Milliman

Cancer Patients Receiving Chemotherapy:

Opportunities for Better Management

Prepared by

Milliman, Inc., NY

Kate Fitch, RN, MEd
Principal and Healthcare Management Consultant

Bruce Pyenson, FSA, MAAA
Principal and Consulting Actuary

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EXECUTIVE SUMMARY

Cancer is an important cost issue for commercial benefit programs. Based on our analysis of Medstat 2007, cancer patients make up 0.68% of a commercially insured population, but account for 10% of the overall healthcare costs. Over the course of a year, a cancer patient receiving chemotherapy (approximately 22% of all cancer patients) incurred, on average, allowed costs of approximately $111,000 a year, almost four times the cost of a cancer patient not receiving chemotherapy. This paper quantifies the medical service utilization and costs of cancer patients receiving chemotherapy, and, in particular, identifies unexplained variation in several utilization and cost measures that indicate opportunities for better quality and cost management. The utilization and cost metrics we examine are:

1. Chemotherapy-related hospitalizations;

2. Chemotherapy-related emergency room visits;

3. Chemotherapy costs;

4. Hospice utilization; and

5. Dying in hospital and chemotherapy administration within 2-4 weeks of dying.

Our analysis focuses on 10 common cancer types where chemotherapy is a key treatment modality. These 10 cancers account for 65% of cancer patients in a commercial population, and 25% of the 10 cancer population receives chemotherapy in a year. The members receiving chemotherapy and having one of the 10 cancers make up about 0.11% of commercial members but account for about 4% of overall healthcare costs.

For the first 3 metrics above, we identified significant regional variation, suggesting an opportunity to reduce costs and utilization and improve quality. Chemotherapy-related inpatient admissions and emergency room visits ranged from 223/1000 to 484/1000 and 465/1000 to 1626/1000 respectively, a 2-3 fold difference in rates. Average per patient chemotherapy costs, ranged from $17,212 to $27,494, a $10,000 difference per chemotherapy patient (Table 1). We did not adjust each region's population of cancer patients receiving chemotherapy by demographics and cancer type distribution mix, but our empirical findings certainly suggest unexplained variation.

Table 1. Variation in Utilization and Costs for Cancer Patients Receiving Chemotherapy (10 cancer groupings only)

	Chemotherapy-Related Inpatient Hospital Admits/1000	Chemotherapy-Related Emergency Room Visits/1000	Average Chemotherapy Drug Costs per Chemotherapy Patient
National Average	378 (average cost per admit $22,000)	929 (average cost per ER visit $800)	$22,353
High Utilizing Region	484	1626	$27,494
Low Utilizing Region	223	465	$17,212

Source: Milliman Analysis of Medstat 2007

The 4th and 5th metric suggest additional quality and cost opportunities. We identified that 3.5% of the cancer patients receiving chemotherapy in a given year died in an inpatient setting including 8% of pancreatic cancer patients and 9% of lung cancer patients. For those patients dying in an inpatient setting, 24% received chemotherapy within 14 days of dying and 51% received chemotherapy within 30 days of dying.

Studies on populations receiving chemotherapy for lung, breast, rectal and ovarian cancer report statistically significant regional variation in the use of chemotherapy along with variation by age, race and socioeconomic factors. [1] [2] [3] [4] [5] In another study, variation in the use of second and third line chemotherapy was identified, and costs for those using second line treatments were substantially higher than those receiving first line only and still higher for those receiving third line chemotherapy.[6] Another study identified two-fold regional variation in the rate of hospitalizations for toxicity from chemotherapy in older women with breast cancer.[7]

Some payers are increasing efforts to manage chemotherapy utilization. Although treatment guidelines are well established, standards for treatment outcomes are lacking. This means that measuring adherence to guidelines rather than outcomes could be a useful tool for payers. Few payers require that providers demonstrate adherence to guidelines to receive reimbursement. Establishing best practice benchmarks for particular cost, utilization and quality metrics could improve the ability to monitor and set targets for improving the quality of care delivery for cancer patients receiving chemotherapy.

The variation in chemotherapy-related inpatient admissions, ER visits and chemotherapy costs suggest opportunities for improvement, and we modeled the impact of a 10% reduction in national average rates for these key quality outcome metrics. The 10% reduction is significantly less than the regional variation we observed for each of these three categories. The cost reduction per chemotherapy patient would be approximately $3,000 or 2.6% of a patient's total annual costs.

Table 2. Modeling Reduction in Medical Utilization and Cost for Cancer Patients Receiving Chemotherapy

Type of cost	Chemotherapy-Related Inpatient Admissions	Chemotherapy-Related Emergency Room Visits	Chemotherapy Drug Costs
Cost per Event	$22,000	$800	$20,000
Frequency of Event Among Chemotherapy Cancer Patients	38%	93%	100%
Modeled Reduction in Use or Cost	10%	10%	10%
Cost Reduction	$836	$74	$2,000

Total Reduction in Cost per Patient	$2,910
Chemotherapy Patients Approximate Annual Cost	$111,000
As a Percent of Total Cost	2.6%

Source: **Milliman Analysis of Medstat 2007**
Milliman Health Cost Guidelines 2009
14 million commercially insured lives, 104,473 cancer patients
Chemotherapy patients exclude patients on hormonal therapy only

Establishing benchmarks for the three quality metrics above would allow health plans and providers to evaluate performance. Targets for chemotherapy-related inpatient admissions and ER visits rates will remain relatively stable from year to year unless the toxicity of chemotherapy in subsequent years is dramatically reduced (or increased). Of course, a particular population's comparison to established benchmarks will need to consider adjustment for demographics and cancer distribution mix.

On the other hand, setting targets for chemotherapy costs is more challenging as chemotherapy costs can fluctuate dramatically from year to year when new chemotherapy agents are introduced. Our Medstat analysis of trends in chemotherapy costs from 2003-2007 produced annual trends varying from 8% to 19%. Because of this variation, alternative methodologies are needed to set expected targets for chemotherapy costs each year. Nonetheless, chemotherapy cost reductions offer the largest potential for cost reduction.

This paper was commissioned by Innovent Oncology, a subsidiary of US Oncology, which has developed evidence-based guidelines for oncology. The paper reflects the research of the authors. It should not be considered an endorsement of any policy or product by Milliman, Inc. Cancer therapy is a rapidly changing field, and readers should note that this paper may not reflect current therapeutic considerations. The figures presented here are, unless otherwise noted, national averages developed from historical databases. Because of the variability in healthcare and health benefits, these figures may not be appropriate for particular organizations or particular purposes.

BACKGROUND ON CHEMOTHERAPY TREATMENT IN CANCER

Primer on Chemotherapy and its Complications

Chemotherapy is one of three pillars of cancer treatment along with surgical treatment and radiation therapy. Chemotherapy treatment can be used for the following intents: curing, prolonging survival, or palliation. Clinical recommendations for cancer treatment depend on the type and stage of cancer along with patient characteristics.

In particular, the clinical recommendations for chemotherapy depend on whether the disease is metastatic (spread of cancer beyond its original site) or non-metastatic cancer type, as well as prior chemotherapy attempts and responses. A course of chemotherapy is generally described using the following terms:

- Neoadjuvant chemotherapy: chemotherapy given prior to a surgical procedure usually to shrink the cancer so that the surgical procedure may not need to be as extensive.

- Adjuvant chemotherapy: chemotherapy given after a tumor is removed surgically to lower the risk that the cancer will recur.

- Induction chemotherapy: chemotherapy given to induce a remission.

- Consolidation chemotherapy: chemotherapy given once a remission is achieved to sustain a remission.

- Maintenance chemotherapy: chemotherapy given after an initial chemotherapy course to prolong a response.

- Palliative chemotherapy: chemotherapy that is given specifically to address symptom management.

- First line chemotherapy: chemotherapy first used for treating cancer that has metastasized.

- Second line chemotherapy: chemotherapy given when a disease has recurred or the patient no longer responds to first line chemotherapy.

- Third and fourth line chemotherapy: chemotherapy given when a disease has recurred or the patient no longer responds to second and third line chemotherapy.

