Title
A Needs Assessment for Standardized Operating Procedures for Long-term Follow-up Care in Adult Stem Cell Transplant Survivors

Author
Bigbee, Korie

Publication Date
2023

Peer reviewed|Thesis/dissertation

UNIVERSITY OF CALIFORNIA

Los Angeles

A Needs Assessment for Standardized Operating Procedures for Long-term Follow-up Care in Adult Stem Cell Transplant Survivors

A dissertation submitted in partial satisfaction of the

requirements for the degree

Doctor of Nursing Practice

by

Korie Bigbee

2023

ABSTRACT OF THE DISSERTATION

A Needs Assessment for Standardized Operating Procedures for Long-term Follow-up in Adult Stem Cell Transplant Survivors

by

Korie Bigbee

Doctor of Nursing Practice

University of California, Los Angeles, 2023

Professor Eden R Brauer, Chair

Background: There have been remarkable achievements and advancements in bone marrow transplant (BMT), also known as hematopoietic stem cell transplant (HSCT), for the treatment of hematologic cancers. Stem cell advancements have improved overall HSCT survival rates and have contributed to HSCT's ability to be a potentially curative treatment. With patients surviving longer after HSCT, attention to transplant-related late complications is needed. These complications significantly influence the quality of life (QoL) and morbidity and mortality.

Objectives: This study assesses quality metrics of HSCT survivorship care and the need for a standardized operating procedure to guide long-term follow-up care in the hematopoietic stem cell transplant survivor, according to National Marrow Donor Program (NMDP) guidelines.

Methods: A retrospective chart review utilizing a convenience sample was conducted to assess patterns of survivorship care delivered to patients at the one-year post-transplant timepoint. The chart review focused on care metrics related to three organ systems (cardiac, pulmonary, and endocrine), which were chosen based on their level of impact and potential organ toxicity. Documentation of care provided was compared to the NMDP recommendations for the three organ systems to illustrate the consistency of care delivered and to identify opportunities to improve guideline-concordant care. Twenty-four metrics were collected and analyzed, some were pertinent to all three systems, but five were cardiac specific, four were pulmonary specific, and seven were endocrine specific. **Results:** Of the 100 charts reviewed, two-thirds (70.1%) did not receive a DEXA scan, 76.3% did not have pulmonary functions tests performed, and 61.9% of the charts reviewed did not have an echocardiogram (ECHO) or an electrocardiogram (EKG). **Conclusions:** The results indicate a need to augment current practice in HSCT survivorship care. A standard operating procedure (SOP) may help to ensure that follow-up care is systematically delivered and reflects the NMDP recommendations. Future work will use these findings to inform the development and implementation of an HSCT SOP.

The dissertation of Korie Bigbee is approved.

Mary-Lynn Brecht

Eunice Eunkyung Lee

Paul Michael Macey

Eden R Brauer, Committee Chair

University of California, Los Angeles

2023

This dissertation is dedicated to my Lord and Savior, Jesus Christ. This project would have been nothing more than a failed attempt had it not been for His grace, favor, wisdom, and love. To my handsome husband who sacrificed, allowed me to pursue my passion, anchored our family, and continually showed me his support and love. To my beautiful daughter Alysa Melena who made my writing snacks, distracted me with Tic Toks, and never got mad at me when I had to miss a game. To my handsome son Isaiah Carter, who gave me shoulder massages and always asked if I needed help before he snuck off with my writing snacks. To my handsome son Jonathan who sat under my desk, at my feet, kept me company for hours, and gave me the sweetest kisses. To my guardian angel, my grandmother, Mildred "Shard" Tabor, who was my reason for pursuing nursing. I did not get to care for you, but I honor you in the way I treat my patients.

To my dad, Daddy, thank you for being one of my best friends, praying for me through every level of education, any hardship, and being my sounding board. To my Auntie Bev, thank you for being one of my best friends, girding me up in prayer, keeping me grounded, and being the best aunt on this side of heaven. To my God mom, Rhonda Flenoy-Younger, I cannot tell you how many times I asked Jesus to bless you; thank you is not enough. To my Kaiser family, who supported, celebrated, and encouraged me along the way. To Jennifer Burnette, Dr. Leonardo Farol, and Dr. Ji-Lan Cai for writing my letters of recommendation and always making me feel like I could change the world. To my City of Hope family, you made me believe I had superpowers and always encouraged me through. To Dr. Saro Armenian, thank you for seeing me as something special. You believed in me, and you were willing to bet on me. I cannot tell you what that meant to me. Cohort 4, this journey would not have been the same without you. To ALL my Florida and Texas family, you all are my heart. I hope to make you proud. I am grateful to all my cheerleaders and friends for your support and love throughout this process.

TABLE OF CONTENTS

List of Figures and Tables

ACKNOWLEDGEMENTS

I want to acknowledge the UCLA School of Nursing for its concerted efforts to produce quality scholars, its investment in nursing innovation, and their reputation for excellence. I want to acknowledge and thank my Chair, Dr. Eden Brauer, for being academically and personally invested in me and seeing me push past my level of comfort. I want to acknowledge and thank my committee members: Dr. Mary-Lynn Brecht, Dr. Paul Macey, and Dr. Eunice Lee, for helping me to curate the best project for the time frame of the program but also one that would have a more significant impact beyond my time at UCLA. Thank you for your time, counsel, and wisdom. I want to thank Dr. Salman Otoukesh for taking a chance on me, providing opportunities to gain experience, and creating seats for me at tables I could not access. You never lowered your expectations. Thank you. I want to acknowledge Dr. Nancy Bush and Dr. Theresa Brown for being women of excellence, committed professors, and now colleagues in the field. There cannot be two more remarkable women who will influence and impact the nursing scientist that will come through this program. I want to acknowledge Mrs. Soo Kwon for all your hard work, devotion, and patience. Your ability to do all that you do is unparalleled and irreplaceable. I want to acknowledge the City of Hope Center for Informatics for the utilization of the POSEIDON platforms for data exploration, visualization, analysis, and discovery. Thank you for your meticulous efforts and careful attention to our data. I want to acknowledge the Department of Computational and Quantitative Medicine, Division of Biostatistics, Beckman Research Institute of City of Hope for their interpretation of our data and ability to create an optimal understanding of our findings.

VITA

Korie M Bigbee, MSN, BSN, NP-C, RN

EDUCATION

Doctor of Nursing Practice [DNP]	University of California, Los Angeles Los Angeles, CA	*In Progress* Expected June 2023
Master of Science in Nursing [MSN]	University of California, Los Angeles Los Angeles, CA Oncology Nurse Practitioner Program	June 2008
Bachelor of Science in Nursing [BSN]	Dillard University New Orleans, LA	May 2005

LICENSURE

California	RN 665677	Aug 31, 2023
California	NP 18482	Aug 31, 2023
California	BLS eCard Code 225414732322	Apr 30, 2024

BOARD CERTIFICATIONS

AANP	A0911030	Aug 31, 2026
RN	665677	Aug 31, 2023

PROFESSIONAL EXPERIENCE

	Kaiser Permanente-Los Angeles Medical Center
June 2014-Present	Nurse Practitioner (Hematology/Oncology)
	City of Hope-Duarte, CA
February 2011-May 2014	Nurse Practitioner (Hematology/Oncology)
December 2009-April 2010	UCLA Center for Health Sciences- Los Angeles, A
	Interim Clinical Nurse Specialist
September 2005-February 2011	UCLA Center for Health Sciences- Los Angeles, A
	Registered Nurse (Hematology/Oncology)

PRESENTATIONS

Fall 2004	Poster Board Presentation of research completed in Thailand- Louisiana Student Nurses State Conference (Alexandria, LA)
Fall 2006	Presentation on Neutropenia Management in the Oncology population (UCLA Center for Health Sciences)
Winter 2007	Presentation on Mucositis Management (UCLA Center for Health Sciences)
Fall 2007	Presentation on Multiple Myeloma (UCLA Center for Health Sciences)
Winter 2007	Presentation on Breast Cancer: Carcinoma in Situ (UCLA Center for Health Sciences)
Winter 2012	Allogenic transplant side effects (HOAG Nursing Conference)
Spring 2013	Presentation on Neutropenia Management in the Oncology Population (Live Strong Foundation)
Spring 2014	Presentation on Neutropenia Management in the Oncology Population (ASBMT, Dallas, TX)
Spring 2023	Poster Presentation on Long-term Follow-up after Hematopoietic Stem Cell Transplant (UCLA JCCC Retreat)

CHAPTER ONE: INTRODUCTION

In early 2022, the National Cancer Institute (NCI) projected there to be over 18 million cancer survivors in the United States of America. This is almost 5.5 % of the general population. Cancer survivors are predicted to grow to 22.5 million by 2032 (*Statistics and Graphs | Division of Cancer Control and Population Sciences (DCCPS)*, n.d.-c). More than 60% of the survivors in this population will be near retirement age or older (Biddle et al., 2020). Cancer survivors have far-reaching health concerns from their initial diagnosis and treatment journey, which mandate surveillance and management for late complications and long-term effects of cancer treatment (Biddle et al., 2020). Patients who have received stem cell transplants for hematologic cancers face long-term health challenges. This group of survivors will live with an average of five comorbidities secondary to their treatment exposures and are at risk for many late complications (Biddel et al., 2020). Even fifteen years after the transplant, the mortality rates for HSCT survivors are twice as high as the general population (Bhatia et al., 2007). Failure to observe, monitor, recognize, and manage post-treatment complications can lead to considerable morbidity and mortality (Giaccone et al., 2020). Therefore, consistent patient-centered survivorship care for long-term HSCT survivors to prevent and manage late complications is the impetus for this Doctor of Nursing Practice (DNP) quality improvement (QI) project.

Background and Significance

In recent decades there have been remarkable achievements and advancements in bone marrow transplant (BMT), also known as hematopoietic stem cell transplant (HSCT). What was once rare and experimental has become the standard of care for hematological malignancies due to collaborative research efforts, research grants, philanthropic support, and technological

innovations (Gratwohl et al., 2012). Over time, there have been some improvements in treatment options, and pioneering therapies have created avenues to deliver less toxic treatments that still have significant long-term complications (Solh et al., 2018). At the same time, new therapies emerge to minimize serious complications such as graft versus host disease (GVHD) or prevent disease relapse, transplant-related mortalities, and morbidities (Solh et al., 2018). Caution is still warranted as these therapies still create late effects. These advancements have improved overall HSCT survival rates and have contributed to the increasing use of HSCTs as potentially curative treatments (Atilla et al., 2017). However, despite this progress, studies indicate that HSCT survivors face a 15-20% risk of late mortality (Battiwalla et al., 2017).

By 2030, there will be over half a million HSCT survivors (Majhail, 2017). As these patients survive longer, healthcare providers (HCP) acknowledge the impact of transplant-related complications on quality of life (QoL). Majhail (2017) reported that among patients who do not experience disease reoccurrence for the first two to five years, approximately nine of ten survivors live for at least a decade. However, the survival rate is 30% lower in the post-HSCT population compared to gender- and age-matched cohorts without a history of cancer (Kaya et al., 2020). The patient's exposure history, including before and during the transplant, heightens the risks of late complications and death. A retrospective study of HSCT survivors by Hierlmeier et al. (2018) found that 74.2% of the participants suffered from early or late complications. Late complications are health challenges that occur months or years post-transplant and can include therapy-related cancers, organ-related toxicities, late infections, reduced quality of life (QoL), psychosocial difficulties, sexual and fertility concerns, financial difficulties, and the inability to reintegrate into their social roles (Majhail, 2017). The prevention and management of this broad range of late complications require close observation and comprehensive survivorship care.

