Financial Burden of Discarded Weight-Based Anti-Neoplastic Drugs to Payers
and Patients in Private Insurance Market

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Abstract

Background: To estimate insurance payments and patient out-of-pocket (OOP) expenses associated with discarded weight-based intravenous anti-neoplastic drugs for privately insured US adult cancer patients.

Methods: We identified patients who received weight-based anti-neoplastic drugs from 2017 MarketScan Health Risk Assessment (HRA) linked to claims data. Using weight information in the HRA, we derived the recommended dose and calculated the percentage of drugs discarded. We applied beta regression to determine factors associated with the discarded percentages. To compare patients with and without high-deductible plans, we employed generalized linear model and two-part model to examine insurance payment and OOP expense, respectively. All statistical tests were 2-sided.

Results: Of 27,350 claims for 58 weight-based anti-neoplastic drugs from 1,970 patients, the median discarded percentage was 9.8% (mean = 12.8%, SD=10.5%). Aside from drug and tumor type, statistically significantly higher discarded percentages were found for patients in the lowest weight group (5.5%, 95% confidence interval = 4.7% - 6.4%; P<0.001, weight <150 vs. ≥200 lb). Private payers spent $5,090 per patient in 2017 on discarded weight-based anti-neoplastic drugs and patients’ mean OOP expense on discarded drugs was $63. 39.7% of patients had high-deductible plans. The adjusted mean OOP expense for discarded drugs was statistically significantly higher for those in high-deductible plans ($95 vs. $47, P<0.001).

Conclusions: Private insurers incurred substantial financial burden from discarded weight-based anti-neoplastic drugs. Although OOP expenses of discarded drugs were modest for most privately insured cancer patients, approximately 5% spent over $400 on the discarded drugs.
Policies designed to reduce drug waste from single-dose, weight-based anti-neoplastic drugs should evaluate their financial consequences for payers and patients.
Spending on cancer drugs in the US has grown 64% from 2013 to 2018, reaching $57 billion in 2018, with the median annual list price of newly approved cancer drugs staying above $150,000 since 2014.[1] Many anti-neoplastic drugs are administered intravenously with the dose depending on a patient’s weight or body surface area (BSA). These weight-based anti-neoplastic drugs are often packaged as single-dose vials. Leftover drug is common with these single-dose vials since the recommended dose based on patients’ weight or BSA often does not exactly match the dose in the vial. Under the prevailing “buy and bill” payment model in the US, insurance companies reimburse physicians for both the drug administered to a patient and the unused proportion.

Bach and colleagues estimated that the total revenues from discarded drugs for the top 20 anti-neoplastic drugs amounted to $1.8 billion dollars in the US in 2016.[2] A portion of the spending on discarded drugs is borne by patients because of the cost-sharing requirement in insurance plans. For cancer patients who receive weight-based anti-neoplastic drugs, the out-of-pocket (OOP) payment of discarded drugs will depend on drug price, amount discarded, and insurance benefit design. The financial burden of discarded drugs is most perceptible for cancer patients who are enrolled in high-deductible plans, which now account for over 40% of adults with employer-based health insurance;[3] high-deductible plans include the consumer-driven health plan and the high-deductible health plan.[4] Importantly, previous research has not provided precise estimates of OOP expenses for discarded cancer drugs because such estimation would require information on each patient’s weight (and height in the case of BSA).

This study linked biometric data from employee health surveys with claims of the employees to obtain refined estimates of the discarded percentage of weight-based anti-neoplastic drugs and estimate the associated insurance payments and OOP expenses. We
distinguished cancer patients enrolled in high-deductible plans because they are most vulnerable to high cost-sharing and OOP costs.

