INTERRUPTING THE PATHWAY OF HEART FAILURE
Planning Committee & Faculty

Jonathan Howlett, MD, FRCPC, FACC (Chair)
Clinical Professor of Medicine, University of Calgary
Libin Cardiovascular Institute of Alberta,
South Health Campus, Calgary
Past President, Canadian Heart Failure Society
Calgary, AB

Caroline McGuinty, MD FRCPC
Clinical Fellow, Heart Failure and Transplantation/Palliative Care
University Health Network
Toronto, ON

Sean Virani, MD, MSc, MPH, FRCPC, FCCS
Associate Professor of Medicine, UBC
Senior Medical Advisor, Cardiac Services BC
President, Canadian Heart Failure Society
Medical Director, HeartLife Foundation
Vancouver, BC

John McMurray, BSc (Hons), MB ChB (Hons), MD, FRCP, FESC, FACC, FAHA, FRSE, FMedSci
Professor of Medical Cardiology and Deputy Director (Clinical),
Institute of Cardiovascular and Medical Sciences,
University of Glasgow
Honorary Consultant Cardiologist,
Queen Elizabeth University Hospital
Glasgow, Scotland

Karen Harkness, RN, PhD, CCN(C), CHFN
Clinical Lead, Cardiac Care Network
Assistant Clinical Professor, McMaster University
Hamilton, Nurse Clinician, Heart Function Clinic
ON
Conflict of Interest
John McMurray, BSc (Hons), MB ChB (Hons), MD, FRCP, FESC, FACC, FAHA, FRSE, FMedSci

My employer, Glasgow University, has been paid for my participation in clinical trials (executive/steering committees, endpoint adjudication committees and data monitoring committees), advisory boards and other meetings/lectures by a number of pharmaceutical companies, including: Amgen, AstraZeneca, Bayer, BMS, DalCor, GSK, Novartis and Theracos.
Conflict of Interest
Sean Virani, MD, MSc, MPH, FRCPC, FCCS

• **Consulting Fees/Honoraria**: AstraZeneca, Bayer, Boehringer Ingelheim, Novartis, Novo Nordisk, Medtronic, Otsuka, Pfizer, Servier, Takeda

• **Clinical Trials**: Bayer, Medtronic, Novartis, Otsuka, Pfizer, Servier
Conflict of Interest
Karen Harkness, RN, PhD, CCN(C), CHFN

• Consulting Fees/Honoraria: Novartis, Servier, Pfizer
Conflict of Interest
Jonathan Howlett, MD, FRCPC, FACC

- **Consulting Fees/Honoraria**: Abbott Vascular, AstraZeneca, Boehringer Ingelheim, BMS/Pfizer Alliance, Medtronic, Novartis, Pfizer, Servier, Bayer, Bristol-Myers Squibb, Otsuka, St. Jude Medical
- **Clinical Trials**: Boehringer Ingelheim, BMS/Pfizer Alliance, Medtronic, Novartis, Servier, Amgen, Bayer, Johnson & Johnson, Otsuka
- **Speaker Fees**: N/A
- **Other**: N/A
Disclosure of Commercial Support

Specific details of relationship:
- This program has received financial support from Novartis Pharmaceuticals Canada in the form of an educational grant
- This program has received in-kind support from the Canadian Heart Failure Society in the form of logistical support

Potential for conflict(s) of interest:
- Speakers have received honoraria from the Canadian Heart Failure Society
- Novartis is the manufacturer and benefits from the sale of Entresto
Mitigating Potential Bias

Potential biases are acknowledged and are mitigated by presenting data supported by national and international guidelines, and as follows:

- Information presented is evidence-based
- Material has been developed and reviewed by a Planning Committee

Off-label uses of drugs will be discussed and identified as such by the speaker
Learning Objectives

After completing the symposium, participants will be able to:

• Describe the hidden risk of “stable” HF and discuss strategies for prevention of HF progression
• Describe and characterize the newly created HF-mrHF type and discuss strategies which may influence its outcome
• Highlight continuing high risk following unstable HF and discuss strategies to optimize HF care for all patients
Accreditation

This event is an Accredited Group Learning Activity (Section 1) as defined by the Maintenance of Certification Program of the Royal College of Physicians and Surgeons of Canada and approved by the Canadian Cardiovascular Society. You may claim a maximum of 1 hour.
## Agenda

<table>
<thead>
<tr>
<th>Time</th>
<th>Session</th>
<th>Speaker</th>
</tr>
</thead>
<tbody>
<tr>
<td>12:25 – 12:30 p.m.</td>
<td>WELCOME AND INTRODUCTIONS</td>
<td>Jonathan Howlett, MD</td>
</tr>
<tr>
<td>12:30 – 12:45 p.m.</td>
<td>EARLY PREVENTION &amp; TREATMENT OF HEART FAILURE</td>
<td>Sean Virani, MD</td>
</tr>
<tr>
<td>12:45 – 1:05 p.m.</td>
<td>HEART FAILURE WITH MID-RANGE EJECTION FRACTION: RATIONALE AND CONTRAST WITH HF-PEF AND HF-REF</td>
<td>John McMurray, MD</td>
</tr>
<tr>
<td>1:05 – 1:20 p.m.</td>
<td>OPTIMIZATION OF HEART FAILURE CARE WITH ALL EJECTION FRACTIONS</td>
<td>Karen Harkness, RN</td>
</tr>
<tr>
<td>1:20 – 1:35 p.m.</td>
<td>QUESTIONS AND ANSWERS</td>
<td></td>
</tr>
<tr>
<td>1:35 – 1:40 p.m.</td>
<td>CLOSING REMARKS AND EVALUATIONS</td>
<td>Jonathan Howlett, MD</td>
</tr>
</tbody>
</table>
Housekeeping Details

