Measures of Treatment Workload for Patients With Breast Cancer

Alex C. Cheng, PhD¹ and Mia A. Levy, MD, PhD¹

PURPOSE Patients with breast cancer spend a large amount of time and effort receiving treatment. When the number of health care tasks exceeds a patient's ability to manage that workload, they could become overburdened, leading to decreased plan adherence. We used electronic health record data to retrospectively assess dimensions of treatment workload related to outpatient encounters, commuting, and admissions.

METHODS Using tumor registry and scheduling data, we evaluated the sensitivity of treatment workload measures to detect expected differences in breast cancer treatment burden by stage. We evaluated the impact of the on-body pegfilgrastim injector on the treatment workload of patients undergoing a specific chemotherapy protocol.

RESULTS As hypothesized, patients with higher stage cancer experienced higher treatment workload. Over the first 18 months after diagnosis, patients with stage III disease spent a median of 81 hours (interquartile range [IQR], 39 to 113 hours) in outpatient clinics, commuted 61 hours (IQR, 32 to 86 hours), and spent \$1,432 (IQR, \$690 to \$2,552) in commuting costs. In contrast, patients with stage I disease spent a median of 29 hours (IQR, 18 to 46 hours in clinic), commuted for 34 hours (IQR, 19 to 55 hours), and spent \$834 (IQR, \$389 to \$1,649) in commuting costs. In addition, we substantiated claims that the pegfilgrastim on-body injector was effective in reducing some dimensions of workload such as unique appointment days.

CONCLUSION Treatment workload measures capture an important dimension in the experience of patients with cancer. Patients and health care organizations can use workload measures to plan and allocate resources, leading to higher quality and better coordinated care.

Clin Cancer Inform. © 2019 by American Society of Clinical Oncology

INTRODUCTION

Patients who have chronic disease experience significant disruption to their lives. These disruptions can come from symptoms of their disease as well as the burden of treatment.¹ Treatment burden is the personal workload of health care and its impact on patient functioning and well-being.^{2,3} Patients who are overburdened with health care tasks have a higher likelihood of nonadherence with treatment plans.⁴ Although previous measures for treatment burden use patient-reported data to assess treatment burden,^{2,5} we believe there is an opportunity to capture one aspect of treatment burden, treatment workload, from electronic health record (EHR) data. Metrics derived from the EHR could allow health care organizations to determine the effort patients put into receiving care over the course of their treatment on a large scale. These quantitative metrics present opportunities to evaluate the impact of new treatments and health care delivery systems on patient treatment workload and to develop interventions to help better

balance workload and patient capacity to manage care. Capacity is a patient's ability to manage treatment burden.⁶ Elements of capacity such as resilience, home environment, and financial well-being allow patients to take on more treatment without being overburdened.⁷ Although this study focuses on treatment workload, the balance between workload and capacity should be considered when providing guidance to patients with cancer.

Outcome measures in cancer capture the effectiveness of treatments to combat illness. Cancer treatment affects patients' lives in complex ways, and no single measure can describe all dimensions of how a patient is affected. Appendix Table A1 lists some commonly used measures in the categories of disease response, host response, treatment burden, and caregiver burden.^{5,8-15} Although each of these measure types may affect others, they are distinct in the aspect of patient life that they describe. For example, a chemotherapy regimen may have a profound effect on tumor size (disease response) but may result in severe adverse

ASSOCIATED CONTENT

Appendix

Author affiliations and support information (if applicable) appear at the end of this article.

Accepted on December 5, 2018 and published at ascopubs.org/journal/cci on February 4, 2019; DOI <https://doi.org/10.1200/CCI.18.00122>

CONTEXT

Key objective: Use electronic health record data to measure workload related to outpatient encounters, commuting, and admissions for patients with breast cancer at a single institution.

Knowledge generated: We confirmed the hypothesis that patients with more advanced disease experienced higher treatment workload. We also substantiated claims that a medication delivery device was effective in reducing some dimensions of workload such as unique appointment days.

