Embracing Electronic Tools to Improve Patient Outcomes

Internal Medicine Grand Rounds

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Purpose and Overview: Dr. Beg will discuss the challenges clinicians and clinical investigators face to assess disease and treatment related toxicity. Electronic patient reported tools and wearable devices are changing the way we perform clinical care and can be powerful tools to incorporate in our practice and in clinical trials. He will discuss strengths and limitations of these tools and present early data demonstrating feasibility in our daily practice.

Educational Objectives:

At the conclusion of this lecture, the listener should be able to:

1) Understand the need for structured Patient Reported Symptom assessment tools in the clinic.

2) Describe the effect of structured electronic Patient Reported Symptom assessment tools on clinical outcomes such as quality of life, emergency department visits and overall survival.

3) Recognize the feasibility of wearable monitors to measure clinical parameters such as physical activity and hemodynamics.

4) Describe the factors that drive how these tools can be implemented in outpatient clinics.

A physician's evaluation of their patient's symptoms is the most critical assessment made during a clinic encounter. But clinicians are unaware of their patient's symptoms up to 50% of the time.[1] The management of these symptoms can affect patient's quality of life and functional capacity. At the same time, there is a direct relationship between degree of patient symptoms and health care utilization. Patients with high symptom burden are more likely to seek acute appointments, contact the clinic for urgent problems, seek care in the emergency department and have poor clinical outcomes.

In the current health system, patients present to the clinic to discuss their health. The physician may approach the clinic visit with a predetermined set of topics to address. Additional provider and health system demands also compete for time making it more difficult to complete their tasks (figure 1). As a result, patients may not have an opportunity to discuss symptoms that are relevant to them. If the patient does present symptoms they may go unrecognized by the clinician. In parallel, when patients experience symptoms at home, they may downplay the symptoms and fail to, or delay in reporting them. Patients who do reach out, can face barriers in the clinic in having their symptoms recognized and managed which can further delay care and result in complications. Because of these factors, our routine current clinical care can be defined as 'reactive' where patients end up having to wait too long to have their symptoms addressed, frequently after complications have developed.

An alternative, 'proactive' approach to symptom monitoring can incorporate data from modern electronic tools, including web based tools, wearable devices and sensors. These can provide objective and quantifiable measures which are not subject to errors and bias of self-reporting and shorter duration of formal testing.[2]
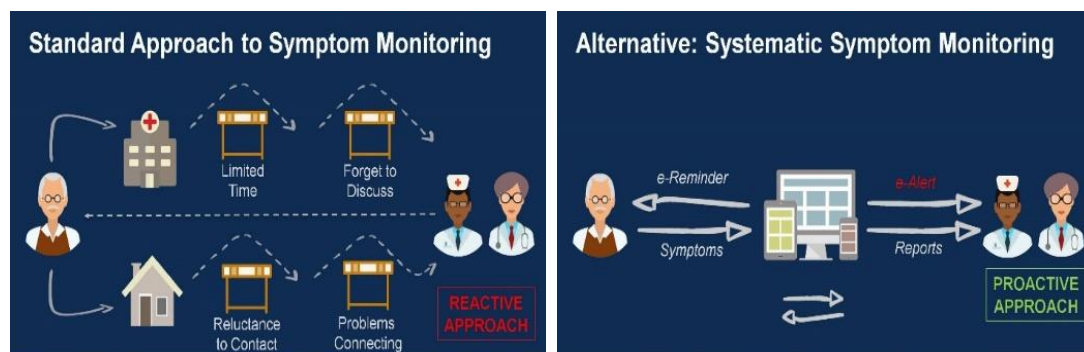

Figure 1: Our current approach to symptom monitoring is 'reactive' and requires patients to report their symptoms in the office or while home, and this leads to physicians not recognizing symptoms up to 50% of the time. A more 'proactive' approach where patients report symptoms at regular intervals can notify clinicians of problems before they cause complications.

