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Systematic Review of Hand Grip Strength and Pilot Study to Measure Hand Grip Strength in  
Participants Receiving Hematopoietic Stem Cell Transplant

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**Abstract**

Systematic Review of Hand Grip Strength and Testing for Strength in Participants Receiving Hematopoietic Stem Cell Transplant

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**Background:** Despite aggressive fall prevention programs, rates of falls in hospitals have increased from 2.7 falls per thousand patient days in 2001 (Halfon, Egli, Van Melle, & Vagnair, 2001) to 3-5 falls per thousand patient days in 2014 (Oliver, Healey, & Haines, 2010). Patients hospitalized for oncological diagnoses are at increased risk of sustaining a fall compared with other hospitalized patients on medical surgical types of units (6.3 vs. 3.1 per thousand patient days) and are more likely to be injured if they do fall (Fischer et al., 2005). One contributing factor to this risk may be weakness. For example, patients hospitalized for Hematopoietic Stem Cell Transplant (HSCT) have been found to have weakness at the time of admission (Mello, Tanaka & Dulley 2003). Although lower extremity muscle weakness is a well-known risk factor for falls (Currie, 2006), assessment of muscle strength is not standard of care in hospitals. Hand grip strength (HGS) by dynamometry has been used to evaluate functional strength in a variety of populations. These populations include patients with a wide variety of diagnoses such as those undergoing kidney transplantation (Garonzik-Wang, et al., 2012), as well as patients with oncological diagnoses (Cantarero-Villanueva, et al., 2012; de Souza, et al., 2012;

Klepin, et al., 2013). In addition, studies of HGS have taken place in both outpatient and inpatient settings (Cantarero-Villanueva, et al., 2012; Norman, et al., 2010). This dissertation is composed of two papers. The first paper is a systematic review of the use of Hand Grip Strength (HGS) in selected clinical studies. The purpose of this review was to delineate methods and identified challenges in studies of HGS by dynamometry in participants who had oncologic diagnoses or were hospitalized for any diagnosis. The second paper reports results of a pilot study that was conducted in a sample of patients undergoing myeloablative HSCT in an inpatient setting. The purposes of the pilot study were to: 1) describe changes in muscle strength as measured by daily HGS measurements; 2) describe relationships between selected laboratory values (Hematocrit [HCT], Hemoglobin [HGB], Absolute Neutrophil Count [ANC]) and HGS during the course of hospitalization; 3) determine the feasibility and acceptability of daily HGS measurements; and 4) compare relative timing of detection of change in muscle strength by HGS measurement and nursing assessment of the participant's need for assistance with mobility.

**Methods:** The first paper describes a systematic review of the literature that was conducted focused on identifying studies related to HGS measurement in hospitalized patients and those with oncologic diagnoses in any care setting (Khan, Kunz, Klejin & Antes, 2003). Medline, CINAHL and Web of Science databases were searched yielding 23 pertinent articles. The articles were then reviewed for quality to ensure that the study designs were appropriate to produce results that were free of bias and could be interpreted accurately. Results were summarized in a table and were used to design a study protocol for a HGS pilot study. The second paper details the results of the pilot observational study. For this study we used a prospective, repeated measures design and enrolled 45 participants hospitalized for HSCT. HGS was measured on admission and daily until discharge from the hospital or study withdrawal. Medications (opioid,

benzodiazepine), physical therapy and laboratory measures of HGB, HCT and ANC were recorded as was nurse assessment of need for assistance with mobility. A single-item survey question developed for study purposes was used to assess feasibility and acceptability of HGS testing from the participant perspective.

**Results:** Twenty-three articles were reviewed for the first paper. Analysis of these articles found that techniques for measuring HGS appeared to be similar but not identical across care settings. This included specific design elements of the studies including positioning, selection of hand for testing, attempts per trial and data included for analysis. Challenges of HGS testing in hospital settings included determining when participants were awake and alert, high percentages of ineligible participants due to complications of care, and interruptions in testing for provision of routine care. For the observational study (2<sup>nd</sup> paper), we enrolled 45 participants undergoing HSCT. Thirty-three (73%) participants completed the study with 20 (61%) followed pre and post-transplant (peri-transplant) and 13 (39%) followed after admission for complications. Nineteen (57%) participants experienced 20% or greater decline in HGS during hospitalization. Nine (45%) of the peri-transplant group experienced decline during the conditioning phase. In the peri-transplant group there was a small positive, statistically significant relationship between both HCT and HGB ( $p < .001$ ) and HGS. In the complication group HGS was negatively correlated with ANC ( $p = .02$ ), HGB ( $p = .007$ ) and HCT ( $p = .001$ ). Patients receiving allogeneic HSCT were more likely to exhibit strength loss of  $\geq 20\%$  than those receiving autologous HSCT ( $p = .02$ ). Gender was highly correlated with HGS with males measuring 13.9-20 Kg higher HGS readings than females ( $p < .001$ ). Nurses documented participant's need for assistance with mobility for 8/19 (42%) of participants with  $\geq 20\%$  strength loss as assessed by dynamometry, although this nursing assessment preceded 20% strength decline in 4 participants and was noted

days after the loss in 4 patients. Participants found the testing to be relatively easy, with a mean score of 1.4 (SD .73) on a 5 point scale in the peri-transplant group, and a mean score of 1.8 (SD 1.3) in the complication group (higher scores indicate greater difficulty). Testing of HGS took 7 minutes (SD 1.95) to complete.

**Conclusion:** It is feasible to test HGS in participants who are hospitalized or have oncologic diagnoses in outpatient or inpatient care settings. Based on the literature review, a standardized protocol for HGS measurement in participants undergoing HSCT was developed and used for the pilot study. A majority of participants experienced clinically significant strength decline during HSCT with a subgroup declining during the conditioning phase. Participants who received allogeneic HSCT were more likely to experience clinically important strength loss than those who received an autologous transplant. Nurses failed to note the participant's need for assistance with mobilization a majority of the time. Participants found the testing to be relatively easy to participate in, however data collection was impacted by issues common to hospitalized participants such as nausea, fatigue and feelings of being overwhelmed. This was the first study to our knowledge, to examine HGS daily in participants receiving HSCT. There appears to be a gap between the timing of clinically important decline of strength and nurse recognition of participants' need for assistance with mobility. The daily use of HGS by dynamometry could be an important tool to assist direct care providers in the evaluation of strength in hospitalized patients.

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## **DEDICATION**

To the love of my life, George Sayre: Thank you for telling me that I was smart! Thank you for taking care of Aaliyah every weekend for the last four years so that I could study. Thank you for being the most amazing partner and friend for thirty-two years! I love you!

## **INTRODUCTION**

Despite aggressive fall prevention programs, rates of falls in hospitals have increased from 2.7 falls per thousand patient days in 2001 (Halfon et al., 2001) to 3-5 falls per thousand patient days in 2014 (Oliver et al., 2010). Reporting falls as rates per thousand patient days may not reveal the true impact of these events. It is estimated that hospitalized patients in the United States experience more than one million falls each year and 30% of those falls result in an injury (Oliver et al., 2007; Oliver et al., 2010). The level of injury sustained may be as minor as a cut or severe enough to cause death (The Joint Commission, 2008).

Although lower extremity muscle weakness is a well-known risk factor for falls (Oliver et al.; Currie, 2006), and although new-onset weakness is often a consequence of hospitalization for treatment of acute and/or life-threatening illness, assessment of muscle strength is not standard of care in hospitals. This is despite the availability of validated, performance-based measures of strength, in particular dynamometry (Ali et al., 2008; Beseler et al., 2014; Bohannon, Magasi, Bubela, Wang, & Gershon, 2012). This dissertation research sought to address this critical gap in healthcare quality and safety.

## **BACKGROUND**

### **Falls and Weakness in Patients with Oncological Diagnoses**

Variability in fall rates is seen in hospitalized patients and is related to the primary diagnosis. For example, fall rates on psychogeriatric units have been reported to be quite high, in the range of 16-67 falls per thousand patient days (Oliver et al., 2010). Patients hospitalized for oncological diagnoses are another group that is at increased risk of sustaining a fall compared with other hospitalized patients on medical surgical types of units (6.3 vs. 3.1 per thousand patient days) and are more likely to be injured if they do fall (Fischer et al., 2005). The etiology

for this increased risk of falling is not clearly understood, but may be related to generalized weakness, sarcopenia, sensory impairments and/or medications.

In a study of 164 patients aged 16-68 (median age 60) who presented for hematopoietic stem cell transplant (HSCT), 50.4% were diagnosed with sarcopenia which was defined as “a level of muscle mass that is two standard deviations below sex-specific norms for young adults” prior to receiving treatment (Morishita, et al., 2012, p 3162). Furthermore, when hand grip strength (HGS) was tested, those with sarcopenia were more likely to exhibit decreased muscle strength measured in kilogram force units (kgf) (R HGS with sarcopenia=26.7 kgf, SD 8.0; without sarcopenia=30.4 kgf, SD 10.3; P=0.012) (Morishita, et al., 2012).

Mello, Tanaka & Dulley (2013) conducted a similar study in 18 patients admitted for HSCT. They found that muscle strength was “lower than normal values” when maximal isometric voluntary strength was tested with a handheld dynamometer. The authors used a “normalized ratio of strength values” to control for age, sex and weight patterns, where a ratio of <1 represents strength that is below normal. The participants were weakest in flexion (ratio .66, p=.008) and extension (ratio .84, p=.052) of the knee. Despite this performance on muscle testing, the authors state that the participants “all had good general status and no functional complaints” (p. 726). The authors go on to state, “hematological disease can cause subclinical alterations in motor function, with disturbance of other mechanisms related to the voluntary recruitment of motor units” (p.726.). Given that weakness is a known risk factor for falls, it follows that patients presenting for HSCT may indeed have an increased risk of falls.

## **Fall Risk Assessment Tools**

The Joint Commission requires acute care hospitals to use valid and reliable fall risk assessment tools. Unfortunately, these tools may lack the sensitivity and specificity to identify all patients at risk for a fall. Many fall risk assessment tools include some type of an assessment of muscle strength or mobility. Two of the widely used fall risk assessment tools are the Morse Fall Scale and The Johns Hopkins Fall Risk Assessment Tool.

The Morse Fall Risk Assessment was one of the earliest fall risk assessment tools to be developed and continues to be widely used in hospital settings (Morse, Morse & Tylko, 1987). The tool assigns risk based on scores in six domains; history of falls, secondary diagnosis, ambulatory aids, IV/heparin lock, gait/transferring, and mental status. Total scores range from 0-140 points, with scores of 25-40 indicating a moderate risk of falling, and scores greater than 45 indicating a high risk of falling. Nurses perform a subjective assessment to score the gait/transferring section. Patients who are “normal” or on bed rest are rated as a 0, those who are “weak” are given a score of 10 and those who are “impaired” are scored as a 20 (Morse, et al., 1987). The sensitivity and specificity of the tool are reported to be 78% and 83% respectively with a positive predictive value of 10.3%. (Morse, et al., 1987).

The Johns Hopkins Fall Risk Assessment tool (JHFRAT) was designed to identify fall risk factors in seven domains; age, fall history, mobility, medication, patient equipment (i.e. items that tether patients such as IVs), altered elimination and cognition (Poe, Cvach, Dawson, Straus & Hill, 2007). Total scores range from 0-37 with a score of 6-13 indicating a moderate risk of falling and scores greater than 13 denoting a high fall risk. In the mobility section, the nurse uses subjective assessment to assign 0-2 points for each of the following three questions; “requires assistance or supervision for mobility, transfer or ambulation”, “unsteady gait” and

“visual or auditory impairment affecting mobility”. Neither sensitivity nor specificity of the tool was reported by the developers. A subsequent study of hospitalized patients in Korea found a sensitivity of 62% and specificity of 69% with a positive predictive value of 33.6% (Kim et al., 2011).

Given the sensitivity and specificity of fall risk assessment tools, it is not surprising that many patients who end up falling were assessed as being “not at risk” when they were screened (Williams & Thomas, 2014). Indeed, the limitations of the fall risk screening tools and subjective nature of some elements in the tools can lead to an underestimation of risk.

### **Hand Grip Strength**

Hand grip strength (HGS) testing by handheld dynamometry has been used to explain and predict outcomes in a variety of patient populations including patients undergoing HSCT (de Souza et al., 2012; Morishita et al., 2013; Pidala et al., 2013). Furthermore, a relationship between HGS and measures of lower extremity strength and mobility has been established (Bohannon et al., 2012; Cantarero-Villanueva et al., 2012). Thus, HGS may serve as an inexpensive, non-invasive tool to objectively measure strength in patients undergoing HSCT as well as patients hospitalized for other diagnoses. Identification of muscle weakness could in turn provide an important means of identifying patients at high fall risk while hospitalized.

