

**ORthopaedic trauma Anemia with Conservative versus Liberal transfusion
(ORACL)
(NCT02972593)**

Brian Mullis, MD
Chief, Orthopaedic Trauma Service
Eskenazi Health, Fifth Third Bank Building
720 Eskenazi Avenue
2nd Floor, Suite 2-S
Indianapolis, IN 46202
Associate Professor
Indiana University School of Medicine
Assistant: 317-880-3600
Office: 317-880-3591
Fax: 317-880-0138

Participating Sites:

Eskenazi Hospital-Orthopaedics (Site PI: Karl Shively, MD)
Methodist Hospital-Orthopaedics (Site PI: Walter Virkus, MD)
WellStar Atlanta Medical Center (Site PI: Jennifer Bruggers, MD)
**Atrium Health Musculoskeletal Institute-Charlotte, NC (Site PI: Laurence
Kempton, MD)**

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1.0 Background

Over 13 million units of blood are transfused each year. While transfusion can certainly be life saving, numerous studies over the last twenty years have shown significant, dose-dependent increases in morbidity, mortality, and cost with each unit of packed red blood cells transfused. {Leal-Noval, 2001 #1} Transfusion is one of the most common interventions made in the critically ill population, however the negative effects of transfusion-related infection is well documented in recent literature. {Leal-Noval, 2001 #1; Leal-Noval, 2001 #1; Hebert, 1999 #2; Carson, 1999 #3; Edna, 1992 #6; Hill, 2003 #8; Vincent, 2002 #9; Taylor, 2002 #10} There is no question that transfusion of blood products can be life-saving to an acutely ill trauma patient, but there is little evidence to help the Orthopaedic Surgeon decide when a transfusion is indicated in an asymptomatic anemic patient who is no longer in need of acute resuscitation.

Several studies have analyzed healthy individuals with an isovolemic reduction in hemoglobin to a level of 5.0 (g/dL). {Leung, 2000 #16; Weiskopf, 1998 #17} They found no significant compromise in oxygen delivery to the tissues. Currently there is a lack of clinical data to suggest adequate red blood cell (RBC) transfusion endpoints in trauma surgery. {Johnston, 2006 #18} Given the lack of evidence to support transfusion triggers for young, healthy, asymptomatic Orthopaedic trauma patients, the purpose of this study will be to investigate the risk of complications associated with permissive anemia in this population.

Orthopaedic trauma patients treated at Eskenazi (previously Wishard) Hospital, a level 1 trauma center, are routinely allowed to be permissively anemic, or allowed to run as low as a Hemoglobin of 5 g/dL if they are young and healthy (see inclusion/exclusion criteria for objective definition) and asymptomatic from anemia. A retrospective review was performed using the inclusion/exclusion criteria proposed in this study to evaluate if a prospective study would be ethical and to provide a power analysis for number of patients needed to reject the null hypothesis. Over a 3 year period (2006-2009), 104 patients were identified who met the inclusion/exclusion criteria proposed in this study and were available for 1 year follow-up. This study controlled for Injury Severity Score, patient age, gender, and whether the patient had received multiple surgeries. We found that patients who were allowed to be permissively anemic (allowed to drop to a Hgb of 5 g/dL if asymptomatic at rest) had a lower complication rate ($p < 0.01$) than those who were transfused to maintain a higher hemoglobin. Additionally, there appeared to be a dose-dependent affect ($p = 0.02$) with higher complications seen in patients receiving multiple units of allogeneic blood. This data was presented at both the American Academy of Orthopaedic Surgery (2011) and Orthopaedic Trauma Association (2011) annual meetings and the manuscript is currently being reviewed for publication. This retrospective study does not prove causation of higher complication rates associated directly with transfusion, but does suggest there may be a lower complication rate in patients allowed to be permissively anemic. The largest barrier to publication of this retrospective study has been the repeated comments by reviewers that a prospective study is needed.

Dr. Mullis, Chief of Orthopaedic Trauma at Eskenazi Hospital, has met with the Chief of Anesthesia at Eskenazi Hospital, John Hasewinkel, and the Chief of Trauma for General Surgery, Gerry Gomez, to develop the inclusion and exclusion criteria listed

below so that this study might be completed in a multi-disciplinary approach with all providers agreeing to the inclusion and exclusion criteria and escape criteria listed below.

2.0 Rationale and Specific Aims

Transfusion of Orthopaedic trauma patients is routinely done in asymptomatic individuals as there is no accepted national standard or recommendations from the American Academy of Orthopaedic Surgeons or the Orthopaedic Trauma Association for what level of anemia is appropriate in an asymptomatic patient. Individual practitioners typically make this decision based on anecdotal experiences and expert opinion. No prospective study has been performed to date to answer this question in this patient population.

The null hypothesis of this proposed pilot study is that no difference will be seen with a liberal transfusion strategy to keep a patient's hemoglobin above 7 g/dL versus a conservative strategy to keep the patient's hemoglobin above 5.5 g/dL in patients asymptomatic at rest. The primary outcome of this pilot study will be infection; defined as postoperative wound infection (superficial or deep) or other perioperative infection but not surgical site (urinary tract infection or pneumonia). Deep infection is defined as the need for intravenous antibiotics or a return to surgery for debridement. Superficial infection is defined as the use of oral antibiotics only successfully treat a surgical site infection. Secondary outcomes will include pulmonary embolism, deep venous thrombosis, acute renal failure or insufficiency, nonunion, delayed union, compartment syndrome, osteomyelitis, nerve palsy, anoxic brain injury, cardiac ischemia or infarct, pancreatitis, or death, and the musculoskeletal functional assessment. These same outcomes were evaluated in the retrospective study done at this institution which found no difference within any one complication, but when all complications were pooled there was a higher complication associated with the liberal transfusion strategy.

3.0 Inclusion/Exclusion Criteria

Inclusion criteria:

- Trauma patients admitted to participating hospital with any Orthopaedic injury who have been determined to be stable by the Trauma Service (General Surgery) and are no longer within the resuscitation phase of initial treatment. This is defined as a normal urine output (greater than 0.5 ml/kg/hr) and a systolic blood pressure greater than 90 mmHg for greater than 6 hours without fluid bolus or transfusion during that time
- Age 18-50
- Hemoglobin less than 9 g/dL or expected drop below 9 g/dL with planned surgery

Exclusion criteria:

- Pregnant (urine pregnancy test will be done as standard of care)
- Prisoner
- Head injury (Glasgow Coma Scale less than 8 over 48 hours from presentation)
- Known cardiac (coronary artery disease, atrial fibrillation, stent placement, congestive heart failure), renal (acute or chronic renal insufficiency or failure,

defined as having Serum Creatinine >1.2 at time of enrollment), liver (Childs C cirrhosis) or pulmonary disease (chronic obstructive pulmonary disease, abnormal pulmonary function tests or history of poor pulmonary function from any cause including acute traumatic conditions such as ARDS)

- Unlikely to follow up in the surgeon's estimation
- Sickle Cell Anemia
- History of cancer
- Preexisting weakness, paresthesias, deformities, or other conditions which might affect functional outcome in the surgeon's opinion
- Spinal cord injury
- Patients with burns expected to require operative treatment
- COVID positive

4.0 Enrollment/Randomization

A consensus opinion was reached in a multidisciplinary manner with multiple members of the Trauma team (General Surgery), Anesthesia, Physical Medicine and Rehab, and the Orthopaedic Trauma Service. This team consisted of members from General Surgery (Timothy Hayward, Erik Streib, Clark Simons, Gerry Gomez), Anesthesia (John Hasewinkel, Jim Mitchell, Leilani Mullis), and Physical Medicine and Rehab (Angela Carbone) along with all members of the Orthopaedic Trauma Service (Jeff Anglen, Janos Ertl, Karl Shively) and the PI (Brian Mullis). The opinions in escape criteria and definitions will be referred to below as "consensus opinion". A biostatistician was consulted after he had reviewed the data from the retrospective study previously performed at this institution to help design an appropriately powered prospective randomized pilot study.

