcomas, so the reported response rates are for the entire group of tumors rather than GIST specifically, and GIST tumors are likely to have even lower response rates than the overall group.

- There is suggestive data that imatinib may improve survival over interferon plus cytarabine for treating chronic myeloid leukemia. While a Phase III controlled trial did not show overall survival benefits for imatinib during the primary study (median 19 months follow up) (O'Brien et al., 2003), in a long-term follow-up of patients continuing on imatinib the 30 month survival of 95 percent compared favorably to the 86 percent survival rates reported for interferon and cytarabine at 36 months in a separate study (Guilhot, 2004; Guilhot et al., 1997). For many of the imatinib studies the results are still early and median survival has not been reached.

- Gefitinib, an epidermal growth factor receptor tyrosine kinase inhibitor (EGFR-TKI) used for treating advanced non small cell lung cancer, did not provide any significant survival benefits over basic supportive care in the Iressa ® Survival Evaluation in Lung (ISEL) Cancer trial. These findings were released in December 2004 after the demonstration began (Astra Zeneca, 2005). The drug was kept in the demonstration, as earlier studies showed dramatic tumor response for some patient subgroups. Later analyses of the ISEL trial showed some patient subgroups did have improved survival on gefitinib -- specifically those of Asian origin or nonsmokers (Tamura and Fukuoka, 2005). Given the genetic variability of the American population, an important outstanding research question for targeted drugs such as the EGFR-TKIs is which specific portion of the

population will achieve such good outcomes.

- Survival benefits over basic supportive care have been shown for a different EGFR-TKI – erlotinib—which was approved for treating metastatic non small cell lung cancer in November 2004 and accepted as a demonstration drug in January 2005. Median survival was 6.7 months in the erlotinib arm compared to 4.7 months in the placebo arm. Head to head trials with Medicare-covered chemotherapeutic agents used at a similar stage of the disease, such as docetaxel, have not been completed. Comparing the median survival times between the erlotinib randomized controlled trial and the two docetaxel trials does not demonstrate a clear advantage for one drug; however, such comparisons are of limited utility due to differences in patient characteristics.

- Survival estimates for thalidomide do not appear to be substantially different from that seen with traditional chemotherapy for treating multiple myeloma. Randomized controlled trials were not available for thalidomide for treating multiple myeloma at the time the evidence review was completed, although a Phase III trial was being conducted. In general, the quality of the studies in this clinical area was poor.

Remission rates

- Imatinib is clearly superior to interferon plus cytarabine in terms of genetic (complete cytogenetic remission of 74 percent versus 9 percent) and molecular tumor response (progression free survival of 92 percent versus 74 percent at 18 months, $p<0.0001$) for treating chronic myeloid leukemia. Cytogenetic and molecular responses predict survival (Hughes et al., 2003).

- There are no significant differences among infliximab, etanercept, or adalimumab in terms of their effects in retarding the disease process for RA; all are significantly more effective than placebo or methotrexate alone (Nixon et al., publication pending).

- Combining methotrexate with the use of adalimumab is significantly more effective than monotherapy with the biologic or methotrexate alone (Breedveld et al., 2006).

Treatment tolerability and compliance with therapy

- Imatinib has far fewer side effects than interferon –used for treating CML – or single agent doxorubicin, single agent ifosfamide, or their combination – used for treating GIST.

- Thalidomide appears to have less intense drug-related side effects with fewer treatment-related deaths than traditional chemotherapy for treating multiple myeloma. However, the use of thalidomide does carry increased risk for peripheral neuropathy, which appears to be cumulative and will need further consideration. Similarly, thalidomide increases the risk for clinically-significant deep vein thrombosis, also needing further consideration. Side effects are dose-dependent and recent clinical studies have looked at decreasing the dose.

- The drug-related side effects of gefitinib and erlotinib are low in all but several percent of patients taking these agents. Drug-related mortality is less than 1 percent. By contrast, docetaxel is associated with grade 3 toxicity in more than 10 percent of subjects for hematologic toxicity (primarily neutropenia), neurosensory toxicity, asthenia, and pulmonary toxicity.[18]

- The major advantages of etanercept, adalimumab, and anakinra over infliximab pertain to the route of administration. Infusion therapy (used for infliximab) carries an independent risk of infection sometimes leading to death; while injection site reactions (used for etanercept, adalimumab or anakinra) are generally mild. However, cases of tuberculosis and other serious opportunistic infections have been reported for all TNF-α antagonists, including systemic lupus erythematosus.

[18] In oncology clinical trials, toxicity (drug-related effects) is often graded according to the Common Toxicity Criteria (CTC). Using this system those indicated as Grade 3 or 4 are the most severe. The criteria are available at http://www.ecog.org/general/common_tox.html.

F. Impact on Medicare Spending

As of December 31, 2005, the ending date of the demonstration, total Medicare spending under the demonstration was $248 million – less than half the $500 million spending limit imposed by Congress.[19] Net Medicare spending, after subtracting out costs for averted Part B drug use, is estimated to be no lower than $218 million. The derivation of the net spending estimate is described later in this section.

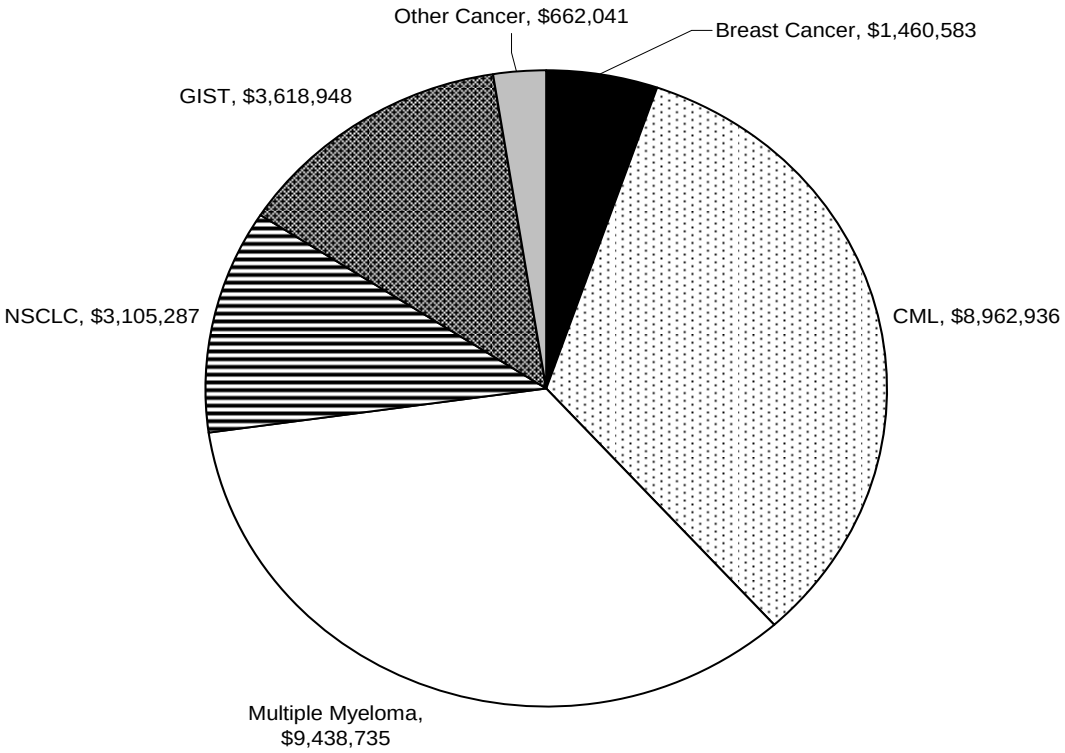
Between September 2004 and June 30, 2005 – the period used for an in-depth claims analysis, total Medicare spending under the demonstration was $90 million. Of the $90 million spent by June 30, 2005, less than one-third of spending was for anticancer drugs ($27 million) with the remainder spent to treat noncancer conditions (Table 13). Despite the wide array of conditions and drugs covered under the demonstration, spending was highly concentrated on just a few conditions. RA and MS alone accounted for 60 percent of demonstration spending. Spending on drug treatments for multiple myeloma and chronic myeloid leukemia accounted for another 20 percent (Figures 6 and 7). Just six of the more than 30 drugs covered under the demonstration accounted for 74 percent of all demonstration spending by June 30, 2005. These were adalimumab ($17.1 million) used for treating RA, etanercept ($15.0 million) used for treating RA, ankylosing spondylitis, psoriasis, and psoriatic arthritis, imatinib mesylate ($12.6 million) used for treating chronic myeloid leukemia and gastrointestinal stromal tumor, glatiramer acetate ($12.4 million) used for treating MS, and thalidomide ($9.4 million) used for treating multiple myeloma.

On average, Medicare covered 79 percent of billed charges, with beneficiaries paying for over 20 percent of drug charges. These proportions varied by drug, reflecting various levels of federal subsidies received for the benefit and duration of treatment.

In the short term, net spending is estimated to be somewhat lower than gross spending, as some demonstration participants replaced Part B covered drugs with demonstration drugs (Table 14). In addition to differences in drug costs, all of the replaceable Part B drugs entailed additional Medicare spending for supplies, physicians' services, and drug administration fees, which have been

[19] These estimates reflect the majority of the claims paid under the demonstration, although claims could continue to be submitted for the next few weeks. These costs do not include year-end reconciliation, where Medicare payments are adjusted to reflect contractual limits that drug price not exceed 82 or 86 percent of average wholesale prices, depending on if the transaction was through mail-order or a retail pharmacy.

