Fall 11-17-2023

LVAD Therapy Versus Medical Management in Heart Failure: An Integrative Review

Megan Cherry
mcherr11@students.kennesaw.edu

Sandi Coker
scoker14@students.kennesaw.edu

LVAD Therapy Versus Medical Management in Heart Failure: An Integrative Review

Megan S. Cherry and Sandi L. Coker

Wellstar School of Nursing, Kennesaw State University

Abstract

Background: Advancements in technology have increased management options for heart failure (HF) patients. Options include guideline-directed medical therapy (GDMT), left ventricular assist device (LVAD) therapy, and/or heart transplant. Due to resource allocations, the most accessible options for many HF patients include GDMT and LVAD therapy. Authors of this integrative review (IR) sought to examine quality of life (QOL) and hospitalization rate outcomes among patients receiving GDMT versus LVAD therapy. **Methods:** 417 articles were screened across multiple databases (CINAHL, Medline, ProQuest, Ovid, PubMed) for inclusion into the integrative review based on inclusion criteria: published within five years, peer-reviewed, written in English, considered adults ages ≥ 18, and considered patients with NYHA HF classification stages III-IV. In total, 13 articles were appraised and thematically analyzed. **Results:** IR findings were presented according to identified themes. Results showed that LVAD therapy poses unique risks: social limitations, higher risk for adverse events, and higher hospitalization rates. Results demonstrated that both GDMT and LVAD therapy improve the following outcome measures in HF patients: survivability, QOL, and functional capacity. It was noted among articles discussing GDMT that combination GDMT has superior outcomes when compared to solo GDMT. Limited research was available that *directly* compared GDMT and LVAD outcomes. Limited research was available surrounding GDMT outcomes. **Conclusions:** While effective, LVAD therapy for HF patients incurs greater complication risk when compared to GDMT. Both therapy options improve QOL, functional capacity, and survivability among HF patients. More research is warranted regarding direct comparisons between LVAD and GDMT outcomes.

Keywords: heart failure, LVAD, guideline-directed medical therapy, quality of life, outcomes

LVAD Therapy Versus Medical Management in Heart Failure: An Integrative Review

Heart failure (HF) is a condition that results when the heart cannot effectively distribute oxygen-rich blood to supply the body's metabolic demands. The consequences of HF can be costly, including increased medical costs, decreased functional capacity, and even death. The incidence of HF is on the rise globally. According to Zimpfer et al. (2020), nearly one million cases of new-onset HF are diagnosed annually. Additionally, more than six million people are living with HF in the United States (Burch et al., 2021). Fortunately, HF is a manageable condition. Patients with HF are classified into four groups by the New York Heart Association (NYHA) according to degree of symptoms. Classes of HF range from class I (no symptoms and no physical limitations) to class IV (symptoms at rest and severe activity limitation). Management options for HF depend on NYHA classification and may include guideline-directed medical therapy (GDMT), left ventricular assist device (LVAD) implant, and/or heart transplant. Current GDMT consists of serial titration of medications to achieve symptom relief (Turgeon et al., 2021). LVAD management involves either destination therapy or bridge-to-transplant therapy (McNamara et al., 2021). Though curative, heart transplant requires the coordination of qualified donors and qualified recipients within a limited timeframe for organ viability. Due to the shortage of viable donor hearts and the growing list of qualified recipients, GDMT and LVAD implant are the most accessible management options for most HF patients.

Background & Purpose

HF management options are worthy of consideration, as new cases of HF are expected to increase as the global population ages (McNamara et al., 2021). In the setting of rising HF diagnoses, further research is warranted regarding the best management approaches. Medical

management of HF involves taking oral or intravenous medications to prevent worsening HF and to maintain adequate organ perfusion. LVAD therapy involves the surgical placement of a mechanical device into the heart that is powered by external battery power. Both options pose the risk of complications. Despite adherence, some medically-managed patients develop refractory HF that fails to respond to prescribed medications. Patients who receive LVAD implants may experience bleeding, stroke, and infection (Zimpfer et al., 2020). There is a plethora of research available that explores physiological outcomes of different HF management strategies. However, a gap exists in current literature regarding direct comparisons among patients who receive GDMT and patients who receive LVAD implant. Specifically, little information is available that compares quality of life (QOL) outcomes and hospitalization rates among both GDMT and LVAD recipients.

This integrative review is being performed to compare QOL measures and hospitalization rates across two HF management options: LVAD therapy and GDMT. Ultimately, the aim of the review is to determine the safest approach to HF management. For the purpose of this review, "safe" is defined as a HF management option that results in greater functional capacity, improved QOL, and fewer hospitalizations. To guide the review, the following PICO question was devised: in adult patients with NYHA class III or IV HF, how does the presence of a LVAD compared to GDMT influence hospitalization rates and QOL?

Methods

In performing the literature search, multiple databases were explored, including CINAHL, Medline, ProQuest, Ovid, and PubMed. Toronto and Remington (2020) recommend utilizing a variety of databases to formulate a more comprehensive review. Database exploration occurred between March and June of 2023. Within databases, Boolean phrases, truncation,

parentheses, and quotation marks were paired with the following search terms: "LVAD," "guideline-directed medical therapy for heart failure," "hospitalization rates," "cardiomyopathy," "outcomes," and "quality of life." The following limits were applied to searches: published within the last five years, scholarly (peer-reviewed) articles, and articles written in English.

Inclusion and Exclusion Criteria

Articles were selected for review based on the following criteria: published within the last five years and peer-reviewed, studied adult patients with HF, studied patients with NYHA classification of III or IV, and published in the English language. Data were restricted to recent publication so that the most current and relevant data could be examined. No geographical limitations were applied in an attempt to widen search results.

Articles were excluded from review based on the following criteria: studied populations under age 18, published before 2018, not published in the English language, and studied populations with NYHA HF classification of I or II.

Screening

Once the search was completed, screening of the articles' abstracts was performed to see if they aligned with researchers' search criteria. If the selected article met inclusion criteria, the article was analyzed in its entirety. In total, 21,072 articles were generated from published literature searches, reference searches, and websites. Of the 21,072 articles, 20,641 were removed before screening due to irrelevance and redundancy. Four hundred seventeen articles were selected for screening in researchers' integrative review based solely on applicable title and abstract. Ultimately, 96 articles were assessed for eligibility and 13 were included in the integrative review. Researchers' search process was tracked and outlined according to a PRISMA flow document to ensure repeatability (see Appendix A). Articles were excluded for the

following reasons: studied pediatric populations, studied patients with NYHA class I and II heart failure, required money or subscription for access to full-text articles, considered heart transplant, compared different types of LVADs, evaluated co-morbid conditions, and explored outcomes other than QOL and hospitalization rates. Types of research articles selected for the integrative review included retrospective observational studies, systematic reviews, literature reviews, descriptive studies, and mixed-method studies.

Data Evaluation & Analysis

Data from relevant articles were placed into a comprehensive data matrix that included the following: author, year of publication, study design, aim of study, method overview, data collection, results, level of evidence, sub-themes identified, and critical appraisal points (see Appendix B). Researchers' comprehensive data matrix was housed as a Google spreadsheet to which researchers had joint, real-time access. This allowed for effective partner work and for researchers to see shared contributions to the integrative review process. Access to selected articles was housed within RefWorks, which served as researchers' citation management system. Quality of evidence was rated according to Melnyk and Fineout-Overholt's (2023) "Level of Evidence Hierarchy" that was specific to interventional and prognostic PICOT questions (see Appendix C). Critical appraisal tools were adapted from University of Oxford (2021).

Thematic analysis was researchers' method of choice for data analysis. According to Braun and Clarke (2006), thematic analysis consists of a “recursive” six step process that includes familiarizing with data, generating initial codes, searching for themes, reviewing themes, defining and naming themes, and producing a report. Toronto and Remington (2020) report that thematic analysis allows researchers to identify repeated patterns across multiple sources of published data to help answer a review question. Thematic analysis was performed

independently by researchers at first. Later, the two researchers came together to discuss perceived sub-themes to review, define, and name the overall themes for the integrative review. Coding and identified themes were placed into a table for overview (see Appendix D).

Thematic analysis generated 10 sub-themes, which were further categorized into three, broad themes: LVAD therapy poses unique risks, LVAD therapy improves health outcomes, and GDMT improves health outcomes (see appendix D). While thematic analysis helped researchers identify broad research findings, the specific research question was not clearly answered. Research revealed that both LVAD therapy and GDMT improve health outcomes in HF patients. However, direct comparisons between the two groups were not able to be drawn due to a lack of existing evidence that directly compared outcomes across the two HF management strategies.

Presentation of Findings

This integrative review was performed to determine the comparative impact of LVAD therapy and GDMT on QOL and hospitalization rates among HF patients. Sub-themes and overall themes identified from thematic analysis helped researchers recognize the need for further research to fully answer the proposed research question. Research findings are presented according to identified themes and subthemes.

LVAD Therapy Poses Unique Risks for HF Patients

Literature revealed that LVAD therapy poses unique risks for HF patients, including increased social burden, increased physiologic complications, and increased hospitalization risk. These sub-themes are demonstrated in Appendix D. These risks are unique to patients receiving LVAD therapy, as LVAD therapy is more invasive than GDMT alone.

LVAD Implant Has Poor Social Implications

Social risks of LVAD therapy include increased reliance, need for a qualified caregiver,

disturbed work and leisure activities, and lack of independence (Carroll et al., 2022; Suzuki et al., 2022). Findings reported by Suzuki et al. (2022) suggest that patients receiving LVAD therapy experience limited participation in social activities. Additionally, Suzuki et al. (2022) report that patients receiving LVAD therapy experience changes to roles, interpersonal relationships, and suffer from a lack of control and independence in their lives. The study performed by Carroll et al. (2022) suggests that patients with LVADs have moderate limitations in their activities of daily living and have an increased need for a caregiver to assist with daily dressing changes and device malfunctions. Overall, it was demonstrated by research findings that LVAD patients suffer disproportionate social consequences when compared to patients receiving GDMT for HF management (Carroll et al., 2022; Suzuki et al., 2022).

