The Multinational Association of Supportive Care in Cancer (MASCC) risk index score:

Neutropenic fever and provider intuition

by Mark Blackmon

A thesis presented to the Honors College of Middle Tennessee State University in partial fulfillment of the requirements for graduation from the University Honors College

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Neutropenic fever and provider intuition

by Mark Blackmon

APPROVED:

Dr. Michelle Finch, Thesis Director Associate Professor, Department of Nursing

Dr. Rebekka King, Thesis Committee Chair Associate Professor, Department of Philosophy and Religious Studies

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## List of Abbreviations

MASCC	The Multinational Association of Supportive Care in	
	Cancer risk index score	
FN	Febrile Neutropenia or Neutropenic Fever	
ICD	International Classification of Disease code	

#### Abstract

**Background:** The purpose of this study retrospectively applied the Multinational Association of Supportive Care in Cancer (MASCC) risk index to examine the relationship between a provider's intuition and how the MASCC would have determined a patient's course of treatment.

**Methods:** Patient records from three sites over three years (n=105) were reviewed to compare their MASCC score to their actual course of treatment, including antibiotics prescribed, precautions, and other factors.

**Results:** Although providers were accurate in admitting patients a majority of the time (58.1%), there is room for improvement for patients need for admittance based on their risk, a patient's needs intravenous or oral antibiotics, and their precautions.

**Conclusion:** Emphasis should be placed on increasing exposure to the MASCC for provider use so that patients can have increased positive outcomes without risk of further complications or delay in oncology treatment.

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#### Introduction

Treatment approaches for cancer vary widely based on a patient's type of cancer, age, gender, comorbidities, and many other characteristics. No matter the age of the patient, chemotherapy and radiotherapy have the potential to wreak havoc on the body in many ways: hair loss, weight loss, nausea, etcetera. Although these treatments generally have empiric success in removing cancerous cells from the body, most do not discriminate; while removing cancerous cells from the body, chemotherapy and radiotherapy also destroy white-blood cells, inhibiting the body's ability to fight infection. This side effect of the body having an insufficient number of white-blood cells is known as neutropenia (Afzal et al., 2015), which is a serious complication for oncology patients. Although empiric research exists regarding the proper course of treatment for neutropenia, this research project seeks to determine whether hospitals are actually following these guidelines and how this affects a patient's outcome.

#### Neutropenia and Febrile Neutropenia

Neutropenia is a condition wherein the body does not have enough neutrophils, the body's most abundant type of white blood cell (Afzal et al., 2015). In neutropenic oncology patients, the chemotherapy or radiotherapy destroys the body's mature white blood cells as well as its ability to reproduce the immature white blood cells (neutrophils). Neutropenia is distributed into three categories: mild (1.0 to 1.5 x 10<sup>9</sup> cells/L), moderate (0.5 to 1.0 x 10<sup>9</sup> cells/L), and severe ( $\leq 0.5 \times 10^9$  cells/L) (Afzal et al., 2015). For reference in a healthy body, the absolute neutrophil count is between 2,500 and 6,000 cells/ $\mu$ L (2.5 x 10<sup>9</sup> cells/L to 6.0 x 10<sup>9</sup> cells/L) versus 500 cells/ $\mu$ L and 1,500 cells/ $\mu$ L for those in the range of neutropenia (American Cancer Society, 2016).

Neutropenia can be either intrinsic (i.e. genetic abnormalities in the production of neutrophils) or acquired, with acquired being the most common. Although neutropenia can be acquired from both cytotoxic and non-cytotoxic medications, it occurs most in patients receiving antineoplastic medications (Nedved & Akhtari, 2015). Additionally, neutropenia is more common in women and the elderly, with women reporting neutropenia twice as often as males and more than half of cases being reported in patients over 60 (Afzal et al., 2015; Nedved & Akharti, 2015). Chemotherapy induced neutropenia is the primary reason oncology patients are hospitalized and can lead to febrile neutropenia (FN); a further diagnosis of FN has the potential to increase mortality 10-20% based on a different range of complications (Bhatt et al., 2015). Febrile neutropenia (i.e. neutropenic fever), is defined as an oral temperature of  $\geq 38.3^{\circ}$  Celsius (101° F) in a patient with an absolute neutrophil count of  $\leq 500$  cells/µL; additionally, common complications include severe sepsis, invasive fungal infections, acute respiratory failure, and clostridium difficile (C. Diff) colitis (Woldie & Soubani, 2015). Despite these serious complications, perhaps the largest issue lies in the fact that often times chemotherapy and radiotherapy dosage or intensity must be reduced, greatly altering their effectiveness in treating the cancer (Bhatt et al., 2015).