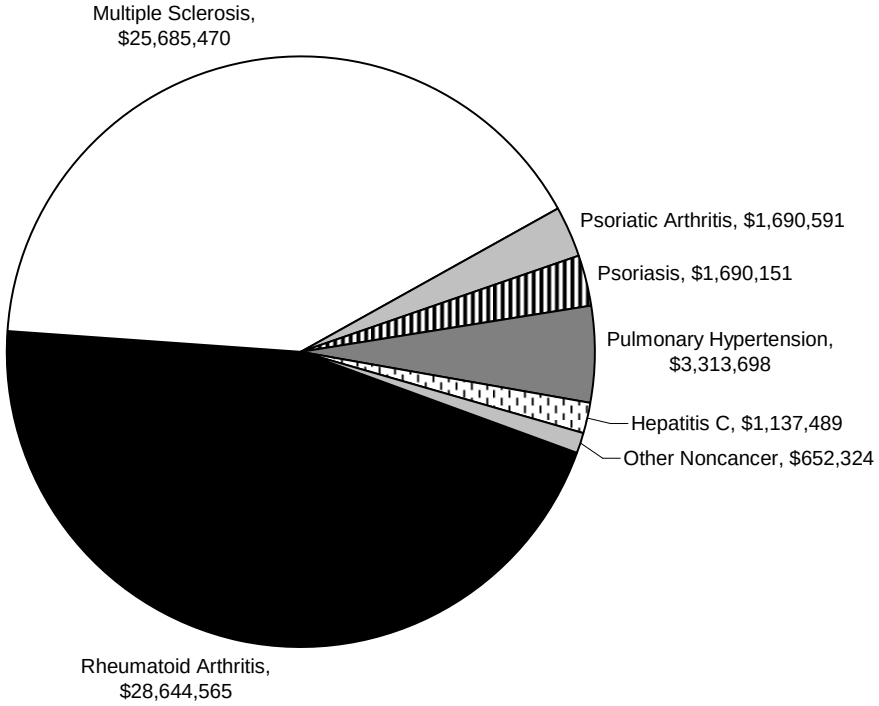
FIGURE 6. MEDICARE SPENDING BY CANCER CONDITION, AS OF JUNE 30, 2005



Total Cancer Spending = $27.2 million

SOURCE: **CMS Analysis of** MRDD Claims Filed Through June 30, 2005

FIGURE 7. MEDICARE SPENDING BY NONCANCER CONDITION, AS OF JUNE 30, 2005



Total Noncancer Spending = $62.8 million

SOURCE: **CMS Analysis of** MRDD Claims Filed Through June 30, 2005

TABLE 13. BILLED CHARGES, MEDICARE AND PATIENT SPENDING UNDER THE MRDD, BY DRUG AND CONDITION as of JUNE 30, 2005

Condition	Drug	Billed Charges	Drug As A Percent of Total Billed Charges	Medicare Payments	Medicare Spending as a Percent of Payments for Drug	Patient Payments	Patient Spending as Percent of Payments for Drug
Total		$113,451,904	100.0%	$90,062,817	79.4%	$23,389,077	20.6%
Cancer		$34,443,504	30.4%	$27,248,530	79.1%	$7,194,965	20.9%
Multiple Myeloma	Thalidomide (Thalomid)	$11,537,103	10.2%	$9,438,735	81.8%	$2,098,368	18.2%
Chronic Myelogenous Leukemia	Imatinib mesylate (Gleevec)	$11,202,050	9.9%	$8,962,936	80.0%	$2,239,114	20.0%
Gastrointestinal Stromal Tumor	Imatinib mesylate (Gleevec)	$4,465,359	3.9%	$3,618,948	81.0%	$846,411	19.0%
Non Small Cell Lung Cancer	All	$4,506,256	4.0%	$3,105,287	68.9%	$1,400,959	31.1%
	Gefitinib (Iressa)	3,623,150		2,487,517		1,135,623	
	Erlotinib (Tarceva)	883,106		617,769		265,337	
Breast Cancer	All	$1,876,371	1.7%	$1,460,583	77.8%	$415,788	22.2%
	Anastrazole (Arimidex)	941,083		674,060		267,023	
	Letrazole (Femara)	718,440		622,848		95,592	
	Exemestane (Aromasin)	158,949		114,417		44,532	
	Tamoxifen	34,417		28,942		5,475	
	Tamoxifen (Novaldex)	22,947		20,272		2,675	
	Toremifene (Fareston)	534		43		491	
Cutaneous T-cell Lymphoma	Bexarotene (Targretin)	$744,430	0.7%	$575,779	77.3%	$168,651	22.7%
Epithelial Ovarian Cancer	Altretamine (Hexalen)	$36,980	0.0%	$24,459	66.1%	$12,521	33.9%
Condition not defined	Imatinib mesylate (Gleevec)	$74,955	0.1%	$61,803	82.5%	$13,152	17.5%

SOURCE: CMS Analysis of Medicare Replacement Drug Demonstration Claims Filed Through June 30, 2005 and Part B Claims January –August 2004.

TABLE 13. BILLED CHARGES, MEDICARE AND PATIENT SPENDING UNDER THE MRDD, BY DRUG AND CONDITION as of JUNE 30, 2005

Condition	Drug	Billed Charges	Drug As A Percent of Total Billed Charges	Medicare Payments	Medicare Spending as a Percent of Payments for Drug	Patient Payments	Patient Spending as Percent of Payments for Drug
Non-cancer Conditions		$79,008,400	69.6%	$62,814,288	79.5%	$16,194,113	20.5%
Rheumatoid Arthritis	All	$35,287,593	31.1%	$28,644,565	81.2%	$6,643,028	18.8%
	Adalimumab (Humira)	19,888,530		17,118,390		2,770,140	
	Etanercept (Enbrel)	15,359,188		11,495,648		3,863,540	
	Anakinra (Kineret)	39,875		30,528		9,348	
Multiple Sclerosis	All	$32,685,145	28.8%	$25,685,470	78.6%	$6,999,674	21.4%
	Glatiramer Acetate (Copaxone)	17,450,807		12,367,223		5,083,584	
	Interferon Beta 1b (Betaseron)	6,897,438		6,592,359		305,079	
	Avonex	4,739,785		3,814,587		925,198	
	Interferon Beta 1a (Rebif)	3,500,600		2,829,836		670,764	
	Rebif Titrin	92,208		77,174		15,034	
	HP Acthar Gel	4,308		4,293		15	
Pulmonary Arterial Hypertension	Bosentan (Tracleer)	4,576,832	4.0%	3,313,698	72.4%	1,263,134	27.6%
Psoriatic Arthritis	Etanercept (Enbrel)	2,247,183	2.0%	1,690,591	75.2%	556,592	24.8%
Psoriasis	All	2,206,007	1.9%	1,690,151	76.6%	515,857	23.4%
	Etanercept (Enbrel)	2,191,123		1,680,700		510,423	
	Efalizumab (Raptiva)	14,884		9,451		5,433	
Hepatitis C	All	1,266,937	1.1%	1,137,489	89.8%	129,448	10.2%
	Pegylated interferon alpha 2a (Pegasys)	1,163,183		1,053,979		109,205	
	Pegylated interferon alpha 2b (Peg-Intron)	103,754		83,510		20,243	

SOURCE: CMS Analysis of Medicare Replacement Drug Demonstration Claims Filed Through June 30, 2005 and Part B Claims January –August 2004.

TABLE 13. BILLED CHARGES, MEDICARE AND PATIENT SPENDING UNDER THE MRDD, BY DRUG AND CONDITION as of JUNE 30, 2005

Condition	Drug	Billed Charges	Drug As A Percent of Total Billed Charges	Medicare Payments	Medicare Spending as a Percent of Payments for Drug	Patient Payments	Patient Spending as Percent of Payments for Drug
Non-cancer Conditions (continued)							
Acromegaly	Pegvisomant (Somavert)	483,444	0.4%	451,619	93.4%	31,825	6.6%
Ankylosing Spondylitis	Etanercept (Enbrel)	127,158	0.1%	103,482	81.4%	23,676	18.6%
Senile Osteoporosis	All	14,669	0.0%	9,444	64.4%	5,225	35.6%
	Calcitonin -- nasal (Miacalcin)	6,996		4,624		2,372	
	Risedronate (Actonel)	5,852		3,691		2,162	
	Alendronate (Fosamax)	1,663		981		682	
	Raloxifene Hydrochloride (Evista)	159		149		10	
Paget's Disease	All	4,125	0.0%	2,759	66.9%	1,366	33.1%
	Risedronate (Actonel)	3,005		2,071		933	
	Alendronate (Fosamax)	1,120		688		432	
Secondary Hyperparathyroidism	Doxercalciferol (Hectoral)	293	0.0%	45	15.3%	248	84.7%
Cytomegalovirus retinitis in AIDS	Valcyte (Valganciclovir)	0	0.0%	0		0	
Chemotherapy-induced Hemorraghic Cystitis	Mesna (Mesnex)	0	0.0%	0		0	
Condition not defined	All	109,014	0.1%	84,975	77.9%	24,040	22.1%
	Etanercept (Enbrel)	53,260		44,792		8,468	
	Risedronate (Actonel)	21,723		15,966		5,757	
	Alendronate (Fosamax)	25,217		17,525		7,692	
	Calcitonin -- nasal (Miacalcin)	5,421		4,332		1,090	
	Raloxifene Hydrochloride (Evista)	3,393		2,359		1,034	

SOURCE: CMS Analysis of Medicare Replacement Drug Demonstration Claims Filed Through June 30, 2005 and Part B Claims January –August 2004.

