Heart Failure and A fib
By the numbers BUT for individuals

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EVIDENCE-BASED PRACTICE IN REALITY

What do Medications Really Achieve?

therapeuticseducation.org/npwebinars/

Heart Failure

A Quick Reflective History Lesson

Why evidence prevails (usually) over opinion

BETA-BLOCKERS WERE CONTRAINDICATED IN HEART FAILURE

Beta Adrenergic Blocking Drugs in the Clinical Management of Cardiac Arrhythmias*

Am J Card 1966;18:444-9

3 patients with HF and sinus tachycardia given IV beta blockers - within 20 minutes - worsened heart failure

An early disturbing finding was that heart failure could be precipitated or aggravated by beta blockade. This untoward effect has been noted by other workers.[3] It presumably results from weakened contractile force of the heart following removal of the catecholamine drive. There is frequently a fall in cardiac output with prolongation of systole.[4] This unwanted effect

arrhythmia. In the presence of myocardial disease, however, these drugs must be used with caution, since they may precipitate or aggravate heart failure. In combination with digitalis,

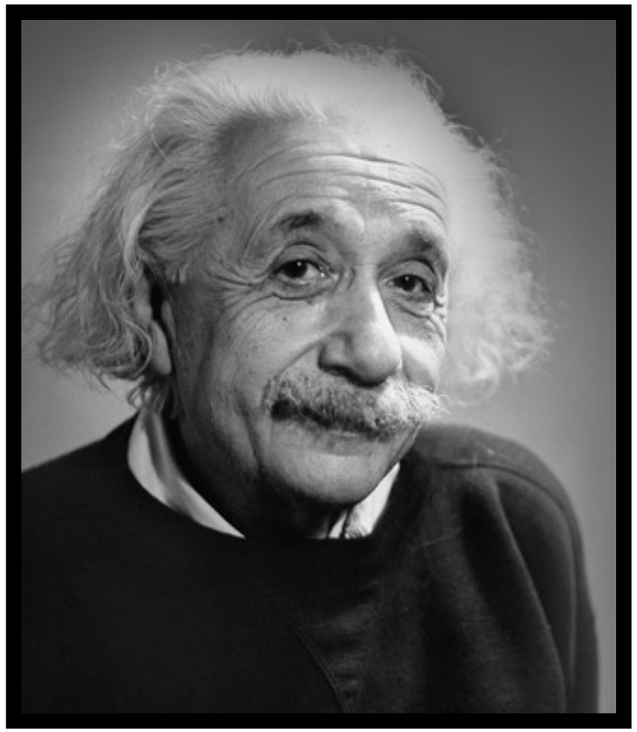
For the next ~25 years beta-blockers were contraindicated

1975 - case series - seven patients - some benefit

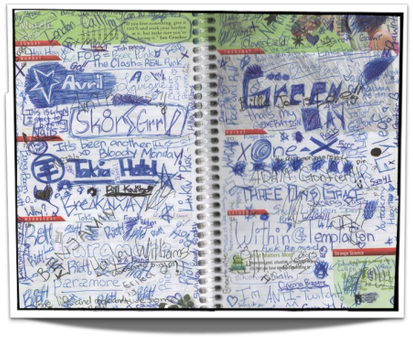
1993 - trials were done showing benefit in HF

Objectives

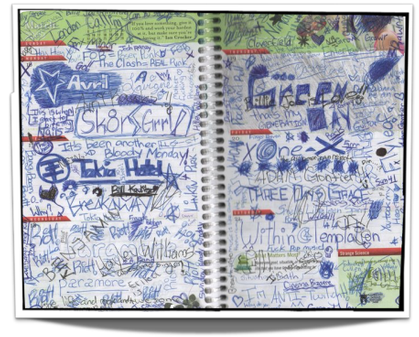
Make HF Simple but not Simpler!!



Looking Behind The Curtain



My Agenda



What guidelines say - and don’t say

A simplified but comprehensive synopsis of the best available evidence

Risks, Benefits, Harms

A SIMPLIFIED APPROACH

SDM, there is time, ⬇side effects, ⬇cost, cutting pills

Tests - for HF - ECHO, BNP, POCUS

What the results mean - measurement variation

Objectives

1. **Understand the basics of heart failure**
   Recognize how symptoms change across NYHA classes and what the main goals of therapy are.
2. **Know what heart failure drugs actually do**
   See which meds help people live longer, feel better, or just reduce symptoms.
   Understand the trade-offs — benefits, side effects, and costs.
3. **Use a simple, rational approach to treatment**
   Learn which medications to start first and how to build combinations over time.
   Appreciate that slower titration is often just as effective.
4. **Make sense of test results and variability**
   Understand what tests (like ejection fraction or BNP) can — and can't — tell you.
   Recognize that small changes often fall within natural variation.
5. **Grasp the key goals in atrial fibrillation**
   Distinguish rate vs. rhythm control, and when each matters.
   Know which drugs reduce stroke risk, by how much and the risk of serious bleeding.
6. **Apply an evidence-based mindset**
   Balance numbers with patient values.
   Focus on what actually helps people, not just what guidelines say.

New York Heart Association (NYHA) functional classification

Class I – No limitation
Ordinary physical activity doesn't cause undue fatigue, palpitations, or shortness of breath.
Example: Can climb stairs, walk briskly, or do housework without symptoms.
Clinical note: Often these patients have cardiac disease detectable on tests (e.g., reduced EF), but they're asymptomatic.

Class II – Mild limitation
Description: Comfortable at rest, but ordinary physical activity (e.g., walking up a hill, carrying groceries) causes symptoms—fatigue, dyspnea, palpitations, or angina.
Example: Feels fine sitting or walking on level ground, but climbing a single flight of stairs brings on symptoms.
Clinical note: Many "stable" ambulatory heart failure patients fall here.

Class III – Marked limitation
Description: Comfortable at rest, but less than ordinary activity triggers symptoms.
Example: Symptoms occur walking 50–100 meters, or with simple tasks like dressing or light chores.
Clinical note: Often used as the cutoff for referral to advanced therapies or palliative support.

Class IV – Symptoms at rest
Description: Symptoms occur at rest or with any physical activity; any effort increases discomfort.
Example: Short of breath sitting in a chair, can't perform any activity without fatigue.
Clinical note: Represents severe heart failure; often corresponds to patients being evaluated for transplant, LVAD, or hospice care.

Heart Failure Guidelines



HF GUIDELINES - CCS 2017 (2020/2021 updates), AHA/ACC/HFSA 2022, ESC 2021

For reduced EF, all recommend **1) ACEI/ARB/ARNIs + 2) BB + 3) MRAs + 4) SGLT2s**

All preferentially say **ARNI** from this **ACEI/ARB/ARNIs**

Can/Amer strongly recommend **Target Doses**, Euro does so without formal recommendations

NONE propose a specific sequence to initiate - there could be **65+** different permutations

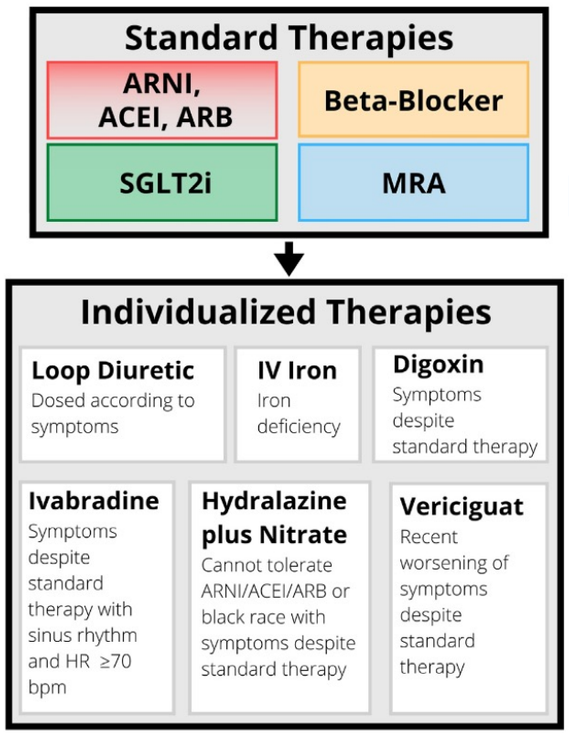
No real mention of **Shared Decision-Making** - HF guidelines worst implementation of SDM in cardiology

VERY UNLIKELY TO BE RCTs OF APPROACHES

Therefore modelling studies have been done using existing evidence - is there a “best” approach?