Although chemotherapy kills cancer cells, it can damage normal cells and cause significant side effects. The side effects vary depending on the particular chemotherapy drug, dosage, route of administration and patient characteristics. Some chemotherapy side effects can be severe enough to require hospitalization. The side effects may include:

- Bone marrow suppression including:

  o Low white blood cell counts which increases the risk of infection

  o Low red blood cell counts (anemia) which can require transfusion

  o Low platelet counts which can lead to bleeding

- Damage and irritation to cells lining the digestive tract which can produce:

  o Nausea and vomiting

  o Diarrhea

- Appetite loss, taste changes and weight changes

- Sores in the mouth and throat including stomatitis, pharangitis, esophagitis and mucositis

- Constipation

- Fatigue

- Pain

- Infertility

- Hair loss

National Evidence-Based Chemotherapy Guidelines

Several organizations produce evidence-based treatment guidelines, including those issued by the National Comprehensive Cancer Network (NCCN), American Society of Clinical Oncology (ASCO), and Innovent Oncology. The guidelines are updated when new therapies or new information on existing therapies are introduced. One literature review on the impact of clinical practice guidelines on improvement in oncology treatment processes or outcomes reported wide variation in guideline adherence, but it reported improved financial outcomes and reduced complication rates with improved guideline adherence.[8]

Chemotherapy Prescribing Patterns

The escalating cost of cancer care has received recent attention with questions raised as to the appropriateness and value of particular chemotherapy treatments. A recent commentary in *Journal of the National Cancer Institute* questioned the value of particular chemotherapies that are marginally effective and costly.[9] Comparative effectiveness efforts are being proposed as a tactic to address the marginal value issue.

Criticism also surrounds the reported variation in chemotherapy utilization; the variation raises quality and cost issues. Studies on populations receiving chemotherapy for lung, breast, rectal and ovarian cancer report statistically significant regional variation in the use of chemotherapy along with variation by age, race and socioeconomic factors.[10] [11] [12] [13] [14] Variation in the use of second and third line chemotherapy was identified, and costs for those using second line treatments were substantially higher than those receiving first line only and still higher for those receiving third line chemotherapy.[15] Another study identified two-fold regional variation in the rate of hospitalizations for toxicity from chemotherapy in older women with breast cancer.[16]

The reasons for variation in physicians' chemotherapy prescribing patterns have not been well documented, although the benefits of following treatment guidelines are well established. One explanation for variation in chemotherapy treatment has been reimbursement practices. A study in *Health Affairs* reported that, although there is no evidence that reimbursement incentives affected oncologists' decisions to administer chemotherapy to metastatic cancer patients, once a decision to give chemotherapy was taken, physicians receiving more generous Medicare reimbursements used more costly treatment regimens.[17]

Some payers are increasing efforts to manage chemotherapy utilization, but few payers require providers to demonstrate adherence to guidelines to receive reimbursement. A few have started to tie coverage or reimbursement for chemotherapy to provider compliance with established guidelines. Medicare recently expanded its list of approved compendia to help set coverage policies for off label anti-cancer treatments.

Establishing benchmarks and targets for metrics that give an indication of the quality of care delivery for cancer patients receiving chemotherapy would allow health plans and providers to evaluate performance. Although claims data has its limitations, it can capture chemotherapy prescribing patterns and costs as well as side effects of chemotherapy. We analyzed commercial claims data to identify the utilization and cost of cancer patients receiving chemotherapy for 5 cost and quality of care outcomes:

1. Chemotherapy-related hospitalizations;

2. Chemotherapy-related emergency room visits;

3. Chemotherapy costs;

4. Hospice utilization; and

5. Dying in hospital rates and chemotherapy administration within 2-4 weeks of dying.

The following sections provide the results of our claims data analysis.

A PAYER VIEW OF CANCER PATIENTS RECEIVING CHEMOTHERAPY

Prevalence

In a typical commercial population, about 0.68% of members will have claims for cancer in a year but will account for about 10% of all medical costs. Even within that 0.68%, costs and intensity of treatment are concentrated in a relatively small portion of patients. Most patients with cancer claims are not receiving active treatment for their cancer. Of all patients with cancer claims, about 22% will receive chemotherapy in a year and these patients incur the majority of costs.

There are numerous types and stages of cancer. Some cancers have a very high cure rate, while for others, treatment success is measured by extending life for a few months. Our analysis focuses on 10 common cancer types where chemotherapy is a key treatment modality. These 10 cancers account for 65% of patients with cancer claims in a commercial population, and 25% of the 10 cancer cohort population receives chemotherapy in a year. The members receiving chemotherapy and having one of the ten cancers make up about 0.11% of commercial members but account for about 4% of all medical costs. The ten cancer groupings are labeled in the figures below along with a category for other cancers not included in the 10.

The prevalence of these cancers varies by age and sex with prevalence generally increasing with age. In the commercial population, women have a slightly lower prevalence of cancer than men. See Figure 1 and 2.
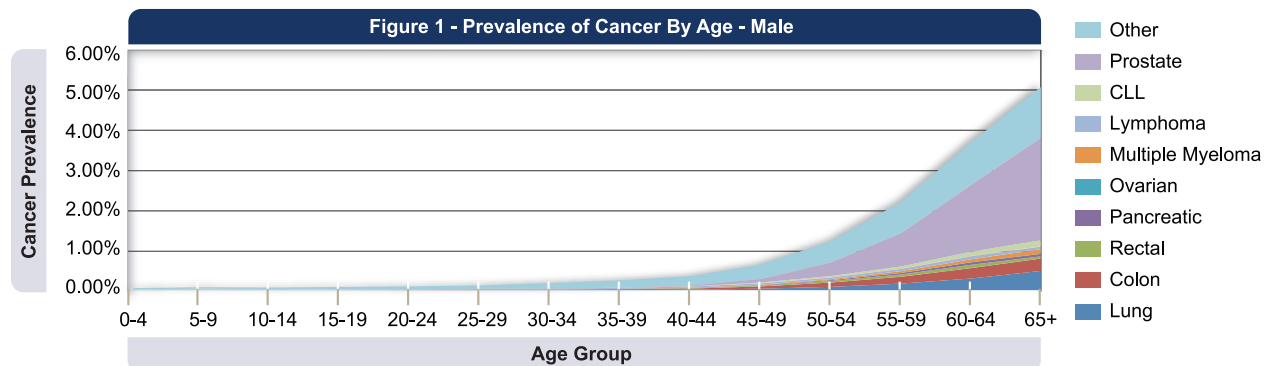
Figure 1 - Prevalence of Cancer By Age - Male

Source: Milliman Analysis of Medstat 2007
Milliman Health Cost Guidelines 2009
14 million commercially insured lives, 104,473 cancer patients
■ Prostate = Prostate Hormone Refractory ■ CLL = Chronic Lymphocytic Leukemia
Chemotherapy patients exclude patients on hormonal therapy only

Figure 2 - Prevalence of Cancer By Age – Female
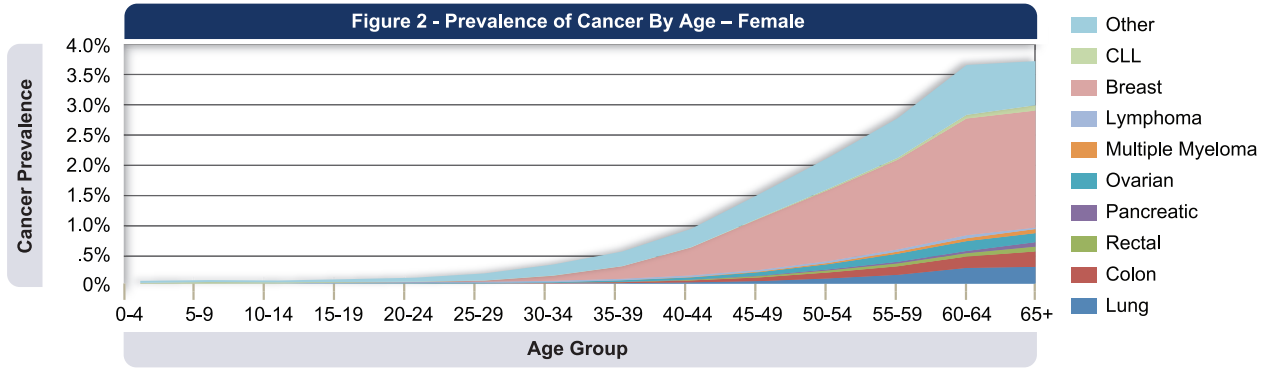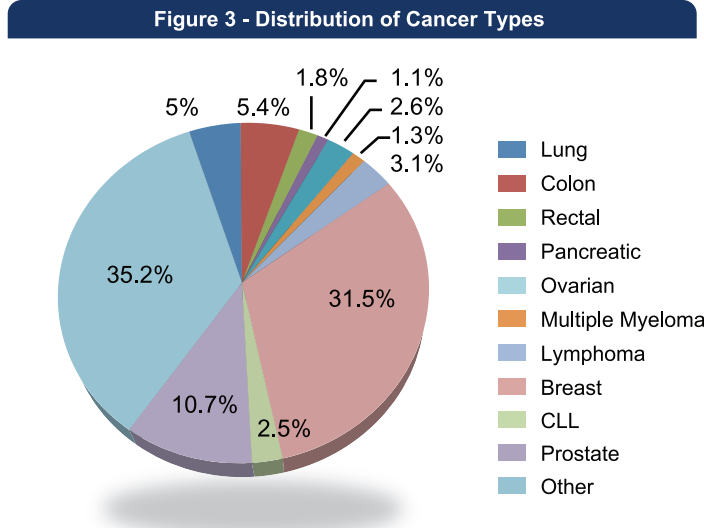