Methods

Data Sources

We linked employees who responded to the Health Risk Assessment (HRA) data in the 2017 MarketScan® Research Databases to their claims in the Commercial Claims and Encounters (CCAE) database via unique enrollee identifiers. The HRA contains biometrics, health risks and behavior collected from employees’ risk assessment questionnaires administrated by US corporations and health plans contributing data to MarketScan. The CCAE covers private-sector health data from approximately 350 private payers and collects paid claims and enrollment information of active employees, early retirees, ex-employees with continued coverage through the Consolidated Omnibus Budget Reconciliation Act, and spouses and dependents covered by employer-sponsored plans.[5] This study was exempt from the Institutional Review Board at the authors’ institution.

Ascertainment of Study Cohort

We identified patients who had cancer via ICD-10 diagnosis code from the linked HRA-CCAE database. Next, we obtained the list of weight-based anti-neoplastic drugs and the associated Healthcare Common Procedure Coding System (HCPCS) codes from the 2017 Centers for Medicare and Medicaid Services Part B Discarded Drug Units Report.[6] We then identified patients who had one or more claims with an HCPCS code indicating weight-based anti-neoplastic drugs from the CCAE claims. We excluded claims with payment ≤ 0 and with service
dates occurring in the month(s) without a valid record of insurance enrollment. The final study cohort consisted of 1,970 privately insured cancer patients who received weight-based intravenous anti-neoplastic drugs.

**Calculation of Discarded Drugs and Associated Costs**

For each drug, we obtained information on the available vial sizes and recommended dose(s) from the IBM MICROMEDEX 2.0.® We derived the recommended dose for each patient based on his/her cancer type, weight or BSA.[7] We then estimated the discarded dose as the difference between the full vial dose based on the vial size and the recommended dose per a patient’s weight or BSA and calculated the discarded percentage as discarded dose divided by the full vial dose. For drugs with multiple vial sizes, we took a conservative approach by using the smallest vial size. Information on the available vial size(s) in the US and the recommended dose for each drug included in our analysis is shown in Supplementary Table 1.

For each claim for a weight-based anti-neoplastic drug, we multiplied the discarded percentage by net payment and OOP expense (sum of deductible, copayment, and coinsurance) to quantify costs associated with the discarded drugs from the payers’ and patients’ perspective, respectively. We then aggregated these claim-level insurance payments and OOP expenses to the patient-level to estimate the per-patient financial burden of discarded weight-based anti-neoplastic drugs for payers and patients over calendar year 2017.

**Statistical Analysis**

Using claims as the unit of analysis, we applied beta regression to determine factors associated with the discarded percentage.[8] Beta regression is well suited for regression models with rates
or proportions as the dependent variable, such as the percentage of drug discarded. Covariates included age category (<50, 50-59, ≥60 y), weight group (<150, 150-199, ≥200 lb), place of service (hospital- vs. office-based), geographic region, cancer type, anti-neoplastic drug, and whether a patient was enrolled in a high-deductible plan. We categorized cancers into 8 groups: breast, lung, gastrointestinal, gynecological, genitourinary, lymphoma, other blood cancer, and all others. Because certain types are gender-specific, we did not include sex as a covariate. Since cancer patients often have multiple claims for their treatment, our analysis also accounted for within patient correlations.

For patient-level analysis, we compared the adjusted mean and median payments and OOP expenses (for total and discarded drugs) between patients with and without high-deductible plans based on multivariable analysis that controlled for age category, weight group, place of service, geographic region, and cancer type. We obtained adjusted mean of insurance payment and OOP expense using the generalized linear model with Gamma family and log link (to account for skewed distribution of cost data) [9] and two-part model (to account for large number of patients with zero OOP expense) [10, 11] respectively. The adjusted median was obtained from quantile regressions [12]. We then categorized payment and OOP expense into five cost ranges, using median, 75th, 90th, and 95th percentile of the distribution from the study cohort (i.e., full sample) as cut points, and compared the distribution across these cost ranges between the subset of patients with high-deductible plans and those without.