Should take into account benefit, side effects (potential to tolerate), convenience and cost - should be as simple as possible but not simpler

CJC Open 5 (2023) 629e640



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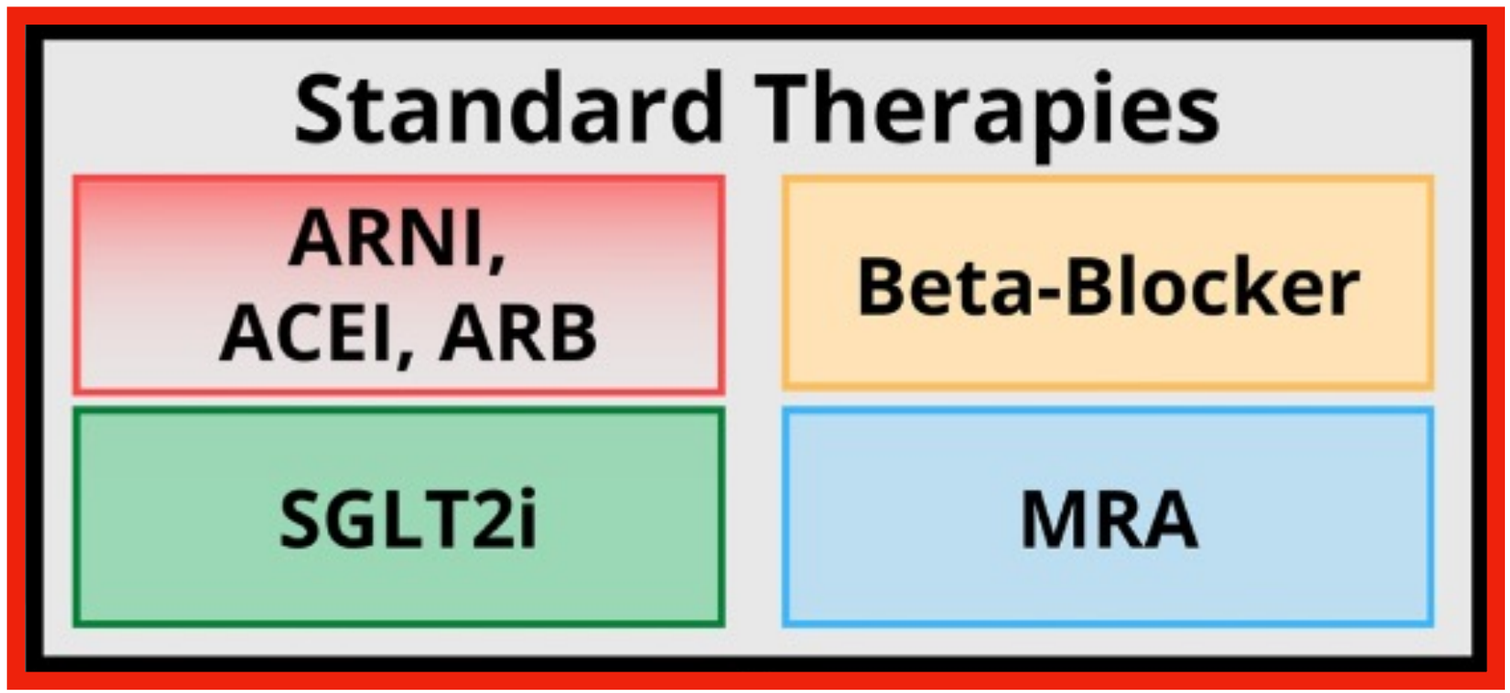
The Focus



BUT HOW TO DO THIS?

Let’s Start at the Very Beginning

A ballpark synopsis of all the numbers…

…from the best available evidence

Goals of Therapy

Reduce mortality

Reduce morbidity

Reduce HF hospitalizations

Reduce HF exacerbations

Treat exacerbating factors

Improve symptoms, exercise tolerance and quality of life

Prevent disease progression

Treat modifiable risk factors

CTC

Meds That May Worsen Heart Failure

Drugs that cause sodium and fluid retention:
Androgens
Corticosteroids
Drugs with high sodium content
Licorice-containing products
Minoxidil
NSAIDs including selective COX-2 inhibitors and high-dose salicylates
Pregabalin
Thiazolidinediones (pioglitazone, rosiglitazone)
Negative inotropes:
Antiarrhythmic agents except amiodarone and dofetilide
Beta-blockers
Itraconazole
Non-dihydropyridine calcium channel blockers
Some anesthesia medications, e.g., propofol

Cardiotoxic drugs:
Alcohol
Amphetamines
Cancer therapies: 5-fluorouracil, alkylating agents (cyclophosphamide, ifosfamide), anthracyclines (doxorubicin, epirubicin, mitoxantrone), bevacizumab, trastuzumab, tyrosine kinase inhibitors (imatinib, sunitinib)
Clozapine
Cocaine

Meds That “Improve” Heart Failure

Category / Class	Examples / Common Drugs in Canada
Diuretics (Loop, Thiazide, etc.)	Furosemide, Bumetanide, Torsemide, Metolazone
Angiotensin-Converting Enzyme Inhibitors (ACE inhibitors)	Enalapril, Lisinopril, Ramipril, Perindopril
Angiotensin Receptor Blockers (ARBs)	Losartan, Valsartan, Candesartan
Angiotensin Receptor-Neprilysin Inhibitors (ARNI)	Sacubitril/Valsartan (Entresto)
Beta-Blockers	Metoprolol succinate, Bisoprolol, Carvedilol
Mineralocorticoid Receptor Antagonists (MRAs, aka Spironolactone / Eplerenone)	Spironolactone, Eplerenone
Sodium-Glucose Cotransporter-2 (SGLT2) Inhibitors	Dapagliflozin, Empagliflozin
Hydralazine + Isosorbide Dinitrate	Hydralazine + Isosorbide dinitrate combination
Ivabradine	Ivabradine
Digoxin	Digoxin
Other adjuncts / supportive	e.g. Iron supplementation (IV iron), anticoagulation (if AF), devices (CRT, ICD)

Diuretics for heart failure

(some withdrawal trials - overall very weak evidence)

2-12 months - all before beta-blockers used

	Mortality (%)	HF worsening (%)
Placebo	12	15
Diuretics (primarily loop)	3	0

Cochrane CD003838

BUT

"the only certainty is that

such therapies can relieve the patient's symptoms and reduce vascular congestion"

Eur Cardiol 2015;10:42-7

The BALLPARK Heart Failure Risk/Benefit/Harm Numbers

all %s are absolute numbers and are for **Class 2-3** (slight to marked limitation) heart failure

1) Over 5 Years, What is the Chance of Death With No Treatment?
Death* ~50%

*SIMILAR absolute risks and benefits for heart failure hospitalizations

If Treated with Medications ➡ New Risk

2) What is the Chance of Death with Different Medication Combinations?**				
ACEI/ARB + BB	ACEI/ARB + BB + MRA	ACEI/ARB + BB + MRA + SGLT2	ARNI + BB + MRA	ARNI + BB + MRA + SGLT2
~35%	~27%	~24%	~23%	~19%

** If VOLUME OVERLOADED - tailored diuretic doses to help control weight and improve symptoms

3) What is the Cost/Yr for Medications?				
~$250-$300	~$350 ~$1,000 if eplerenone	$650 $1,300 if eplerenone	$3,200 $3,900 if eplerenone	$3,500 $4,200 if eplerenone

4) How Many People Get Improved Quality of Life? % of people improved over placebo	
ACE-I	Unknown
ARB	~2%
Beta blocker	No better, or worse
Spironolactone/ eplerenone	Unknown
ARNI (Sacubitril/valsartan)	~3% vs ACEI
SGLT2 inhibitor	~6%

5) What is the ABSOLUTE Benefit of Getting to Target/Higher Doses vs Lower Doses?

% of people benefitted/harmed over 2-4 years

	Mortality	HF Hospitalization	HF worsening	Additional Harm of Higher Doses versus Lower Doses	Dose Tolerability
ACEI/ARB	0%	0%/~3%	~5%/~3%	Hypotension ↑ 3% Dizziness ↑ 5% Increased K ↑ 2-3% Increased Cr ↑ 3-6%	~40-50% can't tolerate TARGET doses
Beta blocker	0%	0%	0%	Dizziness↑14%	
Other Medications	Not studied				

6) What are the Side Effects of These Medications?

