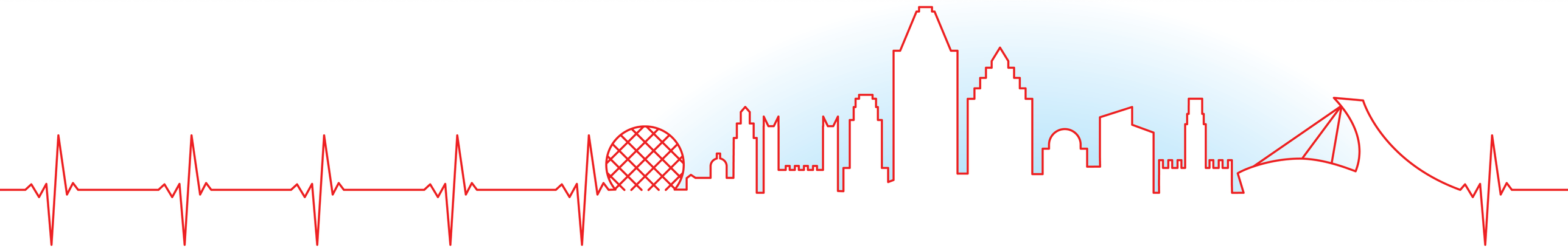

HEART FAILURE UPDATE 2019

CHFS SCIC

Canadian Heart Failure Society
Société canadienne d'insuffisance cardiaque

HOW AND WHEN TO STOP CARDIAC MEDICATIONS IN YOUR HEART FAILURE PATIENTS

Is there ever a time?

May 10, 2019

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Clinical Associate Professor UBC

Disclosures

- **Grants/research support**: Boehringer-Ingelheim
- **Speaker or Consulting fees**: Boehringer-Ingelheim, Eli Lilly, Novartis, Servier, Akea Therapeutics
- **No conflict with respect to the current topic**

Objectives

How and when to stop cardiac medications in your heart failure patients

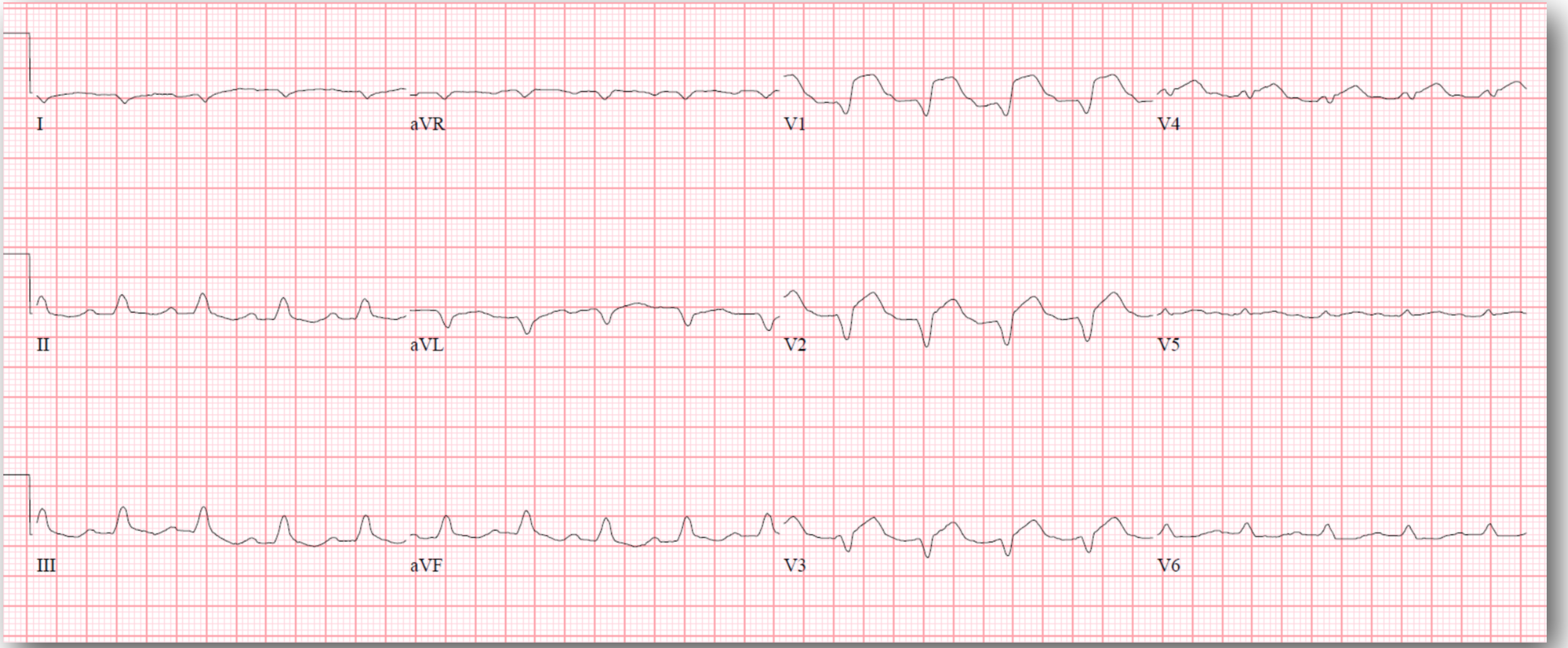
Elizabeth Swiggum, MD

After this workshop, participants will be able to:

1. Understand the implications for withdrawal of evidence-based therapy in patients with recovered ejection fraction
2. Identify clinical scenarios where withdrawal of therapy is likely to be safe
3. Formulate a practical approach to discussing medical withdrawal with HF patients

Case1 WL

- 49 Female Jan 2010
  - 2 d fever, chills, NV, RUQ pain
  - Cardiogenic shock
  - VT
- ECG STE ANT
  - Trop elevated
- Echo LVEF 15-20% (biventricular)
- Angiogram Normal coronaries
  - EMBx performed
    - **Lymphocytic myocarditis**
- ECMO
  - emboli to leg
  - fasciotomy
- transfer to higher level of care
  - Heart Mate II LVAD
    - GI bleed
    - Acute renal injury


