A DNP PROJECT

CREATING A GUIDEBOOK FOR ESTABLISHING A SUCCESSFUL LEFT VENTRICULAR ASSIST DEVICE (LVAD) PROGRAM

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Abstract

Over 6.2 million Americans currently have heart failure (HF) and this number expected to grow to 8 million by 2030. Approximately 5-10% of patients will progress to advanced HF with symptoms refractory to conventional therapies. For these patients, heart transplantation is the best treatment. However, the number of donors is not enough to meet the need. To address this limitation, left ventricular assist devices (LVADs) were introduced as an alternative option. Over the past 20 years, three generations of LVADs have been developed with each generation better than the one before it with outcomes rivaling heart transplant. As a result, the number of device implants over the past several years have been increasing. However, LVAD programs continue to be limited to urban academic centers requiring many patients to travel long distances to access care. This may account for some of the observed disparities with less implants in women and African Americans and other racial minorities. Having LVAD programs in community hospitals may alleviate some of these disparities. The purpose of this DNP project was to review the data supporting the use of LVADs in advanced heart failure patients and to create a comprehensive guidebook to aid community hospitals in establishing an LVAD program. The guidebook was created based on a retrospective analysis of my experience in establishing a Centers for Medicare & Medicaid Services certified LVAD program at my institution. This guidebook also includes information derived from expert consensus and medical society guidelines, heartmate instructions of use and regulatory policies. I created a guidebook that outlines the process of developing clinical practice guidelines, policies, and pathways essential for a successful LVAD program. It also describes the requirements for program certification and provides sample LVAD forms, order sets and clinical protocols. A clinical expert in this field reviewed the guidebook and found it to be comprehensive and cohesive. A new VAD coordinator used the guidebook to establish a Centers for Medicare & Medicaid Services certified VAD center at their institution and found it to be a great tool to navigate the process with ease. This guidebook will be a useful resource for any medical professional interested in establishing an
LVAD program in their community. Having more programs locally will improve access to care and will address some of the observed racial and gender disparities in the treatment of advanced heart failure.

*Keywords:* Left Ventricular Assist Device (LVAD), Ventricular Assist Device (VAD), Centers for Medicare & Medicaid Services LVAD guidelines, advanced heart failure, guidebook, program development, VAD program.
Introduction

Heart failure (HF) is the inability of the heart muscle to pump blood to meet the body’s need for oxygen and blood (American Heart Association [AHA], 2017). It is a highly prevalent, chronic condition resulting in increased morbidity and mortality. The National Health and Nutrition Examination Survey from 2013-2016 reported that 6.2 million adults are currently afflicted with the disorder. The AHA estimates that HF prevalence will increase by 46% to over 8 million by 2030. The total expenditure of treating HF is anticipated to rise by 127% from $30.7 billion in 2012 to $69.8 billion by 2030 (Virani et al., 2020).

The direct cost of HF hospitalizations was over $11 billion in 2014 and when combined with the cost of office visits, medications, procedures, and lost productivity, it poses a significant economic burden to society (Jackson et al., 2018). It was the primary diagnosis in more than 800,000 hospital discharges in 2016 and was responsible for over 80,000 deaths in 2017 (Virani et al., 2020). Despite advances in medical therapies, prognosis remains poor with up to 22% of HF patients dying within a year of diagnosis (Virani et al., 2020). HF was cited as one of the diagnoses in 379,800, death certificates (13.4% of all deaths) in 2018 (Center for Disease Control and Prevention [CDC], 2020).

The clinical course of HF is characterized by progressive decline over time. Early in the diagnosis, utilization of guideline-directed medical therapy, as well as appropriate use of electrical therapies for sudden death prevention and resynchronization, leads to a period of symptom improvement and stability which can last months to years (Chaudhry & Stewart, 2016). However, as the disease progresses, functional status declines, and symptoms worsen leading to acute decompensation and hospitalization. Although initially responsive to the escalation of medical therapy, decompensations become more frequent and eventually become refractory to conventional treatment. It is at this stage that patients are considered to have advanced HF. Heart transplantation is considered the gold standard for the treatment for advanced HF due to the excellent quality of life and longevity that it provides. However, due to
lack of donor availability, only a limited number of patients receive a transplant annually. Some patients are also not candidates for transplantation due to advanced age and co-morbidities. For these patients, a left ventricular assist device (LVAD) is a good option for improving quality of life and survival. The purpose of this DNP project was to create a comprehensive guidebook to help other institutions in establishing a successful LVAD program.

**Background/Significance**

According to the Heart Failure Society of America, advanced HF is the presence of progressive and/or persistent severe signs and symptoms of HF despite optimized medical, surgical, and device therapy. Progression to an advanced HF stage is often gradual, deceptive, and nonspecific making it difficult to diagnose the condition early in the process (Fang et al., 2015). Identification of advanced HF is crucial since the treatment options are limited and need to be considered early as the disease is progressive, and overall survival is poor. According to the landmark Randomized Evaluation of Mechanical Assistance for the Treatment of Congestive Heart Failure (REMATCH) trial, advanced HF patients managed medically had a 25% survival at 1 year and only 8% survival at 2 years (Rose et al., 2001). In the Inotrope Dependent (INTREPID) trial, patients who were ineligible for transplant and treated optimally with inotropes had a survival rate of 22% at 6 months and only 11% at 12 months. (Rogers et al., 2007).

The Acute Decompensated Heart Failure National Registry (ADHERE) indicates that more than 5% of patients will progress to refractory symptoms (Chaudhry & Stewart, 2016). Estimated to number from 250,000 to 500,000, heart transplantation is the gold standard treatment for these patients (Chaudhry & Stewart, 2016; Norton et al., 2011). However, due to the broadening gap between the number of heart donors and transplant candidates, only a small fraction of patients who would benefit from a transplant ultimately obtain one. In 2019, only 3,552 heart transplants were performed in the United States due to the inadequate number of donors (United Network for Organ Sharing [UNOS], 2020). Moreover, patients with advanced
age and co-morbidities such as severe pulmonary, liver or kidney disease, or recent malignancies are ineligible for heart transplantation.

To bridge the gap between demand and donor availability, LVADs were developed as an alternative treatment for end-stage HF patients. The establishment of the Artificial Heart Program funded by the National Heart, Lung, and Blood Institute (NHLBI) in 1964 heralded the development of mechanical circulatory support devices for long-term use (Prinzing et al., 2016). Over the succeeding decades, three generations of LVADs have been created with each generation having improved survival with fewer complications than the one before it. These devices deliver long-term circulatory support and are implanted as a bridge-to-transplant (BTT) for patients who decline while waiting for a heart donor or as destination therapy (DT) for those patients who are ineligible for transplantation (Prinzing et al., 2016).

The first generation LVAD, the HeartMate XVE, introduced in the 1990s, was a pulsatile pump implanted in the abdomen that was connected to the heart via an inflow cannula from the left ventricular apex. After a set volume of blood enters the circular pump, a pusher plate is activated either pneumatically or electrically, propelling the blood to an outflow cannula connected to the ascending aorta. (Prinzing et al., 2016). The REMATCH trial was the first study to demonstrate the superiority of the pulsatile HeartMate XVE LVAD in all-cause survival for advanced HF patients compared to maximal medical therapy (Rose et al., 2001). Survival at 1 year was 52% in the device group compared to 25% in the medical therapy arm, and at 2 years, survival was 23% compared to 8%. Functional capacity and quality of life at 1 year was significantly better in patients who received the device compared to medical therapy, with more patients improving to New York Heart Association (NYHA) functional class II status compared to medical therapy. The results of this revolutionary trial led the Food and Drug Administration (FDA) to approve the HeartMate XVE for long-term use in advanced HF patients. However, widespread adoption of the device was hindered by its relatively large size, noise production, and multiple moving parts that affected its durability (Prinzing et al., 2016; Rose et al., 2001).
Device-related complications were high in the 2001 REMATCH trial with 28% of patients experiencing device infection at three months, and 35% developing device failure at 2 years.