We used SAS 9.4 (SAS Institute Inc, Cary, NC) for data management and STATA 15.1 (StataCorp LLC, College Station, TX) for statistical analysis. To calculate P values, Chi-square tests, Wald tests, and t-tests were used as indicated. All statistical tests were two-sided and P values ≤ 0.05 were considered statistically significant.
Results

Characteristics of Study Cohort

Of the 1,970 cancer patients who received weight-based anti-neoplastic drugs, the mean age was 51.8 years (SD=8.8), and 65.4% were female. Approximately 39.7% of patients were enrolled in high-deductible plans. Breast cancer, gastrointestinal cancer, and lymphoma accounted for 33.8%, 17.6%, and 10.6% of the study cohort, respectively. More patients were in the higher weight categories (41.8% between 150-199 pounds and 31.8% ≥ 200 pounds) than the lowest weight category (26.4%, <150 pounds). The comparison between patients who enrolled in high-deductible plans versus those who did not revealed similar patient characteristics, except that high-deductible enrollees were more likely to receive infused therapy in the office and reside in Northeastern and Southern US regions (Table 1).

Claim-level Analysis of Discarded Percentage

Of the 27,350 claims for 58 weight-based anti-neoplastic drugs, the mean discarded percentage was 12.8% (median = 9.8%, SD=10.5%). Figure 1A plots the mean, minimum and maximum discarded percentage, sorted by the mean values, for each drug with 10 or more claims. The mean discarded percentages varied widely across drugs, ranging from less than 1.0% for ixabepilone (J9207) to 43.2% for pegasparagase (J9266). Figure 1A also shows that for each drug, variations in patients’ weight or BSA resulted in a noticeable range between min and max percentages for some drugs. Figure 1B depicts the share of each drug in the total payment for all discarded anti-neoplastic drugs in 2017 among our study cohort. As shown, drugs with higher mean discarded percentages do not necessary result in high cost share of discarded drugs. The
The top six drugs with the highest share were trastuzumab (28.0%), bevacizumab (10.2%), bortezomib (8.4%), ipilimumab (6.0%), rituximab (5.7%), and bendamustine (4.5%). These six drugs combined accounted for 62.8% of all payment for discarded drugs.

Table 2 shows that after controlling for the list of anti-neoplastic drugs, two covariates statistically significantly associated with the discarded percentages were patients’ weight and cancer type. Specifically, the discarded percentage was 5.5% (95% CI = 4.7% - 6.4%) and 1.1% (95% CI = 0.3% - 1.9%) higher for patients in the lowest (<150 lb) and middle (150-199 lb.) weight categories compared with those in the highest weight category (>200 lb). In addition, compared to patients with gastrointestinal cancer, the discarded percentage was 4.8% (95% CI = 2.0% - 7.5%) lower for those with lung cancer; breast cancer displayed a nearly statistically significant 1.7% increase in discarded percentage.

Patient-level Analysis of Insurance Payment and OOP Expense for Discarded Drugs

On average, private payers spent $43,902 per patient in 2017 on weight-based anti-neoplastic drugs. Of that, $5,090 (11.6%) was spent on discarded drugs. Patients’ mean OOP expense was $522, with $63 on discarded drugs. After controlling for patient characteristics in the multivariable analyses, neither the adjusted mean nor the adjusted median insurance payment for total weight-based anti-neoplastic drugs, as well as discarded drugs, were statistically significantly different between patients enrolled in high-deductible plans and those not (Figure 2A). However, the adjusted mean OOP expense was statistically significantly higher for those in high-deductible plans ($732 vs. $408, P [Wald test] <0.001 for total amount, and $95 vs. $47, P [Wald test] <0.001 for discarded amount). The adjusted median OOP was not statistically significantly different between patients who were in high-deductible plans and those who were
not for total OOP ($42 vs. $37, P [t-test] =0.94), and OOP associated with discarded drugs ($3.13 vs. $2.72, P [t-test]=0.91) (Figure 2B). Other covariates statistically significantly associated with costs of discarded drugs were weight group and the total number of months in chemotherapy (Table 3).