LVAD Therapy Poses Greater Risk for Adverse Physiologic Events

Complications of LVAD therapy represented in the literature include bleeding (33%), neurologic events (17%), device-related infections (57%), hemodynamic compromise (25%), thromboembolic events (2%), and development of right-sided HF (15%) (McNamara et al., 2021; Shah et al., 2018; Weber et al., 2022; Zimpfer et al., 2020). These adverse events relate to pump-related damage to blood components and mechanical pump design, such as artificial pulses (Zimpfer et al., 2020). Additionally, in an article that directly compared LVAD therapy outcomes to GDMT outcomes, it was reported that adverse events were more common in patients receiving LVAD therapy (Shah et al., 2018). These findings highlight physiologic challenges that are unique to LVAD therapy.

Rehospitalization Risk is High in Patients Receiving LVAD Therapy

Collectively, the unique risks of poor social implications and adverse physiologic events increase hospitalization rates among LVAD patients, especially for rural LVAD recipients who

also face limited access to healthcare services (Alonso et al., 2020). This finding is represented well in a study performed by Zimpfer et al. (2020). In the study, 540 LVAD patients were followed for two years, after which only 30.9% of participants were free from rehospitalization (Zimpfer et al., 2020). Additionally, a research study performed by Shah et al. (2018) demonstrated that patients receiving LVAD therapy experience higher rehospitalization rates (28 out of 30 participants; 93%) when compared to patients receiving GDMT (47 out of 66 participants; 71%) within two years of initiating their respective therapies.

LVAD Therapy Improves Health Outcomes in HF Patients

Despite the unique risks posed by LVAD therapy, the benefits of having mechanical circulatory support consistently outweighed the social and physiologic risks in literature results. Weber et al. (2022) reported that QOL and functional metrics improved in LVAD patients, despite adverse events. Thematic analysis revealed the following sub-themes that categorize improvements for specific outcome measures: LVAD therapy improves survivability, QOL, and functional capacity in HF patients.

LVAD Therapy Improves Survivability Among HF Patients

A study performed by Turgeon et al. (2021) demonstrated a survival rating of 83% following LVAD implant. Similar findings were reported by McNamara et al. (2021), which showed that short-term survival ratings for LVAD patients are similar to those seen among heart transplant patients. Furthermore, McNamara et al. (2021) concluded that LVAD recipients demonstrated improved NYHA functional class six months after implant. These findings illustrate that LVAD therapy increases survival.

LVAD Therapy Improves QOL Among HF Patients

Not only were improvements in survivability evident in the literature, but sustained

improvements in QOL were also noted following LVAD implant (Suzuki et al., 2022; Zimpfer et al., 2020; McNamara et al., 2021; Thiha et al., 2019; Shah et al., 2018; Alonso et al., 2020; Weber et al., 2022). Thiha et al. (2019) reported that EQ-5D QOL scores improved from 19 to 28 when compared to pre-implant results reported by study participants. Researchers deduced that improvements in QOL following LVAD implant may result from the improved functional capacity that is also reported among LVAD recipients.

LVAD Therapy Improves Functional Capacity Among HF Patients

When compared to pre-implant scores, LVAD patients demonstrated increased exercise stamina and higher physical activity levels (Suzuki et al., 2022). LVAD patients also demonstrated improved six-minute walk test scores after implant (Zimpfer et al., 2020; McNamara et al., 2021; Thiha et al., 2019; Shah et al., 2019). Literature findings were consistent that LVAD therapy changes the lives of HF patients according to prolonged survival, improved QOL reports, and improved functional performance.

GDMT Improves Health Outcomes in HF Patients

Literature was limited regarding QOL measures and hospitalization rates in HF patients receiving GDMT. Of the 13 articles included in the integrative review, five articles explored GDMT in relation to QOL and hospitalization rates for HF patients. The following sub-themes were identified from the available literature: GDMT improves QOL reports, GDMT serves to improve the functional abilities of HF patients, and combination GDMT correlates with improved health outcomes. It was made clear to researchers from literature results that GDMT improves the lives of HF patients.

GDMT Improves QOL and Functional Capacity Among HF Patients

Moloce et al. (2022) reported that GDMT serves to improve QOL, decrease symptom

burden, and improve functional ability of HF patients. Additionally, Turgeon et al. (2021) reported that GDMT serves to decrease hospitalization rates in HF patients and that GDMT has been shown to improve survival. Literature demonstrated that pharmacotherapy for HF improves patient-reported QOL and reduces the risk of rehospitalization (Burch et al., 2021).

Combination GDMT Leads to Improved Health Outcomes Among HF Patients

GDMT improves survivability and QOL, and research revealed that improvements correlate with use of combination therapy. Jan et al. (2022) concluded that patients receiving triple-therapy GDMT received fewer interventions and suffered fewer hospitalizations than patients receiving only single-therapy GDMT. Furthermore, Jan et al. (2022) report that benefits of triple-therapy GDMT not seen among patients receiving single-therapy GDMT include reduced heart rate and blood pressure, decreased mortality rates at 3- and 12-month follow-up periods, and improved kidney function.

Summary of Findings

Limited literature was available that directly compared patients receiving LVAD therapy with those receiving GDMT for HF. As a result, findings were evaluated independently for LVAD patients and for GDMT patients. An overall comparison of outcomes was then performed based on respective findings. Researchers determined that both LVAD recipients and GDMT recipients show improvements in QOL, functional capacity, and survivability after beginning their respective treatments for HF. However, research findings demonstrated that LVAD patients incur a greater degree of social and physiological risk and experience higher rates of rehospitalization when compared to patients receiving GDMT alone (Shah et al., 2018).

Discussion

Researchers conducted the integrative review to directly compare QOL reports and

rehospitalization rates across two HF management strategies: LVAD therapy and GDMT. A gap in the literature motivated researchers to develop a clinical research question. While a multitude of research studies exist that evaluate LVAD therapy and GDMT independently, little research exists that compares the two HF management strategies directly. As such, it is difficult to draw conclusions from present research regarding the safest HF management approach.

Findings represented in the integrative review serve to emphasize the present knowledge gap found in the literature. In the same way that it was difficult for researchers to answer their research question, it was also difficult for researchers to isolate research articles that directly compared GDMT patients with LVAD recipients. While the gap in literature complicated the integrative review process, findings did extend what is currently known about LVAD therapy and GDMT in the management of HF.

Prior to performing the integrative review, researchers anticipated that both HF management strategies would result in improved QOL measures. Additionally, researchers expected that LVAD patients would suffer a disproportionate number of rehospitalizations when compared to GDMT recipients. As expected, these findings were well-represented among the 13 articles included in the integrative review. However, researchers were surprised to learn that GDMT effectiveness increases with combination therapy (Jan et al., 2022) and that the increased risk that accompanies LVAD therapy does not significantly reduce QOL reports among LVAD recipients (Weber et al., 2022).

Study Limitations

The findings from this integrative review must be considered with respect to study limitations. QOL is a subjective measurement. QOL reports from study participants are subject to external influence and increase risk of bias in research studies. QOL can be influenced by many

confounding variables that might not have been accounted for in studies included in the integrative review, such as degree of social support, prognostic HF measures, comorbid health conditions, access to healthcare services, and financial limitations. Additionally, eight research studies included in the integrative review followed patients for a maximum of two years post-implant or post-initiation of GDMT, while the remaining five articles either failed to mention timeframe for follow-up or did not perform follow-up at all. The limited follow-up represented by the majority of selected studies may be insufficient for determining long-term health outcomes for the two HF management approaches, including morbidity and mortality rates.

Moreover, not all relevant data were explored or included in the integrative review. Data collection was limited by access restrictions within certain databases. The inability to access all available literature surrounding HF management strategies may have excluded data that could have influenced the findings of the integrative review.

Ultimately, researchers were unable to fully answer their proposed research question due to minimal research that compared HF management strategies directly. Additionally, results of the integrative review confirmed that research involving LVAD recipients was more readily available than research involving GDMT patients. As such, further research is warranted to adequately determine which HF management strategy generates the best health outcomes.

Study Implications for LVAD Management

According to the evidence, there is much to be learned regarding HF management strategies. It is known that LVAD therapy incurs greater risk for recipients, and as such, healthcare providers should schedule closer follow-up intervals with LVAD recipients than might be scheduled with GDMT recipients. Additionally, providers are encouraged to explore the degree of social support among LVAD recipients prior to implant. Ensuring increased social

support may involve the inclusion of LVAD patients' family members in the plan of care, referring to social support groups, and/or coordinating home health services when social support is lacking. Prior to implant, LVAD recipients should also be educated about the risks that come with LVAD therapy so that they are better prepared to monitor for and manage complications. While adverse events can occur and health risks are higher among LVAD patients when compared to GDMT patients, LVAD recipients should also be informed of the benefits of LVAD therapy. Research showed that QOL, functional status, and survivability improved after implant, despite adverse events.

Study Implications for GDMT Management

Overall, it was demonstrated by the limited research available for the integrative review that GDMT improves HF outcomes in the same way that LVAD therapy improves outcomes. Patients receiving GDMT showed improvements in QOL and functional status. Additionally, research revealed that patients receiving GDMT incurred lower hospitalization rates when compared to patients receiving LVAD therapy. Lower hospitalization rates were seen among GDMT patients receiving multiple HF medications when compared to GDMT patient receiving solo medication therapy. Therefore, providers are encouraged to consider combination therapy in HF management among GDMT recipients.

Conclusion

Authors conducted an integrative review to explore outcomes of two different HF management strategies. Specifically, the authors sought to learn more about the effects of LVAD therapy and GDMT on QOL reports and hospitalization rates among HF patients. As part of extensive research, 13 articles were rigorously analyzed and included in the integrative review. Thematic analysis generated three themes that broadly depicted integrative review findings:

LVAD therapy poses unique risks for HF patients, LVAD therapy improves health outcomes among HF patients, and GDMT improves health outcomes among HF patients. Authors of the integrative review learned that LVAD recipients experience a disproportionate increase in hospitalization rates and adverse physiologic events. However, authors learned that both LVAD and GDMT recipients experience improved QOL after beginning their respective HF management strategies.