The HeartMate II second-generation LVAD was developed in the mid-2000s to address these issues. By transitioning from a pulsatile to continuous flow design and having only a single moving part, HeartMate II was more durable and much smaller, making it easier to implant even in patients with smaller body habitus. The HeartMate II was found to have less device-related infections, fewer device malfunctions, and better survival at 1 year compared to HeartMate XVE (68% vs 55%) (Slaughter et al., 2009). Patients who underwent HeartMate II implantation also had a better quality of life as assessed by Minnesota Living with Heart Failure and Kansas City Cardiomyopathy Questionnaires and improved functional capacity with 80% improving from NYHA functional class IV symptoms at baseline to class I to II at 6 months (Prinzing et al., 2016; Rogers et al., 2010).

The superiority of the second-generation continuous-flow HeartMate II quickly led to its widespread adoption and a rapid rise in the number of LVADs implanted throughout the United States (Slaughter et al., 2009). However, even with improved survival and better quality of life, the use of continuous-flow HeartMate II LVADs was plagued by high rates of device complications including thrombosis, bleeding, infections, and stroke. Continued efforts to address these complications led to the development of the third-generation HeartMate 3 device. A design change to centrifugal-flow made the HeartMate 3 even smaller than its predecessors allowing for intra-pericardial implantation. It has a magnetically levitated rotor that does not produce heat and wider blood pathways that cause less hemolysis. In addition, a novel algorithm was incorporated that allows the pump to transiently decrease then increase its speed every two seconds before going back to the set speed to decrease the risk of pump thrombosis. All these enhancements led to more consistent left ventricular washout, less aortic insufficiency, and decreased development of arteriovenous malformations (Hanff & Birati, 2019; Prinzing et al., 2016).
In 2019, the Multi-center Study of Maglev Technology in Patients Undergoing Mechanical Circulatory Support Therapy with HeartMate 3 (MOMENTUM 3) trial was published which evaluated the use of the second-generation HeartMate II versus the third-generation HeartMate 3 in patients with advanced HF (Mehra et al., 2019). Results showed that more patients implanted with the HeartMate 3 device were alive and free of incapacitating stroke or pump replacement in 2 years compared to HeartMate II (76.9% vs 64.8%, p=0.001). In addition, LVAD complications such as pump thrombosis, bleeding, and stroke was less frequent with the HeartMate 3 owing to its smaller size, magnetically levitated rotor, and wider blood passages. The incidence of other major complications such as right ventricular failure, renal failure, and hepatic failure was not statistically different for both groups. Since the publication of the MOMENTUM 3 trial, HeartMate 3 became the most common LVAD implanted as BTT or DT in the United States (Mehra et al., 2019).

The Interagency Registry of Mechanical Assisted Circulatory Support (INTERMACS) is a North American registry established in 2005 to collect data on patients who received an FDA-approved left ventricular assist device. A joint effort between the FDA, the Center for Medicaid and Medicare Services (CMS), and NHLBI, and the registry was developed to track outcomes and quality of life after mechanical circulatory support to guide the best practices for LVAD implantation and follow-up care (Prinzing et al., 2016). The latest INTERMACS report in 2019 found that in real-world practice, HeartMate 3 patients have better 1-year survival at 87% compared to 82% for HeartMate II patients. Consistent with the MOMENTUM 3 results, these data show that LVAD survival is increasing and, at least in the short-term, is comparable to heart transplantation whose 1-year survival is 85% (Teuteberg et al., 2020).

Left ventricular assist devices not only increase survival but also improves quality of life (QoL) compared to medical therapy. Using the Kansas City Cardiomyopathy Questionnaire and the Euro-QoL 5 dimensions tool, Emin et al. (2016) assessed the quality of life scores in four groups: 1) patients being assessed for a heart transplant, 2) those listed for transplant on
medical therapy, 3) patients supported with LVADs and 4) patients after a heart transplant. Their findings show that although heart transplant patients had the best quality of life, patients supported with an LVAD reported a significantly better QoL than patients undergoing heart transplant evaluation and those listed for transplant on medical therapy (Emin et al., 2016).

Interventions are considered to be cost-effective if the incremental cost-effectiveness ratio (ICER) is less than $100,000 for every quality-adjusted life-year (QALY) gained. Heart transplant costs $76,000 per QALY gained and is cost-effective owing to its good long-term survival (Patel et al., 2015). Initial analysis of pulsatile assist devices in the REMATCH trial showed that although the HeartMate XVE improved survival, it was a costly intervention with an ICER of $802,700 per QALY gained (Rose at al., 2001). Fortunately, technological advances in device design that resulted in better survival and less complications have also led to a parallel improvement in cost-effectiveness. In a similar cost-analysis by Rogers et al. 2012, the use of the second-generation HeartMate II axial-flow device led to a 75% reduction in ICER to $198,184 per QALY gained. Per Silvestry et al. (2020), the use of the newer centrifugal-flow ventricular assist device increased cost-effectiveness further to an ICER of $69,768 per QALY gained for BTT indication and $102,587 per QALY gained for DT. With continued device innovations in the years to come, it is anticipated that the use of LVADs for advanced HF will not only be more successful but also highly cost-effective and may someday rival heart transplantation.

The need for LVADs is projected to increase over the next decade with the aging of the American population leading to a growing number of people with advanced HF. Furthermore, the change in the heart transplant organ allocation system in 2018 has led to more LVADs being implanted as DT (Teuteberg et al., 2020). With continued technological advances leading to better survival with each new generation of LVAD devices, an increasing number of hospitals are considering establishing an LVAD program to meet the impending demand.
Majority of LVAD programs are currently located in academic institutions in metropolitan areas that are not readily accessible to some patients who must travel great distances for their device implant and follow-up visits. Recently, smaller, community-based hospitals have expressed interest in having their own LVAD programs to decrease the travel burden on patients and their families and keep care local. Most hospitals are reluctant, however, to start a program due to unfamiliarity with the elements necessary to build a successful program. Some organizations do not have expertise in business plan development nor the proficiency in tackling the regulatory requirements essential to obtain CMS certification. Most institutions are unaware of the staffing and equipment needs, and the policies and protocols that must be in place before starting a program. The goal of my DNP project was to create a comprehensive guidebook explaining the steps essential to build a new LVAD program and achieve good outcomes via a multidisciplinary approach to patient selection and management.

**Needs Assessment**

Epidemiologic data show that there are 250,000, to 300,000 patients with end-stage systolic HF who could benefit from advanced therapies (Gustafsson & Rogers, 2017). However, only 3,000 to 3,500 heart transplants are performed in the United States annually, with the number stagnant for many years due to lack of donors. Furthermore, only about 2,500 LVADs are implanted every year. A large gap exists between patients eligible for advanced therapies and those who receive one, suggesting a high demand for LVADs in the future. With continued technological advances and improved survival exhibited with the new generation of LVAD devices, an increasing number of hospitals are considering establishing an LVAD program to meet the impending need.