TABLE 14. ESTIMATED NET MEDICARE SPENDING FOR THE MRDD THROUGH JUNE 30, 2005 FOR SELECTED CONDITIONS

Condition	A. Number of Beneficiaries Filing MRDD Claims by June 30, 2005	B. Average Spending Per Enrollee Week for Demonstration Drugs	C. Average Spending per Enrollee Week for Part B Replaceable Drugs, 2005 prices			D. Proportion of Claimants Estimated to Be Users of Part B Drug In Absence of Demonstration*	E. Net spending per week (B-(CxD))	F. Effect of Part B Substitution on Demonstration Spending (Percentage Reduction Over Gross Spending)	G. Net Spending for Mean Duration of Treatment Through June 30, 2005 (A x E x mean treatment duration)
			Drugs	Administration, Supplies and Adjunct Therapy	Total				
Total (for selected conditions)	14,060	$241	$235	$48	$283	9.8%	$209	11.9%	$63,646,255
Cancer (selected conditions only)	3,928	$201	$171	$108	$278	9.1%	$156	19.5%	$11,730,121
Multiple Myeloma	1,106	$445	$85	$221	$306	5.7%	$427	3.9%	$9,070,302
Non Small Cell Lung Cancer	659	$286	$235	$242	$477	38.9%	$101	61.3%	$1,203,256
Breast Cancer	2,092	$36	$153	$6	$159	0.9%	$34	4.0%	$1,402,372
Cutaneous T-cell Lymphoma	71	$473	$1,425	$96	$1,521	28.2%	$45	90.6%	$54,191
Non-cancer Conditions (selected conditions only)	10,132	$257	$260	$25	$285	10.0%	$230	9.7%	$51,916,134
Rheumatoid Arthritis	5,343	$263	$253		$274	7.5%	$242	7.8%	$26,405,550
Multiple Sclerosis	4,327	$220	$159	$14	$173	13.3%	$197	10.5%	$22,996,602
Pulmonary Arterial Hypertension	462	$522	$1,297	$21 $174	$1,471	8.6%	$396	24.1%	$2,513,982

* Includes the proportion of claimants with a prior diagnosis who used Part B drugs and a proportion of newly diagnosed claimants who were not prior users of demonstration-covered drugs. See Appendix I for details of this calculation.

netted out of gross spending estimates. The analysis of net spending was limited to four cancer conditions (multiple myeloma, non small cell lung cancer, breast cancer, cutaneous t-cell lymphoma) and three noncancer conditions (RA, MS, pulmonary arterial hypertension) for which we had a large enough sample for analyses in the Medicare Part B claims data. Together these conditions accounted for 80 percent of Medicare spending and 84 percent of all enrollees under the demonstration through June 2005. Further details about methods used to estimate net spending, treatment duration under the MRDD and the content and cost of Part B drug administration sessions can be found in Appendix I.

For the seven selected conditions, substitution of Part B drugs reduced gross Medicare spending by 12 percent on average. Gross spending for the selected conditions by June 30, 2005 was $72.2 million. Net spending after subtracting out Part B drug and associated drug administration spending was $63.6 million.

Savings due to replacing a Part B drug with a demonstration drug were generally greatest for the selected cancer conditions. This is due to the relatively high percentage of people estimated to have been Part B drug users in absence of the MRDD with NSCLC and cutaneous T-cell lymphoma (39 and 28 percent, respectively), and the relatively high costs of treating those diseases through conventional chemotherapy regimens. For demonstration participants with cutaneous t-cell lymphoma, savings due to the substitution away from conventional regimens covered under Part B nearly completely offset the additional drug spending for the oral drugs provided under the demonstration.

Part B covered therapies were more costly per week of treatment than were MRDD treatment drugs and biologics for all of the selected study conditions except multiple myeloma and MS. Estimated weekly savings in drug-related spending to Medicare for the subset of participants who replaced Part B drugs range from being more expensive to being less than a third the cost of the Part B substitute. As a striking example of potential savings, average Medicare spending per enrollee week for pulmonary hypertension for the demonstration drug was about $500, while estimated 2005 spending per enrollee week for the Part B replaced drugs was nearly $1000 more. Savings of this magnitude would have resulted in substantial reductions in both Medicare and beneficiary spending had most of the demonstration participants with this condition substituted MRDD drugs for Part B drugs.

There are several important caveats to keep in mind before drawing inferences from this early claims experience to the life of the demonstration. First, these estimates pertain to an average 21-week duration of treatment observed through June 30, 2005. Savings of this magnitude may not accrue over a longer time frame for some regimens. Specifically, the Part B cancer chemotherapy regimens are often of limited duration (commonly four to six months), while the

oral cancer therapies may be taken indefinitely. In addition, many beneficiaries had just attained the catastrophic spending limits after which Medicare pays a higher proportion of their costs. For these reasons, both the estimates of savings for Part B substitution mentioned in the previous paragraph and the aggregate 12 percent reduction of gross spending due to drug substitution would likely be smaller over the course of the entire demonstration, although it is difficult to predict exactly how much smaller.

Additional savings could have accrued to Medicare because of differences in side effects of treatment or clinical outcomes due to the different drug regimens. For example, sepsis related to the indwelling catheter used for continuous intravenous infusion of epoprostenol in the treatment pulmonary arterial hypertension is a common side effect of treatment that would not occur with use of the oral demonstration drug, bosentan. Analyzing these impacts for the diverse diseases and conditions included in the demonstration in the required time frame was beyond the scope of this evaluation. One reason is that Medicare claims for the period when enrollees were using the demonstration-covered drugs would not be available until after this report to Congress is due. Additionally, the net impact is expected to be small, given such a large number of beneficiaries had prior access to MRDD drugs before the demonstration began.

V. Summary and Conclusion

A. Summary

This study presents the results of a Congressionally-mandated evaluation of the MRDD. Specifically, Congress requested that the evaluation address the effects of the demonstration program on three major areas: beneficiary access to care, health outcomes, and Medicare spending, specifically detailing any savings to the Medicare program due to reduced physicians' services and hospital outpatient department services for administration of replaced drugs.

The MRDD sought to improve beneficiary access to drugs prescribed as replacements for those already covered under Part B. Many of the demonstration drugs offered Medicare beneficiaries less toxic, and sometimes more effective, treatment alternatives than the Part B replaced drugs. Because the demonstration drugs are self-administered and do not require visits to physicians' offices for administration, the demonstration was also expected to reduce beneficiaries' time and travel burden, and potentially reduce their financial burden. The demonstration targeted chronically-ill beneficiaries who did not have comprehensive drug coverage and provided them with a drug benefit that was structured similarly to Medicare Part D.

As intended, the demonstration served the poor or near poor who lacked supplemental drug coverage, and reduced the financial burden of drug treatment for a majority of participants. For the minority of participants who substituted Part B with MRDD drugs or who gained new access to drug treatment under the demonstration the benefits were likely substantial, covering many medications that offered economical, life-extending or quality-enhancing clinical advances over those previously covered by Medicare. The plurality of participants, however, did not gain new access to drug treatment under this demonstration.

Initial enrollment was slow, yet the MRDD continued to attract new participants over its 16-month course and nearly attained the Congressionally-imposed limit of 50,000 beneficiaries. Despite steady enrollment trends, no drug claims were filed for about 40 percent of enrollees over the course of the 16-month demonstration. It is unclear why this was the case, as most suffered from conditions that required ongoing drug treatment. Mortality was high among beneficiaries suffering from some conditions, such as non small cell lung cancer and ovarian cancer. However, only a small proportion of beneficiaries died before they used the benefit.

Access. The demonstration did appear to reduce financial burden for a majority of participants, and provided new drug access to some of enrollees. Yet. the experience of early enrollees showed that most had been using demonstration drugs before they enrolled. Consequently, it appears that beneficiary access to these drug therapies was not sharply improved as a result of the demonstration.

Outcomes. Perceived improvements in health or symptoms were sometimes marked for beneficiaries who switched from a Part B-replaceable drug or who had been using some other non-demonstration covered drug to treat their condition before the demonstration, particularly for beneficiaries with cancer or RA. Results from the systematic reviews of the clinical literature for the selected conditions underscore that many of the demonstration drugs offered the potential for significant improvements in survival, disease remission, or reduced drug-related side effects over substitute therapies currently covered under Medicare Part B. The major benefit of drugs used to treat RA – which were used by more than one-third of all demonstration participants– was mainly the added convenience of avoiding regular visits to the physician's office or outpatient clinic to receive lengthy infusions. For the plurality of early enrollees who had previously been using demonstration drugs, the demonstration's probable impact on health outcomes was slight if any.

Spending. For the minority of participants for whom this demonstration enabled them to substitute MRDD for Part B drugs, the demonstration offered several economical alternatives for treatment, as intended. When factoring in the costs of physicians' services and hospital outpatient department services for administration of replaced drugs, our preliminary estimates showed weekly drug-

related spending per enrollee was lower for demonstration-covered drugs versus the Part B replaced drugs for five of the seven conditions selected for the spending analysis. Potential savings in weekly Medicare spending per enrollee for those five conditions ranged from 4 percent to more than a two-fold reduction over the average 20-week therapy observed ten months into the demonstration.

As a preliminary estimate, gross spending was $248 million. Net spending under the demonstration is estimated to $218 million after accounting for savings due to averted Part B drug costs and administration services. This estimate is derived from an analysis of seven conditions representing 80 percent of all spending and 84 percent of all enrollment under the demonstration through mid-year 2005. As few of these early enrollees were using Part B drugs prior to the start of the demonstration, the 'replacement' effect is small. The reduction in net spending due to substitution away from Part B drugs is likely to grow smaller by the end of the demonstration for several reasons: many enrollees were nearing their catastrophic coverage limit for out-of-pocket spending, after which the Medicare program covers a much larger share of drug costs; some cancer beneficiaries who would have been using Part B replaceable drugs in absence of the demonstration would have been nearing the end of their course of chemotherapy, while treatment with oral substitutes offered under the demonstration may continue indefinitely; and toward the end of the demonstration many enrollees filled the maximum allowable days supply for their prescriptions (three months) potentially as a hedge against the uncertainty of transitioning to Medicare Part D. In addition, many of the conditions not included in the analysis of net spending were excluded explicitly because a small fraction had been using Part B replaceable drugs (as described in Appendix I), and the sample size was too small for analysis. Including all demonstration conditions likely would lower the estimate of the proportion of gross spending saved through substitution away from Part B drugs.

B. Conclusion

While this evaluation – by necessity -- reflects the experience of early enrollees, final enrollment reports show the composition of demonstration participants did not change markedly from mid-year 2005 in terms of enrollment condition, qualifications for financial assistance, the likelihood of using the benefit, or reported prior use of demonstration drugs. The key findings – that under the demonstration poor or near poor beneficiaries gained financial assistance for many economical and quality-enhancing treatment alternatives to those previously covered under Medicare, are unlikely to be substantively altered once complete data are available. For the roughly 10-30 percent of beneficiaries who gained new access to these demonstration drugs, the long term clinical benefits could be substantial.

