# Atrial Fibrillation: Keeping Up with the Beat

Atrial Fibrillation Clinic

Heart Rhythm Services

Serena Kutcher, RN, BScN Patient Educator
Sonia Basi, BSc (Pharm)
Belinda-Ann Furlan, NP(F), MSN

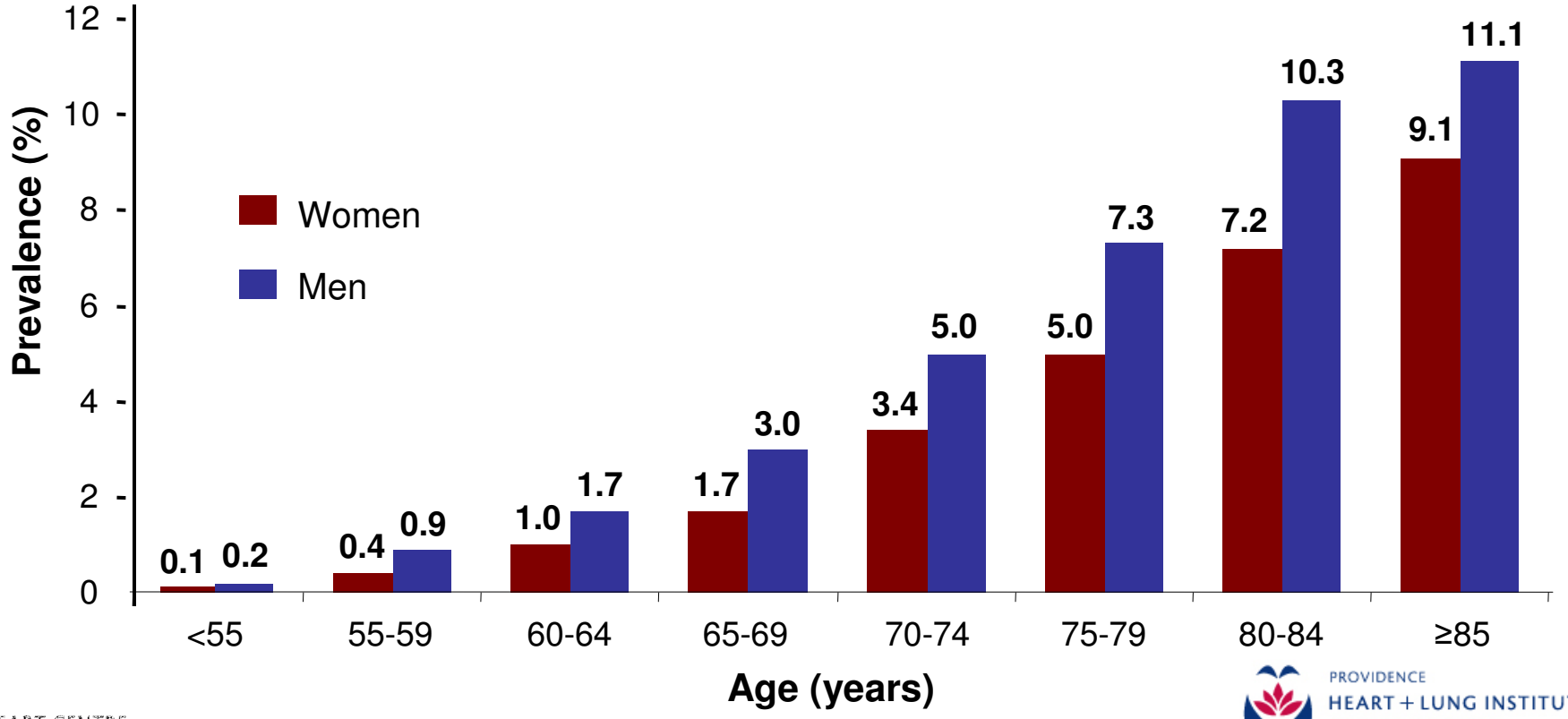
# Objectives

To increase knowledge and understanding of:

- Atrial Fibrillation (AF)
- Stroke Prevention
- Pharmacotherapy for AF
- Procedural Strategies for AF
    - Direct-Current Cardioversion
    - Catheter Ablation