I performed a SWOT analysis to analyze the strengths, weaknesses, opportunities and threats for this DNP project. Evidence shows that LVADs increase survival and improve quality of life and functional capacity. As a result, LVAD implants have been rising over the past several years resulting in an increased interest for community hospitals to start new LVAD programs.
The strength of this project was that having a guidebook makes the process of establishing a new program less time consuming, stress-free, and efficient. The weakness with the guidebook is that although comprehensive, it is a standard tool and may not address every institution’s unique needs.

Despite increasing adoption, there remains significant disparities in LVAD utilization among people of different race/ethnicity and gender. Racial minority groups receive less than one third of all LVAD implants in the US despite accounting for 40% of all heart failure admissions (Breathett et al., 2018). In addition, device utilization is much lower among women than men (Joshi et al., 2019). One factor likely contributing to these disparities is lack of access to advanced heart failure care. The tremendous opportunity for this project is that it will improve access to care by having more LVAD centers in a patient’s own community. The threat I came across is that establishing a new LVAD program is time-consuming and requires expertise in HF and mechanical circulatory support. It requires the knowledge to create new protocols and procedures for device management, and the organizational skills to coordinate with various teams for equipment management. Additionally, extensive device training is required for medical providers and ancillary staff caring for LVAD patients

**Need for LVAD Resource**

When my collaborating physician and I were recruited 3 years ago to start an Advanced HF and LVAD program at our current institution, we searched the medical literature for guidance. We conducted a literature search using PubMed, Google Scholar, Ovid, and CINHAL utilizing the terms “LVAD program”, “left ventricular assist program”, “mechanical circulatory support program” and “advanced heart failure”. We found only one article that describes the process of establishing a successful DT LVAD program. Makdisi et al. (2017) published an editorial in the Journal of Thoracic Disease that outlined 7 steps that are necessary to start a program. It discussed the rationale and importance of a stepwise approach from 1) identifying the need for an LVAD program, 2) getting administrative support, 3) identifying physician
leadership, 4) assembling the clinical team, 5) collaborating with a transplant program, 6) to applying for accreditation 7) to keeping the program successful and profitable. Although the article was informative, it dealt with some of the topics in general terms and did not provide the level of detail necessary for us to develop an action plan and a timeline.

We identified five additional articles each describing a medical center's early experience with starting a new LVAD program. Published between 2015 and 2018, the centers are all located outside of the United States - Chile, Kuwait, the Netherlands, Serbia, and Kazakhstan (Haeck et al., 2015; Nestorovic et al., 2018; Pedemonte et al., 2017; Pya et al., 2016; Tarazi et al., 2017). Although informative, each paper focused more on their center's initial implant volume, patient demographics, and short-term outcomes, and had little information about how their LVAD program was established. Only the paper by Pya et al. (2016) from Kazakhstan went into some detail regarding the training process for staff and patients, team composition, and patient selection criteria utilized in starting the very first LVAD program in their country.

As the medical literature offered little guidance, we had to rely on our initiative and ideas to start an LVAD program at our new institution. Fortunately, my collaborating physician and I have more than 10 years of experience in managing LVAD patients and came from a center that has had an LVAD and heart transplant program for more than 15 years. Relying on our prior experience, we identified the necessary components we had to put in place before our first implant. We organized a multidisciplinary team consisting of cardiologists, surgeons, coordinators, social workers, pharmacists, dietitians, and physiotherapists to form a VAD committee. We created new policies and procedures and educated the appropriate medical providers and ancillary staff who will be caring for our patients. We contacted the device company to procure the necessary equipment and had their representatives instruct our surgeons and perfusionists on their use. We also enlisted the aid of outside financial experts to instruct our billing department on proper coding and reimbursements. And we instituted an education and marketing campaign to inform local cardiologists on the benefits of an LVAD.
Once everything was in place, we arranged for a site inspection and successfully obtained CMS program accreditation 5 months after we started the process. Because of the entire team's hard work, we were fortunate to implant 15 HeartMate 3 devices in our first year with excellent outcomes.

Although we were able to establish a new LVAD program in a relatively short time, we faced many challenges along the way. Despite the use of LVADs for the past 20 years, a large number of our medical staff members were unfamiliar with the device. Also, most of our local cardiologist already had an established referral pattern of sending HF patients to a nearby state for advanced care. Other medical providers were skeptical of the LVAD and felt that it caused unacceptable complications. We also had to justify the expense of the purchase of the device and its components against our expected revenue.

Despite the lack of information from the medical literature, my collaborating physician and I fortunately had the experience, the knowledge, and the connections to overcome those obstacles. Others may not be so fortunate. That is why I think that sharing our experience on how to establish a new LVAD program will be incredibly valuable to people who are new to ventricular assist devices and may not know where to start. I devised a comprehensive guidebook for my DNP project that outlines the steps essential to the creation of a new LVAD program. I provided a detailed framework that includes a local needs assessment, business plan development, and analysis of existing and anticipated staff and equipment needs. I also shared the challenges we faced with CMS certification and insurance billing and how we were able to overcome them. I included ways to track performance metrics and create a vigorous quality assurance and performance improvement process to assure optimal patient outcomes. This comprehensive guidebook will hopefully alleviate some of the apprehension other centers may have about beginning an LVAD program and will allow them to navigate through the process more efficiently and expeditiously.
Problem Statement

With the rising incidence of heart failure and the growing number of people with advanced symptoms, the need for left ventricular assist devices will increase in the coming years. Community hospitals will have to establish LVAD programs to meet this need but most centers are unsure if this is feasible and unaware of how to start the process.

Purpose

The purpose of this DNP project was to review the data supporting the use of LVADs in patients with advanced heart failure and to create a comprehensive guidebook on determining the need, feasibility, and process of establishing an LVAD program in a community hospital.

Aim

The principal aim of this DNP project was to create a comprehensive guidebook as a reference tool for establishing a successful left ventricular assist device (LVAD) program.

Objectives

1. To be able to analyze the existing treatment gaps and the need for new LVAD programs
2. To understand the basic requirements needed to obtain CMS certification as a destination therapy LVAD program.
3. To identify the key members required for building a multidisciplinary team
4. To understand the important forms, clinical practice guidelines and orders set needed
5. To identity quality metrics for a robust quality assurance and performance improvement program as required by CMS.

Review of Literature

Literature Search Strategy

An extensive search of the medical literature was conducted utilizing PubMed, Medline, OVID and Cumulative Index of Nursing and Allied Health Literature (CINAHL) databases using the search terms “left ventricular assist device”, “heart assist device”, “mechanical circulatory support” combined with “end-stage heart failure” or “advanced heart failure”. The search was
limited to include only articles in the English language published between the years 2000 to 2020 in peer-reviewed journals. The year 2000 was chosen as the starting point as LVADs were first introduced around that time. The search was narrowed to exclude review articles, editorials, case reports, case series, and abstracts. Prospective, randomized control trials were prioritized as they provide the highest level of evidence followed by case-cohort studies. Despite an extensive search, only one article was found that describes the process of establishing a successful DT LVAD program. In an editorial published in 2017 in the Journal of Thoracic Disease, Makdisi et al. (2017) outlined the essential steps necessary to start a program. Therefore, the rest of the search was focused on the utility of LVADs in the management of advanced heart failure. The top 10 articles that best met the search criteria were identified and are the subject of this literature analysis.