#### **MASCC Risk Index Score**

Although the complications from FN can be life-threating, not all patients presenting with FN may be at as high of a risk for developing complications. Within the last 20 years an empiric, numeric risk assessment tool has been created: The Multinational Association for Supportive Care in Cancer (MASCC) risk index score. The MASCC has a positive predictive value of 98%, a negative predictive value of 86%, and a sensitivity and specificity of 95%, with a higher total score being predictive of a favorable outcome (Klastersky & Paesmans, 2012; Uys, Rapoprt, & Anderson, 2003).

Prognostic factor	Weight
*Burden of febrile neutropenia (no or mild symptoms)	5
No hypotension (systolic BP > 90 mmHg)	5
No chronic obstructive pulmonary disease (COPD)	4
Solid tumor or hematological malignancy with no previous fungal infection	3
No dehydration requiring parenteral fluids	3
*Burden of febrile neutropenia (moderate symptoms)	3
Outpatient status	3
Age < 60 years	2
*Points attributed to the variable "burden of illness" are not cumulative. The maximum theoretical score is therefore 26.	

Table 1: Multinational association for supportive care in cancer scoring system (Uys,

Rapoprt, & Anderson, 2003)

With the development of the MASCC, it became possible to treat low-risk patients in ambulatory settings rather than inpatient settings, thus reducing the medical costs as well as increasing the quality of life for the patient (Uys, Rapoprt, & Anderson, 2003). Additionally, studies show that outpatient management of FN, in carefully considered patients, is just as effective and safe for the patient as inpatient support (Klastersky & Paesmans, 2012).

Perhaps one of the most important factors in the treatment of FN is the financial cost associated with an occurrence. Other than getting to spend more time at home if discharged early, low risk FN patients also receive the benefit of less cost out of pocket. Those low risk patients hospitalized paid significantly more for treatment compared to

those low risk patients who were discharged early with oral antibiotics for an average stay of 5 days (\$16,341 for hospital versus \$10,977 for home care) (Hendricks, Loggers, & Talcott, 2011). Additionally, the overall success rate and response to initial therapy of both groups are nearly identical, with major complications being rare and equal (Elting et al., 2008).

Despite the implementation of the MASCC and other risk indexes, it appears there is still some ambiguity in exactly how to treat patients with FN. Since the 1980's when FN was first observed to be heterogenous, there have been many research studies seeking the most effective treatments, but it appears the questions remain unanswered as seen in several principles in treating FN remained the same from 1993 to 2018 (Pizzo, 2019). Organizations such as the American Society of Clinical Oncology and Infectious Diseases Society of America have offered guidelines regarding the selection and management of outpatient FN patients that coincide with the MASCC and other empiric treatments of FN, with the goal of inclusivity of treatment rather than exclusivity (Taplitz, Kennedy, & Flowers, 2018).

#### **Antibiotic Treatments**

Of particular importance is the antibiotics used to prophylactically treat any infections of a person with FN (Bhatt et al., 2015). In addition to prophylactic antibiotics, the goal should be to locate the source of infection through obtaining two sources of blood cultures; urine, stool, wound, or other cultures; and chest imaging (Taplitz, Kennedy, & Flowers, 2018). The goal of antibiotic treatment in cases of FN is to eliminate any and all sources of infection before it becomes systemic resulting in septicemia, which is especially life threatening in immunocompromised patients. To

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accomplish this aim, broad spectrum antibiotics are prescribed at first indication of FN until cultures return and a more directed treatment plan can be initiated (Afzal et al., 2015). Broad spectrum antibiotics are a nondiscriminatory, nonspecific medication that are used to prevent systemic infection before a more specific source of infection can be identified.