# Atrial Fibrillation: Prevalence

- **Most common arrhythmia**
- **Risk increases with age**

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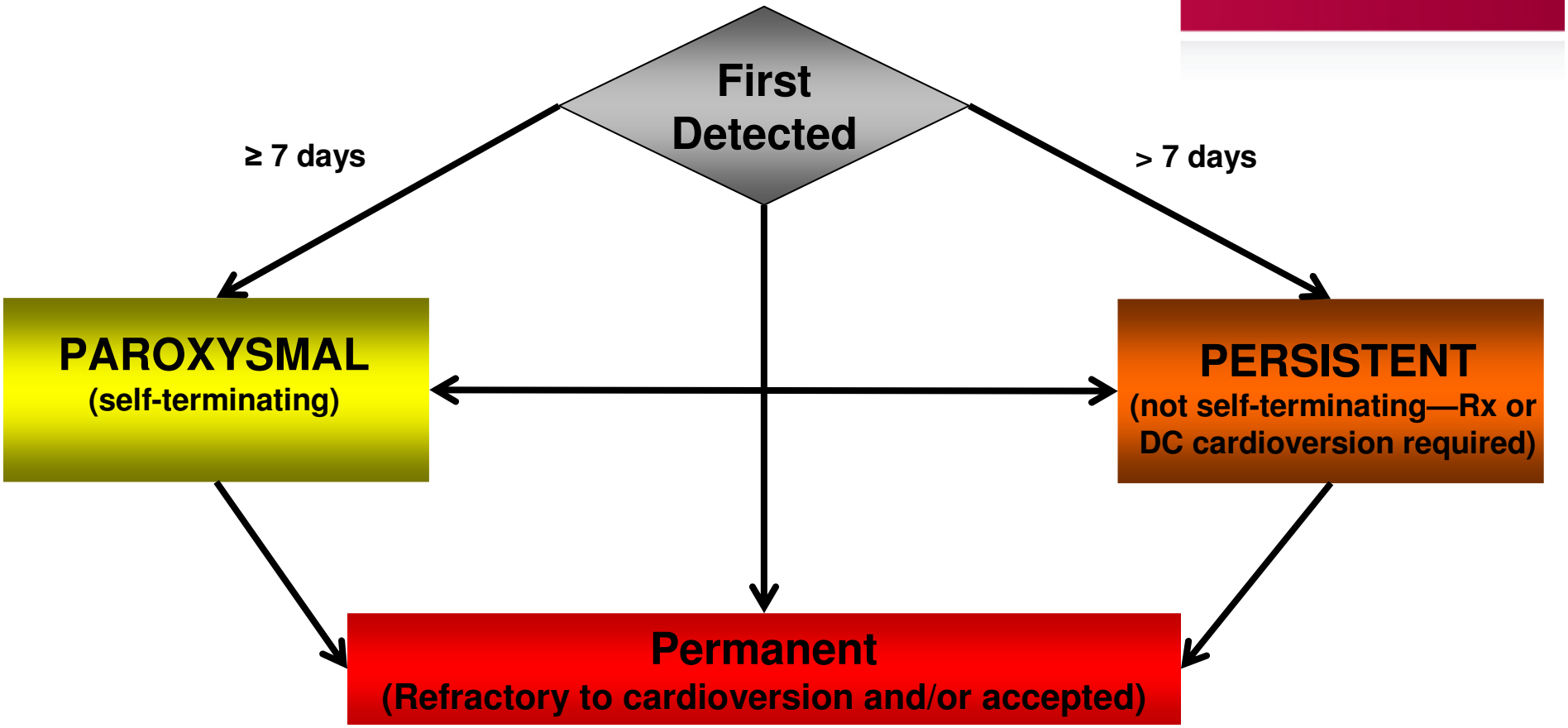
Go A.S., et al. JAMA 2001;285:2370-2375.

# Atrial Fibrillation: Consequences

- **Quality of life (QOL)**
  - May be considerably impaired due to risk of exacerbation of symptoms.[1]
- **Leading cause of hospitalizations for arrhythmia**
  - AF accounts for approximately one-third of hospitalizations for cardiac rhythm disturbances[2]
- **Morbidity and mortality**
  - ~5-fold increase in risk of stroke[3]
    - Stroke associated with AF is typically more severe than ischemic stroke due to other causes[4]
  - 2-fold increase in risk of mortality[5]
  - AF promotes heart failure and HF aggravates AF to worsen a patient's overall prognosis[6]


1. Hamer M.E., et al. Am J Cardiol 1994;74:826-829.
2. Go A.S., et al. JAMA 2001;285:2370-2375.
3. Wolf, et al. Stroke 1991:22:983-988.
4. Dulli D.A., et al. Neuroepidemiology 2003;22(2):118-123.
5. Benjamin E.J., et al. Circulation 1998;98:946-952.
6. Wang T.J., et al. Circulation 2003;107:2920-2925.