Relevance: When patients are prescribed treatment that exceeds their ability to manage care, they are likely to become overburdened. Overburden in cancer treatment could lead to decreased adherence and worse outcomes. Workload measures such as total time in appointments and financial cost of commuting for treatment should be considered alongside existing outcome measures for disease and host response. These measures can be assessed from electronic health record data for patients with breast cancer. Workload measures can be used to inform operational guidelines that mitigate wasted effort for patients. In addition, workload measures and assessments of patient capacity to manage care could lead to clinical decision support for patients who are likely to be overburdened by treatment.

reactions (host response), time missed from work (treatment burden), and stress on family members (caregiver burden). Although disease response and host response measures are commonly measured in the evaluation of new cancer therapies, treatment burden is typically not assessed. We propose that treatment burden measures should be considered alongside existing clinical metrics for cancer care outcomes.

Previous literature has identified dimensions of treatment burden through patient surveys. An online survey of 1,345 patients worldwide showed that patients felt burdened by health care tasks such as frequent tests and doctors' visits.¹⁶ Two other studies developed survey instruments to quantitatively assess treatment burden in patients with chronic conditions.^{2,5} Through the validation of these surveys, both identified medical appointments and coordination of health care tasks as significant contributors to overall feelings of burden.¹⁷ These assessments rely on patient surveys, which can be costly and time consuming to collect. Automated approaches to measuring treatment workload from claims or EHR data could decrease the costs of collecting these outcomes and enable their incorporation into patient care. Although treatment workload measures derived from the EHR are not able to assess felt burden by patients the way a survey can, these measures could provide insight into how treatment interferes with patient lives.

The methods used in this study extend work that used the SEER-Medicare linked database to characterize treatment workload in cancer.¹⁸ Claims data from SEER-Medicare are effective in identifying the number of encounter days for the Medicare population.¹⁹ However, estimating time spent receiving care requires more detailed data from encounter records in the EHR. Information about hours spent in procedures or waiting between appointments can help patients anticipate the amount of disruption to their lives caused by treatment.

Patients could benefit from quantitative measures of treatment workload by allowing them to plan around life disruptions that are a result of their illness. For example, patients with cancer undergo lengthy treatments that result in disruptions to their work schedules and family responsibilities.²⁰ There are many choices that patients and providers have to make on the basis of the patient's disease and goals.²¹ Treatment workload measures would allow care teams to make better informed decisions about treatment plans that match the patient's needs and goals.

Researchers could use treatment workload measures to compare two or more treatment protocols for their impact on patient work. Advertisements for medical services and medications often tout workload-reducing potential by using phrases such as "saving you a trip to the doctor" or needing just "one pill a day." These claims are not typically substantiated with quantitative assessments of patient experience. With an increasing number of curable cancers, providers need to balance the benefit of aggressive treatments with the impact on patients' short-term well-being.

In this study, we derive several simple treatment workload measures from the EHR on the basis of factors that contribute significantly to treatment workload in previous studies. We evaluate these measures on a population of patients with breast cancer at a National Cancer Institute designated comprehensive cancer center, the Vanderbilt-Ingram Cancer Center at Vanderbilt University Medical Center (VUMC; Nashville, TN). In addition, we use these treatment workload measures to assess the effectiveness of a new treatment option in reducing workload for patients with breast cancer undergoing chemotherapy.

METHODS

Using EHR data, we developed measures for treatment workload for clinical encounters and commuting. We then applied these methods to two populations of patients with breast cancer to determine whether the measures were

sensitive to differences in disease stage and treatment protocols. The Vanderbilt Institutional Review Board approved the collection, analysis, and presentation of data for this study (Institutional Review Board No. 151003).

Inpatient and Outpatient Clinical Encounters

Treatment workload as a result of clinical encounters occurs with any event where the patient comes in contact with the health care system, including outpatient appointments, medical procedures, and inpatient hospital admissions. In a previous study,²² we developed a method to measure treatment workload from clinical encounters. We applied this method to calculate the time patients with breast cancer must devote to encounters at VUMC, including those encounters not related to the management of their cancer. Figure 1 shows an example of outpatient encounter data from a single patient including appointment start times and allocated appointment durations from which estimated appointment durations can be derived. Wait times are estimated as the time between appointments, and the total time in clinic is estimated as the time from the start of the first appointment to the end of the last appointment of the day. Other outpatient encounter-related measures include the number of appointments, unique appointment days, and hours in appointments. Inpatient encounters from admission-discharge-transfer data allow for calculation of the number of emergency department visits, hospital admissions, and total length of hospital stay.

Commuting

To estimate patients' commute time from their homes to the locations of their clinic appointments, we again applied a method developed in a previous study.²³ We assumed that patients did not move over the course of their treatment and that driving was the primary mode of transportation.