All Orthopaedic Trauma patients admitted to participating hospital will be screened for inclusion and exclusion criteria after they have been resuscitated and stabilized. The consensus opinion of the "stable" patient was defined as an awake and alert patient with normal urine output and systolic blood pressure greater than 90 mmHG for greater than 6 hours without fluid bolus or resuscitation. If a patient meets criteria for the study as noted above and is stable as defined above, the patient would be approached by either the Principal Investigator (PI) or a co-PI to determine interest and informed consent would be obtained for participation in the study. Patients who either refuse or are unable to consent will be tracked using the screening form. Enrollment would be performed in patients with a Hgb of 9 g/dL or less or in patients expected to drop below 9 g/dL with planned procedures or continued (controlled) bleeding. Randomization would not occur until the patient's Hgb dropped below 7 g/dL at which time a sealed envelope would be opened to determine if the patient would be randomized to a liberal transfusion strategy (transfuse to keep Hgb >7 g/dL) or a conservative strategy (transfuse to keep Hgb > 5.5 g/dL). If the patient's Hgb does not drop below 7.0 g/dL, randomization will not be done. Prior to starting enrollment, envelopes will be made by blinded personnel using a randomization list generated to assign subjects to receive treatment either after hemoglobin drops below 5.5 or after hemoglobin drops below 7.0. Randomization was

done with a block size of 4 to ensure the treatment allocation was balanced throughout the study recruitment period. Escape criteria have been established by the consensus group to allow transfusion in patients with clinical concerns for symptomatic or dangerous levels of anemia despite randomization arm (please see Escape Criteria outlined in section 5.0)

5.0 Study Procedures

If the patient remains asymptomatic at rest (defined as no chest pain, shortness of breath, or dizziness), transfusion would be determined by randomization to the liberal transfusion strategy to maintain Hgb at 7 g/dL or the conservative transfusion strategy of 5.5 g/dL. After each unit of blood is transfused a Hgb level would be checked to ensure appropriate Hgb levels are maintained as well as routine clinical practice (typically daily Hgb levels drawn until at least 2 consecutive days show no further drop with no further procedures or bleeding expected). If the patient's Hgb does not drop below 7.0 g/dL, randomization will not be done but patient will still be followed and patient outcomes will be collected as part of a non-treatment group.

As noted in Section 4.0, a consensus group consisting of multiple physicians and the service chiefs from the Trauma Service (General Surgery), Orthopaedic Trauma Service, Anesthesia, and Physical Medicine and Rehab agreed to the following escape criteria to transfuse regardless of Hgb level or arm of randomization:

Escape Criteria

1. Patient has any of the following symptoms at rest: chest pain, shortness of breath, dizziness
2. Patient has a mean arterial pressure less than 50 mmHg that is not responsive to fluid resuscitation
3. At any time the patient's heart rate increases by more than 30% above baseline while under anesthesia
4. The patient's urine output drops to less than 0.5 mL/kg/hour and remains decreased despite adequate rehydration with fluids
5. Any objective evidence of cardiac ischemia including the following: EKG changes such as ST depression, an elevation of serum cardiac markers, a base deficit greater than 6, lactate greater than 2.5 that does not respond to fluid resuscitation
6. A decrease in systolic blood pressure by 10% or more with exercise (physical therapy) that does not improve with fluid resuscitation
7. Uncontrolled source of hemorrhage

In addition to being followed daily while inpatient, patients would be followed at routine intervals following injury: 2 weeks, 6 weeks, 3 months, 6 months, 9 months, and 1 year. Radiographic and clinical data will be collected specific to the patient's musculoskeletal injury and based on standard of care. The primary outcome is infection defined as superficial infection (cellulitis treated with oral antibiotics) or deep infection (requires IV antibiotics or surgical debridement), osteomyelitis, pneumonia, urinary tract infection.

Secondary outcomes include renal insufficiency, cardiac ischemia or myocardial infarction, deep venous thrombosis, or any other medical complication encountered in the patient's hospital or post-discharge course felt to be possibly related to the patient's injury, procedure, or as a result of transfusion. Secondary outcomes will also include standardized patient outcome scores; specifically, the Musculoskeletal Functional Assessment (MFA) done at baseline, 6 months, and 1 year, and the two minute walk test which would be conducted daily by a certified physical therapist while the patient is an inpatient and after they have been cleared for ambulation. Length of hospital stay will be recorded. Return to surgery or repeat hospitalization due to a complication will be other secondary outcomes. Completion of the Musculoskeletal Functional Assessment at 6 months and 1 year may be done via phone or mail, if the subject is unable or unwilling to return for clinic follow up.

Other possible risks, no matter which group subjects are randomized to, are:

- Infection
- Osteomyelitis
- Pneumonia
- Urinary tract infection
- Renal insufficiency
- Acute renal failure
- Cardiac ischemia or infarct
- Myocardial infarction
- Pancreatitis
- Deep venous thrombosis
- Pulmonary embolism
- Anoxic brain injury
- Death
- Delayed union
- Non-union
- Compartment syndrome
- Nerve palsy

Risk level is the same for all events listed. These risks are possible but there is a low chance for occurrence.

6.0 Reporting of Adverse Events or Unanticipated Problems involving Risk to Participants or Others

Any adverse event identified by a member of the care or research team from any participating site will be documented in writing and the lead site principal investigator will be notified of adverse events as they occur. All serious adverse events, protocol deviations, and noncompliance will be reported to the IRB in accordance with IU IRB policies and procedures. Significant adverse events that meet the policy criteria will be reported to the IRB as they occur. All other adverse events will be documented and reported to the IRB at time of continuing review.

A Data Safety Monitoring Plan (DSMP) will be in place to compare provisional outcomes prior to final enrollment. Per the DSMP, an orthopaedic surgeon not involved with the study will serve as the reviewer, looking at study data for obvious trends in higher complications in one study group. Monitoring of data that has been collected from all participating sites will be done every 6 months and findings will be submitted to the IRB at the time of continuing review. The data safety monitoring board will be comprised of: Todd McKinley-Independent Orthopaedic Surgeon, practices at Methodist (Board Chair), Dana Brock-Anesthesiologist at Eskenazi, Clark Simons-General Surgeon at Eskenazi, and Colin Terry- Biostatistician at Methodist. Qing Yu, PhD- Assistant Research Professor of Orthopaedic Surgery at IU will provide statistical analysis as needed. The DSMB has the independent ability to stop the study at any time if there is a concern for patient safety.

7.0 Study Withdrawal/Discontinuation

Subjects have the right to withdraw from the study at any time and for any reason without prejudice to future medical care. If a subject wishes to withdraw from the study, they must notify a member of the research team. Once withdrawn, no further data will be collected from the subject.