Electronic Patient Reported Symptom Tool:

In one web-based electronic patient symptom reporting tool patients are prompted to complete symptom reports through electronic reminders in between, or immediately before, clinic visits. These can prompt alerts to clinic staff who can act on these reports if clinically indicated. Physicians can be provided with reports during the clinic visits which provides a snapshot of patient symptom burden as well as longitudinal changes with time. This electronic patient symptom reporting tool, in a cohort of patients with advanced cancer, is associated with improved quality of life, reduced emergency department visits and improved overall survival.[3] The observed clinical improvements may stem from early identification of clinical decline from treatment and/or cancer and allows a window of opportunity for appropriate intervention (figure 2). This single-center experience from an urban, academic cancer center, supports the effect of longitudinal patient reported symptom monitoring on patient outcomes in clinical practice which has themes which affect our structure of health care delivery across specialties.
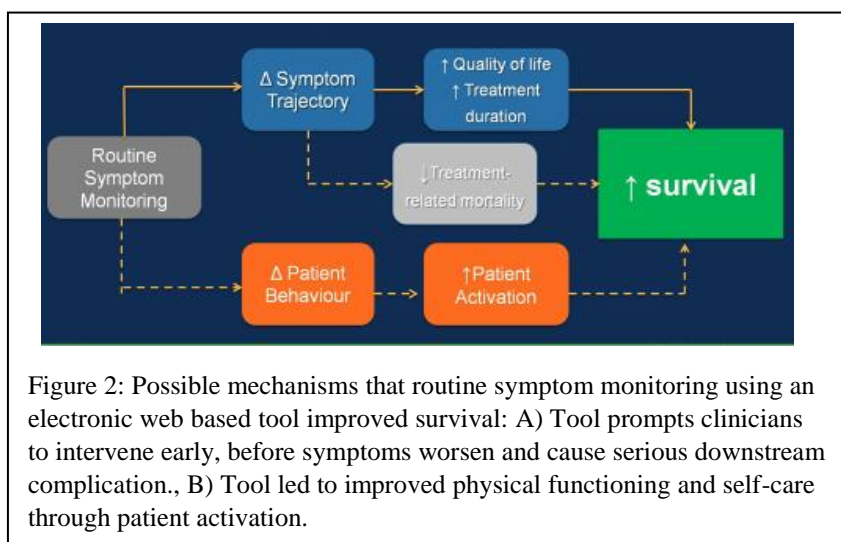

Figure 2: Possible mechanisms that routine symptom monitoring using an electronic web based tool improved survival: A) Tool prompts clinicians to intervene early, before symptoms worsen and cause serious downstream complication., B) Tool led to improved physical functioning and self-care through patient activation.

In this study the vast majority of patient-reported symptoms were grade 1 or 2 (mild to moderate), more than 1,400 were grade 3 or 4 (severe to disabling). In response to e-mail alerts for severe or worsening symptoms, nurses performed direct interventions primarily composed of telephone counseling, medication changes, and ER or hospital referral. Clinical actions may also have been taken in response to symptom reports delivered to clinicians at each office visit including responses to mild/moderate symptoms. Nurses frequently initiated clinical actions in more than 75% of reports.[3,4]

Major conclusions from this study were:

- Health Related Quality of Life (HRQL), improved among more participants in the intervention group than usual care (34% v 18%) and worsened among fewer (38% v 53%; P < .001).
- Patients receiving intervention were less frequently admitted to the ER (34% v 41%; P = .02) or hospitalized (45% v 49%; P = .08) and remained on chemotherapy longer (mean, 8.2 v 6.3 months; P = .002).

- Median overall survival was 31.2 months (95% CI, 24.5-39.6) in the PRO group and 26.0 months (95% CI, 22.1-30.9) in the usual care group (difference, 5 months; P = .03) . In the multivariable model, results remained statistically significant with a hazard ratio of 0.83 (95% CI, 0.70-0.99; P = .04).
- Nurses frequently initiated clinical actions in more than 75% of reports.[3,4]

As such, systematic patient reporting appears to enhance clinician awareness and can augment existing mechanisms for symptom management during routine care. Conversely, when undetected in the absence of patient self-reporting, symptoms may continue to worsen and cause serious complications, lead to hospital visits, limit the ability to safely deliver therapy, and diminish outcomes.