Standardized operating procedures (SOPs) based on evidence-based clinical guidelines can provide a clear process and guide HCPs in addressing the broad needs of HSCT survivors. An SOP is a collection of step-by-step guidelines assembled by the organization to aid personnel in performing everyday operations (Sathyanarayana Rao et al., 2011). SOPs aim to achieve efficacy, quality, and consistency with performed care while minimizing miscommunication, complying with benchmarks, and creating equitable opportunities for care (Sathyanarayana Rao et al., 2011).

A large National Cancer Institute (NCI) designated comprehensive cancer center in Southern California performed its fifteenth thousand bone marrow transplant three years ago. This center is among the first comprehensive cancer centers with such achievement (City of Hope, 2020). According to the Center for International Blood & Marrow Transplant Research (CIBMTR), this highly regarded institution has set a precedent for compelling survival rates. It is a recognized leader in high-quality HSCT care. The one-year survival of patients treated at this center is 78.4%, which is slightly higher than the national average across all transplant centers. The expected one-year survival for patients is between 72.6% and 77.6% (Be the Match, n.d.). The CIBMTR (n.d.) substantiated that this organization's survival rates have been exceptional for fifteen years consecutively. This medical center is the first to reach this historic achievement in the US (City of Hope Lauded for Exceptional Transplant Outcomes, 2022). Given these tremendous achievements in survival rates, consistent and standardized long-term follow-up in the adult survivor population would support post-transplant longevity. This cancer center would benefit from improving long-term follow-up care by observing for and managing long-term complications. In order to enhance survivorship care for this population, it is essential to start by understanding current practice, evaluating provider knowledge, and using this information to

establish an SOP. Without an SOP, follow-up care deficiencies will continue and likely threaten, threatening these patients' QOL and long-term morbidity.

Problem Statement

Survivorship care for HSCT survivors is as complex as the initial diagnosis, and without guideline-driven SOPs, long-term follow-up care will continue to be inconsistent. The failure to provide consistent care creates patient vulnerability to developing significant and preventable transplant-related comorbidities and complications. At the time of this project, guideline-based Due to a lack of resources and funding, SOPs are rarely used in survivorship clinics (Hamblin et al., 2017). Of the five thousand HSCT-accredited medical centers in North America, less than 5% have dedicated HSCT departments, and of these, very few have established long-term follow-up clinics (Hashmi et al., 2018). Depending on initial diagnosis, adult survivors have a 25% to 75% three-year average survival rate after HSCT (Majhail, 2017). Even patients who survive early post-transplant complications remain at substantial risk for long-term complications, including behavioral and mental health difficulties and endocrine, pulmonary, and cardiac problems (Majhail et al., 2012). Survivors are also at higher risk for subsequent therapy-related neoplasms and chronic graft-versus-host disease (cGVHD) (Majhail et al., 2012). These complications heighten mortality and morbidity risks and diminish QoL (Majhail, 2017). Even a decade after the transplant, the survival rate for HSCT patients is three times lower than their peers (Majhail et al., 2012). Thus, understanding provider practice patterns and creating SOPs based on established guidelines are critical to ensure that HSCT survivors receive consistent surveillance to screen for preventable diseases, manage comorbidities, and treat long-term complications (Kaya et al., 2020).

PICO

For providers managing patients one year or more post hematopoietic stem cell transplant, this project aims to examine practice patterns for HSCT follow-up care at the one-year post-HSCT visit using a retrospective chart review and assess concordance with clinical guidelines. Based on these findings, the project will lay the necessary groundwork for developing and implementing an SOP in the future.

Established guidelines for HSCT long-term follow-up

To accelerate advancements in HSCT, collaborations have formed across the globe, and include the American Society for Transplantation and Cellular Therapy (ASTCT), the European Group for Blood and Marrow Transplantation (EBMT), the Center for International Blood and Marrow Transplant Research (CIBMTR), Asia-Pacific Blood and Marrow Transplant Group (APBMT), the Bone Marrow Transplant Society of Australia and New Zealand (BMTSANZ), the East Mediterranean Blood and Marrow Transplantation Group (EMBMT), and the Sociedade Brasileira de Transplante de Medula Ossea (SBTMO). Alliances between these groups have formed to develop surveillance and preventive care guidelines for HSCT survivors (Slater & Hansen, 2021). These recommendations specifically focus on survivors living beyond one-year post-HSCT and are intended to serve as an outline for care related to complications and screening (Slater & Hansen, 2021).

DNP Essentials: Leadership, Interprofessional Collaboration, and Ethics

The effectiveness of the DNP leader stands firm in the capacity to appraise the existing function and efficacy of a healthcare organization, departments within it, policies and

procedures, and pioneer ways to advance or restructure (Regis College Online, 2022). In the context of this project, the DNP leader can examine current data regarding late complications and late effects post-transplant and understand how current practice will affect clinical outcomes. The ability to identify the needed changes will precede the development and promotion of the organizational vision for adult survivorship care. After sharing and fostering the vision, the DNP leader must build strong teams with clear communications and adaptable workflows. Within any group, there are inevitable situational conflicts (scheduling, power dynamics between providers, etc.) that the DNP leader will know how to prevent and alleviate. When there is unmanaged conflict, there is a direct impact on the quality of care rendered, affecting patient outcomes. To mitigate conflicts, the doctorly-prepared nurse strongly encourages a code of ethics that recognizes proper attitudes and behaviors for team members and implements policies that support positive behavior and correct negative actions. This acknowledgment is necessary so that behavior incongruent with teamwork is not supported (i.e., a transplant physician refusing to work with another service line because they prefer to work in a silo) (Regis College Online, 2022).

Out of the eight DNP Essentials, this project focuses on DNP Essential VI, the Interprofessional Collaboration for Improving Patient and Population Health Outcomes (AACN, 2006). HSCT survivorship care is multifaceted, and healthcare management relies heavily on proficient and experienced consultants from various service lines. Healthcare professionals must be highly collaborative to deliver safe, efficient, effective, impartial, and patient-focused care in a complex patient population. The DNP leader understands that providing evidence-based care that influences the QoL of the transplant recipient and strategically meets the complex needs of the survivor through preventative care or effective care management is essential. In collaboration

with interprofessional teams, the DNP leader works to comprehensively improve the quality of care, maintain patient safety, increase patient satisfaction, and enhance patient outcomes. Interprofessional collaboration creates the ability to capitalize on the efficiency of healthcare delivery. In implementing an SOP, the DNP leader creates consistency in patient assessments and care management and collaborates with other services (dermatology, physical therapy, endocrine, cardiology, pulmonary, mental health, etc..) to provide comprehensive care to the survivor (Regis College Online, 2022).

Four provisions from the American Nurses Association Code of Ethics for Nurses speak to the DNP's role in SOP development and implementation. Provision 2: As a nurse leader, the DNP should prioritize the patient as an individual, as a part of a family, group, or community. Interprofessional collaboration in survivorship care is vital, as it promotes best-practice patient care. Provision 6: In managing conflict and power dynamics, the DNP leader institutes, retains, and enhances an ethical work atmosphere and employment prerequisites advantageous to effective quality health care. Provision 7: The nurse leader creates forward progress via research and the construction of nursing and health policies, like SB-987, that are working to increase access to care for cancer patients. The nurse leader can take the evidence-based guidelines and research and apply that scholarly work to current practice. Provision 8: The DNP participates in interprofessional collaboration and works with other health professionals and the community to minimize health disparities through preventative care in the transplant recipient population. This is essential for those survivors with lower-income insurance who are disadvantaged in receiving post-transplant care as insurers do not cover it (Code of Ethics PDF, 2018).

CHAPTER TWO: THEORETICAL FRAMEWORK

Kurt Lewin's Theory of Planned Change was conceptualized in the 1940s, outlining a framework that supports systemic change (Shirey, 2013). This framework is based on Lewin's force field analysis (FFA) model, which helps distinguish and evaluate the components or drivers that will impact a situation (Shirey, 2013). The FFA model includes three steps: unfreezing, moving, and refreezing (Butts & Rich, 2017) (See Figure 1). This paradigm depicts change as a "dynamic force within an organization moving in opposing directions. A driving force pushing individuals toward change, while participants resist the change directed their way" (Butts & Rich, 2017, p. 369). Lewin visualized change as a powerful continuous equalization of forces, not a one-time event.

Framework Steps

The initial phase of *"unfreezing"* involves uprooting the status quo and requires the disintegration of the prior behaviors. For this project, recognizing the problem of inconsistent long-term follow-up sets the stage for change. The research demonstrates that inconsistent follow-up contributes to higher incidences of late complications and gaps in care that necessitate change (Hashmi et al., 2018). Implementing change will begin by partnering with HCPs who will help other HCPs understand the importance of implementing an SOP. In addition to partnering with HCPs with shared goals, another key step is acknowledging the variables that may catalyze or prohibit this change. Successful implementation in practice requires a heavy emphasis on enhancing patient outcomes, increasing survival rates, and strengthening research data for long-term consequences (Shirey, 2013).

Additionally, due to late complications, there must be an adequate understanding of the financial benefits of delivering primary care instead of tertiary care. Unfreezing starts by performing a gap analysis demonstrating differences between current and best practices. Clearly articulating the urgency for change is also paramount at this stage. The proposed solution is to develop a standard operating procedure to create an avenue of change by providing HCPs with clear guidance on long-term care for HSCT survivors. The SOP will provide a strategy to standardize the HCPs into a new consistent practice (Shirey, 2013).

"*Moving or transitioning*" is the second phase of Lewin's theory. This phase visualizes the journey to change as opposed to the result of the change. The process of developing the SOP and embedding it into practice is ongoing. Obtaining HCP input on long-term follow-up, understanding current practices, and educating HCPs on existing international guidelines is essential. Setting this groundwork allows all HCPs to participate in SOP development, acquaint themselves with new practices, and prepare to transition into the best standard of practice. This stage necessitates detailed surveying, frontline engagement with HCPs who may oppose or resist the novel changes in practice, and didactic training. Rehman et al. (2021) notes that 75% of change endeavors fail, as the change processes can be arduous. Many organizations have difficulty implementing practice changes, and the reasons for failures are often multifactorial. For example, team members may be uninformed of the potential benefits of the proposed/intended change, so they become fearful and believe the concept of change is unjust. They generate negative perceptions and display pessimistic attitudes (Rehman et al., 2021). To mitigate these potential antagonistic reactions, the "moving" phase involves one-on-one sessions with HCPs to review the SOP and establish confidence and perceived value of the SOP. It also involves concise communication of the goals and purpose of the changes to keep the bigger

picture/goal in mind: optimal patient outcomes with increased survival outcomes (Shirey, 2013). Conveying the significant opportunity for early detection and appropriate management of post-transplant complications during long-term follow-up is also essential in this phase.

"*Refreezing,"* the third phase of the theory, warrants integrating the SOP into the existing culture, operating policies, and standard practices. In this last step, there must be an overemphasis on the catalyst that creates change and offsets opposition to change. With refreezing, the new change is adopted into practice and is no longer the goal; it becomes the new, improved standard of care. Refreezing promotes the sustainability of the change as it embeds the utilization of the SOP into current and future practice and reaffirms the notion that implementing follow-up care will enhance the survivor's health status and quality of life (Shirey, 2013). Additionally, it maximizes the cost-effective use of health service resources and serves as a driver to continue providing best-practice care with SOP guidance (see Figure 1).