• Please turn your phones to silent mode

• Please remember to complete your evaluation forms at the end of the session, by texting EVALUATION to (647) 696-5222
Early Prevention and Treatment of Heart Failure

Sean Virani, MD, MSc, MPH, FRCPC, FCCS
Associate Professor of Medicine, UBC
Senior Medical Advisor, Cardiac Services BC
President, Canadian Heart Failure Society
Medical Director, HeartLife Foundation
Vancouver, BC
Objectives

(1) Describe the hidden risk of “stable” heart failure

(2) Discuss the need for early prevention

(3) Discuss strategies to prevent disease progression
The Spectrum of Heart Failure Risk

- Poor at identifying or attributing risk
- Poor at communicating risk
- Poor at acting upon our risk assessment
Risk can be defined in many ways

MORTALITY

• 1-year mortality rate: 25%
• 30-day mortality rate after HF hospitalization: 16%
• Median life expectancy: 5 years

HOSPITALIZATIONS

• 30-day readmission rate: 21%
• 2nd highest cause of hospitalization in persons over 65 years of age
• LOS approximately 10 days, $10,000/hospitalization

SYSTEM IMPACT

• Cost of $2.8 billion per year

The Spectrum of Heart Failure Risk

Risk Factors
## Hypertension, LVH and HF

<table>
<thead>
<tr>
<th></th>
<th>Active Treatment</th>
<th>Control Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>LVH</td>
<td>Number randomized</td>
</tr>
<tr>
<td></td>
<td>4 studies</td>
<td>140</td>
</tr>
<tr>
<td></td>
<td>12studies</td>
<td>112</td>
</tr>
<tr>
<td>RR</td>
<td>0.65</td>
<td>CI 0.52-0.79</td>
</tr>
<tr>
<td>RR</td>
<td>0.48</td>
<td>CI 0.38-0.59</td>
</tr>
</tbody>
</table>

Moser and Hebert, JACC 27(5):1214-18
The Spectrum of Heart Failure Risk

Risk Factors

Established Disease
# NYHA Classification of Heart Failure

<table>
<thead>
<tr>
<th>Classes</th>
<th>Description</th>
<th>1 Year Survival Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade I</td>
<td>Early failure; no symptoms with regular exercise or restrictions</td>
<td>&gt;95%</td>
</tr>
<tr>
<td>Grade II</td>
<td>Ordinary activity results in mild symptoms, but comfortable at rest</td>
<td>80 - 90%</td>
</tr>
<tr>
<td>Grade III</td>
<td>Advanced failure, comfortable only at rest; increased physical restrictions</td>
<td>55 - 65%</td>
</tr>
<tr>
<td>Grade IV</td>
<td>Severe failure; patient has symptoms at rest</td>
<td>5 - 15%</td>
</tr>
</tbody>
</table>
Relationship between LVEF and CV Outcomes

![Graph showing the relationship between Ejection Fraction (EF) and annualized incidence of various cardiovascular outcomes.](image_url)
Mortality in HFrEF remains high despite current available therapies

- The average lifespan of HF patients is 5 years
- Approximately 1 in 4 HF patients is readmitted to the hospital within 1 year of discharge
- Prognosis for HF patients remains poor with only slight improvements in overall mortality
- Chronic HFrEF survival rates have improved over time with the introduction of new therapies; however, significant mortality remains
Qualify Centres in Canada

- National Coordinator: Dr. Nadia Giannetti
Qualify: Adherence to GDMT in Canada Score

**Poor adherence** (score ≤ 0.5): use of ≤ 50% of indicated medications in eligible patients

**Moderate** adherence (0.5 < score < 1): use of more than half of indicated medications in eligible patients

**Good adherence** (score = 1): use of all indicated medications in eligible patients
The Spectrum of Heart Failure Risk

Risk Factors → Established Disease → Hospitalization
HFH has a major impact on survival: Death from CV causes

50% of the patients will die within 2.5 years of first hospitalization

Setoguchi, Am Heart J, 2007 Aug, 154(2), 203-205
Communicating Risk

Society Guidelines

2017 Comprehensive Update of the Canadian Cardiovascular Society Guidelines for the Management of Heart Failure

Primary Panel: Justin A. Ezekowitz, MBCh (Chair), Eileen O’Meara, MD (Co-chair), Michael A. McDonald, MD, Howard Abrams, MD, Michael Chan, MBBS, Anique Ducharme, MD, Nadia Giannetti, MD, Adam Grzeslo, MD, Peter G. Hamilton, MBCh, George A. Heckman, MD, Jonathan G. Howlett, MD, Sheri L. Koshman, Pharm D, Serge Lepage, MD, Robert S. McKelvie, MD, Gordon W. Moe, MD, Miroslaw Rajda, MD, Elizabeth Swiggum, MD, Sean A. Virani, MD, Shelley Zieroth, MD

Secondary Panel: Abdul Al-Hesayen, MD, Alain Cohen-Solal, MD, Michel D’Astous, MD, Sabe De, MD, Estrellita Estrella-Holder, RN, Stephen Frenses, MD, Lee Green, MD, Haissam Haddad, MD, Karen Harkness, RN, Adrian F. Hernandez, MD, Simon Kouz, MD, Marie-Hélène LeBlanc, MD, Frederick A. Masoudi, MD, Heather J. Ross, MD, André Roussin, MD, and Bruce Sussex, MBBS
## 2017 Guidelines: Prognostic Risk Scores