# Classification of Atrial Fibrillation

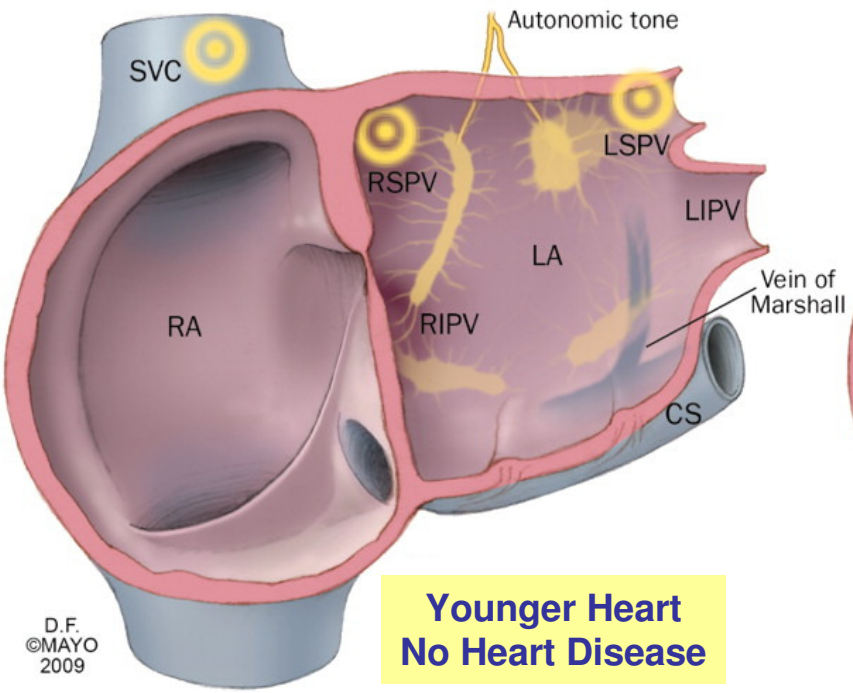





ACC/AHA/ESC 2006 guidelines. J Am Coll Cardiol 2006;48:854-906.