**Literature Review**

The Randomized Evaluation of Mechanical Assistance for the Treatment of Congestive Heart Failure (REMATCH) multi-center trial was the first study to compare the use of the HeartMate XVE LVAD to optimal medical therapy including inotropes in patients with advanced heart failure who are not candidates for heart transplantation (Rose et al., 2001). The HeartMate XVE is a pulsatile pump implanted in the abdomen that connects to the heart via an inflow cannula from the left ventricular apex. Once a set volume of blood enters the circular pumping chamber located within the abdominal wall, a pusher plate is activated either pneumatically or electrically, propelling the blood to an outflow cannula connected to the ascending aorta. A percutaneous driveline connects the pump to external battery packs that powers the device. A total of 129 patients ineligible for transplant primarily due to age were randomized to receive either the HeartMate XVE LVAD or maximal medical therapy. The primary end-point was death of any cause and secondary end-points were any serious adverse events, hospitalization days, quality of life, depression, and functional status. The baseline characteristics of both groups were similar. After two years of follow-up, more patients were
alive in the LVAD group compared to medical therapy. The one-year and 2-year survival for those who received an LVAD was 52% and 23% respectively compared to 23% and 8% in the medical group. At the end of 1 year, patients in the device group had a better quality of life improving to a median NYHA functional class II status versus unchanged class IV status for the medical therapy group. In addition, those who were implanted with a device had statistically better scores on the Beck Depression Inventory and the 36-item Medical Outcomes Study Short-Form General Health Survey (SF-36). However, the device group had a higher incidence of adverse events including a 28% rate of LVAD infection in 3 months, 42% rate of bleeding in 6 months, and a 35% rate of device failure in 24 months. Despite the increased rate of adverse events, the 27% absolute risk reduction in mortality at 1 year compared to medical therapy established LVADs as a new treatment option for advanced heart failure (Rose et al., 2001).

Similar to the REMATCH trial, the Investigation of Non-transplant Eligible Patients who are Inotrope Dependent (INTrEPID) trial assessed the impact of a different pulsatile pump, the Novacor LVAD, in end-stage HF patients who are inotrope-dependent and ineligible for transplant (Rogers et al., 2007). In a prospective, non-randomized clinical trial, the outcomes in 55 patients who received a Novacor LVAD (LVAD group) were compared to 18 patients who continued with optimal medical therapy (OMT group). The primary end-point was all-cause mortality at 6 months while secondary end-points consisted of adverse events, functional capacity, and health-related quality of life. At the end of follow-up, patients who received the Novacor LVAD had better survival at 6 months (46% vs 22%) and at 12 months (27% vs 11%) compared to OMT. There was a higher stroke rate in LVAD patients with 62% experiencing a CVA/TIA compared to 11% in the OMT group. Infection rates were similar in both treatment arms and there were no device failures requiring pump replacement during the trial. At last follow-up, 85% of patients who received an LVAD improved to NYHA FC I or II status while the OMT group did not experience any improvement in their functional capacity from baseline. These results confirmed the findings of the REMATCH trial published in 2001 that advanced
heart failure patients have a high mortality rate and that the use of LVADs confers a survival benefit with improved quality of life despite a higher adverse event risk profile (Rogers et al., 2007).

In spite of the results of the REMATCH and INTRePID trials, broader use of pulsatile LVADs was hindered by its large size, frequent adverse events, noisy operation, and limited durability. The second-generation HeartMate II LVAD was designed in the mid-2000s to overcome those issues. Design innovations made the HeartMate II smaller, quieter, and more durable by shifting from pulsatile to continuous flow and having only a single moving part. To assess the performance of this new LVAD design, a randomized, multi-center trial was conducted comparing outcomes using the pulsatile-flow HeartMate XVE LVAD versus the continuous-flow HeartMate II in patients with advanced heart failure ineligible for transplants (Slaughter et al., 2009). The trial prospectively randomized 200 patients in a 2:1 ratio to either the continuous-flow HeartMate II LVAD (134 patients) or the pulsatile-flow HeartMate XVE (66 patients). The primary end-point was survival free of disabling stroke or reoperation at 2 years, while secondary end-points consisted of actuarial survival, rate of adverse events, functional capacity, and quality of life at 2 years. At the end of 2 years of follow-up, more patients in the HeartMate II group achieved the primary end-point than in the HeartMate XVE group (46% vs 11%). One-year and 2-year actuarial survival was higher in the HeartMate II cohort at 68% and 58% respectively compared to 55% and 24% in the HeartMate XVE arm. While both groups equally had significant improvements in functional status and quality of life, patients who received a HeartMate II device had a lower rate of major adverse events (infections, right heart failure, respiratory and renal failure, cardiac arrhythmia) as well as a 38% relative risk reduction in re-hospitalizations (Slaughter et al., 2009).

Despite the survival benefits of HeartMate II, its use still led to a significant number of adverse events that lead to substantial morbidity and mortality. To address these issues, a newer centrifugal-flow LVAD called HeartWare was designed that utilizes magnetic and
hydrodynamic levitation of the motor eliminating the need for bearings. It has a smaller profile than the HeartMate II device allowing for intra-pericardial implantation. In 2017, a multi-center, randomized clinical trial was conducted involving 446 patients with advanced HF who were ineligible for transplant (Rogers et al., 2017). Patients were randomized in a 2:1 ratio to receive the new HeartWare study device (297 patients) or the HeartMate II LVAD control device (148 patients). The primary endpoint was 2-year survival free of disabling stroke or reoperation due to device malfunction. Secondary end-points included rate of major adverse events, overall survival, and changes in quality of life and health status. The findings showed that HeartWare was non-inferior to HeartMate II with regards to the primary end-point. However, there were significantly more strokes (29.7% vs 12.1%) in patients implanted with the HeartWare LVAD although more patients with HeartMate II required pump replacement for device malfunction or device failure. Overall mortality and improvements in quality of life and functional capacity were similar in both groups. Based on the results, HeartWare was found to be comparable and a viable alternative to the HeartMate II device that was currently in use at that time (Rogers et al., 2017).

Subjects enrolled in all of the LVAD clinical trials until the late 2010s consisted of inotrope-dependent advanced HF patients making it unclear if LVADs will be beneficial in a less sick population. Starling et al. (2017) evaluated the clinical outcome of LVADs compared to continued medical therapy in patients with ambulatory New York Heart Association Functional Class (NYHA FC) IIIB/IV symptoms not requiring inotropes. The ROADMAP trial was a prospective, nonrandomized two-year observational study of 93 patients who were implanted with the HeartMate II LVAD and 103 patients on optimal medical management (OMM). The primary endpoint was survival with an improvement in 6-minute walk distance of greater than or equal to 75 meters. Patients who received an LVAD were sicker at baseline compared to the OMM group with lower health-related quality of life and a lower 1-year predicted survival on the Seattle Heart Failure Model (SHFM). Despite being a sicker cohort, results showed more
patients in the LVAD group met the primary endpoint at 2 years (30% vs 12%) than in the OMM group. Actuarial survival at 2 years was higher in the LVAD group who also experienced greater improvement in their quality of life and functional status. At the end of the study, more patients in the LVAD group improved to NYHA FC I/II compared to OMM (69% vs 37%). However, those who received an LVAD were more likely to be readmitted due to adverse events, predominantly bleeding. Based on the results of the study, less sick patients benefitted from HeartMate II LVAD implantation with higher 2-year survival and quality of life but at the expense of more adverse events and higher hospitalization rate (Starling et al., 2017).