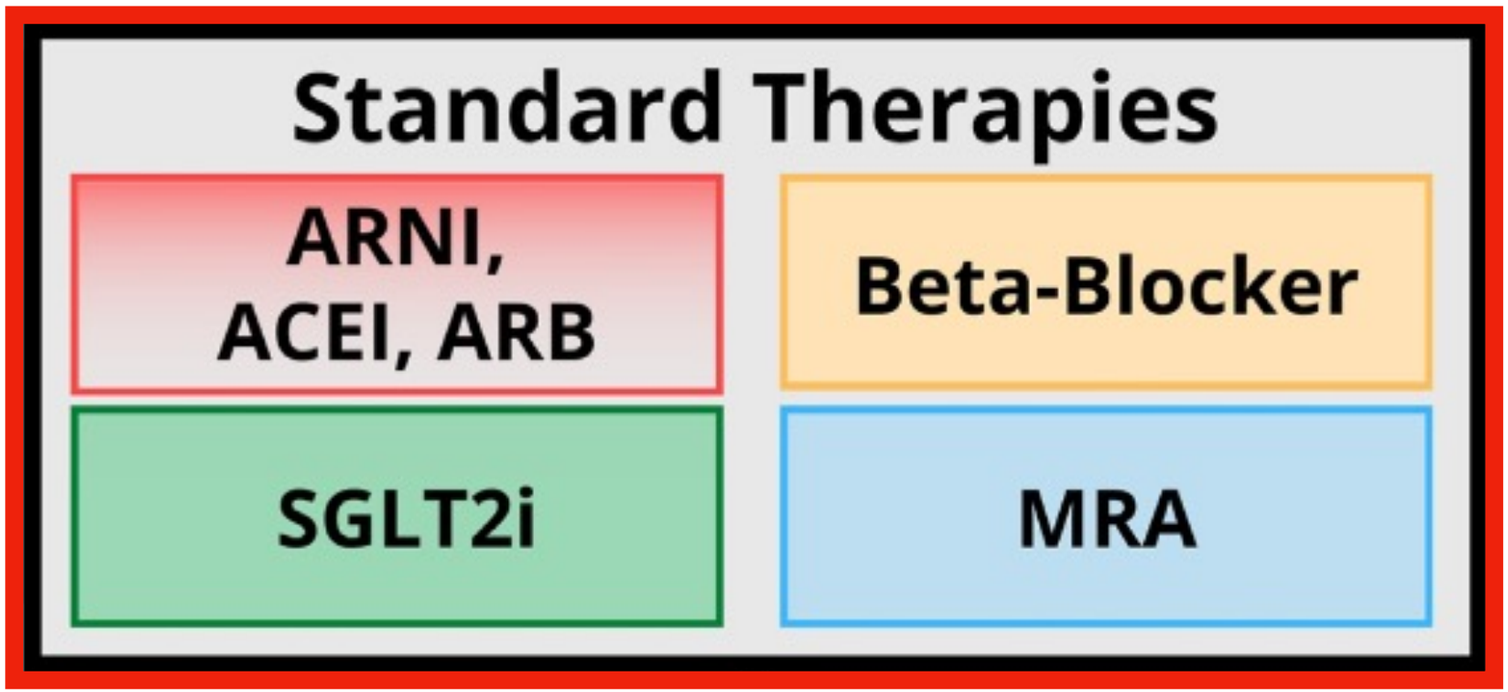
% of people over placebo

ACEI/ ARB	Low blood pressure 5% Dizziness or fainting 7% Decrease in kidney function 3% High potassium 3% Cough 6% - just ACEI Angioedema 0.2% - just ACEI	Also consider the inconveniences of getting and taking the medications PLUS the additional monitoring
Beta blocker	Slow heart rate 3% Dizziness 4% Diarrhea 4% Claudication-type leg pain 2%	
MRA Spironolactone /eplerenone	Decrease in kidney function 2% High potassium 7% Breast growth/tenderness (spironolactone only) 9%	
ARNI (Sacubitril/ valsartan)	Low blood pressure causing symptoms (lightheadedness, dizziness, fatigue, etc.) 5% vs. ACEI	
SGLT2 inhibitor	No differences from placebo in heart failure trials In people with diabetes: Bothersome genital fungal infections 5% Diabetic coma (diabetic ketoacidosis) 0.2%	

Now What?

Category / Class	Pros	Cons
Diuretics (Loop, Thiazide, etc.)	Best for acute symptoms	Hypovolemia, hyonatremia, hypokalemia if over diuresed, no mortality benefit
Angiotensin-Converting Enzyme Inhibitors (ACE inhibitors)	Reduces mortality and hospitalizations	Cough 15%, hyperkalemia, hypotension, worsened renal function
Angiotensin Receptor Blockers (ARBs)	Equals ACEI without a cough - also evidence on QOL (2%)	
Angiotensin Receptor-Neprilysin Inhibitors (ARNI)	Reduces mortality and hospitalizations and improves QOL (3% over ACEI)	Expensive - save money just use an ARB
Beta-Blockers	Reduces mortality and hospitalizations	Bradycardia, hypotension, fatigue, contraindicated in asthma
Mineralocorticoid Receptor Antagonists (MRAs, aka Spironolactone / Eplerenone)	Reduces mortality and hospitalizations	Hyperkalemia, gynecomastia
Sodium-Glucose Cotransporter-2 (SGLT2) Inhibitors	Reduces mortality and hospitalizations and improves QOL (6%)	Genital yeast infection, volume depletion, ketoacidosis

The Focus



BUT HOW DO WE DO THIS?

Present Guideline Recommendations Based on EF%

Ejection Fraction	Typical Categories	YES	MAYBE (Weaker evidence)	AVOID
<40%	Reduced	ARNI, ACEI, ARB; Beta-Blocker; SGLT2i; MRA	Get to Target Doses	N/A
40-49%	Mildly reduced	SGLT2i; MRA	ARNI, ACEI, ARB; Beta-Blocker	N/A
≥ 50%	Preserved	SGLT2i; MRA	ARNI, ACEI, ARB	Unless other reasons for use Vent' arrhythmia, angina AVOID Beta-Blocker

Daily Dose, Guidelines, Evidence

	Available Medications	Guideline suggested times per day	TOTAL DAILY DOSE - multiples 1x	2x	4x	6x	8x	16x	24x
ACEI	Enalapril	2	2.5	5			20	40	60
ACEI	Fosinopril	1	5	10			40		
ACEI	Lisinopril	1	2.5	5			20	35*	
ACEI	Perindopril	1	2	4	8		16		
ACEI	Quinapril	2	5		20				
ACEI	Ramipril	1,2	1.25	2.5	5		10		
ACEI	Trandolapril	1	0.5	1	2		4		
ARB	Irbesartan	Not in a guideline							
ARB	Candesartan	1	4	8	16		32 is this correct		
ARB	Losartan	1	25	50		150			
ARB	Valsartan	1,2	40	80			320		
ARB	Sacubitril-valsartan	2	50/50	100/100	200/200				
BB	Carvedilol	2	6.5		20*		50	100	
BB	Carvedilol CR	1	10				80		
BB	Bisoprolol	1	1.25				10		
BB	Metoprolol (CR/XL)	1	12.5	25				200	
BB	Nebivolol	1	1.25				10		
SGLT2i	Dapagliflozin	1	10						
SGLT2i	Empagliflozin	1	10	25*					
SGLT2i	Canagliflozin	1	100		300*				
MRAs	Spironolactone	1	12.5	25	50				
MRAs	Eplerenone	1	25	50					

20/21 meds **HAVE** target dose recom'

17/22 meds **HAVE NO** dose trials

3 "higher" dose meds (6-16x⬆)

have shown ⬆ benefit

but also ⬆ harm

enalapril 20, lisinopril, losartan

3 "higher" dose meds

have shown no benefit

candesartan, carvedilol, enalapril 40/80

TABLE KEY

Guideline Suggested Starting Doses
Guideline Suggested Target Doses
Target/higher dose tested - ↑ benefit
Target/higher dose tested - NO ↑ benefit
Drugs with no trials of target doses
* = number not exactly the multiple

The BALLPARK Heart Failure Risk/Benefit/Harm Numbers

all %s are absolute numbers and are for **Class 2-3** **(slight to marked limitation)** heart failure

~50% death and ~50% hospitalization in 5 years

If Treated with Medications ➡ New Risk

***SIMILAR absolute risks and benefits for heart failure hospitalizations**

~50% down to ~20% = 30% absolute and 60% relative benefit

ACEI/ARB + BB	ACEI/ARB + BB + MRA	ACEI/ARB + BB + MRA + SGLT2	ARNI + BB + MRA	ARNI + BB + MRA + SGLT2
~35%	**~27%**	**~24%**	**~23%**	**~19%**

** If VOLUME OVERLOADED - tailored diuretic doses to help control weight and improve symptoms

Most of the benefit is from 4 "low" priced medications

~$250-$300	~$350	$650	$3,200	$3,500
	~$1,000 if eplerenone	$1,300 if eplerenone	$3,900 if eplerenone	$4,200 if eplerenone

At most, ~5% get a QOL benefit

ACE-I	Unknown
ARB	~2%
Beta blocker	No better or worse
Spironolactone/ eplerenone	Unknown
ARNI (Sacubitril/valsartan)	~3% vs ACEI
SGLT2 inhibitor	~6%

4-16 X ⬆ dose - ACEI/ARB = hosp' benefit no mort' benefit - but then also harm
BB nothing but harm
~50% can't tolerate ⬆ dose

	Mortality	HF Hospitalization	HF worsening	Additional Harm of Higher Doses versus Lower Doses	Dose Tolerability
ACEI/ARB	0%	0%/~3%	~5%/~3%	Hypotension ↑ 3% Dizziness ↑ 5% Increased K ↑ 2-3% Increased Cr ↑ 3-6%	~40-50% can't tolerate TARGET doses
Beta blocker	0%	0%	0%	**Dizziness↑14%**	
Other Medications	Not studied				

All the meds have side effects and inconveniences

ACEI/ ARB	**Low blood pressure 5% Dizziness or fainting 7% Decrease in kidney function 3% High potassium 3% Cough 6% - just ACEI Angioedema 0.2% - just ACEI**	Also consider the inconveniences of getting and taking the medications PLUS the additional monitoring
Beta blocker	**Slow heart rate 3% Dizziness 4% Diarrhea 4% Claudication-type leg pain 2%**	
MRA Spironolactone /eplerenone	**Decrease in kidney function 2% High potassium 7% Breast growth/tenderness (spironolactone only) 9%**	
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SGLT2 inhibitor	**No differences from placebo in heart failure trials In people with diabetes: Bothersome genital fungal infections 5% Diabetic coma (diabetic ketoacidosis) 0.2%**	

Summary of efficacy of heart failure pharmacotherapy across ejection fraction categories

Medication class	HFrEF (LVEF ≤40%)	HFmrEF (LVEF 41-49%)	HFpEF (LVEF ≥50%)
Death from any cause, ***relative risk reduction****			
ACEI/ARB	~20%	↔	
ARNI (vs ACEI/ARB)	~15%	↔	
Beta-blocker	~35%	~40%	?
MRA	~25%	↔	
SGLT2I	~15%	↔	
Heart failure hospitalization, ***relative risk reduction****			
ACEI/ARB	~25%	~25%	↔
ARNI (vs ACEI/ARB)	~20%	↔	
Beta-blocker	~35%	↔	
MRA	~35%	~20%	
SGLT2I	~30%	~25%	
Quality of life, ***absolute %*** *of people with an increase of a clinically-important improvement*			
ACEI/ARB	+4%	?	
ARNI (vs ACEI/ARB)	+3%	↔	
Beta-blocker	↔	?	
MRA	?	↔	
SGLT2I	+6%		