8.0 Statistical Considerations

Sample size:

This is a pilot study since the primary purpose of this study is to collect preliminary data on estimating the complication rates for orthopedic trauma patients who will receive blood transfusion either with a liberal transfusion strategy or a conservative strategy. The primary outcome of this study is whether a patient develops a complication while following a

conservative or liberal transfusion strategy for anemia. From our retrospective study, we anticipate the true complication rate would be anywhere between 30% and 50%. We want to estimate this proportion with 95% confidence and no more than 14% margin of error. With a sample size of 50 per group we would be able to reach this goal. For example, if the true proportion is 40%, the margin of error will be 13.6% and the maximum margin of error would be 13.9% when the true proportion is 50%.

Up to 370 subjects will be enrolled as part of the non-treatment group.

Data Analysis:

The primary endpoint is a dichotomous outcome, the presence or absence of a complication at post blood transfusion. A point estimate (sample proportion) and a 95% confidence interval for the proportion will be reported. This proportion will be computed for each of the two blood transfusion strategies. Although we did not power the study to detect a difference in complication rate between two strategies, we will compare the complication rates between two groups of patients. Descriptive statistics, like, mean, median, standard deviation for continuous outcomes will be used to describe the subjects' characteristics at baseline. Frequency counts and percent will be used for the categorical outcomes. Baseline clinical and demographic data will be compared between two groups to assess the effectiveness of the randomization. Dichotomous and ordinal variables will be examined using chi-square tests and continuous measures with Student's t-tests. Exploratory analysis will be performed to compute p-values which will be presented as an aid to evaluate the overall comparability of the treatment groups at baseline. Logistic regression model will be used to compare the complication rate or infection rate between two groups and baseline covariates will be included in the model if two groups are found to be significantly different in those covariates.

9.0 Privacy/Confidentiality Issues

Standard HIPAA practices will apply to all sensitive data recorded for study purposes. All attempts will be made to maintain confidentiality between study participants and the research team. Computer/files will be password protected, kept behind locked doors, and located in an area with no public access.

10.0 Follow-up and Record Retention

Duration of the study will last approximately 3 years or until 100 patients have been enrolled with one year follow-up and all necessary data has been collected and analyzed.

Upon study completion, records will be retained for a minimum of 7 years as required by state law. After mandatory retention period, sensitive information will be disposed of by means of hospital provided secure document disposal.

11.0 Investigator Environment and Support

The Orthopaedic research team based at Eskenazi Health has a long history of successful participation in prospective trauma research studies. The PI has successfully partnered with Eskenazi Health to waive fees for research patients to return for appointments in clinic. As it would be unethical to charge patients for research appointments, both facility and physician charges are waived. This helps patients defray costs for parking and travel, and significantly decreases the loss to follow-up.

This study represents a landmark multidisciplinary approach to prospective research at Eskenazi Health. The PI spent over a year recruiting and meeting with 30 IU clinical scientists from the disciplines of Orthopaedic Trauma, General Surgery, Anesthesiology, Physical Medicine & Rehab, and two IU PhD biostatistician. This protocol represents the consensus opinion of all of these faculty. The team consists of clinicians who prefer a conservative transfusion strategy, as well as those who prefer a more liberal transfusion strategy. The protocol was revised multiple times until all clinical scientists felt it was a safe and responsible approach to further study transfusion strategies in this young, healthy patient population.

The research team also consists of two full-time research coordinators, Valda Frizzell and Molly Moore, who have a cumulative experience of decades in participating in prospective studies such as this.

12.0 References:

1. Leal-Noval, S.R., et al., *Transfusion of blood components and postoperative infection in patients undergoing cardiac surgery*. Chest, 2001. **119**(5): p. 1461-8.
2. Hebert, P.C., et al., *A multicenter, randomized, controlled clinical trial of transfusion requirements in critical care. Transfusion Requirements in Critical Care Investigators, Canadian Critical Care Trials Group*. N Engl J Med, 1999. **340**(6): p. 409-17.
3. Carson, J.L., et al., *Risk of bacterial infection associated with allogeneic blood transfusion among patients undergoing hip fracture repair*. Transfusion, 1999. **39**(7): p. 694-700.
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5. Hill, G.E., et al., *Allogeneic blood transfusion increases the risk of postoperative bacterial infection: a meta-analysis*. J Trauma, 2003. **54**(5): p. 908-14.
6. Vincent, J.L., et al., *Anemia and blood transfusion in critically ill patients*. JAMA, 2002. **288**(12): p. 1499-507.
7. Taylor, R.W., et al., *Impact of allogenic packed red blood cell transfusion on nosocomial infection rates in the critically ill patient*. Crit Care Med, 2002. **30**(10): p. 2249-54.
8. Leung, J.M., et al., *Electrocardiographic ST-segment changes during acute, severe isovolemic hemodilution in humans*. Anesthesiology, 2000. **93**(4): p. 1004-10.
9. Weiskopf, R.B., et al., *Human cardiovascular and metabolic response to acute, severe isovolemic anemia*. JAMA, 1998. **279**(3): p. 217-21.
10. Johnston, P., et al., *Is perioperative blood transfusion a risk factor for mortality or infection after hip fracture?* J Orthop Trauma, 2006. **20**(10): p. 675-9.

Appendix A: Screening Form

Subject ID: _____

Date: ____/____/____

	Inclusion: (Must answer YES to all)	
1.	Patients aged 18 to 50 years	<input type="checkbox"/> Yes <input type="checkbox"/> No
2.	Trauma patients admitted to participating hospital with any Orthopaedic injury who have been determined to be stable by the Trauma Service (General Surgery) and are no longer within the resuscitation phase of initial treatment. This is defined as a normal urine output (greater than 0.5 ml/kg/hr) and a systolic blood pressure greater than 90 mmHg for greater than 6 hours without fluid bolus or transfusion during that time	<input type="checkbox"/> Yes <input type="checkbox"/> No
3.	Hemoglobin less than 9 g/dL or expected drop below 9 g/dL with planned surgery	<input type="checkbox"/> Yes <input type="checkbox"/> No
	Exclusion: (Must answer NO to all)	
1.	Women who are pregnant	<input type="checkbox"/> Yes <input type="checkbox"/> No
2.	Prisoner	<input type="checkbox"/> Yes <input type="checkbox"/> No
3.	Head injury(Glasgow Coma Scale less than 8 over 48 hours from presentation)	<input type="checkbox"/> Yes <input type="checkbox"/> No
4.	Known cardiac, renal (defined as having Serum Creatinine >1.2 at time of enrollment), liver, or pulmonary disease	<input type="checkbox"/> Yes <input type="checkbox"/> No
5.	Sickle cell anemia	<input type="checkbox"/> Yes <input type="checkbox"/> No
6.	History of cancer	<input type="checkbox"/> Yes <input type="checkbox"/> No
7.	Preexisting weakness, paresthesias, deformities, or other conditions which might affect functional outcome in the surgeon's opinion	<input type="checkbox"/> Yes <input type="checkbox"/> No
8.	Spinal cord injury	<input type="checkbox"/> Yes <input type="checkbox"/> No
9.	Patients with burns expected to require operative treatment	<input type="checkbox"/> Yes <input type="checkbox"/> No
10.	Unlikely to follow-up, as determined by the attending physician	<input type="checkbox"/> Yes <input type="checkbox"/> No
11.	COVID positive	<input type="checkbox"/> Yes <input type="checkbox"/> No

If you answered yes to any of the exclusion items 1-11, the patient should be excluded.