The study design does not permit a cause and effect link between the demonstration enrollment and reported outcomes. Because of the different trajectories diseases take over time, without an appropriate control population of beneficiaries with similar conditions at similar stages of their disease who did not participate in the demonstration, the impact on outcomes and net spending should be viewed as suggestive of demonstration effects, rather than definitive.

The MRDD and the Medicare prescription drug benefit (Part D) have some very important and distinct differences. These differences include the fact that the Medicare prescription drug benefit is available to all eligible Medicare beneficiaries, while the MRDD targeted specific beneficiaries with chronic diseases who were taking high-cost prescription medications meeting the specifications as defined by the MMA and CMS. Also, the MRDD was designed to reflect the benefit design of the standard Medicare prescription drug benefit, with some important differences. For example, beneficiaries participating in the MRDD were not required to pay a premium. Finally, the MRDD was administered by one Medicare contractor and a pharmacy benefit management company who worked in partnership with each other to process the drug claims. In contrast, multiple private plans administer the Medicare prescription drug benefit for Medicare beneficiaries, with CMS oversight.

Despite the fact that the covered population was very different in nature from the general Medicare population, experience under this demonstration also offered some insights to the new Medicare prescription drug benefit (Part D). Specifically, it takes time to introduce a new, complex change in benefit structure and to attract participants. Early MRDD enrollment was much lower than

anticipated, but it grew steadily, over the course of the demonstration. Although we are still completing a complementary outreach and enrollment study, we learned in part from this demonstration that reaching beneficiaries who were not already getting drug coverage was much more effective through extensive grassroots and local efforts. This was something that was not feasible in the short time frame and limited scope of MRDD. Consequently, subsequent Medicare education and outreach efforts about new benefits like this one have been designed to be much more extensive, local, and personalized.

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Appendix I. Evaluation Methods

Overview of Evaluation Design

The primary research goals of the evaluation were to infer demonstration effects on beneficiaries' access to care, health outcomes, and Medicare spending. For this evaluation, we felt it was important to capture the perspectives of demonstration participants, and as a result we conducted a survey of users. With evidence-based medicine on the rise, we also felt it was important to include systematic reviews of randomized controlled trials conducted outside of the demonstration, which are used to infer potential clinical effects on participants who gained new access to drug treatment. Finally, Medicare's administrative data allow for detailed analyses of spending patterns.

Collection of data from a control or comparison group would have provided a stronger design. Initially, the number of applications was expected to far surpass the Congressionally-mandated cap, and CMS proposed to randomly select participants from the broader pool of applicants. However, when faced with a large excess of slots at the start of the demonstration, CMS felt it was unacceptable to randomize chronically ill applicants to receive no demonstration benefits, and all applicants were accepted into the program. Construction of a historical or concurrent comparison group would have required complex Medicare claims processing or primary data collection that was not feasible given the time frame for the Report to Congress and limited resources available for the evaluation. Specific limitations regarding establishing a control or comparison group included:

- Lack of specificity of administrative claims data:

  For some of the conditions included in the demonstration, ICD-9 diagnosis codes that describe the condition are not specific enough to ensure the beneficiary would be eligible for drug treatment under

the demonstration. For example, the breast cancer drugs were initially made available only to beneficiaries with stage 2-4 breast cancer. Stage, although it was gathered from demonstration enrollees, is not available on the claims data making selection of an appropriate control population from administrative data difficult. The diagnosis code used for gastrointestinal stromal tumor (GIST) covers several soft tissue tumors, of which GIST is a small subset. Similarly, epithelial ovarian cancer and non small cell lung cancer are subsets of the respective diagnoses for ovarian and lung cancer. Many of the demonstration drugs were indicated for use as a second or third-line therapy only after treatment with more conventional therapies failed. This lack of specificity meant that a beneficiary survey would first have to screen potential responders.

- Time lag in the availability of claims data:

  Using retrospective data, the time lag between service date and the development of a final analytic file to use for selection of a potential control cohort can take more than a year. Many of those selected would have died or would have progressed to a more severe stage of the disease by the time they were surveyed or their claims experience was analyzed. Moreover, the complete claims experience concurrent to the demonstration would not have been available until after the Report to Congress was due.

As a result, the evaluation design mainly relies on pre-post comparisons in key outcome variables for a subset of demonstration participants – largely persons who enrolled within the first ten months of the demonstration. (The exact time period varies depending on whether results are from the beneficiary survey, claims analysis, or analysis of enrollment data.) We use this design fully

understanding that pre-post comparisons alone may be subject to their own biases. Specifically, some of the perceived changes, such as changes in health and symptoms, may be the result of secular changes in disease, and may be falsely attributed to the demonstration. In addition, questions that ask about changes from a prior event are subject to recall problems on the part of the beneficiary. For these reasons, the results of the evaluation should be considered suggestive of demonstration effects, rather than definitive.

The primary benefit of the demonstration was to provide new drug coverage to Medicare beneficiaries. The potential benefits on access (both being able to use the drug and being able to afford the drug), health outcomes, and spending would depend greatly on an enrollee's previous access to drug therapy. The evaluation uses the study population's previous drug treatment to draw inferences about study effects. Participants are divided into four groups: 1) those who were already receiving treatment with a drug covered by the demonstration; 2) those who previously had been receiving treatment with a Part B-covered medication that was replaced by a demonstration medication; 3) those who were receiving no drug treatment for their condition before the demonstration; and 4) those who were receiving some drug treatment, but it was neither a demonstration-covered medication nor a Part B-replaceable drug. These people may have been newly-eligible for demonstration drug treatment for their condition, or may have been unable to afford demonstration or Part B drug treatment before the demonstration. Outcomes are considered within the context of this prior drug history.

Beneficiary Survey[1]

The main data file from which the sample for the survey study was drawn was the TrailBlazer Health enrollment data, with additional enrollee characteristics obtained by merging CareMark pharmacy claims data and Medicare enrollment data base (EDB) data. The Trailblazer enrollment file provided information on which beneficiaries were enrolled in the demonstration. The Caremark claims data provided information on which enrolled beneficiaries had a drug claim. The EDB provided beneficiary characteristics such as race/ethnicity, which we used in sampling for the beneficiary survey.

A. Construction of an Initial sample frame

An initial survey sample frame of enrollees consisting of both demonstration users and non-users was constructed using the merged data files described above.[2] The inclusion criterion for this initial sample frame was at least two months of enrollment in the demonstration as of the cutoff date for the sample draw (February 18, 2005). Those with less experience would likely not be able to tell whether their condition had changed since enrollment, and it was expected that the demonstration would take more than two months to affect enrollees on the outcomes of interest.

The three exclusion criteria for the initial sample frame were: (1) relatively long-term non-use of the demonstration, (2) being deceased at the time of the sample construction, and (3) receipt of more than one drug through the demonstration. Relatively long-term non-users were defined as those who had already enrolled by December 1, 2004 but demonstration pharmacy claims had not been filed by February 18 (that is, enrollment for at least 11 weeks without using the demonstration). The initial sample frame thus did contain enrollees

[1] Excerpted from MPR, 2006.
[2] The sample frame is the comprehensive listing of all persons from which the desired sample is to be drawn.

who enrolled between December 1 and December 18 but demonstration claims had not been filed by February 18. The reason for including these enrollees in the initial frame was to leave open the possibility of surveying non-users about reasons they had not yet used the demonstration.

Enrollees who were deceased at the time of the sample construction were excluded from the initial frame as it was felt that asking family proxy respondents about the deceased's experience in the demonstration would be too intrusive. Finally, enrollees receiving more than one drug through the demonstration were excluded for practical reasons of complexity of survey design and respondent burden. Each telephone interview was individualized to the respondent's demonstration-covered drug and primary diagnosis. If enrollees receiving more than one drug had been included in the sample frame, it would first have been necessary to randomly select a primary drug from among the multiple drugs (and a primary diagnosis for those with multiple diagnoses). Interviewers would then have had to be aware of the multiple-drug enrollees, know the primary drug and/or diagnosis that had been randomly selected, and ask the respondents to focus during the interview only on the drug and diagnosis selected for them. Respondents would mostly likely have had great difficulty answering questions under this approach. Furthermore, the number of enrollees receiving more than one drug through the demonstration was a small proportion of the total target population, which made it difficult to justify the resource-intensive effort such an interview protocol would have involved.

Because the demonstration would likely affect enrollees with key characteristics differently, a stratified sampling design was used to ensure that sample sizes within each stratum of interest were large enough for reliable estimates. For this study, the exact nature of the strata was based on the mix of enrollee characteristics in the data from the first four months of enrollment and on research considerations (the subgroups of the greatest interest). The sample

was stratified by three diagnosis categories: (1) cancer, (2) rheumatoid arthritis, and (3) a combined category of multiple sclerosis and all other non-cancer conditions. The other non-cancer conditions (such as pulmonary hypertension, hepatitis C, and secondary hyperparathyroidism) were grouped with multiple sclerosis, because they represented less than 5 percent of the total enrollment and were too few to form their own stratum.

Besides stratifying the sample frame, the frame was also sorted by covariates that may affect enrollee outcomes (a technique known as hierarchical serpentine sorting). This implicit stratification by sorting variables was used to avoid the possibility of extreme concentrations of covariate values among the selected sample. The frame was thus sorted by condition, region of the country, sex, age, race, demonstration benefit level, and whether or not the beneficiary was already taking the covered drug before the demonstration.

Based on a desired total completed sample size for the survey of 3,200 participants, and on assumptions that 95 percent of enrollees would be eligible for the sample and that the response rate would be 85 percent, a sample of 3,962 enrollees was drawn, which yielded 3,269 completed interviews. (The desired number of completed surveys was inflated by the inverse of the expected response rate to arrive at the required sample size).