After the approval by the Food and Drug Administration (FDA) of the HeartMate II in 2009 for destination therapy in patients with advanced HF, more hospitals in the US started offering LVAD therapy. Although most implanting centers at that time were academic-based and had an existing heart transplant program, some community-based, non-transplant hospitals started offering LVADs. Brinkley et al. (2018) conducted a study to determine if any differences in outcomes in patients who had their device implanted at transplant centers compared to non-transplant programs. They analyzed patients from the Interagency Registry of Mechanical Assisted Circulatory Support (INTERMACS) database who received an LVAD from January 2012 to March 2014. INTERMACS is a registry of all durable ventricular assist devices implanted in the United States. Patients were categorized by implanting center as transplant (3,323 patients) or non-transplant (260 patients). Outcomes consisted of overall survival, rates of adverse events, re-hospitalizations, and health-related quality of life. At baseline, patients at non-transplant centers were less sick with more having normal hemodynamics and laboratory values. Their findings showed that even after adjusting for baseline differences, one-month (94.2% vs 94.2%) and 12-month survival (76.4% vs 71.3%) was similar between transplant and non-transplant programs. Risks of adverse events, re-hospitalizations as well as health-related quality of life were likewise similar (Brinkley et al., 2018).
The use of continuous-flow LVADs has been repeatedly shown to improve survival and quality of life compared to medical therapy but continued to be plagued by adverse events including device thrombosis, strokes, and bleeding. The third-generation HeartMate 3 device was developed in an effort to reduce those complications. Switching from an axial-flow to centrifugal-flow design innovations made the HeartMate 3 pump smaller to allow for intrapericardial implantation. A fully magnetically levitated rotor was incorporated that does not generate heat was incorporated into the design as well as wider passages that allow blood to pass with less hemolysis. A novel algorithm was utilized that causes the pump to transiently decrease then increase its speed every two seconds before going back to the set speed to reduce blood stasis. These modifications were designed to reduce pump thrombosis and strokes (Mehra et al., 2019).

Netuka et al. (2015) conducted a single-arm multi-center, prospective study to assess the safety and efficacy of the re-designed HeartMate 3 LVAD. Fifty patients with advanced heart failure who were implanted with HeartMate 3 were enrolled in 10 centers and followed for 6 months. Results showed an excellent 30-day survival of 98% and 6-month survival of 92%, which is better than the 88% 6-month survival rate of appropriately matched historical controls implanted with HeartMate II. In this small, short-term study, no device malfunctions, pump thrombosis, or hemolysis events were observed. This trial showed that the use of the HeartMate 3 device is safe and resulted in high short-term survival rates and a positive adverse event profile (Netuka et al., 2015).

As a follow-up to the study by Netuka et al. 2015, the Multi-center Study of Maglev Technology in Patients Undergoing Mechanical Circulatory Support Therapy with HeartMate 3 (MOMENTUM 3) trial was conducted to directly compare the use of the centrifugal-flow HeartMate 3 device versus the second-generation axial-flow HeartMate II in patients with advanced heart failure (Mehra et al., 2019). It was a larger study involving 69 sites in the US with longer follow-up and enrolled 1,028 patients with advanced HF who were followed for 2
years. Patients were randomly assigned in a 1:1 ratio to receive either the HeartMate II LVAD (512 patients) or HeartMate 3 (516 patients). The same primary end-point employed in prior LVAD studies was also utilized in this trial, which consisted of a composite of survival at 2 years free of disabling stroke or reoperation due to device malfunction. Secondary end-points consisted of pump replacement at 2 years, as well as actuarial survival, re-hospitalizations, functional status, and quality of life. Results showed that at the end of 2 years, even after adjusting for baseline differences, significantly more patients implanted with HeartMate 3 reached the primary end-point of survival free of disabling stroke or pump replacement compared to HeartMate II (76.9% vs 64.8%). Although overall survival was similar in both groups, those implanted with a HeartMate 3 required fewer re-operations for pump replacement at 2 years (2.3% vs. 11.3%). Pump thrombosis, bleeding, and stroke was also less frequent with the HeartMate 3. Improvements in NYHA FC, 6-minute walk distance, and quality of life as measured by the Kansas City Cardiomyopathy Questionnaire (KCCQ), the EuroQol-5D and EuroQol visual analog scale were similar in both groups (Mehra et al., 2019).

The use of aspirin combined with warfarin targeting a goal INR of 2.0-3.0 has been the mainstay of LVAD therapy to prevent pump thrombosis. Although effective, this strategy contributes to the increased frequency of bleeding, primarily from a gastrointestinal source, seen in these patients. The Minimal Anti-coagulation Evaluation to Augment Hemocompatibility (MAGENTUM 1) trial was to evaluate the safety and efficacy of a lower INR goal of 1.5-1.9 in reducing bleeding events without increasing thrombotic complications. In a single-center prospective trial, 15 consecutive patients implanted with HeartMate 3 LVAD were consecutively enrolled. Lower-intensity coagulation was implemented 6 weeks post-implant and patients were followed for at least 6 months. The primary end-point was survival free of pump thrombosis, disabling stroke, and major bleeding. Secondary end-points consisted of thrombotic and bleeding events. Patients with valve prosthesis, atrial fibrillation, or atrial flutter, and significant carotid artery stenosis were excluded. At 6 months, 93% of patients reached the
primary end-point. There were no observed thrombotic events and only one patient (7%) developed recurrent gastrointestinal bleeding. In this short-term, small pilot study, a lower intensity anticoagulation regimen targeting an INR goal of 1.5-1.9 was determined to be safe in reducing bleeding complications without an associated increase in thrombotic events. A large-scale trial is recommended to confirm these findings (Netuka et al., 2018).

The INTERMACS is a North American registry formed in 2005 as a joint effort between the FDA, Center for Medicaid and Medicare Services, and the National Heart, Lung and Blood Institute. It was designed to gather longitudinal clinical information on all patients implanted with any approved left ventricular assist device in the United States and Canada. It currently has 184 active sites and enrolled over 25,000 patients. Since its formation, it periodically releases reports on its cumulative data describing trends in patient demographics, device usage, adverse events, and survival outcomes. In its latest report published in 2020, it evaluated data from the 13,787 patients implanted from January 2014 to December 2018 with follow up through September 2019 (Teuteberg et al., 2020). Yearly implants have been steadily increasing since 2006 with 2,637 LVADs implanted in 2018. Implant volume decreased from 2015 to 2017 likely due to the 1,028 patients that participated in the MOMENTUM 3 trial being conducted at that time that was not included in the registry. Of the 2,603 assist devices implanted in 2014, 46.6% were destination therapy with 70.1% receiving the axial-flow HeartMate 2. This is in contrast to the 1,752 devices implanted from January 2019 to September 2019 where 97.9% were continuous-flow devices implanted as destination therapy in 70.2%. Overall one-month survival was 95%, one-year survival was 82% and 5-year survival was 47%. When evaluated by device type, one-year survival was significantly better in those patients who were implanted with the newer HeartMate 3 device compared to those who received either a HeartMate 2 or HeartWare (87% vs 82% vs 81%). This high one-year survival rate with HeartMate 3 is comparable to the one-year survival with heart transplantation (85%). The rate of adverse events including GI
bleed, stroke, and infections was lower with HeartMate 3 compared to other devices (Teuteberg et al., 2020).

Based on my analysis of all 10 articles arising from my literature search (see Appendix C), the use of LVADs in patients with advanced HF who are not candidates for transplant resulted in better outcomes compared to optimal medical therapy. In the REMATCH and INTrEPID trials, maximal medical therapy confers a one-year survival rate of 11 to 23%. This is in contrast to the 87% one-year survival offered by the latest generation HeartMate 3 LVAD while significantly improving functional capacity and quality of life. While short-term LVAD survival currently approximates that of a heart transplant, with continued innovations, LVADs may someday supplant heart transplant as the gold standard therapy for advanced heart failure.