Figure 1. Kurt Lewin's Change Theory

 **Unfreeze**	 **Change**	 **Refreeze**
1. Identify the need for consistency in long-term follow-up care across the HSCT department 2. Decide that the change should be the development and implementation of a standardized operating procedure (SOP) 3. Involve all the providers to participate in dialogue to understand old behaviors and attitudes so that they can be replaced 4. Ensure that there is dedicated support from management 5. Acknowledge and address provider input, suspicion, and unsettledness	1. Provide a stepwise approach for SOP implementation 2. Develop and implement the SOP 3. Provide didactic training on the SOP 4. Assist providers in learning how to access and utilize the SOP	1. The SOPs are validated, supported, and embedded 2. Assimilate the SOP into daily practice 3. Implement drop-ins to clinic visits, emails to providers with patients nearing the yearly time frame, and leave posters in the clinic with long-term follow-up reminders to sustain change 4. Quarterly review to reward success

It was adapted from: https://online.visual-paradigm.com/app/diagrams/#diagram:proj=0&type=LewinsChangeModel&gallery=/repository/f703210a5dca-44c6-9f7c-e0a53e618d78.xml&name=Lewin%27s%203-Stage%20Model.

CHAPTER THREE: REVIEW OF LITERATURE

Literature Search

A review of available research was performed utilizing resources from the UCLA Library. Databases focused on health, nursing, and medicine were selected for the search. The databases used were PubMed and the Cumulative Index to Nursing and Allied Health Literature (CINAHL). Only articles were included in the search. The advanced search feature allowed for the utilization of multiple combinations of the following key terms: "HSCT" OR "hematopoietic stem cell transplant" OR "allogeneic stem cell transplant," OR "bone marrow transplant," OR "stem cell transplant," AND "late complications," OR "late effects" AND "long-term follow-up," AND "guidelines," AND "standard of practice," OR "standardized operating procedures," AND "survivorship." The literature review focused on long-term follow-up, late complications, survivorship guidelines, survivorship standard of practice, long-term follow-up clinics, survivorship care models, and screenings in adult survivors beyond one-year post-HSCT. International literature was included, but all articles were submitted in English. The articles chosen in the literature search included surveys, systematic reviews, and retrospective studies. Publications were between 2010 and 2022. Literature was also investigated utilizing references from identified articles that directly addressed allogeneic stem cell transplants (adult or pediatric) and specific or general HSCT complications. Articles were excluded if they discussed complications solely after an autologous stem cell transplant.

Literature Synthesis

Overview of late effects and complications

The literature cites the substantial impact of organ-related toxicities secondary to HSCT through retrospective studies and reviews. The regimen-related side effects can lead to severe or life-threatening conditions (Giaccone et al., 2020; *Information for Physicians*, n.d.; Majhail et al., 2012). The late effects range from psychological impairments to chronic graft versus host disease (cGVHD). This synthesis of the literature aims to surmise the major late complications.

Neurologic complications. The intricacies and prevalence of neurological complications post-HSCT vary depending on regimen exposure, pre-existing comorbidities, age, and degree of immunosuppression (which can lead to virus-mediated encephalopathies) (Slater and Hansen, 2021). Complications include cognitive dysfunction, peripheral neuropathy, strokes, secondary leukoencephalopathy related to intrathecal chemotherapy, and secondary brain tumors (Majhail et al., 2012; Slater & Hansen, 2021). After treatment, usually, any decline in neurocognitive function improves with time. However, in 40% of survivors, there can be neurological deficiencies that are more long-term (Majhail et al., 2012). Central nervous system (CNS) and peripheral nervous system (PNS) neurological manifestations of cGvHD are infrequent (Giaccone et al., 2020), with an incidence of polymyositis less than 3% of patients and immune neuropathies and myasthenia gravis occurring in less than 1% of post-HSCT recipients (Giaccone et al., 2020). Other reported syndromes are Guillain-Barre and chronic demyelinating polyneuropathy (Majhail et al., 2012).

GI and liver complications. The late effects of the liver include treatment toxicity, cGVHD, hepatitis B or C virus reactivation, or iron overload (Majhail et al., 2012). Ongoing cGVHD can trigger chronic gastrointestinal inflammation secondary to pseudo gastrointestinal

blockage related to fibrotic cGvHD injuries (Giaccone et al., 2020). cGVHD is a significant element of liver dysfunction, presenting as high liver values (transaminases, alkaline phosphate, and glutamyl transferase) (Majhail et al., 2012). When receiving immunosuppressive treatments for cGvHD, HBV reactivation can affect up to 35% of post-HSCT patients (Giaccone et al., 2020; Majhail et al., 2012). HCV reactivation leads to chronic diseases like cirrhosis, with a cumulative progression incidence of 10% at 15 years and up to 25% at 20 years post-transplant (Giaccone et al., 2020; Majhail et al., 2012). In reactivation cases of Hepatitis B virus (HBV) or Hepatitis C virus (HCV), the clinical manifestation can be mild to moderate, with some survivors being asymptomatic aside from shifting liver function tests (Slater and Hansen, 2021). Iron overload, a common late effect post- HSCT, occurs in 30–60% of long-term survivors and is associated with patients who have required considerable transfusion support and can sometimes be the etiology of elevated liver function tests (Giaccone et al., 2020; Slater and Hansen, 2021). It has also been linked with high infection risks and mortality unrelated to disease relapse. (Giaccone et al., 2020; Slater and Hansen, 2021). The cumulative number of blood transfusions an HSCT receives during periods of pancytopenia makes them vulnerable to developing iron overload (Majhail et al., 2012). Iron overload can imitate liver cGHVD and even place survivors at risk for infections (Majhail et al., 2012).

Airway and pulmonary complications. Lung function can become compromised secondary to an infection, restrictive diseases (i.e., GVHD of lung and bronchiolitis obliterans organizing pneumonia/cryptogenic organizing pneumonia), and obstructive diseases (i.e., chronic obstructive pulmonary disease, bronchiolitis obliterans) (Majhail et al., 2012; Slater & Hansen, 2021; Bhatia, 2014; Giaccone et al., 2020). These late effects typically arise three months to two years post-HSCT and are linked with cGVHD (Bhatia, 2014). The percentage of the HSCT

population that develops delayed pulmonary comorbidities is 10% at two years (Bhatia, 2014); this incidence is slightly higher among those diagnosed with cGVHD at 15.6% (Bhatia, 2014). Pulmonary late effects can be subtle, making a firm diagnosis elusive, but as they progress, these complications become irreversible and are significant sequela for post-HSCT morbidity and mortality (Bhatia, 2014; Giaccone et al., 2020; Majhail et al., 2012; Slater & Hansen, 2021). Rare pulmonary late effects include diffuse alveolar hemorrhage, pulmonary embolism, pleural effusions, and veno-occlusive disease of the lungs (Majhail et al., 2012).

Infectious complications. There are significant infection risks in HSCT recipients for months to years after their transplant, as immune reconstitution does not occur for one to two years post-transplant (Majhail et al., 2012). Risk factors include diseases where bone marrow regeneration can be protracted (i.e., aplastic anemia or myelofibrosis), asplenia, hypogammaglobulinemia, cGVHD, continuing immunosuppressive therapy, cord blood, antigen mismatch, or T cell-depleted graft. (Majhail et al., 2012; Slater & Hansen, 2021). In survivors with cGVHD, necessitating prolonged immunosuppressive therapy, the immune system's ability to recognize and target invading particles for phagocytosis is impaired. Impaired opsonization raises the risk for infections like aspergillus, respiratory syncytial virus (RSV), varicella (VZV), cytomegalovirus (CMV), influenza, pneumonia, adenovirus (ADV), parainfluenza, pneumocystis jirovecii (PJP), and encapsulated bacteria (Neisseria meningitides, Haemophilus influenza, and streptococcus pneumonia) which can be life-threatening (Majhail et al., 2012; Slater & Hansen, 2021).

Cardiovascular complications. Juxtaposed to other post-transplant complications, late cardiac effects are more subtle, and significant cardiovascular events are rare (Majhail et al., 2012). Cardiovascular complications are accountable for 3% of late deaths in the post-HSCT

population; there is a high probability that cardiovascular ailments are grossly underestimated (Majhail et al., 2012). Late cardiac complications can arise years to decades after HSCT. They may present as subclinical idiosyncrasies or as grand as congestive heart failure (CHF) or severe chest pain (Majhail et al., 2012). Assessed alongside the general population, HSCT recipients are four times more likely to develop cardiovascular disease (CD) (Giaccone et al., 2020; Slater & Hansen, 2021). CD complications include hypertension, congestive heart failure (CHF), arrhythmias, cardiomyopathy, arterial diseases, and cerebrovascular disease (Majhail et al., 2012; Slater & Hansen, 2021; Bhatia, 2014). The percentage of the HSCT population that develops arterial disease is greater than 20% at 20 years (Bhatia, 2014). The average age at first heart attack is 53 years, fourteen years sooner than expected compared to the general population (Bhatia, 2014). Metabolic syndrome (hypertension, hyperglycemia, increased abdominal girth, and hyperlipidemia) has acquired more attention in the post-HSCT setting as it increases the risk for CD, strokes, and type 2 diabetes (Majhail et al., 2012; Giaccone et al., 2020). 40% of post-HSCT recipients have high cholesterol, and 70% have hyperlipidemia (Giaccone et al., 2020). Post-transplant heart disease (i.e., cerebrovascular disease, ischemic heart disease, and peripheral arterial disease) augments the vascular landscape (Majhail et al., 2012). These diseases can manifest as stroke, transient ischemic attack, heart attack, chest pain, ischemic leg pain, or chronic coronary artery disease (Majhail et al., 2012).

Ocular complications. Ocular GVHD occurs in 40-60% of HSCT recipients (Slater & Hansen, 2021). It manifests as painful dry eyes, cicatricial conjunctivitis, blepharitis, punctate keratopathy, cataracts, ischemic microvascular retinopathy, and keratoconjunctivitis sicca syndrome (KS) (Majhail et al., 2012). KS is destructive inflammation of the conjunctiva and lacrimal glands that can progress to corneal ulcers or perforation. Patients cannot produce tears

or enough moisture to prevent dry eyes, so they often complain of sensitivities (Giaccone et al.,2020; Majhail et al., 2012; Slater & Hansen, 2021). Cataract formation (50% incidence at one-decade post-HSCT), related to radiation exposure, can occur 4 to 10 years post-transplant (Majhail et al., 2012). Ischemic retinopathy is seen in HSCT survivors who have had radiation and received cyclosporine for GVHD prophylaxis. This retinopathy can also cause decreased visual acuity but is self-limiting as lesions resolve with withdrawal or reduction of the immunosuppression regimen (Majhail et al., 2012). Additional complications include glaucoma, ocular bleeding, optic disc swelling, infectious inflammation of the retina, and ischemic microvascular retinopathy (IMR) (Giaccone et al.,2020; Majhail et al., 2012; Slater & Hansen, 2021).

Oral and dental complications. Pre-existing oral/dental disease can exacerbate oral complications, so pre-transplant oral evaluations are essential. Survivors can develop cGVHD of the buccal mucosa, tongue, gingiva, and salivary glands (Giaccone et al., 2020; Slater & Hansen, 2021; Majhail et al., 2012). In the buccal mucosa, ulcerations can develop, causing oral discomfort, dry mouth (xerostomia), and difficulty swallowing (Giaccone et al., 2020; Slater & Hansen, 2021). Due to these oral changes, HSCT recipients may develop a host of dental diseases and even cancers affecting the oropharynx (i.e., squamous cell carcinoma and salivary gland tumors) (Giaccone et al., 2020; Majhail et al., 2012; Slater & Hansen, 2021). Oral complications can impact nutritional intake and quality of life (Majhail et al., 2012).