The financial cost of commuting was estimated by multiplying the distance traveled by the Internal Revenue Service mileage rate of 54 cents per mile in 2016.²⁴ This rate is meant to capture the cost of fuel and vehicle wear for an average passenger vehicle in the United States.

Patient Populations

Stage 0 to IV cohort. We evaluated our treatment workload measures on two populations of patients with breast cancer. In our first population, we sought to determine whether treatment workload measures were sensitive to expected differences in patients with difference stages of breast cancer. On the basis of an initial analysis of treatment workflows, most patients with early-stage breast cancer received the majority of treatment in the first 18 months after diagnosis. We collected 18 months of data from the date of diagnosis for patients with stage 0 to IV breast cancer who were part of the VUMC Tumor Registry with a date of diagnosis from January 2005 to June 2014. The VUMC Tumor Registry is a hospital-based registry that reports cancer diagnosis, staging, treatment, and outcome data to the Tennessee Cancer Registry and the SEER Program at the National Cancer Institute.^{25,26} We excluded patients with home addresses outside of 150 miles from VUMC because we assumed that it would be unreasonable for them to commute to VUMC from home for each appointment. In addition, we excluded patients with fewer than five outpatient appointments, because our initial analysis showed that most of these patients were only diagnosed at VUMC or received only one mode of treatment (such as surgery) at VUMC. Including these patients who are most likely receiving care elsewhere would not accurately depict the workload that most patients with breast cancer experience.

FIG 1. Summary of outpatient encounter burden measures for an example patient. Over the course of 2 weeks, this patient had 10 appointments lasting a total of 8.75 hours. She waited for 2.25 hours between appointments and was in clinic for 11 hours. She had to travel to the clinic for appointments on 6 unique days, and her commuting took a total of 6 hours. Med Onc, medical oncology.

TABLE 1. Treatment Burden Measures for Patients With Breast Cancer From the Vanderbilt Tumor Registry by Stage Over 18 Months After Diagnosis
Median (IQR)*

Measure	Stage 0 (n = 260)	Stage I (n = 672)	Stage II (n = 495)	Stage III (n = 180)	Stage IV (n = 80)
Outpatient encounters					
No. of appointments	28 (17-41)	38 (23-61)	62 (33-91)	77 (48-119)	75 (39-110)
No. of unique appointment days	20 (11-32)	25 (13-39)	33 (20-52)	41 (24-75)	33 (15-47)
Appointment time, hours	12 (7.2-17)	16 (10 -27)	36 (14-71)	64 (28-83)	40 (17-79)
Wait time between appointments, hours	7.7 (4.2-12)	12 (6.9-19)	18 (9.1-29)	24 (15-35)	25 (10-36)
Time spent in clinic (appointment and wait time), hours	19 (12-28)	29 (18-46)	51 (25 -91)	81 (39-113)	67 (29-108)
Time spent in clinic per month, hours	1.1 (0.69-1.6)	1.6 (1.0-2.6)	2.9 (1.4-5.1)	4.5 (2.2-6.3)	3.7 (1.6-6.0)
Commuting					
Commuting time, hours	26 (14-43)	34 (19-55)	50 (29-81)	61 (32-86)	53 (21-104)
Roundtrip time (clinic and commuting time), hours	49 (32-71)	68 (40-103)	110 (61-177)	149 (91-196)	112 (54-208)
Time from departure to return per month, hours	2.7 (1.8-3.9)	3.8 (2.2-5.7)	6.1 (3.4-9.9)	8.3 (5.1-11)	6.3 (3.0-12)
Distance from VUMC Breast Cancer Clinic, miles	31 (16-74)	35 (16-80)	40 (17-89)	37 (15-79)	54 (23-97)
Cumulative commuting distance, miles	1,153 (568-2,143)	1,545 (720-3,053)	2,315 (1,127-4,329)	2,652 (1,278-4,671)	2,636 (884-5,886)
Commuting cost, \$	622 (307-1,157)	834 (389-1,649)	1,250 (608-2,338)	1,432 (690-2,552)	1,423 (478-3,178)
Admissions					
No. of unique admissions	0 (0-0)	0 (0-0)	0 (0-1)	1 (0-1)	1 (0-2)
% of patients with at least one admission	23	24	31	43	58
Total inpatient length of stay, days	0 (0-0)	0 (0-0)	0 (0-1.3)	0 (0-2.9)	1.9 (0-7.3)
% of patients with at least one emergency department visit	7.6	7.6	15	23	21

Abbreviations: IQR, interquartile range; VUMC, Vanderbilt University Medical Center.