To date, HGS has been studied in patients presenting for HSCT during the pre-transplant phase (Kramer et al., 2013; Morishita et al., 2013; Pidala et al., 2013), at 1 and 3 months post-transplant (Kramer et al., 2013), after discharge (de Souza et al., 2012) and after the diagnosis of graft vs host diagnosis (median 7.3 mos.) (Pidala et al., 2013). The pattern of HGS over the course of the acute care hospitalization has not been studied. This may have important

implications for providers and nurses as they continually assess patients and design and modify safety plans to prevent a patient fall.

## **PURPOSE**

The purpose of this study was to 1) conduct a systematic literature review to delineate methods, identified challenges and results in studies of HGS by dynamometry in participants who had oncologic diagnoses or were hospitalized for any diagnosis and 2) In a sample of patients undergoing myeloablative hematopoietic stem cell transplant in an inpatient setting: a) describe changes in muscle strength as measured by daily HGS measurements; b) describe relationships between selected laboratory values (Hematocrit [HCT], Hemoglobin [HGB], Absolute Neutrophil Count [ANC] ) and HGS during the course of hospitalization; c) determine feasibility and acceptability of daily HGS measurements; and d) compare relative timing of detection of change in muscle strength by HGS measurement and nursing assessment of the patient's need for assistance with mobility.

## **Content of the Dissertation**

This dissertation is composed of two papers. The first paper summarizes a systematic literature review related to the use of handheld dynamometry to measure HGS in participants that were hospitalized or participants with oncological diagnoses in any care setting.

The second paper presents the results of a pilot study. We measured the HGS of participants, provided they were awake and consented to the test, each day of their hospitalization. Potential mediating variables such as opioid and benzodiazepine medications, laboratory results and physical therapy sessions were considered in the analysis. Participants

rated the difficulty of the testing on a 1-5 Likert scale and researchers noted the length of time needed to complete the assessment.

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## PART ONE: Methods of Grip Strength Measurement in Inpatient and Oncology Settings

### Abstract

**Purpose:** To delineate methods, identified challenges and results in studies of Hand Grip Strength (HGS) using dynamometry in hospitalized participants and those with an oncologic diagnosis and to describe a HGS protocol developed to study participants who were hospitalized during Hematopoietic Stem Cell Transplant (HSCT). **Data Sources:** Published studies were identified related to HGS measurement in hospitalized participants and those with oncologic diagnoses in any care setting. Medline, CINAHL and Web of Science databases were searched. Twenty three relevant articles were located. **Data Synthesis:** Technique and equipment used for measuring HGS is similar but not identical across care settings including positioning, selection of hand for testing, attempts per trial and data included for analysis. Challenges of HGS testing in hospital settings included determining when participants were awake and alert, high percentages of ineligible participants due to complications of treatment, and interruptions in testing for provision of routine care. Testing in participants hospitalized for HSCT was impacted by nausea, emesis and fatigue. **Conclusion:** It is feasible to test HGS in participants who are hospitalized or have oncologic diagnoses in any care setting. A standardized protocol for measurement in this population is proposed based on the literature review. **Implications for Nursing:** Measurement of HGS by dynamometry is inexpensive, non-invasive and may serve as a proxy for strength in hospitalized patients and those with oncologic diagnoses in any care setting. Results of HGS testing may assist nurses in detecting weakness which could guide them in designing safety plans to prevent falls. Measurement of HGS in these populations presents unique challenges and may

require adapted techniques. **Key Words: Hand strength, Grip Strength, Hospitalization, Measurement**

## **Introduction**

The measurement of hand grip strength (HGS) by dynamometry is a standard approach in the evaluation of volitional muscle strength (Bohannon, Peolsson, Massy-Westropp, Desrosiers, & Bear-Lehman, 2006; Roberts et al., 2011). HGS has been used in multiple studies across different populations and care settings to predict and/or explain outcomes such as mortality (Ali et al., 2008; Kilgour et al., 2013), and complications of surgery including immobility (Beseler et al., 2014; Chen, Ho-Chang, Huang, & Hung, 2011; Garonzik-Wang, Govindan, Grinnan, & et al., 2012) as well as to quantify deficits in muscle strength (Ansari, Keaney, Taylor, Burns, & Farrow, 2012; de Souza et al., 2012; Keevil et al., 2013).

## **Purpose**

The purpose of this review is to delineate methods, identified challenges and results in studies of HGS by dynamometry in participants who had oncologic diagnoses or were hospitalized for any diagnosis. This includes protocol details for measurement of HGS such as positioning, number of trials and rest periods for each session as well as selection of data for analysis. Finally, a standardized protocol for the measurement of HGS for those participants who are hospitalized and have an oncology diagnosis will be proposed.

## **Background**

### **Handgrip Strength Studies in Hospitalized Participants**

Patients hospitalized for acute or chronic illness may experience weakness and fatigue as a result of immobility, functional limitations and/or general deconditioning. Several studies have been done in the intensive care unit (ICU) setting to evaluate the utility of grip strength testing in

predicting outcomes such as length of stay (Dourado et al., 2006) and mortality (Ali et al., 2008; Baldwin, Paratz, & Bersten, 2013; Kasotakis et al., 2012; Lee et al., 2012a).

Testing grip strength in the acute care setting poses specific challenges which may not be present in the outpatient setting. Waak, Zaremba & Eikermann (2013) broadly categorize these as; subject cooperation (i.e. attention and arousal states), technical considerations (i.e. timing of the test and fatigability), pharmacological paralysis (i.e. neuromuscular blockade) and regional barriers (i.e. pain or fracture). Although these challenges are described in the ICU population, with the exception of the pharmacological paralysis, these factors may well be present for participants being tested in any acute care setting.

The challenges described above may have a negative impact on the percentage of participants who are eligible to participate in HGS testing as well as the percentage who ultimately complete the study. Keevil et al., (2013) note that more than 40% of the eligible participants who were admitted to the geriatric ward were unable to participate in HGS testing because of “feeling unwell, not able to provide consent or not able to use the dynamometer” (p.156). The provision of routine care may also interrupt measures of grip strength in hospitalized participants. In one study, greater than 80% of the subjects had study related assessments interrupted for routine care (Klepin et al., 2011, p. 1839).

### **Handgrip Strength in Patients with Oncologic Diagnoses**

The use of HGS in participants with oncologic diagnoses has been another area of focus for research. Patients with oncologic diagnoses often experience fatigue and weakness, so an approximate measure of overall strength could provide important information to clinicians. Variable degrees of correlation between HGS and fatigue have been reported by researchers. Stone et al.(2000), conducted a study of 227 participants with a variety of cancers and compared

them with a control group of 98 healthy volunteers. The authors report a low but significant correlation between the Fatigue Severity Scale, (a self-report instrument) and HGS ( $r=-.45$ ,  $p<.001$ ) in the participants with cancer. There was no significant correlation between HGS and the Fatigue Severity Scale in the control group ( $r=.08$ ).

Declines in strength as measured by HGS have also been reported in participants undergoing hematopoietic stem cell transplantation (HSCT) (Kramer et al., 2013). When compared to baseline measurement (pre-transplant), a 10% decline in HGS was found at 1 month post-transplant ( $p=.02$ ) with a return to baseline at 3 months post-transplant ( $p=.3$ ). These results seem to suggest that HGS testing is feasible in the oncology population and may provide valuable insight about functional status.

### **Rationale for Literature Review**

As described above, HGS has been studied in hospitalized participants and in participants with oncologic diagnoses. A systematic review of methodology used in measuring HGS in epidemiologic studies of elderly populations has been completed (Roberts et al., 2011). In that review, the authors focused on different techniques used in the measurement of HGS. They found that there was wide variability in the techniques researchers used in measuring HGS including elements such as positioning and number of attempts. In addition, they reported that although the Jamar hand held dynamometer was used in many studies, it was used incorrectly at times.

To date, there has not been a review published which compares and contrasts different methods used to evaluate this parameter in participants who are hospitalized and/or have an oncologic diagnosis. Given the potential clinical uses of HGS measurement by dynamometry and

the potential challenges in using this instrument in these populations, a literature review is required to determine the methods that have been used specifically in these populations.

### **Methods**

A review of literature was conducted to identify studies for inclusion. The review included a search of the Medline, CINAHL and Web of Science databases. MeSH terms were identified and used to build the search including “hand strength”, “hospitals”, “hospitalization”, and “hospital units”. Other non-mesh terms that were added to the search include the terms “grip strength”, “acute care” and “measurement”. The initial search yielded 118 documents. Criteria for inclusion in the review included observational or randomized controlled trials published within the last 10 years, where dynamometry was used to evaluate HGS in participants who were hospitalized with any diagnosis or participants with oncologic diagnoses in either inpatient or outpatient settings. After applying inclusion criteria and reviewing abstracts for relevance, 23 articles were selected for review (Table 1).

### **Review of Literature**

#### **Population and Setting of Studies**

Seventeen of the selected studies were completed in the hospital setting, including two in an inpatient rehabilitation unit (Ali et al., 2008; Baldwin et al., 2013; Beseler et al., 2014; Chen et al., 2011; Di Monaco et al., 2014; Garcia, Meireles, Fuhr, Donini, & Wazlawik, 2013; Garonzik-Wang et al., 2012; Guerra, Fonseca, Pichel, Restivo, & Amaral, 2015; Kasotakis et al., 2012; Keevil et al., 2013; Kerr et al., 2006; Klepin et al., 2011; Klepin et al., 2013; Lasocki et al., 2014; Lee et al., 2012a; Norman et al., 2010). Ten of the studies included in this review were focused on participants with oncologic diagnoses (Cantarero-Villanueva et al., 2012; Chen et al., 2011; de Souza et al., 2012; Kilgour et al., 2013; Klepin et al., 2013; Kramer et al., 2013; Mello,

Tanaka, & Dulley, 2003; Morishita et al., 2012; Norman et al., 2010; Pidala et al., 2013; Roberts, Syddall, Cooper, & Aihie-Sayer, 2012). Four studies involved participants who were hospitalized for oncologic diagnoses (Chen et al., 2011; Klepin et al., 2011; Klepin et al., 2013; Norman et al., 2010).

### **Recruitment and Retention of Subjects**

The ICU was the setting for four of the studies (Ali et al., 2008; Baldwin et al., 2013; Kasotakis et al., 2012; Lasocki et al., 2014). A study conducted by Baldwin et al., (2013) to validate the use of HGS measurement in the ICU exemplifies some of the challenges researchers encounter when performing HGS testing in hospitalized participants. Of the 189 patients who were screened for inclusion, 18 were enrolled and 17 completed the study. Reasons for exclusion were related to neurological impairment, medical contradictions to strength testing and cognitive or psychological impairments (p. 80). Ali et al., (2008) describe similar issues with recruitment. The researchers focused on patients who had been in the ICU for at least 5 days and had required mechanical ventilation. Of the 1458 participants who met inclusion criteria, 174 were enrolled and 136 ultimately completed the study. Of interest, lack of provider or family support for the research was cited as a reason for exclusion of enrollment in 152 of the participants (p. 262).

Chen et al., (2011) studied participants who presented for esophagectomy as a treatment for esophageal cancer. The study completion rate was higher as compared with those conducted in the ICU by Ali et al., (2008) and Baldwin et al., (2013). Out of the sixty-eight participants that met inclusion criteria, sixty-one were able to complete the study including HGS testing. Of note, participants in the study by Chen et al., (2011) were tested prior to surgery which may have improved completion rates.

Of the studies that were focused on participants with oncologic diagnoses, four were related to participants receiving HSCT (de Souza et al., 2012; Kramer et al., 2013; Morishita et al., 2012; Pidala et al., 2013). Completion rates for these studies ranged from 66% (de Souza et al., 2012) to 100% (Morishita et al., 2012). It is important to note that the study conducted by Morishita et al., (2012) consisted of one HGS measurement in participants who were pre HSCT while de Souza's (2012) design included readings pre and post-transplant.

### **Timing of Grip Strength Measurement**

The timing of the grip strength measurement is an important variable to consider and has the potential to change the outcome of the study depending on the population of interest. Ali et al., (2008) focused on participants who were in the ICU for more than five days. The HGS measurement was taken when participants were "awake and attentive". The researchers used the Richmond Agitation Scale (RASS), a validated tool that measures sedation level in ICU patients to determine timing of the study (Sessler et al., 2002). Lee et al., (2012) describes a similar approach, using the RASS tool and waiting until participants were awake and alert before HGS testing. In contrast, the protocol used by Kasotakis et al., (2012), specified that HGS and strength testing be completed on the day after admission to the Surgical ICU. The authors cite the different timing of HGS measurement as one possible reason their results did not concur with the finding by Ali et al., (2008) that HGS was correlated to manual muscle testing.