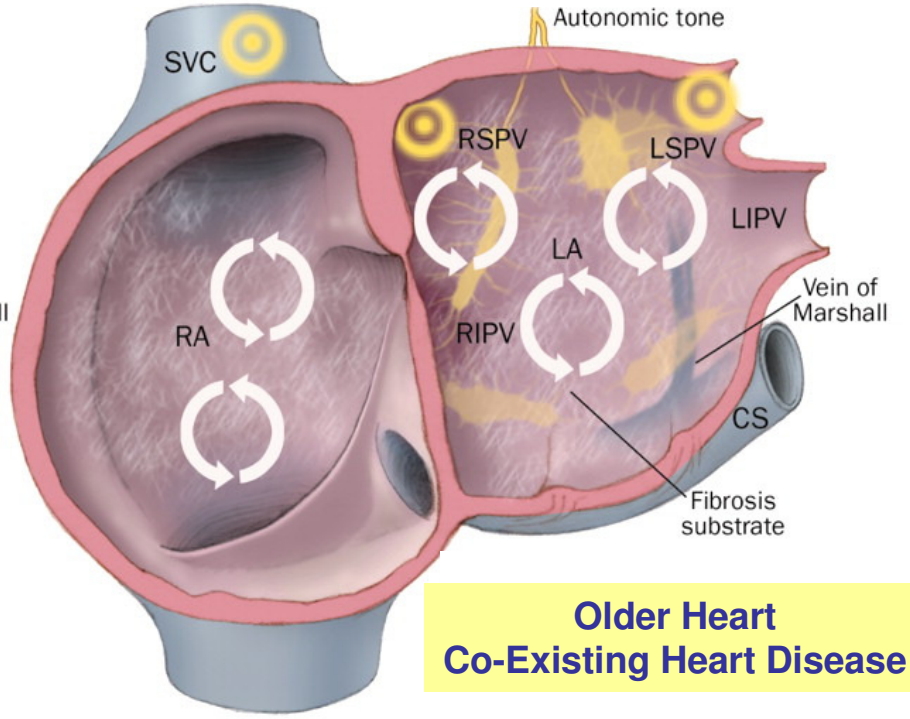
# Atrial Fibrillation

## Paroxysmal




**Younger Heart**
**No Heart Disease**

## Persistent

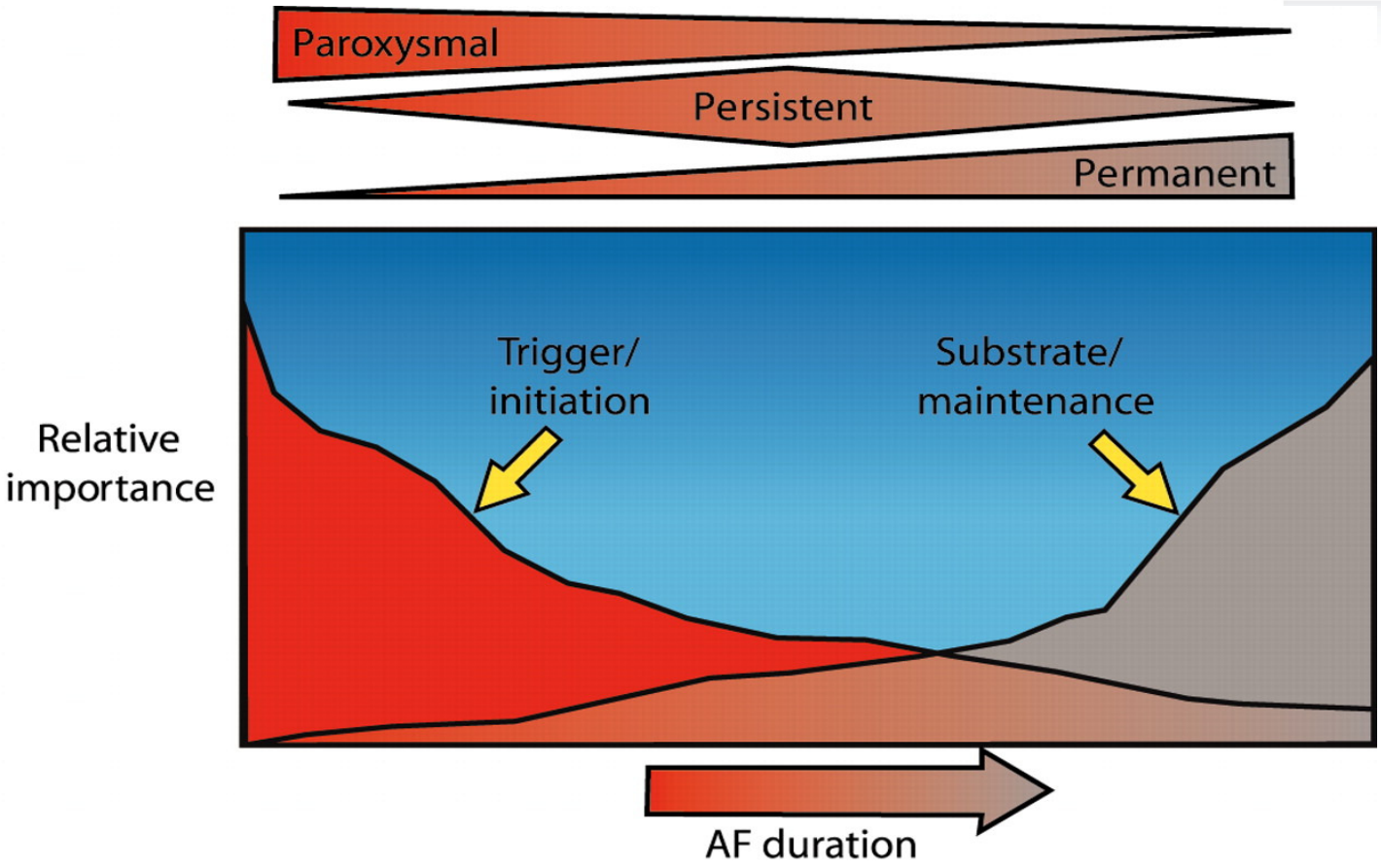



**Older Heart**
**Co-Existing Heart Disease**



http://www.mayoclinicproceedings.com/content/84/7/643.figures-only

# Atrial Fibrillation: Spectrum of Pathology

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# Symptoms of Atrial Fibrillation

- Palpitations
- Fatigue
- Dizziness, presyncope or syncope
- Nausea or diaphoresis
- Chest pain
- Asymptomatic

# Atrial Fibrillation: Assessing Symptom Burden

- Increasing emphasis on patient-defined outcomes
- CCS Severity in Atrial Fibrillation (SAF) Scale
  - Class 0 Asymptomatic
  - Class 1 Minimal effect on quality of life (QOL)
  - Class 2 Minor effect on QOL
  - Class 3 Moderate effect on QOL
  - Class 4 Severe effect on QOL