Endocrine complications. Endocrine dysfunction frequently occurs in the post-HSCT setting (Bhatia, 2014). Radiation, chemotherapy, cGVHD, and long-term steroid use can significantly impair the functionality of the endocrine system (Majhail et al., 2012). Thyroid gland irregularities post-HSCT include hypothyroidism (primary), hyperthyroidism (rare), and

thyroid carcinoma. Thyroid ailments usually begin during the early years post-transplant, but there have been reports of occurrence more than 20 years post-HSCT (Giaccone et al.,2020). Metabolic syndrome and thyroid dysfunction (hypothyroidism) occur in 7-50% of HSCT survivors, depending on their exposure history (Slater & Hansen, 2021). It usually occurs within the first three years after HSCT but can occur as late as fifteen years later (Slater & Hansen, 2021). Complications post-HSCT include dyslipidemia, diabetes (DM), altered growth patterns (pediatrics), and adrenal insufficiency. Hypogonadism (ovarian failure and germ cell damage) not only has a significant impact on the HSCT recipients' physical health, but it also impacts their QoL. Post-HSCT recipients have stated that infertility was as devastating as the cancer diagnosis (Bhatia, 2014). Irreversible gonadal impairment and infertility are notorious regimen-related toxicities. Advanced age at the time of transplantation, female gender, and TBI have been linked to causes of infertility (Bhatia, 2014). In female adults, ovarian failure is typically irreversible (Slater & Hansen, 2021). Germ cell damage impacts over 90% of male HSCT recipients (Slater & Hansen, 2021; Bhatia, 2014). Adrenal insufficiency (AI) occurrence is greater than 10% in the post-HSCT population (Giaccone et al., 2020). Once steroid therapy is tapered off, the hypothalamus-pituitary-adrenal axis automatically resumes its normal function; however, in high-dose, long-term steroid use, it does not. Clinical presentation and patient-reported symptoms of adrenal insufficiency can emulate GvHD (Giaccone et al., 2020).

Musculoskeletal complications. Osteoporosis from prolonged steroid use has a 30-50% incidence of compression fractures within the first five years (Giaccone et al., 2020; Majhail et al., 2012; Slater and Hansen, 2021). Within the first six months post-HSCT, the greatest loss in bone mineral density occurs (Bhatia, 2014). The reduced bone mineral density is secondary to steroid use, hypogonadism, sedentariness, and low vitamin D and calcium intake (Bhatia, 2014).

Myopathy is the weakness of proximal muscles, typically the quadriceps. Avascular necrosis (AVN) has an incidence of 4–19% (Giaccone et al., 2020; Slater & Hansen, 2021). It occurs when there is poor perfusion of the bone (Bhatia, 2014). It usually affects bilateral weight-bearing joints like the hips, knees, ankles, and wrists. (Slater & Hansen, 2021). Sclerosis impacts the integumentary system and subcutaneous tissues with different grades of severity and is a diagnostic indicator of cGVHD. In the initial stages, the connective tissues and tendons have swelling eosinophilia, which can later advance to scarring and joint deformities. These changes are present in fingers, carpal bones (wrists), shoulders, antecubital fossa (elbows), and ankles (Majhail et al., 2012). Inflammation of the synovium may create fluid within the joint (Majhail et al., 2012).

Therapy-related malignancies. Influential complications post-HSCT are secondary malignancies (Bhatia, 2014). Any person diagnosed with cancer has a two-fold risk of developing second cancer (Slater & Hansen, 2021). HCT survivors have a three-fold risk (Giaccone et al., 2020; Slater & Hansen, 2021). The occurrence of new cases of secondary malignancies at ten years is less than 5% and slightly over 10% at 15 years post-HCT (Slater & Hansen, 2021). Common secondary solid tumors in HSCT survivors are basal cell and squamous cell cancers (6.5% incidence and 3.4% incidence at 20 years, respectively) (Bhatia, 2014), breast cancer (11% incidence at 25 years) (Bhatia, 2014), liver, cervix, bone, thyroid, and central nervous system (CNS) tumor (Slater & Hansen, 2021). The proportion of post-HSCT survivors that develop solid tumors after HSCT is between 7% to 11% at 15 years post-transplant (Bhatia, 2014). The risk is three times higher in patients 15 or more years post-HSCT. Additional risk factors for solid carcinomas include infection with tumor-causing viruses (HBV, HCV: liver cancer; HPV: cervical cancer) and cGVHD of the mouth (squamous cell carcinoma) (Bhatia,

2014). Common secondary hematological malignancies are non-Hodgkin lymphoma (NHL), myelodysplastic syndrome (MDS), acute leukemia, and post-transplant lymphoproliferative disorder (PTLD) (Slater & Hansen, 2021; Bhatia, 2014).

Psychosocial Effects and Social Wellbeing. HSCT recipients verbalize symptoms of depression, distress, anxiety, and post-traumatic stress disorder (PTSD) related to disease reoccurrence, sexual dysfunction, and financial obligations (Giaccone et al., 2021). They also express fatigue, neurocognitive complications, cancer-associated fatigue, suicide, returning to work, social assimilation difficulties becoming sexually aroused, or feeling sexual satisfaction which can create relationship dilemmas (Giaccone et al., 2021; Slater and Hansen, 2021). The symptoms can heighten the physical aspects of recovery from HSCT (Slater & Hansen, 2021; Giaccone et al.,2020). The elevated frequency of infertility and the parallel anguish increases the need for providers to present fertility-preserving options before HSCT when possible, as disease aggression may dictate otherwise. Physicians must also offer family expansion options and supportive care measures to HCT survivors (Slater & Hansen, 2021). In a study of long-term survivors after allo-HSCT, Bhatia (2014) found that psychosocial and spiritual QoL increased about six months after the transplant. Survivors with advanced age noted poorer physical QoL but had enhanced social welfare. Having the capability to maintain employment is a crucial gauge of re-acclimatization. Inadequate health related to cGVHD was the primary reason for regaining employment (Bhatia, 2014).

Morbidity and Late Mortality. Disease relapse is the primary cause of mortality among HSCT survivors (Giaccone et al., 2020). Almost half (45%) of sibling-donor survivors and one-third of unrelated-donor survivors will inevitably experience disease reoccurrence (Giaccone et al., 2020). Osteopenia can increase morbidity secondary to pain, impaired mobility, and poor

QoL (Slater & Hansen, 2021). The probability of surviving 10-20 years post-HSCT is greater than 80% for those individuals who were alive and without relapse two to five years after HSCT (Bhatia, 2014). Thirty years post-HSCT, mortality rates were still nearly ten times higher than in the general population (Bhatia, 2014). Initial disease relapse and cGVHD are the prominent reasons for premature death (Bhatia, 2014). Juxtaposed to the HSCT survivor's peers, allogeneic HSCT recipients are almost four times more likely to perish from therapy-related malignancies, 15 times more likely to pass away from respiratory complications, and two times more likely to die of cardiovascular adversities (Bhatia, 2014).

Renal Complications. Chronic kidney disease (CKD) occurs in 20-60% of HSCT recipients and is clinically evident approximately six months to 1-year post-HSCT (Giaccone et al., 2020; Majhail et al., 2012). Kidney dysfunction can present as nephrotic syndrome, thrombotic microangiopathy, or glomerulonephritis. Nevertheless, most survivors develop an idiopathic form of CKD that has no relation to the diseases mentioned above. It can develop secondary to a virus-mediated acute kidney injury, the pre-and post-transplant exposures, age at the time of transplant, radiation, diagnosis, certain medications, baseline kidney function, and chemotherapy (Giaccone et al., 2020; Majhail et al., 2012). Nephrotic syndrome occurs in 5%-10% of HSCT survivors (Slater & Hansen, 2021). Renal insufficiency and nephrotic syndrome can initiate the onset of imbalanced lipids or worsen a pre-existing lipid disease (Giaccone et al., 2020).

Literature Review

The relevant literature included in this review cuts across various dimensions of survivorship care. The included articles focus on late complications, avenues of survivorship care

delivery (actual clinics vs. standardized templates of post-HSCT care), guidelines for screening, and elements of follow-up care. The literature acknowledged that the risks and outcomes congruent with poor long-term follow-up are significant. It also recognizes types of late complications and the necessity for standardized care using accredited guidelines. Included literature consists of one retrospective, observational, case-control study (Kaya et al., 2020), three retrospective studies (Gifford et al., 2013; Hierlmeier et al., 2018; Abou-Mourad et al., 2010), and one cohort survey study (Sun et al., 2010). The study settings were all international, with study locations in Australia, Canada, Turkey, Germany, and Japan (see Table of Evidence).

Review of the Literature

In a retrospective, observational, case-control study by Kaya et al. (2020), they aimed to provide insight into their follow-up experiences using their guideline-driven approach for follow-up of late effects, including chronic graft versus host disease (cGVHD). The guideline is based on the Recommended screening and preventive practices for long-term survivors after hematopoietic cell transplantation (Majhail et al., 2012). Their study included ninety-one allogeneic stem cell transplant patients. In this cohort, they used descriptive statistics and found that ocular complications occurred in 50.6% of patients, oral complications occurred in 15.4% of patients, 8.8% had respiratory complications, and 5.5% suffered from cardiac complications. Over a quarter (37.4%) of the patients had metabolic syndrome; even more staggering is that skeletal complications were found in 66.7% of the patients assessed. Endocrine complications accounted for 12.1%, elevated blood pressure was found in 5.5% of the patients, and type 2 diabetes mellitus was present in 8.8%. Almost 76 % of the patients had ferritin levels lower than 1000 ng/mL, but 24% of patients had ferritin levels ≥ 1000 ng/mL, which places them at

increased risk for cGVHD, 26% had grade 12 acute GVHD, and 17% had grade 3-4 acute GVHD. Concerning cGVHD, which increases the risk of morbidity and mortality, 7% developed mild, 13% had moderate, and 11% had severe cGVHD. A limitation of this study is the failure to share the degree of match between donors and recipients, as that can impact GVHD development. Descriptive statistics were used to analyze the data.

Australia has been undertaking allo-HSCTs since 1970, yet there has been little literature on the late complications of HSCT survivors (Gifford et al., 2013). A single-center retrospective chart review utilizing allo HSCT transplant data from January 2000 to December 2007. After exclusionary criteria were met, 99 charts were used. Late complications in this study were: cGVHD (70%), respiratory problems (66%), ocular complications (40%), skeletal diseases (33%), and impaired renal function (26%). A limitation of this study was its inability to be generalizable. Additionally, due to the retrospective nature of the survey, the assessments were incomplete as they could not collect every parameter on all the participants.

Long-term morbidity burdens among HCT survivors are considerable (Sun et al., 2010). The team used the Bone Marrow Transplant Survivor Study (BMTSS) resources to ascertain the prevalence and gravity of ongoing comorbidities in HCT survivors compared to those with a healthy familial cohort. It aimed to distinguish subpopulations at higher risk. Participants completed a 255-item BMTSS-validated questionnaire comprising general areas: diagnosis by a medical provider of health problems with age at the time of diagnosis, the grade of chronic GVHD (if any), accessibility of and use of health care, and sociodemographic characteristics. Post-HSCT comorbidities were graded using the Common Terminology Criteria for Adverse Events. This instrument grades acute and chronic health issues in cancer patients and survivors. It categorizes grades one through four with clinical explanations of the severity of each event.

The Sun et al. (2010) study found that almost two-thirds (66%) of the HSCT survivors reported a minimum of one chronic condition; nearly 20% reported severe/life-threatening conditions. The cumulative incidence of a chronic health condition among HCT survivors was almost 60% one decade after HSCT. Survivors had two times the likelihood of developing a chronic disease. The HSCT survivors with cGVHD were nearly five times as likely to develop severe/life-threatening conditions. A limitation of the study was that the sample only included live patients. Patients may have died of missed chronic health conditions when describing the morbidity after HSCT.

A retrospective analysis by Hierlmeier et al. (2018) aimed to identify prognostic indicators, outline future follow-up measures, and support exposure-based stem cell transplantation strategies to diminish short and long-term toxicities. This retrospective study analyzed complications of stem cell transplant and the long-term effects afterward. They found infections and pulmonary complications were the top late complications within HSCT that significantly contribute to morbidity and mortality. Limitations in this study were the limited follow-up time (stopped after 2.5 years) and the studied population being pediatrics, so exposure to specific therapies and the amounts are limited. This may lessen or completely diminish late effects. Additionally, some complications (cardiac, pulmonary, or renal) present after a more extended period and may not have had a high occurrence due to the limited follow-up window.