The study completed by Cantarero-Villanueva et al., (2012) raises another consideration regarding timing. The authors state that the study measures were completed between 8pm-11pm to avoid influence of the circadian cycle. Depending on the population of interest it is clear that timing of the HGS testing may indeed have impact on the results. In addition to the time of day when testing is completed, researchers must give thoughtful consideration to the timing of the

testing related to other variables such as medical treatments and hospitalization days. The optimal timing of the testing depends on the question of interest i.e. whether the goal is to determine strength at a potential peak or to determine a time of greatest weakness. In addition, daily routines of hospitalized participants should be identified so that the researchers can take these factors into consideration when designing the study.

## **Positioning**

Fourteen of the twenty-three studies included information on how participants were positioned for the measurement of HGS. These descriptions ranged from quite brief, i.e. “modified recumbent” (Baldwin et al., 2013) to detailed information on positioning of feet, hips, knees, arms and wrists (Garcia et al., 2013). In general, studies that were conducted in the inpatient setting included more detailed information on positioning than those conducted in outpatient settings.

### **Body Position**

Six of the studies conducted in the hospital had participants seated for HGS testing (Beseler et al., 2014; Di Monaco et al., 2014; Garcia et al., 2013; Kasotakis et al., 2012; Keevil et al., 2013; Norman et al., 2010). Garcia et al (2013) give the most detail about the seated position, stating that patients had hips and knees at 90 degree angles. Positioning of the participants in the four studies completed in ICU settings was less clear and described as “close to sitting as possible” (Ali et al., 2008; Lee et al., 2012a) or not described at all (Baldwin et al., 2013; Kasotakis et al., 2012; Lasocki et al., 2014). Only one study described participants being tested in the standing position (Chen et al., 2011). This author describes the standing position as the “standard position” although every other study in this review specified that patients were

seated for testing (p.2). Differences in positioning may affect HGS readings and need to be considered when interpreting study findings.

### **Shoulder and Elbow Position**

Six of the studies describe the positioning of the shoulder (Beseler et al., 2014; Di Monaco et al., 2014; Garcia et al., 2013; Keevil et al., 2013; Lee et al., 2012a; Norman et al., 2010) . In each of these studies the shoulder is described as “adducted”.

The position of the elbow is described in nine of the studies (Ali et al., 2008; Beseler et al., 2014; Chen et al., 2011; Di Monaco et al., 2014; Garcia et al., 2013; Kasotakis et al., 2012; Keevil et al., 2013; Lee et al., 2012a; Norman et al., 2010) and is noted to be flexed at a 90 degree angle in most of the studies. Only one study (Chen et al., 2011) describes the elbow as being “extended” (p.2).

Specificity around positioning is important and needs to be held constant as it may affect results of HGS testing. Roberts et al., (2011) state that there may be variability in HGS readings related to posture and degree of flexion and support of the elbow during testing. Utilizing a standardized protocol, adhered to by each team member will increase the accuracy of the readings. In addition, inclusion of these details in the dissemination of the research enhances the ability of future researchers to replicate and possibly validate the findings.

### **Hand Chosen for Testing**

The majority of studies refer to the selection of hand for strength testing. This may be important as readings can vary depending on whether the dominant or non-dominant hand is tested. In a study of 60 healthy adults, Ozcan et al., (2004) found that participants with right hand dominance demonstrated significantly higher HGS in the dominant hand compared with the non-

dominant hand ( $p < .05$ ). Those with left hand dominance did not demonstrate significant difference between the dominant and non-dominant hands ( $p > .05$ ).

Eleven of the studies included bilateral testing (Baldwin et al., 2013; Beseler et al., 2014; de Souza et al., 2012; Keevil et al., 2013; Kerr et al., 2006; Klepin et al., 2011; Klepin et al., 2013; Kramer et al., 2013; Lasocki et al., 2014; Morishita et al., 2012; Roberts et al., 2012) while others selected the dominant hand for testing, (Ali et al., 2008; Chen et al., 2011; Kasotakis et al., 2012; Kilgour et al., 2013; Lee et al., 2012a; Pidala et al., 2013). Two of the studies used clinical indicators to determine which hand would be tested including the affected side for breast cancer patients (Cantarero-Villanueva et al., 2012) and the side without intravenous access (Garcia et al., 2013). Valid results can be obtained whether the dominant, non-dominant or both hand(s) is (are) used as long as that choice remains constant during the repeated measurements. Prior surgeries, injuries or other medical conditions such as stroke may also decrease the grip strength of the affected side.

### **Number of attempts and rest periods**

The number of attempts per trial is included in all but one of the studies involving participants who were hospitalized. Each of these studies describes three attempts per trial. Garcia et al., (2013) allowed one “pre-test...allowing the patient to become familiar with the apparatus” (p.51). There was only one study that reported including two trials and no rationale was provided for this (Cantarero-Villanueva et al., 2012).

Rest periods between attempts were specified in six of the studies (Cantarero-Villanueva et al., 2012; de Souza et al., 2012; Guerra et al., 2015; Kasotakis et al., 2012; Kilgour et al., 2013; Norman et al., 2010). These ranged from a “small interval” (de Souza et al., 2012) to 3 minutes (Cantarero-Villanueva et al., 2012). The number of attempts and the rest period between

attempts requires thoughtful consideration during the design of the study. Participants may need more than one attempt to become familiar with the dynamometer and achieve their maximum HGS. Watanabe et al. (2005) found that repeated testing of HGS without rest intervals resulted in gradually declining HGS measurements. When participants were given 1 minute rest periods between tests, there was no decline in strength. Participant burden and time required to perform testing are other factors to consider when deciding the number of trials and rest intervals to include. Based on this review, it seems prudent to include at least two trials with a rest interval in a study designed to evaluate HGS.

### **Data included for analysis**

As described above, the majority of studies collected several HGS readings. In general, researchers used the best or highest reading of HGS for analysis (Ali et al., 2008; Di Monaco et al., 2014; Garcia et al., 2013; Kasotakis et al., 2012; Keevil et al., 2013; Kerr et al., 2006; Lasocki et al., 2014; Lee et al., 2012a; Norman et al., 2010; Roberts et al., 2012). Klepin, et al., (2011) state that the “best performance of three trials was selected for each hand, with averages of the left and right hand used in analyses” (p.1838). Baldwin et al., (2013) also used an averaged score of the two hands and took an additional step of log transforming the data for “reliability analysis” (p.79).

The decision of which data to include depends on the research question that is posed. For example, if the research question is centered on the maximal volitional force that a participant can generate, then it seems reasonable to include only the highest reading for analysis.

Alternatively, if the research question is related to functional status, perhaps an average of all readings would yield better information as participants may not exert maximum effort at all times.

In summary, measurement protocols for participants who are hospitalized require special consideration of factors such as timing, positioning and data to include in analyses that are most appropriate for the acute care setting. For example, having the participant remain in the bed with the head in the most upright position can be a reasonable surrogate for being seated in a chair. In terms of timing, researchers must balance the data collection requirements of the study with the needs of participants who are acutely ill. This may require a flexible approach in terms of time of the day when HGS is collected. Participants who are not feeling well will be more likely to decline testing, thus researchers should target times during hospitalization when participants are awake, alert and ready to participate.

### **Measurement Error**

Test-re-test reliability is of some concern in the measurement of HGS by dynamometry, particularly if more than one person is collecting data. As discussed above, there are many variables such as positioning, number of trials and rest intervals that can impact results of HGS testing. Baldwin, et al., (2013) designed a study with the primary aim of determining test-re-test reliability in testing of HGS in participants who were critically ill. The design also included a control group of “healthy subjects”. A second examiner was utilized for the re-test measures of peripheral strength including HGS about 2-3 hours after the first set of measurements. The reported agreement of the two examiners was .95 (95% CI 0.848, 0.987,  $p < .001$ ) and .96 (95% CI 0.837, 0.991,  $p < .001$ ) for the left and right hands respectively. Although the inter-rater reliability was high, the authors recommend using one examiner and the dominant hand to further enhance the reliability and to decrease errors of HGS and peripheral muscle testing (p. 85). This study also found that participants in the ICU needed more time to generate peak force (4.35 seconds SD 1.05) compared with the healthy controls who produced peak forces at 3.75

(SD 0.77seconds,  $p \leq .001$ ). This may be of greater importance in the ICU setting, as the participants were much weaker than in the oncology settings.

## Results

### Outcomes of HGS Studies

The studies reviewed focused on many outcomes both predictive and associative. Mortality was the outcome of interest in several of the studies including two that were conducted in the ICU. Ali et al (2008) studied the association between HGS and mortality in the ICU setting. The authors found an inverse relationship between HGS and mortality with participants below threshold having the highest mortality risk (OR 4.5 95% CI 1.5, 13.6,  $p=.007$ ). Kasotakis et al., (2012), as part of a validation of the Surgical Intensive Care Unit Optimal Mobility Score (SOMS), investigated whether HGS was predictive of LOS in the ICU as well as whether HGS was predictive of mortality. The authors found that HGS was not predictive for length of stay ( $p=.5$ ) or mortality ( $p=.19$ ). Of note, the SOMS was predictive of mortality ( $p=.001$ ) and HGS was correlated with the SOMS score ( $r = .51$ ;  $p= .008$ ).

Pidala et al., (2013) also studied the relationship between HGS and mortality amongst participants with chronic Graft vs. Host Disease. In this study, HGS was not associated with overall survival (.95; 95% CI.999, .983;  $p=1.017$ ). The study by Kilgour et al (2013) focused on HGS as a predictor of survival in cancer survivors. In this study the authors reported that those with HGS in the 25<sup>th</sup> percentile range had a mortality HR of 1.96(95% CI 1.26, 3.04,  $p<.01$ ) and those with HGS <10<sup>th</sup> percentile had an HR of 3.2 (95%CI 2.0, 5.1  $p<.001$ ) compared to those with strength >50<sup>th</sup> percentile.

HGS has also been used in the study of physical and emotional functioning. Cantarero-Villanueva, et al., (2012), focused on the relationship between HGS and measures of physical

function in breast cancer survivors. The study found variable levels of correlation ranging from a fair association between HGS and fatigue (0.36,  $p < .001$ ) to a moderate association between HGS and the static trunk curl (0.519,  $p < .001$ ).

Other studies have focused on the relationship between HGS and hospital length of stay and discharge destination. In a study of older medical inpatients in Malaysia, Keevil et al., (2013), examined the relationship between HGS and the likelihood of being discharged to the participant's usual residence. Interestingly, the hazard ratio was modeled as the chance of being discharged to the participant's usual residence. The study found that each 1 kg increase in grip strength was associated with a hazard ratio (HR) (being discharged to usual residence) of 1.05 (95% CI 1.00, 1.09;  $p = 0.03$ ). Roberts et al., (2012) found similar results in their study of older participants admitted for rehabilitation. The HR of being discharged to the participant's usual residence when adjusted for HGS was 1.05 (95% CI 0.99; 1.11,  $p = 0.14$ ) and did not reach statistical significance. However, when adjusted for age and size and analyzed by gender subgroups, the HR was statistically significant at 1.09 for every kg increase in HGS (95% CI 1.01, 1.17,  $p = .02$ ).

### **Relationship Between Hand Grip Strength and Lower Body/Global Strength**

Three of the studies included in this review found correlations between HGS and other measures of physical function. Cantarero-Villanueva et al., (2012) found a fair correlation between HGS and two widely used functional tests; the timed Sit to Stand test (-0.302,  $p = 0.003$ ) and the 6 minute walk test (0.334;  $p = 0.002$ ). Similarly, Kramer et al., (2013), found correlation between HGS and knee extensor and foot dorsiflexion strength in a validation study with data collected pre HSCT (knee=.6,  $p < .01$ ; foot =.7,  $p < .01$ ) and at 1 month (knee=.6,  $p < .01$ ; foot=.6,  $p < .01$ ) and 3 months (knee=.6,  $p < .001$ ; foot=.4,  $p < .001$ ) post-transplant. Norman et al.,

also found that HGS was highly correlated with knee extension strength ( $r = 0.752$ ,  $p < 0.001$ ). Thus, there is growing evidence that HGS is correlated with lower extremity strength as well as with overall strength.