If we take the oncology treatment landscape as an example, it has evolved over the last 2 decades. More recently, the rise of molecular targeted therapies and immune checkpoint inhibitors have forced the development of novel clinical trial designs. [5-7] The success in using electronic web based symptom reporting on clinical practice has contributed to the development of a National Cancer Institute (NCI) Patient-Reported Outcomes Version of the Common Terminology Criteria for Adverse Events (PRO-CTCAE). PRO-CTCAE is being developed as a tool to bridge the strength of PRO tools with validated toxicity assessment measures (e.g NCI-CTCAE) on which current clinical trials rely. [8] This tool uses self-reported PRO-CTCAE items which are conducted via wireless devices and can measure adverse events at multiple time points. Validation of the PRO-CTCAE tools is needed to formally assess treatment toxicity, on which clinical trial outcomes including decisions of dose limiting toxicities can be made.

Wearable Devices and Sensors: Medical 'Internet of Things' and the 'Quantified Patient':

The web-based electronic patient symptom reporting tools, such as those used above, are a decade old in development, are still vulnerable to recall bias and are designed to assess symptoms only for the prior 7 days. Newer generation electronic sensors and wearable monitors can objectively, and semi-autonomously, report longitudinal data to a central data repository for grading and assessment and can overcome many of these issues.

Wearable devices can offer clinicians, and investigators involved in clinical trials, access to a degree of detail about the lives of patients, which is not possible with current pen and paper quality-of-life tools. The future application of 'Quantified-Self' and the 'Internet of Things' data in the medical field relies on the feasibility of using these devices in our patient population, and the clinical relevance of collected data.

The measures farthest along in development are continuous blood glucose monitoring for diabetic patients and physical activity assessment. Other examples of health parameters which can be measured with wearable devices include: heart rate with an oximeter built into a ring, a wireless patch for blood pressure, muscle activity with an electromyographic sensor embedded

into clothing, stress with an electodermal sensor incorporated into a wristband, sleep patterns via an accelerometer in a watch and detailed body temperature tracking.

This can also allow clinicians from different specialties to better assess the real-world tolerability of drugs and interventions. These have broad applications based on the clinical scenario being examined and can help answer questions that have been difficult to study using current tools. Many modern day clinical dilemmas may be answered using these tools. Some examples of this can be the real world effect of an intervention for pain control, the degree of debility from statin-induced myopathy on elderly patients, identify patients most likely to benefit from joint replacement, quantify deconditioning from surgery and also measure the frequency of fever in patients with cancer.[9,10]

The relationship between wearable-derived, and clinician-assessed measures are important to establish as wearable data and electronic medical records (EMR) become more integrated. Clinicians and investigators will have access to unprecedented data for clinical decision-making at their disposal. This can allow deep learning algorithms to begin to look at subtle effects of treatment, which can predict long-term toxicity, or to identify departures from baseline, which may be the initial signs of clinical decompensation.

Physical Activity:

In recent years, commercially available wearable physical activity monitors are making their way into clinical research related to obesity, depression and physical activity. Wearable physical activity monitors can inform clinical practice and provide a measure of patient functional status that is free of patient and provider bias. Among wearable devices, the most commonly used devices are physical activity monitors (PAMs). A higher level of physical activity is associated with improved outcomes in patients undergoing chemotherapy and this assessment can influence decisions on cancer therapy, eligibility for clinical trials and track the impact of therapy[11-13]. The level of physical activity is also an important predictor of outcome, and patients with poor performance status who undergo chemotherapy have poor survival, reduced response rates and worse quality of life[14]. Functional status has historically been recorded via clinical judgment and patient questionnaires such as the Karnofsky Performance Status (KPS), Eastern Cooperative Oncology Group (ECOG) or Zubrod Scale, and

Figure 3: Commonly used performance status assessment tools, are subjective, and can lack inter-observer agreement.
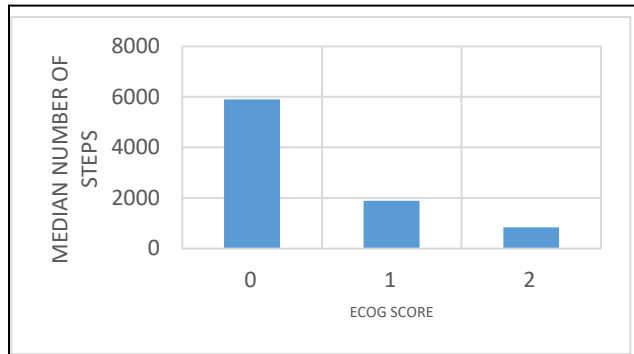
Figure 4: Difference in median number of steps based on clinician assessed ECOG score

the Functional Assessment of Cancer Therapy (FACT) score (figure 3)[15]. These assessments are subjective, and are prone to inter-observer differences and bias, which can be especially relevant for elderly patients where subtle differences in activity can carry more clinical significance.