Device implants have risen over the years with over 2,600 devices placed in 2018. Previously confined to large academic transplant centers, community-based, non-transplant programs have begun offering LVADs due to their tremendous benefit with outcomes similar to larger institutions. Given that there are currently around 250,000 people with advanced heart failure who could potentially benefit from an assist device, there will be a need for more LVAD programs throughout the country to meet their needs.

**Theoretical Framework**

For my DNP project, I created a comprehensive guidebook that outlines the various steps needed for an institution to establish and maintain a successful LVAD program. The role of durable LVADs in the management of advanced HF has been growing over the past 20 years. These devices were implanted and managed primarily at large academic centers due to their complexity. However, as the next-generation devices became smaller and more patient-friendly combined with accumulated experience in device management, a growing number of community-based, non-transplant hospitals are planning to establish LVAD programs to serve their communities.
The theoretical framework that I utilized for this project is the Ottawa Model of Research Use (OMRU). This model identified the steps and processes necessary to introduce an innovation such as LVADs to an institution. This model was initially created by Logan and K. Graham in 1998 and revised in 2004 (White et al., 2021). The OMRU describes the three stages and six fundamentals essential for translating research into practice (see Appendix A). The three stages consist of (1) assessing barriers and support, (2) monitoring intervention and degree of use, and (3) evaluating outcomes (White et al., 2021). The first stage identifies the existing support and anticipated obstacles to introducing innovations and consists of three elements: evidence-based innovation, potential adopters, and the practice environment. The second stage evaluates the transfer and utilization of new knowledge and is comprised of two elements, implementation intervention strategies, and adoption. The last stage consists of a single element, outcomes, which evaluates the effects of the intervention on patients, practitioners, and the entire program (White et al., 2021).

The introduction of a new evidence based innovation involves numerous steps. During the initial phase of the OMRU, I described the design and functionality of LVADs and introduced the clinical evidence supporting their use in advanced HF. I outlined ways to engage potential adopters such as hospital managers, cardiologists, cardiac surgeons, and nurses and addressed their concerns or gaps in knowledge. Lastly, I explained how LVADs improve quality of life, functional capacity, and survival of advanced HF patients and how it positively affects healthcare finances by reducing recurrent heart failure admissions.

During the second phase of OMRU, I sketched the steps in creating policies and protocols on patient selection and evaluation to ensure appropriate device use. I explained the process for purchasing the device and its components from the vendor as well as appropriate equipment inspection and maintenance. I provided training schedules for various providers and staff members so they can be proficient in device use and patient management. Finally, once all elements are in place, I shared the steps required to schedule, prepare for, and undergo a
successful initial LVAD program survey and obtain Centers for Medicare & Medicaid Services (CMS) certification as required by various health insurers.

The final stage of the OMRU model emphasizes evaluating outcomes from the perspective of the patients, medical providers, and hospital administrators. This stage is vital in determining if the innovation is generating the projected outcome or is causing any inadvertent consequences. I outlined how patient satisfaction is determined through health questionnaires before and after LVAD and how functional capacity is measured objectively via a six-minute walk test. I discussed ways to assess and incorporate provider feedback through regular reviews of processes and procedures to ensure efficiency. Lastly, I described methods of tracking patient survival, length of stay, readmission rates, and complications that influence program outcomes. Tracking relevant metrics allows a program to institute a robust quality assurance and performance improvement process to identify and address any deficiencies ensuring a high-quality LVAD program.

In summary, I utilized OMRU for this DNP project as illustrated in Appendix B. It had all the fundamentals I needed to create a framework outlining the steps necessary to establish and maintain a successful LVAD program. Hopefully, by sharing my experience, my project will be useful to other institutions who are contemplating starting an LVAD program.

**Methodology**

**Overview**

The purpose of my DNP project was to create a guidebook containing all the necessary steps to establish a left ventricular assist device program that complies with CMS guidelines. As this was a program development and evaluation project, it did not follow the structure of a traditional DNP project.

**Design**

**Setting**
The setting for this project is any hospital or community medical center that is contemplating starting an LVAD program.

Population

The population I focused on are advanced heart failure (HF) patients.

Guidebook

The guidebook included various chapters discussing the steps needed to establish a new LVAD program from the planning to implementation stage including CMS accreditation. All of the information are evidence-based and derived from expert consensus and medical society guidelines (Givertz et al., 2019; Mehra et al., 2019; Slaughter et al., 2009), Heartmate instructions for use (Thoratec corporation, 2017), and CMS regulatory guidelines (Centers for Medicare & Medicaid Services [CMS], 2020).

Guidebook chapter overview

Chapter 1: Do you need an LVAD program in your community?
- Discussed need to evaluate catchment area demographics and health needs to see if establishing an LVAD program is appropriate and feasible
- Described benefits and challenges having an LVAD program poses to an institution

Chapter 2: Enlisting administrative support
- Underlined importance of identifying people that can serve as program champions
- Emphasized need for a business proposal detailing benefits a local LVAD program will provide to patients and its impact on the hospital’s long-term economic goals

Chapter 3: Performing a Gap analysis
- Reviewed CMS requirements for an LVAD program (mandated team composition, competencies, experience, infrastructure, equipment) and the need to fill any gaps

Chapter 4: The CMS Certification Process
- Listed the minimum requirements necessary for program certification
• Described the differences in the inspection process between the two CMS-contracted certifying bodies – The Joint Commission (TJC) and Det Norske Veritas-Germanischer Lloyd (DNV-GL)

Chapter 5: Patient Selection and Management

• Highlighted importance of having a multidisciplinary LVAD team that includes cardiologists, surgeons, social worker, and palliative care specialists to evaluate patient candidacy for LVAD implant

• Discussed need for standardized criteria for patient selection and protocols for pre- and post-operative management

Chapter 6: Policies and procedures

• Explained how to formulate program policies and procedures and clinical practice guidelines for perioperative and long-term management of LVAD patients

Chapter 7: Equipment purchase and inventory management

• Reviewed need to coordinate with hospital finance administrators on setting budget for initial equipment purchase and refurbishment

• Shared algorithm for LVAD pump and ancillary equipment (batteries, chargers, monitors, controllers, cables) purchase, inventory and maintenance in coordination with the biomedical department

Chapter 8: Training requirements

• Listed the minimum LVAD training requirements for medical staff, nursing, perfusionists, coordinators, surgeons, and cardiologists, commensurate to the degree of their involvement with LVAD care

Chapter 9: Quality Assurance and Performance Improvement metrics

• Discussed the need for a robust program performance improvement program to ensure good outcomes and determine opportunities for improvement
• Stressed adoption of a performance improvement model to address any program weaknesses

**Chapter 10: How to maintain a successful and profitable LVAD program**

• Enumerated various ways to promote a new LVAD program and create a steady referral stream

• Emphasized importance of proper coding and billing to obtain the appropriate reimbursements for implants and have a sustainable program

Included in the appendix are the following:

1. Sample of LVAD consent
2. Home safety checklist
3. Patient education flowsheet
4. Validation of LVAD training form
5. LVAD equipment checklist at discharge
6. Letter for emergency services
7. Written test for patient and caregiver
8. Table of required clinical practice guidelines and samples
9. Sample of patient satisfaction survey
10. LVAD order set example

**Results**

All the steps outlined in the guidebook from planning to implementation were derived from my experience in establishing an LVAD program at our institution in less than 6 months. Our program passed the initial CMS survey without any non-conformities and implanted 12 patients in the first year. To ensure accuracy, completeness, and applicability to other institutions, I had the guidebook reviewed by a clinical expert from the device company and received excellent feedback. The suggestions were incorporated into the final manuscript. The guidebook was also shared with a RN LVAD coordinator in Georgia who used this book as a
resource tool. She found it to be extremely useful in establishing an LVAD program at her institution and getting CMS certification.