### **Summary of Results**

HGS has been found to be useful in describing and predicting outcomes in many, but not all settings. Of the twenty-three studies included in this review, sixteen found correlations between HGS and the outcome of interest. Five of the studies did not demonstrate correlation of HGS and the designated outcome (Garcia et al., 2013; Kasotakis et al., 2012; Lasocki et al., 2014; Lee et al., 2012a; Pidala et al., 2013) and two of the studies used HGS as just one element of a more comprehensive battery of tests (Klepin et al., 2011; Klepin et al., 2013).

### **Recommendation for Measurement of Handgrip Strength Protocol**

Assessing HGS in participants who are hospitalized and/or have oncologic diagnoses presents many unique challenges. Standard protocols that have been used in community dwelling participants may well need to be adapted to these unique populations. Based on this comprehensive review of literature, the following protocol adaptations for the study of participants who are hospitalized are recommended (Appendix A).

#### **Timing**

As noted in this review, the timing of the HGS measurement can have impact on data collection and the results. Measurements should be timed so that there is a high likelihood that patients will be able to fully participate with minimum impact on hospital staff. Conducting measurements during day time hours is recommended. The researcher needs to be flexible and may need to return at a later time if the participants are away for a test, receiving care from a member of the team, napping or feeling unwell.

### **Body Position**

The participant who is hospitalized will remain in the bed, with the head of the bed in the most upright position possible to the degree it is tolerated for testing. The participant will be assisted to sit as upright as possible with hips back toward the head of the bed. The legs and feet will be on the bed. This will allow for standardization of testing across many participants, some of whom may not feel well enough to sit at the side of the bed or in a chair. Including details about body position adds more clarity than a description of “sitting as upright as possible” which was seen in 2 of the studies in the ICU (Ali et al., 2008; Lee et al., 2012a)

### **Shoulder and Elbow**

The shoulder will be adducted and held close to the body. This is based on the fact that this position was described by almost all of the studies in this review. The elbow will be held at a 90 degree angle. The elbow at 90 degrees was the preferred position for the vast majority of the studies reviewed. Given the acute care setting-an adaptation may need to be made to allow for proper positioning of the elbow. Pillows may be placed under the arm as needed to achieve the correct elbow position. The elbow will be supported during the testing because an unsupported elbow can dramatically change the results of testing (Roberts et al., 2011).

### **Hand Chosen for Testing**

HGS will be tested on each hand during every episode of testing. This will control for potential confounders such as arthritis, injury or IV access. The patient will be asked whether one hand is considered dominant and that will be recorded by the researcher. Nine of the studies in this review used both hands for HGS testing. This appears to allow for the most robust data collection and analysis.

### **Number of Attempts**

The participant will be asked to perform HGS testing a total of three times on each hand. No pre-test for familiarization will be given. A one minute rest period will be given between each attempt. This will be important to ensure that fatigue is minimized so that the best effort will be demonstrated and can be recorded. Most of the studies reviewed allowed for repeated attempts in each trial. A standardized and specified rest period will decrease the likelihood of spurious results.

### **Time to Reach Peak Force**

Participants will be asked to hold the maximum grip for 4 seconds to ensure adequate time to reach threshold performance. This recommendation is based on the study by Baldwin et al., (2013) which found that allowing extra time to achieve peak force was helpful in overcoming errors in measurement.

### **Data Included for Analysis**

The best or highest HGS reading for each hand will be used for analysis. Right and left hands will be analyzed separately with notation of hand dominance. The decision to analyze the data this way is related to the proposed research question which is “What is the pattern or trend of HGS for participants hospitalized for HSCT”.

### **Implications for Nursing**

Ensuring that patients are safe and free from harm is a primary consideration of every nurse providing care in the acute care setting. Falls with injury are one of the most common adverse events occurring in hospitals. The outcomes from a fall may be a minor to severe physical injury as well as a subsequent fear of falling.

Currently, nurses evaluate strength and the need for mobility assistance using subjective measures, primarily observation. Clinically important changes in strength may not be detected by subjective observation. The use of HGS offers nurses and other clinicians the ability to trend patient's strength over time and to intervene when a clinically important decline is detected. Fall prevention interventions can then be initiated which may include assisted mobility, use of a gait belt, fall mats and possibly a bed alarm.

Further studies involving HGS in participants receiving HSCT will advance nursing science as nurse researchers begin to understand patterns of strength that occur within this intense treatment period. The patient's need for autonomy and the fact that patients do not always recognize their own declining strength may make them less likely to heed nursing advice to ask for assistance when mobilizing. In addition, nurses may decide incorrectly that patients are safe to mobilize independently. The use of HGS by dynamometry provides an objective measure of strength that nurses can discuss with their patients. This objective measure has the potential to provide data that will inform the nurse's assessment of patients' ability to mobilize independently as well as the patient's ultimate decision to ask for assistance.

### **Conclusion**

As demonstrated in this review the measurement of HGS to explain and predict outcome variables has been shown to be effective in a variety of settings. It is an attractive option as an approximation of global strength in patients who are hospitalized for any disease process and for patients with oncologic diagnoses, regardless of their care setting. Many features of evaluation of HGS by dynamometry contribute to its' utility; it is non-invasive, inexpensive and does not appear to impose undue burden on the participant or the researcher. The statistical analysis of HGS readings can be performed in a variety of ways depending on the specific research question.

Although HGS has been studied in participants hospitalized for HSCT, to date, there has been no study that has examined the pattern of grip strength over the course of hospitalization in this population. Based on this review, there is a clear recommendation for the structure of a protocol to measure HGS. In addition, no insurmountable barriers to this testing for hospitalized participants have been identified in the literature. In summary, this is an exciting area of nursing research which may lead to improved detection of strength loss and allow for the development of targeted fall prevention plans. Thus, it is recommended that a pilot study be conducted to determine patterns of strength in participants receiving HSCT and to evaluate the feasibility and acceptability of daily HGS testing.

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**Table 1. List of Studies in the Systematic Review (Listed Alphabetically)**

<b>Author</b>	<b>Design</b>	<b>Sample</b>	<b>Hand Selection</b>	<b>Position</b>	<b>Number of attempts</b>
Ali et al., (2008)	Prospective cohort; Predictive	Medical ICU patients N=136	Dom*	Close to sitting Elbows at 90 °	3 each day x 2 days
Baldwin et al., (2013)	Repeated measures	Mixed ICU patients N=17	Bilat**	Modified recumbent	3x (2 on day one and 1 on subsequent day)
Beseler et al., (2014)	Prospective, Observational	Inpatients who were bedridden N=50	Bilat**	Seated or in a semi-seated position, Shoulder adducted and neutrally rotated, Elbow flexed at 90° forearm in a neutral position, Wrist between 0° and 30° dorsiflexion and between 0° and 15° ulnar deviation.	3 trials One at baseline and one after 4 week training or achievement of ambulation
Cantarero-Villanueva et al.,(2012)	Cross-Sectional	Breast cancer survivors N=95 Age-18-75	Affected side	Not described	2 trials with 3 min rest between
Chen, et al., (2011)	Prospective observational	Patients presenting for esophagectomy for esophageal cancer N=61 Age-34-83	Dom*	Standing position, upper limb relaxed down to the sides of the body, palm towards the torso. Elbow extended	At least 3 times several days pre-op

**Table 1. List of Studies in Systematic Review-Continued**

<b>Author</b>	<b>Design</b>	<b>Sample</b>	<b>Hand Selection</b>	<b>Position</b>	<b>Number of attempts</b>
deSouza et al., (2012)	Prospective	Stem cell transplant patients N=50 Age-24-67	Bilat**	Not described	3 trials for each hand small rest between
Di Monaco et al., (2014)	Observational	Women with hip fracture admitted to rehab hospital N=123	Non-dominant	Sitting position shoulder adducted and neutrally rotated, elbow flexed at 90°, forearm in the neutral position, and wrists between 0° and 30° of flexion and between 0° and 15° of ulnar deviation	Best of 3 attempts
Garcia et al., (2013)	Cross sectional	Hospitalized patients N=118 Age-19-85	Side without vascular access	Seated, hips and knees at 90° of flexion, adducted shoulder close to the trunk, flexed elbow at 90 °	1 pretest trial 3 measurement trials

**Table 1. List of Studies in Systematic Review-Continued**

Author	Design	Sample	Hand Selection	Position	Number of attempts
Garonzik-Wang et al.,(2012)	Prospective	Kidney Transplant patients N=183 Mean Age 53(SD-14)	Not described	Not described	Not described
Guerra et al.,(2013)	Cross sectional	Hospitalized patients N=688 Age 18-91	Non Dominant	Not described	3 trials 1 minute rest interval
Kasotakis et al., (2012)	Prospective single center cohort	Surgical ICU N=113 Age-18-93	Dom*	Sitting upright, elbows at 90 °	3 trials 1 minute rest interval
Keevil et al.,(2013)	Prospective cohort	Patients admitted to geriatric ward N=80 Mean age 80.6 male 77.8 female	Bilat**	sitting with shoulder adducted and elbow flexed to 90 °.	3 trials on each arm
Kerr et al., (2006)	Prospective cohort	Older patients admitted to Medical Admissions Unit N=120 Median age=83.7	Bilat**	Not described	3 trials on each side
Kilgour et al., (2013)	Prospective	Patients with non-small cell lung, pancreatic or Gastrointestinal cancer N=203 Age-64.3(SD 12.8)	Dom*	Seated, feet touching ground Test arm at 90 ° on arm rest	1-2 introductory trials to familiarize subject with technique Then 3 trials with 1 minute rest interval
Klepin et al., (2011)	Prospective Observational Cohort	Inpatient leukemia unit N=54 Age 60+	Bilat**	Not described	3 trials

**Table 1. List of Studies in Systematic Review-Continued**

<b>Author</b>	<b>Design</b>	<b>Sample</b>	<b>Hand Selection</b>	<b>Position</b>	<b>Number of attempts</b>
Klepin et al., (2013)	Prospective Cohort	Inpatients with leukemia N=74 Mean age-70(SD 6.4)	Bilat**	Not described	Not described
Kramer et al., (2013)	Prospective repeated measures	Stem Cell transplant N=40 Age-16-69	Bilat**	Elbow at 90 ° Wrist and arm in neutral position	3 trials
Lasocki et al.,(2014)	Prospective observational	ICU patient N=107 Mean age-59-64 (SD 18.4)	Bilat**	Not Described	3 trials
Lee et al., (2012)	Prospective observational	Surgical ICU N=95 Age- Mean 61.2(SD 18.3)	Dom*	Sitting upright as possible Shoulder in neutral position Elbow 90 °	3 trials
Morishita et al., (2012)	Prospective observational	Stem cell transplant N=164 Age 16-68	Bilat**	Not described	Not described
Norman et al., (2010)	Prospective Cross sectional Observational	Patients admitted for cancer N=189 Mean age 60.8(SD 12.7)	Non-dominant	Seated with shoulder adducted and forearm neutrally rotated, elbow flexed to 90 ° forearm and wrist in neutral position	3 trials with 30 second rest interval

**Table 1. List of Studies in Systematic Review-Continued**

<b>Author</b>	<b>Design</b>	<b>Sample</b>	<b>Hand Selection</b>	<b>Position</b>	<b>Number of attempts</b>
Pidala et al., (2013)	Multicenter Observational Cohort	Stem cell transplant with chronic GVHD*** N=584 Age-2-79	Dom*	Not described	3 trials
Roberts et al., (2012)	Prospective Observational	Elderly patients admitted for rehab N=101 Age>70	Bilat**	Refers to “standard protocol”	3 trials

\*Dominant \*\*Bilateral \*\*\*Graft vs. Host Disease

## **PART TWO: Patterns of Hand Grip Strength and Detection of Strength Loss in Patients Undergoing Hematopoietic Stem Cell Transplantation: A Pilot Study**