While evidence was available that compared LVAD therapy and GDMT outcomes independently, little research was available that compared the two HF management strategies directly. Additionally, fewer research studies were available that evaluated outcomes of GDMT when compared to studies that evaluated outcomes of LVAD therapy. These limitations for the integrative review made answering researchers' proposed question difficult.

Though researchers were unable to fully answer their research question and thus propose the safest approach to HF management, the integrative review did highlight the existing need for further research surrounding GDMT in HF management. The integrative review also emphasized the need for further research that directly compares LVAD outcomes to those of GDMT in HF management. Researchers posit that the safest approach to HF management is one that improves QOL, improves functional capacity, and leads to fewer hospitalization rates. While the integrative review results were inconclusive regarding the safest (as defined for this integrative review) HF management strategy, researchers can confidently support that LVAD therapy and GDMT are both viable options to promote survival and improve the lives of HF patients.

References

Alonso, W. W., Faulkner, K. M., Pozehl, B. J., Hupcey, J. E., Kitko, L. A., & Lee, C. S. (2020). A longitudinal comparison of health-related quality of life in rural and urban recipients of left ventricular assist devices. *Research in Nursing & Health, 43*(4), 396–406. https://doi.org/10.1002/nur.22052

Braun V., Clarke V. (2006) Using thematic analysis in psychology. *Qualitative Research in Psychology, 3*(2), 77-101. https://doi.org./10.1111/j.1365-2702.2010.03336.x

Burch, A. E., Colley, B. J., Döring, M., Gummadi, S., Perings, C., Robertson, M., Sanchez, R., Shroff, G., Veltmann, C., & Sears, S. F. (2021). Increased quality of life among newly diagnosed patients with heart failure with reduced ejection fraction in the months after initiation of guideline-directed medical therapy and wearable cardioverter defibrillator prescription. *Journal of Cardiovascular Nursing, 36*(6), 589-594. https://doi.org/10.1097/jcn.0000000000000864

Carroll, A. J., Hahn, E. A., & Grady, K. L. (2022). Research engagement and experiences of patients pre- and post-implant of a left ventricular assist device from the mechanical circulatory support measures of adjustment and quality of life (MCS A-qol) study. *Quality of Life Research, 31* (8), 2457–2470. https://doi.org/10. 1007/s11136-022-03111-4

Jan, R. K., Alsheikh- Ali, A., Mulla, A. A., Sulaiman, K., Panduranga, P., Al- Mahmeed, W., Bazargani, N., Al- Suwaidi, J., Al- Jarallah, M., Al- Motarreb, A., Salam, A., & Al-Zakwani, I. (2022). Outcomes of guideline-based medical therapy in patients with acute heart failure and reduced left ventricular ejection fraction. *Medicine, 101*(23). https://doi.org/10.1097/md.0000000000029452

McNamara, N., Narroway, H., Williams, M., Brookes, J., Farag, J., Cistulli, D., Bannon, P., Marasco, S., Potapov, E., & Loforte, A. (2021). Contemporary outcomes of continuous-flow left ventricular assist devices—a systematic review. *Annals of Cardiothoracic Surgery, 10*(2), 186–208. https://doi.org/10.21037/acs-2021-cfmcs-35

Melnyk, B. M., & Fineout-Overholt, E. (2023). *Evidence-based practice in nursing & healthcare: A guide to best practice* (5th ed.). Wolters Kluwer.

Moloce, M.-A., Costache, I.-I., Nicolae, A., & Onofrei Aursulesei, V. (2022). Pharmacological targets in chronic heart failure with reduced ejection fraction. *Life, 12*(8), 1112. https://doi.org/10.3390/life12081112

Page, M. J., McKenzie, J., Bossuyt, P., Boutron, I., Hoffmann, T., mulrow, cindy, Shamseer, L., Tetzlaff, J., Akl, E., Brennan, S. E., Chou, R., Glanville, J., Grimshaw, J., Hróbjartsson, A., Lalu, M. M., Li, T., Loder, E., Mayo-Wilson, E., McDonald, S., … Moher, D. (2020). *The Prisma 2020 Statement: An Updated Guideline for Reporting Systematic Reviews*. https://doi.org/10.31222/osf.io/v7gm2

Shah, K. B., Starling, R. C., Rogers, J. G., Horstmanshof, D. A., Long, J. W., Kasirajan, V., Stehlik, J., Chuang, J., Farrar, D. J., & Estep, J. D. (2018). Left ventricular assist devices versus medical management in ambulatory heart failure patients: An analysis of INTERMACS profiles 4 and 5 to 7 from the Roadmap Study. *Journal of Heart and Lung Transplantation, 37*(6), 706–714. https://doi.org/10.1016/j.healun.2017.12.003

Suzuki, F., Sato, H., Akiyama, M., Akiba, M., Adachi, O., Harada, T., Saiki, Y., & Kohzuki, M. (2022). Changes in the quality of life of patients with left ventricular assist device and their caregivers in Japan: Retrospective observational study. *The Tohoku Journal of Experimental Medicine, 257*(1), 45–55. https://doi.org/10.1620/tjem.2022.j016

Thiha, S., Zaidi, A. R., Robert, C. A., Abbas, M. K., & Malik, B. H. (2019). A rising hope of an artificial heart: Left ventricular assisted device - outcome, convenience, and quality of life. *Cureus.* https://doi.org/10.7759/cureus.5617

Toronto, C. E., & Remington, R. (2020). *A step-by-step guide to conducting an Integrative Review*. Springer.

Turgeon, R. D., Barry, A. R., Hawkins, N. M., & Ellis, U. M. (2021). Pharmacotherapy for heart failure with reduced ejection fraction and health-related quality of life: A systematic review and meta-analysis. *European Journal of Heart Failure, 23*(4), 578–589. https://doi.org/10.1002/ejhf.2141

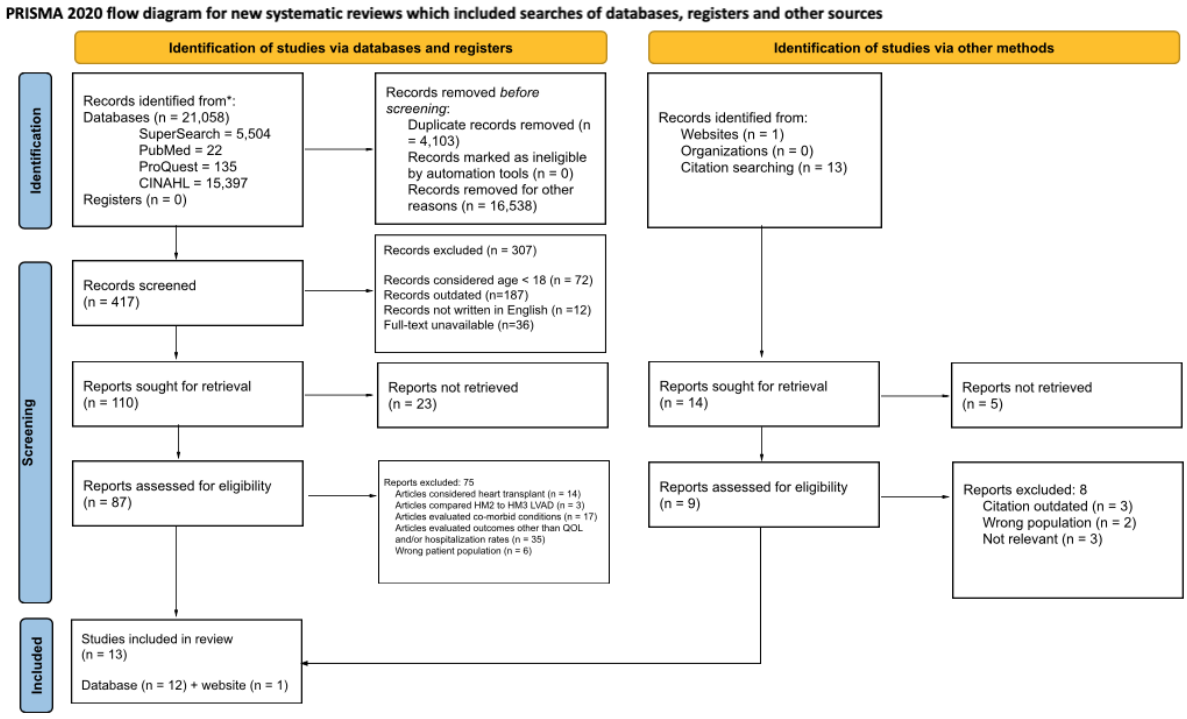
University of Oxford. (2021, June 14). *Critical appraisal tools*. Centre for Evidence-Based Medicine (CEBM), University of Oxford. https://www.cebm.ox.ac.uk/resources/ebm-tools/critical-appraisal-tools

Weber, M. P., Stulak, J., Maltais, S., Pagani, F. D., Cowger, J., & Tchantchaleishvili, V. (2022). Quality of life metrics in LVAD patients after hemocompatibility- related adverse events. *Artificial Organs, 46*(8), 1616–1625. https://doi.org/10.1111/aor.14235

Zimpfer, D., Gustafsson, F., Potapov, E., Pya, Y., Schmitto, J., Berchtold-Herz, M., Morshuis, M., Shaw, S. M., Saeed, D., Lavee, J., Heatley, G., Gazzola, C., & Garbade, J. (2020). Two-year outcome after implantation of a full magnetically levitated left ventricular assist device: Results from the Elevate Registry. *European Heart Journal, 41*(39), 3801–3809. https://doi.org/10.1093/eurheartj/ehaa639

Appendix A

PRISMA Flow Document (Page et al., 2020)