Source: Milliman Analysis of Medstat 2007
 Milliman Health Cost Guidelines 2009
 14 million commercially insured lives, 104,473 cancer patients
 ■ CLL = Chronic Lymphocytic Leukemia
 Chemotherapy patients exclude patients on hormonal therapy only

The ten cancer groupings in our analysis capture approximately 65% of all commercially insured members with cancer claims as shown in Figure 3. Breast cancer is the most prevalent of the 10 cancers. This distribution reflects a snapshot of the members in a commercially insured plan that have one or more claims coded with a cancer diagnosis. Individuals who have been diagnosed in the past with cancer but are not being actively managed for cancer (no claims coded with cancer during the analysis year) are not included in our sample.
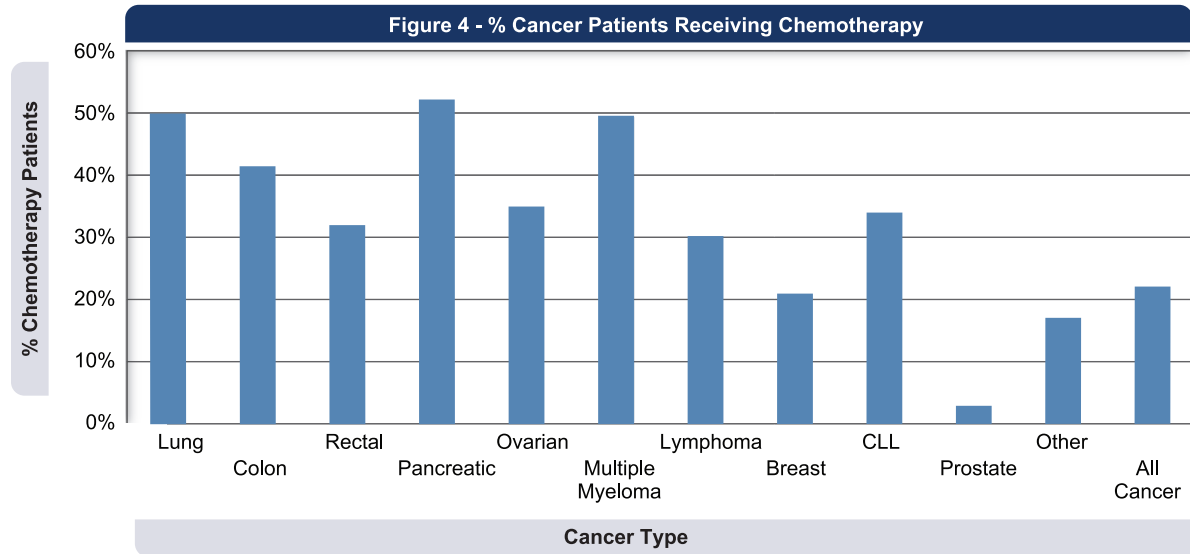
Figure 3 - Distribution of Cancer Types

Source: Milliman Analysis of Medstat 2007
 Milliman Health Cost Guidelines 2009
 14 million commercially insured lives, 104,473 cancer patients
 ■ CLL = Chronic Lymphocytic Leukemia ■ Prostate = Prostate Hormone Refractory
 Chemotherapy patients exclude patients on hormonal therapy only

Of people in a commercial population with these 10 cancer types, about 25% will receive chemotherapy in a year compared to approximately 18% of other cancer patients and 22% of all cancer patients. As shown in Figure 4, approximately 50% of lung, pancreatic and multiple myeloma patients receive chemotherapy at some point during the year. We do not include patients on hormonal therapy only, as these patients are often on long-term maintenance therapy or in remission.

Figure 4 - % Cancer Patients Receiving Chemotherapy

Source: **Milliman Analysis of Medstat 2007**
Milliman Health Cost Guidelines 2009
14 million commercially insured lives, 104,473 cancer patients
■ CLL = Chronic Lymphocytic Leukemia ■ Prostate = Prostate Hormone Refractory
Chemotherapy patients exclude patients on hormonal therapy only

Costs and Medical Utilization

On average, patients receiving chemotherapy cost about $111,000 per year. By contrast, the average annual per capita medical cost of a commercial population member is approximately $4,000. In Figure 5 we show the per patient per month (PPPM) costs for cancer patients compared to non cancer patients whose demographics have been adjusted to match that of the cancer patient population.

Figure 5 - Cost of Chemotherapy Cancer Patients compared to Non Cancer Patients

■ Cancer Patient with Chemotherapy
■ Non Cancer Patient with Chemotherapy Patient Demographics

Source: **Milliman Analysis of Medstat 2007**
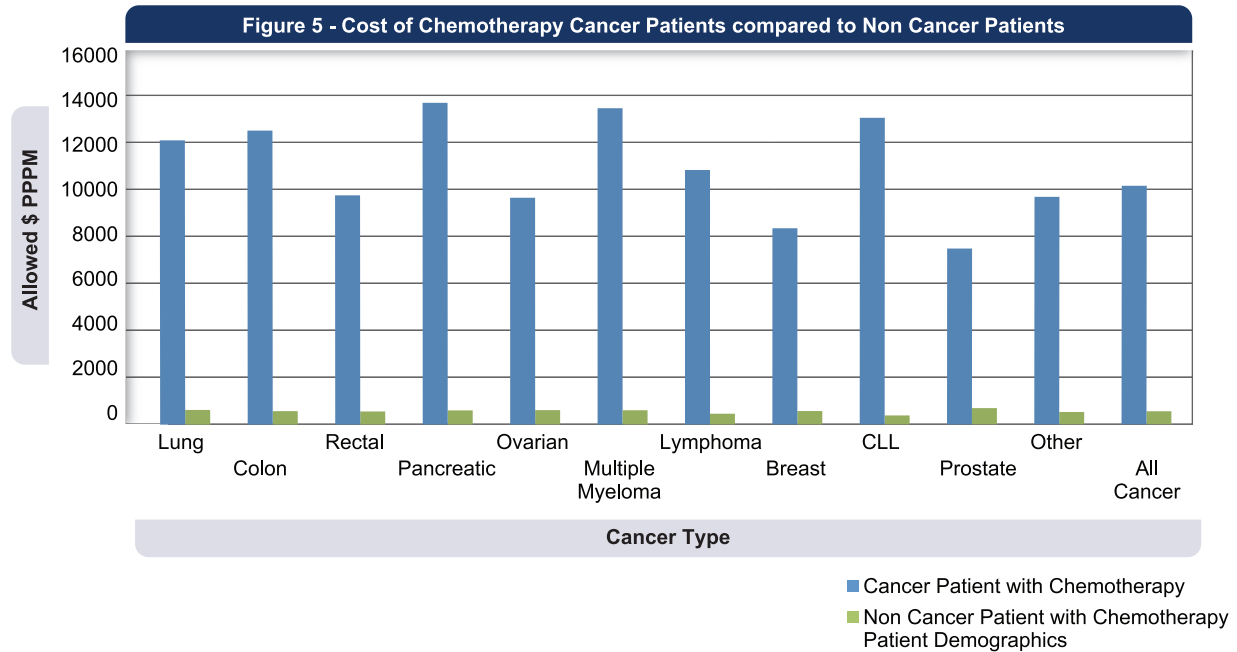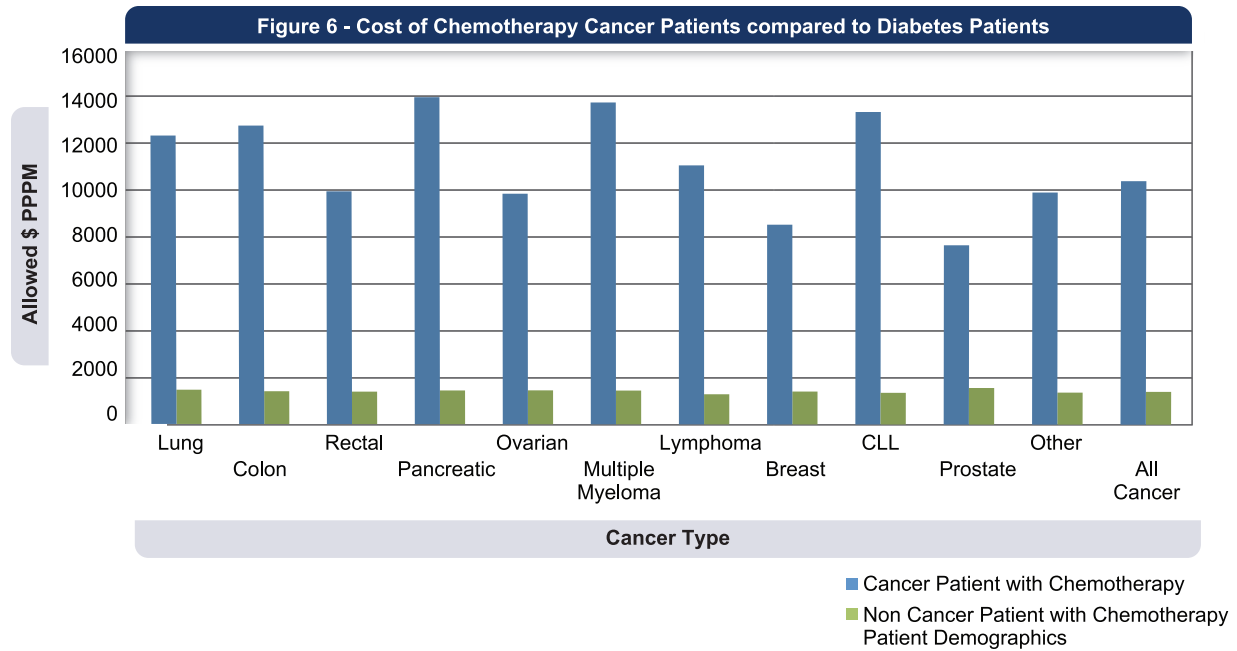**Milliman Health Cost Guidelines 2009**
14 million commercially insured lives, 104,473 cancer patients
■ CLL = Chronic Lymphocytic Leukemia ■ Prostate = Prostate Hormone Refractory
Chemotherapy patients exclude patients on hormonal therapy only
Non cancer patient demographics adjusted to demographics of the cancer patient population