I
aVR
V1
V4
II
aVL
V2
V5
III
aVF
V3
V6

Case WL 6 mo later

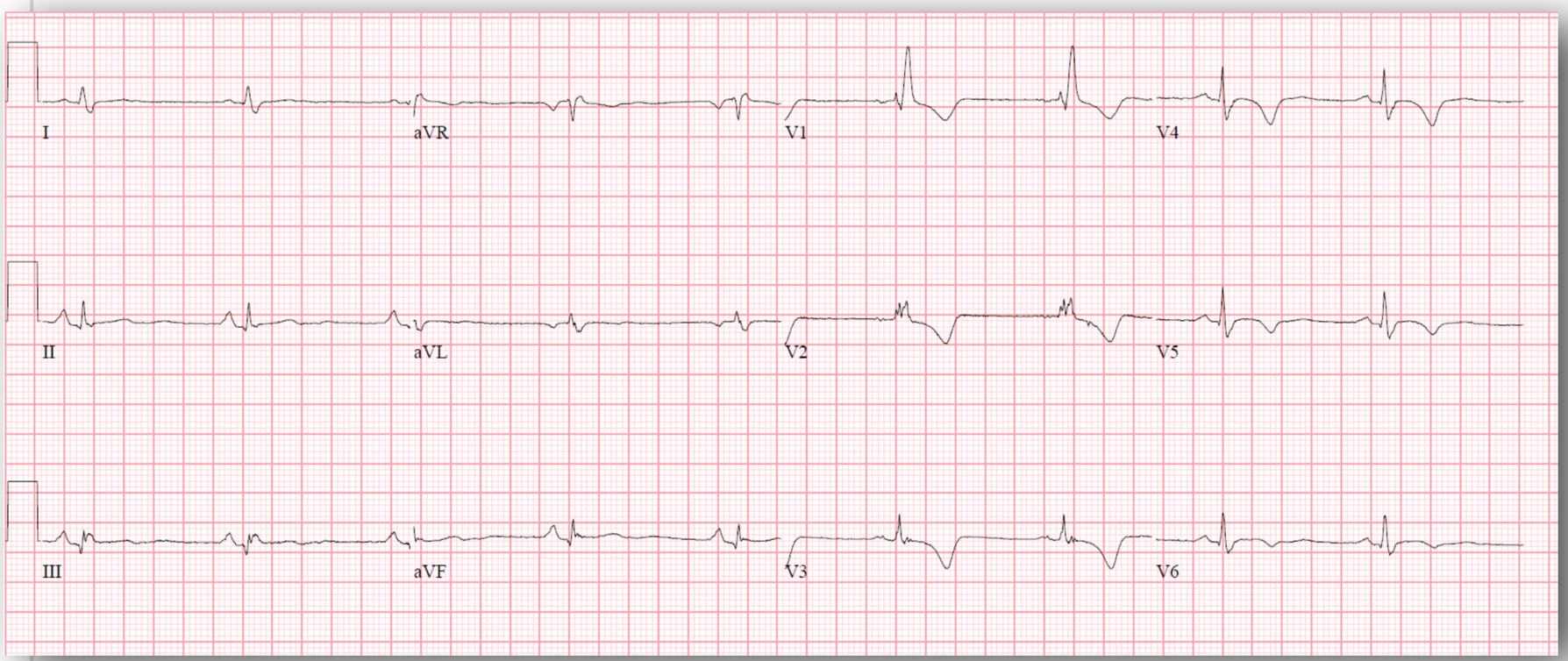
- Referred to home HFC
- Echo VAD insitu
  - April 2010 EF 70%
- Post Explant VAD 1 mo
  - June 2010 EF 60%

- Physical
  - 110/60, HR 60 Sinus
  - JVP +3cm ASA

- **Medications**
  - **Carvedilol 6.25 mg BID**
  - Esomeprazole 40 mg OD
  - Trazodone 100 qhs
  - Calcium 500 mg TID
  - Ferrous gluconate 600 mg qhs
  - Colace 200 mg daily
  - Immune 7 BID
  - Zinc 50 mg daily

Case WL 6 mo later

- NYHA I-II
  - Trainer 1 hr per day
- **<u>Laboratory</u>**
  - NT proBNP 2025 pg/mL (14,004)
  - eGFR 54



WHERE DO WE GO FROM HERE?

Where do we go from here?

- Increase guideline directed medication
- Reduce medication
  - which ones?
- Surveillance of heart function

Canadian Journal of Cardiology 33 (2017) 1342–1433

Society Guidelines

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

Primary Panel: Justin A. Ezekowitz, MBBCh (Chair),[a] Eileen O'Meara, MD (Co-chair),[b] Michael A. McDonald, MD,[c] Howard Abrams, MD,[c] Michael Chan, MBBS,[d]

Table 12. Potential scenarios in which evidence-based medical therapy for heart failure might be withdrawn

Clinical presentation	Conditions to justify stepwise withdrawal of GDMT after 6-12 months of full medical therapy	Comments
Tachycardia-related CM	• Normal EF and LV volumes • NYHA I • Underlying tachycardia controlled	Usually due to atrial fibrillation/flutter with increased HR, might rarely occur because of PVCs. Might need long-term BB for rate control
Alcoholic CM	• Normal EF and LV volumes • NYHA I • Abstinence ETOH	Nutritional deficiency, obesity, and obstructive sleep apnea might coexist and require therapy
Chemotherapy-related CM	• Normal EF and LV volumes • NYHA I • No further drug exposure	Certain types of chemotherapy are more likely to reverse than others (trastuzumab—high rate of LVEF improvement when it is discontinued whereas patients who received anthracyclines should continue LV enhancement therapy) Long-term surveillance strongly recommended
Peripartum CM	• Normal EF and LV volumes • NYHA I	Repeat pregnancy might be possible for some. Consultation at high-risk maternal centre should be undertaken
Valve replacement surgery	• Normal EF and LV volumes • NYHA I • Normally functioning valve	Less consensus on regurgitant lesions with ongoing dilation of LV

Withdrawal of pharmacological treatment for heart failure in patients with recovered dilated cardiomyopathy (TRED-HF): an open-label, pilot, randomised trial

Brian P Halliday, Rebecca Wassall, Amrit S Lota, Zohya Khalique, John Gregson, Simon Newsome, Robert Jackson, Tsveta Rahneva, Rick Wage, Gillian Smith, Lucia Venneri, Upasana Tayal, Dominique Auger, William Midwinter, Nicola Whiffin, Ronak Rajani, Jason N Dungu, Antonis Pantazis, Stuart A Cook, James S Ware, A John Baksi, Dudley J Pennell, Stuart D Rosen, Martin R Cowie, John G F Cleland, Sanjay K Prasad

Summary

Background Patients with dilated cardiomyopathy whose symptoms and cardiac function have recovered often ask whether their medications can be stopped. The safety of withdrawing treatment in this situation is unknown.