Figure 3 illustrates the distribution of insurance payment and OOP expense for weight-based anti-neoplastic drugs, and for their discarded amount in 2017 for all patients in the full sample and stratified by whether patients enrolled in high-deductible plans. The distribution of insurance payment was similar between patients who enrolled in high-deductible plans and those who did not, with median payment (per patient) around $13,500 for anti-neoplastic drugs (Figure 3A) and $1,400 for discarded drugs (Figure 3B). Distribution of OOP expense indicates although close to 60.0% of patients had zero expense, a higher proportion of patients in high-deductible plans incurred expenses higher than the 95th percentile. Figure 3C shows 8.2% of patients in high-deductible plans spent $3,100 or more OOP on weight-based anti-neoplastic drugs, compared to 3.0% of patients who did not enroll in high-deductible plans. For OOP expense on discarded drugs, Figure 3D shows 7.3% of patients in high-deductible plans and 2.7% in non high-deductible plans spent $400 or more OOP on discarded drugs.

Discussion

Our study reports the financial burden of discarded weight-based anti-neoplastic drugs for payers and patients of commercial insurance. We found that although OOP expenses of discarded drugs were modest for the majority of privately insured patients, approximately 4.5% of patients paid more than $400 in 2017 for discarded drugs alone. The percentage was even higher (7.3%) for the subset of patients enrolled in high-deductible plans. These numbers are noteworthy both
because of the trend of rising enrollment in high-deductible plans and the state of financial preparedness among American families. Indeed, a 2018 survey on the economic well-being of US households reported that 4 in 10 adults could not cover an unexpected expense of $400.[13] Another notable finding is the high costs of discarded anti-neoplastic drugs for third party payers, with the estimated payment on the leftover amount averaging over $5,000 per patient in 2017. Although not directly paid by the patients, these costs are ultimately transmitted to the insured population as higher premiums. The National Academies of Sciences, Engineering, and Medicine (NASEM) recently released a consensus study report on discarded drugs.[14] The report suggests that if regulatory action is taken to require rebates from manufacturers, the rebates should first be directed to cover patients’ OOP expense for the discarded drugs. Estimates from this study offers useful information to policy discussions regarding such rebates.

Undoubtedly, the high price tag of discarded weight-based anti-neoplastic drugs is driven by the high costs of cancer drugs in the US. The definitive solution is to develop policies to lower the price of prescription drugs – a point emphasized in the above NASEM report.[14] Still, small incremental changes may help reduce drug waste caused by leftover from single-dose vials. Researchers have proposed to mitigate this problem through three channels: drug delivery and administration, manufacturing, and reimbursement.[2, 15] Proposed strategies under each channel can potentially reduce costs of discarded drugs for some stakeholders in the US healthcare system but also face unique regulatory and/or implementation challenges.

Vial sharing is a drug delivery practice that deploys strategies to safely administer the leftover portion of the drug in a single-use vial to a second patient instead of discarding it. Safety of vial sharing is enhanced by technologies like closed system drug transfer devices that reduce the risk of microbial contamination.[16] Per the infection control guideline of the Centers for
Disease Control and Prevention (CDC), vial sharing is prohibited as the guideline requires a new syringe and needle (as in the case of single-dose vials) to be used by one patient.[17] The United States Pharmacopeia (USP) imposes less strict requirements than the CDC. Under USP Chapter 797 standards, single-use drugs must be discarded within six hours of use if the drug was opened and kept in International Organization for Standardization (ISO) 5 air conditions and within one hour if outside ISO 5 air conditions.[18] These regulatory requirements contribute to the less frequent vial-sharing practices observed in the US compared with other countries despite evidence of cost-effectiveness of the vial sharing practice.[19] From patients’ perspective, it is unclear whether vial sharing will ease the financial burden associated with discarded cancer drugs because providers may charge payers for the full vial under the buy-and-bill model.[20]

Another proposed strategy urged regulators to require biopharmaceutical companies to manufacture drugs in multiple vial sizes. Bach and colleagues estimated that this strategy could save the healthcare system around $2 billion dollars from wastage avoided for the top 20 infused cancer drugs.[2] Economists have cautioned that as long as drug manufacturers hold monopoly power in setting drug prices, an unintended consequence of regulating multiple vial sizes could be a compensatory increase in drug prices.[21] In that case, patients could actually be worse off financially. In addition, it is possible that even with the option of multiple vial sizes, providers may choose to purchase only one size to reduce inventory costs and administrative burden.