<table>
<thead>
<tr>
<th>Score Name</th>
<th>Population</th>
<th>Endpoint</th>
<th>Other Considerations</th>
<th>Access</th>
<th>Variables</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Seattle Heart Failure Model</strong>645</td>
<td>HFrEF</td>
<td>Mortality risk at 1, 2 and 5 years with or without intervention. Mean life expectancy.</td>
<td>Restricted to clinical trial patients with ‘severe’ HF; Lab data entry non-SI units; More than 20 variables to enter.</td>
<td><a href="https://depts.washington.edu/shfm/">https://depts.washington.edu/shfm/</a></td>
<td>Age, gender, NYHA class, weight, EF, SBP, ischemic etiology, diuretic dose, Na, lymphocyte count, Hgb, cholesterol, uric acid, use of ACEi/ARB/BB/aldosterone blocker/allopurinol/statins, QRS&gt;120msec, use of device therapy</td>
</tr>
<tr>
<td><strong>MAGGIC Risk Score</strong>646</td>
<td>HFrEF and HfPfEF</td>
<td>Mortality risk at 1 and 3 years</td>
<td>Cohorts from many sites; missing data in the overall analysis.</td>
<td><a href="http://www.heartfailurerisk.org">www.heartfailurerisk.org</a></td>
<td>Age, gender, NYHA class, diabetes, COPD, timing of diagnosis, EF, smoking, SBP, creatinine, BMI, use of beta-blocker/ACEi/ARB</td>
</tr>
<tr>
<td><strong>3C-HF</strong>647</td>
<td>HFrEF and HfPfEF</td>
<td>Mortality risk at 1 year</td>
<td>Patients from centres with experience with HF management; mostly Caucasian patients; Lab data entry in non-SI units.</td>
<td><a href="http://www.3chf.org/site/home.php">http://www.3chf.org/site/home.php</a></td>
<td>Age, NYHA class, AF, valvular heart disease, EF, anemia, diabetes, hypertension, creatinine, use of ACEi/ARB or beta-blockers.</td>
</tr>
<tr>
<td><strong>BCN- Bio-HF</strong>648</td>
<td>HFrEF and HfPfEF</td>
<td>Mortality risk at 1,2 and 3 years</td>
<td>Limited to patients with chronic HF treated in HF unit in a tertiary hospital. Lab data entry in US units. Use of biomarkers improves accuracy but is optional.</td>
<td><a href="http://www.BCNBioHFcalcator.cat">www.BCNBioHFcalcator.cat</a></td>
<td>Age, gender, NYHA class, Na, eGFR, Hgb, EF, diuretic dose, use of statins, beta-blockers or ACEi/ARB. Optional: hs-cTnT, ST2, Nt-pro-BNP</td>
</tr>
<tr>
<td><strong>EFFECT</strong>649</td>
<td>Hospitalized HFrEF and HfPfEF</td>
<td>30-day and 1-year mortality</td>
<td>Limited to hospitalized patients; missing current clinically important variables</td>
<td><a href="http://www.ccort.ca/Research/CHFRiskMode.aspx">http://www.ccort.ca/Research/CHFRiskMode.aspx</a></td>
<td>Age, respiratory rate, SBP, BUN, Na, CVD, dementia, COPD, cirrhosis, cancer, Hgb</td>
</tr>
<tr>
<td><strong>EHMRG</strong>650</td>
<td>HFrEF and HfPfEF patients presenting to the ED</td>
<td>7 day mortality</td>
<td>Limited to patients presenting to the ER and only short-term mortality; missing current clinically important variables</td>
<td><a href="https://ehmrg.ices.on.ca">https://ehmrg.ices.on.ca</a></td>
<td>Age, arrival by ambulance, triage SBP, triage HR, triage O2 sat, potassium, creatinine, active cancer, metolazone, troponin. Optional: BNP</td>
</tr>
<tr>
<td><strong>ELAN</strong>651</td>
<td>Hospitalized HFrEF and HfPfEF</td>
<td>180-day mortality</td>
<td>Limited to hospitalized patients</td>
<td></td>
<td>Age, edema, SBP, serum sodium, serum urea, NYHA class at discharge, NT-proBNP at discharge and change in NT-proBNP</td>
</tr>
<tr>
<td><strong>ADHERE</strong>652</td>
<td>HFrEF and HfPfEF</td>
<td>In-hospital mortality</td>
<td>Limited to hospitalized patients</td>
<td>BUN, creatinine, SBP</td>
<td></td>
</tr>
<tr>
<td><strong>LACE</strong>653</td>
<td>Hospitalized patients</td>
<td>30-day mortality or readmission</td>
<td>Limited to hospitalized patients</td>
<td>Length of stay, acute admission, comorbidity index, # of ED visits in last 6 months</td>
<td></td>
</tr>
</tbody>
</table>
Prognostic Risk Scores

- Facilitate discussion about expectations and reasonable goals of therapy by incorporating objective measures into discussion
- Avoid relying on single, opinion-based prognostic factors
- Help plan approach to patient care moving forward
- To date, risk stratification has largely relied on NYHA and LVEF (hence the guidelines)
  An opportunity for pragmatic clinical trials?
The Heart Failure Paradox™

Acting upon our risk assessment

• How does risk assessment impact our clinical decision making?