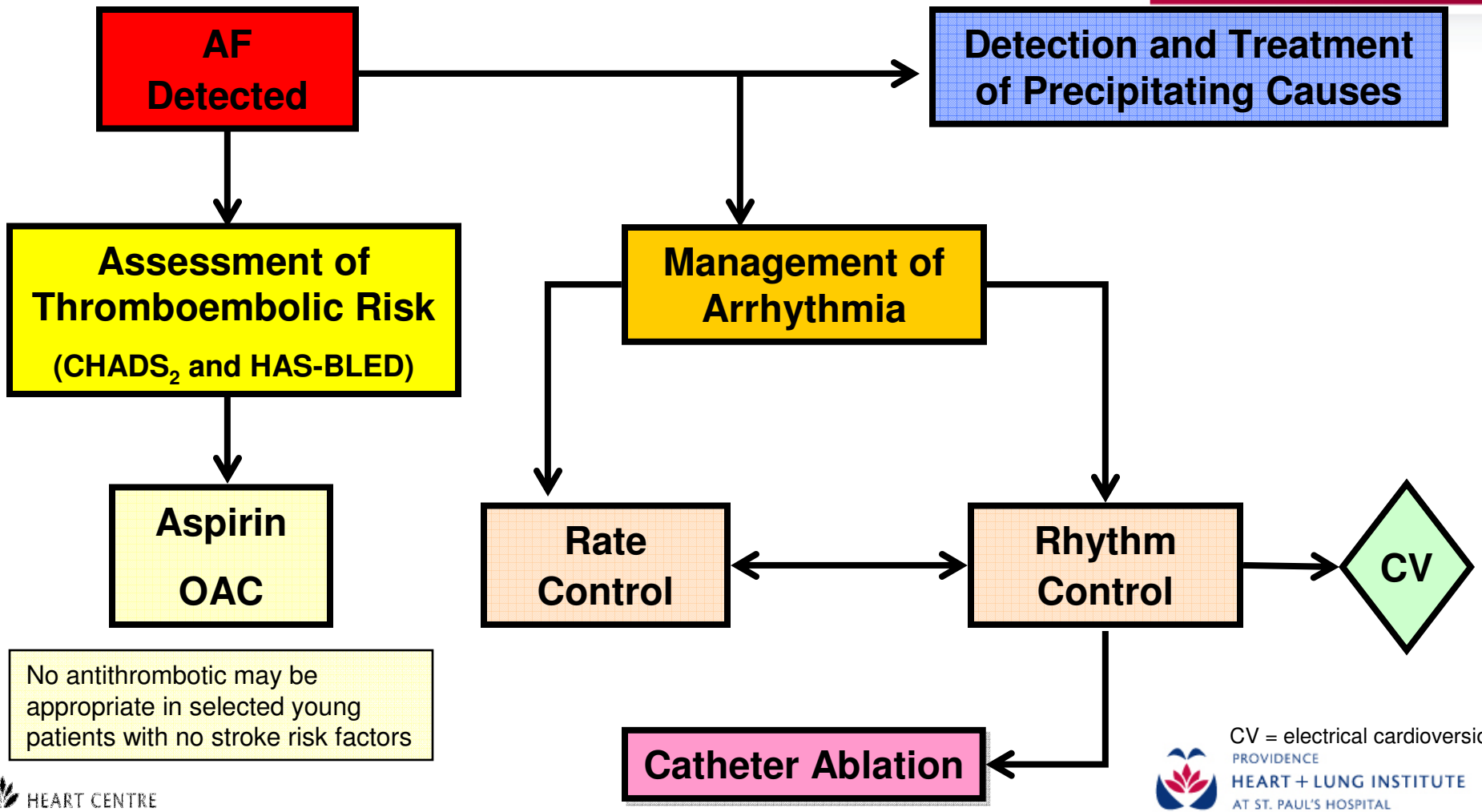
# CCS SAF Scale: Assessing Symptom Burden

| Class 0 |
| --- |
| Asymptomatic with respect to AF |
| **Class 1** |
| Symptoms attributable to AF have *minimal* effect on patient's quality of life (QOL)<br>Minimal and/or infrequent symptoms, or<br>Single episode of AF without syncope or heart failure |
| **Class 2** |
| Symptoms attributable to AF have *minor* effect on patient's QOL<br>Mild awareness of symptoms in patients with persistent/permanent AF, or<br>Rare episodes (e.g. less than a few per year) in patients with paroxysmal or intermittent AF |
| **Class 3** |
| Symptoms attributable to AF have a *moderate* effect on patient's QOL<br>Moderate awareness of symptoms on most days in patients with persistent/permanent AF, or<br>More common episodes (e.g. more than every few months) or more severe symptoms, or both, in patients with paroxysmal or intermittent AF |
| **Class 4** |
| Symptoms attributable to AF have a *severe* effect on patient's QOL<br>Very unpleasant symptoms in patients with persistent/paroxysmal AF and/or<br>Frequent or highly symptomatic episodes in patients with paroxysmal or intermittent AF and/or<br>Syncope thought to be due to AF and/or<br>Congestive heart failure due to AF |

# Atrial Fibrillation: Goals of Therapy

- Reduce symptom burden and improve QOL
- Prevent tachycardia-induced cardiomyopathy and CHF
- Decrease risk of stroke

# Overview of AF Management




CV = electrical cardioversion

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Gillis AM et al. Can J Cardiol. 2010;27:47-59.

# Investigations

- Electrocardiogram
- Event monitor PRN
- Identify etiology
- Basic lab work
  - CBC, electrolytes, renal, thyroid, and liver function, fasting lipid profile, fasting glucose, INR
- Echocardiogram
  - LA size, LA volume, LV function, valve abnormalities
- Holter Monitor



Gillis AM et al. Can J Cardiol. 2010;27:31-37.