**Discussion/ Implications**

Use of the guidebook will help any nurse practitioner or provider who has limited experience in LVADs be able to establish a new LVAD program in any institution. It outlines all the necessary steps to create an LVAD team, develop clinical practice guidelines and polices, and meet all the requirements for CMS certification. This guidebook could be used as a template for program- building for novice leaders in the field of heart failure.

**Dissemination**

The contents of the guidebook will be disseminated via the final project paper, poster, and oral presentation and stored in the Rutgers University community electronic repository. The guidebook could be published as a journal article and/or be made available for viewing on medical websites and could be used for future doctorate level students to evaluate and implement.

**Plans for Future Scholarship**

This guidebook provides opportunities for future project implementation. Prospective DNP students interested in education, training, policy implementation, or quality assurance projects could take any one section of this guidebook and conduct independent projects. They can also update the entire guidebook or certain chapters periodically as LVAD technology advances and practice guidelines change due to ongoing research.

**Conclusion**

Heart failure prevalence is rising and as the technology evolves, LVAD utilization is expanding owing to improved patient survival and quality of life. More programs are needed that can implant and care for these patients due to growing demand. However, there is very little information available on how to establish an LVAD program. It is vital to have a resource tool to help institutions build and sustain excellent device programs. This program development and
evaluation project is unique because it involved creation of a guidebook that details the various processes necessary to put together an LVAD program. This information is derived from my extensive clinical experience managing LVAD patients and is written from the perspective of an advanced practice nurse. It will be a valuable resource for a novice LVAD coordinator or nurse practitioner.
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https://doi.org/10.1161/CIR.0000000000000757

Appendix A

Ottawa Model of Research Use

Appendix B

Implementation of Ottawa Model of Research Use in this DNP Project

### Table of Evidence Grid

<table>
<thead>
<tr>
<th>Article #</th>
<th>Author &amp; Date</th>
<th>Evidence Type</th>
<th>Sample, Sample Size &amp; Setting</th>
<th>Study findings that help answer the EBP question</th>
<th>Limitations</th>
<th>Evidence Level &amp; Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Rose et al. (2001)</td>
<td>Prospective multi-center randomized control trial (REMATCH trial)</td>
<td>129 end-stage HF pts LVEF &lt; 25% were assigned randomly to either LVAD HeartMate XVE (68 pts) or OMT (61 pts)</td>
<td>Pts who received device therapy had a 48% reduction in mortality in 2 years vs. the OMT group</td>
<td>Not possible to blind pts and investigators to treatment assignment which could lead to bias</td>
<td>Level of evidence II – randomized, multi-center clinical trial of good quality</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Comparison of optimal medical therapy (OMT) to HeartMate XVE LVAD</td>
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<td>2</td>
<td>Rogers et al. (2007)</td>
<td>Prospective non-randomized clinical trial (INTrEPID trial)</td>
<td>81 patients were screened, and 55 patients were enrolled. 37 patients to LVAD and 18 to OMT</td>
<td>Patient treated with LVAD had better survival at 6 months 946% vs. 22% p=0.03) and 12 months (27% vs.11%; p =0.02). OMT noted to have higher adverse events</td>
<td>Potential institutional or investigator bias contributing to patients a choice to continue medical therapy rather than receive an LVAD due to the study design</td>
<td>Level of evidence III - non-randomized trial (quasi-experimental) – moderate quality</td>
</tr>
</tbody>
</table>
| 3 | Slaughter et al. (2009) | Prospective multi-center randomized control trial  
Comparison of HM XVE to HM II | 200 pts with end-stage HF LVEF < 25% refractory to OMT randomized 2:1 ratio to continuous-flow LVAD HM II (134 pts) vs pulsatile-flow LVAD HM XVE (66 pts)  
The primary end-point was composite of survival at 2 yrs., free of disabling stroke or reoperation to replace pump; secondary end-points were actuarial survival, frequency of adverse events, functional status, and quality of life. | More pts in the HM II group achieved the primary end-point than those who received HM XVE (46% vs. 11%, HR 0.38, 95% CI 0.27-0.54, p < 0.001)  
For secondary end-points, actuarial survival at 2 yrs. was better for HM II vs HM XVE (58% vs. 24%, p = 0.008).  
The rate of re-hospitalization was 38% lower in the HM II group while functional status and quality of life metrics improved | Potential bias as not possible to blind pts and investigator’s to treatment assignment  
Some sites had limited experience implanting and managing HM II devices which could impact outcomes  
Applicability to less sick population unknown | Level of evidence II – randomized clinical trial, multi-center study – good quality |
<table>
<thead>
<tr>
<th></th>
<th>Rogers et al. (2017)</th>
<th>Prospective multi-center randomized clinical trial of HeartWare HVAD (study device) to HM II (control device) to test for non-inferiority.</th>
<th>446 pts with NYHA FC IIIB-IV despite OMT, LVEF &lt; 25% randomly assigned in 2:1 ratio to either HeartWare HVAD or HM II. The primary end-point was a composite of 2-yr survival free from disabling stroke with the original device in place or explanted due to heart transplant or LV recovery. Secondary endpoints include incidence of major adverse events, overall survival, change in the quality of life measures, and change in 6-minute walk distance.</th>
<th>The study device was non-inferior to the control device. The primary endpoint was not statistically different in the study device group vs. control device group (55% vs. 57.4%, p = 0.67). More pts in the study device group had strokes (ischemic or hemorrhagic) vs. the control device group (29.7% vs. 12.1%, p &lt; 0.001). Overall mortality, improvement in the quality of life measures, and 6-minute walk distance were similar in both groups.</th>
<th>Not able to blind pts and investigators to treatment assignment potentially leading to bias. Anticoagulation management was left to investigators. Did not address device durability beyond 2 years.</th>
<th>Level of evidence II – randomized clinical trial, multi-center study- good quality.</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>Starling et al. (2017)</td>
<td>Prospective non-randomized observational study</td>
<td>200 pts with ambulatory NYHA FC IIIB/IV symptoms were enrolled.</td>
<td>At 2 yrs., more pts in the LVAD group were alive with improvement in 6MWD &gt;</td>
<td>The study was observational and non-randomized</td>
<td>Level of evidence IV – a well-designed cohort study- moderate quality.</td>
</tr>
<tr>
<td></td>
<td>Brinkley et al. (2018)</td>
<td>Retrospective cohort observational study</td>
<td>Comparison of patients’ outcomes after continuous low-LVAD as DT at a transplant center vs. nontransplant centers.</td>
<td>Patients implanted with continuous-flow LVAD as DT between January 2012 and March 2014 from INTERMACS were included. Implanting centers were categorized as transplant and non-transplant centers. 3583 patients with continuous-flow LVAD were enrolled. 260 at nontransplant centers and 3323 at transplant centers.</td>
<td>The nontransplant center had less sick patients with higher INTERMACS profiles and normal lab and hemodynamic a value. The study showed both transplant centers and non-transplant centers showed similar primary and secondary endpoints and there was no difference in Biased lesser sick patient selection by non-transplant centers. Missing data was high in the secondary outcome for HRQL and few pre-implant variables.</td>
<td>Biased lesser sick patient selection by non-transplant centers. Missing data was high in the secondary outcome for HRQL and few pre-implant variables.</td>
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</table>
The primary outcome was patent survival, censored at device explant for recovery or transplant.