Appendix B

Data Matrix

Integrative Review Data Matrix: LVAD vs. GDMT in Heart Failure

Article # & Database	Reference	Study Design/Type	Study Aim(s)	Methods Overview	Data Collection	Results	Level of Evidence	Sub-Themes Identified from Thematic Analysis	Quality Appraisal
1 SuperSearch on EBSCO platform **M.C.**	Suzuki, F., Sato, H., Akiyama, M., Akiba, M., Adachi, O., Harada, T., Saiki, Y., & Kohzuki, M. (2022). Changes in the quality of life of patients with left ventricular assist device and their caregivers in Japan: Retrospective observational study. *The Tohoku Journal of Experimental Medicine, 257*(1), 45–55. https://doi.org/10.1620/tjem.2022.j016	Retrospective observational study	Investigate the changes in the QOL of patients and caregivers before and after LVAD implantation Identify the factors that reduce the patients' QOL	**Sample size**: 32 (20 patients in the improved group and 12 patients in the unimproved group) + 24 live-in caregivers **Sample characteristics:** - Patients with end-stage HF (NYHA class III-IV) - Median age of patients: 48 - Median age of caregivers: 52 - 75% of patients were males Participants were grouped in the unimproved group or the improved group based on whether the Euro-QOL 5 Dimensions 5 Levels (EQ-5D-5L) index score improved after LVAD implant	Data were collected preoperatively and postoperatively. Caregivers were asked to complete the patients' current QOL using EQ-5D-5L as estimated by them to examine correlation between the patients' QOL perceived by the caregivers and the patients' own perceptions. Measures: patient background (age, sex, duration of LVAD implant, primary disease, medical history, reason for LVAD, LVAD model, pre- and post-operative states, total number of days of hospitalization after LVAD implant, and frequency of hospitalization following LVAD implant) via review of medical records, caregivers' information (age, sex, relationship to patient) via medical record and interviews, QOL (EQ-5D-5L and 12-item Short Form Health Survery), Minnesota Living with HF Questionnaire, symptoms of depression/anxiety (Hospital Anxiety and Depression Scale), activity (Frenchay Activities Index), present status (Barthel Index for activities of daily living, 6-minute walk distance test, and burden of caregivers (burden index of the caregiver (BIC-11)).	Average number of hospitalizations after LVAD implant: 4 Patients showed improvement after LVAD implant in the EQ-5D-5L, MLHFQ, and HADS. There was no improvement in the FAI Caregivers' QOL revealed no change in many indicies after LVAD implant. Total and anxiety indicators improved in the HADS. Burden of caregivers did not worsen after LVAD implant. Social QOL and level of activity did not improve after LVAD implant, suggesting that the social participation and activities of LVAD patients are limited. Patients' QOL perceived by the caregivers did not always match the patients' perceptions.	Level IV	**Quality of life improves after LVAD implant** **Functional ability improves after LVAD implant** **LVAD implant has poor social implications**	**Factors that increase risk of bias and threaten validity:** - Study performed in a single institution in Japan (Tohoku University Hospital), which limits generalizability - Surveys relied on patients' retrospective recall of pre-implant status (recall bias) - Degree of social support = confounding variable - Degree of rehabalitation and physical therapy post-discharge after implant = confounding variable **Valid and reliable measurement tools used:** - EQ-5D-5L - Hospital Anxiety and Depression Scale (HADS) - Frenchay Activity Index - Burden Index of Caregiver (BIC-11) - Minnesota Living with Heart Failure Questionnaire (MLHFQ) **Follow-up considerations**: - Single administration of questionnaire to caregivers and patients hospitalized February-October 2019 - Questionnaires returned same-day or at next scheduled outpatient follow-up visit - Limited time frame/single snapshot in time **Applicability**: - Relevant to PICO question as a result of studying LVAD patients and complications of LVAD therapy - Does not consider comparison to GDMT patients **Ethics:** - Study received ethical approval by the Medical Ethics Committee of Tohoku University Hospital - Participants provided written informed consent
2 SuperSearch on EBSCO platform **M.C.**	Turgeon, R. D., Barry, A. R., Hawkins, N. M., & Ellis, U. M. (2021). Pharmacotherapy for heart failure with reduced ejection fraction and health-related quality of life: A systematic review and meta-analysis. *European Journal of Heart Failure, 23*(4), 578–589. https://doi.org/10.1002/ejhf.2141	Systematic review	Synthesize the evidence on the effect of heart failure with reduced ejection fraction pharmacotherapy on health-related quality of life	**Sample size:** 37 studies included from 5770 total articles reviewed **Inclusion criteria:** Placebo-controlled RCTs that enrolled patients with HFrEF, evaluated an intervention that consisted of ≥ 1 agent recommended for the chronic management of HFrEF in contemporary heart-failure guidelines, reported HRQoL as an outcome **Study characersitics:** Median study values were a sample size of 263 participants (20-8442), age 63 years (49-81), female 26% (9-52%), EF 28% (19-42%), and NYHA class II 53% (0-86%) 2 reviewers independently screened article titles and abstracts, reviewed full-text articles for inclusion, extracted data, evaluated trials for risk of bias, and graded evidence Databases searched: CENTRAL, MEDLINE, Embase, CINAHL, clinicaltrials.gov, and WHO's International Clinical Trials Registry Platform.	The following data was extracted from each study using a standardized data collection form: lead author, publication year, sample size, inclusion criteria [EF, NYHA class], baseline characteristics (age, sex, NYHA class, ischemic cardiomyopathy, a-fib, EF, serum BNP concentration), baseline use of HFrEF medications, intervention and comparator characteristics (agent, target dose, and achieved dose), HRQoL outcome characteristics (instruments, timing of follow-up, proportion completing HRQoL assessment, values at baseline and last lab follow-up, and change from baseline).	6 classes of medications (ARB's, ARNI's, SGLT2 inhibitors, ivabradine, hydralazine-nitrate, and IV iron) produced statistically significant improvements in HRQoL in patients with HFrEF IV iron produced a moderate improvement in HRQoL ARB's, ARNIs, SGLT2 inhibitors, ivabradine, hydralazine-nitrate produced small improvements in HRQoL	Level I	**GDMT improves QOL reports in HF patients**	**Search strategy:** - Multiple databases searched - Included RCTs (increases reliability and validity) - Clearly-defined inclusion and exclusion criteria (repeatable) **Methods:** - Contained multiple reviewers to decrease risk of bias - Bias assessed for each included study with "high/unclear bias in 27 studies" **Statistical analysis:** - Used standardized mean difference values to evaluate effect size - Numerous HrQOL surveys complicated analysis **Applicability:** - Relevant to PICO question as a result of studying GDMT patients - Does not consider comparison to LVAD patients
3 SuperSearch on EBSCO platform **M.C.**	Zimpfer, D., Gustafsson, F., Potapov, E., Pya, Y., Schmitto, J., Berchtold-Herz, M., Morshuis, M., Shaw, S. M., Saeed, D., Lavee, J., Heatley, G., Gazzola, C., & Garbade, J. (2020). Two-year outcome after implantation of a full magnetically levitated left ventricular assist device: Results from the Elevate Registry. *European Heart Journal, 41*(39), 3801–3809. https://doi.org/10.1093/eurheartj/ehaa639	Prospective, observational, multinational registry study	Study long-term outcomes with the HM3 in a real-world population	**Sample size:** 540 (primary implant = 463, pump exchange = 19, anonymous = 58) **Sample characteristics:** - Patients with HM3's implanted in Europe and Middle East - NYHA classification breakdown: class IIIA (42), class IIIB (165), class IV (231), not provided (25) - Mean age: 55.6 +/- 11.7 years - In primary implant cohort: 412 males (89%) and 51 females (11%)	Patients were followed for 24 months post-implant or until an outcome (transplant, explant, expiration, withdrawal). Data (demographics, comorbidities, previous CV history, hemodynamic profile, lab values, echocardiogram parameters, NYHA classification, 6-minute walk test, INTERMACS profle, Euro-QOL-5 scores) were collected at baseline. Post-implant, patients were evaluated at 6, 12, and 24 months for their clinical and functional status	HM3 implant for advanced HF with reduced EF is associated with 2-year survival rate of 74.5% and results in sustained improvement of NYHA functional class and QOL. Complications observed: stroke (10.2%), GI bleed (9.7%), pump thrombosis (1.5%), outflow graft twists (3.5%) Median duration spent out of hospital in primary implant cohort (n=426) was 671.5 days. After 24 months, majority of patients were in NYHA classes 1 and 2 (82%) Freedom from re-hospitalization at 2 years was 30.9% and the majority of re-hospitalizations were for adverse events (75%). 8.2% of patients were transplanted within the first 2 years after implant, 25% of patients expired on their device, the device was explanted in 1.3% of patients, and 0.7% of patients were lost to follow-up	Level IV	**QOL improves after LVAD implant** **Functional ability improves after LVAD implant** **Re-hospitalization risk is high in LVAD patients** **LVAD implant poses risk of adverse physiologic effects**	**Factors that increase risk of bias and threaten validity:** - No randomization - No control group - Patients selected based on enrollment in ELEVATE registry (purposive sampling) - Study funded by Abbott (manufacturer of HM3 device) - Sample localized to Europe and Middle East (limits generalizability) **Valid and reliable measurement tools used:** - EQ-5D VAS QOL questionnaire - 6MWD test **Follow-up considerations**: - Patients followed for 2 years with follow-up intervals of 6, 12, and 24 months - Reasons were provided for non-follow-up **Applicability**: - Relevant to PICO question as a result of studying LVAD patients and complications of LVAD therapy - Does not consider comparison to GDMT patients **Ethics:** - Study conducted according to Declaration of Helsinki - Protocol and informed consent forms were approved by ethics committes at each institution