#### **Purpose of Study**

With the understanding that in some cases broad spectrum oral antibiotics are just as effective as intravenous (IV) antibiotics, the implementation of the MASCC has the potential to save FN patients from an in-patient hospital stay if it is used effectively to identify high and low risk patients. The aim of this study was to retrospectively review patient records and apply the MASCC to objective symptoms and findings to identify high and low risk patients with the goal of observing if a provider's intuition agreed with the patient's MASCC and empiric treatment was followed.

#### Methods

#### Sample

All patients admitted with the primary diagnosis of febrile neutropenia at one of three research sites between January 1, 2017 and January 1, 2020 were included in the original population (N=1,036) with exclusion criteria of those patients who develop febrile neutropenia while in the hospital but without a primary diagnosis of febrile neutropenia. Inclusion criteria for the population was derived from the International Classification of Disease (ICD) codes of "agranulocytosis secondary to chemotherapy" (D70.1), "neutropenia, unspecified" (D70.8), and "other neutropenia" (D70.9), regardless of socioeconomic status, race, ethnicity, or gender. Only patients 18 and older were included in the sample in order to exclude any vulnerable populations.

#### **Study Design**

After initial Institutional Review Board (IRB) and research site approval was received, data collection began in April 2020 and ended in August 2020. A retrospective report was generated to include all patients admitted with the primary diagnosis of "neutropenia, unspecified" (ICD Code D70.9), "other neutropenia" (ICD Code D70.8), or "agranulocytosis secondary to chemotherapy" (ICD Code D70.1) between January 1, 2017 and January 1, 2020 at the three research sites. The report was sorted into length of stay and date of admission, then a random number generator was used to select patients from the population to participate in the study. For the four-month data collection period, a total of 603 charts were reviewed with a final sample size of appropriate patients of n=105. It was intended for the full population to be included in the sample; however, a significant number of patients were excluded based on not meeting the diagnosis criteria of febrile neutropenia despite their ICD code. Eligible cases were identified based on primary diagnosis at admission, and manual data extraction was completed to perform a retrospective MASCC score. A study investigator then reviewed the electronic medical record of each eligible case to gain more descriptive information about the patient's clinical status.

#### Instrument

A form was created in REDCap to pull objective information from a patient's chart in order to complete a MASCC for a particular patient; however, since this study is intended to compare provider intuition to objective means, there is some room left for the researcher to interpret the provider's clinical writings. The full instrument can be found in Appendix II.

## Results

## **Characteristics at Presentation**

Characteristic	n (%)
Male	44 (41.9)
Female	61 (58.1)
ICD diagnosis	
D70.1	22 (21)
D70.8	1 (0.9)
D70.9	82 (78.1)
Race/Ethnicity	
Asian	1 (0.9)
African American/Black	18 (17.1)
White (non-Hispanic)	85 (80.1)
Of Hispanic/Latino Descent	1 (0.9)
Avg length of stay (days)	4.40
Avg neutrophil count (x10 <sup>9</sup> )	2.390
Avg temperature (°F)	99.570
Clinically neutropenic	84 (80.0)
Clinically febrile neutropenic	38 (36.2)
Burden of febrile neutropenia	, , , , , , , , , , , , , , , , , , ,
None/Mild	59 (56.2)
Moderate	38 (36.2)
Severe	8 (7.6)
Hypotensive	15 (14.3)
History of COPD/Requiring O2	28 (24.8)
No prior fungal infection	99 <i>(94.3)</i>
Dehydrated	55 (52.4)
Previously outpatient	103 (98.1)
Age less than 60	43 (41.0)
Avg total MASCC score	19.91
Appropriate to admit	61 (58.1)
Placed on neutropenic precautions	38 (36.2)
Avg days on neutropenic precautions	4.16
Placed on IV antibiotics	88 (83.8)
Avg days on IV antibiotics	6.87
Placed on oral antibiotics	17 (16.2)
Avg days on oral antibiotics	6.87
Discharged with antibiotics	36 (34.3)