There is Time To Titrate

what do you lose if you did nothing other than treat with a diuretic

Over 5 years

5-year risk Death ~50% Hospitalization for HF ~50%
Risk with max meds and doses Death ~20% Hospitalization for HF ~20%

50 minus 20 = lose **~30%** absolute benefit over 5 years

30%/60 months = lose **~0.5%** absolute benefit per month

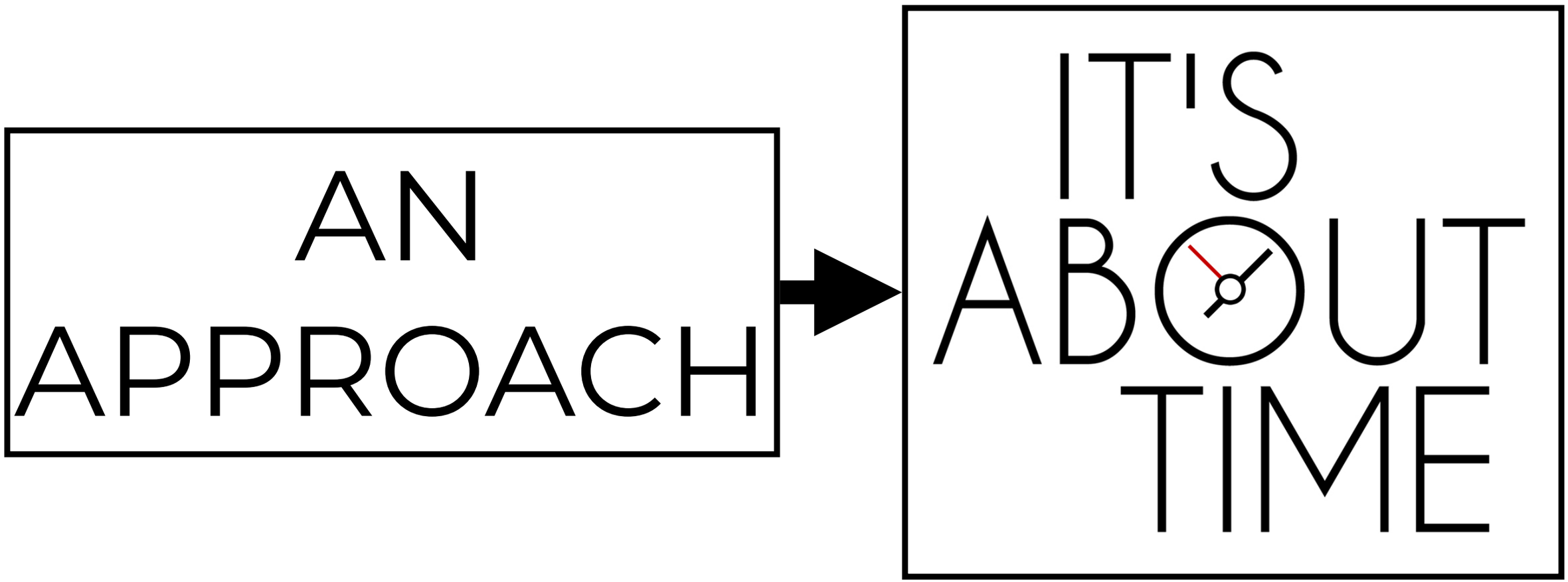
Over 1 year

1-year risk Death ~20% Hospitalization for HF ~8%
Risk with max meds and doses Death ~??% Hospitalization for HF ~8%

If benefit front-loaded - use 1 year

20 minus 8 = lose **~12%** absolute benefit over 1 year

12%/12 months = lose **~1%** absolute benefit per month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APPROACH
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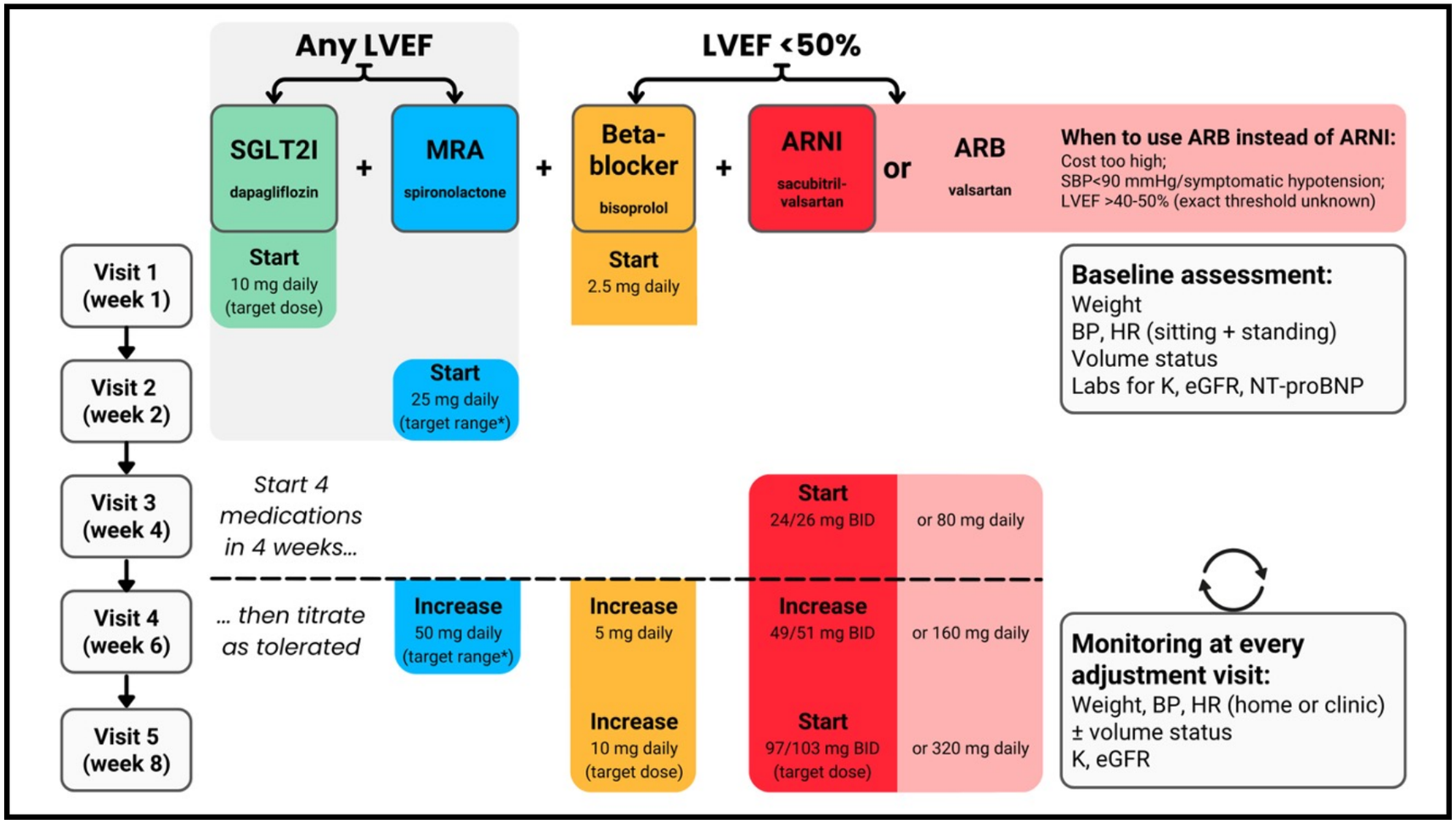
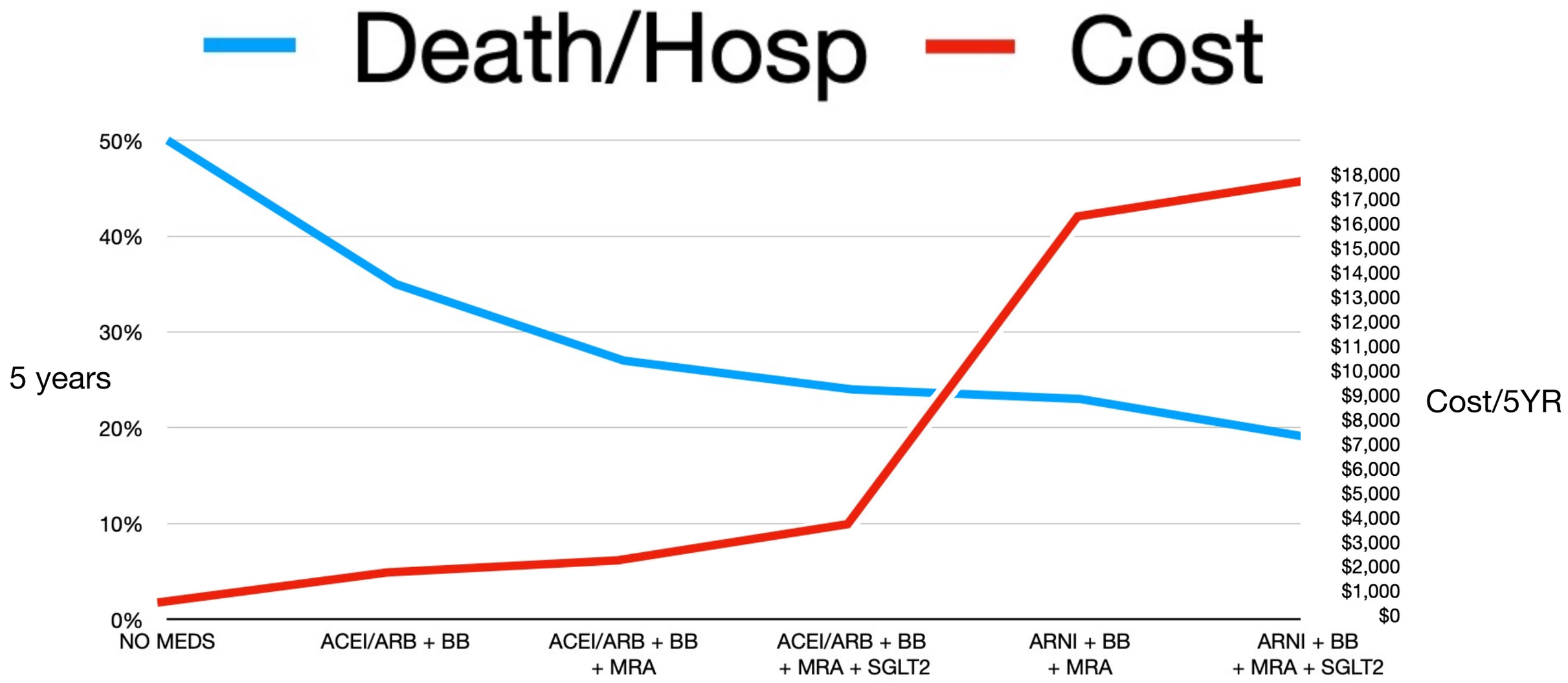
TIME