# Potential Causes of Atrial Fibrillation

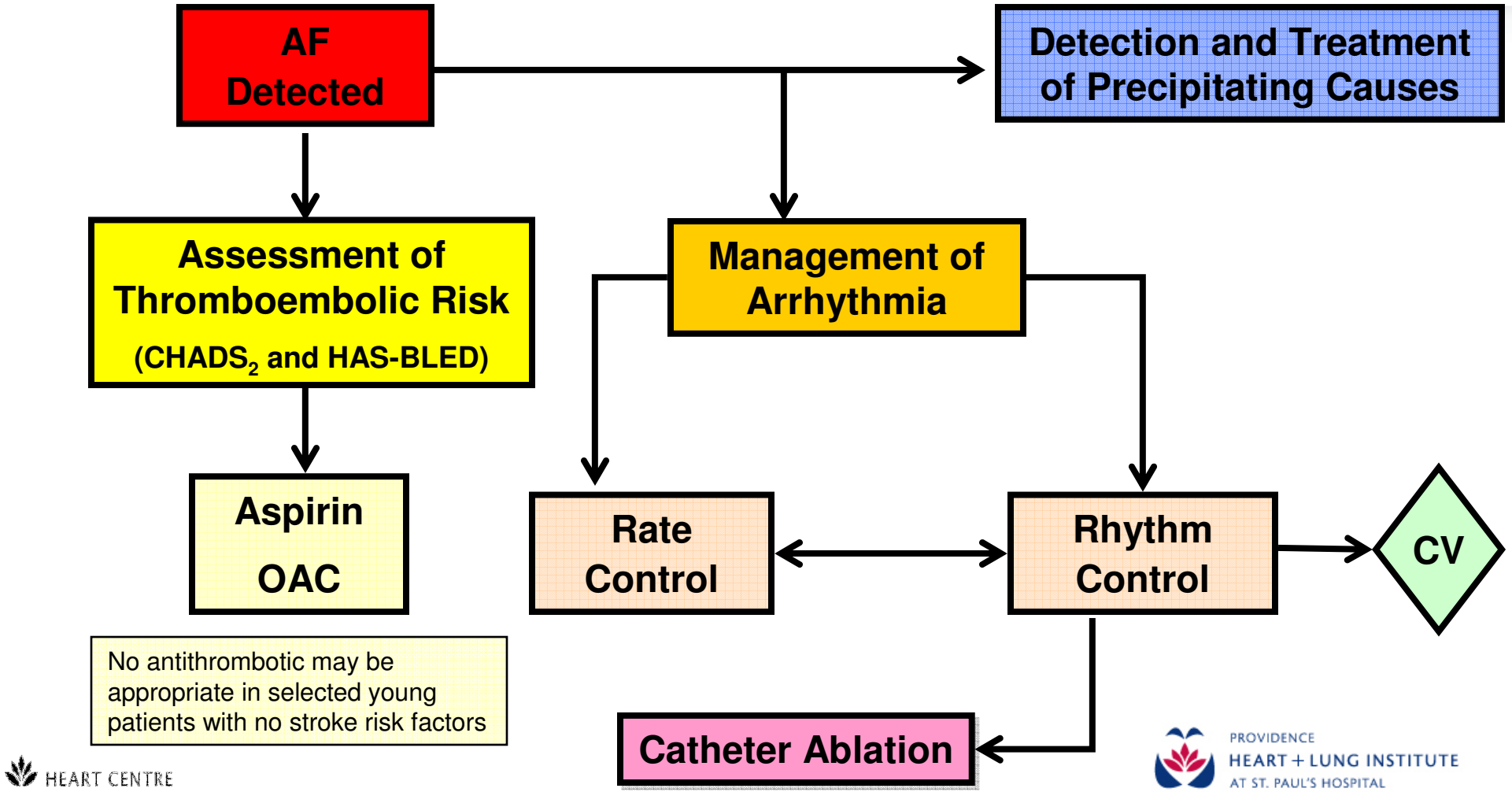
| CARDIAC | NON-CARDIAC | IDIOPATHIC |
|---|---|---|
| • HTN<br>• CHF*<br>• MI<br>• CMO<br>• LV dysfunction*<br>• Valvular disease<br>• Congenital heart disease*<br>• Sick Sinus Syndrome<br>• AF 2° to ventricular pacing*<br>• SVT*<br>• Post cardiac surgery<br>• Genetic/ familial | • OSA*<br>• Pneumonia<br>• COPD<br>• Pulmonary embolism<br>• Pulmonary hypertension<br>• Hyperthyroidism*<br>• Excessive alcohol*<br>• Aerobic training<br>• Obesity* | • Lone AF |

*treatment of cause may prevent the development or recurrences of AF



Gillis AM et al. Can J Cardiol. 2010;27:31-37.