Cancer patients receiving chemotherapy also dwarf the costs of commercial members with chronic disease. Figure 6 shows more than a six-fold higher cost for all cancer patients receiving chemotherapy compared to the cost of patients with diabetes whose demographics have been adjusted to the demographics of the cancer patients receiving chemotherapy.

Figure 6 - Cost of Chemotherapy Cancer Patients compared to Diabetes Patients

Legend:
- Cancer Patient with Chemotherapy
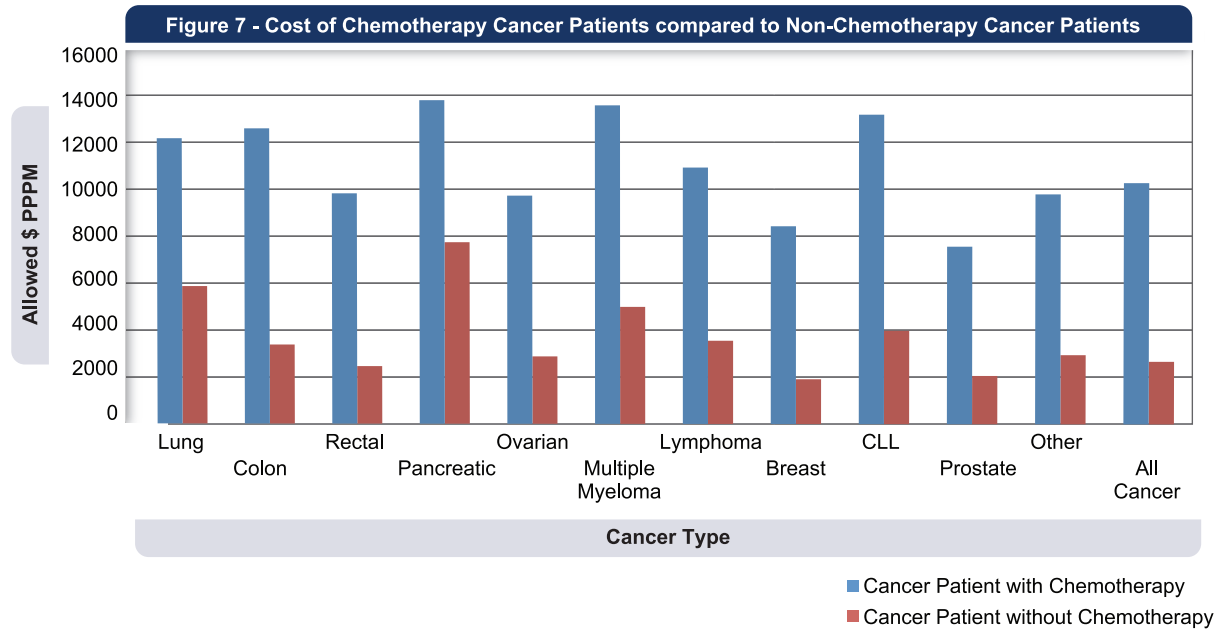- Non Cancer Patient with Chemotherapy Patient Demographics

Source: **Milliman Analysis of Medstat 2007**
Milliman Health Cost Guidelines 2009
14 million commercially insured lives, 104,473 cancer patients
■ CLL = Chronic Lymphocytic Leukemia ■ Prostate = Prostate Hormone Refractory
Chemotherapy patients exclude patients on hormonal therapy only
Diabetes patient demographics adjusted to demographics of the cancer patient population

For each cancer, Figure 7 compares the PPPM costs of patients receiving chemotherapy to those not receiving chemotherapy. On average, medical costs tend to increase with age for all people, but the much higher costs for chemotherapy patients (4 times the cost of the non-chemotherapy cancer patients) overwhelm age adjustments.

Figure 7 - Cost of Chemotherapy Cancer Patients compared to Non-Chemotherapy Cancer Patients

- Cancer Patient with Chemotherapy
- Cancer Patient without Chemotherapy

Source: **Milliman Analysis of Medstat 2007**
Milliman Health Cost Guidelines 2009
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Chemotherapy patients exclude patients on hormonal therapy only

The high cost of chemotherapy patients is driven by care received in an outpatient setting, as shown in Figure 8. Outpatient care includes all medical services other than costs incurred in an inpatient setting and prescription drug costs. Outpatient costs include chemotherapy infusion costs, chemotherapy drugs billed under the medical benefit as well as outpatient physician, lab, radiology, and ambulatory surgery.