• How do we design/redesign our system and care processes to reflect risk assessment?
The majority (>80%) of deaths in PARADIGM-HF had a CV cause. The mortality benefit of LCZ696 is related to the observed reduction in sudden cardiac death and death due to worsening heart failure.
The annual rate of SCD in the treatment arm of PARADIGM-HF was 3.0%
# The HF Paradox™ - Atrial Fibrillation

<table>
<thead>
<tr>
<th>Item</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Congestive heart failure</td>
<td>1</td>
</tr>
<tr>
<td>Hypertension</td>
<td>1</td>
</tr>
<tr>
<td>Age ≥75 years</td>
<td>1</td>
</tr>
<tr>
<td>Diabetes Mellitus</td>
<td>1</td>
</tr>
<tr>
<td>Stroke/TIA</td>
<td>2</td>
</tr>
</tbody>
</table>

**Add Points Together**

<table>
<thead>
<tr>
<th>CHADS₂</th>
<th>Stroke rate (95% CI)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>6</td>
<td>18.2 (10.5-27.4)</td>
</tr>
<tr>
<td>5</td>
<td>12.5 (8.2-17.5)</td>
</tr>
<tr>
<td>4</td>
<td>8.5 (6.3-11.1)</td>
</tr>
<tr>
<td>3</td>
<td>5.9 (4.6-7.3)</td>
</tr>
<tr>
<td>2</td>
<td>4.0 (3.1-5.1)</td>
</tr>
<tr>
<td>1</td>
<td>2.8 (2.0-3.8)</td>
</tr>
<tr>
<td>0</td>
<td>1.9 (1.2-3.0)</td>
</tr>
</tbody>
</table>
Figure 1. Predictors of In-Hospital Mortality and Risk Stratification for the Derivation Cohort

The HF Paradox™
The Spectrum of Heart Failure Risk

- Risk Factors
- Established Disease
- Hospitalization

Poor at identifying or attributing risk

Poor at communicating risk

Poor at acting upon our risk assessment
Heart Failure with Mid-Range Ejection Fraction: Rationale and Contrast with HF-pEF and HF-rEF

John McMurray, BSc (Hons), MB ChB (Hons), MD, FRCP, FESC, FACC, FAHA, FRSE, FMedSci
BHF Cardiovascular Research Centre, University of Glasgow & Queen Elizabeth University Hospital, Glasgow.
Describing Heart Failure: Terminology

- borderline
- systolic
- HFmrEF
- HFpEF
- HFnEF
- LVEF
- HFFrEF
- mid-range
- improved
- normal
- LVSD
- recovered
- diastolic
- diastolic
- ejection fraction
- intermediate
- recovered
Confused?
How did we get here?

No LVEF
CONSENSUS
V-HeFT

<25%
COPERNICUS

≤35%
SOLVD-T
CIBIS-2
RALES
SHIFT
SCD-HeFT
CARE-HF

≤40%
MERIT-HF

LVEF (%) 25 30 35 40 45 50 55 60

HFrEF
CHARM Executive committee – LVEF above 40% not clearly reduced but not normal either. What do we call this? “Preserved”!
CHARM Executive committee – LVEF above 40% not clearly reduced but not normal either. What do we call this? “Preserved”!
How did we get here?

- <25% COPERNICUS
- 35% SOLVD-T
- CIBIS-2
- RALES
- SHIFT
- SCD-HeFT
- CARE-HF

- 40% MERIT-HF
- CHARM-REF
- PARADIGM-HF

- ≥45% I-Preserve
- PARAGON-HF

LVEF (%)
How did we get here?

- **≤25%**
  - COPERNICUS

- **≤35%**
  - SOLVD-T
  - CIBIS-2
  - RALES
  - SHIFT
  - SCD-HeFT
  - CARE-HF

- **≤40%**
  - MERIT-HF
  - CHARM-REF
  - PARADIGM-HF

- **≥45%**
  - I-Preserve
  - PARAGON-HF

LVEF (%)

- <25%
- ≤35%
- ≤40%
- ≥45%
How did we get here?

LVEF (\%)

- <25\%
  - COPERNICUS
- ≤35\%
  - SOLVD-T
  - CIBIS-2
  - RALES
  - SHIFT
  - SCD-HeFT
  - CARE-HF
- ≤40\%
  - MERIT-HF
  - CHARM-REF
  - PARADIGM-HF
- ≥45\%
  - I-Preserve
  - PARAGON-HF

“Grey area”

DIG ancillary
How did we get here?

“Grey area” (LVEF 41-44%)
“HFmrEF” (LVEF 40-49%)
The source of the problem?

<table>
<thead>
<tr>
<th>HFrEF</th>
<th>HFmrEF</th>
<th>HFP EF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptoms ± Signs*</td>
<td>Symptoms ± Signs*</td>
<td>Symptoms ± Signs*</td>
</tr>
<tr>
<td>LVEF &lt;40%</td>
<td>LVEF 40–49%</td>
<td>LVEF ≥50%</td>
</tr>
</tbody>
</table>

---

1. Elevated levels of natriuretic peptides;
2. At least one additional criterion:
   a. relevant structural heart disease (LVH and/or LAE),
   b. diastolic dysfunction (for details see Section 4.3.2).
My response?

SORRY!

WE APOLOGIZE
### Classification | EF (%) | Description
--- | --- | ---
I. Heart failure with reduced ejection fraction (HFrEF) | ≤40 | Also referred to as systolic HF. Randomized controlled trials have mainly enrolled patients with HFrEF, and it is only in these patients that efficacious therapies have been demonstrated to date.  
II. Heart failure with preserved ejection fraction (HFpEF) | >50 | Also referred to as diastolic HF. Several different criteria have been used to further define HFpEF. The diagnosis of HFpEF is challenging because it is largely one of excluding other potential noncardiac causes of symptoms suggestive of HF. To date, efficacious therapies have not been identified.  
a. HFpEF, borderline | 41 to 49 | These patients fall into a borderline or intermediate group. Their characteristics, treatment patterns, and outcomes appear similar to those of patients with HFpEF.
<table>
<thead>
<tr>
<th>Transatlantic consensus? Almost……</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>ACC/AHA 2013</th>
<th>ESC 2016</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>HFrEF</strong></td>
<td><strong>HFrEF</strong></td>
</tr>
<tr>
<td>• LVEF ≤40%</td>
<td>• LVEF &lt;40%</td>
</tr>
<tr>
<td><strong>HFpEF borderline</strong></td>
<td><strong>HFmrEF</strong></td>
</tr>
<tr>
<td>• LVEF 41-49%</td>
<td>• LVEF 40-49%</td>
</tr>
<tr>
<td><strong>HFpEF</strong></td>
<td><strong>HFpEF</strong></td>
</tr>
<tr>
<td>• LVEF ≥50%</td>
<td>• LVEF ≥50%</td>
</tr>
</tbody>
</table>

ACC/AHA: American College of Cardiology/American Heart Association  
ESC: European Society of Cardiology
Is the problem categorization of LVEF?