On the reimbursement front, Bach et al. suggested requiring drug manufacturers to refund the cost of leftover drug in exchange for allowing them to select their vial sizes;[2] such refund could be extended to patients. In fact, the JW modifier mandated by CMS may offer a viable mechanism to refund payers and patients for the discarded proportion of weight-based drugs. The JW modifier is a HCPCS Level II modifier created by CMS in July 2007 for providers to report
drug amount discarded/not administered to any patient as a separate line in drug claims.[22] Effective January 1, 2017, CMS mandated providers to report the JW modifier for discarded drugs on Part B claims.[23] Some private insurance plans, such as Blue Cross and Blue Shield, have also adopted this CMS mandate.[24] If providers adhere to the use of the JW modifier when submitting their claims, policy makers can leverage this information to mark claims to request for refund and waive the associated copayment for patients. Unfortunately, a recent study suggested a wide variation across providers in the billing practice of using the JW modifier to report discarded drugs.[25] Price transparency could potentially inform patients of the impact of discarded drugs on their OOP expense and incentivize policy actions. However, despite efforts from state legislators and private sectors in promoting price transparency[26, 27], price transparency in the context of OOP expense remains challenging.[28]

Several study limitations warrant discussion. First, our study was based on a convenient sample of employees who responded to their employers’ risk assessment questionnaire; thus, the study cohort may not be representative of the entirety of privately insured cancer patients. Although the biometric information available in our data offer a rare opportunity to obtain patient-specific cost estimate, interpretations of the drug-to-drug variations should note that for drugs with a small number of users the discarded percentages documented in our study would more likely reflect the biometric characteristics of patients than the available vial sizes. Second, weight and height information in the HRA were self-reported and static, and studies have found self-reported weight tends to be under-reported for both overweight and obese individuals.[29, 30] Third, our use of the smallest vial size to calculate discarded percentage could underestimate the discarded percentages and associated costs for weight-based drugs with multiple vial sizes. Lastly, our analysis did not consider dose-rounding as such practice cannot be reliably
determined from claims data. This may over-estimate costs associated with discarded drugs as research has shown dose-rounding can reduce drug wastage.[31] Nevertheless, our estimates from the perspective of payers and patients in private insurance add important information to the literature as the study by Bach et al. derived their estimates from Medicare payment,[2] which tend to have lower mark-up than private payers. Another unique contribution of our study is our elucidation of the financial impact of discarded drugs for patients.

In conclusion, private insurers incurred about $5,000 per patient per year to reimburse oncology practices for the discarded proportion of weight-based anti-neoplastic drugs. Although OOP expenses of discarded drugs were modest ($63 on average), over 7.0% of those enrolled in high-deductible plans spent more than $400 per year on the discarded drugs alone. Policies designed to reduce drug waste from single-dose, weight-based anti-neoplastic drugs should consider their financial impact at both the societal level, e.g., waste is translated to higher insurance premiums for employees, and the individual level where select patients may have high OOP expenses.

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Data Availability

Access to the data used in this study (i.e., MarketScan) is strictly limited to members of the research team who signed the Data Use Agreement (DUA) at the corresponding author’s
institution. Per the DUA, authors of this study cannot grant data access nor distribute any subset of data to individual outside the research team.