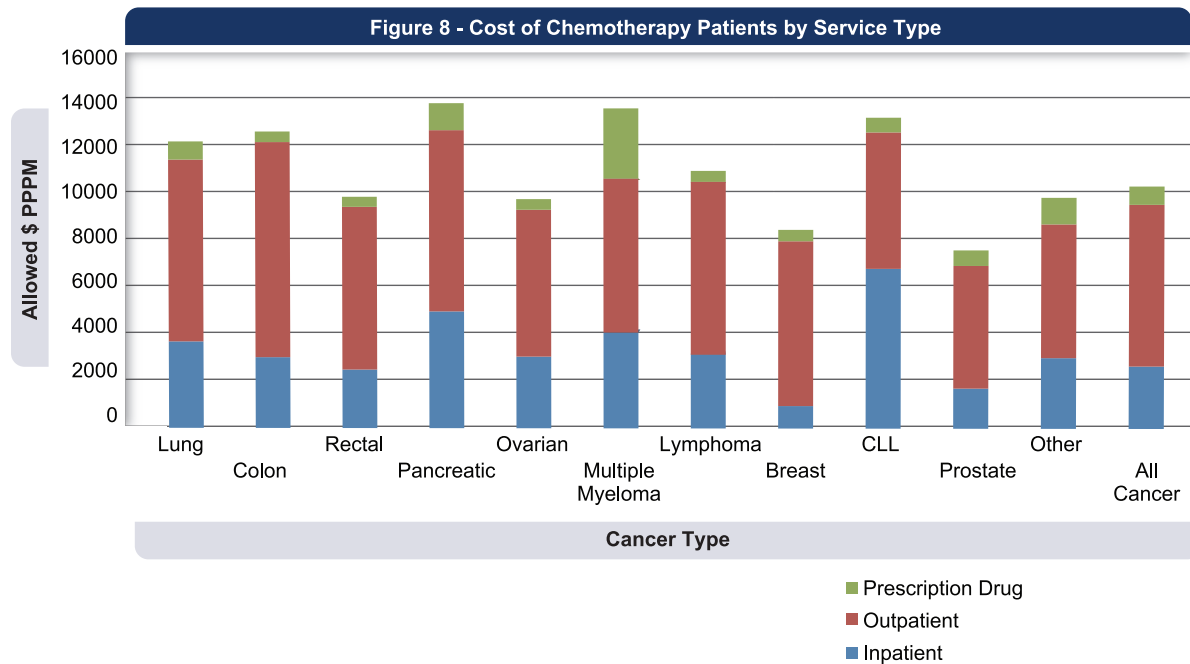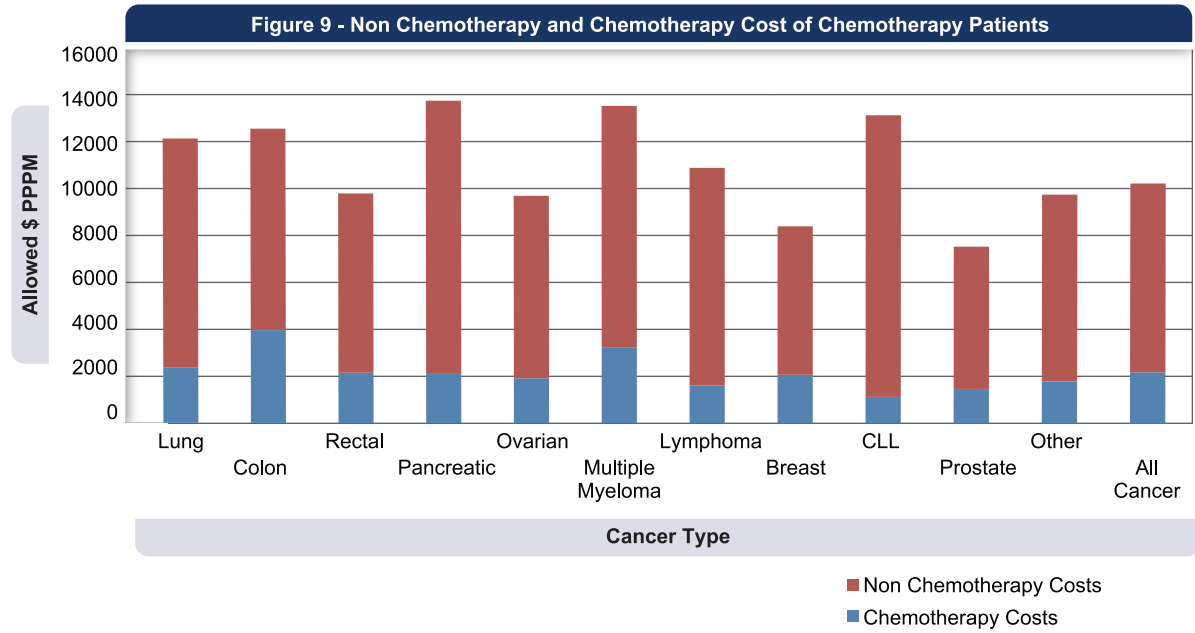Figure 8 - Cost of Chemotherapy Patients by Service Type

Source: Milliman Analysis of Medstat 2007
Milliman Health Cost Guidelines 2009
14 million commercially insured lives, 104,473 cancer patients
■ CLL = Chronic Lymphocytic Leukemia ■ Prostate = Prostate Hormone Refractory
Chemotherapy patients exclude patients on hormonal therapy only

In Figure 9, we split total cost for cancer patients receiving chemotherapy into chemotherapy and non-chemotherapy costs. Chemotherapy costs account for 25% of total costs or approximately $2,200 PPPM. We do not include the costs associated with infused chemotherapy administration as part of the 25%.

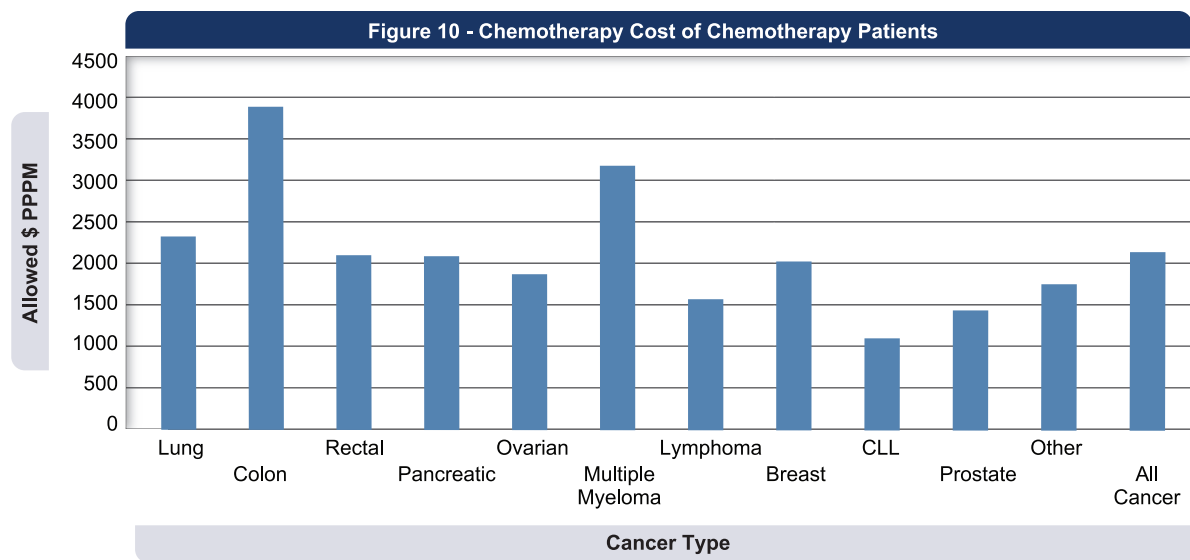Figure 9 - Non Chemotherapy and Chemotherapy Cost of Chemotherapy Patients

Source: Milliman Analysis of Medstat 2007
Milliman Health Cost Guidelines 2009
14 million commercially insured lives, 104,473 cancer patients
■ CLL = Chronic Lymphocytic Leukemia ■ Prostate = Prostate Hormone Refractory
Chemotherapy patients exclude patients on hormonal therapy only

OPPORTUNITIES FOR COST AND QUALITY IMPROVEMENT

Several cost drivers for cancer patients receiving chemotherapy have the potential for better management, including:

- Cost of chemotherapy drugs;

- Utilization of chemotherapy-related admissions;

- Utilization of chemotherapy-related emergency room visits; and

- End-of-life care including hospice enrollment, dying in an acute care setting and receiving chemotherapy within a few weeks of dying.

For our 10 cancer category study cohort, we analyzed these metrics. The cost of chemotherapy drugs across all cancer patients averages approximately $20,000 annually for cancer patients receiving chemotherapy, but the cost varies by disease state -- ranging from approximately $4,000 PPPM for colon cancer to $1,100 PPPM for chronic lymphocytic leukemia as shown in Figure 10. The cost is dependent on the selection of drug therapies, the number of lines of therapy and the duration of each round of therapy. For example, the PPPM cost of chemotherapy for colon cancer is approximately twice that of chemotherapy for breast cancer.

Figure 10 - Chemotherapy Cost of Chemotherapy Patients

Source: **Milliman Analysis of Medstat 2007**
Milliman Health Cost Guidelines 2009
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Chemotherapy patients exclude patients on hormonal therapy only

We identified the admission rates for the 10 cancer groupings and identified the subset of admissions we refer to as chemotherapy-related conditions that are known to be side effects of chemotherapy. Appendix B describes our methodology. Figure 11 shows cancer patients receiving chemotherapy utilize approximately 1 inpatient admission per person per year and approximately 40% of these are considered chemotherapy-related.