Four hundred and twenty-nine HSCT survivors who underwent an allo HSCT at British Columbia in Vancouver, Canada, were assessed in the Abou-Mourad et al. (2010) study. This study evaluated long-term outcomes. Data was collected from the medical record and via communications between the community provider and the transplant physicians. Survival analyses were done according to the method of Kaplan and Meier and compared using the log-rank test. Univariate and multivariate analyses were performed using a Cox proportional hazard

technique. Late effects were outlined as complications in long-term survivors. In this study, 50% of the patients had obstructive airway disease, 21% had hypertension, 36% had hypogonadism, and 24% had osteoporosis secondary to long-term complications. A limitation of this study was that it was a single-center study, so results are not generalizable,

CHAPTER FOUR: METHODS

Project Design

This project utilized a descriptive comparative QI design to understand the current care of long-term follow-up care for HSCT survivors. At the culmination of this project, an understanding of practice patterns was identified based on retrospective patient chart data. The utility of an SOP for long-term follow-up, guided by the National Marrow Donor Program (NMDP), was recognized as an approach to delivering comprehensive survivorship care.

Setting and Sample

The project involved a retrospective chart review at a large NCI-designated comprehensive cancer center in Southern California. The research informatics team used convenience sampling to select 100 unique patients who had undergone an allogeneic stem cell transplant (matched or unmatched, haploidentical and cord blood transplants) from January 2017 through December 2019. To be included in the study sample, these patients were required to be alive at the 12-month to 18-month post-HSCT mark.

Data Collection

The institutional research informatics team performed a retrieval of retrospective chart data. Socio-demographic and clinical variables collected from the chart included: age at time of

transplant, sex, cancer diagnosis, transplant type, and graft-vs-host disease (GVHD) status. Data was also collected on outcomes focused on recommended care for three major organ systems (cardiac, pulmonary, and endocrine). Using specific recommendations from the NMDP guidelines, documentation of guideline-concordant consults/referrals, radiographic studies, clinical exams, vital signs, and serum studies at follow-up appointments within the 12 to 18-month post-HSCT period were extracted from the chart and converted into indicator variables. Additionally, variables related to past medical history and current medications were retrieved to determine whether specific recommendations were appropriate for each patient.

Data Analysis

Descriptive statistics were performed to summarize the patient, disease, transplant characteristics, GVHD status, and care the patients received after the transplant. Medians and ranges were used for continuous variables, and frequencies and percentages were used for categorical variables. There was no hypothesis testing. The point estimates, and 95% confidence intervals are provided whenever appropriate. Using the NMDP guidelines (Majhail et al., 2012), a gap analysis was performed by calculating the rate of concordant care for each recommendation and at the organ system level across the sample to compare the consistency of care delivered and identify opportunities for enhancements. All statistical analyses were conducted using statistical analysis software (SAS). The recommendations are presented in the results section for ease of interpretation.

Ethical Considerations/Protection of Human Subjects

Prior to the project's initiation, this project was granted an exemption from the cancer center's institutional review board (IRB). The cancer center's IRB board reviewed and approved all data preparation, collection, and analysis activities. The patients' charts under review had careful intent (omitting patient identifiers) to protect their Health Insurance Portability and Accountability Act (HIPAA) rights. Furthermore, this project adhered to the ethical principles of human action, respect for persons, beneficence, and justice, as described in the Belmont Report (Adashi et al., 2018). Chart review data were stored in a file on a locked desktop computer inside a secure office building. Substitution codes were used in place of participant identifiers. The chart review was retrospective; patient charts were only included if they signed consent to participate in data-related studies.

CHAPTER FIVE: RESULTS

A total of 100 patient charts were requested for review. A total of 97 of the 100 charts were utilized in this project. Three patients did not consent to have their data accessed for research. Over half of the charts, 52.6% (n=51) were from 2017, 35.1% (n=34) were from 2018, and 12.4% (n=12) were from 2019. The sample included both males (n=59) and females (n=38), although the male transplant recipients were the more significant majority. The sample was ethnically diverse, though a sizable portion of the transplant recipients were White (n=41, 42.3%). The patient’s age ranged from 18-72 years, with an average age of 55. Table 1 presents more in-depth information about the patients’ characteristics.

Table 1: Patient Characteristics and Clinical Features from the Chart Review

Characteristic and Clinical Features	No. (%)
Ethnicity	
White	41 (42.3%)
African American	6 (6.2%)
Asian	12 (12.4%)
Hispanic	38 (39.2)
Age	
Median	55
Interquartile range	34, 65
Range	18-72
Gender	
Male	59 (60.8%)
Female	38 (39.2%)
Primary Diagnosis	
Acute Myeloid Leukemia	18 (18.6%)
Acute Lymphoblastic Leukemia	23 (23.7%)
Myelodysplastic Syndromes/Myeloproliferative Neoplasm	24 (24.7%)
Lymphoma (Non-Hodgkin's and Hodgkin's)	20 (20.6%)
Chronic Myeloid Leukemia/Chronic Myelomonocytic Leukemia	5 (5.2%)
Non-Malignant (Aplastic Anemia and Sickle Cell)	4 (4.1%)
Multiple Myeloma	3 (3.1%)
Donor age, years	
Median	32
Conditioning Intensity	
Myeloablative	17 (17.5%)
Non-Myeloablative	14 (14.4%)
Reduced Intensity	66 (68%)
Donor Type	
Matched Related Donor	25 (25.8%)
Matched Unrelated Donor	55 (56.7%)
Haploidentical	15 (15.5%)
Cord Blood	2 (2.1%)

Table 2. Summary of Follow-Up Care from the Chart Review

NMDP Recommendations at 1-Yr Post-HSCT	No. (%) of Patients Who Received Guideline-Concordant Care
Cardiovascular Care Recommendations:	
Echo/EKG	37 (38.1%)
Clinical Exam	96 (99%)
Vital Sign Assessment	96 (99%)
Serum Lipid Evaluation	58 (59.8%)
Endocrine Care Recommendations:	
DEXA	29 (29.9%)
Hgb A1C Evaluation	26 (26.8%)
Vitamin D Level	26 (26.8%)
Hormone Evaluation	20 (20.6%)
Clinical Exam	96 (99%)
Pulmonary Care Recommendations:	
CT/CXR (if indicated)	50(51.5%)
PFT	23 (23.7%)
Clinical Exam	96 (99%)

Practice Patterns Related to NMDP Recommendations for Cardiovascular Care:

According to the NMDP guidelines, related to cardiovascular follow-up care, providers should complete a clinical exam consisting of an assessment of blood pressure, an ECHO with ventricular function, or an EKG (in patients at risk and symptomatic patients), and a fasting lipid profile (including HDL-C, LDL-C, and triglycerides) at the one-year post-HSCT visit. The vital signs assessment should include blood pressure, heart rate, oxygen saturation, and weight. Medical management and patient education are recommended if the blood pressure is elevated. A lipid panel should be evaluated for dyslipidemia, and medication should be prescribed if warranted. Other important risk factors described in the guidelines include those who received anthracyclines, had radiation exposure, are older at HSCT (>55yo), have cardiovascular risk factors (hypertension, dyslipidemia, or diabetes) before/after HSCT, have chronic kidney disease or metabolic syndrome. The chart review of the 97 patients revealed 31.9% had radiation

exposure, 49.4% were >55yrs of age, and 30.9% had a past medical history of cardiovascular issues (n=30). Normal blood pressure was found in 64.9% (n=63), and 43.3% were on cardiovascular medications (n=42). 61.9% of the patients (n= 67) had not had an ECHO or an EKG, and 59.8% (n=58) had not assessed their lipid levels. Of the 97 patient charts reviewed, normal blood pressure was found in 64.9% (n=63), 43.3% were on cardiovascular medications (n=42), 61.9% of the patients (n= 67) had not received an ECHO or an EKG, and 59.8% (n=58) had not received a lipid evaluation. Table 2 summarizes findings by organ system, including four specific cardiovascular recommendations.

The guidelines also describe other important factors that can further increase cardiovascular risk in HSCT patients, including receipt of anthracyclines, radiation exposure, older age at HSCT (>55 years), presence of other cardiovascular risk factors (hypertension, dyslipidemia, or diabetes) before or after HSCT, chronic kidney disease or metabolic syndrome. Among the 97 patients included in the chart review, 31.9% had radiation therapy exposure, 49.4% were >55yrs of age at HSCT, and 30.9% had a past medical history of cardiovascular issues. Of the 97 charts reviewed, 69.01% (n=67) had no documented baseline cardiovascular ailments, but 30.9% (n=30) did. At 12 months post-HSCT, 43.40% (n=42) of the charts indicated medication management for cardiovascular issues. Although there is no direct correlation between the 30.9% of patients with a cardiac history before HSCT and the 43.4% with cardiac issues requiring medical management post-transplant, the substantial proportion of patients affected does speak to the concern for late cardiac effects in HSCT patients.

Practice Patterns Related to NMDP Recommendations for Endocrine Care:

According to the NMDP guidelines related to endocrine follow-up care, providers should complete a clinical exam and draw blood to evaluate serum levels of fasting blood sugars, Hemoglobin A1C, Vitamin D, gonadal assessments (FSH, LH, and testosterone) respective to gender and order DEXA scans at the one-year post-HSCT visit. Of the 97 reviewed charts, 73.2% (n=71) did not have a documented evaluation of hemoglobin A1C or Vitamin D levels. A substantial percentage, 78.4% of the patients (n=76), also lacked documentation of hormone levels, and 64.9% (n=63) did not have documented serologic thyroid evaluations. The majority of patients (n=68, 70.1%) also did not receive a DEXA scan. Other important risk factors for the endocrine function described in the guidelines include inactivity, young age at the time of HSCT, chemotherapy exposure, radiation exposure, corticosteroid usage, GVHD, and hypogonadism. In this study sample, 30.9% (n=30) of the patients had a history of endocrine issues before transplant, and 50.5% (n=49) were on endocrine-related medications at one-year post-transplant, emphasizing the concern for monitoring late endocrine effects after HSCT. Table 2 summarizes results by organ system, including five specific endocrine recommendations.

Practice Patterns Related to NMDP Recommendations for Pulmonary Care:

According to the NMDP guidelines for pulmonary follow-up care, providers should complete a clinical exam and order PFTs at approximately one-year post-HSCT. Providers should request a focused radiologic assessment if warranted (e.g., signs or symptoms of lung compromise in allogeneic HSCT recipients). In the study sample, 51.5% (n=50) had received a chest x-ray or CT scan. Despite the guideline recommendation that all allo-HSCT patients have

PFTs performed, 76.3% (n=74) of the patients did not receive this recommendation. Table 2. summarizes findings by organ system, including three specific pulmonary recommendations.

Other important pulmonary risk factors described in the guidelines include busulfan exposure, radiation exposure to the chest, GVHD, and pre-or post-HSCT pulmonary infection(s). Of the 97 charts reviewed, 55.6% (n=54) of patients had active GVHD, and 31.9% (n=31) had radiation as part of their conditioning regimens (n=31). Before the transplant, 11.3% (n=11) had a documented history of pulmonary disease. Still, at the one-year post-HSCT timepoint, this number increased to 21 patients (21.6%) with pulmonary issues requiring medication management, highlighting the importance of pulmonary monitoring in HSCT follow-up care.