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Table 1: Patient Characteristics, Total Cohort and by Enrollment in High-deductible Plans

| Patient Characteristics | Full Sample No. (%) | Enrolled in High Deductible Plans No. (%) | Not in High Deductible Plans No. (%) | \( P^a \) |
|-------------------------|---------------------|-----------------------------------------|-------------------------------------|---------|
| Total                   | 1,970 (100.0)       | 782 (100.0)                             | 1,188 (100.0)                       |         |
| Age, y                  |                     |                                         |                                     |         |
| <50                     | 655 (33.2)          | 269 (34.4)                              | 386 (32.5)                          | 0.51    |
| 50-59                   | 904 (45.9)          | 359 (45.9)                              | 545 (45.9)                          |         |
| ≥60                     | 411 (20.9)          | 154 (19.7)                              | 257 (21.6)                          |         |
| Sex                     |                     |                                         |                                     |         |
| Male                    | 681 (34.6)          | 263 (33.6)                              | 418 (35.2)                          | 0.48    |
| Female                  | 1,289 (65.4)        | 519 (66.4)                              | 770 (64.8)                          |         |
| Weight, lb              |                     |                                         |                                     |         |
| <150                    | 520 (26.4)          | 203 (26.0)                              | 317 (26.7)                          | 0.86    |
| 150-199                 | 824 (41.8)          | 333 (42.6)                              | 491 (41.3)                          |         |
| ≥200                    | 626 (31.8)          | 246 (31.5)                              | 380 (32.0)                          |         |
| Place of service        |                     |                                         |                                     |         |
| Office-based            | 934 (47.4)          | 407 (52.1)                              | 527 (44.4)                          | 0.001   |
| Hospital outpatient     | 1,036 (52.6)        | 375 (48.0)                              | 661 (55.6)                          |         |
| Cancer Type             |                     |                                         |                                     |         |
| Breast                  | 666 (33.8)          | 288 (36.8)                              | 378 (31.8)                          | 0.17    |
| Gastrointestinal        | 346 (17.6)          | 131 (16.8)                              | 215 (18.1)                          |         |
| Genitourinary           | 96 (4.9)            | 40 (5.1)                                | 56 (4.7)                            |         |
| Gynecological           | 167 (8.5)           | 52 (6.7)                                | 115 (9.7)                           |         |
| Lung                    | 101 (5.1)           | 40 (5.1)                                | 61 (5.1)                            |         |
| Lymphoma                | 208 (10.6)          | 78 (10.0)                               | 130 (10.9)                          |         |
| Other blood cancers     | 117 (5.9)           | 50 (6.4)                                | 67 (5.6)                            |         |
| Others                  | 269 (13.7)          | 103 (13.2)                              | 166 (14.0)                          |         |
| Region                  |                     |                                         |                                     |         |
| Northeast               | 291 (14.8)          | 140 (17.9)                              | 151 (12.7)                          | <0.001  |
| Region       | Patients (Mean) | Active (Mean) | Quiescent (Mean) | Average months in chemo (SD) | P value |
|-------------|----------------|--------------|-----------------|-------------------------------|---------|
| North Central | 609 (30.9)      | 193 (24.7)   | 416 (35.0)      | 4.52 (2.98)                  |         |
| South       | 700 (35.5)      | 309 (39.5)   | 391 (32.9)      | 4.60 (2.94)                  |         |
| West        | 370 (18.8)      | 140 (17.9)   | 230 (19.4)      | 4.46 (3.02)                  | 0.28b   |

*P values from two-sided Chi-Squared tests. SD=standard deviation.

*b P value from two-sided t-test.
Table 2: Claims-level Analysis of Factors Associated with Discarded Percentage