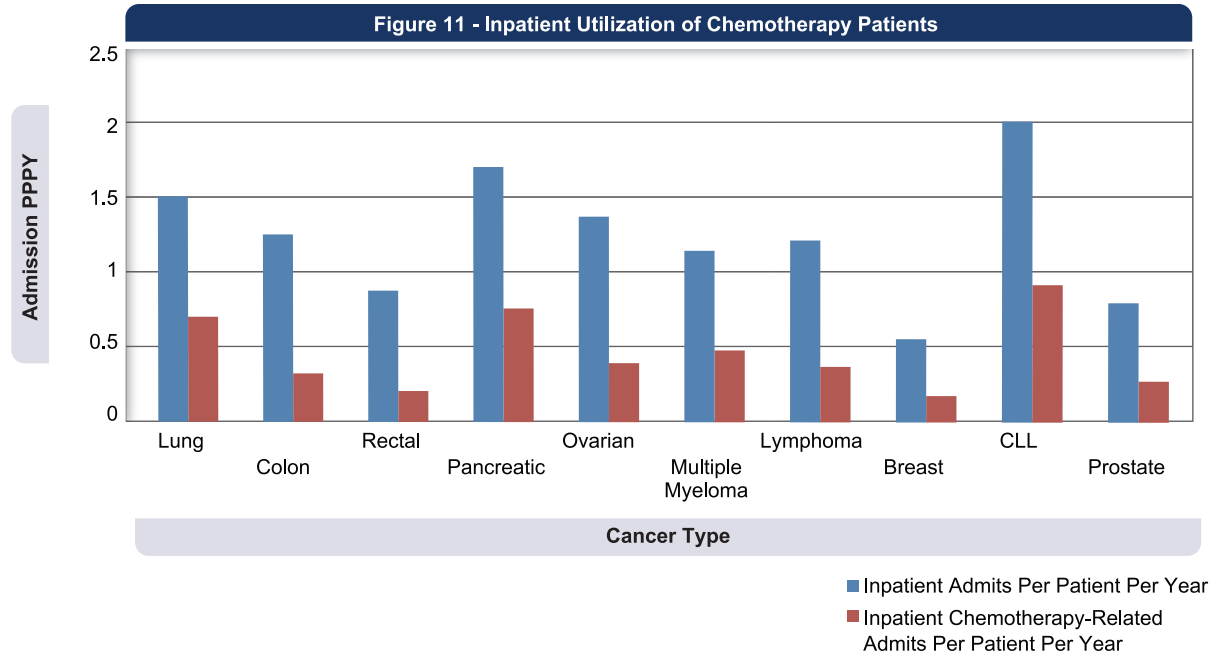**Figure 11 - Inpatient Utilization of Chemotherapy Patients**

Source: Milliman Analysis of Medstat 2007
Milliman Health Cost Guidelines 2009
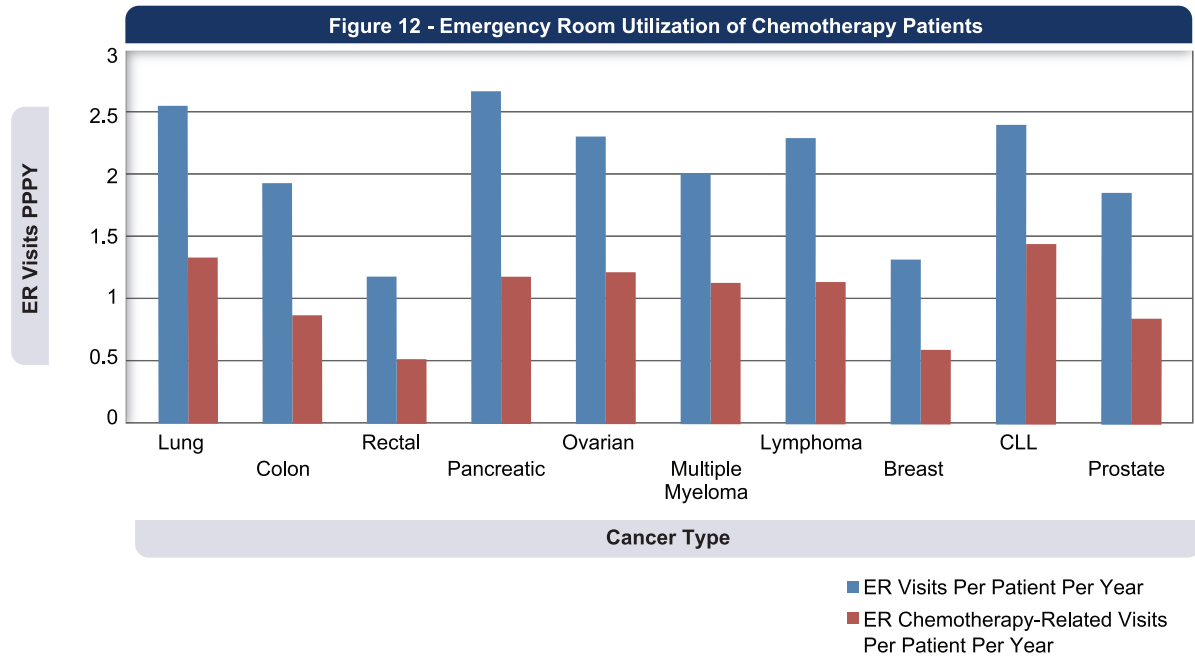14 million commercially insured lives, 104,473 cancer patients
■ CLL = Chronic Lymphocytic Leukemia ■ Prostate = Prostate Hormone Refractory
Chemotherapy patients exclude patients on hormonal therapy only

We analyzed ER utilization for our 10 cancer cohorts and found chemotherapy patients have approximately 2 visits per person per year and close to half of those are chemotherapy-related (Figure 12).

Figure 12 - Emergency Room Utilization of Chemotherapy Patients

Source: Milliman Analysis of Medstat 2007
Milliman Health Cost Guidelines 2009
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■ CLL = Chronic Lymphocytic Leukemia ■ Prostate = Prostate Hormone Refractory
Chemotherapy patients exclude patients on hormonal therapy only

On average, 3.5% of cancer patients receiving chemotherapy in a year die in an inpatient setting in that year. The portion of chemotherapy patients who die as inpatients is higher for the cancers with higher mortality. Figure 13 shows that over 8% of lung cancer and pancreatic cancer patients die in an inpatient acute care setting, which may be considered a quality issue for terminally ill patients who have hospice as an option.

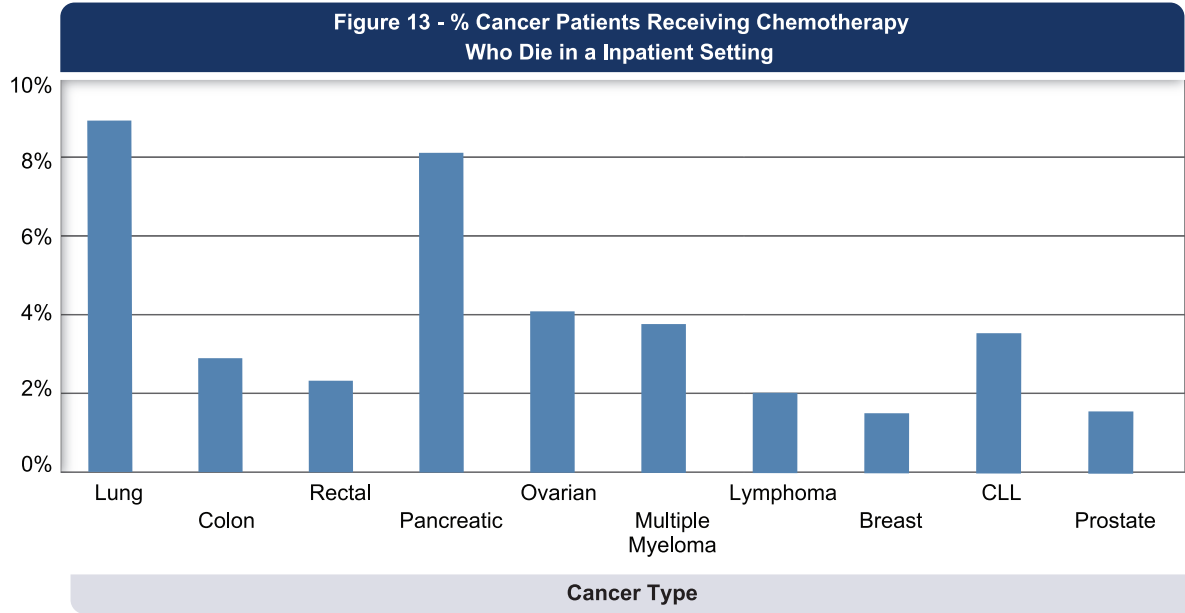Figure 13 - % Cancer Patients Receiving Chemotherapy Who Die in a Inpatient Setting