Secondary outcomes included freedom from death or major adverse events, individual adverse event rates, hospitalization, and health-related QoL (HRQL) assessed at 6 months.

<table>
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<th></th>
<th>Netuka et al. (2015)</th>
<th>Prospective multicenter nonblinded nonrandomized trial</th>
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<tr>
<td>7</td>
<td>To evaluate the performance and safety of fully magnetically levitated LVAD in a patient with advanced HF</td>
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<tr>
<td></td>
<td>50 patients were enrolled at 10 centers in different countries with ejection fraction less than or equal to 25%, cardiac index less than or equal to 2.2 l/min/m² without inotropes, or were inotropic dependent on OMT or listed for transplant. Written informed consent was required from all participants.</td>
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<tr>
<td></td>
<td>The primary endpoint was survival at 6 months</td>
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<tr>
<td></td>
<td>Fully magnetically levitated centrifugal-flow chronic LVAD noted to be safe with 98% survival at 30 days, 92% 6-month survival vs 88% performance goal.</td>
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</tbody>
</table>

Lack of randomization and controls. The study included all patients meeting the standards for advanced HF and without demarcation by indication (BTT or DT).

Level of evidence III- The quality of the study was moderate.
months with a performance goal obtained from Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS).

Secondary study end-point compared 6 months predicted survival using the Seattle Heart Failure Model (SHFM), European Quality of Life Questionnaire 5 level (EQ-5D), functional status, adverse event rates, and occurrence of the device malfunction, reoperation, rehospitalization, and survival free of a devastating stroke.

<table>
<thead>
<tr>
<th>Year</th>
<th>Study</th>
<th>Design</th>
<th>Patients</th>
<th>Primary Outcome</th>
<th>Secondary Outcomes</th>
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<tbody>
<tr>
<td>2019</td>
<td>Mehra et al.</td>
<td>Prospective multi-center randomized control trial (MOMENTUM 3)</td>
<td>1,028 pts with end-stage HF were randomized 1:1 ratio to either HM II (512 pts) or HM 3 LVAD (516 pts)</td>
<td>The primary end-point was a composite of survival free of disabling stroke</td>
<td>At 2 yrs., more pts on HM 3 met the primary end-point than pts on HM II (76.9 vs. 64.8%, RR 0.84, p&lt; 0.001). Pump replacement at 2 yrs. was</td>
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<td>Comparison of HM II axial-flow LVAD to HM 3 centrifugal-flow LVAD</td>
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<td>Non-blinded Variations in pt. management depending on the center practice</td>
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<td>Level of evidence II–randomized clinical trial, multi-center study- good quality</td>
</tr>
</tbody>
</table>
or device replacement at 2 years
Secondary endpoints were pump replacement at 2 yrs., actuarial survival, rehospitalization, functional status, and quality of life (QoL).

| 9 | Netuka et al.(2018) | A prospective, single-center cohort study. (MAGENTUM 1 trial)
A study performed to evaluate the safety and probability of a low-intensity anticoagulation protocol in HeartMate 3 patients |
|---|---|---|
15 patients enrolled irrespective of the intended goal of therapy between November 20, 2016, and September 4, 2017
The primary outcome was survival free pump thrombosis, disabling stroke, and major bleeding at 6 months
The secondary endpoint was to evaluate adverse events in the hemocompatibility domain (thrombosis and bleeding).

less in the HM 3 group vs. HM II (2.3% vs. 11.3%, RR 0.21, p<0.001)
No difference in overall survival, functional status, or quality of life measures between the two groups

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A single-center study, small sample size, closer monitoring required
Level of evidence- IV
Study quality is moderate.
| 10 | Teuteberg et al. (2020) | Retrospective multicenter cohort observational study | Adults from age 19 yrs. with a durable implant from Jan 2014 to December 2018 was followed till September 30th, 2019. 13,016 patients were isolated and were used to compare baseline patient characteristics over time, survival, freedom from major adverse events, and cumulative hospitalizations. The study showed that patients receiving implant during 2017-2018 were sicker than compared to 2014-2016 implants (17.1% vs 14.3%, P less than .001) and had pre-implant temporary mechanical circulatory support (34.8% vs 29.3%, P less than .001) CF-LVAD was noted to become a more dominant technology over the past 5 years. Also noted to have lesser adverse events and better survival. | During the period of comparison, the patient who was not BTT did not receive either CF-HL or CF-FML so there was a potential bias in patients undergoing these implants. CF-FML was only approved initially for BTT whereas CF-HL was indicated for both BTT and DT. There could be also variation in baseline characteristic, the center bias in device selection which may have affected the result. | Level of evidence III The quality of the study is good |
Appendix E

Letter of Cooperation

Date: 11/10/2020

Re: Letter of Cooperation for

Dear [Name],

This letter confirms that I, as an authorized representative of [Organization Name], allow the PI access to conduct study related activities at the listed site(s), as discussed with the PI and briefly outlined below, and which may commence when the PI provides evidence of IRB approval for the proposed project.

- **Research Site(s):** [Redacted]
- **Study Purpose:** The purpose of the DNP project is to create a guidebook for establishing a successful left ventricular assist device program.
- **Study Activities:** The study doesn’t involve any site employee interview or intervention, however may access the quality assurance and performance improvement of left ventricular assist device program with no patient identifiers.
- **Subject Enrollment:** No subject enrollment required.
- **Site(s) Support:** Provide access to get quality assurance data required for the project with no patient identifiers.
- **Data Management:** No direct patient data would be collected.
- **Other:** n/a
- **Anticipated End Date:** 8/30/2021

We understand that this site’s participation will only take place during the study’s active IRB approval period. All study related activities must cease if IRB approval expires or is suspended. I understand that any activities involving Personal Private Information or Protected Health Information may require compliance with HIPAA Laws and Rutgers Policy.

Our organization agrees to the terms and conditions stated above. If we have any concerns related to this project, we will contact the PI. For concerns regarding IRB policy or human subject welfare, we may also contact the Rutgers IRB (see [website]).

Regards,

[Signature]

Date Signed: 11/10/2020

[Full Name]

[Job Title]
Appendix F

DETERMINATION OF NON-HUMAN SUBJECT RESEARCH

November 16, 2020

To:       Dreamy James
From:     Research Integrity Office
Re:       Research Project Determination Letter

Title:   Guidebook for establishing a successful left ventricular assist program

Thank you for your submission to the Research Integrity Office. Upon review of the materials provided, it has been determined that your proposal, as submitted, does not meet the definition of research involving human subjects as defined by DHHS and FDA regulations. Therefore, review and approval by the Institutional Review Board (IRB) is not required. This determination applies only to the activities described in the Human Subjects Research Determination Worksheet and may not apply should any changes to the activities be made.

If you desire to make changes to the design of your proposal, you should re-submit the amended proposal to the IRB to ensure that the changes do not change the nature of the project in such a way that would require IRB review and approval.

If you have any questions, comments, complaints or concerns or wish to provide input, please do not hesitate to contact the Research Integrity Office at [email protected] or by email at [email protected]

Sincerely,