Simple sequencing: a rational and generalizable approach to starting, titrating, and monitoring HF pharmacotherapy



Unpublished - created by RD Turgeon, BJ MacDonald, NM Hawkins, JP McCormack


Death/Hosp
Cost
50%
40%
30%
20%
10%
0%
5 years
$18,000
$17,000
$16,000
$15,000
$14,000
$13,000
$12,000
$11,000
$10,000
$9,000
$8,000
$7,000
$6,000
$5,000
$4,000
$3,000
$2,000
$1,000
$0
Cost/5YR
NO MEDS
ACEI/ARB + BB
ACEI/ARB + BB + MRA
ACEI/ARB + BB + MRA + SGLT2
ARNI + BB + MRA
ARNI + BB + MRA + SGLT2

Tests

“Only do a test if the result will influence management”
Lots of people

“If you aren’t sick, you just haven’t had enough tests”
Bob Rangno, MD

Echocardiogram

The GOLD standard for diagnosing heart failure

BUT

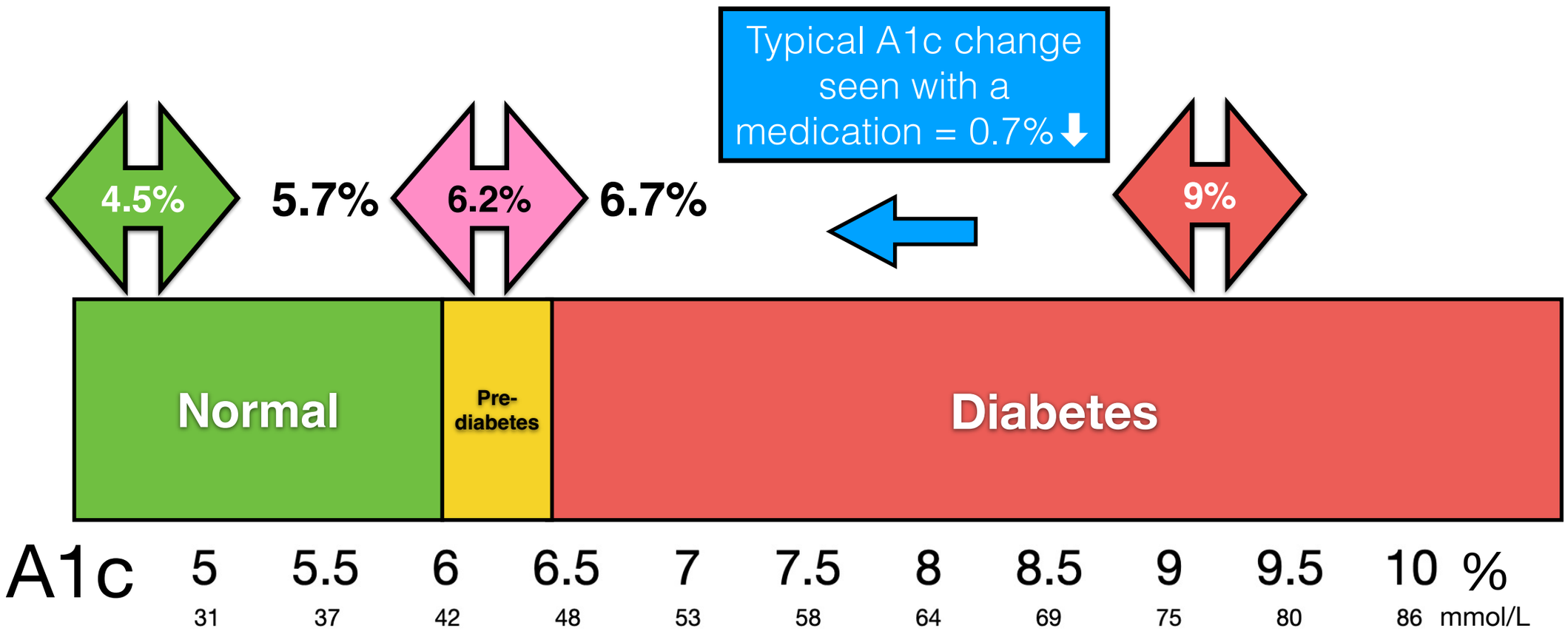
Your Results May Vary: The Imprecision of Medical Measurements

Every test has…

2020

…measurement variation

Diabetes Measurement Issues - A1c



Echo Ejection Fraction%

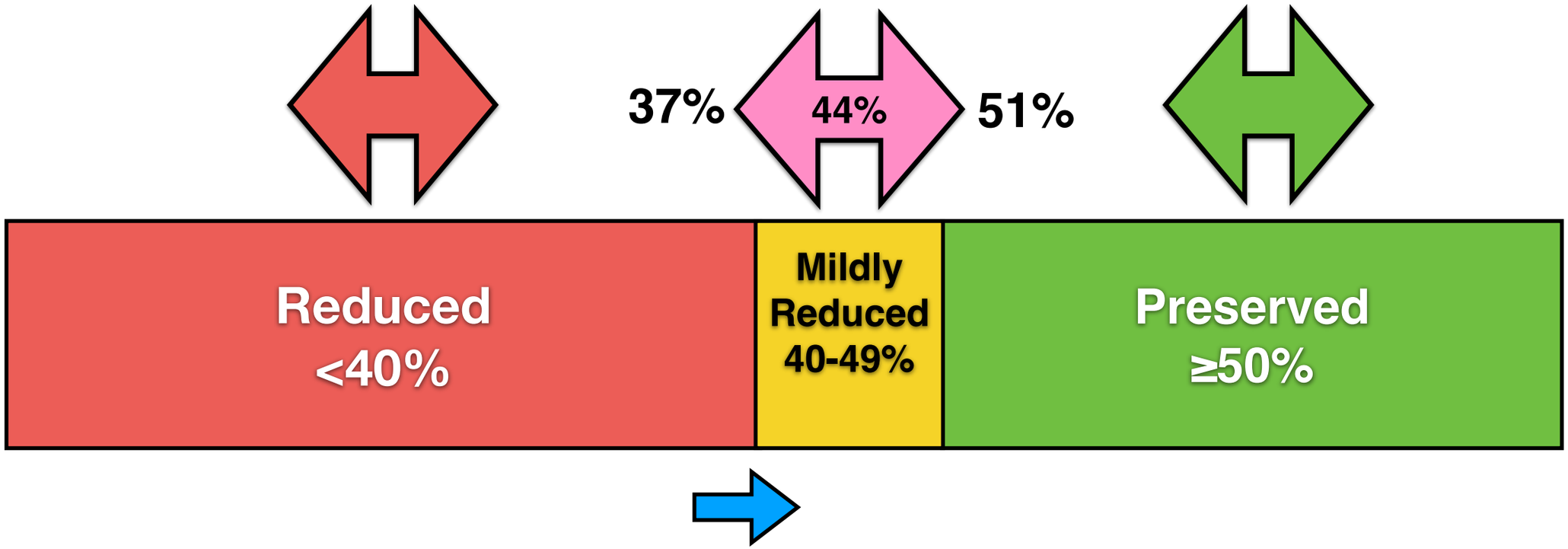
is at least +/- 5 to 7%

"An LVEF of 44% assessed on a Monday could be 37% on Wednesday and 51% on Friday, leading a physician to diagnose HFrEF, HFmrEF, and HFpEF in the same patient within a 7-day period"

J Am Heart Assoc. 2024;13:e034642. DOI: 10.1161/JAHA.124.034642 2

Echo Ejection Fraction%

at least +/-5 to 7%

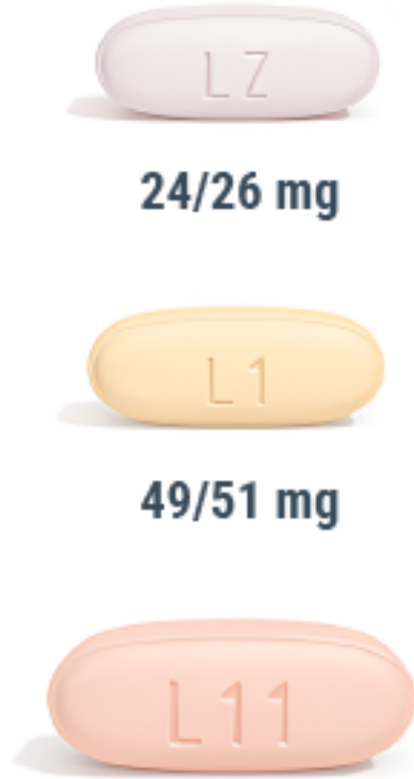


Echo Ejection Fraction

A category redo?