LVEF is a continuous variable
LVEF distribution in CHARM

7,599 patients with NYHA class II-IV heart failure and no LVEF exclusion
Alternative approach?

Clinical syndrome (symptoms, signs) +

Elevated natriuretic peptides +

Structural/functional heart disease
CHARM-Programme: cause of death by LVEF

Proportion of deaths non-CV: 15% 18% 20% 21% 37%

Solomon et al Circ 2005
More fundamental problems?

- Method – echocardiography, RNVG, CMR (comparing echo and CMR, limits of agreement for LVEF -18.1% to 8.3%)
- Inter-observer variability (up to 15% with echo)
- Intra-observer variability (up to 10% with echo)
Variability around measurement of LVEF

Interobserver variability around echo measurement of LVEF

LVEF (%)

HFrEF | HFmrEF | HFpEF
More fundamental problems?

- Method – echocardiography, RNVG, CMR (*comparing echo and CMR, limits of agreement for LVEF -18.1% to 8.3*)
- Inter-observer variability (*up to 15% with echo*)
- Intra-observer variability (*up to 10% with echo*)
- A patient with “HFmrEF” could be categorized as any of the three HF phenotypes, depending on the imaging modality used. *The same patient could be assigned a diagnosis of HFrEF, HFmrEF or HFpEF within an hour if they were imaged by different individuals or by different modalities!*
What is a “normal” LVEF?

- Pooling of individual-person data from 43 globally representative, population-based, echocardiography studies (22,404 adults)
- Age-, sex- and racially/ethnically appropriate adult reference values for LVEF.
- Using the 5th percentile as the lower reference value, then “normal” in an older man of European ancestry is 50% and that in an older European woman 51% (these values are higher in Asian men and women).
Alternative nomenclature?

LVEF (%)

25 30 35 40 45 50 55 60

HFrEF  HFpEF  HFnEF

HFrEF  HFmrEF  HFpEF
What do we know about HFmrEF?

*Pubmed analysis 1/1/2014-5/5/2018*

((mid range[Title]) AND ((ejection[Title] OR systolic[Title]))) AND ((borderline[Title] OR grey area[Title]))

![Graph showing number of publications over time with ACC/AHA guideline and ESC guideline annotations.](image)
Some of the best article titles in recent memory!

**Beta-blockers for the treatment of heart failure with a mid-range ejection fraction: deja-vu all over again?**

*Heart failure with mid-range ejection fraction. Looking for Middle Earth?*

**Heart Failure With a Mid-Range Ejection Fraction**

*Culture and Cardiovascular Research; Cardiovascular Division and Division of Bone and Mineral Metabolism, Department of Medicine, Washington University School of Medicine, St Louis, MO, USA*

Milton Packer, MD

**Scompenso cardiaco con frazione di eiezione intermedia. Alla ricerca della Terra di Mezzo?**

*Heart failure with mid-range ejection fraction. Looking for Middle Earth?*
Existing trials which included “HFmrEF” patients
Effect of candesartan across the range of LVEF

Heart failure with mid-range ejection fraction in CHARM: characteristics, outcomes and effect of candesartan across the entire ejection fraction spectrum

Lars H. Lund¹*, Brian Claggett², Jiankang Liu², Carolyn S. Lam³, Pardeep S. Jhund⁴, Giuseppe M. Rosano⁵, Karl Swedberg⁶, Salim Yusuf⁷, Christopher B. Granger⁸, Marc A. Pfeffer², John J.V. McMurray⁴, and Scott D. Solomon²
### Baseline characteristics by HF phenotype

<table>
<thead>
<tr>
<th></th>
<th>HFrEF</th>
<th>HFmrEF</th>
<th>HFpEF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr.)</td>
<td>65</td>
<td>65</td>
<td>67</td>
</tr>
<tr>
<td>Female (%)</td>
<td>26</td>
<td>30</td>
<td>46</td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>30</td>
<td>44</td>
<td>58</td>
</tr>
<tr>
<td>Hx hypertension (%)</td>
<td>49</td>
<td>56</td>
<td>69</td>
</tr>
<tr>
<td>Hx MI (%)</td>
<td>58</td>
<td>58</td>
<td>37</td>
</tr>
<tr>
<td>AF (%)</td>
<td>26</td>
<td>26</td>
<td>31</td>
</tr>
<tr>
<td>DM (%)</td>
<td>29</td>
<td>29</td>
<td>28</td>
</tr>
</tbody>
</table>
Outcomes according to LVEF in CHARM

CV death or HF hospitalization

HF hospitalization

CV death
Effects of candesartan across the LVEF spectrum

CV death or HF hospitalization  HF hospitalization  CV death

- CV death or HF hospitalization
  - p for trend = 0.34
  - Overall p = 0.15

- HF hospitalization
  - p for trend = 0.53
  - Overall p = 0.14

- CV death
  - p for trend = 0.17
  - Overall p = 0.37
Existing trials which included “HFmrEF” patients

HFrEF  HFmrEF  HFpEF

CHARM-Preserved

DIG ancillary trial

LVEF (%) 25 30 35 40 45 50 55 60
Effect of digoxin in patients with heart failure and mid-range (borderline) left ventricular ejection fraction

Azmil H. Abdul-Rahim¹, Li Shen², Christopher J. Rush², Pardeep S. Jhund², Kennedy R. Lees², and John J.V. McMurray²*, on behalf of the VICCTA-Heart Failure Collaborators†