Patient Enrollment Status:

- ☐ Included
- ☐ Excluded
- ☐ Refusal to consent (otherwise met inclusion/exclusion criteria)
- ☐ Inability to consent (otherwise met inclusion/exclusion criteria)

Appendix B: Patient Contact Form

Subject ID: _____

Date: ____/____/____

Patient Name: _____

DOB: ____/____/____

Address: _____

City: _____

Zip Code: _____ Home Phone: (____) ____ - _____

Cell Phone: (____) ____ - _____

Alternate Contact # 1

Name: _____

Relationship to patient: _____

Address: _____

City: _____

Zip Code: _____ Home Phone: (____) ____ - _____

Cell Phone: (____) ____ - _____

Alternate Contact # 2

Name: _____

Relationship to patient: _____

Address: _____

City: _____

Zip Code: _____ Home Phone: (____) ____ - _____

Cell Phone: (____) ____ - _____

Appendix C: Pre-Injury Musculoskeletal Function Assessment (MFA)

Subject ID: _____

Date: ____/____/____

Visit Interval: ☒ Pre-injury

Musculoskeletal Function Assessment

We would like you to answer the questions in this survey based on your condition before your injury.

Please answer "YES" or "NO" to each question by putting a check in the box ☐ next to the question. If the question was true for you before your injury, choose "YES". If the question was not true for you before your injury, choose "NO".

If you wish to comment on any of the questions, please use the space in the margins. Please answer all questions, even though some of the questions may not seem to apply to you.

Appendix C: Pre-Injury Musculoskeletal Function Assessment (MFA)

Subject ID: _____

Date: ____/____/____

Visit Interval: ☒ Pre-injury

ACTIVITIES USING YOUR ARMS OR LEGS

This first set of questions is about using your arms or legs to do such things as reaching, walking, and carrying. ***Before your injury . . .***

1. Were you able to walk?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
2. Did you feel unsteady on your feet?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
3. Was it difficult for you to reach up high?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
4. Did you straighten or bend your arm(s) completely?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
5. Did you straighten or bend your leg(s) completely?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
6. Did you pivot?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
7. Did you climb up and down ladders?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
8. Did you have to rest often when walking?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
9. Did you avoid stairs?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
10. Did you stand for long periods of time?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
11. Was it hard for you to get moving after you'd been sitting or lying down?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
12. Did you always walk with a limp?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
13. Did your leg sometimes lock or give-way?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
14. Did you have trouble getting in or out of a low chair?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
15. Did you have trouble getting in or out of bed?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
16. Did you kneel?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
17. Did you pick up things from the floor?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
18. Did you run at all?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
19. Did you have trouble getting in or out of a car?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
20. Had you stopped using public transportation because of your physical condition?	<input type="checkbox"/> Yes	<input type="checkbox"/> No

Before your injury, how much were you bothered by problems using your arms or legs?

(Please check one)

<input type="checkbox"/> 1 Not at all bothered	<input type="checkbox"/> 2 A little bothered	<input type="checkbox"/> 3 Somewhat bothered	<input type="checkbox"/> 4 Quite bothered	<input type="checkbox"/> 5 Extremely bothered
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Appendix C: Pre-Injury Musculoskeletal Function Assessment (MFA)

Subject ID: _____

Date: ____/____/____

Visit Interval: ☒ Pre-injury

ACTIVITIES USING YOUR HANDS

The following questions are about activities <u>using your hands</u> . Before your injury . . .		
1. Did you have difficulty squeezing things?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
2. Could you make a tight fist?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
3. Was it hard for you to put your hand in your pocket?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
4. Did you have difficulty turning knobs or levers (for example, opening doors, rolling down car windows)?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
5. Did you have trouble holding a book?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
6. Did you have difficulty writing or typing?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
7. Did you have trouble opening medicine bottles or jars?	<input type="checkbox"/> Yes	<input type="checkbox"/> No

Before your injury, how much were you bothered by problems using your hands? (*Please check one*)

<input type="checkbox"/> 1 Not at all bothered	<input type="checkbox"/> 2 A little bothered	<input type="checkbox"/> 3 Somewhat bothered	<input type="checkbox"/> 4 Quite bothered	<input type="checkbox"/> 5 Extremely bothered
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WORK AROUND YOUR HOME

These questions are about <u>activities around your home, including such things as cooking, cleaning, maintenance, or repairs</u> . Before your injury . . .		
1. Did you need help with housework or yard work?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
2. Did you do as <u>much</u> housework or yard work as you wanted?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
3. Was it difficult for you to do household chores because they took so <u>much effort</u> ?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
4. Did you mop or sweep or vacuum?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
5. Was scrubbing a pan or dish difficult?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
6. Did you need someone to cook for you?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
7. Did it take you a <u>long time</u> to do household chores?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
8. Was it difficult for you to shop for groceries or other thing?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
9. Had you stopped doing car, house, or maintenance repairs because of your physical condition?	<input type="checkbox"/> Yes	<input type="checkbox"/> No

Appendix C: Pre-Injury Musculoskeletal Function Assessment (MFA)

Subject ID: _____

Date: ____/____/____

Visit Interval: ☒ Pre-injury

Before your injury, how much were you bothered by problems doing work around your home? *(Please check one)*

<input type="checkbox"/> 1 Not at all bothered	<input type="checkbox"/> 2 A little bothered	<input type="checkbox"/> 3 Somewhat bothered	<input type="checkbox"/> 4 Quite bothered	<input type="checkbox"/> 5 Extremely bothered
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SELF CARE ACTIVITIES

The following questions are about <u>taking care of yourself</u> . <i>Before your injury . . .</i>		
1. Did you wear things that were easier to get into?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
2. Did you <u>sometimes</u> need help from others to get dressed?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
3. Did you struggle with buttons, snaps, hooks, zippers?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
4. Did you have trouble pulling clothes on over your head?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
5. Was it difficult for you to put on shoes, socks, or stockings?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
6. Was it a chore for you to dress because it took so long?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
7. Was it difficult to brush your teeth?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
8. Did you have a difficult time cutting your fingernails?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
9. Did you need help keeping yourself clean after going to the bathroom?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
10. Was it difficult for you to get on or off the toilet?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
11. Was it hard for you to get in or out of the bathtub or shower?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
12. Did you sit while showering?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
13. Did you need help washing yourself?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
14. Did you need help eating?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
15. Was it hard for you to cut food?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
16. Were you stuck at home because of your physical condition?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
17. Had you stopped going out by yourself?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
18. Had you stopped driving because of your physical condition?	<input type="checkbox"/> Yes	<input type="checkbox"/> No

Before your injury, how much were you bothered by problems caring for yourself? *(Please check one)*

<input type="checkbox"/> 1 Not at all bothered	<input type="checkbox"/> 2 A little bothered	<input type="checkbox"/> 3 Somewhat bothered	<input type="checkbox"/> 4 Quite bothered	<input type="checkbox"/> 5 Extremely bothered
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Appendix C: Pre-Injury Musculoskeletal Function Assessment (MFA)

Subject ID: _____

Date: ____/____/____

Visit Interval: ☒ Pre-injury

SLEEP AND REST

These questions are about changes or problems you may have experienced with sleep and rest. **Before your injury . . .**