Lancet 2019; 393: 61–73

Published Online

The Lancet
Volume 393, Issue 10166, Pages 61-73 (January 2019)

Withdrawal of pharmacologic therapy in patients with dilated CMO

- 51 patients randomized open label trial
  - stepwise withdrawal
  - continued therapy
    - single X-over at 6 mo for withdrawal

6 mo follow up

- Inclusion
  - Prior CMO LVEF <40%
  - Asymptomatic on therapy
  - Current LVEF >50%
    - Normal LVEDVi
  - NT proBNP <250 ng/L

1º Brian Halliday, senior author Sanjay Prasad Bromptom Hospital, London

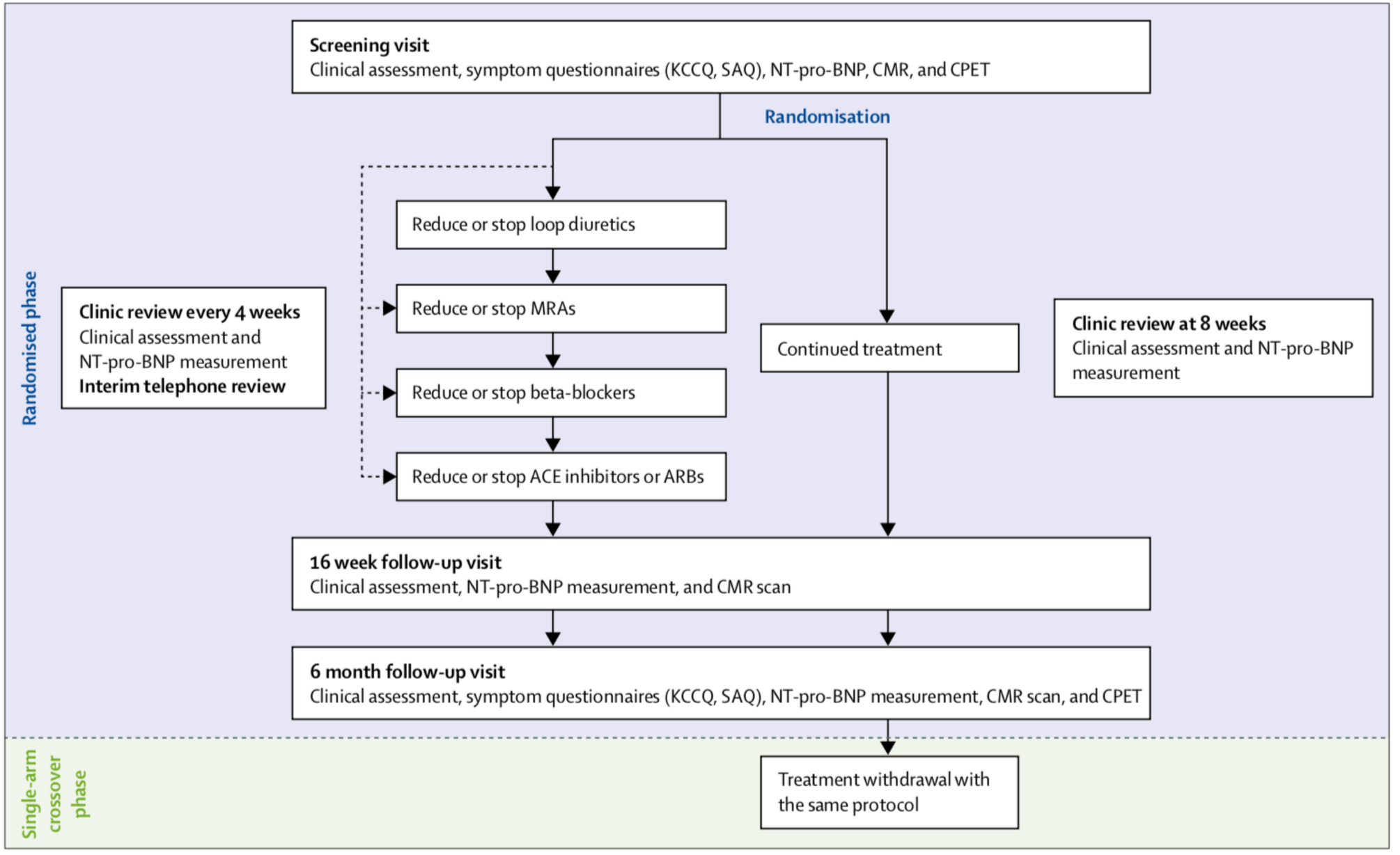


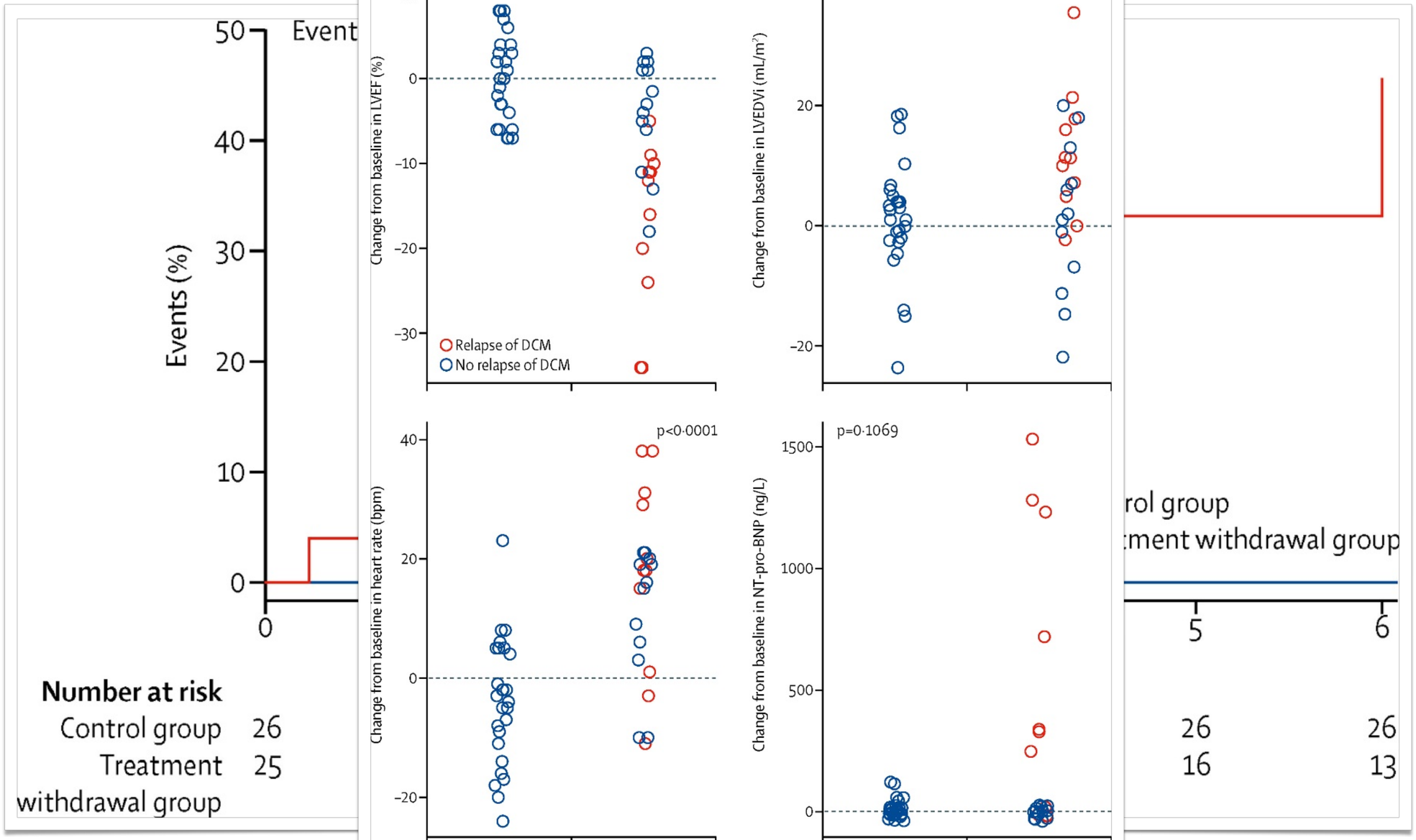
Figure 1: **Flowchart of TRED-HF study design**

Withdrawal of pharmacologic therapy in patients with dilated CMO

Endpoint measure

Relapse of dilated CMO

- LVEF worse by 10% and <50%
- LVEDV increase by 10%
- 2X rise in NT-pro BNP and >400 ng/L
- Clinical HF


Event
50
40
30
20
10
0
Events (%)
0
Number at risk
Control group 26
Treatment withdrawal group 25
rol group
tment withdrawal group
5
6
26
26
16
13
p=0·0001
Change from baseline in LVEF (%)
10
0
−10
−20
−30
Relapse of DCM
No relapse of DCM
p=0·1361
Change from baseline in LVEDVi (mL/m²)
40
20
0
−20
p<0·0001
Change from baseline in heart rate (bpm)
40
20
0
−20
Control
Treatment withdrawal
Treatment group
p=0·1069
Change from baseline in NT-pro-BNP (ng/L)
1500
1000
500
0
Control
Treatment withdrawal
Treatment group

Lessons from TRED HF

- 40% had relapse within 6 mo of medication withdrawal
  - majority had deterioration within 16 weeks

- 50% of patients had successful medication withdrawal
  - is 6 mo long enough?

Lessons from TRED HF

- Recovery ≠ Cure
- But does it mean Remission?

How does this apply to my patient?