Investigators and providers often use clinical and functional status measures to evaluate treatment- and disease- symptom burden. Standardized scales are used to classify therapy and disease related toxicities by assigning grades based on clinical descriptions of severity, need or level of required intervention or hospitalization, and the patient's ability to perform activities of daily living. The strength of these grading systems is in their ability to accurately classify adverse events that rely on numerical variables (e.g. cell counts, level of transaminases). However, there may be a disconnect between patient and provider perception of reported symptoms such as fatigue, malaise and pain which are subject to individual patient and provider interpretation and reporting, and also recall bias and reporting bias. PAMs can therefore identify 'at risk' patients with suboptimal performance which is the first step to targeting interventions aimed at increasing physical activity. Clinicians and clinical trial investigators do not currently have tools to accurately assess or report functional status and impact, either positive or detrimental, of therapy on activity. Many clinical trials depend on functional assessment scales as surrogates for level of physical activity. Commonly used scales in Oncology, mentioned above, such as the KPS and ECOG have evolved into accepted tools for clinical care in assessing physical activity level, prognosis, tolerability of therapy and even as clinical trial eligibility criteria. These scales are generally reproducible but have low associations with quality of life and symptom measures. While there is acceptable agreement in comparing broad, 'good' (ECOG 0-2) versus 'poor' (ECOG 3-4) functional status, inter-observer agreement is lost while making observations with higher resolution (e.g. ECOG 0 vs 1 vs 2).[16] Due in part to the lack of accurate assessment of tolerability, some therapies deemed to be effective in clinical trials have not seen broad adoption in clinical practice due to poorer than expected treatment tolerance in the real world.

PAMs may be able to provide a more accurate measure of functional status, thus guiding therapy and eligibility in clinical trials. These tools may accurately reflect the fluctuation of symptoms between visits, are less likely to be compromised by missing data and user fatigue which can pose a challenge to assign clinical meaningfulness of other obtained data. PAM devices are worn for extended periods of time, have relatively automated 'passive' data capture and therefore provide longitudinal, potentially more clinically relevant, data.

The experiences from prior published reports of electronic tools is a necessary first step to understand what these resources can achieve. Future work will help us understand how to implement these tools in the real world. As an example, patients with cancer tend to be older and frail, and are less likely to be technologically literate. Also, clinical trial participants are not representative of the general patient population seen in most clinics. The logistics of implementing commercial grade wearable devices will vary based on the type of clinic (academic vs private, urban vs rural). We performed a pilot study to determine the feasibility of PAMs to longitudinally assess physical activity and performance status in cancer patients receiving chemotherapy at the Harold Simmons Cancer Center. This was a pilot study of a commercially available wearable PAM, the 'Fitbit flex' in adult cancer patients. The primary objective was to assess feasibility of a commercially available wearable PAM, the 'Fitbit Flex', in subjects receiving therapy for cancer.

In our cohort, 80% participants adhered to wearing the PAM for more than 70% of the observation period. Patients completed a post-study questionnaire which revealed that 74% of patients rated their experience of using the PAM to be ≥4 on a scale of 1-5 (1=very poor, 5= very good). The average number of steps differed significantly between ECOG 0, 1 and 2 patients (Figure 4). This is an essential first step before wearable derived data are used as a surrogate for legacy performance status instruments like ECOG and KPS. [17] We also tested the association of wearable-derived data with patient reported quality of life tools. There are multiple patient reported outcome assessment tools available for use in cancer patients. Survey tools require a face-to-face visit and only provide a snap shot around the time of the encounter. They also demand significant research staff (and patient) time. However, these surveys are well validated across many clinical indications and are therefore routinely incorporated in clinical trials. We showed that minimum, but not average, number of steps correlated with the Brief Fatigue Index (BFI), Functional Assessment of Cancer Therapy-General (FACT-G) and the Quick Inventory of Depressive Symptomatology (QIDS).[17]