*Values are provided as median (IQR), where applicable.

Pegfilgrastim cohort. To assess whether these measures were useful for capturing the impact of new treatment protocols on patients, we applied each measure to a population of patients with early-stage breast cancer who received systemic infusion therapy in the adjuvant or neoadjuvant setting at VUMC. We sought to determine whether the introduction of the pegfilgrastim (Neulasta; Amgen, Thousand Oaks, CA) on-body injector (OBI) on April 20, 2015, had any effect on the treatment workload of patients with breast cancer receiving the dose-dense doxorubicin and cyclophosphamide (ddAC) chemotherapy protocol.²⁷ Before 2015, the granulocyte colony-stimulating factor pegfilgrastim was typically given by subcutaneous injection 24 to 72 hours after chemotherapy to increase neutrophil production and decrease the risk of infection and febrile neutropenia.^{28,29} Patients receiving pegfilgrastim via subcutaneous injection would either return to the infusion clinic the day after their chemotherapy to receive the injection³⁰ or self-administer the injection at home. In contrast, an OBI is a device that is attached to the patient during the patient's infusion appointment and programmed to automatically inject medication at a time

specified by the provider.³¹ Previous studies have shown that pegfilgrastim administered via OBI is pharmacokinetically similar to manually injected pegfilgrastim.³²

To identify patients receiving pegfilgrastim with their ddAC chemotherapy protocol, we first identified patients with breast cancer by the presence of a respective ninth revision (174) or 10th revision International Classification of Diseases (C50) administrative billing code for any encounter between January 2005 and July 2017. We captured patients who received both doxorubicin and cyclophosphamide on the same day between 12 and 19 days apart for no more than four consecutive cycles. We collected data from the same sources as the stage 0 to IV cohort from the start of each patient's first ddAC administration to 14 days after their last ddAC administration.

In the pegfilgrastim cohort, we compared the treatment workload of patients with breast cancer with pegfilgrastim administered by one of the following three routes: subcutaneous injection administered in the infusion center 24 to 72 hours after chemotherapy, subcutaneous injection administered at home 24 to 72 hours after chemotherapy,

FIG 2. Total time spent in clinic (appointment time plus wait time) for patients with breast cancer at Vanderbilt University Medical Center per month over 18 months after diagnosis.

or OBI injection placed on the body in the infusion center on the same day as the chemotherapy treatment.

RESULTS

Stage 0 to IV Cohort

Of the 1,987 patients with breast cancer diagnosed at VUMC from January 2010 to June 2014, 1,687 had at least five outpatient appointments at VUMC and home addresses with zip codes within 150 miles of VUMC (Fig A1). Appendix Table A2 lists the characteristics of patients in this cohort. Table 1 lists the treatment workload measures among these tumor registry patients. For most outpatient encounter-related tasks such as time spent in clinic and appointment count, stage III patients experienced the highest workload, followed by stage IV patients, stage II

FIG 3. Appointment time for patients with breast cancer per month by department.

patients, stage I patients, and stage 0 patients. Stage I patients spent a median of 29 hours (interquartile range [IQR], 18 to 46 hours) in clinic over 18 months compared with 81 hours (IQR, 39 to 113 hours) for stage III patients. The median commuting cost over 18 months was \$834 (IQR, \$389 to \$1,649) for stage I patients compared with \$1,432 (IQR, \$690 to \$2,552) for stage III patients. For inpatient measures such as percentage of patients admitted, stage IV patients experienced the highest workload. Kruskal-Wallis H tests showed that the differences between stages was significant for all measures with $P < .001$, except for distance from VUMC breast cancer clinic ($P = .039$).

For encounter-related measures, we plotted the mean workload experienced over 18 months after diagnosis (Figs 2 and 3). We observed that total time spent in clinic was highest in the first 5 months after diagnosis and tended to taper off over 18 months. Figure 3 shows the breakdown of appointment time for all patients by department. Imaging and surgery appointments were most prevalent during the first few months of a patient's treatment, whereas chemotherapy and radiation therapy were most often used in months 3 to 5.