| Covariatesa | Estimate (95% CI), % | Pb |
|-------------|---------------------|----|
| High-deductible plan | 0.01 (-0.7 to 0.7) | 0.98 |
| Age (reference: age <50 y) | | |
| 50-59 y | -0.5 (-1.3 to 0.2) | 0.18 |
| ≥60 y | -0.1 (-1.0 to 0.8) | 0.84 |
| Weight (reference: >200 lb) | | |
| <150 lb | 5.5 (4.7 to 6.4) | <0.001 |
| 150-199 lb | 1.1 (0.3 to 1.9) | 0.008 |
| Place of service (reference: office-based) | | |
| Hospital-based | 0.4 (-2.2 to 1.1) | 0.20 |
| Cancer type (reference: Gastrointestinal) | | |
| Breast | 1.65 (-0.1 to 3.4) | 0.06 |
| Genitourinary | -0.03 (-3.1 to 3.0) | 0.98 |
| Gynecological | -1.4 (-3.2 to 0.3) | 0.11 |
| Lung | -4.8 (-7.5 to -2.0) | 0.001 |
| Lymphoma | -0.5 (-2.3 to 1.4) | 0.61 |
| Other blood cancers | -0.4 (-3.5 to 2.8) | 0.81 |
| Other cancer | 0.4 (-1.0 to 1.8) | 0.56 |
| Region (reference: Northeast) | | |
| North Central | -0.7 (-1.7 to 0.4) | 0.22 |
| South | 0.4 (-0.6 to 1.4) | 0.43 |
| West | 0.6 (-0.4 to 1.7) | 0.25 |

a Other covariates include the list of weight-based anti-neoplastic drugs. CI = confidence interval.

b P values from Wald tests; all P values were two-sided.
Table 3: Patient-Level Analysis of Factors Associated with Insurance Payment or Out-of-Pocket Payment for Discarded Drugs

| Covariates                        | GLM: Insurance Payment Estimate (95% CI) | Quantile Regression: Insurance Payment Estimate (95% CI) | Two-Part Model: OOP Payment Estimate (95% CI) | Quantile Regression: OOP Payment Estimate (95% CI) |
|-----------------------------------|----------------------------------------|----------------------------------------------------------|-----------------------------------------------|---------------------------------------------------|
| High-deductible plan              | -533 (-1463 to 397)                    | -234 (-725 to 257)                                        | 40 (24 to 56)                                 | 0.18 (-2.9 to 3.2)                                |
| Age (reference: age <50)          |                                        |                                                          |                                               |                                                   |
| 50-59 y                           | -855 (-2017 to 307)                    | -8.7 (-554 to 536)                                       | -0.8 (-17 to 16)                              | -0.00001 (-3.4 to 3.4)                           |
| ≥60 y                             | -682 (-2132 to 768)                    | -56 (-735 to 622)                                        | 13 (-9 to 34)                                 | 0.08 (-4.1 to 4.3)                               |
| Weight (reference: >200 lb)       |                                        |                                                          |                                               |                                                   |
| <150 lb                           | 1843 (661 to 3024)                     | 567 (-77 to 1211)                                        | 34 (14 to 55)                                 | 0.08 (-3.9 to 4.1)                               |
| 150-199 lb                        | 1420 (161 to 2680)                     | 193 (-370 to 755)                                        | 21 (3 to 39)                                  | -0.00001 (-3.5 to 3.5)                           |
| Place of service (reference: office) |                                        |                                                          |                                               |                                                   |
| Hospital                          | 3586 (2366 to 4806)                    | 775 (289 to 1262)                                        | -17 (-32 to -2)                               | -0.9 (-3.9 to 2.1)                               |
| Cancer type (reference: Gastrointestinal) |                                        |                                                          |                                               |                                                   |
| Breast                            | 2158 (1020 to 3296)                    | 813 (110 to 1516)                                        | 30 (8 to 51)                                  | 0 (-4.4 to 4.4)                                  |
| Genitourinary                     | -99 (-2609 to 2412)                    | 568 (-658 to 1793)                                       | -14 (-50 to 21)                               | 2.1 (-5.5 to 9.7)                                |
| Gynecological                     | -3321 (-5343 to -1298)                 | -468 (-1463 to 527)                                      | -43 (-79 to -7)                               | -0.08 (-6.3 to 6.1)                              |
| Lung                              | 506 (-1379 to 2392)                    | 599 (-602 to 1801)                                       | -17 (-59 to 25)                               | -0.69 (-8.1 to 6.8)                              |
| Lymphoma                          | 7679 (5837 to 9520)                    | 2071 (1143 to 2998)                                      | 62 (37 to 87)                                 | 1.0 (-4.8 to 6.8)                                |
| Other blood cancers               | 9349 (683 to 11860)                    | 4520 (3389 to 5651)                                      | 72 (41 to 103)                                | 0.92 (-6.1 to 7.9)                               |
| Other cancer                      | 4302 (1397 to 7206)                    | 309 (-549 to 1168)                                       | -3 (-35 to 30)                                | 0 (-5.3 to 5.3)                                  |
| Region (reference: Northeast)     |                                        |                                                          |                                               |                                                   |
| North Central                     | 294 (-1185 to 1773)                    | -297 (-1060 to 466)                                      | -3 (-29 to 23)                                | 0 (-4.7 to 4.7)                                  |
| South                             | 311 (-930 to 1552)                     | 20 (-729 to 769)                                         | 8 (-17 to 33)                                 | 0.08 (-4.6 to 4.7)                               |
| West                              | 865 (-499 to 2228)                     | 210 (-628 to 1048)                                       | -10 (-38 to 18)                               | -0.84 (-6.0 to 4.4)                              |
| Months on chemotherapy            | 1927 (1606 to 2247)                    | 902 (821 to 983)                                         | 12 (10 to 15)                                 | 0.92 (0.4 to 1.4)                                |