1. Were you tired all of the time?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
2. Did you have trouble falling asleep at night?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
3. Did you have difficulty sleeping the whole night?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
4. Was it hard for you to get comfortable to sleep?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
5. Did you wake up sooner than you would like?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
6. Did you have disturbing dreams?	<input type="checkbox"/> Yes	<input type="checkbox"/> No

Before your injury, how much were you bothered by problems with sleep and rest? (*Please check one*)

<input type="checkbox"/> 1 Not at all bothered	<input type="checkbox"/> 2 A little bothered	<input type="checkbox"/> 3 Somewhat bothered	<input type="checkbox"/> 4 Quite bothered	<input type="checkbox"/> 5 Extremely bothered
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LEISURE and RECREATIONAL ACTIVITIES

The following questions are about changes or problems you may have had before your injury with leisure time or recreational activities. These activities may include such things as hobbies, sports, crafts, gardening, aerobics, or volunteering. **Before your injury . . .**

1. Was your physical fitness worse because of your health or physical condition?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
2. Did you do less of your usual physical recreational activities because of your health or physical condition?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
3. Had you stopped doing all of your usual physical recreational activities?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
4. Were you doing fewer leisure activities (such as hobbies, crafts, gardening, card playing, going out with friends) because of your health or physical condition?	<input type="checkbox"/> Yes	<input type="checkbox"/> No

Before your injury, how much were you bothered by problems doing leisure and recreational activities? (*Please check one*)

<input type="checkbox"/> 1 Not at all bothered	<input type="checkbox"/> 2 A little bothered	<input type="checkbox"/> 3 Somewhat bothered	<input type="checkbox"/> 4 Quite bothered	<input type="checkbox"/> 5 Extremely bothered
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Appendix C: Pre-Injury Musculoskeletal Function Assessment (MFA)

Subject ID: _____

Date: ____/____/____

Visit Interval: ☒ Pre-injury

RELATIONSHIPS: FAMILY and FRIENDS

These questions are about your relationships with family, friends, and other important people in your life. ***Before your injury . . .***

1. Was there a strain in your relationships with either your friends or family?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
2. Did you feel you just didn't want to be around anybody?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
3. Was it hard for you to get either your family or friends to help you do things?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
4. Were you lonely?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
5. Did you feel that either your friends or family had shied away from you?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
6. Did you often act irritable towards those around you (for example, snap at people, give sharp answers, criticize easily)?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
7. Did you miss being with either your friends or family?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
8. Did you feel like being less intimate because of your physical condition?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
9. Had your sexual life changed because of your physical condition?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
10. Did you enjoy sex less because of your physical condition?	<input type="checkbox"/> Yes	<input type="checkbox"/> No

Before your injury, how much were you bothered by problems you had with your friends, family, and other important people in your life? *(Please check one)*

<input type="checkbox"/> 1 Not at all bothered	<input type="checkbox"/> 2 A little bothered	<input type="checkbox"/> 3 Somewhat bothered	<input type="checkbox"/> 4 Quite bothered	<input type="checkbox"/> 5 Extremely bothered
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THINKING

These questions are about thinking, concentrating, or remembering. ***Before your injury . . .***

1. Did it take you a long time to figure things out?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
2. Did you have problems with concentration?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
3. Were you confused and scattered?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
4. Were you forgetful?	<input type="checkbox"/> Yes	<input type="checkbox"/> No

Before your injury, how much were you bothered by problems with thinking, concentrating, and remembering? *(Please check one)*

<input type="checkbox"/> 1 Not at all bothered	<input type="checkbox"/> 2 A little bothered	<input type="checkbox"/> 3 Somewhat bothered	<input type="checkbox"/> 4 Quite bothered	<input type="checkbox"/> 5 Extremely bothered
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Appendix C: Pre-Injury Musculoskeletal Function Assessment (MFA)

Subject ID: _____

Date: ____/____/____

Visit Interval: ☒ Pre-injury

LIFE CHANGES and FEELINGS

The following questions are about the day to day adjustments and feelings you may have been experiencing in your life before your injury. ***Before your injury . . .***

1. Did you sometimes use your physical condition as an excuse <u>not</u> to do things?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
2. Did you have to concentrate when using your hands, arms, legs, or feet?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
3. Did you avoid using your hands, arms, legs, or feet?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
4. Did you protect your hands, arms, legs, or feet?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
5. Did you accept you physical condition?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
6. Did you feel your life had changed because of your health or physical condition?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
7. Did you feel your physical condition was getting worse over time?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
8. If you did too much in one day, did it affect what you did the next day?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
9. Did you feel disabled, even though you may have looked fine to others?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
10. Did you feel useless?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
11. Did you feel unattractive?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
12. Did your physical condition make you feel less capable?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
13. Did you feel sorry for yourself?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
14. Did you feel like you complained a lot?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
15. Did you have to ask for help a lot?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
16. Did you feel angry or frustrated about your health or any physical condition?	<input type="checkbox"/> Yes	<input type="checkbox"/> No

Before your injury, how much were you bothered by the day to day adjustments you were making and the feelings you were experiencing in your life?

<input type="checkbox"/> 1 Not at all bothered	<input type="checkbox"/> 2 A little bothered	<input type="checkbox"/> 3 Somewhat bothered	<input type="checkbox"/> 4 Quite bothered	<input type="checkbox"/> 5 Extremely bothered
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Appendix C: Pre-Injury Musculoskeletal Function Assessment (MFA)

Subject ID: _____

Date: ____/____/____

Visit Interval: ☒ Pre-injury

WORK ACTIVITIES

Were you working before you injury?

☐ No.....Were you unable to work because of your health or physical condition?

☐ No

☐ Yes

☐ Yes..... (please answer the questions below)

Please answer these questions as they describe your experiences at work before your injury. ***Before your injury . . .***

1. Were you making changes in your job?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
2. Was it more difficult for you to do your job because of your health or physical condition?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
3. Were you slow at your job because of your health or physical condition?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
4. Did you take more breaks because of your health or physical condition?	<input type="checkbox"/> Yes	<input type="checkbox"/> No

Before your injury, how much were you bothered by problems with work activities, because of your physical condition?
(Please check one)

<input type="checkbox"/> 1 Not at all bothered	<input type="checkbox"/> 2 A little bothered	<input type="checkbox"/> 3 Somewhat bothered	<input type="checkbox"/> 4 Quite bothered	<input type="checkbox"/> 5 Extremely bothered
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Appendix D: Follow-up Musculoskeletal Function Assessment (MFA)

Subject ID: _____

Date: ____/____/____

Visit Interval: ☐ 6month ☐ 1 year

Musculoskeletal Function Assessment

We are interested in finding out how you are managing with your injury or arthritis this week.

Please answer "YES" or "NO" to each question by putting a check in the box ☐ next to the question. If the question was true for you and is related to your injury or arthritis, choose "YES". If the question was not true for you and is not related to your injury or arthritis, choose "NO".

If you wish to comment on any of the questions, please use the space in the margins. Please answer all questions, even though some of the questions may not apply to your injury or arthritis.