The boxplot in Figure 4 visualizing the distribution of appointment count by stage is also helpful for identifying outliers. The median number of appointments over 18 months was 38 appointments (IQR, 23 to 61 appointments) for stage I patients and 77 (IQR, 48 to 119 appointments) for stage III patients. There were also 48 patients who had more than 150 unique appointments during that time.

Pegfilgrastim Cohort

To study the effect of pegfilgrastim delivery mechanism on treatment workload, we identified 371 patients with breast cancer who received the ddAC chemotherapy protocol from January 2010 to August 2017. Among these patients, 343 had home addresses with zip codes within 150 miles of VUMC (Appendix Fig A1). Table 2 shows these results. In total, these 343 patients received 1,158 cycles of ddAC. For those cycles, 464 doses of pegfilgrastim were administered by the OBI, 303 doses by subcutaneous injection in the infusion center 24 to 72 hours after chemotherapy, and 391 doses by self-administration by subcutaneous injection at home. Over the course of their ddAC chemotherapy, 40 patients had more than one mode of pegfilgrastim administration from cycle to cycle. Patients receiving pegfilgrastim by subcutaneous injection in the infusion center spent approximately 40 minutes longer in appointments and had 1 additional day in clinic per cycle. Cycles where patients received the subcutaneous injection of pegfilgrastim in the infusion center were also admitted at VUMC at a higher rate than OBI and take-home pegfilgrastim cycles. Patients who received pegfilgrastim via self-administered injection tended to live further from clinic

FIG 4. Distribution of the number of appointments experienced over 18 months after diagnosis by stage.

(median, 64 miles; IQR, 24 to 112 miles) compared with patients who received pegfilgrastim with the OBI (median, 40 miles; IQR, 22 to 91 miles) and patients who received the clinic-administered injection (median, 30 miles; IQR, 12 to 61 miles).

DISCUSSION

The goals of this work were to develop a framework for calculating and reporting quantitative measures of patient treatment workload derived automatically from the EHR and to demonstrate that these measures are sensitive to expected differences in treatment workload across a population of patients with breast cancer. The measures of patient treatment workload are derived from data elements commonly found in most EHR systems including patient and facility addresses, admissions, and outpatient appointments. The measures themselves are also simple calculations of event counts and time between events. A strength of the framework is that other health care delivery systems with different EHRs can reproduce these measures. For our two cohorts of patients with breast cancer, we demonstrated that these measures of treatment workload are sensitive to expected differences in the intensity of treatment by cancer stage and to subtle differences in similar treatment protocols.

Although outpatient appointment records and inpatient admission records are all reliable sources of data, there are limitations to how completely the EHR at a single institution captures workload for patients. We were unable to capture care given at other health care organizations. We

TABLE 2. Treatment Burden Experienced per Cycle for Patients With Breast Cancer Receiving Various Modes of Pegfilgrastim Administration as Part of Their ddAC Chemotherapy

Measure	Median (IQR)*		
	OBI	Next-Day SubQ Injection	Take Home SubQ Injections
No. of cycles	464	303	391
Outpatient encounters			
No. of appointments	4 (3-5)	5 (4-6)	3 (3-4)
No. of unique appointment days	1 (1-2)	2 (2-3)	1 (1-2)
Appointment time, hours	3.7 (3.6-4.6)	4.4 (4.1-5.6)	3.6 (3.6-4.6)
Time spent waiting between appointments, hours	1.2 (0.92-2.7)	1.4 (0.92-2.1)	1.4 (1.0-2.1)
Time spent in clinic (appointment and wait time), hours	5.3 (4.5-7.8)	6.0 (5.3-7.7)	5.3 (4.8-6.7)
Communting			
Communting time, hours	2.3 (1.1-4.0)	3.0 (1.8-5.0)	3.0 (1.8-4.5)
Roundtrip time (clinic and commuting), hours	8.4 (6.5-12)	10 (7.3-12.7)	8.6 (6.9-11)
Distance from VUMC Breast Cancer Clinic, miles	40 (22-91)	30 (12-61)	64 (24-112)
Communting distance, miles	121 (52-231)	136 (74-280)	165 (87-264)
Communting cost, \$	65.46 (27.88-124.82)	73.50 (39.86-150.94)	88.91 (46.92-142.75)
Admissions			
No. of unique admissions	0 (0-0)	0 (0-0)	0 (0-0)
% of cycles with an admission	1.1	4.3	1.3
Total inpatient length of stay, days	0 (0-0)	0 (0-0)	0 (0-0)
% of cycles with an emergency department visit	1.1	1.7	2.1

NOTE. Cycles were between 12 and 19 days apart.