4 PubMed on NIH platform **M.C.**	McNamara, N., Narroway, H., Williams, M., Brookes, J., Farag, J., Cistulli, D., Bannon, P., Marasco, S., Potapov, E., & Loforte, A. (2021). Contemporary outcomes of continuous-flow left ventricular assist devices—a systematic review. *Annals of Cardiothoracic Surgery, 10*(2), 186–208. https://doi.org/10.21037/acs-2021-cfmcs-35	Systematic Review	Systematically review the literature to quantify survival and the incidence of adverse events following implantation of continuous-flow LVADs used as both bridge to transplant (BTT) and destination therapy (DT)	**Sample size:** 63 studies (9,280 patients) included after a total of 627 studies were reviewed (including observational studies, single- or multi-center case series) **Sample characteristics:** - Mean age: 57 - Majority male **Inclusion criteria:** studies reporting survival or adverse event outcome data for patients who had undergone insertion of a continuous-flow LVAD for heart failure **Exclusion criteria:** reviews or editorials, conference proceedings, studies with non-human participants, surgical techniques, pediatric studies, studies that did not separate data for pulsatile and continuous flow devices, studies reporting on mechanical assist devices other than isolated implantable LVADs, studies reporting on risk modeling, studies examining post-transplant outcomes in patients bridged with LVAD, studies that were updated by newer publications and sub-analyses of previously reported results 3 reviewers screened title and abstract, and if relevant, reviewed full-text copies of the articles. Before final inclusion, full-text copies of all selected articles were examined for eligibility Databases searched: MEDLINE, Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, Database of Abstracts and Reviews of Effects for English-Language Studies	Data extraction points: number of patients implanted with cf-LVAD, device model, duration of follow-up or mean duration of support or defined time at risk, patient demographics and outcome measures (survival, adverse events, OHT, functional status, QOL measure) **Primary outcomes:** survival, frequency of adverse events **Secondary outcomes:** QOL and assessment of functional status	Most commonly reported adverse events: GIB, device-related infection, neurological events, RHF QOF (as measured by Kansas City Cardiomyopathy Questionnaire) and functional status (as measured with 6-minute walk test) improved after cf-LVAD implant with no decline evident 2 years after implantation Long-term survival post-implant remains limited d/t incidence of adverse events. Short-term survival is comparable to heart transplant. All patients were reported as NYHA class III or IV at baseline, with 79%-85% improving to NYHA I-II at 6-months and no evidence of deterioration in status at 24 months "LVAD therapy offers patients with ESHF the potential for improved survival, HRQoL, and functional status compared to medical therapy alone."	Level I	**LVAD implant poses risk of adverse physiologic events** **Quality of life improves after LVAD implant** **Functional ability improves after LVAD implant** **LVAD implant improves survivability**	**Search strategy:** - Multiple databases searched - Clearly defined inclusion and exclusion criteria (repeatable) - Clearly defined outcomes - Examined 13 years of published studies - Utilized MeSH and keyword approaches (repeatability) **Methods:** - Contained multiple reviewers to decrease risk of bias - Adherence to PRISMA - Few RCTs/cohort studies meant that each study was treated as a case-series, which weakens evidence **Statistical analysis:** - Significant heterogeneity between studies - No meta-analysis related to lack of standard definitions and varying durations of follow-up, **Applicability**: - Relevant to PICO question as a result of studying LVAD patients and complications of LVAD therapy - Does not consider comparison to GDMT patients
5 ProQuest on Galileo Platform **M.C.**	Thiha, S., Zaidi, A. R., Robert, C. A., Abbas, M. K., & Malik, B. H. (2019). A rising hope of an artificial heart: Left ventricular assisted device - outcome, convenience, and quality of life. *Cureus*. https://doi.org/10.7759/cureus.5617	Literature review	To evaluate the outcome and convenience regarding the usage of continuous-flow LVAD, both as definitive therapy and as bridge to cardiac transplant To assess the consequences, cardiac output performance, life expectancy, and quality of life in end-stage HF patients within one to two years of treatment with LVAD implant	**Sample size:** 71 articles screened; 50 studies included; 3,574 patients **Sample characteristics:** - Databases: PubMed and Google Scholar - Inclusion criteria: articles related to human studies, studies less than 5 years old, clinical trials, literature reviews - Exclusion criteria: HF with normal EF - Limiters: full-text, English - Study designs: case reports, observational studies, RCTs, SR, MA - Mean age of patients: 58 years - Majority male (84-85%) **Sampling technique:** - MeSH keywords: "LVAD," "EF," "death," and "QOL"	**Measures**: cardiovascular and device-related problems (ventricular arrhythmia, CVA, pump thrombosis, infections, GI bleed, right HF), outcomes (EF, QOL, exercise time, peak workload, total cardiac output, peak oxygen consumption, anaerobic threshold), total cost	For patients with NYHA class III and IV HF with max medication therapy, there was significant increase in mean EF from 4-6% and an increase in 6-minute walk distance from 98 meters to 130 meters QOL improved when compared to pre-LVAD stage with a mean increase of EQ-5D QOL score from 19 to 28 55% of re-hospitalizations are due to adverse events following DT LVAD implant	Level VII	**Quality of life improves after LVAD implant** **Functional ability improves after LVAD implant** **Re-hospitalization risk is high in patients with LVAD implant** **LVAD implant poses risk of adverse physiologic events**	**Search strategy:** - Clearly defined inclusion and exclusion criteria (repeatable) - Included studies ≥ 10 years old (outdated evidence) - Utilized MeSH headings, keyword searching, and hand-searching methods (repeatability) - Defined limiters: English language, peer-reviewed **Methods:** - Contained multiple reviewers - Evaluated outcomes according to valid and reliable measures: EQ-5D-5L, 6MWD **Applicability**: - Relevant to PICO question as a result of studying LVAD patients and complications of LVAD therapy - Does not consider comparison to GDMT patients
6 Recommended from classmate in DB5 **M.C.**	Shah, K. B., Starling, R. C., Rogers, J. G., Horstmanshof, D. A., Long, J. W., Kasirajan, V., Stehlik, J., Chuang, J., Farrar, D. J., & Estep, J. D. (2018). Left ventricular assist devices versus medical management in ambulatory heart failure patients: An analysis of INTERMACS profiles 4 and 5 to 7 from the Roadmap Study. *Journal of Heart and Lung Transplantation, 37*(6), 706–71. https://doi.org/10.1016/j.healun.2017.12.003	Non-randomized, controlled, observational study **Relevant context/data from initial ROADMAP study:** - Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS) profiles are qualitative clinical profiles developed to describe symptomatic HF patients on a scale of 1 (most severly ill) to 7 (advanced NYHA class III) - Patients with INTERMACS profiles 1-3: inotrope dependent - ROADMAP study evaluated ambulatory, non-inotrope dependent HF patients (INTERMACS profiles 4-7) who were not candidates for heart transplant	Provide insight to benefits and complications associated with earlier LVADs Define which patients may benefit from LVAD implant Compare outcomes between patients with LVAD therapy versus medical management in HF	**Sample size:** 195 patients; 94 selecting LVAD therapy and 101 selecting OMM **Sample characteristics:** - Patients with non-inotrope dependent HF - Patients characterized as INTERMACS profiles 4-7 from a previously-performed observational study (ROADMAP) - Patients were enrolled from October 2011-July 2013 - NYHA class IIIB in IM4: 30; NYHA class IIIB in IM5-7: 69 - NYHA class IV in IM4: 45; NYHA class IV in IM5-7: 28 **Inclusion criteria:** FDA-approved indications for HMII LVAD destination therapy (patients with NYHA class III or IV HF who received optimal medical therapy for at least 45 of the last 60 days who are not candidates for heart transplant) + the following: at least 1 hospitalization for HF in 12 months, 6-minute walk distance < 300 meters **Exclusion criteria:** - Inotrope use within 30 days of enrollment Patients were separated into INTERMACS profile 4 (IM4) and INTERMACS profile 5-7 (IM5-7) and comparisons were made between groups	**Outcomes**: survival on original therapy (LVAD vs. optimal medical management [OMM]), 6-minute walk test distance, adverse events, health-related QOL, hospitalization rates Baseline characteristics: demographics, health history, NYHA class, INTERMACS profile, 6MWD, lab measurements, medications, HRQoL, PHQ-9 Clinical follow-ups were made every 6 months for up to 24 months, which included assessment of HRQoL, depression, functional status, and lab parameters **Primary end-point**: composite of survival on original therapy with improvement in 6MWD ≥ 75 meters at 12 months after enrolllment	Patients who received LVAD therapy were more likely to be alive and have an improvement in 6MWD at 12- and 24-month follow up. LVAD patients had greater improvements in QOL, depression, and HF symptoms when compared to HF patients who opted for medical therapy. For INTERMACS Profile 4, more LVAD patients met primary end-point (survival on original therapy with improvement in 6-minute walk distance ≥ 75 meters at 1 year) compared with OMM patients (40% vs 15%). Adverse events trended higher in LVAD patients compared with OMM patients. Rehospitalization rates for LVAD patients vs. OMM patients were similar between treatment arms in IM4 but were higher for LVAD in IM5-7 For both IM4 and IM5-7, GI bleed was the most common adverse event for LVAD patients and worsening HF was the most common adverse event for OMM patients Findings clarified the primary ROADMAP study findings: LVAD compared with OMM therapy provided better survival with improvement in 6MWD at 1 year and continued at 2-year follow up Only IM4 patients had more improvements in 6MWD, QOL, and depression with LVAD compared with OMM	Level III	**Quality of life improves after LVAD implant** **Functional ability improves after LVAD implant** **LVAD implant improves survivability** **Re-hospitalization risk is high in patients with LVAD implant** **LVAD implant poses risk of adverse physiologic events**	**Factors that increase risk of bias and threaten validity:** - No randomization (observational study) - Relied on results of previous study - Grant and research support received from Abbott (LVAD manufacturer) - Some patients included in the study were missing outcome data, which could skew data results **Valid and reliable measurement tools used:** - 6MWD - EQ-5D-5L - PHQ-9 **Statistical analysis:** - Outcomes reported in odds ratios and p values **Follow-up considerations**: - Follow-up performed every 6 months for up to 2 years **Applicability**: - Relevant to PICO in that the study considers both LVAD and GDMT patients