### **Abstract**

**Background:** Patients hospitalized for oncological diagnoses are at increased risk for falls and falls with injury compared with patients on medical surgical units (Fischer et al., 2005). Although lower extremity muscle weakness is a well-known risk factor for falls (Currie, 2006; Oliver et al., 2010), and although new-onset weakness is often a consequence of hospitalization for treatment of acute and/or life-threatening illness, assessment of muscle strength is not standard of care in hospitals. Hand grip strength (HGS) by dynamometry has been used to evaluate functional strength (Cantarero-Villanueva et al., 2012). **Purposes:** The purposes of this study were to 1) describe changes in muscle strength as measured by daily HGS measurements; 2) describe relationships between selected laboratory values (hematocrit [HCT], hemoglobin [HGB], absolute neutrophil count [ANC]) and HGS during the course of hospitalization; 3) determine feasibility and acceptability of daily HGS measurements; and 4) compare relative timing of detection of change in muscle strength by HGS measurement and nursing assessment of the patient's need for assistance with mobility in participants undergoing myeloablative hematopoietic stem cell transplant (HSCT) in an inpatient setting. **Methods:** Prospective, repeated measures design to study participants hospitalized for HSCT. HGS was measured on admission and daily until discharge from the hospital or study withdrawal. Medications (opioid, benzodiazepine), physical therapy and laboratory measures of ANC, HGB and HCT were recorded, as was nurse assessment of mobility. A Likert-scaled single survey item was used to assess acceptability of HGS testing to study participants. Feasibility of the testing (i.e., daily HGS measurement with dynamometer) was assessed based on time required to complete the HGS testing and degree of difficulty of using the dynamometer. **Results:** Forty-five participants

enrolled in the study; thirty-three (73%) completed the study. Twenty (61%) were followed pre and post-transplant (peri-transplant) and thirteen (39%) were followed after admission for complications. Nineteen (57%) participants experienced 20% or greater decline in HGS during hospitalization. Nine (45%) of the peri-transplant group experienced decline during the conditioning phase. Male participants had significantly higher levels of strength in both the peri-transplant and complication groups ( $p < .001$ ). Univariate analyses in the peri-transplant group demonstrated a small positive, statistically significant relationship between gender, HCT and HGB ( $p < .001$ ) and HGS. Age, gender and HGB remained significant in the multivariate model ( $p = .001$ ). In the complication group HGS was negatively correlated with ANC ( $p = .02$ ), HGB ( $p = .007$ ) and HCT ( $p = .004$ ). Age and gender remained significant in the multivariate model ( $p = .02$ ). Those receiving allogeneic HSCT were more likely to experience clinically important strength loss than those receiving autologous transplants ( $p = .02$ ). Nurses documented participants need for mobility assistance for 8/19 (42%) of participants with 20% strength loss. Participants found the testing to be relatively easy, with the peri-transplant group scoring it 1.4 (SD .43) and complication group scoring 1.8 (SD 1.3) on a 5 point difficulty scale. HGS testing took 7.15 (SD 1.95) minutes to complete. Research assistants reported that the dynamometer was easy to use. **Conclusion:** A majority of participants experienced strength decline during HSCT with a subgroup declining during the conditioning phase. There was a positive relationship between HGS and HGB and HCT in participants admitted for conditioning for HSCT. Nurses failed to note participant's need for assistance with mobility the majority of time, despite clinically important strength loss. Participants and researchers found the testing to be relatively easy to perform.

## **Introduction**

According to the Joint Commission, accidental falls continue to be one of the most commonly reported adverse events experienced by patients who are hospitalized (The Joint Commission, 2014). Despite aggressive fall prevention programs, rates of falls in hospitals increased from 2.7 falls per thousand patient days in 2001 (Halfon et al., 2001) to 3.4 falls per thousand patient days in 2011 (Staggs, Mion, & Shorr, 2014).

Patients hospitalized for oncological diagnoses are at increased risk of sustaining a fall compared with other hospitalized patients on medical surgical types of units (6.3 vs. 3.1 per thousand patient days) and are more likely to be injured if they do fall (Fischer et al., 2005). The etiology for this increased risk of falling is not clearly understood, but may be related to generalized weakness, sarcopenia, sensory impairments and/or medications. Although lower extremity muscle weakness is a well-known risk factor for falls (Currie, 2006; Oliver et al., 2010), and although new-onset weakness is often a consequence of hospitalization for treatment of acute and/or life-threatening illness, assessment of muscle strength is not standard of care in hospitals. This is despite the availability of validated, performance-based measures of strength, in particular dynamometry (Ali et al., 2008; Beseler et al., 2014; Bohannon et al., 2012).

## **Background**

### **Weakness in Patients Undergoing HSCT**

There is evidence that patients may already have mild weakness when they present for Hematopoietic Stem Cell Transplantation (HSCT), although the change may be imperceptible to the patient (Mello et al., 2003). In their study of fifty-six patients receiving HSCT (mean age of 43.9 [SD 11]), White et al., (2005) found that Hand Grip Strength (HGS) was “reduced to less than 80% predicted in 39% of subjects and less than 60% predicted in 15% of subjects” prior to

transplant. Similarly, 58% of subjects in this study performed the six minute walk test at less than 80% predicted distance.

Declines in strength as measured by HGS also occur during the course of HSCT. Kramer et al., (2013) studied 40 patients who were treated with HSCT. When compared to baseline measurement (pre-transplant), a 10% decline in HGS was found at 1 month post-transplant ( $p=.02$ ) with a return to baseline at 3 months post-transplant ( $p=.3$ ). Of interest, HGS was not correlated to the 2 minute walk test (2MWT) at the baseline measurement ( $r=.1$ ,  $p>.05$ ) but was correlated at 1 month ( $r=.5$ ,  $p=.05$ ) and 3 months ( $r=.6$ ,  $p=.05$ ). One explanation for this variable correlation between baseline and post-transplant measures is that the study was designed to evaluate the effects of graft vs. host disease on the physical measures of HGS and 2MWT. This complication was not present at the baseline measurement but was ultimately experienced by about a third of the participants. In addition, the study had a relatively small sample of twenty-seven participants which may have skewed the results.

### **Limitations of Fall Risk Assessment in Patients Undergoing HSCT**

The Joint Commission has designated fall prevention as a National Patient Safety Goal and has mandated the use of a standardized, validated risk assessment for every hospitalized patient as one of the expected elements of performance needed to achieve accreditation. The subjective nature of some elements of fall risk screening tools can lead to an underestimation of risk. In a study of 25,000 falls in academic medical centers, the authors note that 88% of the patients who fell had been screened for risk prior to the fall. As many as 17% of those who fell had been deemed to be not at risk (Williams, Szekendi, & Thomas, 2014).

The conventional wisdom that weights confusion and age as risk factors for falls may actually serve to confound fall risk assessment in patients undergoing HSCT (Tzeng & Yin, 2013). These patients tend to be younger than the general hospitalized population and are rarely confused.

### **Hand Grip Strength**

Hand grip as assessed by dynamometry is a well-established physiologic measure of muscle strength and has been used in a variety of settings (Ali et al., 2008; Bohannon et al., 2012; Cantarero-Villanueva et al., 2012; Kramer et al., 2013). Normed HGS values have been published that stratify strength by age and gender, thus allowing for easy comparisons amongst subjects (Mathiowetz et al., 1985). There is evidence of a positive correlation between HGS and tests of mobility, such as the two and six minute walk ( $r=.334$ ,  $p=.002$ ) and with functional strength as determined by the Sit to Stand test ( $r=.330$ ,  $p=.003$ ) as well as measures of manual muscle (lower extremity) strength such as knee extension ( $r=.56-.68$ ,  $p<.001$ ) (Bohannon, Magasi, Bubela, Wang, & Gershon, 2012; Cantarero-Villanueva, et al., 2012). Thus, HGS may represent a non-invasive, inexpensive and objective measure that can serve as a proxy for global functional strength.

Research has been done to establish the minimum clinically important difference (MCID) for HGS. In a study of 50 patients who had sustained a distal radius fracture and subsequent volar locking plate fixation, the MCID was found to be a decrease of 6.25 kg (19%) (Kim, Park, & Shin, 2014). This was calculated by correlating HGS changes with patient subjective report of grip in addition to ensuring that the expected standard error in management was accounted for.

Lang et al., (2008), conducted a similar study in patients who had experienced a stroke. Strength testing of the upper extremity, including grip strength was performed at days 9 and 26

post-stroke. Patients were asked to rate their perception of improvement at each time period (Lang, Edwards, Birkenmeier, & Dromerick, 2008). The authors found that a change in grip strength of 5.0 and 6.2 kg for the affected dominant and non-dominant sides respectively represented the MCID.

### **Research Gap**

Previous studies in participants undergoing HSCT have assessed HGS pre-transplant (Kramer et al., 2013; Morishita et al., 2012; Pidala et al., 2013), at 1 and 3 months after transplant (Kramer et al., 2013), “after discharge” (de Souza et al., 2012) and after the diagnosis of graft vs. host disease (median 7.3 months post-transplant) (Pidala et al., 2013). The pattern and timing of HGS changes over the course of hospitalization for a participant undergoing HSCT is not known. This is important to establish, as changes in HGS over time may be reflective of change in functional status. Declines in functional status may increase the risk of falls and thus timely, accurate assessment is important as fall prevention plans are being developed and implemented.

In addition, patients receive different types of stem cell transplants; allogeneic (from a donor) or autologous (patient’s cells are treated and returned). Those receiving allogeneic HSCT often have more aggressive disease and receive stronger doses of chemotherapy and radiation therapy in their conditioning regimen. de Souza (2012) compared HGS between participants receiving allogeneic vs. autologous HSCT at the time of admission for HSCT, and found no significant difference  $p=.61$ ). No study has been done that compares these two groups throughout hospitalization.

The relationship between the nurse’s subjective determination of a patient’s ability to mobilize independently and HGS has not been studied to date. A study is indicated to examine

whether use of an objective measure of strength (HGS) may be more sensitive to changes in strength than a nurse's subjective assessment.

Furthermore, there has been limited study of laboratory values related to HGS in patients receiving HSCT. Pidala et al., (2013) included platelet counts at the time of enrollment, de Souza et al., (2012), included engraftment of neutrophils and platelets as an outcome measure and Morishita et al., (2012) collected baseline data on hemoglobin (HGB). No studies to date in this population have examined the relationship between HGS and absolute neutrophil count (ANC), HGB or hematocrit (HCT).

### **Objectives**

The objectives of the study in a sample of participants undergoing myeloablative hematopoietic stem cell transplant in an inpatient setting were thus to: 1) describe changes in muscle strength as measured by daily HGS measurements; 2) describe relationships between selected laboratory values ( [HCT], [HGB], [ANC]) and HGS during the course of hospitalization; 3) determine feasibility and acceptability of daily HGS measurements; and 4) compare relative timing of detection of change in muscle strength by HGS measurement and nursing assessment of the patient's need for assistance with mobility.

### **Methods**

#### **Design and Setting**

This prospective, repeated measures study utilized a within subject design. The setting was two inpatient units specializing in the care of patients undergoing HSCT. These units are part of a large quaternary academic medical center within a designated National Comprehensive Cancer Center Network.

## **Participant Recruitment**

After receiving Institutional Review Board approval, patients presenting to an academic medical center for their first myeloablative HSCT or being admitted within 20 days of HSCT for complications of HSCT were approached for enrollment. Participants were >18 years of age and were able to speak, understand and read English. A maximum of 7 participants were enrolled at any one time. Participants were excluded if they required droplet isolation or intensive care treatment.

## **Measures**

### **Demographics**

Demographic information collected included age, gender, hand dominance, transplant type (allogeneic vs autologous) diagnosis and date of diagnosis.

### **HGS by dynamometry**

Prior to data collection, research assistants completed a competency validation with a patient volunteer. HGS was tested using a Jamar 200 KG Hydraulic Handheld dynamometer. Participants were tested at the time of enrollment. Testing was then conducted each day of the hospitalization, provided participants were awake at the time of testing and agreed to proceed. Participants were positioned with their legs and feet on the bed and the head of the bed in the most upright position possible. The elbow was flexed at a 90 degree angle and the shoulder was adducted. Each hand was tested 3 times with the dominate hand tested first. Participants were asked to hold the maximum torque for 4 seconds. A 1 minute rest period was given between tests (Appendix A).

### **Clinical Data**

The nurse assessment from the mobility section of the Johns Hopkins Fall Risk Assessment Tool (JHFRAT) (Poe, Cvach, Dawson, Straus, & Hill, 2007), which is completed

every 12 hours and charted in the electronic medical record (EMR), was abstracted. This included nurse response to the following parameters; “requires assistance or supervision for mobility, transfer or ambulation” and “unsteady gait”. Data were collected on each day that HGS was measured. The assessment that was most proximate to the time of HGS testing was abstracted.

Abstracted laboratory data included HGB, HCT and ANC as well as any blood transfusions that occurred. These data were abstracted for each day the HGS was measured. Use of benzodiazepines and opioids within 12 hours of the testing time was also recorded on each day of HGS measurement.

Information regarding physical therapy intervention within 24 hours of each HGS testing was abstracted from the EMR from the clinical notes section.