CHAPTER SIX: DISCUSSION

With the increasing number of HSCTs conducted globally and HSCT survival rates following suit (Majhail et al., 2017), there is momentum in advancing and implementing comprehensive long-term follow-up care for the rising number of HSCT survivors. Research studies demonstrate plateaus in mortality rates among HSCT recipients near the 5-year mark (Majhail et al., 2017). This patient population will have to confront elevated risks for chronic comorbidities and premature death years after their transplant (Majhail et al., 2017). Common late complications, similar to the ones reviewed in our study, included hypothyroidism and pulmonary and cardiovascular diseases (Kanagasundram and Amini, 2019). Complications such as elevated lipids place survivors at risk for heart attacks, arterial disease, and stroke (Hilgendorf et al. (2015). Hilgendorf et al. (2015) found that an average of 45% of their sample of HSCT survivors developed dyslipidemias. This is striking with the understanding that this can only be diagnosed if assessed, and our study found that 58.2% of patients were not evaluated. Our

retrospective chart review found that only 20.6% of the charts had hormone levels assessed. Hilgendorf et al. (2015) found that over 90% of patients experience gonadal dysfunction. Kaya et al. (2020) found that late pulmonary adverse effects occur in 15% to 20% of HSCT recipients with conditioning regimens with radiation and certain chemotherapies and those diagnosed with cGVHD. Their study demonstrated the importance of consistent interval clinical pulmonary observations via clinical exams and PFTs (in the presence or absence of symptoms). Our study showed that 55.6 % of the charts reviewed had active GVHD at the one-year mark, 32% had conditioning regimens that included radiation, yet only 23% had PFTs ordered. Implementing comprehensive survivorship care that includes surveillance, preventive care, and chronic disease management is crucial in this population. Interprofessional collaboration with the transplant physician, primary care providers, and referral services will help to minimize and prevent complications. However, access to a multidisciplinary team is rare in most transplant centers due to insufficient resources and staffing (Hamblin et al., 2017). A multi-centered study by Hamblin et al. (2017) found that of the twenty-seven centers studied, nearly all (90%) had dedicated late-effect clinics, and most of the centers (nearly 70%) had standard operating procedures.

Future research must focus on collecting data to illustrate the need for insurance coverage for the increasing number of HSCT survivors and support healthcare policy change. More studies are also required to identify the pathology of late effects, patient-reported outcomes, and unmet needs of survivors. The increase in morbidity and mortality, the profound impact of late complications, and the adverse effects on quality of life justify the research and current work to ensure optimal patient-centered outcomes (Solh et al., 2018). The model for survivorship care will have to be institution-driven as there is significant resource utilization (Hamblin et al., 2014), and each organization has its limitations. Even still, developing a guideline-driven SOP

will ensure that any provider assuming care of the transplant survivor has the tools to deliver best-practice care. It is also the initial step in creating realistic long-term follow-up care that can be translated within any care setting to this vulnerable patient population and facilitate continuity of survivorship care. The consequences of delayed or absent care are substantial, and implementation of standardized follow-up care is a high priority.

Limitations

Findings from this project shed important light on current gaps in HSCT follow-up care, but several limitations should be noted. A threat to internal validity includes history. The coronavirus disease 2019 (COVID) resurge impacted care delivery during the study period, which may have included less provider availability and delays in care. Another threat to validity is maturation. If a patient develops a recurrence, long-term follow-up is redirected to the acute management of active/recurrent disease. The patient's care must transition back to active care, and the SOP for long-term follow-up is no longer applicable (Majhail et al., 2017). During data collection, if a chart revealed disease reoccurrence, this necessitated a request for a chart replacement. This occurred on three occasions. Attrition also threatens validity, as some patients receive follow-up care by a primary care provider one-year post-transplant. In these cases, the chart at the transplant center will not necessarily contain details of follow-up care received at an outside facility. The actual chart review's limitations include a narrow focus on follow-up care as the review was limited to three organ systems due to project constraints. There is also the inability to account for barriers to care, such as a change in insurance or co-payments, and undocumented care, such as verbal conversations or emails.

Finally, this project is a needs assessment to validate the need for the SOP. However, after the SOP is developed, there may be potential barriers to implementation, including the provider's failure to access or follow the SOP. Additionally, providers may not consider a clinical guideline valuable to their practice or feel it does not align with their "usual" approach, resulting in barriers to SOP adoption. Selection bias is another possible threat to validity, as some providers may be more inclined to address survivorship issues or have a personal stake in the SOP than others. Also, the providers collaborating with an APP may be more likely to reference the SOP since the nurse practitioner or physician assistant can order the required labs or radiographic studies.

Conclusion

Transplant providers and researchers worldwide have acknowledged that comprehensive guidelines for long-term follow-up of HSCT survivors are deficient. The CIBMTR, the EBMT, and the ASTCT gathered a group of experts in 2012 to revise previous guidelines initially created in 2006. The recommended guidelines focus on late complications and risks for adult HSCT recipients who have survived one year or more following transplantation. HSCT-related complications may be preventable or minimized if guidelines are implemented and adhered to in alliance with risk factors and individual exposures. Findings from this project suggest many barriers to guideline uptake remain, as there were significant gaps between clinical care and recommended care in the post-transplant period. These gaps create missed opportunities to impact overall survival and quality of life positively. This project indicates opportunities for growth in current practice at a large comprehensive cancer, particularly in monitoring for HSCT's cardiovascular, endocrine, and pulmonary complications. Translationally, these findings

in a large cancer center could also be disparities experienced in post-transplant care at small cancer centers. As HSCT patients live longer and older patients with multiple comorbidities are given access to transplants, consideration must be taken beyond mere "survival rates." Long-term follow-up care guidelines were established to provide a framework for monitoring treatment's potential long-term and late effects. These guidelines are geared toward specialized HSCT clinicians. Still, they can also be helpful for long-term HSCT recipients who are transitioned back to their primary care providers for follow-up care. Creating SOP can provide a shared long-term follow-up care plan for all clinicians involved in patient care.

Implications for Practice and Research

With the number of HSCTs conducted globally increasing and HSCT survival rates following suit (Majhail et al., 2012), there is momentum in advancing and implementing comprehensive cancer long-term follow-up care for the rising number of HSCT survivors. Research studies demonstrate plateaus in mortality rates among HSCT recipients near the 5-year mark. Still, even ten to fifteen years after their transplant, this population faces elevated risks for chronic comorbidities and premature death (Majhail et al., 2012). Implementing comprehensive survivorship care that includes surveillance, preventive care, and chronic disease management is crucial in this population. Interprofessional collaboration with the transplant physician, primary care providers, and referral services will help to minimize and prevent complications, and standardized processes can reduce variations in care. Given the significant resource utilization needed, the model for survivorship will likely be institution driven. Future research should focus on comparing various models of care, with specific attention to the role of insurance coverage and the need for healthcare policy changes for these patients. More studies are also required to identify the pathology of late effects, patient-reported outcomes, and unmet needs of survivors,

particularly many years beyond HSCT. The increase in morbidity and mortality, the profound impact of late complications, and the adverse effects on quality of life justify the research and current work to ensure optimal patient-centered outcomes. Various circumstances can prohibit recipients from following provider advice for surveillance and preventive care. The factors include miscommunications, insufficient finances, inadequate insurance coverage, reduced physical well-being, or lack of awareness (Giaccone et al., 2021). HSCT recipients with marginal education or information needs and minimal information impediments have better QoL with decreased anxiety and depression (Slater and Hansen, 2021; Giaccone et al.,2020). Developing a guideline-driven SOP will ensure that any provider assuming care of the transplant survivor is fully equipped to deliver best-practice care. It is also the initial step in creating a realistic LTFU care model that can be translated within any care setting to this vulnerable patient population and facilitate continuity of survivorship care. The consequences of delayed or absent care are substantial, and implementation of standardized follow-up care is a high priority (Giaccone et al.,2020; Majhail et al., 2012; Slater and Hansen, 2021).

APPENDICES

TABLE OF EVIDENCE

CITATION	PURPOSE	SAMPLE/SETTING	METHODS (Design, Interventions, Measures)	RESULTS	DISCUSSION, INTERPRETATION, LIMITATIONS
Sun, C. L., Francisco, L., Kawashima, T., Leisenring, W., Robison, L. L., Baker, K. S., Weisdorf, D. J., Forman, S. J., & Bhatia, S. (2010). Prevalence and predictors of chronic health conditions after hematopoietic cell transplantation: A report from the bone marrow transplant survivor study. Blood, 116(17), 3129–3139. https://doi.org/10.1182/blood2009-06-229369	It aimed to establish the prevalence and severity of chronic health comorbidities in HCT survivors and compare outcomes to healthy sibling cohorts. It aimed to identify subpopulations at increased risk.	Participants: HCT recipients at the City of Hope National Medical Center (COH) or the University of Minnesota (UMN) between 1974 and 1998 Transplanted for a hematologic malignancy or severe aplastic anemia (SAA) 2-year survivor at minimum Alive, 18 years of age or older, and able to read and speak English	Data were analyzed using SAS Version 9.1 (SAS Institute). All statistical tests were 2-sided, and $P < .05$ was considered statistically significant. Relative risk regression was also used for analyses restricted to HCT survivors. A fixed set of explanatory variables were selected to assess their impact on the risk of chronic health conditions.	HCT survivors were twice as likely as siblings to have a chronic health condition (95% CI, 1.6-2.1) of any severity, 1.9 times as likely to have a grade 1 or 2 condition (95% CI, 1.6-2.2), and 3.5 times as likely to have a grade 3 or 4 condition (95% CI, 2.3-5.4). Allogeneic recipients were likelier to report auditory or visual impairment (RR = 3.7; 95% CI, 1,1-12.2).	Succinct communications between the transplant provider and the primary care physicians regarding the details of the long-term care of post-HSCT recipients are critical. The prevalence of any chronic health condition is high: 66.4% have at least one chronic health condition, 18.3% have a severe or life-threatening illness, more than one-half have two or more conditions, and more than one-third have three or more conditions.

		A total of the 2175 patients underwent HCT at COH or UMN Of the 1633 survivors alive during study participation, 1468 (90%) were successfully contacted, and 1022 (70%) participated. Participants were older at HCT (mean age, 34 vs. 29 years) Non-Hispanic whites vs. Caucasians (65% vs. 56%) Females vs. Males (67% vs. 60%) A comparison was made with a noncancer population with a nearest-age sibling to the study.	Comparisons between HCT survivors and siblings were conducted using relative risk regression for expected outcomes and were reported as relative risks (RR) with 95% confidence intervals (CIs). Standard parametric and nonparametric techniques were used to compare clinical and demographic subgroups.	Survivors of unrelated donor HCT had a 4.6x more risk of having a grade 3 or 4 chronic health condition than siblings (95% CI, 2.87.6). HCT survivors, 89 (9%) reported psychological distress as indicated by the Brief Symptom Inventory-18 Global Severity Index scores. The cumulative incidence of a chronic health condition among allogeneic HCT survivors was 64% at 10 years and approached 71% at 15 years after HCT.	HCT survivors had 3.5 times the likelihood of developing a severe or life-threatening health condition compared to their siblings. A survivor having cGVHD added to an increased risk of severe or life-threatening conditions and the occurrence of multiple diseases Limitations: The participation rate was 63% of all eligible subjects and 70% of those successfully contacted.