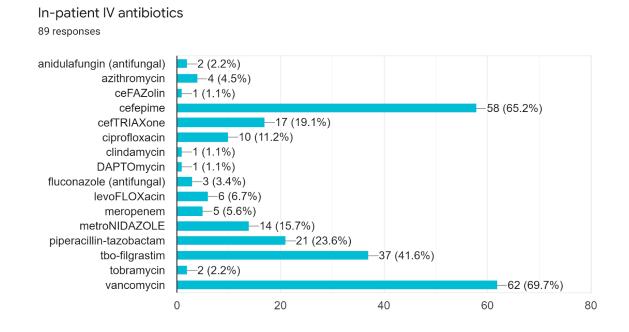
# Table 2: Characteristics of Patients at Presentation to the Emergency Department andtheir Following Treatment

Since women were the majority (58.1%) in the sample, breast cancer, uterine cancer, and ovarian cancer were most seen. The area surrounding these hospitals is predominately white (non-Hispanic), which is reflected in the amount of each race admitted. It additionally became clear that there was no set way to code for FN, leading to the three ICD codes of D70.1, D70.8, and D70.9, although D70.9 was most often used (78.1%). The average patient was not truly neutropenic or febrile, with only 36.2% of patients truly meeting the criteria to be assessed for the MASCC. Although the majority of this sample did not meet the criteria for the MASCC, the providers specifically outlined admitting the rest of the sample (63.8%) for FN.

Thirty-five patients identified as high risk had none/mild symptoms while the remaining twenty-four were categorized as low risk; additionally, eighteen with moderate symptoms were categorized as high risk and twenty as low. All eight with severe symptoms were categorized as high risk with an average MASCC of 10.38. While the range of symptoms varied for each patient, the most consistent factor in determining whether a patient was high or low risk was whether or not they were dehydrated with 52.4% of the latter. Since dehydration is weighted at three points on the MASCC, only one other factor would push the patient over the edge into the high-risk category. Only thirty-eight patients who were appropriately identified to have FN were placed on neutropenic precautions (34.2%). Additionally, only thirty-four of the total eighty-four patients who were neutropenic were placed on neutropenic precautions (40.5%).

#### **Antibiotic Prescription**

The most common antibiotics prescribed overwhelmingly was cefepime and vancomycin for in-patient intravenous use at 65.2% and 69.7% of the total. The length of time IV antibiotics was prescribed varied with an average of 6.87 days.



# *Figure 1: Prescription Percentage and Total Number for In-Patient Intravenous Antibiotics*

In addition to in-patient IV antibiotics, seventeen of the patients additionally received oral antibiotics, with the greatest prescription being sulfamethoxazole/trimethoprim (29.4%). Of note, the patients who received both IV antibiotics and oral antibiotics were switched from IV antibiotics to oral antibiotics after an initial dose of IV antibiotics. The average length of time for oral antibiotics was also 6.87. The length of time being identical for oral antibiotics and IV antibiotics is indicative of complications in reviewing patient records where all medications were listed in one format without a clear indication of how long each medication was taken; therefore, it was assumed that patients received their antibiotics over the course of their stay.

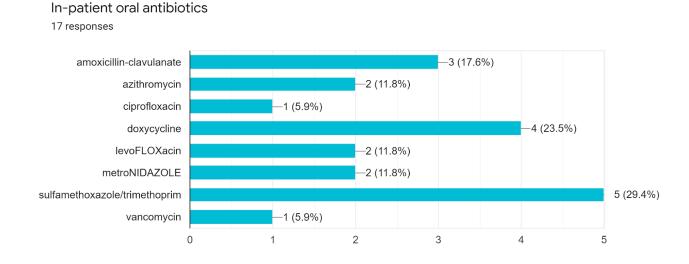


Figure 2: Prescription Percentage and Total Number for In-Patient Oral Antibiotics

Lastly, patients discharged with oral antibiotics overwhelmingly received levofloxacin (28.9%) and amoxicillin-clavulanate (26.3%). No patients were prescribed more than one antibiotic at discharge. Additionally, many patients' health records did not indicate how long the antibiotic should be taken at home, so that information was unavailable for collection.