### **HGS Feasibility Survey**

A simple Likert-scaled survey tool was administered at the conclusion of each HGS testing session. The survey was administered verbally with the researcher asking the question: “on a scale of 1 to 5, with 5 being very difficult, how difficult was it for you to participate in the Hand Grip Strength testing today”?

### **Statistical Analysis**

Stata 12.1 software was used for all statistical analyses (Stata Corp, 2011). Descriptive statistics were used to evaluate each participant’s pattern of strength over the course of the hospitalization. Given the different number of data points in each group, subgroup analysis of the peri-transplant and complication groups was conducted. A threshold for clinically significant change in HGS was set a priori at 20% per recommendations by Kim et al., (2014) cited above.

After determining that the variables HGS, HCT, HGB and ANC in the peri-transplant group were non-linear across the transplant continuum, we divided the data into two groups; day

-7 to day 0, representing the pre-transplant phase and day 1-8 representing the post-transplant phase. Variables were linear when examined at these time points. We then ran univariate multilevel analyses examining the relationship between HGS and each of the following independent variables; transplant day, age, gender, transplant type (allogenic vs. autologous) HCT, HGB and ANC, controlling for transfusion, in the peri-transplant group for days -7 to 0 and for days 1-8. Given the wide range of ANC readings (0-10,000) we transformed the data by dividing by 500 to better see effects of ANC on HGS. The same analyses were completed on the complication group data. Since the complication group had only post-transplant data we did not further subdivide into groups. We chose to use multilevel modeling in the univariate and multivariate analyses to account for the fact that each participant had multiple data points, thus each observation was nested within the individual and a simple linear regression would have been inadequate (Snijders, 2014).

The variables that were found to be statistically significant ( $p \leq .05$ ) were then included in a multivariate, multilevel regression analysis. These included transplant day (TD), HGB, age, gender, transplant type, and transfusion received. HCT was not included in the multivariate model as it was highly correlated with HGB. ANC was not included in the multivariate model in the peri-transplant group only as it was found to be statistically insignificant in univariate analysis. In the complication group, the multivariate analysis included TD, Age, gender, HGB, and ANC. Chi square analyses were also conducted to examine differences between the strength loss and no strength loss groups in the peri-transplant subgroup.

## Results

### Participants

Fifty patients met inclusion criteria and were approached for enrollment. Five patients declined enrollment with two giving specific reasons (not wanting sleep interrupted; enrolled in too many studies). Of the 45 who gave informed consent, 33 (20 peri-transplant; 13 complication) completed the study (Table 2). Reasons for not completing the study included; declining to continue participation due to feeling unwell or overwhelmed (5), broken dynamometer (2), early discharge (2), being placed in droplet precautions (1), researcher illness (1), and insufficient data (1). In addition, participants were not wakened for daily testing. Participants who missed data collection for 4 days for any reason were dis-enrolled from the study. Peri-transplant patients that dropped out of the study prior to day 0 of the transplant and any patient with <3 data points were excluded from data analysis.

### Dependent Variable-Hand Grip Strength

#### *Peri-Transplant Group*

A total of 756 HGS readings were collected on the right hand of participants, and 759 readings on the left hand over the course of the study. For each session, the maximum grip from the right and left hands were recorded and included in the analysis. Sixty five percent (13/20) of the peri-transplant group experienced a 20% or greater strength loss during the course of hospitalization (our definition of clinically important change) (Kim et al., 2014; Lang et al., 2008). Participants experienced the strength loss between transplant day (TD) -6 (i.e. 6 days before transplant) to 11 (mean=TD -1.46, SD 4.3). Nine (69%) of the participants in the strength loss group reached the 20% decline during the conditioning phase of the transplant (Figure 1). Seven participants experienced >40% strength loss, with one of those participants declining by

52% (Table 3). The nadir of HGS in the strength loss group appeared between transplant day -6 to 19 (mean=TD 6.3, SD 7.2) (Table 3).

Chi square analyses were performed to examine differences in selected characteristics between participants in the strength loss group and those with no strength loss. Age, gender and mean time since diagnosis were not statistically significant (Table 4). Those receiving allogeneic transplants were more likely to be in the strength loss group than participants who received autologous transplants ( $p=.02$ ).

#### *Complication Group*

A total of 204 HGS readings were collected from the right hand of the participants and 204 from the left hand. As in the peri-transplant group, the maximum reading from each session was included in the analysis. Forty six percent (6/13) of the complication group experienced a 20% or greater loss of HGS during hospitalization, with 5 participants declining by >40%. Participants experienced this loss between TD 5 to 11 (mean=TD7.3, SD 2.8) with the HGS nadir occurring on transplant day 9.8 (SD 4.1) (Table5).

#### **Clinical Data**

##### *Peri-transplant group-Univariate Analysis*

In the univariate analysis, statistically significant relationships were found between HGS and age, HGB and HCT, (Table 6). In addition, male gender was strongly correlated with HGS ( $p<.001$ ). Receiving an allogeneic HSCT was strongly negatively correlated with HGS. Those receiving allogeneic HSCT had HGS that was about 11-12 KG lower than those receiving autologous HSCT ( $p<.001$ ). ANC was not significantly associated with HGS..

### ***Peri-transplant group-Multivariate Analysis***

Variables that were found to be statistically significant ( $p \leq .05$ ) in the univariate analyses were included in the multivariate analysis. One exception was HCT which was not included due to collinearity between HGB and HCT. Gender, and HGB remained positively correlated with HGS when adjusted for transplant day and transfusions received (Table 7). Allogeneic transplants were negatively associated with HGS ( $p < .001$ ).

### ***Complication group-Univariate and Multivariate Analysis***

In the complication group, there was a very small but statistically significant negative correlation between HGS and ANC, HGB, HCT and Age (Table 8). As in the peri-transplant group male gender was strongly associated with HGS ( $p < .001$ ). When these variables were added to the multivariate analysis, only age and gender remained significant (Table 9).

### **Other Independent Variables**

Nine patients in the Peri-transplant group (45%) and five patients in the complication group (38%) received patient controlled analgesia (PCA) at some point in the study. Given that PCA doses are not recorded in the medical record, they were not included in the analysis. No correlation was seen between opioid ( $p = .36$ ) or benzodiazepine ( $p = .41$ ) use and HGS. Only 2 participants in the peri-transplant group and 4 in the complication group received physical therapy evaluation.

### **Nurse Assessment of Mobility**

Nurses documented limitations in mobility for 8/19 (42%) participants in the strength loss group when data were analyzed from both the peri-transplant and complication groups. Of interest, nurse documentation preceded declines in HGS by 1-6 days for four of the participants. Conversely, there were also 1-12 day lags in documentation of mobility limitations for four

participants. No nurse documented the need for assistance with mobilization on the day of the 20% strength decline.

### **Feasibility and Acceptability**

The time required to perform HGS testing was 7.12 (SD 1.95) minutes. We were able to train and validate competency for the research assistants (RAs) in about 30 minutes. The RAs reported that obtaining the measurements was simple.

Participants in the peri-transplant group rated the difficulty of performing the grip strength at 1.4 (SD=.73) on a scale of 1-5 with 5 being most difficult. Similarly, the complication group rated the difficulty at 1.8 (SD= 1.3). In addition to the feasibility score, many patients commented that they felt tired or weak at the time of testing.

### **Discussion**

While there have been studies that have examined changes in strength pre and post HSCT (de Souza et al., 2012; Kramer et al., 2013; Mello et al., 2003; Pidala et al., 2013), to our knowledge, this is the first study to measure HGS daily in participants undergoing HSCT. We found that clinically important changes in HGS occurred in the majority of participants (57%) in this study, with a subgroup experiencing strength loss early in the HSCT process, during the conditioning phase. There was a high degree of variability for the day of nadir of HGS. In addition, a large percentage (46%) of patients admitted for complications of HSCT experienced continued strength loss after admission.

HGS appeared to be associated with gender, with males having higher grip strengths across both the Peri-tx and Complication groups. Based on the results of this study, the correlation between age and HGS is not clear. Of interest, there was a small but statistically significant positive correlation between HGS and age, HCT and HGB in the peri-transplant

group. The positive relationship between age and HGS was not expected. The age related norms provided by Mathiowetz (1985) demonstrate that HGS peaks between the ages of 25-39. One explanation for this counter-intuitive finding is that the majority (53%) of the peri-transplant group were male. Males in this group had HGS about 19 kg higher than females ( $p < .001$ ). Thus, the effect of gender may have confounded the effect of age. When age and gender were added to a bivariate analysis, gender remained statistically significant ( $p = .03$ ) but age did not ( $p = .94$ ). In the complication group there was a negative relationship between age and HGS, as would be expected. This group was more evenly distributed between genders with 46% of the participants being male.

In contrast to the findings in the Peri-transplant group, we found a small ( $< 1\text{kg}$ ) negative correlation between HGS and ANC, HCT, HGB and ANC in the univariate analyses, in the complication group. These results are similar to the findings of Kilgour et al (2013) of negative correlation between HGB and HGS for those in the 10<sup>th</sup> ( $-19.7$ ,  $p < .001$ ) and 25<sup>th</sup> ( $-9.76$ ,  $p < 0.01$ ) percentiles. In addition, age was negatively correlated with HGS in the complication group ( $p = .015$ , 95% CI  $-0.498$ ,  $-0.054$ ).

Of interest, those who received allogeneic transplants were more likely to experience clinically important strength loss than those who received autologous transplants ( $p = .02$ ). Of the five studies of HGS in patients receiving HSCT that were reviewed for this study, four included only patients receiving allogeneic transplants (Kramer et al., 2013; Mello et al., 2003; Morishita et al., 2013; Pidala et al., 2013). deSouza et al., (2012) studied patients receiving allogeneic and autologous HSCT. The authors found no significant difference in HGS between the groups at baseline ( $p = .61$ ) and did not compare the two groups post HSCT.

Additionally, we found that nurses may not fully appreciate a patient's weakened state as demonstrated by lack of documentation of patient's need for assistance with mobilization when scoring the JHFRAT, despite participant's clinically important declines in strength of  $\geq 20\%$ . This may be related to the study by Mello, Tanaka & Dulley (2013), which examined muscle strength in 18 patients presenting for HSCT. Although the participants in the study had strength that was lower than expected, they had no complaints and seemed to function well (p.726). Thus, the strength loss may not be appreciated during subjective assessments, further highlighting the need for an objective measure of strength.

Testing HGS in patients hospitalized for HSCT was feasible. In general, participants found the HGS testing to be relatively easy to perform. The mean time to complete the testing was 7.15 minutes (SD 1.95) minutes. This time included instructions given to the patient as well as any positioning required. Many of the participants were interested in learning how the HGS was changing over time. No adverse events such as injury or infection related to the HGS testing occurred during this study.

Data collection was interrupted at three points during the study due to equipment failure of the dynamometer instrument (JAMAR-200) used in the study. This instrument was chosen because many of the studies reviewed used this model and it is reported to be the "gold standard" (Roberts, 2011, p.524). Although the dynamometer was calibrated by the health sciences clinical engineering department prior to initial use, it broke once early on in the data collection period and required replacement. There were two other dynamometer failures during the study period that required repair. The failures were detected by the research team at the time of daily calibration checks prior to data collection.

## **Limitations**

There were some limitations to this study. First, this pilot, feasibility study was conducted in a single medical center and although there were more than one thousand HGS measurements, the sample size was small with thirty-three participants completing the study. Thus the results may not be generalizable to other inpatient settings.

The research team did not waken patients for testing and, as would be expected, participants were asleep at various times of the day. Participants were asked on each day “are you ready for a grip strength test”? in an effort to ensure ongoing assent to participate in the study. Many patients declined on various days for reasons such as nausea, diarrhea, or just generally feeling unwell. Participants were dis-enrolled from the study if they refused data collection or were sleeping at the time of data collection for 4 consecutive days. In addition, there were many missing data points due to our decision to minimize burden and disruption to participants by not wakening them for testing. As participants progressed in the HSCT process, they tended to nap during the day which limited their availability for testing. In total we collected data on 78% of the potential days for the peri-transplant group and 85% of the potential days for the complication group. Despite gaps in data collection, we were able to see trends of HGS over the course of the hospitalization, however, missing data points may have impacted our results.

Another limitation is that we did not control for conditioning regimens. While every participant received a myeloablative HSCT, some conditioning regimens were more intense (i.e. higher doses of chemotherapy and radiation) than others. There is a possibility that those with intense conditioning regimens had a higher degree of strength loss, but this study was not designed to examine that question.

Although the impetus for this study was identification of an objective method of quantifying strength loss in order to potentially prevent falls, it is important to recognize that we did not measure falls, lower body strength or gait. Therefore we are not able to draw conclusions about the relationship between HGS and falls.