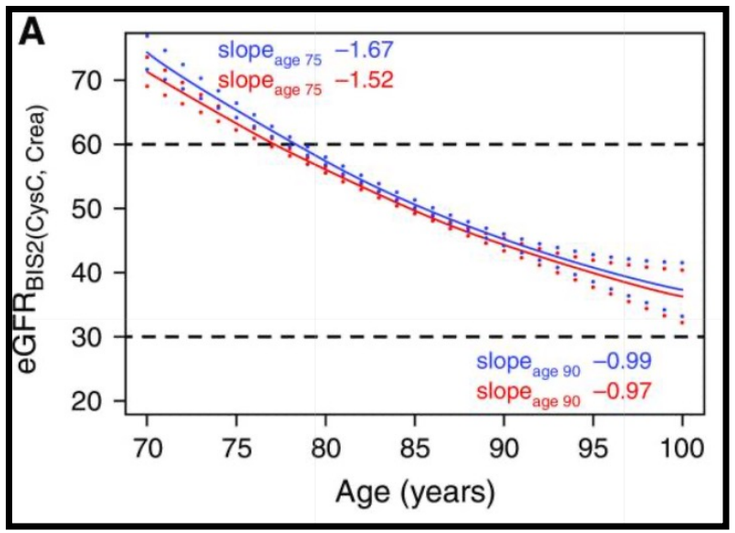
J Am Heart Assoc. 2024;13:e032257. DOI: 10.1161/JAHA.123.032257
J Am Heart Assoc. 2024;13:e034642. DOI: 10.1161/JAHA.124.034642 2

Entresto - Cutting Pills

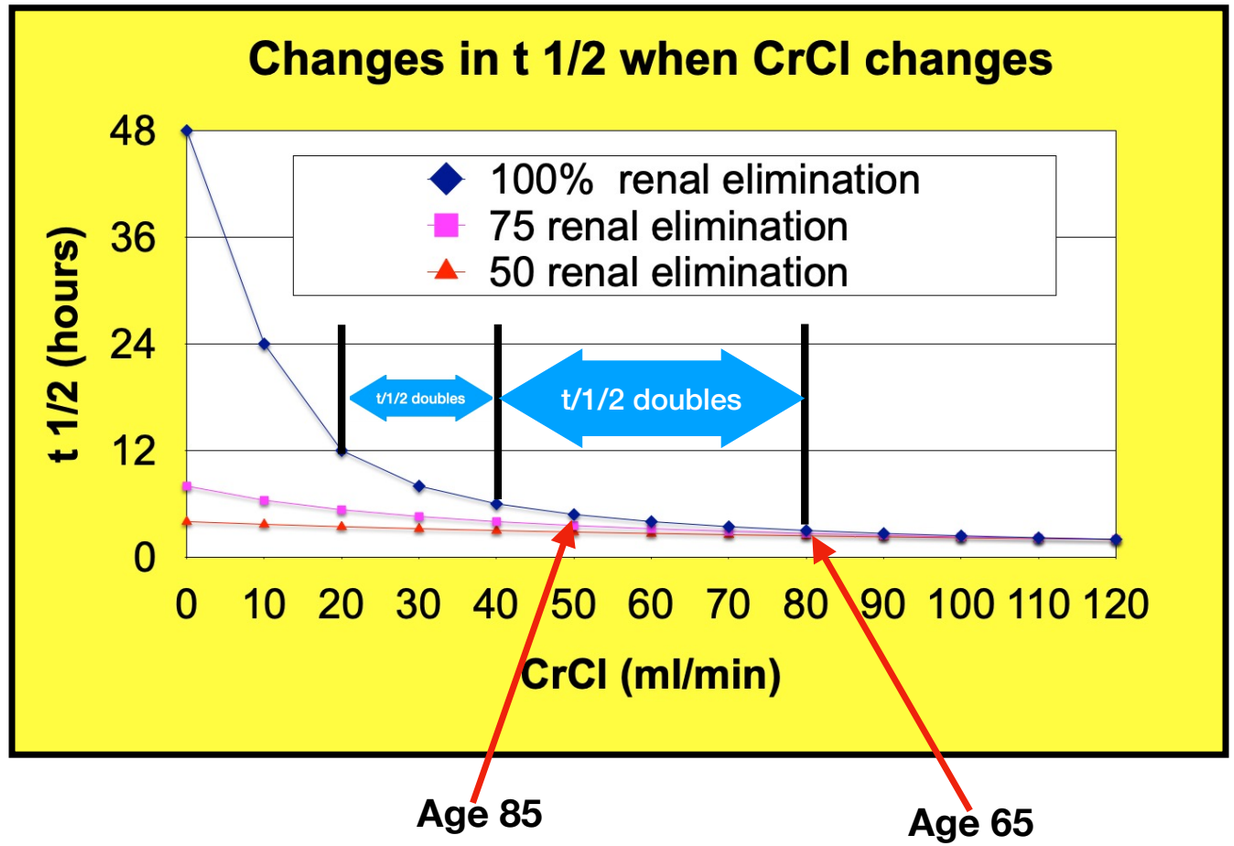


into 1/2s is easy - 1/4s are a !@#$% mess

Elderly = “sustained release”



Clin J Am Soc Nephrol. 2022
Aug;17(8):1119–1128



ACEI - primarily renal
ARB - primarily hepatic
Bisoprolol - 50/50
Dapagliflozin - primarily renal

Sodium restriction

TOOLS FOR PRACTICE #368 | June 24, 2024

Sodium Restriction in Heart Failure: Beneficial or pouring salt in the wound?

CLINICAL QUESTION

Does sodium restriction improve outcomes in patients with chronic heart failure?

BOTTOM LINE

In patients with chronic heart failure, restricting dietary sodium to <2 grams/day does not reduce death or hospitalization compared with 2-3 grams/day.

Top Tips for HF and Meds

Medications - more = better

20%+ absolute benefits but STILL “most” get no mortality/hosp’ benefit

You do have time!!

Lower dose = 90+% of the benefit

Target/High doses - more (not BB) = a bit better but also a bit worse

Higher price = a bit better - split all tablets in 1/2

IMHO - side effects unacceptable

Top Tips for HF and Meds

If hypotensive (symptom) - over-diuresed? - not necessarily from the “BP” meds?

If newly hypotensive - with meds - still think about over-diuresed?

After discharge from hospital - reassess volume and vitals a week after discharge - because often aggressive treatment early so not sure of SS when at home on diuretics

If still slightly fluid overloaded - give SGLT2 - better than ⬆ dose of diuretic - SGLT2 6% get ⬆ QOL regardless of EF

New HF elderly - 60%+ are >40% EF

If post MI and if on BB - stop as if EF >~50% as no benefit on QOL CJC Open 6 (2024) 639e648

“The answers are all out there, we just need to ask the right questions.”