Source: Milliman Analysis of Medstat 2007
Milliman Health Cost Guidelines 2009
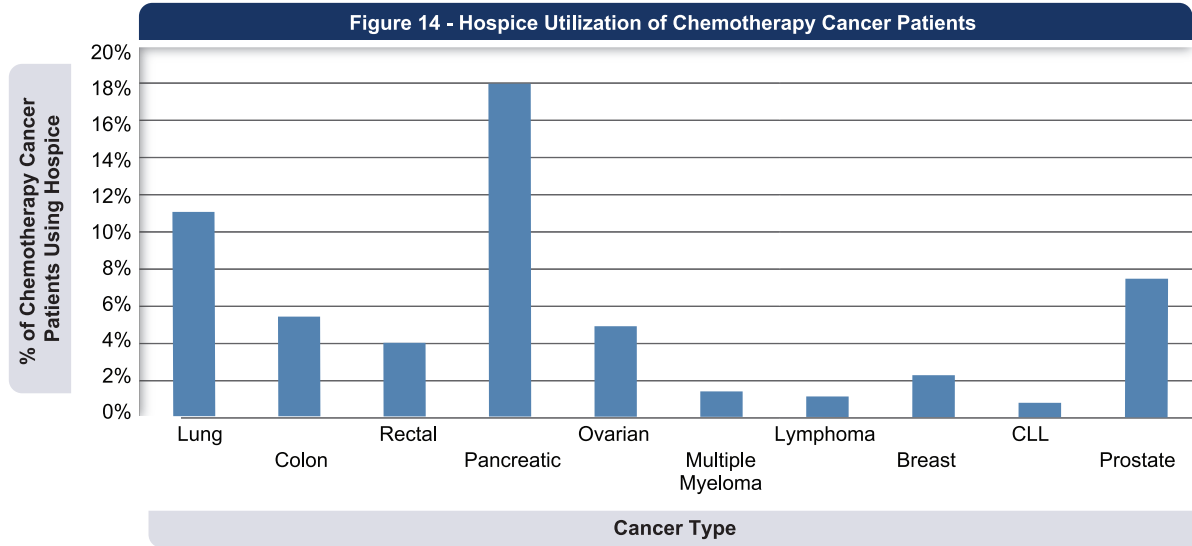14 million commercially insured lives, 104,473 cancer patients
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Approximately 5% of chemotherapy patients receive hospice care during the same year. Not surprisingly, the frequency of seeking hospice care is generally higher for cancers with very high mortality and short post-diagnosis survival, such as lung and pancreatic cancer. Hormone refractory prostate cancer, with post-diagnosis survival of less than 3 years, also has high hospice use. The low survival rate of some of these cancers suggests an opportunity for more access to hospice services.

Figure 14 - Hospice Utilization of Chemotherapy Cancer Patients

Source: **Milliman Analysis of Medstat 2007**
Milliman Health Cost Guidelines 2009
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■ CLL = Chronic Lymphocytic Leukemia ■ Prostate = Prostate Hormone Refractory
Chemotherapy patients exclude patients on hormonal therapy only

A quality and cost concern is whether patients receiving end-of-life care are receiving appropriate chemotherapy. While some chemotherapy is palliative, our data analysis raises the question of whether too many patients are receiving chemotherapy shortly before death. In commercial databases, it is difficult to distinguish between a member who dies and one who leaves the health plan for other reasons. This limits our ability to analyze mortality rates and other important statistics associated with death. However, it is possible to identify an individual who dies in hospital because the recorded discharge status is death. Our analysis showed that 3.5% of all cancer patients receiving chemotherapy died in the hospital. Table 3 shows the portion of these chemotherapy patients who die within 14 and 30 days of receiving chemotherapy. We have not analyzed these events in detail to determine whether these admissions were for cancer or that the chemotherapy provided shortly before death was inappropriate. However, this data does suggest an opportunity for further scrutiny and care improvement.

Table 3. Chemotherapy Utilization Near the Time of Death

	Cancer Patients Who Died in Hospital and Received Chemotherapy within 14 Days of Death	Cancer Patients Who Died in Hospital and Received Chemotherapy within 30 Days of Death
Proportion	24%	51%
Total Allowed Cost per Patient During last 14 Days	$25,960	N/A
Total Allowed Cost per Patient During Last 30 Days	N/A	$42,731
Average Allowed Cost of Last Inpatient Stay	$15,022	$22,010

Data based on the 3.5% of Cancer Patients Receiving Chemotherapy who Died in the Hospital
Source: Milliman Analysis of Medstat 2007

Geographic Variation in Cost and Utilization Related to Chemotherapy Cost Drivers

Geographic variation in medical utilization, such as inpatient length of stay and admission rates, is well established, and it is not surprising to find similar variation in utilization associated with chemotherapy side effects. Much geographic variation in medical utilization is explained by differences in medical practice and decision-making by physicians, and the lower utilizing areas do not show worse quality outcomes. Lower utilizing areas are held as models of superior efficiency.18

We performed a geographic variation analysis for 3 cost drivers and identified significant variation for each cost driver as shown in Table 4.

Table 4. Variation in Chemotherapy-Related Metrics for Patients in the 10 Cancer Groupings Receiving Chemotherapy

	Chemotherapy-Related Inpatient Hospital Admits/1000	Chemotherapy-Related Emergency Room Visits/1000	Average Chemotherapy Drug Costs per Chemotherapy Patient
National Average	378 (average cost per admit $22,000)	929 (average cost per ER visit $800)	$22,353
High Utilizing Region	484	1626	$27,494
Low Utilizing Region	223	465	$17,212

The above table shows the variations in per-capita utilization, where the regions were defined by 2-digit zip codes. The figures shown above should not be interpreted as the highest or lowest nationally, as the data was limited to 20 geographic regions (out of a possible 100 2-digit zip regions) that generated significant chemotherapy patient volumes. Furthermore, the above numbers were not adjusted to account for different mixes of cancers or demographics. The same region does not produce all the high or all the low figures. Nevertheless, these figures suggest, as with other regional variation analyses, the potential to reduce chemotherapy-related costs in many regions of the country.

Reducing Variation: Using Pathways in Cancer Treatment

Many studies have shown that adherence with evidence-based pathways is associated with improved outcomes and reduced cost. Several organizations have developed pathways for treating cancer, including Innovent Oncology, who commissioned this paper.

Pathways for treating cancer generally specify details of surgery, radiation therapy and chemotherapy treatment based on the particular kind of cancer and its stage. Additional factors in the pathway may include the patient response (including side effects), laboratory values, and history of treatment and response. Often, chemotherapy recommendations vary by the "line" of therapy. A patient whose cancer does not respond or progresses after "first line" agents may then be treated with "second line" agents.

Determining the clinical value of pathways must start with validating that they are based on high quality evidence, and there are established methodologies for grading such evidence.

Two retrospective approaches are generally used to assess the potential economic value of pathways:

- Detailed chart audits. A set of patient charts is examined and their treatments are compared to the treatments specified in the pathway. A determination is made about the On/Off pathway status for each patient. Patients are split into On and Off pathway cohorts, risk adjusted or otherwise matched, and their costs and outcomes tabulated. This approach may be retrospective or prospective.

- Claims data. Patients meeting certain disease or treatment criteria are identified in medical claims data using some combination of diagnosis, procedure codes, drug codes, demographic information and dates. The patients are then evaluated using algorithms that make an On/Off pathway determination based on criteria converted into a set of computer program logic statements. The patients are stratified by risk and other characteristics and their costs and outcomes tabulated. This approach is almost always retrospective.

Each method has its weaknesses and strengths. The chart audit method captures cancer stage and the clinical status of the patient in ways that are impossible for claims data. For some cancers, On/Off pathway determinations are impossible with claims data because it is difficult or impossible to determine cancer stage or line of therapy. Claims data can be a more complete record of all the care a patient receives, especially if the patient obtains services from several providers who may not be coordinating or even aware of each other. Claims data can generate many more cases and much larger sample sizes, because large claims databases have longitudinal records of tens of millions of individuals.

Claims data can be used to measure the impact of cancer treatment care on several quality and cost metrics including:

- The cost of chemotherapy drugs

- Side effects of chemotherapy which can lead to inpatient and emergency room admissions

- Avoiding death in hospital and promoting hospice for appropriate patients

Targets for chemotherapy-related inpatient admissions and ER visits rates will remain relatively stable from year to year unless the toxicity of chemotherapy in subsequent years is dramatically reduced (or increased). Targets for chemotherapy use within 4 weeks of death as well as hospice utilization should also remain relatively stable from year to year. Of course, a particular population's comparison to established benchmarks will need to consider adjustment for demographics and cancer distribution mix.

On the other hand, setting targets for chemotherapy costs is more challenging as chemotherapy costs can fluctuate dramatically from year to year when new chemotherapy agents are introduced. Our Medstat analysis of trends in chemotherapy costs from 2003-2007 produced annual trends varying from 8% to 19%. Because of this variation, alternative methodologies are needed to set expected targets for chemotherapy costs each year. Nonetheless, chemotherapy cost reductions offer the largest potential for cost reduction.