Appendix D: Follow-up Musculoskeletal Function Assessment (MFA)

Subject ID: _____

Date: ____/____/____

Visit Interval: ☐ 6month ☐ 1 year

ACTIVITIES USING YOUR ARMS OR LEGS

This first set of questions is about changes or problems you may have using your arms or legs to do such things as reaching, walking, and carrying. ***This week, because of your injury or arthritis . . .***

1. Are you able to walk?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
2. Do you feel unsteady on your feet?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
3. Is it difficult for you to reach up high?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
4. Do you straighten or bend your arm(s) completely?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
5. Do you straighten or bend your leg(s) completely?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
6. Do you pivot?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
7. Do you climb up and down ladders?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
8. Do you have to rest often when walking?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
9. Do you avoid stairs?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
10. Do you stand for long periods of time?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
11. Was it hard for you to get moving after you'd been sitting or lying down?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
12. Do you always walk with a limp?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
13. Do your legs sometimes lock or give-way?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
14. Do you have trouble getting in or out of a low chair?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
15. Do you have trouble getting in or out of bed?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
16. Do you kneel?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
17. Do you pick up things from the floor?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
18. Do you run at all?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
19. Do you have trouble getting in or out of a car?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
20. Had you stopped using public transportation because of your physical condition?	<input type="checkbox"/> Yes	<input type="checkbox"/> No

How much are you bothered by problems you are **now** having using your arms or legs?
(Please check one)

<input type="checkbox"/> 1 Not at all bothered	<input type="checkbox"/> 2 A little bothered	<input type="checkbox"/> 3 Somewhat bothered	<input type="checkbox"/> 4 Quite bothered	<input type="checkbox"/> 5 Extremely bothered
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Appendix D: Follow-up Musculoskeletal Function Assessment (MFA)

Subject ID: _____

Date: ____/____/____

Visit Interval: ☐ 6month ☐ 1 year

ACTIVITIES USING YOUR HANDS

The following questions are about activities using your hands. ***This week, because of your injury or arthritis . . .***

1. Do you have difficulty squeezing things?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
2. Do you have difficulty making a tight fist?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
3. Is it hard for you to put your hand in your pocket?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
4. Do you have difficulty turning knobs or levers (for example, opening doors, rolling down car windows)?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
5. Do you have trouble holding a book?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
6. Do you have difficulty writing or typing?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
7. Do you have trouble opening medicine bottles or jars?	<input type="checkbox"/> Yes	<input type="checkbox"/> No

How much are you bothered by problems you are **now** having using your hands? *(Please check one)*

<input type="checkbox"/> 1 Not at all bothered	<input type="checkbox"/> 2 A little bothered	<input type="checkbox"/> 3 Somewhat bothered	<input type="checkbox"/> 4 Quite bothered	<input type="checkbox"/> 5 Extremely bothered
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WORK AROUND YOUR HOME

These questions are about activities around your home, including such things as cooking, cleaning, maintenance, or repairs. ***This week, because of your injury or arthritis . . .***

1. Do you need help with housework or yard work?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
2. Do you do as <u>much</u> housework or yard work?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
3. Do you do household chores but find that it takes more <u>effort</u> ?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
4. Do you mop or sweep or vacuum?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
5. Is scrubbing a pan or dish difficult?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
6. Do you need someone to cook for you?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
7. Does it take you <u>longer</u> to do household chores?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
8. Is it difficult for you to shop for groceries or other thing?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
9. Have you stopped doing car, house, or maintenance repairs because of your injury or arthritis?	<input type="checkbox"/> Yes	<input type="checkbox"/> No

How much are you bothered by problems you are **now** having doing work around your home? *(Please check one)*

<input type="checkbox"/> 1 Not at all bothered	<input type="checkbox"/> 2 A little bothered	<input type="checkbox"/> 3 Somewhat bothered	<input type="checkbox"/> 4 Quite bothered	<input type="checkbox"/> 5 Extremely bothered
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Appendix D: Follow-up Musculoskeletal Function Assessment (MFA)

Subject ID: _____

Date: ____/____/____

Visit Interval: ☐ 6month ☐ 1 year

SELF CARE ACTIVITIES

The following questions are about taking care of yourself. ***This week, because of your injury or arthritis .***

1. Do you wear things that are easier to get into?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
2. Do you <u>sometimes</u> need help from others to get dressed?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
3. Do you struggle with buttons, snaps, hooks, zippers?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
4. Do you have trouble pulling clothes on over your head?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
5. Is it difficult for you to put on shoes, socks, or stockings?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
6. Is it a chore for you to dress because it took so long?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
7. Is it difficult to brush your teeth?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
8. Do you have a difficult time cutting your fingernails?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
9. Do you need help keeping yourself clean after going to the bathroom?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
10. Is it difficult for you to get on or off the toilet?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
11. Is it hard for you to get in or out of the bathtub or shower?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
12. Do you sit while showering?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
13. Do you need help washing yourself?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
14. Do you need help eating?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
15. Is it hard for you to cut food?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
16. Are you stuck at home?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
17. Have you stopped going out by yourself?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
18. Have you stopped driving because of your physical condition?	<input type="checkbox"/> Yes	<input type="checkbox"/> No

This week, because of your injury or arthritis, how much were you bothered by problems caring for yourself? (*Please check one*)

<input type="checkbox"/> 1 Not at all bothered	<input type="checkbox"/> 2 A little bothered	<input type="checkbox"/> 3 Somewhat bothered	<input type="checkbox"/> 4 Quite bothered	<input type="checkbox"/> 5 Extremely bothered
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Appendix D: Follow-up Musculoskeletal Function Assessment (MFA)

Subject ID: _____

Date: ____/____/____

Visit Interval: ☐ 6month ☐ 1 year

SLEEP AND REST

These questions are about changes or problems you may be experiencing with sleep and rest. ***This week, because of your injury or arthritis . . .***

1. Are you tired all of the time?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
2. Do you have trouble falling asleep at night?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
3. Do you have difficulty sleeping the whole night?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
4. Is it hard for you to get comfortable to sleep?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
5. Do you wake up sooner than you would like?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
6. Do you have disturbing dreams?	<input type="checkbox"/> Yes	<input type="checkbox"/> No

How much are you bothered by problems you are **now** having with sleep and rest? (*Please check one*)

<input type="checkbox"/> 1 Not at all bothered	<input type="checkbox"/> 2 A little bothered	<input type="checkbox"/> 3 Somewhat bothered	<input type="checkbox"/> 4 Quite bothered	<input type="checkbox"/> 5 Extremely bothered
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LEISURE and RECREATIONAL ACTIVITIES

We would also like to know about changes or problems you are having with leisure time or recreational activities. These activities may include such things as hobbies, sports, crafts, gardening, aerobics, or volunteering. ***This week, because of your injury or arthritis . . .***

1. Is your physical fitness worse because of your health or physical condition?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
2. Do you do <u>less</u> of your usual physical recreational activities because of your health or physical condition?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
3. Have you stopped doing <u>all</u> of your usual physical recreational activities?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
4. Are you doing fewer leisure activities (such as hobbies, crafts, gardening, card playing, going out with friends) because of your health or physical condition?	<input type="checkbox"/> Yes	<input type="checkbox"/> No

How much are you bothered by problems you are **now** having with leisure and recreational activities? (*Please check one*)

<input type="checkbox"/> 1 Not at all bothered	<input type="checkbox"/> 2 A little bothered	<input type="checkbox"/> 3 Somewhat bothered	<input type="checkbox"/> 4 Quite bothered	<input type="checkbox"/> 5 Extremely bothered
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Appendix D: Follow-up Musculoskeletal Function Assessment (MFA)

Subject ID: _____

Date: ____/____/____

Visit Interval: ☐ 6month ☐ 1 year

RELATIONSHIPS: FAMILY and FRIENDS

These questions are about your relationships with family, friends, and other important people in your life. ***This week, because of your injury or arthritis . . .***