B. Sample selection

To meet precision requirements on key analytic domains, as well as to minimize the total variance, the sample was allocated among the three strata in proportion to the number of beneficiaries in each stratum. Proportional allocation has several advantages over an equal allocation of the sample. It minimizes sample weight variation, which improves the precision of overall survey estimates. Moreover, because the distribution of beneficiaries across the three strata is essentially equal, the sample sizes in each stratum are large enough for precise estimation.

Using an equal probability systematic sample selection procedure, participants were selected independently within the strata, based on the sample size allocation. This procedure ensured that the implicit strata, defined by the sorting variables, contained sample sizes approximately proportional to their population sizes.

C. Construction of final analytic sample

Since enrollees who had never used the demonstration to cover any medications (in other words, for whom medication claims had never been filed under the demonstration) would have no opinions or useful information on the benefits of the demonstration, the initial sample described above was modified by excluding respondents who had not used drugs covered by the demonstration by the time of the survey. Sample members for whom at least one demonstration pharmacy claim had not been filed by the time of the start of the survey (May 5, 2005) were excluded, yielding a final analytic sample of 2,649 sample members.

Based on the TrailBlazer enrollment data, this final analytic sample represented an underlying population of 9,613 demonstration enrollees who met the criteria for the initial sample described above, and who then met the additional criterion of having had at least one demonstration pharmacy claim filed by the start of the survey on May 5, 2005.

D. Weighting and Estimation

Because the goal of the survey is to produce results that are representative of all beneficiaries in the underlying population of interest (in this case, demonstration users), to calculate means, rates, and other statistics from survey responses, weights must be attached that account for the number of beneficiaries represented by each response in the sample. Sample weights were calculated as the inverse of the probability that a beneficiary was selected from a

stratum. Because the sample had been allocated proportionally across all strata, the sample weights were equal across strata.

Potential nonresponse bias was compensated for by adjusting for nonresponse independently within weighting classes. Weighting class adjustments were made by partitioning the sample into groups, called weighting classes, and then adjusting the weights of respondents within each class so that they summed to the weight total for nonrespondents and respondents from that class. Implicit in the weighting class adjustment is the assumption that—had the nonrespondents responded—their responses would have been distributed in the same way as the responses of the other respondents in their weighting class. Moreover, two separate weighting adjustments were made to attempt to compensate for nonresponse, because eligibility determination and cooperation have distinct response patterns. First, sampling weights were adjusted to account for sampled beneficiaries for whom eligibility status could not be determined. For this adjustment, the weighting classes were defined on the basis of race, age, and region of the country. Second, incomplete or missing questionnaires from beneficiaries known to be eligible were adjusted for. For the second adjustment, the weighting classes were defined by age, sex, and whether or not the beneficiary was already taking the covered drug before the demonstration.

1. Post-survey Weight Adjustment

The eligibility determination adjustment factor for the c^{th} weighting class is defined as:

(1) $$A_c^E = \frac{\sum_{i \in c} W_i}{\sum_{i \in c} \delta_E W_i} \text{ for beneficiaries with eligibility status determined}$$
$$= 0 \text{ otherwise}$$

where W_i is the sample weight and δ_E is equal to 1 for enrollees whose eligibility status was determined and 0 otherwise. The eligibility determination adjusted weight for the i^{th} sample record from the c^{th} weighting class is then calculated as:

$$W_{ci}^{E} = A_{c}^{E} \times W_{i} \quad (2)$$

The completion adjustment factor for the d^{th} weighting class is defined as:

$$A_{d}^{C} = \frac{\sum_{i \in d} W_{i}^{E}}{\sum_{i \in d} \delta_{C} W_{i}^{E}} \text{ for eligible beneficiaries}$$
$$= 1 \text{ for ineligible beneficiaries} \quad (3)$$
$$= 0 \text{ otherwise}$$

where W^E is the eligibility determination adjusted weight and δ_C is equal to 1 for enrollees who completed the survey and 0 otherwise. The completion adjusted weight for the i^{th} respondent in the d^{th} weighting class was then calculated as:

$$W_{dci}^{C} = A_{d}^{C} \times W_{ci}^{E} \quad (4)$$

Poststratification adjustments were also calculated to correct for sample variation in estimated population totals for medical conditions in the final analytic population (that is, demonstration users), using population totals that were available from the intake data. Poststratification has the added advantage of improving the precision of estimates if "medical condition," the characteristic of beneficiaries used to create the poststrata, is related to the measures of interest. The poststratification adjustment factor for the h^{th} poststratum is defined as:

$$A_{h}^{PS} = \frac{N_{h}}{\sum_{i \in h} W_{dci}^{C}} \quad (5)$$

where N_h is the total number of beneficiaries in the sample frame associated with the h^{th} poststratum. The poststratified adjusted weight for the i^{th} sample record from the h^{th} poststratum is then calculated as:

(6) $$W_{hdci}^{PS} = A_h^{PS} \times W_{dci}^{C}$$

Therefore, when summed over all respondents in poststratum h, the poststratified weights now total N_h.

2. Variance Estimation

Because this survey design is complex, using the usual variance formulas based on a simple random sample yields incorrect results. Standard statistical software assumes equal probabilities of selection to compute the standard errors of survey estimates and often underestimates the true standard errors for complex surveys. Special techniques are necessary for computing proper variance estimates. The Taylor series linearization method, which uses the final weight along with key design variables, such as stratification variables, was used. Taylor series linearization is available in many of the popular software packages for analyzing survey data, such as SUDAAN, SAS, and Stata.

Analysis of Administrative Data

Administrative data were used to examine trends in demonstration enrollment and evaluate the impact of the program on Medicare spending. Four primary sources of administrative data were used, including: Part B Medicare claims data (outpatient, durable medical equipment, and physician/supplier files for 2004), Medicare enrollment and entitlement data, demonstration program enrollment data, and drug claims data from the demonstration. Administrative data were also linked to the 2003 Area Resource File to determine whether the beneficiary resided in an urban or rural county.

Because of lags in the availability of Part B claims data (not considered complete until 6 months after the service date, data request processing periods of 2 to 6 months, and the development of analytic files requiring an additional 3 months), this analysis reflects Medicare Part B drug use patterns in the eight months prior to the start of the demonstration (January 2004-August 2004) and demonstration drug experience from September 2004 through June 30, 2005.

To facilitate analysis, beneficiaries with multiple demonstration conditions were dropped from the analysis (e.g., cancer with rheumatoid arthritis). Beneficiary condition was primarily defined from the physician's reported condition for the beneficiary at the time of enrollment. However, three additional sources of information were used to assess the validity of physician-reported condition. These were: beneficiary self-reported condition; concordant drug claims filed under the demonstration; and concordant ICD-9 codes for those beneficiaries with Part B claims in the 8 months preceding the demonstration. (A list of ICD-9-CM diagnosis codes related to those conditions is provided in Appendix II.) If two or more of these latter sources agreed with each other, and they were not consistent with the physician's reported condition, the data were

cleaned to reflect the agreeing sources. Of 16,238 beneficiaries who had demonstration claims filed by June 30, 2005, data were cleaned for 48 persons (0.1 percent) – of these 31 were set to 'multiple' for having more than one demonstration condition. An additional 53 people were dropped from further analysis because the various sources for their condition could not be reconciled.

A number of beneficiaries (171) had claims for osteoporosis drugs under the demonstration, although they had enrolled for a condition other than senile osteoporosis or Paget's disease and also had claims for their original enrollment condition (e.g., beneficiary enrolled for rheumatoid arthritis with claims for adalimumab and alendronate). It was not clear whether these beneficiaries also met the criteria for coverage for senile osteoporosis drugs (homebound), if they also had Paget's disease, or if they were receiving these drugs without qualifying for the demonstration by either of these conditions (controls on claims for these drugs were mainly upon intake rather than at the retail or mail-order level). These beneficiaries were not dropped from the analysis and their original enrollment condition was retained. In detailed analyses of spending by condition, spending was examined only for those drugs used to treat their original enrollment condition.

For the Medicare Part B claims analysis, beneficiaries were selected from the National Medicare Utilization Data (NMUD) final action claims files who were participants in the Section 641 demonstration program as of February 15, 2005 (identified by their Medicare health insurance claims (HIC) number). In order to ensure relatively-complete claims history, the Part B drug spending cohort had to meet the following additional eligibility criteria:

- Were enrolled in Part A and Part B for all periods of Medicare eligibility in the 8 months prior to the demonstration;

- Were never enrolled in an HMO in the 8 months prior to the demonstration;
- Were never covered by a primary payer other than Medicare in the 8 months prior to the demonstration.

In addition to being required not to have multiple qualifying health conditions for the demonstration, beneficiaries with end stage renal disease in the 8 months prior to the demonstration were also excluded. Of 19,908 beneficiaries who had enrolled in the demonstration by February 15, 2005, 15,496 met all the eligibility criteria.

Replaceable Part B drugs for each demonstration drug were defined prior to conducting the analysis using published systematic reviews of the clinical literature, reviews commissioned by CMS for the detailed analysis of potential clinical outcomes under the demonstration, and/or the judgment of the clinical panel charged with evaluating which drugs to include in the MRDD. A Part B drug was listed as 'replaceable' only if the demonstration drug offered a substitute treatment at the specific stage of disease for which the drugs were taken. In other words, rheumatoid arthritis is typically first treated with non-steroidal anti-inflammatory drugs and methotrexate. If these fail, the TNF-α antagonists may be used in combination with methotrexate or alone. While Medicare will cover physician-administered methotrexate, that drug alone is used at an earlier stage of treatment; it is not considered to be a replaceable drug for this study. Infliximab is the only Medicare-covered drug considered to be a replaceable drug under the demonstration for treatment of rheumatoid arthritis. As another example, the aromatase inhibitors covered under the demonstration and used to treat breast cancer are considered to be adjunct therapy to conventional chemotherapies. As such, the aromatase inhibitors do not replace conventional chemotherapies, but are considered a replacement for the

Medicare-covered fulvestrant. A list of replaceable Part B drugs by condition can be found in Table II-2 and Table II-3 in Appendix II.