Modeling Cost Reduction Opportunity

As described earlier, chemotherapy patients are expensive and have a high frequency of chemotherapy-related inpatient admissions and chemotherapy-related emergency room admissions. We have provided evidence of geographic variation for these utilization metrics and for chemotherapy costs. Table 5 provides average utilization and costs for a typical commercial population during a one-year period which we use to model a potential for cost reduction.

Table 5. Annual Cost and Utilization Metrics for Cancer Patients Receiving Chemotherapy

Cost of Chemotherapy Drugs per Patient	$20,000
Inpatient Admits per Patient	1.0
Inpatient Chemotherapy-Related Admits per Patient	0.38
ER Visits per Patient	1.9
ER Chemotherapy-Related Admits per Patient	0.93
% Chemotherapy Cancer Patients With Hospice Claims	5%
% Chemotherapy Cancer Patients Dying in Hospital	3.5%

In Table 6, we show the potential cost reduction for a typical chemotherapy patient with one of the ten common cancers that are the subject of this paper. We have assumed a 10% reduction in national average rates of chemotherapy-related admissions and emergency room visits, and a 10% reduction in chemotherapy costs. The 10% is less than the regional variation we observed for each of these three categories. The total cost reduction per patient is about $2,900. This is about 2.6% of the total annual cost for these patients.

Table 6. Potential to Reduce Per Patient Costs

Type of cost	Chemotherapy-Related Inpatient Admissions	Chemotherapy-Related Emergency Room Visits	Chemotherapy Drug Costs
Cost per Event	$22,000	$800	$20,000
Frequency of Event Among Chemotherapy Cancer Patients	38%	93%	100%
Modeled Reduction in Use or Cost	10%	10%	10%
Cost Reduction	$836	$74	$2,000

Total Reduction in Cost per Patient	$2,910
Chemotherapy Patients Approximate Annual Cost	$111,000
As a Percent of Total Cost	2.6%

Source: **Milliman Analysis of Medstat 2007**
Milliman Health Cost Guidelines 2009
14 million commercially insured lives, 104,473 cancer patients
Chemotherapy patients exclude patients on hormonal therapy only

The variation in cost and utilization of medical services for cancer patients receiving chemotherapy that we identified suggests significant opportunity for commercial payers and employers. The quality and cost concerns raised by unexplained regional variation in medical service utilization is well established although not for cancer patients receiving chemotherapy. We hope our analysis sheds light on this opportunity and raises the awareness of the role clinical treatment guidelines can play in reducing unexplained variation.

APPENDIX A: DESCRIPTION OF KEY DATA SOURCES AND THEIR APPLICATION

Medstat claims data. This dataset contains all paid claims generated by approximately 28 million commercially insured lives. The Medstat database represents the inpatient and outpatient healthcare service use of individuals nationwide who are covered by the benefit plans of large employers, health plans, government and public organizations. The MarketScan database links paid claims and encounter data to detailed patient information across sites and types of providers, and over time. The annual medical database includes private sector health data from approximately 100 payers. This data represents the medical experience of insured employees and their dependents for active employees, early retirees, COBRA continuees and Medicare-eligible retirees with employer-provided Medicare Supplemental plans. No Medicaid or Workers Compensation data is included.

Member identification codes are consistent from year-to-year and allow for multi-year longitudinal studies. Information includes diagnosis codes, procedure codes and DRG codes, NDC codes along with site of service information, and the amounts paid by commercial insurers. For this study, we used MedStat 2007.

Milliman's 2009 Health Cost Guidelines. The Guidelines provide a flexible but consistent basis for the determination of health claim costs and premium rates for a wide variety of health plans. The Guidelines are developed as a result of Milliman's continuing research on healthcare costs. First developed in 1954, the Guidelines have been updated and expanded annually since that time. The Guidelines are continually monitored as they are used in measuring the experience or evaluating the rates of health plans, and as they are compared to other data sources. The Standard Demographics in the Guidelines were developed to be representative of the age and sex distribution for a typical large insured group. The Standard Demographics were developed using data from large insurers combined with Department of Labor Sources. We use the Guidelines to demographically adjust our target population to a typical working age population.

Milliman Medical Index (MMI). The MMI examines key components of medical spending and the changes in these components over time. The MMI incorporates proprietary Milliman studies to determine representative provider-reimbursement levels over time, as well as other reliable sources, including the Kaiser Family Foundation/Health Research and Educational Trust 2008, Annual Employer Health Benefit Survey (Kaiser/HRET), to assess changes in health plan benefit levels by year. The MMI includes the cost of services paid under an employer health-benefit program, as well as costs paid by employees in the form of deductibles, coinsurance, and copayments. The MMI represents the total cost of payments to healthcare providers, the most significant component of health insurance program costs, and excludes the non-medical administrative component of health plan premiums. The MMI includes detail by provider type (e.g., hospitals, physicians, and pharmacies), for utilization, negotiated charges, and per capita costs, as well as how much of these costs are absorbed by employees in the form of cost sharing. We used the annual MMI cost trends to trend the MedStat cost data to 2009 dollars.

APPENDIX B: METHODOLOGY FOR CLAIM ANALYSIS

Identification Methodology

We used Medstat 2007 for this analysis. From the Medstat starting population of approximately 28 million lives, we selected the members with drug coverage, eliminated members in HMOs or capitated PPOs, and included members whose primary beneficiary had full time or other/unknown status, with age <70. Our analysis contained about 14 million lives as a starting population.

We considered a patient to have cancer if they had one inpatient or emergency room claim or two physician E&M claims on separate days with the following codes in any position of the claim:

140.xx through 172.xx	174.xx through 208.9x

We identified approximately 105,000 individuals using this method.

We selected a subset with the 10+ cancer types in the table below, which produced a cohort of approximately 70,000 individuals. Again, we used the criteria of one inpatient or emergency room claim or two physician E&M claims on separate days with the cancer ICD9 in any position of the claim.

For individuals coded with more than one cancer, we used the order of the listing below to establish a hierarchy and assign individuals to the cancer highest in the list.

Cancer Type	ICD9 Code
Non small and small cell lung cancer	162.XX
Colon	153.XX
Rectal	154.XX
Pancreatic	157.XX
Ovarian	183.XX
Multiple myeloma	203.0X
Hodgkins, nonhodgkins, diffuse large B cell lymphoma, mantle cell	201.XX, 200.3X, 200.4X, 200.6X, 200.7X, 202.0X
Breast	174.XX, 175.XX
Chronic lymphocytic leukemia	204.0X, 204.1X, 204.2X
Prostate	185.XX

Physician E&M codes	99201-99205, 99211-99215, 99217-99220, 99241-99245, 99304-99337, 99341-99350, 99381-99387, 99341-99350, 99381-99387, 99391-99397, 99401-99404, 99411, 99412, 99420, 99429, 99455, 99456, 99499

We identified individuals receiving chemotherapy if they had one or more claim with a chemotherapy J code or NDC code (list provided upon request). We did not include individuals who were on hormone therapy only but did include those with claims for hormones along with non-hormone chemotherapy claims.

Costs

We report allowed costs trended to 2009 using our Milliman Medical Index. In this report, chemotherapy costs are for the drug component and do not include costs associated with chemotherapy administration for infused products.

Several studies report costs associated with infused chemotherapy, although the reported costs vary. A study of the costs of IV administration in a metastatic breast cancer population identified chemotherapy per visit costs of $2,477, with IV administration accounting for approximately 10% ($252); the study drug accounting for 59% ($1,463); and other drugs and services accounting for 31% ($763).[19] Another study of chemotherapy cost for small cell lung cancer patients reported a cost per chemotherapy visit of $787, with 50% of the cost for the IV chemotherapy drug ($395); 12% of the cost for IV chemotherapy administration procedures ($93); and 38% for other visit related drugs and services ($300).[20]

Chemotherapy-Related Inpatient Admissions and ER Visits

We identified admissions as chemotherapy-related if they had either:

1. A primary diagnosis with one of the chemotherapy-related ICD9 codes

2. A secondary diagnosis with one of the chemotherapy-related ICD9 codes and a primary diagnosis of cancer but not a surgical admission

The list of chemotherapy-related ICD9 codes was created from combining a search of the literature, an analysis of the primary diagnoses for inpatient admissions incurred by our cohort of cancer patients receiving chemotherapy, and clinical judgment.

The list of chemotherapy-related ICD9 codes is available upon request.

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