1. Is there a strain in your relationships with either your friends or family?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
2. Do you feel you just don't want to be around anybody?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
3. Is it hard for you to get either your family or friends to help you do things?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
4. Are you lonely?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
5. Do you feel that either your friends or family had shied away from you?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
6. Do you often act irritable towards those around you (for example, snap at people, give sharp answers, criticize easily)?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
7. Do you miss being with either your friends or family?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
8. Do you feel like being less intimate?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
9. Has your sexual life changed?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
10. Do you enjoy sex less?	<input type="checkbox"/> Yes	<input type="checkbox"/> No

How much are you bothered by problems you are **now** having with your friends, family, and other important people in your life? (*Please check one*)

<input type="checkbox"/> 1 Not at all bothered	<input type="checkbox"/> 2 A little bothered	<input type="checkbox"/> 3 Somewhat bothered	<input type="checkbox"/> 4 Quite bothered	<input type="checkbox"/> 5 Extremely bothered
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THINKING

These questions are about thinking, concentrating, or remembering. ***This week, because of your injury or arthritis . . .***

1. Does it take you a long time to figure things out?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
2. Do you have problems with concentration?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
3. Are you confused and scattered?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
4. Are you more forgetful?	<input type="checkbox"/> Yes	<input type="checkbox"/> No

How much are you bothered by problems you are **now** having thinking, concentrating, and remembering? (*Please check one*)

<input type="checkbox"/> 1 Not at all bothered	<input type="checkbox"/> 2 A little bothered	<input type="checkbox"/> 3 Somewhat bothered	<input type="checkbox"/> 4 Quite bothered	<input type="checkbox"/> 5 Extremely bothered
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Appendix D: Follow-up Musculoskeletal Function Assessment (MFA)

Subject ID: _____

Date: ____/____/____

Visit Interval: ☐ 6month ☐ 1 year

LIFE CHANGES and FEELINGS

These questions are about the day to day adjustments you may be making because of your injury or arthritis and feelings you may be having about your experiences. ***This week, because of your injury or arthritis . . .***

1. Do you sometimes use your physical condition as an excuse <u>not</u> to do things?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
2. Do you have to concentrate when using your injured limb or arthritic joints?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
3. Do you avoid using your injured limb or arthritic joints?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
4. Do you protect your injured limb or arthritic joints?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
5. Do you think everything will work out in the long run?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
6. Do you accept your current situation?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
7. Do you feel everything is back to normal?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
8. Do you feel your life has changed quite a bit?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
9. Are you getting worse?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
10. If you do too much in one day, does it affect what you do the next day?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
11. Do you feel disabled, even though you may look fine to others?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
12. Do you feel useless?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
13. Do you feel unattractive?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
14. Does your injury or arthritis make you feel less capable?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
15. Do you feel sorry for yourself?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
16. Do you feel like you complained a lot?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
17. Do you have to ask for help a lot?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
18. Do you feel angry or frustrated that you have this injury or arthritis?	<input type="checkbox"/> Yes	<input type="checkbox"/> No

How much are you bothered by the day to day adjustments you are making in your life and the feelings you are **now** experiencing, because of your injury or arthritis? (*Please check one*)

<input type="checkbox"/> 1 Not at all bothered	<input type="checkbox"/> 2 A little bothered	<input type="checkbox"/> 3 Somewhat bothered	<input type="checkbox"/> 4 Quite bothered	<input type="checkbox"/> 5 Extremely bothered
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Appendix D: Follow-up Musculoskeletal Function Assessment (MFA)

Subject ID: _____

Date: ____/____/____

Visit Interval: ☐ 6month ☐ 1 year

WORK ACTIVITIES

Are you working now?

☐ No.....Are you unable to work because of your injury or arthritis?

☐ No (Please skip to the next section)

☐ Yes (Please skip to the next section)

☐ Yes..... (Please answer the questions below)

Please answer these questions as they describe your experiences at work. ***This week, because of your injury or arthritis . . .***

1. Are you making changes in your job?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
2. Is it more difficult for you to do your job now?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
3. Are you slower at your job?	<input type="checkbox"/> Yes	<input type="checkbox"/> No
4. Do you take more breaks?	<input type="checkbox"/> Yes	<input type="checkbox"/> No

How much are you bothered by problems you are **now** having with work activities, because of your injury or arthritis?
(Please check one)

<input type="checkbox"/> 1 Not at all bothered	<input type="checkbox"/> 2 A little bothered	<input type="checkbox"/> 3 Somewhat bothered	<input type="checkbox"/> 4 Quite bothered	<input type="checkbox"/> 5 Extremely bothered
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Appendix D: Follow-up Musculoskeletal Function Assessment (MFA)

Subject ID: _____ Date: ____/____/____ Visit Interval: ☐ 6month ☐ 1 year

If you have completed this survey before, please answer the following three questions. If you are completing this survey for the first time, please skip them.

1. Have you had any injuries or other important changes in your health since you completed the last survey?

☐ No

☐ Yes... If yes, please list whatever injuries or health changes you have had:

2. Have you had any surgeries or hospitalizations since you completed the last survey?

☐ No

☐ Yes... If yes, please list whatever injuries or health changes you have had:

3. How is your injury or arthritis now, compared to when you completed the last survey? (*Check one*)

Much worse.....☐

Slightly worse.....☐

About the same.....☐

Slightly better.....☐

Much better.....☐

Appendix E: 2 Minute Walk Test

Subject ID: _____

Date: ____/____/____ Assistance Level: _____ O₂ %: _____

Assistive Device Used: _____ Distance ambulated in 2 minutes: _____

____ Vitals before test: HR: ____ BP: ____/____ O₂ ____ Vitals after test: HR: ____

BP: ____/____ O₂ ____

Pt unable to complete test due to:

- ☐ Pending OR/on bed rest
- ☐ Physical inability to complete due clinical indication such as pain/decrease in vitals.

Completed by: _____

—

Date: ____/____/____ Assistance Level: _____ O₂ %: _____

Assistive Device Used: _____ Distance ambulated in 2 minutes: _____

____ Vitals before test: HR: ____ BP: ____/____ O₂ ____ Vitals after test: HR: ____

BP: ____/____ O₂ ____

Pt unable to complete test due to:

- ☐ Pending OR/on bed rest
- ☐ Physical inability to complete due clinical indication such as pain/decrease in vitals.

Completed by: _____

—

Date: ____/____/____ Assistance Level: _____ O₂ %: _____

Assistive Device Used: _____ Distance ambulated in 2 minutes: _____

____ Vitals before test: HR: ____ BP: ____/____ O₂ ____ Vitals after test: HR: ____

BP: ____/____ O₂ ____

Pt unable to complete test due to:

- ☐ Pending OR/on bed rest
- ☐ Physical inability to complete due clinical indication such as pain/decrease in vitals.