Of the 15,496 beneficiaries selected for the Part B claims analysis, only 1,877 had claims for replaceable Part B drugs in the 8 months prior to the demonstration. Conditions with fewer than 20 beneficiaries with a history of Part B drug administration sessions were dropped from further analysis. These included: gastrointestinal stromal tumor, chronic myeloid leukemia, hepatitis C, senile osteoporosis, and psoriatic arthritis. The Part B spending analysis was therefore limited to the remaining 1,867 enrollees who had the following seven conditions: breast cancer, cutaneous t-cell lymphoma, multiple myeloma, non small cell lung cancer, multiple sclerosis, pulmonary arterial hypertension, and rheumatoid arthritis. Together these conditions accounted for 80 percent of Medicare spending and 84 percent of all enrollees under the demonstration through June 2005.

Originally, CMS intended to compare pre-post drug spending changes for beneficiaries who had demonstration drug claims under the demonstration. However, by restricting our analysis to only those enrollees who had a drug claim under the demonstration during the first several months, our analytic cohort was reduced by another 70 percent (N= 588), and several more conditions would have had to have been dropped from the analysis due to small sample size. For this reason, spending patterns for Part B drugs were examined for enrollees irrespective of whether they also had claims for demonstration drugs. These were compared with spending patterns for demonstration drugs for those who had an MRDD claim by mid-summer. The assumption we are making is that the content of a Part B drug administration session is reasonably consistent across beneficiaries for the same drugs (e.g., infusion services, evaluation and management services, laboratory tests, and drugs).

In order to make spending estimates comparable between the demonstration drugs and the Part B replaceable drugs, CMS calculated average weekly spending for the drug for the duration of therapy. Duration of therapy was estimated by using the difference between the first date of therapy in the study period (January – August 2004 for Part B drugs and September 2004 – June 2005 for demonstration drugs) and calculating the number of weeks until the last claim filed adjusted for days supply for the claim. Days supply is a specific field in the demonstration drug claims data. For the Part B drugs, days supply was set to equal the typical periodicity of drug administration for the specific type of therapy. As an illustration, one-hour docetaxel infusions are given to patients with non small cell lung cancer every three weeks. In this case, 21 days would be added to the date of the last claim to estimate an ending date for that therapy. The durations of Part B therapies were derived from their FDA product labels and are presented in Table II-4 in Appendix II.

Part B drug administrations were defined as all services furnished on the same day that at least one Part B replaceable drug was given to treat a beneficiary's enrollment condition. Claims data for durable medical equipment (DME), hospital outpatient department, and physician/supplier bills were merged to create unique session-level data for each beneficiary in the analytic cohort. For a session to have occurred, at least one claim had to have been billed by a hospital outpatient department or a physician. This was not the case for the treatment of pulmonary arterial hypertension, where a number of DME claims were filed without any associated hospital outpatient department or physician drug administration session. These were exclusively for external infusion pump supplies and drug refills that were obtained by beneficiaries directly from suppliers. The pump supplies and drug spending for these DME claims were averaged over all sessions for administering pulmonary arterial hypertension drugs. Source of claim and site of visit are summarized in Table I-1. Nearly ¾ of all drug administration sessions for the selected conditions took place at a

physician's office. The number of beneficiaries used for the Part B spending analysis, calculated mean duration of treatment, and average number of sessions per week by condition are presented in Table I-2.

TABLE I-1. SOURCE FILE FOR DRUG ADMINISTRATION SESSIONS

Site of Session and Claim Source	Number of Sessions	Percentage of Sessions
Physician's office or infusion suite	15,237	**74.8%**
Physician/Supplier alone	14,997	73.6%
Physician/Supplier and DME	240	1.2%
Outpatient department	5,143	**24.3%**
Outpatient alone	2,523	12.4%
Physician/Supplier and Outpatient	2,343	11.5%
Physician/Supplier, Outpatient and DME	67	0.3%
Outpatient and DME	20	0.1%
DME alone*	190	**0.9%**
	20,380	100.0%

SOURCE: CMS Analysis of Medicare Part B Claims for January-August 2004
NOTES: *largely pump supplies and refills for external infusion pumps.
Visit numbers include counts for conditions later excluded due to small sample size.

TABLE I-2. UTILIZATION STATISTICS FOR ENROLLEES WITH PART B REPLACEABLE DRUG USE IN THE EIGHT MONTHS PRIOR TO THE MRDD

Condition	Number of Enrollees with Part B Drug Use, January – August 2004	Number of Part B Drug Administration Sessions	Mean Duration of Treatment (Weeks)	Mean Number of Sessions Per Week
Breast Cancer	23	109	19.91	0.2
Cutaneous T-cell Lymphoma	48	1,334	21.78	1.3
Multiple Myeloma	104	492	12.20	0.4
Non-small Cell Lung Cancer	628	4,901	18.12	0.5
Multiple Sclerosis	504	11,338	28.85	0.8
Pulmonary Arterial Hypertension	24	33	29.40	0.05
Rheumatoid Arthritis	536	1,983	22.72	0.2
Total	1,867	20,190	21.6	0.5

SOURCE: CMS Analysis of Medicare Part B Claims for January-August 2004

Once a drug administration session was identified, CMS needed to estimate what Part B spending would have been in the absence of the demonstration for 2005. Several major changes in Medicare policies to pay for drugs and administration of drugs were implemented in 2005 that would not have been reflected in the 2004 data used for the analysis. First, Medicare began paying based on average sales price plus 6 percent, rather than a percentage of average wholesale price for drugs furnished in a physician's office, effectively decreasing average payments for drugs. Second, Medicare increased payments for drug administration services.. CMS also launched a nationwide demonstration project to improve the quality of cancer care that provided additional payments to oncologists if they administered a standardized assessment scale examining their patient's levels of pain, vomiting and nausea, and fatigue (The Demonstration of Improved Quality of Care for Cancer Patients

Undergoing Chemotherapy). Finally, Medicare updates the amounts paid under the fee schedule every year.

To reflect these changes, codes that were billed for at least two percent of drug administration session for treating a specific condition were identified (or more than 2 sessions for conditions with fewer than 100 sessions over the study period). These codes were then priced at 2005 levels using Medicare fee schedules for physicians' services, hospital outpatient department services, laboratory services, and durable medical equipment. The 2005 per service fee was multiplied by the percentage of sessions for which that service was billed to obtain a weighted average payment per drug administration session. Prices for a particular service depended on the source of the bill (e.g., from a physician/supplier or hospital outpatient department) and the setting. Thus, an evaluation and management service could be billed by both the hospital outpatient department and the physician for the same session. Prices paid for the former were derived from the Outpatient Prospective Payment System (OPPS) and for the latter from the physician fee schedule.

For the cancer conditions, demonstration oncology codes were added to the visit for the proportion of times an eligible cancer chemotherapy service was billed for intravenous (96410 (G0359) –chemotherapy infusion for up to one hour) or push therapy (96408 (G0357)-- chemotherapy administration IV push technique). The codes listed below correspond to four patient assessment levels for each of the three patient symptom areas: nausea and/or vomiting; pain; and fatigue.

G9021-G9024	Assessment of vomiting and nausea
G9025-G9028	Assessment of pain
G9029-G9032	Assessment of fatigue

In 2005, practices reporting data on all three factors on a Medicare claim qualified for an additional payment of $130 per encounter (Medicare would pay $104 and beneficiary coinsurance of $26 applied). Monitoring data for the oncology demonstration project for January – June 2005 showed these codes were billed for 77-78 percent of eligible cancer drug administrations. The corresponding percentage was applied to the number of drug administrations reporting the eligible infusion codes to derive a proportion of administrations likely to have submitted bills for cancer care assessments in 2005.

An example of how 2005 payments were applied to the content of a drug administration is shown in Table 1-3 for multiple sclerosis. A detailed examination of the content of a multiple sclerosis drug administration shows care that reasonably could be considered to be routinely provided when the drug is administered at the outpatient department or the physician's office. While some of this care may have been provided even for beneficiaries on self-injected therapy (e.g., therapeutic procedure), the occurrence is rare enough to not make a large difference in the cost estimates for administration. On average, for this condition, 2005 drug payments were $254 and payments for drug administration and ancillary services were $23.

TABLE I-3. CONTENT OF MULTIPLE SCLEROSIS DRUG ADMINISTRATION VISIT UNDER MEDICARE, 2005 PRICES

HCPCS Code	Descriptor	Medicare 2005 Payment	Percent of sessions
	Outpatient Department		
Q3025	**Injection, Interferon Beta 1-a, 11 mcg**	$262.07	23%
Q3025	**Injection, Interferon Beta 1-a, APC 9022**	$215.88	55%
90782	Injection, sc/im	$18.95	15%
90782	Level II injections, APC 353	$22.68	57%
J1825	**Injection, Interferon Beta-1A, 33 MCG**	**$109.00**	**15%**
99211	Office/outpatient visit, est -- level 1	$9.10	8%
99211	Low level clinic visits, APC 600	$51.47	7%
Q0083	Chemotherapy Administration -- SC/ IM	$90.58	8%
G0001	Routine venipuncture for collection of specimens	$3.00	6%
99212	Office/outpatient visit, est -- level 2	$24.25	2%
99212	Low level clinic visits, APC 600	$51.47	5%
85025	CBC	$14.68	5%
97110	Therapeutic procedure, each of 15 minutes	$56.65	5%
99213	Office/outpatient visit, est -- level 3	$35.62	3%
99213	Mid level clinic visits, APC 601	$56.11	1%
99214	Office/outpatient visit, est -- level 4	$59.12	2%
99214	High level clinic visits, APC 602	$79.65	1%
Q0081	Infusion therapy using other than chemotherapeutic drugs, APC 120	$111.80	3%
80053	Comprehensive metabolic panel	$19.96	3%
80076	Hepatic function panel	$15.43	2%
	Weighted Avg.	$234.95	1655
	Physician's Office		
Q3025	**Injection, Interferon Beta 1-a, 11 mcg**	**$262.07**	**101%**
90782	Injection, sc/im	$18.95	66%
99211	Office/outpatient visit, est -- level 1	$21.60	19%
99213	Office/outpatient visit, est -- level 3	$52.68	4%
99212	Office/outpatient visit, est -- level 2	$38.66	3%
	Weighted Avg	$284.17	9,648
	Weighted Avg Both Settings	$276.97	
	Drug	$254.10	
	Administration	$22.87	

SOURCE: CMS Analysis of Medicare Part B Claims for January-August 2004

Finally, net spending under the demonstration was determined by using the following formula:

1) $NS_{ij} = (MRDD_i \times wks) - (M \times B_i \times wks)$

where:

NS = net spending under the demonstration for condition i through June 2005;
MRDD = average weekly MRDD spending on drugs for condition i;
wks = average duration of MRDD drug therapy for beneficiaries with condition i;
M = average weekly Medicare spending on Part B replaceable drugs, administration and ancillary services for condition i in 2005 prices;
B = proportion of enrollees with condition i likely to have been using Part B drugs in absence of the demonstration.