Oscar Wilde

A fibrillation

primarily the stroke reduction part

Goals of Therapy

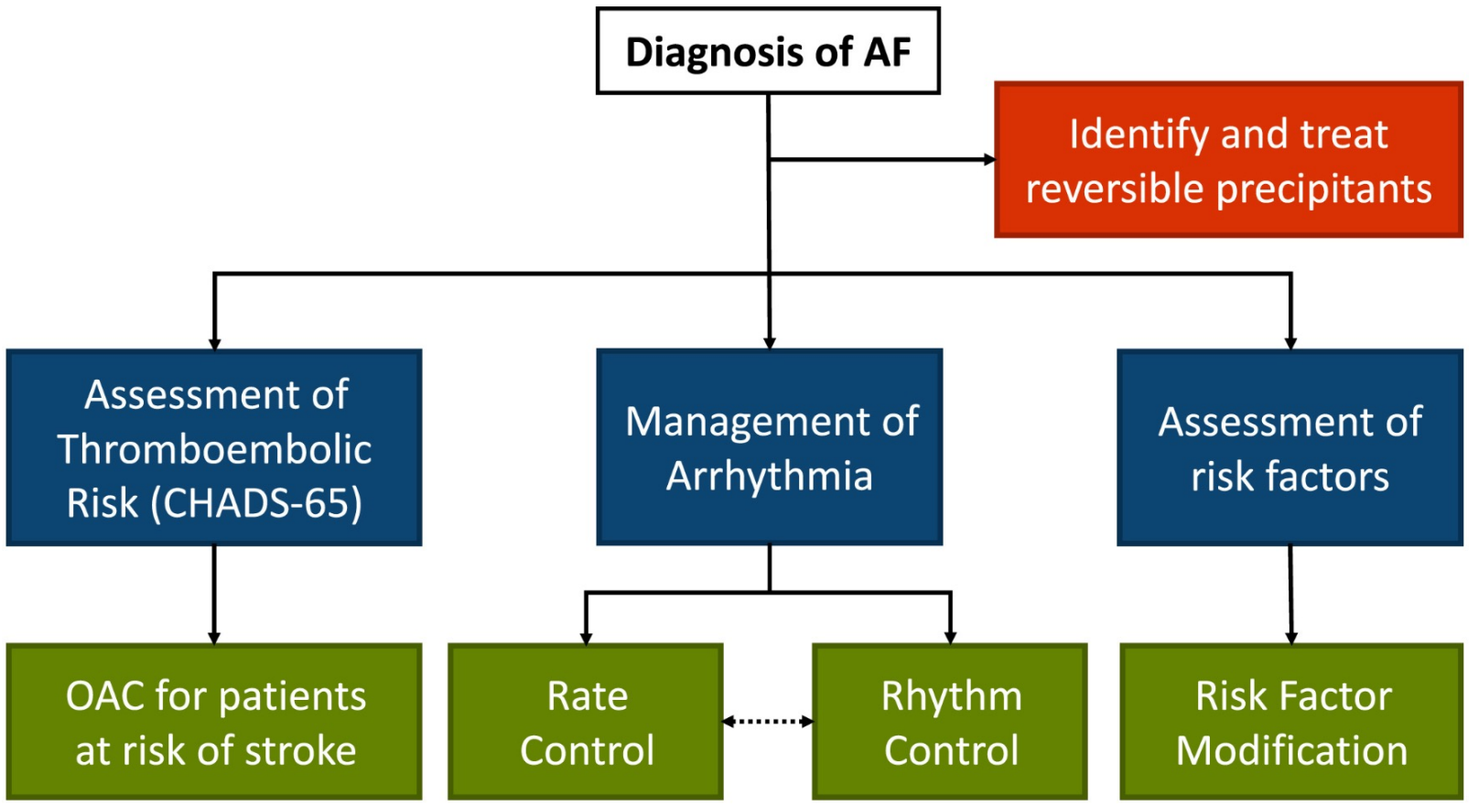
In the acute stage - restore sinus rhythm; rhythm control should always be possible in re-entrant arrhythmias (Atrioventricular RT or AV-Nodal RT)

Rhythm control may not be possible or desirable in some patients - in these situations, the goal is to control the rate of the supraventricular tachycardia

Prevent arrhythmia recurrence or substantially reduce the overall arrhythmia burden

Reduce the risk of thromboembolic events (stroke) in patients with AF/atrial flutter

CTC



Major Goals of AF Management	Anticipated Outcome
Prevent stroke or systemic thromboembolism	Improvement in survival
Cardiovascular Risk Reduction	
Improve symptoms, functional capacity, and QOL	Reduction in healthcare utilisation (e.g. ED visits or hospitalizations)
Prevent complications (e.g. LV dysfunction, falls)	

2020 Canadian Cardiovascular Society/Canadian Heart Rhythm Society Comprehensive Guidelines for the Management of Atrial Fibrillation

Cryoablation or Drug Therapy for Initial Treatment of Atrial Fibrillation

303 adults (mean age ≈ 58 yr; ≈ 70 % male) with symptomatic, untreated paroxysmal AF

CANADIAN TRIAL	Recurrence (%)	Symptom recurrence (%)	Serious adverse events (%)	Hospitalization (%)
Cryoablation	43	11	3	3
Antiarrhythmic drugs*	68	26	4	8

*__flecainide__, sotalol, propafenone, dronedarone

NEJM 2021; 384:305-15 (EARLY-AF Trial)

Effect of alcohol reduction on recurrent A fib

One RCT where they were randomized to oral and written advice to abstain from alcohol with monthly follow-up followed for 6 months

140 patients with A fib for ~6 years **16 drinks/week avg**	**Drinks/week**	**Recurrence of Atrial fibrillation**	**A fib related hospital admissions**	**Weight loss**
ADVICE	2 61% complete abstinence	53%	9%	3.7kg less than control
NO ADVICE	13	73%	20%	

https://cfpclearn.ca/tfp271/

Meds That Can Cause A fib

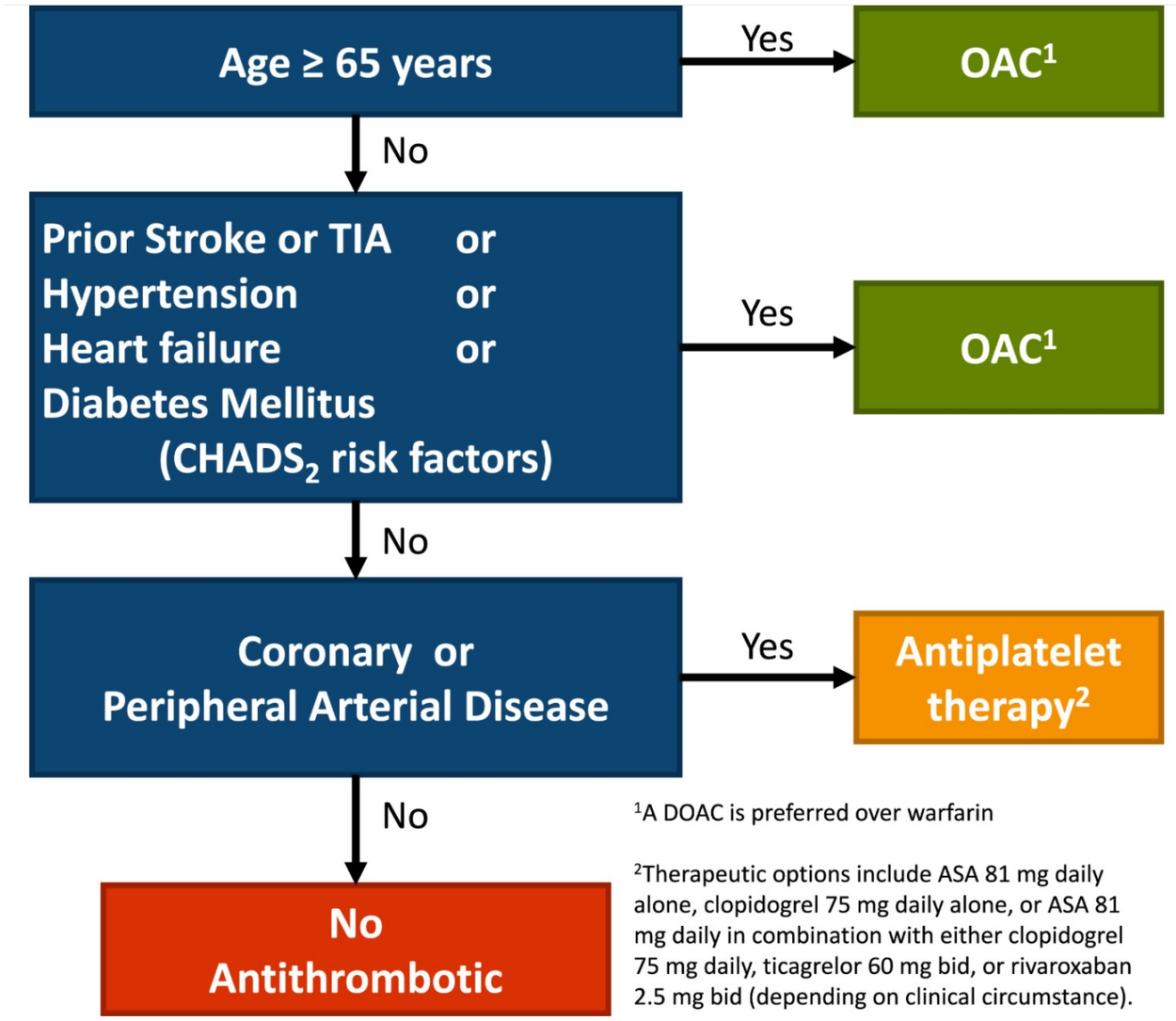
Very common/frequent (≥10%)
Cardiovascular drugs
Acetylcholine test: 8-17%
Adenosine: 1-15%
Aminophylline/theophylline: 2.5-13%; OR 1.8 (95% CI 1.0-3.9)
β-adrenergic agonists (in patients undergoing cardiac surgery): 39% with dopamine and 44% with dobutamine vs 20% with an α-adrenergic agonist (phenylephrine)
Dobutamine: 0-18%
Dopamine, renal doses: 23-39%; OR 3.35 (1.38-8.12)
Flecainide: 6-13.5%*
Propafenone: 9-12%*
Common (1-<10%):
Cardiovascular drugs
Amiodarone: 1.3%*
Arbutamine: 1%
Dobutamine (0.4-1.2% for stress echocardiography; 6-7.6% in patients with HF)
Enoximone: 8.3%
Icosapent ethyl: HR 1.5 (1.14-1.98); in patients with previous AF: HR 1.96 (1.19-3.21)
Ivabradine: HR 1.23 (1.08-1.41)
Levosimendan: 9% (low cardiac output after surgery: 12%)
Milrinone: 4.6-5.0%; OR 4.86 (2.31-10.25)
n-3 polyunsaturated fatty acids: HR 1.35 (1.1–1.66)
Verapamil: 5% (in patients with HCM)
Non-cardiovascular drugs
Drugs acting on the central nervous system
Antipsychotics: chlorpromazine 1.96 (1.44-2.67); clozapine aOR 2.81 (1.64–2.39); olanzapine 1.81 (1.44–2.88); prochlorperazine 1.22 (1.15–1.29); quetiapine 1.55 (1.25–1.92); risperidone 1.25 (1.00–1.55)
Empty Cell
Cannabis: HR 1.35 (1.30–1.40)
Empty Cell
Lacosamide: 1.5-2.3%
Empty Cell
Mitoxantrone: 1.4%
Empty Cell
Morphine: HR 4.37 (3.56–5.36)
Empty Cell
Opioids (hydrocodone, propoxyphene, tramadol): HR 1.35 (1.16-1.57)
Anti-inflammatory drugs
Oral corticosteroids 1.8-5.6%; OR 2.7 (1.9–3.8)
High-doses of corticosteroids: 5.8%; ≥ 7.5 mg of prednisone equivalents: OR 6.07 (3.90-9.42)
Non-aspirin NSAIDs: OR 1.33 (1.26-1.41)
Diclofenac: OR 1.2 (1.1-1.4); paracetamol 1.4 (1.2-1.6); ibuprofen 1.1 (1.0-1.3); naproxen 1.3 (1.0-1.7)
Empty Cell
COX-2 inhibitors: HR 1.16 (1.05–1.29); etoricoxib 1.35 (1.19–1.54)
Empty Cell
Orphenadrine: 2.5%
Bisphosphonates
Yearly i.v. zolendronic acid: OR 1.30 (1.18-1.43); alendronate: OR 1.86 (1.09-3.15); nitrogen containing bisphosphonates: aHR 1.55 (1.03–2.39)
Hormones
Levothyroxine (>0.075 mg/d): aOR 1.29 (1.23-1.35)
Respiratory drugs
Antimuscarinics: OR 1.2 (0.9-1.5)
Empty Cell
Long-acting β2-agonists: 1-2.7%; OR 2.54 (1.59-4.05)
Uncommon (<1%)
Non-cardiovascular drug
Fingolimod (0.22%), ipratropium (0.5%), salbutamol, tiotropium (<1%)