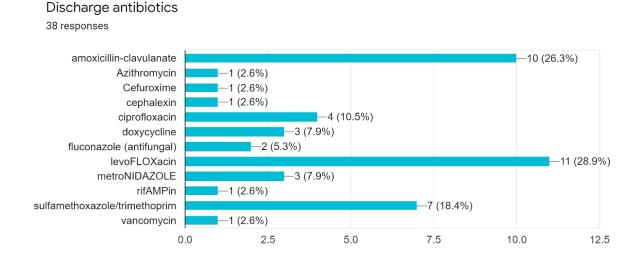


Figure 3: Prescription Percentage and Total Number for Discharge Oral Antibiotics

Of note, seventeen patients did not receive any form of antibiotic treatment whether IV, oral in-patient, or oral at discharge. The range of length of stay for those that received no antibiotic treatment was from zero to twenty days and an average of 2.12 days. All of these patients had a cancer diagnosis and an average absolute neutrophil count of  $1.50 \times 10^9$  for sixteen patients (there is an outlier with an absolute neutrophil count of 13.3 who was not admitted and therefore excluded from this sample).

#### Discussion

#### **Early Implementation of MASCC**

With forty-four patients being admitted when they could have otherwise taken at home oral antibiotics there clearly is some discrepancy between a provider's intuition and the MASCC identified high and low risk. Based on the information presented in Hendricks, Loggers, and Talcott (2011), those forty-four patients ended up paying a large sum of money for a potentially unnecessary hospital stay. There is no doubt that neutropenia, especially FN, is a life-threatening condition; however, as a study by Elting et al. (2008) showed that the patient and their family cope better while performing at home as well as have empirically identical outcomes at low risk levels, there is no reason to not offer them the opportunity.

Perhaps the greatest reason for this lack of clarity in admitting patients is the constant changing tide of medicine. There are countless tools and resources available to providers with guidelines constantly changing for the care of patients. Although the MASCC has been validated over the last twenty years, only one provider out of all who saw the 105 patients mentioned using the MASCC and appropriately categorized a patient based on their score. This is a great disservice to many patients who are already struggling with a potentially grave diagnosis. Therefore, the first aspect that needs to be addressed is to increase the awareness of the MASCC. If more providers are aware of this resource, word will spread of its efficacy and use in treating FN patients.

The next avenue to be discussed is how the MASCC should be implemented in the emergency department or clinic setting. The Hendrich II Fall Risk Model and the Braden scale for rating skin integrity are two tools commonly used by front line nursing

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staff when a patient is first seen (Hendrich, 2020; Agency for Healthcare Research and Quality, 2014). Both the scales are graded similarly to the MASCC, offering the opportunity to nurses to implement the MASCC at triage or other first assessment. Although nursing staff may not have the clinical knowledge to assess the burden of febrile neutropenia as effectively as a provider, the remaining information could easily be gathered similarly to the other two measures. Having this information at first assessment by the provider would paint a much better picture of how the patient's care should proceed. Before the provider even sees the patient, blood cultures and urine cultures can be drawn with routine labs. Additionally, the patient could already be started on empiric antibiotics before a decision is made on admitting or not. However the MASCC is implemented, it is evident that early use of the MASCC has potential to more consistently treat patients according to their needs.

#### Subjective vs. Objective Patient Symptoms

The greatest variable of the MASCC is the subjective assessment made by the provider. There will always be a "gut feeling" on the part of the provider for which an objective measure such as the MASCC cannot accurately account. The MASCC attempts to account for this through weighing the burden of symptoms as mild, moderate, or severe. Based on the results, it is clear that a provider's subjective intuition is accurate the majority of the time when it is appropriate to admit a patient. The issue lies in the recognition of a patient who may not need to be admitted. Although a patient's care should always err on the side of caution, there is great potential for this objective measure to be incorporated into a provider's subjective view of a patient's symptoms. The

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MASCC will never replace a provider's decision; however, it provides a wonderful lens for the provider to view the patient's situation most accurately.