The proportion of enrollees likely to have been using Part B drugs in absence of the demonstration was derived in a three-step process. First, the claims analysis cohort was divided into four groups, based on the presence of a diagnosis code for their condition in the 8 months prior to the demonstration and physician-reported[3] prior use of MRDD drugs from the intake form (Table 1-4).

TABLE I-4. PRIOR USE OF MRDD DRUGS AND PRIOR DIAGNOSIS IN MEDICARE CLAIMS FOR SELECTED CONDITIONS

Drug Use Groups	Prior use of MRDD drugs	No prior use of MRDD drugs	Total
Prior diagnosis	A (N=7,722)	B (N=4,077)	(N=11,799)
No prior diagnosis	C (N=959)	D (N=698)	(N=1,657)
Total	(N=8,681)	(N=4,775)	

SOURCE: CMS Analysis of Medicare Part B Claims for January-August 2004 and demonstration enrollment data September 2004 -July 15, 2005.
NOTES: Prior MRDD drug use from physician-report on the enrollment intake form. Prior diagnosis derived from analysis of Medicare claims data 8 months prior to the demonstration start.

[3] Physician-reported medication use was felt to be more reliable than patient-reported use.

Next, for each condition, the proportion of Part B drug use among previously-diagnosed enrollees (Cohorts A and B) was calculated using prior evidence of Part B claims for the replaceable drugs. It was assumed that Cohort C – physician-reported users of MRDD drugs before the demonstration and no history of claims data -- would have continued to use those drugs in absence of the demonstration (0 percent Part B drug use). Finally, it was assumed that the proportion of Part B drug users among enrollees who had not been previously diagnosed and were not previously using the MRDD drug would be the same as the weighted average of those with a prior diagnosis (Cohorts A and B). Part B drug use in the three months prior to the start of the demonstration was used as the gold standard for evidence of prior Part B drug use.[4] The percentage used in the net spending analysis (Column D in Table 14) represents a weighted average of Part B drug use across all four cohorts.

[4] The two time periods (8 and 3 months) were used for different purposes in this study; the 8-month period was used for analyses of patterns of drug use and the 3-month period as an estimate of prior Part B drug user. We felt evidence of use of Part B drugs more proximal to the start date of the demonstration (e.g., within the three months before the start of the demonstration) was a better indicator of whether or not a beneficiary substituted demonstration drugs for Part B-covered drugs. However, a longer time period (8-months) was important to observe frequency and duration of drug therapy.

Appendix II. Codes of Conditions and Drugs Used in the Evaluation and Specified Replaceable Part B Drugs

TABLE II-1. LIST OF CONDITIONS AND DIAGNOSIS CODES INCLUDED IN THE DEMONSTRATION

Condition	Diagnosis codes	Number Enrolled on 2/15/2005	Notes about the specificity of diagnoses
Non-cancer		12,185	
Acromegaly	*253.0*	*41*	
Ankylosing Spondylitis	*720.0*	*1*	
Chemotherapy-induced hemorraghic cystitis	*595.39*	*0*	
Chronic viral hepatitis C	070.44, 070.51, 070.54	186	
Cytomegalovirus retinitis in AIDS	363.00-363.08, 363.10-363.15, 363.2	*0*	
Multiple sclerosis	340.*	4,622	
Paget's disease	731.0	*20*	
Psoriasis	*696.1*	*96*	
Psoriatic arthritis	696.0	379	
Pulmonary arterial hypertension	416.0	320	
Rheumatoid arthritis	714.* not 714.9	6,427	
Senile osteoporosis	*733.**	*81*	*Homebound specified by receiving home health care*
Cancer		7,545	
Breast cancer	174.* 175.*	2, 619	Stage 2-4 not specified
Chronic myeloid leukemia	205.1*	1,379	
Cutaneous t-cell lymphoma	202.1 202.2 202.8	165	
GI stromal tumor	151.2, 151.9	512	Stomach neoplasm, pyloric antrim or unspecified
Non small cell lung cancer (NSCLC) – primary	162.2 – 162.9, 197.0	1,386	NSCLC not specified; secondary neoplasm (197) not indicated for drugs
Multiple myeloma	203.0	1,466	
Epithelial ovarian cancer	*183.0*	*18*	*Epithelial not specified*

* Diseases with less than 100 enrollees were dropped from the analysis and are listed in italics.

TABLE II-2. LIST OF MEDICARE PART B DRUGS REPLACEABLE UNDER THE DEMONSTRATION – NONCANCER CONDITIONS

Condition	Replacement Drug	Replaceable Drug	J Code	Dosage
Chronic viral hepatitis C	Pegylated interferon alpha-2a (Pegasys)	Interferon alpha-2a, recombinant (Roferon A)	J9213	3 million units-SC,IM
		Interferon alpha 2b (Intron A)	J9214	1 million units SC, IM
		Interferon alpha con1 (Infergen)	J9212	1 mcg SC
	Pegylated interferon alpha 2b (Peg-Intron)	Interferon alpha-2a, recombinant (Roferon A)	J9213	3 million units-SC,IM
		Interferon alpha 2b (Intron A)	J9214	1 million units SC, IM
		Interferon alpha con1 (Infergen)	J9212	1 mcg SC
Multiple sclerosis	Interferon beta 1a (Rebif)	Interferon beta-1a (Avonex)	J1825	33 mcg-IM
		Interferon beta-1a (Avonex)	Q3025	11 mcg-IM
	Glatiramer acetate (Copaxone)	Interferon beta-1a (Avonex)	J1825	33 mcg-IM
		Interferon beta-1a (Avonex)	Q3025	11 mcg-IM
	Interferon beta 1b (Betaseron)	Interferon beta-1a (Avonex)	J1825	33 mcg-IM
		Interferon beta-1a (Avonex)	Q3025	11 mcg-IM
Psoriatic arthritis**	Etanercept (Enbrel)	Infliximab injection (Remicade)	J1745	10 mg-IV
Pulmonary arterial hypertension	Bosentan (Tracleer)	Epoprostenol (Flolan)	J1325	0.5 mg-IV
		Treprostinil (Remodulin)	Q4077	1 mg-SC infusion
Rheumatoid arthritis	Adalimumab (Humira)	Infliximab injection (Remicade)	J1745	10 mg-IV
	Anakinra (Kinaret)	Infliximab injection (Remicade)	J1745	10 mg-IV
	Etanercept (Enbrel)	Infliximab injection (Remicade)	J1745	10 mg-IV
Senile osteoporosis	Alendronate (Fosamax)	Pamidronate disodium	J2430	per 30 mg-IV
		Etidronate disodium	J1436	per 300 mg-IV
		Calcitriol	J0636	0.1 mcg-IV
		Calcitriol	J0635	1 mcg-IV
		Calcitonin – salmon	J0630	Up to 400 units
	Calcitonin –nasal (Miacalcin)	Pamidronate disodium	J2430	per 30 mg-IV
		Etidronate disodium	J1436	per 300 mg-IV
		Calcitriol	J0636	0.1 mcg-IV
		Calcitriol	J0635	1 mcg-IV
		Calcitonin – salmon	J0630	Up to 400 units
	Raloxifene Hydrochloride (Evista)	Pamidronate disodium	J2430	per 30 mg-IV
		Etidronate disodium	J1436	per 300 mg-IV
		Calcitriol	J0636	0.1 mcg-IV
		Calcitriol	J0635	1 mcg-IV
		Calcitonin – salmon	J0630	Up to 400 units
	Risedronate (Actonel)	Pamidronate disodium	J2430	per 30 mg-IV
		Etidronate disodium	J1436	per 300 mg-IV
		Calcitriol	J0636	0.1 mcg-IV
		Calcitriol	J0635	1 mcg-IV
		Calcitonin – salmon	J0630	Up to 400 units

*Note: Demonstration conditions excluded from the claims analysis are not listed.