Abbreviations: ddAC, dose-dense doxorubicin and cyclophosphamide; IQR, interquartile range; OBI, on-body injector; SubQ, subcutaneous; VUMC, Vanderbilt University Medical Center.

*Values are provided as median (IQR), where applicable.

determined from the tumor registry that 31% of patients in the stage 0 to IV cohort had some portion of their cancer treatment at a non-Vanderbilt institution. Future work will include data sources that capture services provided outside our institution such as payer claims data.

There are several uses for our measures in cancer care delivery. A provider could use Figure 2 to help patients plan at diagnosis for how much time they should expect to spend at the clinic in the upcoming months. This preparation may allow patients to make the necessary arrangements in their work or caregiver schedules to make way for the care that will give them the best chance for recovery. Health care organizations could use Figure 3 to ensure that capacity is available in coming months for newly diagnosed patients. Furthermore, health care management could use Figure 4 to identify patients who are at risk for overutilization or overburden. Patients who are experiencing a high workload compared with others with comparable disease may be candidates for interventions that alleviate some patient work, such as home visits or telehealth encounters.

Although previous studies may have implied that using the OBI would decrease work for patients, researchers can strengthen these claims through the treatment workload measures proposed in this study. Table 2 shows that in cycles where VUMC administered pegfilgrastim with the OBI, patients had 1 less unique appointment day compared with cycles where VUMC used next-day injections. Presenting this evidence would help make the case that patients who live further away from an infusion clinic should

receive the OBI. Treatment workload measures can provide data-driven evidence for the increased convenience for new treatments. In addition, these measures could be used to inform patient-centric organizational guidelines that eliminate wasted treatment workload by improving efficiency.

An important point to note is that patients experience treatment workload differently. Treatment workload needs to be assessed alongside patients' capacity to manage care. Although some aspects of capacity are fixed, others can be coached or enhanced through education or access to resources. The next step to providing guidelines or clinical decision support to address treatment workload is to identify characteristics of patients that cause them to feel overburdened. Helping providers identify patients who are at risk for overburden and nonadherence could lead to treatment that is personalized for patients and better clinical outcomes.

In conclusion, treatment burden is an important dimension of the experience of patients with cancer. This study demonstrates that measurement of treatment workload derived from EHRs can differentiate patient populations with breast cancer by stage. We also demonstrate that providers can use these measures to understand how changes in treatment protocol can affect the work patients put into their care. Future work will attempt to use treatment workload measures to inform operational guidelines that improve efficiency and clinical decision support for patients who are likely to become overburdened.

AFFILIATION

¹Vanderbilt University Medical Center, Nashville, TN

CORRESPONDING AUTHOR

Alex C. Cheng, PhD, Vanderbilt University Medical Center, 2525 West End Ave, Ste 1475, Nashville, TN 37203; e-mail; a.cheng@vumc.org.

SUPPORT

Supported by Grant No. OG 180003 from the Susan G. Komen Foundation and Informatics Training Grant No. 4 T15 LM007450-15 from the National Library of Medicine.

AUTHOR CONTRIBUTIONS

Conception and design: All authors

Administrative support: Mia A. Levy

Collection and assembly of data: All authors

Data analysis and interpretation: All authors

Manuscript writing: All authors

Final approval of manuscript: All authors

Accountable for all aspects of the work: All authors

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST AND DATA AVAILABILITY STATEMENT

The following represents disclosure information provided by authors of this manuscript. All relationships are considered compensated. Relationships are self-held unless noted. I = Immediate Family Member, Inst = My Institution. Relationships may not relate to the subject matter of this manuscript. For more information about ASCO's conflict of interest policy, please refer to www.asco.org/rwc or ascopubs.org/jco/site/ifc.

Mia A. Levy

Employment: SeqTech Diagnostics (I)

Leadership: Personalis

Consulting or Advisory Role: Personalis, GenomOncology, Roche

Research Funding: GenomOncology

Patents, Royalties, Other Intellectual Property: Royalties from GenomOncology for licensing of MyCancerGenome content

No other potential conflicts of interest were reported.