#### **Empiric Course of Antibiotic Treatment**

These antibiotics are generally prescribed together as broad-spectrum coverage until blood cultures return and more focused antibiotic can be administered (Wishart et al., 2018). The goal of broad-spectrum antibiotic use is to stop a systemic infection from occurring so that the patient will not suffer further adverse consequences. Additionally, any sort of complication leads to a withholding of chemotherapy or radiation treatments, thus putting the patient at greater risk for complications from their cancer specifically. In this study, the patients that received primarily oral antibiotics while in-patient were identified as low risk which indicates oral antibiotics would have been sufficient for treatment. Therefore, these patients had the opportunity to receive their oral antibiotics as an outpatient prescription rather than staying at the hospital per their MASCC. Starting patients from the outset with empiric antibiotics could potentially show improvement in symptoms that would negate any need for an in-patient stay. However, if a patient receives the antibiotic and symptoms do not improve or there are worsening symptoms, then certainly the patient should be admitted.

#### **Limitations and Future Directions**

#### **Small Sample Size**

One of the main limitations of this study is the small sample size based on the larger available population. Given more time, a larger population size would be utilized by including more years of patient admission and utilizing more research sites. The full population was not able to be assessed due to the timeframe of this project; however, it became evident early on that not every patient with ICD D70.1, D70.8, or D70.9 was actually neutropenic. A great deal of time was therefore spent sifting through a patient's presentation criteria to determine if they fit the criteria for the MASCC. While the MASCC is a great resource for true FN, it is not intended to be utilized for simple neutropenia. This led to a gray area in the inclusion of participants who were severely neutropenic yet did not have a clinical fever. Due to both lack of time and the niche criteria of the MASCC, the sample size was significantly limited.

#### **Subjective Intuition**

Obviously one limitation of a retrospective study into subjective information is the lack of objective view on a subjective decision. Great care was taken into making a case for why a provider may have admitted a patient even if their MASCC did not indicate an admission to give the aspect of provider intuition. Oftentimes, the patient had a new diagnosis of cancer or had recently started a new chemotherapy regiment.

#### **Comparison to Previous Studies**

Other studies utilizing the MASCC had the benefit of prospectively applying the MASCC to discover its effectiveness in treating patients and studying their outcomes. Unfortunately, the limitations of this study (i.e. time, funds, accessibility) did not allow for any prospective use of the MASCC. Because of this, comparisons could not very well be drawn from this study to those used in the literature review process as no other studies have been conducted retrospectively.

#### **Future Directions**

An ultimate extension of this project is to prospectively use the MASCC in clinical practice rather than retrospectively. This study shows that although provider intuition is effective regardless of a true risk index, patient outcomes could be better improved if the MASCC was implemented in the case of FN in order to save patients time, money, and potentially worsening conditions. However, if prospective studies are not possible, a larger sample size would certainly improve the reliability of the conclusions presented.

#### Conclusion

Although providers were accurate in assessing a patient's need for admission the majority of the time, it is clear there is still room for improvement. The goal in empiric treatment of patients should be to provide patients with the greatest possible outcome with the least amount of cost or adverse consequences. Increasing awareness of the MASCC and implementing it early and effectively has been shown to positively impact patient outcome and will be critical to further patient success in the face of a terrifying diagnosis. Oncology patients generally show great strength in their fight, so it should be the mission of all clinical staff to support patients with all available resources, including the MASCC. Implementation of the MASCC offers patients earlier access to antibiotic treatment while also allowing the patient and their family the opportunity to recover at home if appropriate. Accurately assigning a patient as low or high risk and swiftly eliminating any infection with the least damage to the patient are integral to keeping them on track for chemotherapy or radiation treatments.