NB all patients in sinus rhythm
## Baseline characteristics by HF phenotype

<table>
<thead>
<tr>
<th></th>
<th>CHARM</th>
<th></th>
<th></th>
<th>DIG</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HFrEF</td>
<td>HFmrEF</td>
<td>HFpEF</td>
<td>HFrEF</td>
<td>HFmrEF</td>
<td>HFpEF</td>
</tr>
<tr>
<td>Age (yr.)</td>
<td>65</td>
<td>65</td>
<td>67</td>
<td>63</td>
<td>65</td>
<td>67</td>
</tr>
<tr>
<td>Female (%)</td>
<td>26</td>
<td>30</td>
<td>46</td>
<td>21</td>
<td>29</td>
<td>47</td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>30</td>
<td>44</td>
<td>58</td>
<td>26</td>
<td>43</td>
<td>59</td>
</tr>
<tr>
<td>Hx hypertension (%)</td>
<td>49</td>
<td>56</td>
<td>69</td>
<td>44</td>
<td>54</td>
<td>63</td>
</tr>
<tr>
<td>Hx MI (%)</td>
<td>58</td>
<td>58</td>
<td>37</td>
<td>65</td>
<td>63</td>
<td>45</td>
</tr>
<tr>
<td>AF (%)</td>
<td>26</td>
<td>26</td>
<td>31</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>DM (%)</td>
<td>29</td>
<td>29</td>
<td>28</td>
<td>28</td>
<td>30</td>
<td>29</td>
</tr>
</tbody>
</table>
Relationship between CV death or HF hospitalization and LVEF

**CHARM**

**HFmrEF**

**DIG**

**HFmrEF**
Effect of digoxin across the LVEF spectrum

HFmrEF

95%CI

Digoxin/placebo HR

HR = 1.0
Beta-blockers for heart failure with reduced, mid-range, and preserved ejection fraction: an individual patient-level analysis of double-blind randomized trials

John G.F. Cleland¹, Karina V. Bunting², Marcus D. Flather³, Douglas G. Altman⁴, Jane Holmes⁴, Andrew J.S. Coats⁵, Luis Manzano⁶, John J.V. McMurray⁷, Frank Ruschitzka⁸, Dirk J. van Veldhuisen⁹, Thomas G. von Lueder¹⁰,¹¹, Michael Böhm¹², Bert Andersson¹³, John Kjekshus¹⁴, Milton Packer¹⁵, Alan S. Rigby¹⁶, Giuseppe Rosano¹⁷,¹⁸, Hans Wedel¹⁹, Åke Hjalmarson¹³, John Wikstrand²⁰, and Dipak Kotecha²,¹¹*; on behalf of the Beta-blockers in Heart Failure Collaborative Group
Effect of beta-blockers across the LVEF spectrum
TOPCAT: Effects of spironolactone according to LVEF

European Heart Journal (2016) 37, 455–462
doi:10.1093/eurheartj/ehv464

Influence of ejection fraction on outcomes and efficacy of spironolactone in patients with heart failure with preserved ejection fraction

Scott D. Solomon¹*, Brian Claggett¹, Eldrin F. Lewis¹, Akshay Desai¹, Inder Anand², Nancy K. Sweitzer³, Eileen O’Meara⁴, Sanjiv J. Shah⁵, Sonja McKinlay⁶, Jerome L. Fleg⁷, George Sopko⁷, Bertram Pitt⁸ and Marc A. Pfeffer¹, for the TOPCAT Investigators
TOPCAT: Primary composite endpoint

![Graph showing treatment effect incidence rate ratio vs. ejection fraction](image-url)
Can we conclude anything?

- Not surprisingly, patients with HFmrEF have a clinical phenotype somewhere in between HFrEF and HFpEF (although more HFrEF than HFpEF?)
- The few data we have about treatment are in relatively small subgroups with few events
- The limited evidence we have suggests that there may be some (but attenuated) benefit of treatments that are effective in HFrEF in patients with HFmrEF.
- My personal take home message is give patients with a borderline LVEF “the benefit of the doubt” when considering treatment (N.B. remember variability in LVEF measurement).
Where next? Back to the future??

- HFrEF
- HFmrEF
- HFpEF
- EMPEROR-Reduced
- EMPEROR-Preserved
- PARAGON-HF
- I-Preserve
- CHARM-Preserved
- DIG ancillary trial

*ongoing trials
Optimization of Heart Failure Care with all Ejection Fractions

Karen Harkness, RN, PhD, CCN(C), CHFN-K
Clinical Lead, Cardiac Care Network
Assistant Clinical Professor, McMaster University
Nurse Clinician, Heart Function Clinic
Hamilton, ON
Objectives

- Highlight continuing high risk following unstable heart failure
- Discuss strategies to optimize heart failure care for all patients
- Provide practical tips to ensure your patient can stay out of hospital
The Heart Failure Cycle

Acute Heart Failure → Hospitalization → End-of-life Planning → Death → Hospital discharge → Clinical stability → Clinical instability → Acute Heart Failure
Going home…. and coming back!