# AF Management: Stroke Risk Modification

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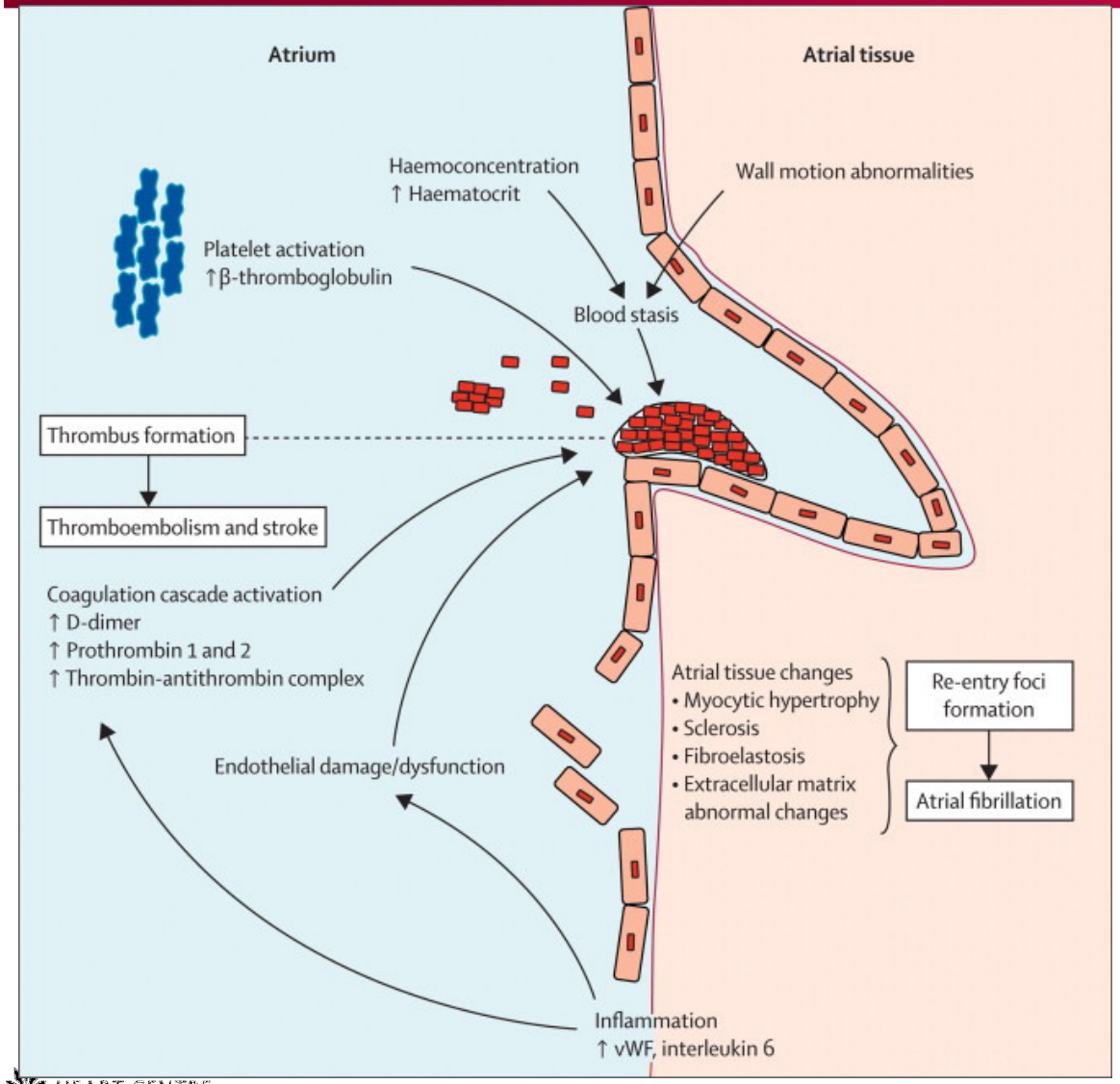
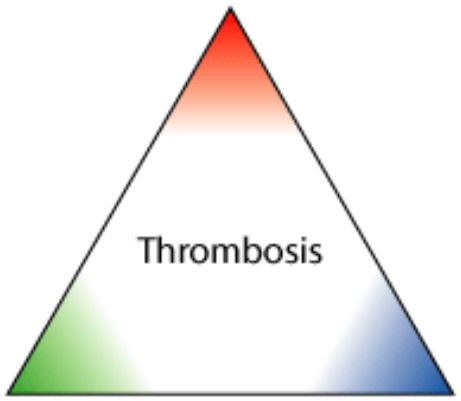
# Thrombogenesis in AF: Applying Virchow's Triad




**Circulatory Stasis**




**Endothelial Injury**

**Hypercoagulable State**

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Watson T, Shantsila E, Lip GY. Lancet. 2009;373:155-166.