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### Appendix I

Middle Tennessee State University Institutional Review Board Approval Letter

**IRB INSTITUTIONAL REVIEW BOARD** Office of Research Compliance, 010A Sam Ingram Building, 2269 Middle Tennessee Blvd Murfreesboro, TN 37129



#### **IRBN001 - EXPEDITED PROTOCOL APPROVAL NOTICE**

Tuesday, April 21, 2020

Principal Investigator	Mark Blackmon (Student)
Faculty Advisor	Kathleen Darby
Co-Investigators	NONE
Investigator Email(s)	mdb8z@mtmail.mtsu.edu; kathleen.darby@mtsu.edu
Department	Social Work
Protocol Title	The Multinational Association for Supportive Care in Cancer
	(MASCC) Risk Index Score and Physician Intuition: Febrile
	Neutropenia and Patient Outcome
Protocol ID	20-2170

Dear Investigator(s),

The above identified research proposal has been reviewed by the MTSU Institutional Review Board (IRB) through the **EXPEDITED** mechanism under 45 CFR 46.110 and 21 CFR 56.110 within the category *(5) Research involving materials*. A summary of the IRB action and other particulars in regard to this protocol application is tabulated below:

IRB Action	APPROVED for ONE YEAR		
Date of Expiration	<mark>4/30/2021</mark>	Date of Approval 4/21/20	
Sample Size	1,000 (ONE THOUSAND) Records		
Participant Pool	Target Population: Primary Classification: Non-Research data from Adults (18 or older) Specific Classification: Patients admitted to healthcare providers (list on file)		
Exceptions	1. Analysis of non-research purpose data is permi	tted	
Restrictions	1. Identifiable data/artifacts, such as, audio/video data, photographs, handwriting samples, personal address, driving records, social security number, and etc., must be used only for the research purpose as proposed; the data must be deidentified after data processing. 3. Mandatory Final report (refer last page).		
Approved Templates	NONE		
Comments	COVID-19: Refer to the Post-Approval Action sect	· · · · ·	

IRBN001

Version 1.4

Revision Date 06.11.2019

# Appendix II

# REDCap Data Collection Instrument

	MASCC RISK INDEX STUD Page
PT HX Form	
Record ID	
FIN Number	
Facility	
ICD diagnosis	
Payor	
Sex	O Male O Female
Race or Ethnicity	American Indian or Alaskan Native Asian Black or African American Native Hawaiian or Pacific Islander White Hispanic or Latino or Spanish Origin Not Hispanic or Latino or Spanish Origin
Date of Birth	
Date of Death	
Date of Entrance	
Date of Discharge	
Total LOS	
Initial Neutrophil Count (x10^3)	
Initial Temperature	
Clinically Neutropenic?	O Yes O No
Clinically Febrile Neutropenic?	O Yes O No

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Burden of Febrile Neutropenia	O None/Mild O Moderate O Severe
Hypotensive?	O Yes O No
Initial Systolic	
Initial Diastolic	
History of COPD/currently requiring O2 treatment?	O Yes O No
Solid tumor or hematological malignancy with no prior fungal infection ?	O Yes O No O Information unavailable
Dehydration requiring parenteral fluids?	O Yes O No
Previously outpatient?	O Yes O No
Age less than 60?	O Yes O No
Total MASCC Score	
Appropriate to admit based on MASCC Score?	O Yes O No
Possible reasons for admit if not appropriate	
Placed on Neutropenic Precautions?	O Yes O No
Days on Neutropenic Precautions	
Comorbidities per pt hx	
Neutrophil Count with Subsequent Lab Draws (x10^3)	
Date and Time of Lab Draw	

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O Yes O No	
O Yes O No	
O Yes O No	
	O Yes

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#### **Appendix III**

#### Description of REDCap

Saint Thomas Health has adopted a software toolset and workflow methodology for electronic collection and management of research and clinical trial data. REDCap (Research Electronic Data Capture) data collection projects rely on a thorough studyspecific data dictionary defined in an iterative self-documenting process by all members of the research team with planning assistance from the Saint Thomas Research Services Center. Due to the iterative development and testing process used in REDCap, investigators are able to formulate a well-planned and carefully constructed data collection strategy for individual studies. REDCap servers are housed in a local data center at Saint Thomas Health and all web-based information transmission is encrypted. REDCap was developed specifically around HIPAA-Security guidelines and is recommended to Saint Thomas Health researchers by both its Privacy Officer and parent company health information security leaders. REDCap has been disseminated for use locally at other institutions and currently supports 240+ academic/non-profit consortium partners on six continents and over 26,000 research end-users (www.project-redcap.org).