CITATION	PURPOSE	SAMPLE/SETTING	METHODS (Design, Interventions, Measures)	RESULTS	DISCUSSION, INTERPRETATION, LIMITATIONS
Kaya, A., Namdaroğlu, S., Kayıkcı, M., Merdin, A., Batgi, H., İskender, D., Dal, M., Kızıl Çakar, M., Tekgunduz, E., & Altuntas, F. (2020). Impact of guideline-driven approach in the follow-up of long-term complications after allogeneic hematopoietic cell transplant: single center experience. *Experimental and clinical transplantation, 18*(3), 359–367. https://doi.org/10.6002/etc.2018.0007	To share their familiarity with a guideline-driven approach for follow-up of long-term complications posttransplant.	Hematology and Bone Marrow Transplant Unit, Dr. Abdurrahman Yurtaslan Ankara Oncology Education and Research Hospital, Ankara, Turkey Allogeneic HSCT patients that underwent transplant procedures between July 2009 and March 2016 at the medical center N=91 patients (35 female and 56 male. median age of the patients at the time of their evaluation was 39 years (range, 18-64 y) The median posttransplant follow-	A retrospective, observational, case-control study Data were extracted from patient files and stored in electronic format Patients were routinely followed for 1-year post-transplant at a minimum. The screening program was applied to all cases between 2/2016 and 2/ 2017. Categorical and quantitative variables are presented with descriptive statistics and shown as	69 patients had < 1000 ng/mL, and 22 had≥ 1000 ng/mL ferritin levels. Twenty-four patients had grade 1-2 acute GVHD 16 had grade 3-4 acute GVHD. Seven patients had mild chronic GVHD (cGVHD) patients 12 had moderate cGVHD 10 had severe cGVHD.	Posttransplant follow-up screening is recommended after allo-HCT Patients and physicians should be vigilant of the long-term complications after allo-HCT. Long-term evaluations should be detailed assessments of organs and systems, observing for late effects. Early recognition of late effects can lead to decreased mortality and morbidity.

CITATION	PURPOSE	SAMPLE/SETTING	METHODS (Design, Interventions, Measures)	RESULTS	DISCUSSION, INTERPRETATION, LIMITATIONS
		up duration was 36 months (range, 12-84 months) The median follow-up duration after the initial diagnosis was 51 months. The median count of transplanted CD34-positive stem cells was 7×10^6	frequency or median. Comparisons for statistical significance were made using chi-square analyses for categorical variables. $P \leq .05$ was considered statistically significant. Statistical analyses were performed with SPSS software.		Limitations: Unmentioned elements that can affect GVHD were unmentioned in the study: -Degree of donor/recipient match -Disease status at the time of transplant -Type of GVHD prophylaxis

CITATION	PURPOSE	SAMPLE/SETTING	METHODS (Design, Interventions, Measures)	RESULTS	DISCUSSION, INTERPRETATION, LIMITATIONS
Hierlmeier, S., Eyrich, M., Wölfl, M., Schlegel, P., and Wiegering, V. (2018). Early and late complications following hematopoietic stem cell transplantation in pediatric patients – A retrospective analysis over 11 years. *PLOS ONE, 13*(10), e0204914. https://doi.org/10.1371/journal.pone.0204914	Identify prognostic markers that guide follow-up measures, and support individualized stem cell transplant strategies to minimize long-term toxicities	A total of 229 (105 females, 124 males; median age was 7 y) pediatric patients who underwent HSCT between Jan 1, 2005, and Dec 31, 2015, at the University Hospital Wuerzburg, Children's Department of Oncology, Hematology and Stem Cell Transplantation, Wuerzburg, Germany 55.0% (n = 126) of patients received allo-HSCT, 45.0% (n = 103) auto-HSCT	Retrospective analysis Statistical evaluation was done with IBM SPSS Statistics 23 Premium 02. Correlations and differences between the two groups were calculated with the Chi-square test. Fisher's exact test calculated low cell frequency variables with a 2x2-contingency table.	74.2% (n = 175) had late complications 25.8% (n = 59) were free of complications More complications occurred after allo-HSCT than after auto-HSCT (88.9% [n = 112] vs. 56.3% [n = 58])	Establishing a customized risk-adjusted and exposure-specific, long-term follow-up plan should be the focus of future treatment protocols. There is a need for more prospective and systematically collected multicenter studies. Limitations: The population was pediatric, and the average follow-up time was 2.5 years.

CITATION	PURPOSE	SAMPLE/SETTING	METHODS (Design, Interventions, Measures)	RESULTS	DISCUSSION, INTERPRETATION, LIMITATIONS
			The Mann-Whitney U test was used for nonparametric values to calculate the significance of metric variables. Survival curves were calculated according to Kaplan and Meier.	Allo transplant patients had a greater risk of severe bacterial infection/sepsis 8.7%, viral reactivations (26.2, 59.5% developed an aGvHD (acute Graft versus-Host-Disease), increased incidence of pulmonary impairment (lung dysfunction): 43.6%, CNS-disorders: 62.5%, ECG abnormalities: 26.9%	

CITATION	PURPOSE	SAMPLE/SETTING	METHODS (Design, Interventions, Measures)	RESULTS	DISCUSSION, INTERPRETATION, LIMITATIONS
Abou-Mourad, Y., Lau, B. C., Barnett, M. J., Forrest, D. J., Hogge, D. E., Nantel, S. H., Nevill, T. J., Shepherd, J. D., Smith, C., Song, K. W., Sutherland, H. J., Toze, C. L., & Lavoie, J. C. (2010). Long-term outcome after allo-SCT: close follow-up on a large cohort treated with myeloablative regimens. *Bone Marrow Transplantation*, *45*(2), 295–302. https://doi.org/10.1038/bmt.2009.128	To reveal survivors' late outcomes and long-term complications after allo-HSCT, discuss the health issues seen in long-term survivors, and highlight the importance of medical surveillance.	Charts of 429 patients were alive and disease free of their original illness for at least two years post-transplantation. A total of 60 patients died of relapsed disease or non-relapse causes. A total of 369 long-term survivors were included in the study. Leukemia/BMT Program of British Columbia in Vancouver, Canada.	Retrospective chart review Survival analyses were done according to the method of Kaplan and Meier and compared using the log-rank test. The competing risk method calculated relapse's cumulative incidence (CI), non-relapse mortality, and secondary malignancy.	Major non-relapse causes of death were chronic GVHD (cGVHD), secondary malignancy, and infection. The probabilities of OS and EFS were 85% (95% cumulative incidence (CI) (81–89%)) and 79% (95% CI (74–83%)) at ten years, respectively. Hypogonadism was seen in 68.8% of women	Limitations: Potential bias in capturing patients' complications since it is a single-center study Gonadal failure is the most frequent endocrine complication of high-dose chemotherapy and radiotherapy post-allo-HSCT, and recovery is rare. Dyslipidemia and hypertension are significant contributors to developing cardiac complications. Surveillance and treatment of known cardiac risk factors are recommended.

CITATION	PURPOSE	SAMPLE/SETTING	METHODS (Design, Interventions, Measures)	RESULTS	DISCUSSION, INTERPRETATION, LIMITATIONS
			Univariate and multivariate analyses were performed using a Cox proportional hazard technique	cGVHD was diagnosed in 53.1% of survivors. Endocrine and metabolic complications: hypogonadism in 36.3% of patients, osteopenia/ osteoporosis in 24.4% of patients, dyslipidemia in 8.9% of patients, hypothyroidism in 7.6% of patients and diabetes in 28 7.6%. Hypertension was diagnosed in 21.4% of patients	Lifelong surveillance is recommended. Late effects like chronic GVHD, infections, secondary cancers, and cardiac, endocrine, psychological, mood, and musculoskeletal diseases are common complications for long-term survivors.

CITATION	PURPOSE	SAMPLE/SETTING	METHODS (Design, Interventions, Measures)	RESULTS	DISCUSSION, INTERPRETATION, LIMITATIONS
Gifford, G., Sim, J. S., Horne, A. W., & Ma, D. (2014). Health status, late effects, and long-term survivorship of allogeneic bone marrow transplantation: a retrospective study. *Internal Medicine Journal*, *44*(2), 139–147. https://doi.org/10.1111/imj.12336	To recognize late complications of survivorship, such as organ dysfunction, secondary neoplasms, emotional health, return to vocation or study, and social acclimatization after transplant in post-allo-HSCT survivors.	Allo-HSCT patients surviving at least 2 years after transplantation (N=99) The median age was 43 years (range 18–64 years). There were 55 men and 44 women. St Vincent's Public Hospital in Australia	A single-center, retrospective chart review Data was collected from all patients who underwent allo-HSCT between January 2000 and December 2007. Descriptive statistics The overall survival probability was calculated using Kaplan–Meier analysis.	47% had late cardiovascular effects. 6% had hypothyroidism and were on thyroid replacement therapy. 4% experienced steroid-induced diabetes that resolved after steroids were discontinued. 21% of women and three men were on hormonal replacement therapy (HRT).	This study demonstrated that chronic health conditions are high in allo-HSCT survivors: 91% of study participants reported chronic physical health conditions. Allo-HSCT survivors have poor cardiovascular outcomes and an increased incidence of type 2 diabetes mellitus. < 50% of allo-HSCT survivors testify to normal functional status, QOL issues persist over time, and 5% of long-term survivors (>10 years post-transplant) qualify their health as poor.

CITATION	PURPOSE	SAMPLE/SETTING	METHODS (Design, Interventions, Measures)	RESULTS	DISCUSSION, INTERPRETATION, LIMITATIONS
				32% had normal follicle-stimulating hormone, luteinizing hormone, and either estrogen or testosterone levels for age and gender. 68% of patients were hypogonadal.	Management should be preventative through education and control of modifiable risk factors, particularly obesity, tobacco, hypertension, and dyslipidemia. Limitations: -Data regarding long-term HSCT survivorship in Australia are scarce. -The study was a single-center, so the results may not be generalizable. -Retrospective analyses are incomplete assessments of patients.

REFERENCES

AACN. (2006). *DNP Essentials*. https://www.aacnnursing.org/DNP/DNP-Essentials. Retrieved Nov 14, 2021, from https://www.aacnnursing.org/DNP/DNP-Essentials

Abou-Mourad, Y., Lau, B. C., Barnett, M. J., Forrest, D. J., Hogge, D. E., Nantel, S. H., Nevill, T. J., Shepherd, J. D., Smith, C., Song, K. W., Sutherland, H. J., Toze, C. L., & Lavoie, J. C. (2010). Long-term outcome after allo-SCT: close follow-up on a large cohort treated with myeloablative regimens. *Bone Marrow Transplantation, 45*(2), 295–302. https://doi.org/10.1038/bmt.2009.128

Adashi, E. Y., Walters, L. B., & Menikoff, J. A. (2018). The Belmont Report at 40: Reckoning With Time. *American Journal of public health, 108*(10), 1345–1348. https://doi.org/10.2105/AJPH.2018.304580

Atilla, E., Atilla, P. A., Toprak, S. K., & Demirer, T. (2017). A review of late complications of allogeneic hematopoietic stem cell transplantations. *Clinical Transplantation*, *31*(10). https://doi.org/10.1111/ctr.13062

Battiwalla, M., Hashmi, S., Majhail, N., Pavletic, S., Savani, B., and Shelburne, N. (2017). National Institutes of Health Hematopoietic Cell Transplantation Late Effects Initiative: Developing recommendations to improve survivorship and long-term outcomes. *Biology of Blood and Marrow Transplantation, 23*(1), 6–9. https://doi.org/10.1016/j.bbmt.2016.10.020

Battiwalla, M., Tichelli, A., and Majhail, N. S. (2017). Long-term survivorship after hematopoietic cell transplantation: Roadmap for research and care. *Biology of blood and marrow transplantation: journal of the American Society for Blood and Marrow Transplantation*, *23*(2), 184–192. https://doi.org/10.1016/j.bbmt.2016.11.004.