** Application for FDA approval for Remicade for this indication was pending as of January 2005.

TABLE II-3. LIST OF MEDICARE PART B DRUGS REPLACEABLE UNDER THE DEMONSTRATION – CANCER CONDITIONS

Condition	Replacement Drug	Replaceable Drug	J Code	Dosage
Breast cancer	Anastrazole (Arimedex)	Fulvestrant (Faslodex)	J9395	Injection, 25 mg
	Exemestane (Aromasin)	Fulvestrant (Faslodex)	J9395	Injection, 25 mg
	Letrazole (Femara)	Fulvestrant (Faslodex)	J9395	Injection, 25 mg
	Tamoxifen (Novaldex)	Fulvestrant (Faslodex)*	J9395	Injection, 25 mg
	Toremifene (Fareston)	Fulvestrant (Faslodex)	J9395	Injection, 25 mg
Chronic myeloid leukemia	Imatinib mesylate (Gleevec)	Interferon alpha 2b (Intron A)	J9214	1 million units SC, IM
		Interferon alpha-2a, recombinant (Roferon A)	J9213	3 million units-SC,IM
Cutaneous t-cell lymphoma	Bexarotene (Targretin) – oral****	Photochemotherapy (PUVA)	96912	
		Photochemotherapy (PUVA)	96913	
		Photopheresis (extracorporeal) (Methoxsalen/Oxsoralen--Ultra)	36522	
		Interferon alpha-2a, recombinant (Roferon A)	J9213	3 million units-SC,IM
		Interferon alpha 2b (Intron A)	J9214	1 million units SC, IM
		Denileukin Diftitox (Ontak)	J9160	300 mcg
		Alemtuzumab	J9010	10 mg
		Doxorubicin HCL, lipid (Adriamycin, Doxil)	J9000	Per 10 mg IV
		Doxorubicin HCL, all lipid (Adriamycin, Doxil)	J9001	Per 10 mg IV
		Cyclophosphamide, oral	J8530	25 mg
		Cyclophosphamide (Cytoxan)	J9070	100 mg IV
		Cyclophosphamide (Cytoxan)	J9080	200 mg IV
		Cyclophosphamide (Cytoxan)	J9090	500 mg IV
		Cyclophosphamide (Cytoxan)	J9091	1 g IV
		Cyclophosphamide (Cytoxan)	J9092	2 g IV
		Cyclophosphamide lyophilized	J9093	100 mg IV
		Cyclophosphamide lyophilized	J9094	200 mg IV
		Cyclophosphamide lyophilized	J9095	500 mg IV
		Cyclophosphamide lyophilized	J9096	1 g IV
		Cyclophosphamide lyophilized	J9097	2 g IV
		Pentostatin (Nipent) (Deoxycoformycin)	J9268	10 mg

* Fulvestrant is typically taken after tamoxifen therapy fails.

****Indicated for patients who are refractory to at least one prior systemic therapy. Electron beam therapy is also used, but the codes for radiation therapy are nonspecific to the type of radiation therapy.

TABLE II-3. LIST OF MEDICARE PART B DRUGS REPLACEABLE UNDER THE DEMONSTRATION – CANCER CONDITIONS (continued)

Condition	Replacement Drug	Replaceable Drug	J Code	Dosage
Non-small cell lung cancer	Gefitinib** (Iressa)	Carboplatin (Paraplatin, Paraplatin solution)	J9045	50 mg IV
		Cisplatin (Platinol)	J9060	10 mg IV
		Cisplatin (Platinol)	J9062	50 mg IV
		Gemcitabine (Gemzar)	J9201	200mg IV
		Vinolrelbine tartrate (Navelbine)	J9390	10 mg
		Paclitaxel (Taxol, Onxol)	J9265	30mg IV
		Docetaxel (Taxotere)	J9170	20mg IV
	Erlotinib**(Tarceva)	Carboplatin (Paraplatin, Paraplatin solution)	J9045	50 mg IV
		Cisplatin (Platinol)	J9060	10 mg IV
		Cisplatin (Platinol)	J9062	50 mg IV
		Gemcitabine (Gemzar)	J9201	200mg IV
		Vinolrelbine tartrate (Navelbine)	J9390	10 mg IV
		Paclitaxel (Taxol, Onxol)	J9265	30mg IV
		Docetaxel (Taxotere)	J9170	20mg IV

** Platinum-based chemotherapies used to treat non-small cell lung cancer are often used in combination or with other chemotherapeutic drugs, known as a cocktail. Common combinations include cisplatin with gemcitabine, vinolrelbine, or paclitaxel or carboplatin and gemcitabine.

TABLE II-3. LIST OF MEDICARE PART B DRUGS REPLACEABLE UNDER THE DEMONSTRATION – CANCER CONDITIONS (continued)

Condition	Replacement Drug	Replaceable Drug	J Code	Dosage
Multiple myeloma	Thalidomide*** (Thalomid)	Vincristine sulfate	J9370	1 mg IV
		Vincristine sulfate	J9375	2 mg IV
		Vincristine sulfate	J9380	5 mg IV
		Carmustine	J9050	100 mg IV
		Melphalan hcl (Alkeran)	J9245	50 mg IV
		Cyclophosphamide, oral	J8530	25 mg
		Cyclophosphamide (Cytoxan)	J9070	100 mg IV
		Cyclophosphamide (Cytoxan)	J9080	200 mg IV
		Cyclophosphamide (Cytoxan)	J9090	500 mg IV
		Cyclophosphamide (Cytoxan)	J9091	1 g IV
		Cyclophosphamide (Cytoxan)	J9092	2 g IV
		Cyclophosphamide lyophilized	J9093	100 mg IV
		Cyclophosphamide lyophilized	J9094	200 mg IV
		Cyclophosphamide lyophilized	J9095	500 mg IV
		Cyclophosphamide lyophilized	J9096	1 g IV
		Cyclophosphamide lyophilized	J9097	2 g IV
		Doxorubicin HCL, lipid (Adriamycin, Doxil)	J9000	Per 10 mg IV
		Doxorubicin HCL, all lipid (Adriamycin, Doxil)	J9001	Per 10 mg IV

***Standard chemotherapy regimens for multiple myeloma are combinations of the replaceable drugs. Specifically, VBMCP (vincristine, carmustine, melphalan, cyclophosphamide, and prednisone) and VAD (vincristine, doxorubicin, and dexamethasone (a steroid)).
****Indicated for patients who are refractory to at least one prior systemic therapy.

TABLE II-4. PERIODICITY OF DRUG ADMINISTRATION

Condition	Replaceable Drug	Periodicity of Administration*
Chronic viral hepatitis C	Interferon alpha-2a, recombinant (Roferon A)	6 MIU 3x per week for 1st 3 months followed by 3 MIU 3x per week for 9 mos
	Interferon alpha 2b (Intron A)	3 MIU 3x per week over 6 months
Multiple sclerosis	Interferon beta-1a (Avonex)	Once a week
Psoriatic arthritis**	Infliximab injection (Remicade)	Not indicated
Pulmonary arterial hypertension	Epoprostenol (Flolan)	Chronic infusion using portable infusion pump through in-dwelling catheter; dosage gradually increased daily over 7-day period; periodic pump re-filling
	Treprostinil (Remodulin)	Continuous sc infusion via a self-inserted subcutaneous catheter using portable infusion pump
Rheumatoid arthritis	Infliximab injection (Remicade)	At 2 and 6 weeks and once every 8 weeks thereafter
Senile osteoporosis (homebound)	Pamidronate disodium	Indicated for hypercalcemia and Paget's disease (not indicated for osteoporosis)
	Etidronate disodium	Indicated for hypercalcemia, Paget's disease, and ossification (not indicated for osteoporosis) -- for hypercalcemia 2hours infusion for 3 consecutive days
	Calcitriol	Indicated for hypercalcemia (not indicated for osteoporosis)
	Calcitriol	Indicated for hypercalcemia (not indicated for osteoporosis)
	Calcitonin – salmon	100 units IM 3x per week

*Data obtained from package inserts or cancer guidelines.

TABLE II-5. PERIODICITY OF DRUG ADMINISTRATION (continued)

Condition	Replaceable Drug	Periodicity of Administration*
Breast cancer	Fulvestrant (Faslodex)	IM Injection monthly
Chronic myeloid leukemia	Interferon alpha 2b (Intron A)	Not indicated for CML
	Interferon alpha-2a, recombinant (Roferon A)	9 MIU daily SC
Cutaneous t-cell lymphoma	Photochemotherapy (PUVA)	No more than 200 treatments every other day
	Photopheresis (extracorporeal) (Methoxsalen)	
Non-small cell lung cancer	Carboplatin (Paraplatin, Paraplatin solution)	Varies according to the combination of chemotherapy drugs used: Docetaxol treatments consist of 1-hour infusions every three weeks. Gemcitabine/Cisplatin: Gemcitabine on days 1 and 8 and cisplatin on day one of a 21-day cycle. 6 cycles. Paclitaxel/carboplatin: Paclitaxel on day 1 and Carboplatin on day 6 of 21 day cycle. 6 cycles Vinorelbine/cisplatin: Vinolrelbine once weekly plus cisplatin on days 1 and 29 then every 6 weeks.
	Cisplatin (Platinol)	
	Cisplatin (Platinol)	
	Gemcitabine (Gemzar)	
	Vinolrelbine tartrate (Navelbine)	
	Paclitaxel (Taxol, Onxol)	
	Docetaxel (Taxotere)	
Multiple myeloma**	Vincristine sulfate	Varies according to the combination of chemotherapy drugs used. Standard chemotherapy regimens for multiple myeloma are combinations of the replaceable drugs. Specifically, VBMCP (vincristine, carmustine, melphalan, cyclophosphamide, and prednisone) and VAD (vincristine, doxorubicin, and dexamethasone (a steroid)). A VBMCP cycle is 35 days. A VAD cycle is 21 days. Treatment length for VAD is typically 6 cycles. Carmustine: administered every 6 weeks.
	Vincristine sulfate	
	Vincristine sulfate	
	Carmustine	
	Melphalan hcl (Alkeran)	
	Cyclophosphamide (Cytoxan)	
	Cyclophosphamide (Cytoxan)	
	Cyclophosphamide (Cytoxan)	
	Cyclophosphamide (Cytoxan)	
	Cyclophosphamide (Cytoxan)	
	Cyclophosphamide lyophilized	
	Cyclophosphamide lyophilized	
	Cyclophosphamide lyophilized	
	Cyclophosphamide lyophilized	
	Cyclophosphamide lyophilized	
	Doxorubicin HCL, lipid (Adriamycin, Doxil)	
	Doxorubicin HCL, all lipid (Adriamycin, Doxil)	

*Data obtained from package inserts or cancer guidelines.
**Bortezomib (velcade) was included as a Part B replaceable drug for treatment of multiple myeloma, but no demonstration beneficiaries with multiple myeloma had been using that drug between January and August 2004.