Figure 5: A) Cardio MEMS Pulmonary artery pressure monitor system sensor (B) Transcatheter is implanted into a distal branch of the descending pulmonary artery. (C) Patient takes daily pressure readings from home. (D) Information transmitted is immediately available for review. (E) Pressure trend information and pulmonary artery pressure

Heart Failure:

As technology advances, sensors and wearable devices are being developed which can accurately measure clinical variables of interest such as heart rate, blood pressure, EKG tracings, pulse oximetry and even degree of pulmonary edema. A recently approved implantable wireless
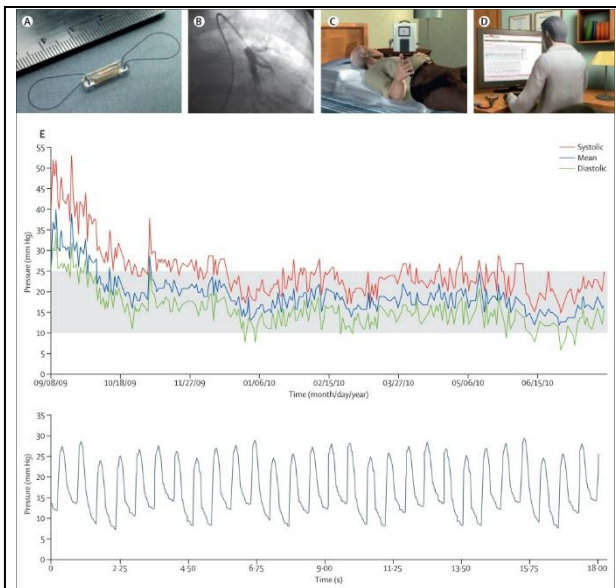
pulmonary artery pressure remote monitor, the CardioMEMS HF System, has been shown to be effective in reducing hospitalizations among New York Heart Association (NYHA) class III HF patients (figure 5). The 'CardioMEMS Heart Sensor Allows Monitoring of Pressure to Improve Outcomes In NYHA Class III Heart Failure Patients' (CHAMPION) randomized single-blind trial found that transmission of pulmonary artery pressure data from the device reduced HF-related hospitalizations at six months (31 versus 44 percent, HR 0.70, 95% CI 0.60-0.84). [18] There was a 1.5 percent rate of device- or system-related complications. An exploratory subgroup analysis found that device-guided management reduced HF-related hospitalization in patients with preserved left ventricular ejection fraction (LVEF ≥40 percent or LVEF ≥50 percent), as well as in patients with LVEF <40 percent. Results of this trial have been called into question due to study design concerns and possible bias but still speaks to the advancements technology continues to make.[19] Regardless of the validity/reproducibility of this trial, it is clear that the sensor technology has progressed tremendously in recent years and that remote monitoring of advanced hemodynamic parameters is feasible and can inform clinical care.

Implementation of Electronic Technology:

The factors that may limit the impact of these technologies on clinical practice will revolve around how successfully investigators, clinics and health systems implement these in their environment. The International Society for Quality of Life Research provided a framework for implementation of QOL measures that can also be adapted for electronic tools (figure 6). The most important step in implementation is to define the goal and have a clear marker of impact. The goal of these tools could be improving clinic efficiency, reduce emergency rooms visits, improve patient satisfaction or improve clinical care.

Next, the health system should assess available resources and scale the implementation based on what is available and avoid a mismatch. The chosen electronic tool would have to be a good match based on these factors and whenever possible, the tools used in clinic should match those used in clinical trials. Other questions the team should ask while implementing such a process include: How would results be reported? Should results be reported before, during or after the clinic visit? Can results reporting be incorporated into the clinic workflow or should it be kept in a parallel system? Would the patient, physician, nurse or consulting teams receive results? Can the release of results be automated like laboratory and imaging reports are in our Electronic Medical Record? How will the medical team respond to results? Mostly importantly, a predetermined measure of success is needed to determine whether the intended goals are met and how much continued resources can be applied to these tools.