Case WL 7 yr later

- Periodic follow up in HFC
- Echo EF 50-55%
  - apical aneurysm from VAD

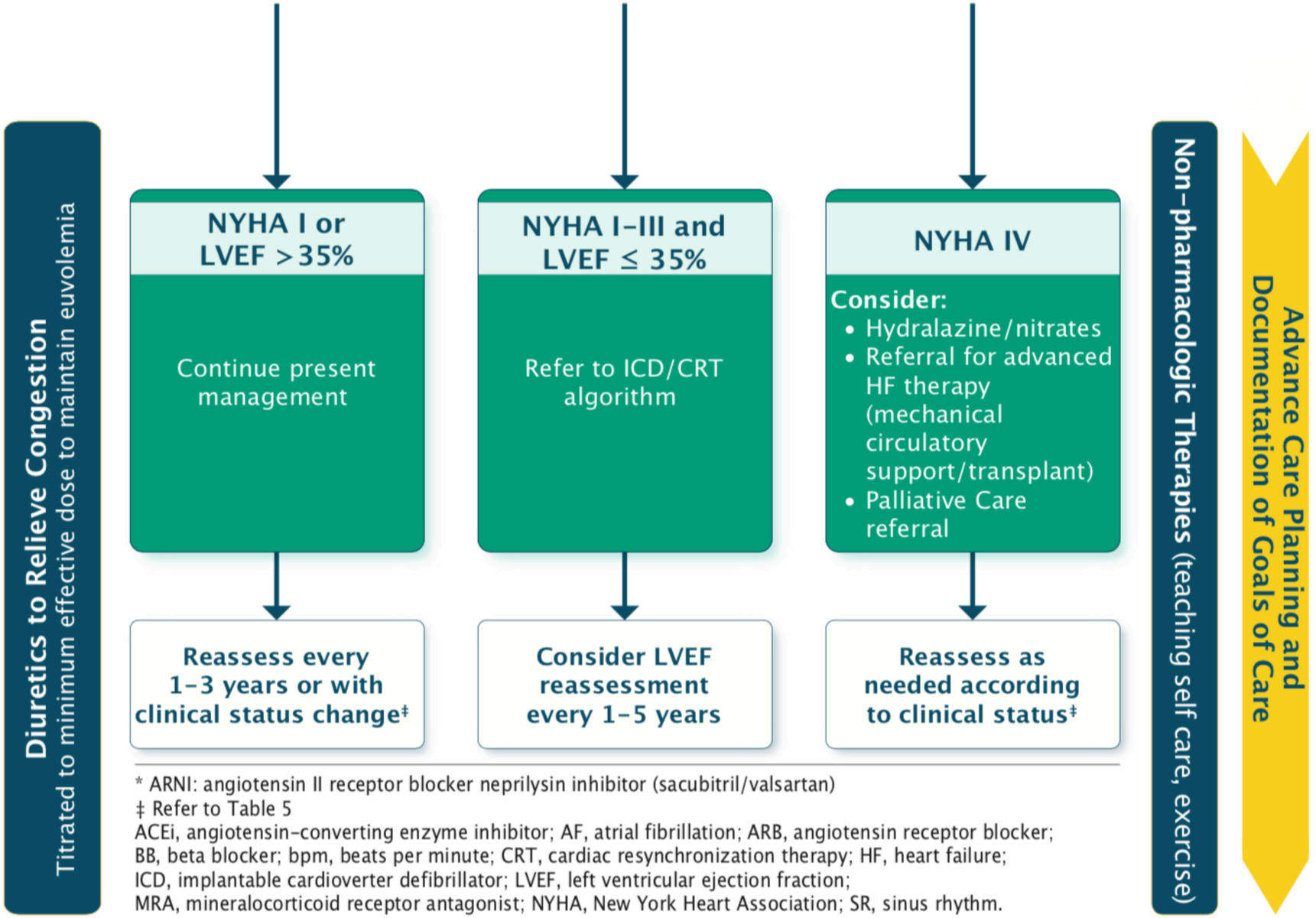
- Physical
  - 102/59, HR 66 Sinus
  - JVP ASA
  - wide split 2nd HS

- **<u>Medications</u>**
  - Cipralex 20 mg
  - Trazodone 25 qhs

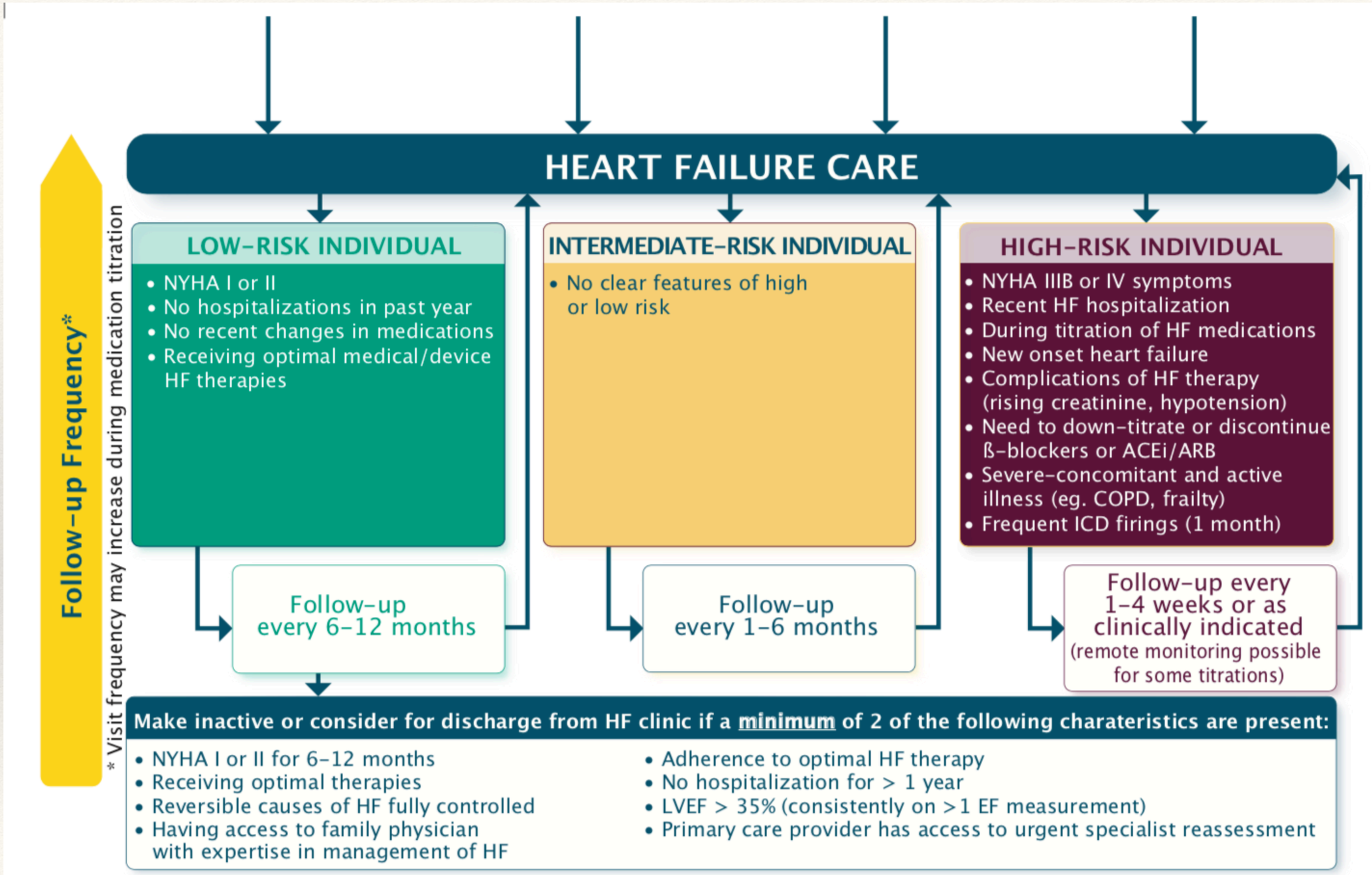
eGFR 47

NT proBNP 386 pg/mL

What would you recommend for surveillance?