7 CINAHL on EBSCO platform **S.C.**	Moloce, M. A., Costache, I. I., Nicolae, A., & Onofrei Aursulesei, V. (2022). Pharmacological targets in chronic heart failure with reduced ejection fraction. *Life, 12*(8), 1112. https://doi.org/10.3390/life12081112	Literature review	Provide overview of current guideline-directed medical therapy of HFrEF and novel treatments tested in clinical trials To present new therapeutic targets based on the current understanding and progression of molecular and cellular mechanisms leading to heart failure.	**Sample size:** not provided **Sample characteristics:** - Patients with HRrEF < 40% - Patients with NYHA class II or III HF **Limiters:** English language, published between January 1, 2000 and June 2022 **Inclusion criteria:** Focuses on meta-analysis, randomized clinical trials, and clinical practice guidelines, experimental studies with positive results, major clinical trials with guideline-recommended drugs, RCT's **Exclusion criteria:** Trials and studies excluding acute HF, advanced HF, HFpEF, trials and studies with negative results **Databases searched:** MEDLINE, Embase, CDSR **Key words**: pharmacological treatments, heart failure with reduced ejection fractions, trials	The following medication classes and medications were examined in current guidelines and in current practice: ARNI, SGLT2i, vericiguat, ivabradine, aldosterone, digoxin, combination isosorbide dinitrate and hydralazine	ARNI and SGLT2 inhibitors have shown great benefit in improving HF progression and will continue to make strides in the treatment of heart failure. There is still much to learn about the balance between hemodynamic and neurohormonal modulators to create a personalized adaptive therapy. There are currently three different therapeutic models used to develop treatment for HFrEF but none of these can properly explain disease progression completely. Current models need to be expaned or more inclusive models need to be adapted for effective and safe therapy practices. Goals of HF treatment: improved QOL, improved symptoms, and greater functional capacity	Level VII	**GDMT serves to improve functional capacity & QOL in HF patients**	**Search Strategy:** Multiple databases searched, 22-year seach timeline (weakens current reliability), clearly defined outcomes, utilized keyword approaches and clear inclusion/exclusion criteria (increases repeatability) **Application:** Relevant to current PICO question as a result of studying GDMT for patients with HRrEF
8 CINAHL on EBSCO platform **S.C.**	Alonso, W. W., Faulkner, K. M., Pozehl, B. J., Hupcey, J. E., Kitko, L. A., & Lee, C. S. (2020). A longitudinal comparison of health‐related quality of life in rural and urban recipients of left ventricular assist devices. *Research in Nursing & Health, 43*(4), 396–406. https://doi.org/10.1002/nur.22052	Descriptive study	To compare generic and HF-specific HRQOL longitudinally from pre-implantation to 1-, 3-, and 6- months post-implant in a cohort of rural and urban LVAD recipients	**Sample size:** 95 patients (32 rural, 63 urban) **Sample characteristics:** - Patients consented and enrolled at a single academic medical center in the northestern US between May 2012 and August 2016. - 83.1% white, 80% male, NYHA Class III or IV (96.3%). **Inclusion criteria:** Subjects must be 21 years or older and have an Interagency Registry of Mechanically Assited Circulatory Support Profile designation of 1-4. **Exclusion criteria:** Previously received heart transplant or LVAD, patient undergoing treatment for a life-limiting illness, patients medically diagnosed with a serious cognitive impairment such as Alzheimer's	Data was collected pre-implant and at 1-, 3-, and 6-month marks post-implant **Data collected of patients at baseline:** - Demographic information (age, gender, race, ethnicity, education level, employment, zipcode of primary residence) - HF etiology and duration - EF - NYHA class - Implant strategy (BTT vs. DT) **Primary outcome:** HRQOL **Measures:** - Rural and urban residence (determined by zipcode) - HRQOL via the European Quality of Life Visual Analog Scale (EQ-VAS) for generic HRQOL and the Kansas City Cardiomyopathy Questionnaire (KCCQ) for HF-specific QOL	Nearly all subjects experienced at least one adverse event during the 6-month study period. Infection was the most common adverse event (57 occurrences) followed by bleeding (37 occurrences), device thrombosis (26 events), and neurologic dysfunction (25 events). A total of 107 hospital admissions were recorded among 58 subjects (18 of which were rural patients). Median length of stay for hospitalizations was 4 days (range from 0-109 days). Both rural and urban patients demonstrated significant improvements in generic and HF-specific HRQOL in the first month following LVAD implant. Rural patients with HF report a lower HF-related QOL before LVAD implantation. Both rural and urban have two phases of improvement post-implantation in both generic and HF-spcefic QOL. Ongoing monitoring of HRQOL during LVAD therapy could lead to higher QOL in both rural and urban patients.	Level VI	**Rural LVAD patients are at high risk for poor health outcomes** **Re-hospitalization risk is high in patients with LVAD implant** **Quality of life improves after LVAD implant**	**Factors that increase risk of bias and threaten validity:** - Barriers experienced by rural patients, such as poorer access to health care and travel/finacial considerations - Limited generalizabilty of results secondary to small, homogenous (male, white) sample (limited representation) - Rural sample was smaller than urban sample, which can skew data **Valid and reliable measurement tools used:** - EQ-VAS (generic) - KCCQ (HF-specific) **Follow-up considerations:** - Follow-up was arranged at 1-, 3-, and 6-month intervals post-implant, which could skew HRQOL reports - HRQOL monitoring for longer period of time (5-10 years) is recommended **Applicability:** - Relevant to PICO question as a result of studying LVAD patients and complications of LVAD and HRQOL
9 CINAHL on EBSCO platform **S.C.**	Carroll, A. J., Hahn, E. A., & Grady, K. L. (2022). Research engagement and experiences of patients pre- and post-implant of a left ventricular assist device from the mechanical circulatory support measures of adjustment and quality of life (MCS A-qol) study. *Quality of Life Research, 31*(8), 2457–2470. https://doi.org/10.1007/s11136-022-03111-4	Mixed methods design	To understand the experiences of adults with mechanical circulatory support (MCS) who are eligible for and enrolled in a study for HRQOL To describe research engagements and experiences among adults prior to or living with MCS in a secondary analysis of data from the MCS A-QOL study Finding solutions to overcome research participation barriers in patients with HF is essential for increasing generalizability and representativeness of research findings, particularly for HRQOL research given the MCS-related challenges to HRQOL	**Sample size of the MCS A-QOL (parent) study:** - 1011 approached for the study of which 86.7% enrolled, 12.7% declined, and 0.6% were ineligible. - 877 participants enrolled of which 272 were pre-implant and 605 were post-implant **Sample characteristics:** - Primarily male (78%), < 60 years of age (range 19-83 years), non-Hispanic white (63%), and college-educated (57%) - 86% of pre-implant group had NYHA class III or IV HF; 83% of post-implant group had NYHA class III or IV HF **Inclusion criteria for parent study**: age ≥ 19 years, able to speak and understand English, sufficient cognitive ability present to provide self-report data **Exclusion criteria for parent study:** scheduled for implant of a second or subsequent LVAD, scheduled for a biventricular (bi)VAD, right (R)VAD, or total artificial heart 2 groups of participants were recruited from 12 sites in the U.S. between 10/2016 and 02/2021. Patients were divided into 2 groups: group 1 (pre-implant) and group 2 (post-implant)	Data collection for group 1 participants was longitudinal: assessments were completed prior to MCS surgery and at 3- and 6-months post-implant Data collection from group 2 participants was cross-sectional: a one-time assessment was completed ≥ 3 months post-implant Administered questionnaires assessed HRQOL, treatment satisfaction, symptoms, self-efficacy, social support, financial resources, and health literacy Following each study assessment, a research coordinator conducted a debrief interview either in-person or by telephone **Measures from participants:** - Demographic variables (age, gender, race/ethnicity) - Clinical variables (etiology of HF, NYHA class) - MCS characteristics (goal of MCS therapy, INTERMACS profile) - Research study engagement (numbers and proportions of patients who were eligible, enrolled in, and completed the study) - Research study experiences (semi-structured interviews)	The study found that patients enjoyed participating in HRQOL research focused on MCS. However, these participants felt that the questionnaires could be improved to decrease the burden of participation. Group 1 participants were likely to be ≥ 60 years of age compared to group 2 participants MCS population is characterized by unique challenges that limit comprehensiveness and sensitivity of available HRQOL measures Among adults with HF, refusal to participate in research studies include: lack of interest, busy schedules, travel distance and cost, high acuity of illness, family problems, study time requirements, and privacy concerns	Level VI	**LVAD implant poses risk of adverse physiologic events** **LVAD implant has poor social implications**	**Factors that increase risk of bias and threaten validity:** - Study relies on patients' preceptions of HRQOL pre-implant and at 3 and 6 months post-implant - Study participants were primarily younger, white males **Valid and reliable measurement tools used:** - None were described transparently. The parent study aimed to develop a measurement system to assess adjustment to MCS and HRQOL among adults who undergo LVAD implant **Follow-up considerations:** - Single administration of questionnaire to the group 2 patients - Limited time frame/single snapshot in time **Applicability:** - Relevant to PICO question as a result of studying LVAD patients and HRQOL research **Ethics:** - Study approved by each site's IRB - Written informed consent was signed by each patient
10 MEDLINE **S.C.**	Weber, M. P., Stulak, J., Maltais, S., Pagani, F. D., Cowger, J., & Tchantchaleishvili, V. (2022). Quality of life metrics in LVAD patients after hemocompatibility‐related adverse events. *Artificial Organs, 46*(8), 1616–1625. https://doi.org/10.1111/aor.14235	Retrospective study with time series design	To evaluate QOL and impact on functional status after a patient has an adverse event with an LVAD, specifically a hemocompatability-related adverse event (HRAE). HRAEs are neurologic events, thromboembolic events, or non-surgical bleeding occurring within 6 months of implant. Researchers hypothesized that HRAEs adversely impact HRQOL and functional outcomes	**Sample Size:** 21,552 patients identified in database (3,509 with one HRAE and 18,043 non-HRAE). **Sample characteristics:** - Median age: 59 years - Median height:175.3 cm - Median weight: 85.8 kg - 78.5% of patients were male - All patients were adults - 76.1% of the sample was documented NYHA class IV and 16.9% class III The study used the INTERMACS (Interagency Registry for Mechanically Assisted Circulatory Support) database to query patients undergoing LVAD implant between 2008-2017	QOL data was collected pre-implant, pre-HRAE, and post-HRAE within a period of 12 months post-operatively. QOL was measured using the KCCQ QOL, the KCCQ PLS, and the EQ-5D. Functional status was measured according to 6MWT. Pre-defined time points for time-series analysis of data were: QOL scores pre-HRAE, first score post-HRAE, and score closest to one-year post-op Patients were asked to complete questionnaires on QOL preceived by the patient. Each patient was also asked to complete a fuctional status assessment (6MWT).	HRAE patients were more likely to hold a pre-operative NYHA class 4 representation. Near the time of a HRAE, decreases in QOL metrics and functional status metrics were noted for patients. However, recovery in these metrics were noted in the post-HRAE. When comparing broad HRAE and non-HRAE cohorts at 12-month follow up post-operatively, all scores were reduced in HRAE patients when compared to non-HRAE patients. Patients are likely to experience a sharp decrease in fuctional status and quality of life after a HRAE. 6MWT distance is the most responsive and representative metric of patient status after adverse events. Results of 6MWT data failed to significantly improve from pre- to post-HRAE timepoints, unlike other metrics. There is a need for longer-term data to fully understand patients' quality of life and funtional status.	Level IV	**Quality of life improves after LVAD implant** **Functional ability improves after LVAD implant** **LVAD implant poses risk of adverse physiologic events**	**Factors that increase risk of bias and threaten validity:** - No randomized groups, no control groups - Patients selected via INTERMACS database meant a limited number of patients with complete cases (some patients included in the study were missing outcome data, which could skew data results) **Validity and Reliable measurement tools:** - EQ-5D VAS QOL questionnaire - KCCQ QOL and PLS - 6MWT test **Follow up consideration:** - 12 month post-HRAE - Time-series design creates a more holistic snapshot **Applicability:** - Relevant to PICO question as a result of studying LVAD patients QOL