Finally, results of HGS can be affected by the effort that a participant puts in to the testing process. Researchers have found decreased HGS performance as a result of depression (Philips, Biland, Costa, & Souverain, 2011) or lack of sincerity of effort (Philips et al., 2011). Given both the diagnoses that necessitated HSCT and the intensity of the treatment which caused fatigue, nausea and pain, mood states of the participants were variable from day to day. Sincerity of effort did not appear to pose an issue as most participants exhibited consistent interest and participation in the testing.

### **Conclusion**

A majority of patients who present for HSCT appear to experience a clinically important decline in strength over the course of hospitalization and those receiving allogeneic HSCT are more likely to experience this decline than patients receiving autologous transplants. Given this strength loss, patients receiving HSCT are likely to be at an increased risk of falls and falls with injury. Furthermore, our study demonstrates that clinically important declines may occur early in the transplant period, during the conditioning phase. Current fall prevention screening tools rely on subjective nursing assessment of patients' ability to mobilize independently; our study provides new data that suggests that nurse assessment of a patient's need for assistance with mobility does not correspond closely to declines in the patient's muscle strength as measured by dynamometry. HGS may be a more sensitive, real-time indicator of declines in strength. In addition, although not directly assessed in our study, it is likely that patients, themselves, may

not recognize their own strength decline. Thus, nursing and patient decisions about the need for assistance with mobility may not be fully informed. HGS by dynamometry provides an essential objective measure of strength that will allow care providers to identify clinically significant weakness as soon as it occurs. This identification may provide health care providers critical information that will inform the design of an individualized fall prevention plan.

The HGS test by dynamometry was found to be feasible for use in the inpatient setting for participants receiving HSCT. In the future it would be useful to perform the HGS test when the participant is already awake for vital signs or some other routine care, which would increase the days when data could be collected. Engaging participants in the process of measuring and trending HGS over the hospitalization is an important factor. One participant stated that he would like to see a chart that would allow him to track his HGS over time.

In summary, this study adds to the body of literature that has emerged about the use of HGS in acute care settings. We have demonstrated that it is feasible to test HGS daily in hospitalized participants who are acutely ill. Given the success of this pilot, a study with a larger sample size, sufficiently powered for statistical significance is indicated. The design of this pilot study could be utilized for such a future study with a few modifications to improve data capture and interpretation of results. For example, HGS measurements should be timed to coincide with vital signs to minimize missing data. Information on conditioning regimens should be collected and considered in the analysis. Differences in HGS between participants receiving allogeneic and autologous HSCT should be further explored. Based on the results of this study, inclusion of lab data could be limited to HGB as HCT was found to be collinear with HGB and ANC did not appear to be correlated to HGS. Trended HGS readings could be posted in the room and participants could be surveyed regarding their perceptions of the trending tool and whether it

made them more or less likely to ask for assistance with mobility. Once this proposed study is accomplished, there is the possibility of yet another study to examine the use of HGS as a fall prevention intervention. HGS results could be displayed for patients and nurses to see. Having objective, trended information about one's strength may increase the likelihood that a patient would call for assistance prior to mobilizing when HGS has declined, which could potentially prevent a devastating fall.

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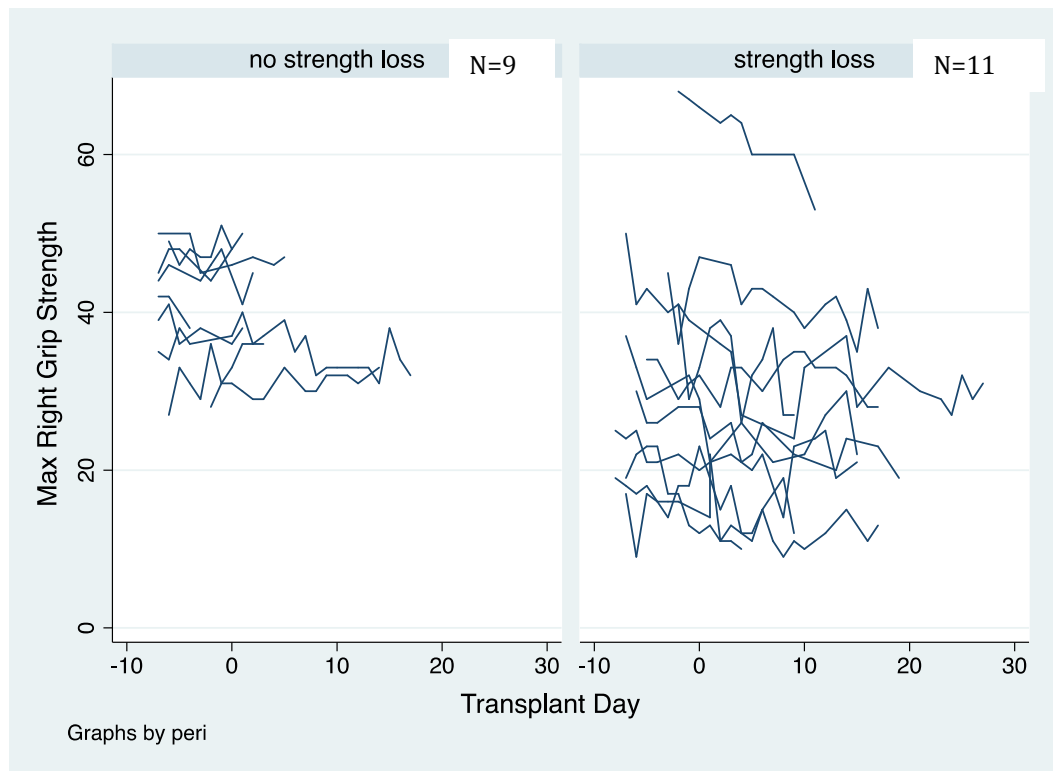
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Table 2. Characteristics of Participants

	<b>Peri-Transplant</b> N=20	<b>Complication</b> N=13
<b>Mean Age (yrs.)</b> (Min-Max)	51.5 (SD 11.4) (32-71)	56.1 (SD 12.9) (27-71)
<b>Gender (%)</b>	M=15(75) F=5 (25)	M=6 (46) F=7 (54)
<b>Hand Dominance (%)</b>	R=17 (85) L=3 (15)	R=13 (100) L=0
<b>Diagnosis (%)</b>		
AML	N=5 (25)	N=1 (8)
Lymphoma	N=5 (25)	N=4 (29)
Myelofibrosis	N=3 (15)	N=0
Multiple Myeloma	N=2 (10)	N=6 (47)
Myelodysplastic Syndrome	N=1 (5)	N=1(8)
CLL	N=0	N=1(8)
Other	N=4 (20)	N=0
<b>Mean Time Since Diagnosis (mos.)</b> (Min-Max)	12.35 mos.(SD 10.9) (4-42)	18.76 mos. (SD 28.73) (5-107)
<b>Transplant Type</b>		
Allogeneic	N=11 (55)	N=3 (23)
Autologous	N=9 (45)	N=10 (76)
<b>Length of Study Participation(Hospital Days)</b> (Min-Max)	17.3 days (SD 7.4) (8-35)	6 days (SD 3.1) (3-12)

Figure 1. Patterns of strength in Peri-Transplant group for strength loss (Right side of graph) and no strength loss groups (Left side of graph).



**Table 3. Characteristics Strength Loss and No Strength Loss-Peri-Transplant Group**

Characteristic	No Strength Loss N=9	Strength Loss N=11	p value
Age	55.6 yrs. (SD 3.84)	48.5 (SD 3.75)	.22
Gender (Male)	7 (87.5%)	7(64%)	.27
Time Since Diagnosis	14.2 mos. (SD 4.0)	10.8 mos. (SD 3.6)	.51
Transplant Type			
Allogeneic	2 (22%)	7 (64%)	.02*
Autologous	7 (78%)	4 (36%)	

\*Significant

Table 4. Peri Transplant Group-HGS and Data Collection

<b>ID</b>	<b>Age</b>	<b>Right Grip (kg) % change from baseline</b>	<b>HGS decline 20% from baseline TD*</b>	<b>HGS Nadir(TD*)</b>	<b>Data points (% collected)</b>
6	43	47%	-3	4	24/24 (100)
10	35	42%	-6	5	32/36 (88)
11	64	36%	-1	7	24/24 (100)
12	38	47%	-6	-6(R), 6(L)*	42/50(84)
13	59	No Strength loss	N/A	-3(L)*	44/48 (92)
19	60	22%	-2	15	34/42(80)
20	32	7%	-5	8(R)**, 3(L)*	12/20(60)
22	59	22%	11	11	28/38((74)
24	57	52%	-3	17(R)**, 15(L)*	42/70(60)
26	56	6%	N/A	-5(R)**,- 4(L)*	16/16(100)
28	56	7%	N/A	1(R)**	16/20(80)
32	40	44%	0	8	38/48(79)
34	32	36%	1	19	33/52(63)
35	60	No Strength Loss	N/A	2(L)*	25/34(73)
36	71	3%	N/A	-6	16/22(73)
37	54	2%	N/A	-2(R)**	12/16(75)
38	65	43%	-5	1(R)**, 7(L)*	24/32(75)
39	51	10%	N/A	-3(R)**, 5(L)*	14/26(54)
40	41	18%	-2	2(R)**, 14(L)*	36/46(78)
45	57	21%	2	3(R)**,- 2(L)*	22/26(85)

\*L=Left \*\* R=Right

Table 5. Complication Group-HGS and Data Collection

<b>ID</b>	<b>Age</b>	<b>Right Grip (KG) % change from baseline</b>	<b>HGS Nadir(TD*)</b>	<b>Data points (% collected)</b>
1	27	2%	10	6/6(100)
2	43	8%	6	6/6(100)
7	71	59%	6	16/16 (100)
8	54	No Strength Loss	N/A	6/6(100)
9	61	46%	11	8/8 (100)
14	63	48%	8	16/20(75)
18	71	No Strength Loss	N/A	14/24(58)
21	54	45%	14	18/24(75)
23	37	27%	7	12/14(86)
31	69	No Strength Loss	14	12/12(100)
33	56	No Strength Loss	N/A	6/6(100)
41	60	6%	5	10/10(100)
44	64	5%	11	6/8(75%)

Table 6. Summary Results of 20% Strength Loss and Nadir of Strength

	<b>Peri-Tx Group N=20</b>	<b>Complication Group N=13</b>
20% Strength Loss	13(65%)	6(46%)
Mean TD 20% Strength Loss Range	TD -1.46 (SD 4.3) (TD -6 to 11)	TD 7 (SD 2.8) (TD 5 to 11)
Mean HGS Nadir Range	TD 6.3(SD 7.2) (TD -6 to 19)	TD 9.8(SD 4.1) (TD 5 to 14)

Table 7. Univariate Analyses with Hand Grip Strength-Peri Transplant Group

Variable	Transplant Day -7 to Day 0			Transplant Day 1-8		
	Coefficient	p value	95% CI	Coefficient	p value	95% CI
TD*	-.2766	.65	-1.48, .924	-.368	.65	-1.96, 1.22
Age	.590	<.001	.397, .794	.51	<.001	.314, .711
HGB	4.10	<.001	2.75, 5.44	4.47	<.001	2.65, 6.29
HCT	1.29	<.001	.811, 1.77	1.36	<.001	.737, 1.98
ANC**	.026	.90	-.390, .442	.266	.22	-.162, .695
TT***	--10.99	<.001	-15.69, -6.29	-13.31	<.001	-18.40, -8.22
Gender (M)	19.6	<.001	15.02, 24.21	18.1	<.001	13.33, 22.00

\*TD-Transplant Day \*\*Divided by 500 \*\*\*Allogeneic Transplant

Table 8. Multivariate Analysis with Hand Grip Strength-Peri Transplant Group

Variable	Transplant Day -7 to Day 0			Transplant Day 1-8		
	Coefficient	p value	95% CI	Coefficient	p value	95% CI
TD	-.04	.91	-.7930, -7102	-.11	.81	-1.03, .816
TT*	-7.32	<.001	-10.92, -3.72	-3.82	.11	-8.58, .932
Age	-.269	.02	-.492, -.046	.093	.46	-.159, .347
HGB	2.01	.001	.845, 3.19	1.54	.08	-.179, 3.25
Gender (M)	20.29	<.001	15.14, 25.44	13.75	<.001	7.77, 19.73

\*TT-Transplant type =allogeneic

Table 9. Univariate Analyses with Hand Grip Strength-Complication Group  
Transplant Day 0-15