* ARNI: angiotensin II receptor blocker neprilysin inhibitor (sacubitril/valsartan)
‡ Refer to Table 5
ACEi, angiotensin-converting enzyme inhibitor; AF, atrial fibrillation; ARB, angiotensin receptor blocker; BB, beta blocker; bpm, beats per minute; CRT, cardiac resynchronization therapy; HF, heart failure; ICD, implantable cardioverter defibrillator; LVEF, left ventricular ejection fraction; MRA, mineralocorticoid receptor antagonist; NYHA, New York Heart Association; SR, sinus rhythm.


HEART FAILURE CARE
Follow-up Frequency*
* Visit frequency may increase during medication titration
LOW-RISK INDIVIDUAL
• NYHA I or II
• No hospitalizations in past year
• No recent changes in medications
• Receiving optimal medical/device HF therapies
INTERMEDIATE-RISK INDIVIDUAL
• No clear features of high or low risk
HIGH-RISK INDIVIDUAL
• NYHA IIIB or IV symptoms
• Recent HF hospitalization
• During titration of HF medications
• New onset heart failure
• Complications of HF therapy (rising creatinine, hypotension)
• Need to down-titrate or discontinue ß-blockers or ACEi/ARB
• Severe-concomitant and active illness (eg. COPD, frailty)
• Frequent ICD firings (1 month)
Follow-up every 6-12 months
Follow-up every 1-6 months
Follow-up every 1-4 weeks or as clinically indicated (remote monitoring possible for some titrations)
Make inactive or consider for discharge from HF clinic if a minimum of 2 of the following charateristics are present:
• NYHA I or II for 6-12 months
• Receiving optimal therapies
• Reversible causes of HF fully controlled
• Having access to family physician with expertise in management of HF
• Adherence to optimal HF therapy
• No hospitalization for > 1 year
• LVEF > 35% (consistently on >1 EF measurement)
• Primary care provider has access to urgent specialist reassessment

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Peripartum CM	• Normal EF and LV volumes • NYHA I	Repeat pregnancy might be possible for some. Consultation at high-risk maternal centre should be undertaken
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>80g per day for 5 yr or longer
>6 drinks per day

141 patients ACM
716 DCM
445 controls

CENTRAL ILLUSTRATION: Alcohol Consumption and Genetic Background Act in Concert to Determine Cardiac Phenotype

ALCOHOL + GENETICS

PHENOTYPE

Alcoholic Cardiomyopathy (ACM)	Dilated Cardiomyopathy (DCM)
Prevalence of rare genetic variants in cardiomyopathy genes: ACM: 13.5% Controls: 2.9% $P_{Fisher} = 0.000012$	LVEF according to titin truncating variant (TTNtv) status and alcohol intake: no TTNtv or excess alcohol intake: 39.6 ± 12.2% TTNtv only: 39.8 ± 13.2% excess alcohol intake only: 37.8 ± 11.8% TTNtv AND excess alcohol intake: 27.7 ± 12.7% $P_{Multivariate} = 0.007$

Ware, J.S. et al. J Am Coll Cardiol. 2018;71(20):2293-302.

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Case 2 SL

- 2005 woman 25 y.o.
- Right Breast CA - ductal carcinoma
  - ER+, PR+, Her/neu+
  - Excision, CEF x 6, radiation
  - Herceptin x 9 weeks
- EF 33%
- Herceptin discontinued
  - Ramipril
  - Bisoprolol
- LVEF 55%

Case SL Can I Stop my cardiac medications?

- 2007 woman 27 y.o.
- REALLY???
  - Well…ok let’s try one

- Bisoprolol weaned off EF dropped within 3mo
  - Ramipril
  - Bisoprolol
- LVEF 55%

Case SL Doctor I’m pregnant…with twins

- 2009 woman 29 y.o.
- REALLY???
  - Well…ok let’s not panic
  - Ramipril stopped
  - Tamoxifen stopped
  - Fetal screening
    - Everyone was ok
- Medications
  - NTG/Hydralazine
  - Bisoprolol
- LVEF 40-45%
- Returned to usual Rx post delivery
- LVEF 50%

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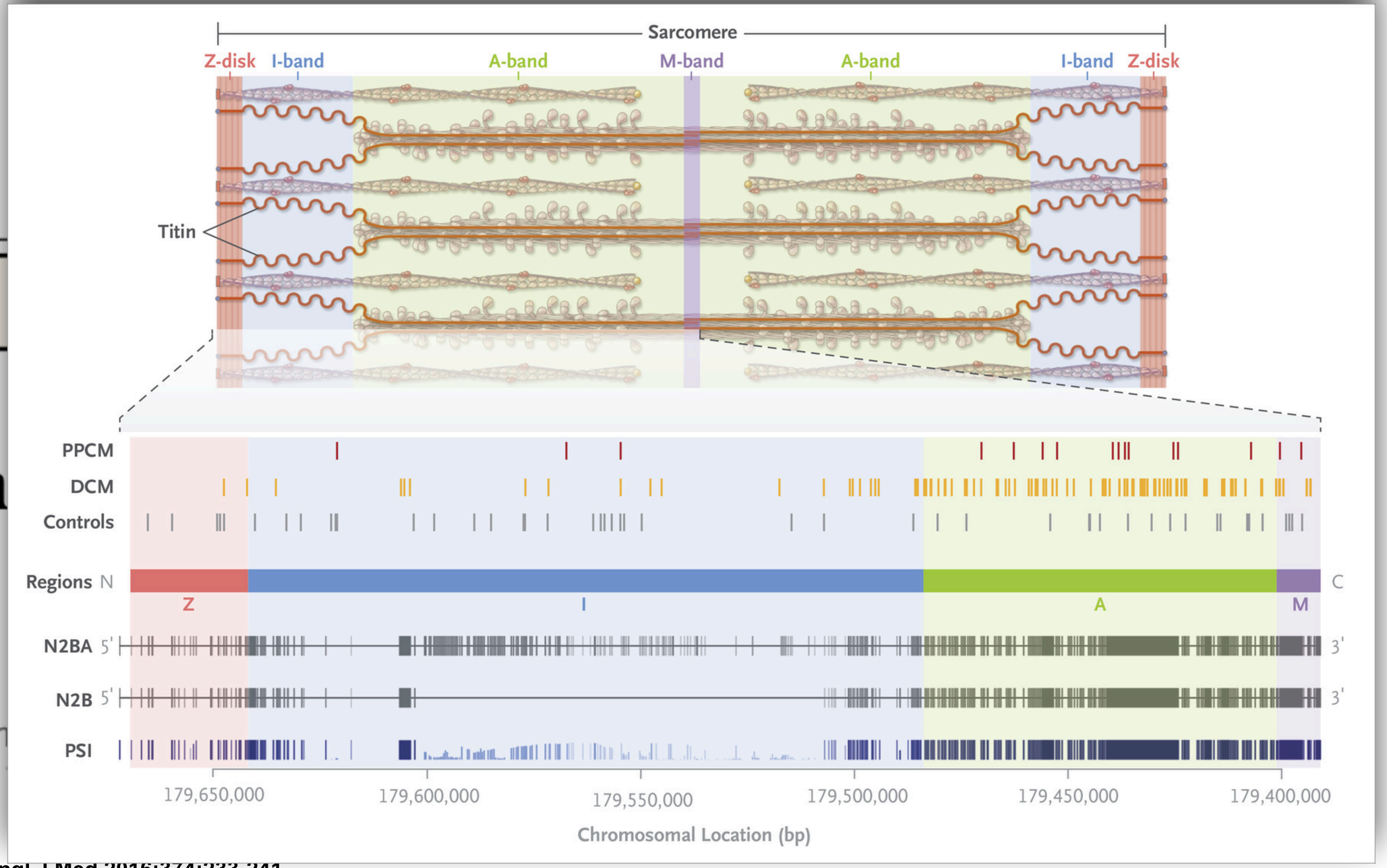