30-day readmission rate in Canada- 18.1%

Retrospective study:
Admitted to hospital with primary diagnosis of HF and discharged alive (9 Provinces)
n=217,039 patients
Mean age: 76.8 years
Male: 50%

McAlister et al., J Am Heart Assoc, 2017
### Characteristics of well-executed transitions

<table>
<thead>
<tr>
<th>Characteristic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Early discharge planning</td>
</tr>
<tr>
<td>Interprofessional communication and collaboration, and standardized handoff procedures</td>
</tr>
<tr>
<td>Timely, clear, and organized information</td>
</tr>
<tr>
<td>Medication reconciliation</td>
</tr>
<tr>
<td>Engagement of community support groups</td>
</tr>
<tr>
<td>Self-care coaching on monitoring and managing heart failure signs and symptoms after discharge</td>
</tr>
<tr>
<td>Early and intense follow-up, including home visits and structured telephone support</td>
</tr>
<tr>
<td>Advance care planning</td>
</tr>
</tbody>
</table>

Heckman et al., Curr Opin Cardiol 2018
Characteristics of well-executed transitions

<table>
<thead>
<tr>
<th>Early discharge planning</th>
</tr>
</thead>
<tbody>
<tr>
<td>Interprofessional communication and collaboration, and standardized handoff procedures</td>
</tr>
<tr>
<td>Timely, clear, and organized information</td>
</tr>
<tr>
<td>Medication reconciliation</td>
</tr>
<tr>
<td>Engagement of community support groups</td>
</tr>
<tr>
<td><strong>Self-care coaching on monitoring and managing heart failure signs and symptoms after discharge</strong></td>
</tr>
<tr>
<td>Early and intense follow-up, including home visits and structured telephone support</td>
</tr>
<tr>
<td>Advance care planning</td>
</tr>
</tbody>
</table>

Heckman et al., Curr Opin Cardiol 2018
Self-care in Heart Failure

- **Symptom Perception**: What are my symptoms of heart failure and are they different from my usual pattern?
- **Management**: What do I need to do about my symptoms when they are changing?
- **Maintenance**: What do I do to help feel well and help prevent my heart failure from getting worse?

Self care maintenance
RECOMMENDATION

74. We suggest daily morning weight should be monitored in patients with HF with fluid retention or congestion that is not easily controlled with diuretics, or in patients with significant renal dysfunction (Weak Recommendation; Low-Quality Evidence).

**Practical tip.** Weight should be closely monitored for unstable or frail patients. Any rapid weight gain (ie, > 1.5 or 2 kg) should prompt a rapid medical visit. Weight loss should also be addressed medically.
75. We suggest that restriction of daily fluid intake to approximately 2 L/d should be considered for patients with fluid retention or congestion that is not easily controlled with diuretics (Weak Recommendation; Low-Quality Evidence).

**Practical tip.** The appropriate quantity of fluid intake is a subject of debate. Strict limits should be imposed when there is clear fluid overload or demonstrated sensitivity to fluid intake.

**Practical tip.** Severely limiting daily fluid intake to < 1.5 L might have adverse consequences on nutrition, renal function, and quality of life without known additional benefit and should be applied selectively.

**Practical tip.** Special consideration for hyponatremic patients should be applied.
RECOMMENDATION

73. We suggest that patients with HF should restrict their dietary salt intake to between 2 g/d and 3 g/d (Weak Recommendation; Low-Quality Evidence).

Practical tip. The optimal quantity of salt in the diet is still a subject of debate. The amount should be adapted to the clinical situation, the severity of symptoms, and baseline consumption without interfering with other nutritional content.
RECOMMENDATION

71. We recommend regular exercise to improve exercise capacity, symptoms, and quality of life in all HF patients (Strong Recommendation; Moderate-Quality Evidence).

72. We recommend regular exercise in HF patients with reduced EF to decrease hospital admissions (Strong Recommendation; Moderate-Quality Evidence).

Values and Preferences. These recommendations have placed a high value on regular exercise and not emphasized structured exercise training because it is recognized that not all patients will be able to participate in a structured exercise training program because of patient preferences or availability of resources.
Medication Adherence

• Based on your experience, what proportion of patients do you think are adherent to taking medications as prescribed?
  (Adherent- taking the medication as prescribed at least 80% of the time)
  
  <50%
  50%
  60%
  70%
  80%
  90%
Medication Adherence

Based on your experience, what proportion of patients do you think are adherent to taking medications as prescribed?

(Adherent- taking the medication as prescribed at least 80% of the time)

- <50%
  USA- discharged with HF Apr 2006-Oct 2012, Age 65+ years, n=9878
- 50%
  At 90 days, medication adherence:
  Beta Blocker 58%
- 60%
  ACE/ARB 48%
- 70%
  MRA 48%
- 80%
  1 year (n= 6615)
  Beta Blocker 53%
- 90%
  ACE/ARB 48%
  MRA 36%

Chang et al, J Am Heart Assoc, 2018 Epub
<table>
<thead>
<tr>
<th>Problem</th>
<th>Patient indicated for a treatment who</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lack of treatment</td>
<td>Is not receiving the treatment</td>
</tr>
<tr>
<td>Suboptimal treatment</td>
<td>Is receiving the wrong medication</td>
</tr>
<tr>
<td>Undertreatment</td>
<td>Is receiving a subtherapeutic dose</td>
</tr>
<tr>
<td>Inaccessible treatment</td>
<td>Is unable to obtain medication</td>
</tr>
<tr>
<td>Overdose</td>
<td>Is receiving a toxic dose</td>
</tr>
<tr>
<td>Adverse reaction to treatment</td>
<td>Is receiving an indicated dose and experiences treatment-related side effects</td>
</tr>
<tr>
<td>Drug interaction</td>
<td>Is receiving an indicated dose and experiences side effects due to interactions with other treatments or dietary components</td>
</tr>
<tr>
<td>Off-label use</td>
<td>Has no FDA-approved indication for the treatment being used</td>
</tr>
</tbody>
</table>

Table 1 Common drug-related problems in patients with heart failure. Reprinted from Journal of Cardiac Failure, 19(5), Milfred-LaForest SK et al. Clinical pharmacy services in heart failure: an opinion paper from the Heart Failure Society of America and American College of Clinical Pharmacy Cardiology Practice and Research Network, 354–369, Copyright (2013), with permission from Elsevier [5]

Andersonand Marrs. Adv Ther 2018
What are my early HF symptoms

Was that a good decision? Do I feel better?