Appendix E: 2 Minute Walk Test

Subject ID: _____

Completed by: _____

—

Appendix F: Adverse Event

Subject ID: _____

Report Date: ____/____/____

Interval: ☐ 2 weeks ☐ 6 weeks ☐ 3 months ☐ 6 months ☐ 9 months ☐ 1 year

Date of event: ____/____/____

- | | | |
|---|--|--|
| <input type="checkbox"/> Osteomyelitis | <input type="checkbox"/> Urinary tract infection | <input type="checkbox"/> Pneumonia |
| <input type="checkbox"/> Renal insufficiency | <input type="checkbox"/> Cardiac ischemia | <input type="checkbox"/> Myocardial infarction |
| <input type="checkbox"/> Deep venous thrombosis | <input type="checkbox"/> Reoperation | <input type="checkbox"/> Re-hospitalization (____/____/____) |
| <input type="checkbox"/> Infection | | |
| <input type="checkbox"/> Superficial (cellulitis treated with oral antibiotics) | | |
| <input type="checkbox"/> Deep (requires IV antibiotics or surgical debridement) | | |
| <input type="checkbox"/> Other: _____ | | |

Please list any details of event: _____

Event related to treatment?

- ☐ Related ☐ Probably Related ☐ Possibly Related ☐ Not Related

Classification of AE:

- ☐ Expected
- ☐ Unexpected
- ☐ Serious (check below)
- ☐ Requires/prolongs inpatient hospitalization
- ☐ Immediately life-threatening
- ☐ Permanently disabled
- ☐ Fatal

Outcome:

- ☐ Resolveddate resolved ____/____/____
- ☐ Resolved with impairment....date resolved ____/____/____
- Degree of impairment: ☐ Mild ☐ Moderate ☐ Severe
- ☐ Ongoing

Appendix G: Protocol Deviation

Subject ID: _____

Report Date: ____/____/____

1. Date of deviation: ____/____/____

2. Please describe protocol deviation: _____

Appendix H: Escape Criteria

Subject ID: _____

Report Date: ____/____/____

1. Transfusion Time: ____:

2. Reason patient was transfused:

- ☐ Patient has any of the following symptoms at rest: chest pain, shortness of breath, dizziness
- ☐ Patient has a mean arterial pressure less than 50 mmHg that is not responsive to fluid resuscitation
- ☐ At any time the patient's heart rate increases by more than 30% above baseline while under anesthesia
- ☐ The patient's urine output drops to less than 0.5 mL/kg/hour and remains decreased despite adequate rehydration with fluids
- ☐ Any objective evidence of cardiac ischemia including the following: EKG changes such as ST depression, an elevation of serum cardiac markers, a base deficit greater than 6, lactate greater than 2.5 that does not respond to fluid resuscitation
- ☐ A decrease in systolic blood pressure by 10% or more with exercise (physical therapy) that does not improve with fluid resuscitation
- ☐ Uncontrolled source of hemorrhage
- ☐ Asymptomatic- Hgb dropped below randomization threshold

3. Lowest Hgb prior to transfusion: _____ g/dL

Appendix H: Escape Criteria

Subject ID: _____

Report Date: ____/____/____

Appendix I: Length of Stay

Subject ID: _____

Report Date: ____/____/____

1. Date of hospital admission: ____/____/____

2. Date of hospital discharge: ____/____/____

3. Length of hospital stay: ____ days

Appendix J: American Academy of Orthopaedic Surgeons Abstract February 2011 San Diego, CA (Podium Presentation)

Does Anemia or Transfusion Increase the Risk of Complications in Orthopaedic Trauma Patients?

Introduction: Transfusion of young, healthy, asymptomatic Orthopaedic trauma patients is routine at many institutions due to concerns for anemia. The purpose of this study is to assess whether anemia, with or without allogeneic blood transfusion, contributes to an increased complication rate in healthy orthopaedic trauma patients and whether the transfusion itself might be an independent risk factor for a complication.

Methods: A retrospective review of 104 patients treated at a level-one trauma center from September 2006-February 2009 was conducted. Inclusion criteria were patients 18-50 years of age, a hemoglobin concentration of 9.0 g per deciliter (g/dL) or less at any time during their admission. Head injured patients or patients with history of pulmonary or cardiac conditions were excluded. The patients were initially divided into two cohorts by their lowest hemoglobin level prior to first transfusion of < 7.0 (g/dl) and >7.0 (g/dl); this was followed by further division depending on whether the patients were transfused. Logistic regression analysis was performed.

Results: There was no increased risk for complication related to anemia itself ($p=0.3$). However, there was a significant risk for complication related to transfusion ($p<0.01$); furthermore, there was a dose-dependent effect with complication risk increasing with each unit transfused ($p=0.02$). Other factors such as age, injury severity score (ISS), and gender were considered and when adjusted did not change these results.

Conclusion: In young, healthy Orthopaedic trauma patients anemia does not appear to act as an independent risk factor for complications; however, allogeneic blood transfusion does appear to be a significant independent risk factor for complication and has a dose-dependent effect.

Does Anemia or Transfusion Increase the Risk of Complications in Orthopaedic Trauma Patients?

Mullis BH, Fisk E, Weaver D, Zhao Q, Daggy J Indiana University School of Medicine Department of Orthopaedics

Introduction: Transfusion of young, healthy, asymptomatic Orthopaedic trauma patients is routine at many institutions due to concerns for anemia. The purpose of this study was to assess whether anemia, with or without allogeneic blood transfusion, contributed to an increased complication rate in healthy Orthopaedic trauma patients and whether the transfusion itself might be an independent risk factor for a complication.

Methods: A retrospective review of 104 patients treated at a level 1 trauma center by a single surgeon from September 2006- February 2009 was conducted. Inclusion criteria were patients 18-50 years of age and a hemoglobin concentration of 9.0 g per deciliter (g/dL) or less at any time during their admission. Patients with head injury, pregnancy, or patients with a pre-existing history of pulmonary, cardiac, or renal conditions were excluded. The patients were initially divided into two cohorts by their lowest hemoglobin level prior to first transfusion of < 7.0 (g/dl) and >7.0 (g/dl); this was followed by further division depending on whether the patients were transfused. Logistic regression analysis was performed. Patients' charts were reviewed for complications extending through a one-year period after initial discharge from the inpatient service. Patients who had not received follow-up treatment through a known outpatient clinic were contacted by telephone to ascertain outcome. Overall, 5 out of 104 patients were lost at one-year follow-up. Among other variables, postoperative complications were recorded as our primary outcome. Superficial wound infection was defined as cellulitis within one year requiring oral antibiotics; deep wound infection was defined as any infection within 1 year of injury which required intravenous antibiotics or surgical debridement in the operating room. Complications included (not all were found but the following were specifically searched) superficial infection (defined as cellulitis requiring oral antibiotics), deep infection (defined as requiring intravenous antibiotics or surgical debridement), urinary tract infection, pneumonia, pulmonary embolism, deep venous thrombosis, acute renal failure or insufficiency, nonunion, delayed union, compartment syndrome, osteomyelitis, nerve palsy, anoxic brain injury, cardiac ischemia or infarct, pancreatitis, or death.

Results: There was no increased risk for complication related to anemia itself ($p=0.3$). However, there was a significant risk for complication related to transfusion ($p<0.01$); furthermore, there was a dose-dependent effect with complication risk increasing with each unit transfused ($p=0.02$). Other factors such as age, injury severity score (ISS), and gender were considered and when adjusted did not change these results.

Conclusion: In young, healthy Orthopaedic trauma patients anemia does not appear to act as an independent risk factor for complications; however, allogeneic blood transfusion does appear to be a significant independent risk factor for complication and has a dose-dependent effect. Based on our findings from this retrospective study, we are designing a multi-specialty prospective study on Orthopaedic Trauma patients at our institution to determine if transfusion simply acts as a marker for patients at higher risk for complication due to injury or if transfusion might contribute directly to these complications.