CI = confidence interval; GLM = generalized linear model

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Figure Legends

**Figure 1.** Discarded percentage of each weight-based anti-neoplastic drug and its share in total payment for discarded drugs in 2017, sorted by mean discarded percentages. A) Mean, minimum and maximum discarded percentage of each weight-based anti-neoplastic drug calculated from patients’ biometric information linked to drug claims and sorted by mean discarded percentages. A plus (+) indicates less than five patients in our study cohort received the drug. B) Share of each weight-based anti-neoplastic drug among total payment for discarded drugs in year 2017 varies widely across drugs.

**Figure 2.** Comparison of the adjusted mean and median insurance payment and OOP expenses for total and discarded amount of weight-based anti-neoplastic drugs between cancer patients enrolled in high-deductible plans and those not in high-deductible plans (N=1970). A) No statistically significant difference by enrollment to HD plans was observed in the adjusted mean and median net payment for total and discarded amount of weight-based anti-neoplastic drugs. B) Mean OOP of total and discarded weight-based anti-neoplastic drugs were statistically significantly higher for patients enrolled in HD plans. No statistically significant difference in median OOP was found between patients in HD and non-HD plans. OOP = out-of-pocket; HD = high-deductible.

**Figure 3.** Distribution of Insurance Payment and Out-of-Pocket Expense on Total vs. Discarded Weight-Based Anti-Neoplastic Drugs (N=1,970). A) Distribution of insurance
payment on weight-based anti-neoplastic drugs was similar between patients in HD and non-HD plans. B) Distribution of insurance payment on discarded weight-based anti-neoplastic drugs was similar between patients in HD and non-HD plans. C) Distribution of OOP expenses on weight-based anti-neoplastic drugs showed a higher proportion of patients with HD plans in higher cost categories and a lower proportion of HD patients had zero OOP expense. D) Distribution of OOP expenses on discarded weight-based anti-neoplastic drugs showed a higher proportion of patients with HD plans in higher cost categories and a lower proportion of HD patients had zero OOP expense …The cut point of each cost category corresponds to median, 75th, 90th, and 95th percentile of the distribution of the full sample. HD = high-deductible; OOP = out-of-pocket.
Figure 1

A Discarded Percentage of Weight-based Anti-neoplastic Drugs, Sorted by Mean Discarded %

B Share of Total Payment in 2017 for Discarded Drugs, Sorted by Mean Discarded %
Figure 2

A

Adjusted mean and median net pay by enrollment to HD Plans

B

Adjusted mean and median OOP by enrollment to HD Plans