Do I have any early HF symptoms today?

I wonder why my symptoms changed?

What should I do?

Do I need to do anything about my symptoms?

Self care monitoring & management
Symptom Perception and Interpretation - tips

- Personalize Signs and Symptoms - How do you know if you are starting to retain fluid?
- Expect a large variety of vague descriptions from patients/family caregivers.
- Help clarify signs and symptoms that are probably not related to HF.
- Story telling – ‘tell me about…a typical day… the last week…. highlight signs or symptoms that reflect HF decompensation (e.g. what did you feel like just prior to hospitalization?)
- Repeat reinforcement is often necessary
Beyond knowledge..

CCS guidelines
The 2012 Canadian Cardiovascular Society Heart Failure Management Guidelines Update: Focus on Acute and Chronic Heart Failure

Health care professionals

How do we apply to our patients?
Case studies/scenarios

Patient education materials

Patients and caregivers

How do we apply to our patients?
Explore examples/plan ahead

Health care professionals

How do we apply to our daily life/routines?
## Factors Affecting Self-Care

<table>
<thead>
<tr>
<th>Domain</th>
<th>Tips</th>
</tr>
</thead>
<tbody>
<tr>
<td>Confidence</td>
<td>- Self-care confidence is critical to a patient’s management of their heart failure.</td>
</tr>
<tr>
<td></td>
<td>• Counselling to recognize benefits and overcome barriers of self-care</td>
</tr>
<tr>
<td></td>
<td>• Reinforcing positive behaviours</td>
</tr>
<tr>
<td></td>
<td>• Setting mutual and realistic goals</td>
</tr>
<tr>
<td></td>
<td>• Celebrating successes</td>
</tr>
<tr>
<td>Cognitive status</td>
<td>- Subtle cognitive deficits often go undetected but can interfere with learning and problem solving</td>
</tr>
<tr>
<td></td>
<td>• Consider screening for mild cognitive impairment in patients with ongoing challenges with engaging in self-care</td>
</tr>
<tr>
<td></td>
<td>• Consider underlying subtle delirium if you notice trouble with attention (e.g. infection, recent ETOH, side effects from medications)</td>
</tr>
</tbody>
</table>

Howlett et al., CCS Heart Failure Companion, 2016
MoCA Test Examples

Case 1- 65 year old male, NYHA III, EF 15%, Total MoCA 15. Lots of confusion with appts.

Case 2- 69 year old male, NYHA II, EF 40, Total MoCA 18 (wife manages pills)

Case 3- 78 year old male, NYHA III, EF 30, Total MoCA 23. Primary caregiver for his wife.

Case 4- 84 year old male, NYHA III, EF 20, Total MoCA 19. Wife manages care.
Factors Affecting Self-Care

<table>
<thead>
<tr>
<th>Domain</th>
<th>Description</th>
<th>Tips</th>
</tr>
</thead>
</table>
| Emotional Status | Symptoms such as anxiety and depression can have a negative impact on engaging in self-care. | • Counselling to recognize benefits and overcome barriers of self-care  
• Reinforcing positive behaviours  
• Setting mutual and realistic goals  
• Celebrating successes |

“Considering how I used to be and now…that has change drastically…..I find it very hard sometimes to deal with it…it’s very emotional. This morning after I got into the office for a while I just, uh, cried a little bit, a sense of hopelessness….I’m not capable of doing the walking that I used to…I fell a sense of inadequacy…Sometimes you just get fed up and think that was a day I just had a real down spiraling. I just ate what I wanted. I put salt on everything and I didn’t care”

Harkness et al., J CV Nurs, 2016
### Factors Affecting Self-Care

<table>
<thead>
<tr>
<th>Domain</th>
<th>Description</th>
<th>Tips</th>
</tr>
</thead>
</table>
| Learning environment    | Patients need a safe environment (e.g. not punitive) to explore real or potential situations where self-care is difficult. Patients may experience many difficulties despite deliberate attempts to make healthy choices. | • Creative problem-solving, cognitive behavioural strategies and mutual goal setting are necessary.  
• Let patients know that others have difficulties and encourage them to share concerns or problems.  
• Repeat reinforcement is often necessary. |

*Howlett et al., CCS Heart Failure Companion, 2016

“They told me not to have any canned foods, no canned soups and no lunch meats…. I didn’t have any canned foods and lunch meats. I had pizza and hot wings and Pepsi Cola.*

*Riegel et al., 2007 in Spaling et al. JAN, 2015*
## Factors Affecting Self-Care

<table>
<thead>
<tr>
<th>Domain</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Caregivers</td>
<td>Caregivers often provide a substantial amount of support for patients and need to be seen as partners in the overall care plan. Their contribution cannot be underestimated.</td>
</tr>
<tr>
<td></td>
<td>Be mindful of caregiver burden.</td>
</tr>
</tbody>
</table>

Howlett et al., CCS Heart Failure Companion, 2016  
Buck et al., Eur J Cardiovasc Nurs, 2014
“The relationship”

“People don't care how much you know until they know how much you care”

Theodore Roosevelt

“They listen... like my input... I feel so much better. They don’t argue with me... respect me as a person. That is really, really important to me... they are interested in me”

Currie et al., Eur J Cardiovasc Nurs, 2014
Summary

• Regardless of ejection fraction, optimizing care for people living with heart failure must include self-care support for patients.

• Patients regard self-care within a process of adaptation that strives to maintain independence and quality of life.

• Self-care is a skill- it is not always easy and requires practice and learning over time.
 QUESTIONS?

Please fill out the evaluation form by texting EVALUATION to (647) 696-5222
THANK YOU!

Please fill out the evaluation form by texting EVALUATION to (647) 696-5222

Co-presented by