ACKNOWLEDGMENT

We thank Christine Micheel for helping to develop this article.

REFERENCES

1. Leppin AL, Montori VM, Gionfriddo MR: Minimally disruptive medicine: A pragmatically comprehensive model for delivering care to patients with multiple chronic conditions. *Healthcare (Basel)* 3:50-63, 2015

2. Eton DT, Yost KJ, Lai JS, et al: Development and validation of the Patient Experience with Treatment and Self-management (PETS): A patient-reported measure of treatment burden. *Qual Life Res* 26:489-503, 2017
3. Shippee ND, Shah ND, May CR, et al: Cumulative complexity: A functional, patient-centered model of patient complexity can improve research and practice. *J Clin Epidemiol* 65:1041-1051, 2012
4. Haynes RB, McDonald HP, Garg AX: Helping patients follow prescribed treatment: Clinical applications. *JAMA* 288:2880-2883, 2002
5. Tran V-T, Montori VM, Eton DT, et al: Development and description of measurement properties of an instrument to assess treatment burden among patients with multiple chronic conditions. *BMC Med* 10:68, 2012
6. May C, Montori VM, Mair FS: We need minimally disruptive medicine. *BMJ* 339:b2803, 2009
7. Boehmer KR, Shippee ND, Beebe TJ, et al: Pursuing minimally disruptive medicine: Disruption from illness and health care-related demands is correlated with patient capacity. *J Clin Epidemiol* 74:227-236, 2016
8. Eisenhauer EA, Therasse P, Bogaerts J, et al: New response evaluation criteria in solid tumours: Revised RECIST guideline (version 1.1). *Eur J Cancer* 45:228-247, 2009
9. Paiva B, van Dongen JJM, Orfao A: New criteria for response assessment: Role of minimal residual disease in multiple myeloma. *Blood* 125:3059-3068, 2015
10. Saad ED, Katz A, Buyse M: Overall survival and post-progression survival in advanced breast cancer: A review of recent randomized clinical trials. *J Clin Oncol* 28:1958-1962, 2010
11. Colevas AD, Setser A: The NCI Common Terminology Criteria for Adverse Events (CTCAE) v 3.0 is the new standard for oncology clinical trials. *J Clin Oncol* 22, 2004 (suppl 14; abstr 6098)
12. Krohe M, Hao Y, Lamoureux RE, et al: Patient-reported outcomes in metastatic breast cancer: A review of industry-sponsored clinical trials. *Breast Cancer (Auckl)* 10:93-102, 2016
13. Zafar SY, Peppercorn JM, Schrag D, et al: The financial toxicity of cancer treatment: A pilot study assessing out-of-pocket expenses and the insured cancer patient's experience. *Oncologist* 18:381-390, 2013
14. Grunfeld E, Coyle D, Whelan T, et al: Family caregiver burden: Results of a longitudinal study of breast cancer patients and their principal caregivers. *CMAJ* 170:1795-1801, 2004
15. Sklenarova H, Krümpelmann A, Haun MW, et al: When do we need to care about the caregiver? Supportive care needs, anxiety, and depression among informal caregivers of patients with cancer and cancer survivors. *Cancer* 121:1513-1519, 2015
16. Tran VT, Barnes C, Montori VM, et al: Taxonomy of the burden of treatment: A multi-country web-based qualitative study of patients with chronic conditions. *BMC Med* 13:115, 2015
17. Spencer-Bonilla G, Quiñones AR, Montori VM: Assessing the burden of treatment. *J Gen Intern Med* 32:1141-1145, 2017
18. National Cancer Institute: SEER-Medicare publications by journal and year. https://healthcaredelivery.cancer.gov/seermedicare/overview/pubs_jour_year.php
19. Presley CJ, Soulos PR, Tinetti M, et al: Treatment burden of Medicare beneficiaries with stage I non-small-cell lung cancer. *J Oncol Pract* 13:e98-e107, 2017
20. Henry DH, Viswanathan HN, Elkin EP, et al: Symptoms and treatment burden associated with cancer treatment: Results from a cross-sectional national survey in the U.S. *Support Care Cancer* 16:791-801, 2008
21. Tinetti ME, Naik AD, Dodson JA: Moving from disease-centered to patient goals-directed care for patients with multiple chronic conditions: Patient value-based care. *JAMA Cardiol* 1:9-10, 2016
22. Cheng AC, Levy MA: Data driven approach to burden of treatment measurement: A study of patients with breast cancer. *AMIA Annu Symp Proc* 2016:1756-1763, 2017
23. Cheng A, Levy M: Determining burden of commuting for treatment using online mapping services: A study of breast cancer patients. *AMIA Annu Symp Proc* 2017:555-564, 2018
24. Internal Revenue Service: 2016 standard mileage rates for business, medical and moving announced. <https://www.irs.gov/uac/newsroom/2016-standard-mileage-rates-for-business-medical-and-moving-announced>
25. Tennessee Department of Health: Tennessee Cancer Registry. <https://www.tn.gov/health/health-program-areas/tcr.html>
26. National Cancer Institute: What is a cancer registry? https://seer.cancer.gov/registries/cancer_registry/cancer_registry.html
27. Citron ML, Berry DA, Cirincione C, et al: Randomized trial of dose-dense versus conventionally scheduled and sequential versus concurrent combination chemotherapy as postoperative adjuvant treatment of node-positive primary breast cancer: First report of Intergroup Trial C9741/Cancer and Leukemia Group B Trial 9741. *J Clin Oncol* 21:1431-1439, 2003
28. Biganzoli L, Untch M, Skacel T, et al: Neulasta (pegfilgrastim): A once-per-cycle option for the management of chemotherapy-induced neutropenia. *Semin Oncol* 31:27-34, 2004 (suppl 8)
29. Crawford J: Once-per-cycle pegfilgrastim (Neulasta) for the management of chemotherapy-induced neutropenia. *Semin Oncol* 30:24-30, 2003 (suppl 13)
30. Burris HA, Belani CP, Kaufman PA, et al: Pegfilgrastim on the same day versus next day of chemotherapy in patients with breast cancer, non-small-cell lung cancer, ovarian cancer, and non-Hodgkin's lymphoma: Results of four multicenter, double-blind, randomized phase II studies. *J Oncol Pract* 6:133-140, 2010
31. Holt MD, Cairns AS, Romacker M: Drug delivery device. 2015
32. Yang B-B, Morrow PK, Wu X, et al: Comparison of pharmacokinetics and safety of pegfilgrastim administered by two delivery methods: On-body injector and manual injection with a prefilled syringe. *Cancer Chemother Pharmacol* 75:1199-1206, 2015