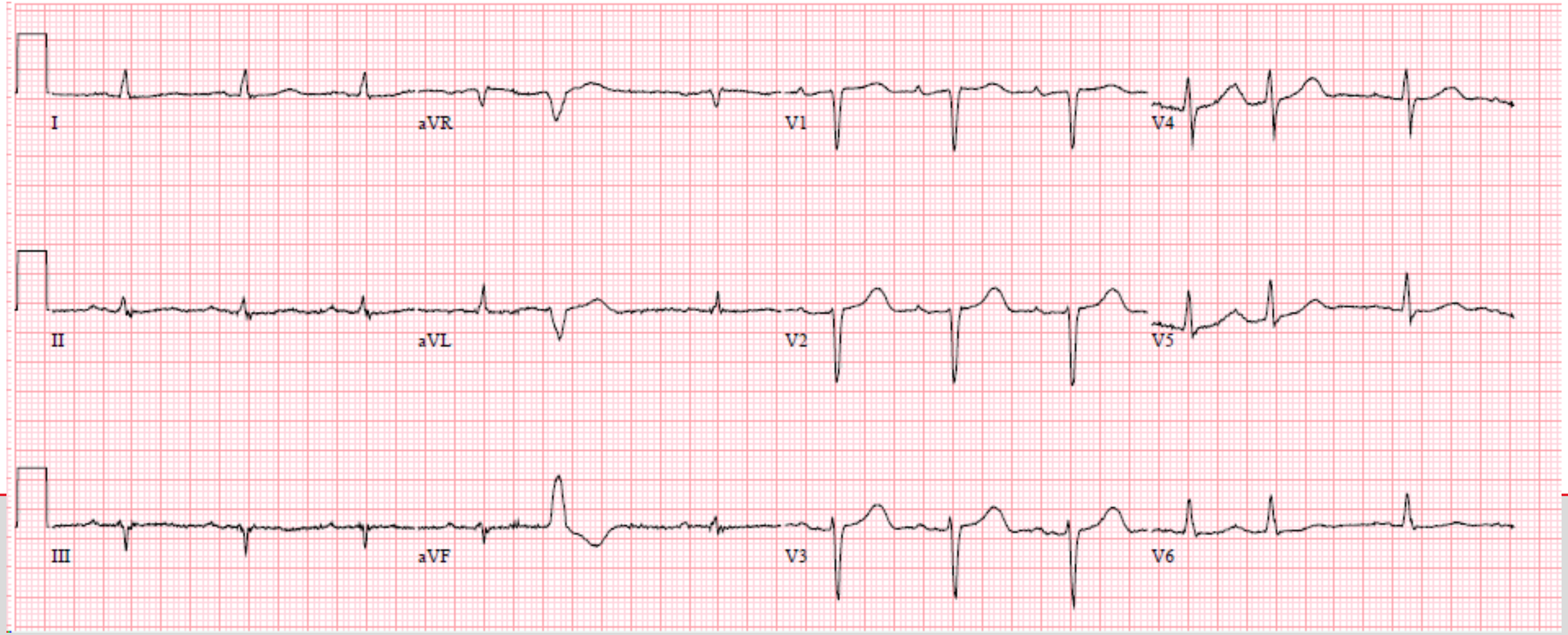
Ware JS et al. N Engl J Med 2016;374:233-241

THERE IS A PLACE AND TIME

Mr. Tu Lo

Mr. P. Lee Yate

Case 3 Tu Lo 2016



Tu Lo 2017

- RHC and biopsy 2016
  - wt ATTR CA

- Medications
  - nebivolol
  - Ramipril 1.25
  - furosemide 120 mg BID
  - amiodarone
  - apixaban
  - rosuvastatin

Tu Lo 2017

- He tells you he is fatigued and dizzy upon standing

- Should the medications be adjusted?

- Medications
  - nebivolol
  - Ramipril 1.25
  - furosemide 120 mg BID
  - amiodarone
  - apixaban
  - rosuvastatin

Tu Lo 2017

- He tells you he is fatigued and dizzy upon standing
- Should the medications be adjusted?