Be The Match. (n.d.). *Patient survival information for this center*. Be The Match. Retrieved September 11, 2022, from http://bethematch.org/tcdirectory/index/104/

Bhatia, S., Francisco, L., Carter, A., Sun, C. L., Baker, K. S., Gurney, J. G., McGlave, P. B., Nademanee, A., O'Donnell, M., Ramsay, N. K., Robison, L. L., Snyder, D., Stein, A., Forman, S. J., & Weisdorf, D. J. (2007). Late mortality after allogeneic hematopoietic cell transplantation and functional status of long-term survivors: report from the bone Marrow Transplant Survivor Study. *Blood*, *110*(10), 3784–3792. https://doi.org/10.1182/blood-2007-03-082933

Bhatia, S. (2014). Caring for the long-term survivor after allogeneic stem cell transplantation. *Hematology*, *14*(1), 495–503. https://doi.org/10.1182/asheducation-2014.1.495.

Biddell, C., Spees, L., Mayer, D., Wheeler, S., Trogdon, J., Rotter, J., & Birken, S. (2020). Developing personalized survivorship care pathways in the United States: Existing resources and remaining challenges. *Cancer*, *127*(7), 997–1004. https://doi.org/10.1002/cncr.33355

Butts, J., and Rich, K. (2017). *Philosophies and theories for advanced nursing practice* (3rd ed.). Jones & Bartlett Learning. City of Hope. (2020, Jan 29). *City of Hope lauded for exceptional transplant outcomes.* Retrieved Jun 11, 2022, from: https://www.cityofhope.org/breakthroughs/city-of-hoperecognized-for-exceptional-transplant-outcomes

City of Hope lauded for exceptional transplant outcomes. (2022, August 19). City of Hope. https://www.cityofhope.org/breakthroughs/city-of-hope-recognized-for-exceptional-transplant-outcomes

Code of Ethics PDF. (2018, February 15). ANA. https://www.nursingworld.org/practice-policy/nursing-excellence/ethics/code-of-ethics-for-nurses/coe-view-only/

Field, A. (2017). *Discovering Statistics Using IBM SPSS Statistics: North American Edition* (5th ed.). SAGE Publications Ltd. Giaccone, L., Felicetti, F., Butera, S., Faraci, D., Cerrano, M., Dionisi Vici, M., Brunello, L., Fortunati, N., Brignardello, E., & Bruno, B. (2020). Optimal Delivery of Follow-Up Care After Allogeneic Hematopoietic Stem-Cell Transplant: Improving Patient Outcomes with a Multidisciplinary Approach</p> *Journal of Blood Medicine, Volume 11*, 141–162. https://doi.org/10.2147/jbm.s206027

Gifford, G., Sim, J. S., Horne, A. W., & Ma, D. (2014). Health status, late effects, and long-term survivorship of allogeneic bone marrow transplantation: a retrospective study. *Internal Medicine Journal*, *44*(2), 139–147. https://doi.org/10.1111/imj.12336

Gratwohl, A., Brand, R., McGrath, E., van Biezen, A., Sureda, A., Ljungman, P., Baldomero, H., Chabannon, C., & Apperley, J. (2014, Jan 31). Use of the quality management "JACIE" and outcome after hematopoietic stem cell transplantation. *Haematologica*, *99*(5), 908–915. https://doi.org/10.3324/haematol.2013.096461

Gratwohl, A., & Niederwieser, D. (2012). History of Hematopoietic Stem Cell Transplantation: Evolution and perspectives. *Transplantation Dermatology*, 81–90. https://doi.org/10.1159/000335266

Hahn, T., Paplham, P., Austin-Ketch, T., Zhang, Y., Grimmer, J., Burns, M., Balderman, S., Ross, M., & McCarthy, P. L. (2017, November). Ascertainment of unmet needs and participation in health maintenance and screening of adult hematopoietic cell transplantation survivors followed in a formal survivorship program. *Biology of Blood and Marrow Transplantation*, *23*(11), 1968–1973.

https://doi.org/10.1016/j.bbmt.2017.07.024

Hamblin, A., Greenfield, D. M., Gilleece, M., Salooja, N., Kenyon, M., Morris, E., Glover, N., Miller, P., Braund, H., Peniket, A., Shaw, B. E., & Snowden, J. A. (2017). Provision of long-term monitoring and late effects services following adult allogeneic hematopoietic stem cell transplant: A survey of UK NHS-based programmes. *Bone Marrow Transplantation*, *52*(6), 889–894. https://doi.org/10.1038/bmt.2017.67

Hashmi, S., Lee, S., Savani, B., Burns, L., Wingard, J., Perales, M., Palmer, J., Chow, E., Meyer, E., Marks, D., Mohty, M., Inamoto, Y., Rodriguez, C., Nagler, A., Sauter, C., Komanduri, K., Pidala, J., Hamadani, M., Johnston, L., Shah, N., Shaughnessy, P., Hamilton, B.K., Majhail, N., Kharfan-Dabaja, M.A., Schriber, J., DeFilipp, Z., Tarlock, K., Fanning, S., Curtin, P., Rizzo, J., and Carpenter, P. (2018). ASBMT practice guidelines committee survey on long-term follow-up clinics for hematopoietic cell transplant survivors. *Biology of Blood and Marrow Transplantation*, *24*(6), 1119–1124. https://doi.org/10.1016/j.bbmt.2018.03.023

Health Resources and Services Administration. (2022, Apr 14). *Transplant Activity Report*. Blood stem cell. Retrieved Aug 20, 2022, from https://bloodstemcell.hrsa.gov/data/donation-and-transplantation-statistics/transplantactivity-report#summary

Hierlmeier, S., Eyrich, M., Wölfl, M., Schlegel, P., and Wiegering, V. (2018). Early and late complications following hematopoietic stem cell transplantation in pediatric patients – A retrospective analysis over 11 years. *PLOS ONE*, *13*(10), e0204914. https://doi.org/10.1371/journal.pone.0204914

Hilgendorf, I., Greinix, H., Halter, J., Lawitschka, A., Bertz, H., & Wolff, D. (2015). Long-Term

Follow-up After Allogeneic Stem Cell Transplantation. Deutsches Arzteblatt International. https://doi.org/10.3238/arztebl.2015.0051

Inamoto, Y., & Lee, S. J. (2017, Feb 23). Late effects of blood and marrow transplantation. *Haematologica*, *102*(4), 614–625. https://doi.org/10.3324/haematol.2016.150250

Kaya, A., Namdaroğlu, S., Kayıkcı, M., Merdin, A., Batgi, H., İskender, D., Dal, M., Kızıl Çakar, M., Tekgunduz, E., and Altuntas, F. (2020). Impact of guideline-driven approach in follow-up of long-term complications after allogeneic hematopoietic cell transplant: A single-center experience. *Experimental and Clinical Transplantation*, *18*(3), 359–367. https://doi.org/10.6002/ect.2018.0007

Information for Physicians. (n.d.). Fred Hutch. https://www.fredhutch.org/en/research/patient-treatment-support/long-term-follow-up/bone-marrow-stem-cell-transplant-ltfu/information-for-physicians.html

Kanagasundram, S., & Amini, F. (2019). Late Complications of Allogenic Stem Cells Transplantation in Leukaemia. *Tissue Engineering and Regenerative Medicine*, *16*(1), 1–9. https://doi.org/10.1007/s13770-018-0157-3

Kurosawa, S., Mori, A., Tsukagoshi, M., Onishi, Y., Ohwada, C., Mori, T., Goto, H., Asano-Mori, Y., Nawa, Y., Hino, M., Fukuchi, T., Mori, Y., Yamahana, R., Inamoto, Y., and Fukuda, T. (2020). Current status and needs of long-term follow-up clinics for hematopoietic cell transplantation survivors: Results of a nationwide survey in Japan. *Biology of Blood and Marrow Transplantation*, *26*(5), 949–955. https://doi.org/10.1016/j.bbmt.2020.01.008

Lewin's 3-Stage Model (n.d.) *Lewin's Change Model Template*. Online Visual Paradigm.

Retrieved Jun 29, 2022, from https://online.visualparadigm.com/diagrams/templates/lewins-change-model/lewins-3-stage-model/.

Majhail, N. S. (2017). Long-term complications after hematopoietic cell transplantation. *Hematology/Oncology and Stem Cell Therapy*, *10*(4), 220–227. https://doi.org/10.1016/j.hemonc.2017.05.009

Majhail, N., Rizzo, J., Lee, S., Aljurf, M., Atsuta, Y., Bonfim, C., Burns, L., Chaudhri, N., Davies, S., Okamoto, S., Seber, A., Socie, G., Szer, J., van Lint, M., Wingard, J., & Tichelli, A. (2012). Recommended screening and preventive practices for long-term survivors after hematopoietic cell transplantation. *Bone Marrow Transplantation*, *47*(3), 337–341. https://doi.org/10.1038/bmt.2012.5

Morken, C., Tevaarwerk, A., Swiecichowski, A., Haine, J., Williams, Z., Norslien, K., Arroyo, N., Zhang, X., Campbell, B., Mendonca, E., Juckett, M., & Sesto, M. (2019). Survivor and clinician assessment of survivorship care plans for hematopoietic stem cell transplantation patients: An engineering, primary care, and oncology collaborative for survivorship health. *Biology of Blood and Marrow Transplantation*, *25*(6), 1240–1246. https://doi.org/10.1016/j.bbmt.2019.02.003

Regis College Online. (2022, Jun 17). *DNP Nursing Leadership Role and Skills*. Retrieved Sept 5, 2022, from https://online.regiscollege.edu/blog/dnp-nursing-leadership/

Rehman, N., Mahmood, A., Ibtasam, M., Murtaza, S., Iqbal, N., & Molnár, E. (2021). The psychology of resistance to change: The antidotal effect of organizational justice, support, and leader-member exchange. *Frontiers in Psychology*, *12*.

https://doi.org/10.3389/fpsyg.2021.678952Shirey, M. (2013). Lewin's theory of planned change as a strategic resource. *The Journal of Nursing Administration*, *43*(2), 69–72. https://doi.org/10.1097/nna.0b013e31827f20a9

Sathyanarayana Rao, T., Radhakrishnan, R., & Andrade, C. (2011b). Standard operating procedures for clinical practice. *Indian Journal of Psychiatry*, *53*(1), 1. https://doi.org/10.4103/0019-5545.75542

Shirey, M. (2013). Lewin's Theory of Planned Change as a Strategic Resource. *JONA: The Journal of Nursing Administration*, *43*(2), 69–72. https://doi.org/10.1097/nna.0b013e31827f20a9

Simplify, E. (2022, Aug 11). *ANA Code of Ethics: What are the 9 Provisions of Nursing?* Educate Simplify. Retrieved Sept 5, 2022, from https://educatesimplify.com/anacode-of-ethics-9-provisions-nursing/

Slater, S. S., & Hansen, L. K. (2021). Long-term follow-up and survivorship. *Blood and Marrow Transplant Handbook*, *3*, 807–828. https://doi.org/10.1007/978-3-030-53626-8_51

Solh, M. M., Bashey, A., Solomon, S. R., Morris, L. E., Zhang, X., Brown, S., & Holland, H. K. (2018, Jan 15). Long-term survival among patients who are disease free at 1-year post allogeneic hematopoietic cell transplantation: a single center analysis of 389 consecutive patients. *Bone Marrow Transplantation*, *53*(5), 576–583. https://doi.org/10.1038/s41409-017-0076-2

Statistics and Graphs | Division of Cancer Control and Population Sciences (DCCPS). (n.d.-b). Retrieved Sept 20, 2022, from https://cancercontrol.cancer.gov/ocs/statistics

Sun, C. L., Francisco, L., Kawashima, T., Leisenring, W., Robison, L. L., Baker, K. S.,

Weisdorf, D. J., Forman, S. J., & Bhatia, S. (2010, October 28). Prevalence and predictors of chronic health conditions after hematopoietic cell transplantation: a report from the Bone Marrow Transplant Survivor Study. *Blood*, *116*(17), 3129–3139. https://doi.org/10.1182/blood-2009-06-229369