APPENDIX

FIG A1. Patient flow diagram for breast cancer stage 0 to IV and dose-dense doxorubicin and cyclophosphamide (ddAC) with pegfilgrastim cohort selection. VUMC, Vanderbilt University of Medical Center.

TABLE A1. Summary of Outcome Measures Used in Cancer Treatment

Measure Type	Description	Examples	Assessment Methods
Disease response	Biologic effect of treatment on disease	Response Evaluation Criteria in Solid Tumors (RECIST) ⁸ Minimal residual disease ⁹	Radiology assessment Pathology assessment
Host response	Morbidity and mortality effect of treatment on patient	Overall survival ¹⁰ Common Terminology Criteria for Adverse Events ¹¹ European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire ¹²	Physical exam Patient reported Surveys
Treatment burden	Logistical and emotional effect of treatment on patients' lives	Financial toxicity ¹³ Treatment Burden Questionnaire ⁵	Surveys
Caregiver burden	Logistical and emotional effect of treatment on patients' caregivers	Zarit Burden Inventory ¹⁴ Supportive Care Needs Survey ¹⁵	Surveys

TABLE A2. Patient Demographic Characteristics and Disease Stage for Stage 0 to IV and Pegfilgrastim Cohorts

Characteristic	Breast Cancer Stage 0 to IV Cohort	ddAC With Pegfilgrastim Cohort
Median age, years (range)	57 (14-95)	50 (26-80)
Race, No. (%)		
White	1,466 (87)	280 (82)
Black	180 (11)	54 (16)
Other	41 (2)	9 (2)
Disease stage, No. (%)		
0	260 (15)	0 (0)
I	672 (40)	59 (17)
II	495 (29)	179 (52)
III	180 (11)	103 (30)
IV	80 (5)	2 (1)

Abbreviation: ddAC, dose-dense doxorubicin and cyclophosphamide.