Lastly, the security of data from wearable devices will need strict governance. This will vary based on the variables being measured, where the Protected Health Information (PHI) linked data will reside and whether there is integration with electronic health records.

Lessons From Existing UTSW Electronic Patient Portals:

For web-based, wearable and sensor based tools to become ubiquitous, outpatient clinics need to optimize allocated resources. Using a focus group of clinic nurses from the Simmons Cancer Center we studied the effect of electronic patient portals (i.e. MyChart) on nursing workflow. [20] We discovered that the primary consideration of this technology on nursing staff was its impact on work volume and flow. Nurses reported notable differences in the workflow of how patient portal communications are handled between physicians, even within the same clinic. Nurses raised concerns about the perceived substantial increase in the volume of electronic communications, burden of docum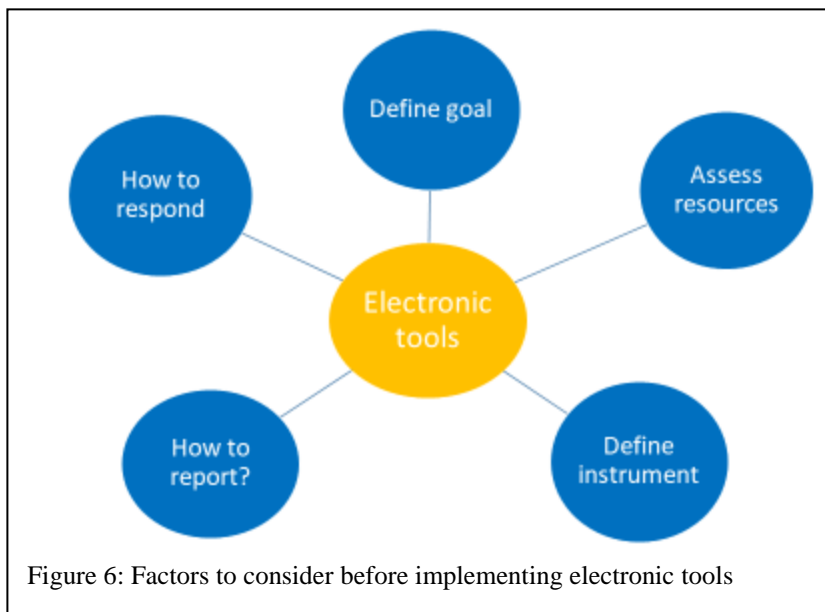entation, potential for multiple exchanges between patients and staff members. We identified a huge opportunity to streamlining workflow and improving patient and staff experience. Increasing patient and caregiver education regarding appropriate use and expectations was a widely agreed upon approach. Key nursing themes that emerged include work volume and flow, patient expectations and safety, variation in use of communication technologies, and education and management.

Figure 6: Factors to consider before implementing electronic tools

Conclusions

Recent years have seen tremendous growth in technology including electronic web-based tools, wearable monitors and sensors. These tools are poised to change the way we practice medicine in the coming years and have the potential to improve our ability to quantify relevant measures for our patients. Clinic and research programs should prepare to systematically implement these devices into their workflow in an adaptable and iterative manner.

In summary, we can evaluate the effect of electronic tools on the management of chronic diseases from three perspectives:

> 1. Patient: Continuous monitoring for disease or treatment related toxicities. This allows physicians to anticipate impending decompensation and to implement timely medical treatment accordingly.

2. Public health: Decrease the need for emergency hospitalizations and improve quality of life. This will help alleviate the heavy healthcare burden of chronic disease.

3. Technology: Physicians and health system have an opportunity to better inform the development of these tools and make them most relevant to the care we offer our patients and can help streamline clinical care into a more patient centric model.

Future studies will help us better understand the strengths and limitations of these technologies. Physicians should lead the effort to standardize the processes to incorporate these in outpatient Internal Medicine clinics.