Anticancer Drugs
Alkylating agents
Cisplatin 6.6-32% (intrapericardial/intrapleural)
Cisplatin+cetuximab 4.5%
Cyclophosphamide 2.2% (6.4% plus busulfan)
Dacarbazine
Ifosfamide 9.6%
Melphalan high-dose 6.9-13% (22.5% in elderly)
Antimicrotubules/
Taxanes
Docetaxel
Paclitaxel 0.18-< 2%
Anthracyclines
Daunorubicin
Doxorubicin 1.4-10.3%
Idarubicin
Endocrine therapy
Abiraterone 0.7-2.6% (grade 3: <1%)
GnRH analogues 16%
Leuprolide 0.73%
Fluoropyrimidines
Azacitidine+lenalidomide 2.5-5%
Capecitabine 1.1% (up to 31% if prior cardiac comorbidities)
Clofarabine 7.4-18.7%
Decitabine 10% (15% in patients with renal dysfunction)
Fluorouracil 0.4-1.7% (0.4-6.5% + cisplatin; 5.1% + sorafenib)
Gemcitabine 8.1%
Histone deacetylase inhibitors
Romidepsin 4.6%
Venetoclax 4.6-5.6%
Immune checkpoint inhibitors
All 0.3-7.6% (30% with ICI-related cardiotoxicity)
Darvalumab 0.8-2.8%
Ipilimumab
Nivolumab 1.6-4%
Pembrolizumab 1.7%
Tremelimumab 0.19%
Immunomodulating agents
Aldesleukin (Interleukin-2) High-dose: 4.2-8%. Low-dose: 1.5%.
Dexamethasone 0.9%
Lenalidomide
Lenalidomide+dexamethasone 1.9-3.8% (6.6% in patients >65 years)
Pomalidomide
Temsirolimus 1%
Thalidomide+ dexamethasone 4.7% (3.4% with dexamethasone+placebo)
Monoclonal antibodies
Alemtuzumab ≤ 1%
Isatuximab 4.6%
Obinutuzumab
Ofatumumab1%
Rituximab1-1.5%
Trastuzumab 0.4-0.6% (19% in women with cardiac comorbidities)
Proteasome inhibitors
Carfilzomib 0-3.9%
Bortezomib 3.3-6.8%
Tyrosine kinase inhibitors
Acalabrutinib 4-9.4% (grade ≥3: 1.3%)
Bosutinib 0.34-2.4%
Ibrutinib 4.5-29% (up to 38% at 2 years follow-up)
uPPR: 5.96 (5.70–6.23)
aROR: 8.68 (8.14-9.26)
Idelalisib
Midostaurin
Nilotinib 0.1-1.2%
Osimertinib
Pirtobrutinib 2.7% (grade ≥ 3: 1%)
Ponatinib 0.44-5.1%
Ribociclib
Trametinib
Zanubrutinib 1.8-5.2% (grade ≥ 3: 1%)
VEGF inhibitors: pazopanib, sorafenib, sunitinib 2.7-3.5%
Vemurafenib 1.5%
Miscellaneous drugs
Interferon-alpha2 6.8-12%
T-cell therapy
CD19-directed CAR T 0.6-11.1%
Axicabtagene ciloleucel 2.4%
Idecabtagene vicleucel 1.6-10.3%
Tisagenlecleucel 1.4%
Bispecific T-cell engagers (BiTEs)
Blinatumomab

https://doi.org/10.1016/j.phrs.2024.107077

Meds Used For A fib

Category / Class	Examples / Common Drugs in Canada
Rate Control	Metoprolol, Bisoprolol, Carvedilol, Atenolol, Propranolol, Diltiazem, Verapamil, Digoxin
Rhythm Control (Antiarrhythmic Drugs)	Class IC: Flecainide, Propafenone Class III: Amiodarone Class III: Sotalol Class III: Dronedarone
Anticoagulants (Stroke Prevention)	Warfarin (INR 2–3) DOACs: Dabigatran, Rivaroxaban, Apixaban, Edoxaban Antiplatelets: Aspirin, Clopidogrel



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In your patient with atrial fibrillation, which of the following stroke or bleeding risk factors are present?

Reset

Stroke Risk (CHA2DS2-VASc)

Age	◉ <65 ○ 65-74 ○ 75+		
TIA or stroke (at any time in the past)	☐	**CHF/LV dysfunction** (diagnosed at any time in the past)	☐
Prior MI, peripheral artery disease, or aortic plaque	☐	**Hypertension** (controlled or uncontrolled)	☐
Female	☐	**Diabetes Type I or II** (controlled or uncontrolled)	☐
		CHA2DS2-VASc SCORE (0-9):	**0**

Major Bleeding Risk (HAS-BLED)

Abnormal renal function (dialysis, SCr>200 mcmol/L, or transplant)	☐	**History of labile INR** (time in therapeutic range <60%)	☐
Hypertension (SBP>160mmHg)	☐	**Current use of alcohol** (>8 drinks per week)	☐
Abnormal liver function (cirrhosis or liver enzymes >3x ULN)	☐	**Currently taking antiplatelet drug or NSAID**	☐
History of major bleeding (any cause)	☐	**HAS-BLED SCORE (0-9):**	**0**

PERCENT PER YEAR

	annual risk of **stroke/embolism**	annual risk of **major bleeding** (intracranial bleeding, bleeding requiring hospitalization, HgB decrease of > 20 g/L, or need for transfusion secondary to bleeding)
NO THERAPY	4.3%	0.6%
ASPIRIN	3.4%	1.1%
WARFARIN	1.4%	2.2%
DABIGATRAN 110	1.4%	1.8%
DABIGATRAN 150	0.9%	2.2%
RIVAROXABAN	1.4%	2.2%
APIXABAN	1.1%	1.5%

http://www.sparctool.com

Meds That Can Reduce Stroke Risk

Therapy	Relative risk reduction (vs no therapy)
Aspirin (ASA)	**34%**
ASA + clopidogrel	**44%**
Warfarin (INR 2–3)	**66%**
Dabigatran 110 mg bid	**66%**
Dabigatran 150 mg bid	**78%**
Rivaroxaban 20 mg qd	**66%**
Apixaban 5 mg bid	**74%**
Edoxaban 30 mg qd	**66%**
Edoxaban 60 mg qd	**71%**

https://www.sparctool.com/

	Warfarin	**DOACs (avg across Apixaban, Rivaroxaban, Dabigatran, Edoxaban)**
Therapeutic range time (INR 2–3)	60–65% of time	Not applicable
Onset of action	2–4 days to therapeutic effect	2–4 hours
Offset after stopping	3–5 days	1–2 days
Side effects	Bleeding	Bleeding
Drug interactions (clinically relevant)	> 100 known	≈ 20–30 known
Food interactions (vitamin K related)	YES	None
Lab monitoring	Every 1–4 weeks	None routine
Cost (Canada, 2025)	90 days ≈ $20	90 days ≈ $100 - dabigatran $250
Renal dose limits (eGFR mL/min)	Usable down to < 15	Generally avoided < 30
Half-life	36–42 h	8–15 h
Reversal availability (typical hospital)	> 95%	Possible but usually not needed

DOACs*	Pros	Cons
Dabigatran **110, 150 mg**	150 mg ~0.5-1% ⬆ stroke benefit over other NOACs	Twice daily 150 mg ~0.5% ⬆ bleeding risk over other DOACs More expensive
Rivaroxaban	Once daily	
Apixaban	~0.5%⬇ in bleeding risk versus D and R	Twice daily
Edoxaban **30, 60mg**	Once daily 30 mg ~ 1%⬇ in bleeding risk versus D and R	

* but **NO head-to head trials** (all studied against warfarin) so outcome differences not definitive