11 Ovid **M.C.**	Burch, A. E., Colley, B. J., Döring, M., Gummadi, S., Perings, C., Robertson, M., Sanchez, R., Shroff, G., Veltmann, C., & Sears, S. F. (2021). Increased quality of life among newly diagnosed patients with heart failure with reduced ejection fraction in the months after initiation of guideline-directed medical therapy and wearable cardioverter defibrillator prescription. Journal of Cardiovascular Nursing, 36(6), 589–594. https://doi.org/10.1097/jcn.0000000000000864	Prospective, non-randomized, international (U.S. and Germany) study	Examine change in patient-reported outcomes in newly diagnosed patients with HF and reduced EF prescribed a wearable cardioverter defibrillator (WCD) Prospectively measure change in patient-reported outcomes (including QOL) among newly-diagnosed HF patients with HFrEF prescribed a WCD while initiating GDMT	**Sample size:** 210 patients **Sample characteristics:** - Participants from U.S. and Germany - Mean age of participants: 58 years - 26% of participants identified as female (n = 54) - 85% of participants were white; 13% African American/Black **Inclusion criteria:** - Adults hosptialized for new-onset HF and prescribed a WCD within 10 days **Exclusion criteria:** - Patients witch unipolar pacemakers, first hospitalization for HF occurred within 30 days before enrollment, patients with a psychological or physiologic condition that would inhibit wearing WCD Study intitiated March 2017	Patients completed Kansas City Cardiomyopathy Questionnaire (KCCQ) at 3 points: baseline, day 90, and day 180	All KCCQ subscales (physical limitation, symptom frequency, QOL, and social limitation) showed improvement from baseline to day 90. Only QOL continued to improve from day 90 to day 180. By day 90, 70% of patients showed improved QOL, and by day 180, 80% reported improvement. 3.7% of patients reported a net decrease, and 13.4% had no net change. Pursuing GDMT for HFrEF (while being proctected by WCD) is likely to provide symptom relief and improve QOL On average, patients reporting higher QOL had higher baseline EF Patient burden of adhering to GDMT is an important consideration for providers Symptom burden and QOL did not differ between men and women	Level IV	**GDMT improves QOL reports in HF patients**	**Factors that increase risk of bias and threaten validity:** - Considered only patients in U.S. and Germany - Predominately white, male sample **Study design/logistics flaws:** - Confounding variables unaccounted for (medication side effects, social support, functional status, etc.) - Wear time and shock data were not provided for analysis - No control group (non-wearable CD group with which to compare QOL) - "GDMT" was undefined in the study and no details were provided about what types of medications patients were prescribed. Medication side effects can affect QOL reports. **Follow-up considerations:** - No follow-up data to indicate whether GDMT was achieved or whether there were improvements in EF **Valid and reliable measurement tools:** - Kansas City Cardiomyopathy Questionnaire (KCCQ) **Applicability:** - Relevant to PICO question as a result of studying HFrEF patients, GDMT, and QOL - Does not consider comparison to LVAD patients
12 OVID **M.C.**	Jan, R. K., Alsheikh-Ali, A., Mulla, A. A., Sulaiman, K., Panduranga, P., Al-Mahmeed, W., Bazargani, N., Al-Suwaidi, J., Al-Jarallah, M., Al-Motarreh, A., Salam, A., & Al-Zakwani, I. (2022). Outcomes of guideline-based medical therapy in patients with acute heart failure and reduced left ventricular ejection fraction. Medicine, 101(23). https://doi.org/10.1097/md.0000000000029452	Retrospective observational study	Report on the use, predictors, and outcomes of guideline-based medical therapy (GBMT) in patients with HFrEF of < 40% from 7 countries in the Arabian gulf	**Sample size:** 2680 patients considered from Gulf CARE registry of patients with acute HF admitted to 47 hospitals in 7 Middle Eastern Gulf countries **Sample characteristics:** - Majority of patients were on dual (39%) and triple (39%) GBMT modalities, 14% received one, and 7.2% were not on any GBMT medications. - Mean average age: 58 +/- 15 years - 72% males - GBMT was achieved as follows: RAS blockers (80%), BB (75%), and MRAs (56%) **Inclusion criteria:** - Males and females age ≥ 18, admitted to any participating hospitals with admission diagnosis of acute HF (rapid onset of symptoms and signs secondary to abnormal cardiac function) **Exclusion criteria:** - Patients with HF who were discharged from the ED without admission, no informed consent, patients transferred from non-registry hospital, EF > 40%	Data collected post-discharge at 3 months and at 1 year Data collected at the point of initial care and during hospitalization included: demographics, HF etiology, risk and precipitating factors for acute HF, comorbidities, clinical presentation, troponin and BNP levels, drug history, defibrillator use, and in-hospital outcome Mortality data were collected at 3 months and 12 months Measured outcomes: numbers and types of GDMT use, their predictors as well as the impact on GBMT use on 3-month and 12-month all-cause mortality Follow-up was completed in 2,418 patients, after excluding patients who died in-hospital (5.7%) and those lost to follow-up (4%)	Triple GBMT prescribing and dosing in patients with HFrEF were suboptimal Patients on triple GBMT were less likely than those on single GBMT to require interventions such as PCI/CABG or in-hospital courses, including infection requiring therapy, requirement for inotropes, and non-invasive ventilation Having a cardiologist as the main treating physician was associated with increased likelihood of patients being prescribed triple GBMT Lack of treatment of HFrEF with GBMT and/or treatment with suboptimal dosages are associated with increased mortality Benefits of being treated with triple GBMT in comparison to a single GBMT medication include: decreased 3- and 12-month mortality, decreased HR, decreased systolic BP, decreased BG and creatinine, and improved eGFR on follow-up Co-morbidities (CAD, HLD, DM, CKD, asthma/COPD, OSA) were more likely to be present in patients on a single GBMT in comparison to those taking triple GBMT	Level IV	**Increased GDMT improves health outcomes in HF patients**	**Factors that increase risk of bias and threaten validity:** - Considered only patients enrolled in the Arabian GULF registry - Predominately male sample **Study design/logistics flaws:** - Confounding variables unaccounted for (medication side effects, social support, functional status, etc.) that might have influenced GDMT compliance, access, and use - No control group - No randomization - Recent GBMT modalities (example: Entresto) not considered due to data being collected in 2012 - Pro-BNP and echocardiographic data were missing in a majority of patients - EF was not measured at 3- and 12-month intervals **Follow-up considerations:** - Patients were followed-up with at 3- and 12-month intervals **No valid and reliable measurement tools used.** **Applicability:** - Relevant to PICO question as a result of studying HFrEF patients, GDMT - Does not consider comparison to LVAD patients - Does not consider QOL outcomes
13 SuperSearch on EBSCO platform **S.C.**	Joseph, J., P S, S., James, J., Abraham, S.,& Abdullakutty, J. (2020). Guideline-directed medical therapy in heart failure patients: Impact of focused care provided by a heart failure clinic in comparison to general cardiology out-patient department. *The Egyptian Heart Journal, 72*(1). https://doi.org/10.1186/s43044-020-00088-8	Retrospective observational study Performed in a tertiary care hospiral in southern India	Assess the impact of HF clinics in medication therapy management, including usage of GDMT To evaluate if target dose (specified by GDMT) was achieved and how much time it took to reach target dose in HF clinics compared to outpatient cardiology (OPC) offices	**Sample size:** 400 patients (200 in HF clinics, 200 in OPC offices) **Sample characteristics:** - Mean age of patient in HF clinic: 60.64 (+/- 11.4 years) - Mean age of patient in OPC office: 63.62 (+/-10.48 years) - More smokers in HF clinic group - Most common co-morbidity: anterior wall MI - Most common risk factor: DM - Male predominance in both groups **Inclusion criteria:** - Patients must have a diganosis of HFrEF Study performed in 2017	Data were obtained from electronic medical records and were compared between study groups Data collected: attainment of evidence-based target doses of disease-modifying drugs, time to reach target dose, EF at first visit and after 12 months Data were collected at 3 points in time: at 3, 6, and 12 months following the patient's first visit After data collection, participants were grouped into 4 categories based on the percentage of target dose achieved: group 1 (0-25%), group 2 (26-50%), group 3 (51-75%), and group 4 (75-100%)	Use of GDMT was higher in HF clinics when compared to OPC offices. A significantly higher number of patients in HF clinic achieved target dose when compared to OPC offices Patients in HF clinic attained target doses faster when compared to OPC offices Among patients managed in a HF clinic, EF improved and patients demonstrated decreased rates of rehospitalization and mortality HF clinics showed greater ability to manage medication therapy for HF when compared to OPC offices Only 55% of patients in OPC offices received GDMT compared to 81% of the patients in HF clinics Improvement in EF was seen (from 28.12 to 38.59) by end of 12 months in patients receiving GDMT and managed in HF clinic No significant improvement in EF was seen among patients treated with GDMT in OPC offices (33.87 in first month and 34.03 in twelfth month) Significant difference existed for re-hospitalization rates (65 in HF clinic and 189 in OPC offices), which was attributed to increased usage and better adherence to guidelines among patients treated in HF clinic	Level IV	**Increased GDMT improves health outcomes in HF patients**	**Factors that increase the risk of bias and threaten validity:** - No randomization or control group was noted. The study was strictly observational. - Predominately male sample - Considered only patients in India **Ethics:** - Institutional Review Board and institutional Ethics Committee approvals were approved before the study was conducted **Follow up considerations:** - Followed up at 3-,6-, and 12-month intervals following initial visits **No valid and reliable measurement tools used.** **Applicability:** - Relevant to the PICO question because it considers effects of GDMT on HF outcomes