References:

1.   Pakhomov SV, Jacobsen SJ, Chute CG, Roger VL. Agreement between patient-reported symptoms and their documentation in the medical record. *Am J Manag Care.* 2008;14(8):530-539.
2.   Beg MS, Gupta A, Stewart T, Rethorst CD. Promise of Wearable Physical Activity Monitors in Oncology Practice. *J Oncol Pract.* 2017;13(2):82-89.
3.   Basch E, Deal AM, Dueck AC, et al. Overall Survival Results of a Trial Assessing Patient-Reported Outcomes for Symptom Monitoring During Routine Cancer Treatment. *JAMA.* 2017;318(2):197-198.
4.   Basch E, Deal AM, Kris MG, et al. Symptom Monitoring With Patient-Reported Outcomes During Routine Cancer Treatment: A Randomized Controlled Trial. *J Clin Oncol.* 2016;34(6):557-565.
5.   Beg MS, Azad NS, Patel SP, et al. A phase 1 dose-escalation study of NEO-102 in patients with refractory colon and pancreatic cancer. *Cancer Chemother Pharmacol.* 2016;78(3):577-584.
6.   Beg MS, Brenner AJ, Sachdev J, et al. Phase I study of MRX34, a liposomal miR-34a mimic, administered twice weekly in patients with advanced solid tumors. *Invest New Drugs.* 2017;35(2):180-188.
7.   Woodcock J, LaVange LM. Master Protocols to Study Multiple Therapies, Multiple Diseases, or Both. *N Engl J Med.* 2017;377(1):62-70.
8.   Basch E, Pugh SL, Dueck AC, et al. Feasibility of Patient Reporting of Symptomatic Adverse Events via the Patient-Reported Outcomes Version of the Common Terminology Criteria for Adverse Events (PRO-CTCAE) in a Chemoradiotherapy Cooperative Group Multicenter Clinical Trial. *Int J Radiat Oncol Biol Phys.* 2017;98(2):409-418.
9.   Crawford J, Ozer H, Stoller R, et al. Reduction by granulocyte colony-stimulating factor of fever and neutropenia induced by chemotherapy in patients with small-cell lung cancer. *N Engl J Med.* 1991;325(3):164-170.
10.   Chiauzzi E, Rodarte C, DasMahapatra P. Patient-centered activity monitoring in the self-management of chronic health conditions. *BMC Med.* 2015;13:77.
11.   Dimeo FC, Stieglitz RD, Novelli-Fischer U, Fetscher S, Keul J. Effects of physical activity on the fatigue and psychologic status of cancer patients during chemotherapy. *Cancer.* 1999;85(10):2273-2277.
12.   Mishra SI, Scherer RW, Snyder C, Geigle P, Gotay C. The effectiveness of exercise interventions for improving health-related quality of life from diagnosis through active cancer treatment. *Oncology nursing forum.* 2015;42(1):E33-53.
13.   Fong DY, Ho JW, Hui BP, et al. Physical activity for cancer survivors: meta-analysis of randomised controlled trials. *Bmj.* 2012;344:e70.
14.   Schnipper LE, Smith TJ, Raghavan D, et al. American Society of Clinical Oncology identifies five key opportunities to improve care and reduce costs: the top five list for oncology. *J Clin Oncol.* 2012;30(14):1715-1724.
15.   Garman KS, Cohen HJ. Functional status and the elderly cancer patient. *Critical reviews in oncology/hematology.* 2002;43(3):191-208.

16. Sorensen JB, Klee M, Palshof T, Hansen HH. Performance status assessment in cancer patients. An inter-observer variability study. *Br J Cancer.* 1993;67(4):773-775.

17. Beg MS ST, Gupta A, Dong Y, Rahimi Z, Paul T, Crane K, Rethorst C. Feasibility of wearable physical activity monitors in cancer patients (PAMCaP). *J Clin Oncol* 2017;35:(suppl; abstr 6577).

18. Abraham WT, Adamson PB, Bourge RC, et al. Wireless pulmonary artery haemodynamic monitoring in chronic heart failure: a randomised controlled trial. *Lancet.* 2011;377(9766):658-666.

19. Dhruva SS, Krumholz HM. Championing Effectiveness Before Cost-Effectiveness. *JACC Heart Fail.* 2016;4(5):376-379.

20. Gerber DE, Beg MS, Duncan T, Gill M, Craddock Lee SJ. Oncology Nursing Perceptions of Patient Electronic Portal Use: A Qualitative Analysis. *Oncol Nurs Forum.* 2017;44(2):165-170.