- Medications
  - spironolactone 12.5 mg daily
  - furosemide 80 mg BID
  - amiodarone
  - apixaban renal dose
  - rosuvastatin

LAST CASE

Case 4 Mr. P. Lee Yate

- 74 y.o male
- MI, CABG age 43
  - EF 35% RV impaired
- Afib, prior stroke
- PVD, CVD
- CKD eGFR 18
  - MPO vasculitis
- Bladder CA
- T2DM

- NYHA IV
- Abdominal ascites
  - poor appetite
- BP 137/57, HR 61
- JVP mandible in sitting position

Mr. P. Lee Yate

- Medications
- NTG patch 0.4 mg
- Hydralazine 50 mg TID
- Amlodipine 10 mg
- Furosemide 80-120 mg BID
- Metalozone
- spironolactone 12.5 mg daily
- Atorvastatin 20 mg daily
- ASA 81 mg
- Insulin
- Pantoprazole 40 mg
- Azathioprine 12.5 mg daily
- Alpha calcidiol 0.25 mug MWF
- Ferrous fumarate 300 mg qhs
- hydromorphone 1-3 mg daily pen

Can we deprescribe anything?

Mr. P. Lee Yate

- Medications
- NTG patch 0.4 mg
- Hydralazine 50 mg TID
- Amlodipine 10 mg
- Furosemide 80-120 mg BID
- Metalozone
- spironolactone 12.5 mg daily
- **Atorvastatin 20 mg daily**
- ASA 81 mg
- **Insulin**
- Pantoprazole 40 mg
- **Azathioprine 12.5 mg daily**
- **Alpha calcidiol 0.25 mug MWF**
- **Ferrous fumarate 300 mg qhs**
- hydromorphone 1-3 mg daily pen
-

Can we deprescribe anything? Not on a beta blocker…

What if your patient has symptomatic hypotension?

Mr. P. Lee Yate with symptomatic hypotension

- Medications
- NTG patch 0.4 mg
- **Hydralazine 50 mg TID**
- **Amlodipine 10 mg**
- Furosemide 80-120 mg BID
- Metalozone
- spironolactone 12.5 mg daily
- **Atorvastatin 20 mg daily**
- ASA 81 mg
- **Insulin**
- Pantoprazole 40 mg
- **Azathioprine 12.5 mg daily**
- **Alpha calcidiol 0.25 mug MWF**
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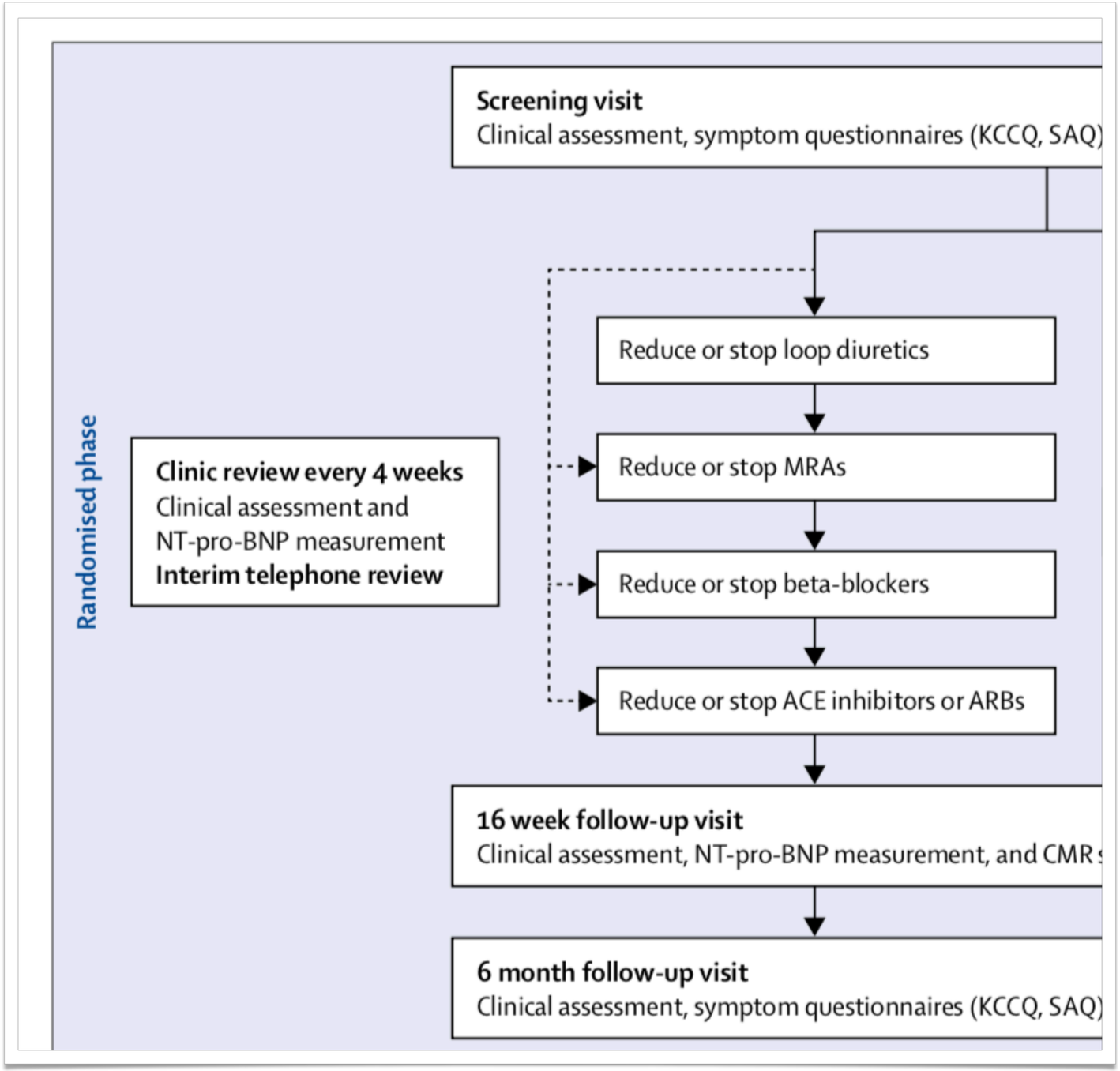
- hydromorphone 1-3 mg daily pen
-

Can we deprescribe anything?

PRACTICAL DEPRESCRIBING



Commitment to the patient

Wean off
Reassess
Wean off
Reassess

Ongoing surveillance

Can you delegate the surveillance?

Comments and Considerations

- Medication withdrawal has a high likelihood of relapse
- When considering it requires a tailored approach
  - Information
  - Surveillance
  - Willingness to re-engage