<b>Variable</b>	<b>Coefficient</b>	<b>p value</b>	<b>95% CI</b>
TD*	-.04	.90	-.674, .590
Age	-.28	.015	-.498, -.054
HGB	-.92	.007	-3.32 , -.525
HCT	-.70	.001	-1.11, -.300
TT***	-.55	.86	-6.99, 5.89
ANC**	-.51	.02	-2.81, -.214
Gender (M)	15.45	<.001	11.22-19.70

\*TD-Transplant Day \*\* Divided by 500 \*\*\* Transplant type=allogeneic

Table 10. Multivariate Analysis with Hand Grip Strength-Complication Group  
Transplant Day 0-15

<b>Variable</b>	<b>Coefficient</b>	<b>p value</b>	<b>95% CI</b>
TD*	-.185	.53	-.759, .390
Age	-.377	.02	-.682, -.051
HGB	-.877	.20	-2.23 , -.480
ANC**	-1.19	.054	-2.41, .019
Gender (M)	13.60	<.001	8.99, 18.22

\*TD-Transplant Day \*\* Divided by 500

## Appendix A: Protocol for Hand Grip Strength Measurement

1. Perform hand hygiene prior to entering the hospital room
2. If participant is sleeping, do not awaken them
3. Ask participant “are you ready for a grip strength test?”
4. If participant is in contact isolation precautions, perform hand hygiene and don gown and gloves prior to entering room.
5. Note the measurement start time on data collection tool.
6. Position participant in bed for testing:
  - a. Assist the participant to move up on the mattress if needed
  - b. Raise head of bed as high as possible.
  - c. Assist participant to sit as upright as possible with hips back toward the head of bed and legs on the bed with ankles uncrossed.
  - d. Ensure that shoulder is in neutral flexion/extension position.
  - e. Place Right elbow at 90 degree angles.
  - f. Instruct the patient to hold the shoulder close to the body.
7. To calibrate the instrument, ensure that the indicator needle is at 0.
8. Ensure the dynamometer is set to the second handle position.
9. Rotate the red peak-hold needle counter clockwise to 0.
10. If patient is in contact precautions, have them don gloves
11. Ask the participant: “Which hand is your dominant hand?” Place the dynamometer in the participant’s dominate hand. Record.
  - a. If participant is unable to state which hand is dominant, start with right hand.
12. Instruct the participant by saying out loud: “Squeeze the dynamometer as hard as you can for up to 4 seconds. Get ready, squeeze. One one thousand, two one thousand, three one thousand, four one thousand and Stop.” Record the maximum KG torque reached by looking at the dial on the dynamometer and record number on separate piece of paper. Allow for 1 minute rest time between each reading. Repeat this 2 more times for a total of 3 readings on one hand. Use the same instructions each time: “Get ready, squeeze. One one thousand, two one thousand, three one thousand, four one thousand and Stop.” Record highest reading on data collection form.
13. Place dynamometer in the participant’s non-dominate hand.
14. Instruct the participant to squeeze as hard as they can and hold for up to 4 seconds. “Get ready, squeeze. One one thousand, two one thousand, three one thousand, four one thousand and Stop.” Record the maximum KG torque reached by looking at the dial on the dynamometer and noting this number on the data collection form. Allow for 1 minute rest time between each reading. Repeat this 2 more times for a total of 3 readings on one hand.
15. Note the measurement stop time on data collection sheet
16. Share the results with the patient and/or nurse if requested.
17. Note any comments made by the participant about the testing procedure on the data collection form in the comment section (i.e. difficulty, emotions during testing etc.).
18. Ask the participant “On a scale of 1-5, with 5 being the most difficult, how difficult was it for you to complete the hand grip strength test today?” Record answer on data collection form.
19. Perform hand hygiene upon exiting the hospital room.
20. Clean all surfaces of dynamometer with Sani-Wipe outside of the room.
21. If participant is in contact precautions use a bleach wipe to clean the dynamometer.

## Appendix B Recruitment Flyer

### Hand Grip Strength Research Study

#### ***A new study to measure hand grip strength in patients who are admitted to the hospital for a blood/marrow transplant***

Researchers in the School of Nursing at University of Washington are evaluating the use of a hand-held instrument (dynamometer) to measure the strength of patients admitted for a blood/marrow transplant.

#### **Who is eligible to participate?**

- ✓ Age 18-65
- ✓ Planning to be in the hospital for a blood/marrow transplant
- ✓ Has not previously received a blood/marrow transplant
- ✓ Able to speak English and understand directions



#### **Goals**

- Determine if there are changes in strength during hospitalization for blood/marrow transplant and how quickly changes can be detected
- Determine if patients are willing to have their grip strength tested in the hospital

#### **Process**

Once patients have agreed to participate, they will have their grip strength tested once at the time of enrollment and then each day that they are in the hospital. Grip strength will be shared with the patient after every test.

#### **How will this contribute to science?**

Researchers have measured grip strength before and after hospitalization for blood and marrow transplant. No study has been done to measure strength levels throughout the hospital stay.

#### **How do I enroll in the study?**

Participation is completely voluntary. If you are qualified to participate, the researcher will contact you to determine if you are interested.

***For more information, contact:***

**Cindy Sayre-casayre@uw.edu**  
425-923-5730

## **Appendix C- HGS Study Consent Form**

Fred Hutchinson Cancer Research Center

### **Feasibility of Use of Hand Grip Strength as a Determinant of Functional Strength in Patients Undergoing Hematopoietic Stem Cell Transplant: A Pilot Study**

*Principal Investigator:* Kathleen Shannon Dorcy, RN, PhD., Fred Hutchinson Cancer Research Center (206-667-3648) Cindy Sayre RN, ARNP, PhD(c), University of Washington; (206-598-6913)

**Emergency number (24 hours): 206-598-8902**

A team of investigators at the Fred Hutchinson Cancer Research Center (FHCRC) and the University of Washington School of Nursing (UWSON) are conducting this study.

The care you get will be at University of Washington Medical Center (UWMC), a nonprofit hospital which provides complete patient care services.

#### **WHAT IS THE PURPOSE OF THIS CONSENT FORM?**

This form is called a consent form. The purpose of this form is to let you know about a research study being done at (UWMC). It tells you about the purpose, risks and benefits, and describes what is involved in the study. It also tells you what other choices you have. This consent form gives you the opportunity to consider participating in a study about hand grip strength in patients who will be receiving or have already received a Hematopoietic Stem Cell Transplant (HSCT)

#### **We would like you to join this research study.**

Since you are undergoing a hematopoietic stem cell transplant, we would like to ask you to join this research study. We will enroll up to 45 people.

Research is not the same as treatment or medical care. The purpose of a research study is to answer scientific questions.

You do not have to be in this study. You are free to say yes or no, or to drop out after joining. There is no penalty or loss of benefits if you say no. Whatever you decide, your regular medical care will not change.

#### **Why are we doing this study?**

We are doing this study to examine if patients' hand grip strength changes during the course of being hospitalized for a HSCT. We want to know if testing hand grip strength daily while patients are in the hospital will be acceptable to them and whether this testing will detect a decrease in strength before it is recognized by the nurse.

### **What research tests, procedures, and treatments are part of this study?**

If you decide to join this study, we will do these tests and procedures:

- **Hand Grip Strength Testing.** We will test your Hand Grip Strength within 24 hours of being admitted to the hospital and each day afterwards. This should take no more than 15 minutes each day.
- **Questionnaire.** We will ask you to answer a question each day about the difficulty of performing the Hand Grip Strength test. The researcher will record your answer. If the question makes you feel uncomfortable, you may choose not to answer.
- **Medical Record Review.** We will review your medical records to find information about your diagnosis and medical history, the medications you are receiving and whether you have had physical therapy. We will also look at your red blood cell (hemoglobin and hematocrit) and white blood cell counts (neutrophils).

### **How long will I be in this study?**

We think you will be in this study until one of these things happen; you reach day 30 of hospitalization, your absolute neutrophil count (white blood cells) is 500 or higher for 3 days or you are discharged from the hospital.

The total time includes no more than 30 days.

The researcher may take you out of this study at any time. This would happen if:

- They think it is in your best interest not to continue in the study.
- You are unable or unwilling to follow study procedures.
- The whole study is stopped.

If you are thinking about dropping out of this study, please tell the researcher. There will be no changes in your treatment or care should you decide to drop out of the study.

If you leave the study, your test results and information cannot be removed from the study records.

### **What are the side effects (risks)?**

In this part of the consent form, we tell you the side effects we expect from the tests in this study. There may be side effects we do not know about yet. If we learn about other side effects, we will tell you.

We carefully watch everyone in the study for side effects. If you want more information about side effects and risks, ask the researcher.

### **Non-physical risks are:**

You may feel embarrassed, anxious, annoyed or worried by having your grip strength measured.

## **Physical Risks**

No physical risks related to testing of handgrip strength have been reported in the literature and we do not anticipate that there will be any physical risk to anyone participating in this study.

### **What are the benefits?**

Although the study will not benefit participants directly, we hope the information we learn will help people undergoing HSCT in the future.

We hope the information from this study will help us test the utility of measuring hand grip strength in patients who are hospitalized for an HSCT. In the future, nurses and doctors may use hand grip strength testing to determine which patients are at the greatest risk for an accidental fall.

### **You have other choices besides this study.**

You do not have to join this study. You are free to say yes or no. Your regular medical care will not change.

## **Protecting your Privacy as an Individual and the Confidentiality of Your Personal Information**

Some people or organizations may need to look at your research records for quality assurance or data analysis. They include:

- Researchers involved with this study.
- Institutional Review Boards (IRB), including the Fred Hutchinson Cancer Research Center IRB. An IRB is a group that reviews the study to protect your rights as a research participant.
- Fred Hutchinson Cancer Research Center, University of Washington School of Nursing.

We will do our best to keep your personal information confidential. But we cannot guarantee total confidentiality. Your personal information may be given out if required by law. For example, workplace safety rules may require health workers to contact you about lab tests. Or a court may order study information to be disclosed. Such cases are rare.

We will not use your personal information in any reports about this study, such as journal articles or presentations at scientific meetings.

Federal regulations and the policies of the University of Washington (UW Medicine) and the Seattle Cancer Care Alliance (SCCA) require that certain information about your participation in this research be made a part of your permanent medical record.

The information in your permanent medical record will include:

- Name of the study
- The name of the researcher.
- The name of the study coordinator.
- Contact phone number for the study.
- Contact email address for the study.
- Emergency phone number for the study.
- Expected start and end dates for your time in the study.
- Whether this study includes healthy volunteers.

Information about your research procedures and test results may also be put in your medical record. This will include: Hand Grip Strength testing

In the future, if you give permission to any person or group to look at your medical record (such as an insurance company or employer), they could receive this research information. If you have already given permission to anyone (such as your life or health insurance company) to look at your medical record, they may receive this information if they ask for a copy of your medical record.

**Will you pay me to be in this study?**

There is no payment for being in this study.

**How much will this study cost me?**

There are no extra costs for being in this study.

**What if I get sick or hurt in this study?**

If you get sick or hurt in this study, tell the study researcher in person or call 425-923-5730.

Emergency medical treatment is available at the usual charge. You or your insurance company will have to pay for medical care or hospitalization. There are no funds to pay you for a research-related injury, added medical costs, loss of a job, or other costs to you or your family.

If you get sick or hurt in this study, you will get medical treatment. You or your insurer will have to pay for treatment.

You will not lose your legal right to seek payment for treatment if you sign this form.

**Your rights**

- You do not have to join this study. You are free to say yes or no. Your regular medical care will not change.
- If you join this study, you do not have to stay in it. You may stop at any time (even before you start). There is no penalty for stopping. Your regular medical care will not change.

- If you get sick or hurt in this study, you do not lose any of your legal rights to seek payment by signing this form.
- During the study, we may learn new information you need to know. For example, some information may affect your health or well-being. Other information may make you change your mind about being in this study. If we learn these kinds of information, we will tell you.

**For more information**

If you have questions or concerns about this study, you may talk to your doctor anytime. Other people you can talk to are listed below.

<b>If you have questions about:</b>	<b>Call:</b>
This study (including complaints and requests for information)	206-667-3648 Dr. Kathleen Shannon Dorcy 206-598-6913 Cindy Sayre, MN PhD (c)
If you get sick or hurt in this study	206-667-3648 Dr. Kathleen Shannon Dorcy
Your rights as a research participant	206-667-4867 (Karen Hansen, Director of Institutional Review Office, Fred Hutchinson Cancer Research Center) 206-543-0098 (Human Subjects Division, University of Washington)

**Emergency number (24 hours): 206-598-8902**