Appendix C

Melnyk and Fineout-Overholt: Level of Evidence Hierarchy

Examples of Different Types of Clinical Questions in PICOT Format and Their Associated Levels of Evidence Hierarchy

Types of Clinical Questions With PICOT Example	Levels of Evidence to Answer This Type of Question
Intervention: In patients living in long-term care facilities who are at risk for pressure injuries (***P***), how does a pressure injury prevention program (***I***) compared to the standard of care (e.g., turning every 2 hours) (***C***) affect signs of emerging pressure injuries (***O***)? **OR Diagnosis or diagnostic test:** In patients with suspected deep vein thrombosis (***P***) is D-dimer assay (***I***) compared to ultrasound (***C***) more accurate in diagnosing deep vein thrombosis (***O***)?	1. Systematic review/meta-analysis (i.e., synthesis) of RCTs 2. RCTs 3. Non-RCTs 4. Cohort study or case–control studies 5. Meta-synthesis of qualitative or descriptive studies 6. Qualitative or descriptive single studies 7. Expert opinion
Prognosis/prediction: In patients who have a family history of obesity (BMI > 30 kg/m^2) (***P***), how does dietary carbohydrate intake (***I***) predict healthy weight maintenance (BMI < 25 kg/m^2) (***O***) over 6 months (***T***)? **OR Etiology:** Are fair-skinned females (***P***) who have prolonged unprotected ultraviolet ray exposure (>1 hour) (***I***) compared to darker-skinned females without prolonged unprotected ultraviolet ray exposure (***C***) at increased risk of melanoma (***O***)?	1. Synthesis of cohort study or case–control studies 2. Single cohort study or case–control studies 3. Meta-synthesis of qualitative or descriptive studies 4. Single qualitative or descriptive studies 5. Expert opinion

Appendix D

Thematic Analysis Table

Overall Themes: LVAD vs. GDMT in HF Management
1. LVAD therapy poses unique risks. 2. LVAD therapy improves health outcomes. 3. GDMT therapy improves health outcomes.

Thematic Analysis: LVAD vs. GDMT in HF Management		
Article #	**Codes/Evidence**	**Sub-Themes Identified**
1	Improved HADS and FAI scores post-implant	**Quality of life improves after LVAD implant** **Functional ability improves after LVAD implant**
	LVAD implant improves QOL and survival	
	Improved EQ-5D-5L scores after LVAD implant	
	Activity levels, QOL, and anxiety/depression improved after implant	
	Higher exercise tolerance and physical activity levels in LVAD implants	
	Role change	**LVAD implant has poor social implications**
	Lack of independence	
	Change in interpersonal relationships	
	Need for caregivers	
	Absence of social support systems	
	Disturbed work and leisure activities of patients	
	Severe restrictions on LVAD patients/caregivers	
	Social participation and activities of LVAD patients are limited	
2	GDMT goal is to reduce death and hospitalizations in HF	**GDMT improves QOL reports in HF patients**
	Pharmacotherapy improves HRQOL and prolongs survival	
	6 classes of medications resulted in improved HRQOL	
3	Overall survival rate after 2 years post-HM3 implant = 83.4%	**Quality of life improves after LVAD implant** **Functional ability improves after LVAD implant**
	Functional capacity and QOL showed improvement at 6 months	
	2-year survival was 83% for primary VAD implant	
	Sustained improvement of NYHA functional class and QOL	
	Sustained improvement in 6-minute walk test	
	QOL improved and was sustained up to 2 years post-implant	
	QOL was not decreased by adverse events	
	Freedom from re-hospitalization at 2 years was 30.9%	**Re-hospitalization risk is high in patients with LVAD implant**
	Majority of re-hospitalizations (75%) were for adverse events	**LVAD implant poses risk of adverse physiologic events**
	Major bleeding in 33.3% of patients	
	Stroke in 10.2% of patients	
	Right heart failure in 9% of patients	
	Infection/sepsis in 24% of patients	
4	LVADs are associated with a significant number of adverse events	**LVAD implant poses risk of adverse physiologic events**
	Most commonly reported adverse events: GI bleed, device-related infection, neurological events, right HF	
	Adverse events limit long-term survival	
	Hemolysis, pump thrombosis, infection, GI bleeding	
	Risks associated with LVAD devices can limit survival	
	LVAD devices can prolong life and improve QOL	**Quality of life improves after LVAD implant** **Functional ability improves after LVAD implant** **LVAD implant improves survivability**
	Quality of life improved after continuous-flow LVAD implant with no decline evident at 2-year follow-up	
	6MWT improved after continuous-flow LVAD implant with no decline evident at 2-year follow-up	
	Short-term survival in LVAD patients is comparable to heart transplant	
	Benefits of LVAD therapy	
	No deterioration in NYHA status at 24 months	
	NYHA status improved in 79-85% of patients post-implant from class III/IV at baseline to I/II at 6 months	
	6MWT distance improvement was seen at 6 months and maintained through 24 months	
	LVAD offers potential for improved survival	
5	EF increased to roughly 50% after 10-25 days of LVAD use	**Quality of life improves after LVAD implant** **Functional ability improves after LVAD implant**
	6MWT distance improved post-LVAD	
	Substantial improvement in QOL	
	Mean increase in EQ-5D QOL score from 19 to 28 post-LVAD	
	Device-relate problems include: ventricular arrhythmia, CVA, pump thrombosis, infection, GI bleed, right HF	**Re-hospitalization risk is high in patients with LVAD implant** **LVAD implant poses risk of adverse physiologic events**
	50-60% of rehospitalizations due to device-related complications	
	Several unfavorable outcomes related to improper function and failure of LVAD, which can increase re-hospitalization risk	
6	LVAD patients were more likely to be alive and show improved 6MWT distance at follow-up when compared to GDMT patients	**Quality of life improves after LVAD implant** **Functional ability improves after LVAD implant** **LVAD implant improves survivability**
	LVAD patients showed greater improvements in QOL, depression, and HF symptoms when compared to GDMT patients	
	GI bleed was the most common adverse event for LVAD patients	**Re-hospitalization risk is high in patients with LVAD implant** **LVAD implant poses risk of adverse physiologic events**
	Worsening HF was the most common adverse event for GDMT patients	
	More LVAD patients required re-hospitalization that GDMT patients	
7	Prevent progression of HF	**GDMT serves to improve functional capacity & QOL in HF patients**
	GDMT targets neurohormonal and hemodynamic modulators to control HF symptoms	
	Personalized adaptive therapy	
	Goals of GDMT: improved QOL, impoved symptoms, greater functional capacity	

8	Poor HRQOL has been reported in rural HF populations	Rural LVAD patients are at high risk for poor health outcomes Re-hospitalization risk is high in patients with LVAD implant
	Disadvantages and outcome disparities	
	Limited access to appropriate care for HF	
	Rural LVAD patients experience a greater number of hospitalizations	
	Rural patients visited ED a mean of 1.28 times compared to urban subjects who visited a mean of 0.41 times during the study	
	Cardiac workforce reduced/absent in some rural areas	
	LVAD implant improves re-admission rates, HF-related mortality, and HRQOL	Quality of life improves after LVAD implant
	Comparable improvements in HRQOL in rural and urban LVAD recipients	
9	LVAD patients face unique challenges, including LVAD-related self-care and adverse events	LVAD implant poses risk of adverse physiologic events
	Limitations in activities of daily living imposed by LVADs	LVAD implant has poor social implications
	Need for trained caregiver	
10	HRQOL and functional metrics improved in LVAD patients, despite adverse events	Quality of life improves after LVAD implant Functional ability improves after LVAD implant
	Burden of adverse events did not negatively impact HRQOL	
	LVAD patient metrics improve over time after adverse events	
	Adverse events experienced by LVAD patients include: stroke, TIA, seizure, thromboembolic events, bleeding	LVAD implant poses risk of adverse physiologic events
11	Improvement in QOL reported by GDMT patients after initiation	GDMT improves QOL reports in HF patients
	Patient-reported QOL improved significantly among patients newly-diagnosed with HF	
	Pursuing GDMT for HFrEF is likley to provide symptom relief and improve QOL	
	GDMT provides the best opportunity for HF patients to reduce morbidity and mortality	
	Scores for physical limitation, symptom frequency, QOL, and social limitation all improved from baseline to day 90	
	Only QOL continued to improve significantly from day 90 to day 180	
	Most patients experience an increase in QOL after beginning GDMT	
12	Patients taking triple-therapy GDMT were less likely to receive in-hospital invasive treatments and more likely to be treated by a cardiologist	Increased GDMT improves health outcomes in HF patients
	Patients taking triple-therapy GDMT demonstrated significantly reduced all-cause mortality at 3- and 12-month follow-ups compared to HF patients not taking GDMT	
	Maximally tolerated doses of appropriate GDMT recommended by ACC	
	More co-morbidities present in HF patients on single-therapy GDMT	
13	Re-hospitalization rates decreased among HF clinic patients when compared to outpatient cardiology clinic patients due to increased use of and compliance with GDMT	Increased GDMT improves health outcomes in HF patients
	EF improved in HF clinic patients when compared to OPC patients due to increased use of and compliance with GDMT	
	GDMT use has been shown to reduce morbidity and mortality	
	Improves functional capacity, reduces HF hospitalization, and reduces mortality	