# Evaluating Stroke Risk: $CHADS_2$

- **$CHADS_2$**

| | |
|---|---|
| **C**ongestive Heart Failure | 1 point |
| **H**ypertension | 1 point |
| **A**ge ≥ 75 years | 1 point |
| **D**iabetes | 1 point |
| **S**troke or TIA | 2 points |



Gillis AM et al. Can J Cardiol. 2010;27:74-90.

# Evaluating Stroke Risk Further: $CHA_2DS_2$-VASc

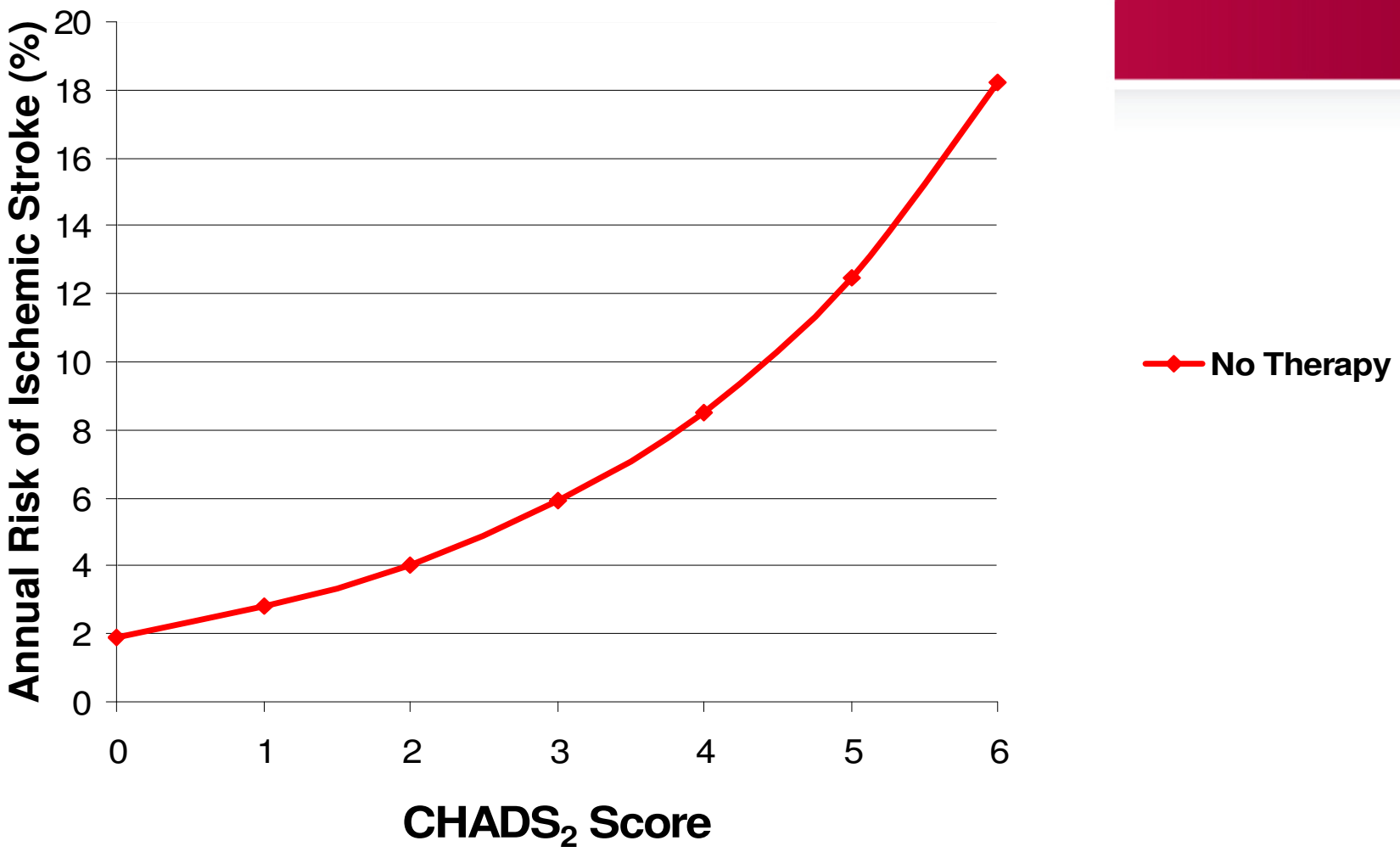
- **$CHA_2DS_2$-VASc**

| | |
|---|---|
| **C**ongestive Heart Failure | 1 point |
| **H**ypertension | 1 point |
| **A**ge ≥ 75 years | 2 point |
| **D**iabetes mellitus | 1 point |
| **S**troke/TIA/TE | 2 points |
| **V**ascular disease | 1 point |
| **A**ge 65 to 74 years | 1 point |
| **S**ex **c**ategory is female | 1 point |



http://www.escardio.org/congresses/esc-2010/congress-news/Pages/guidelines-atrial-fibrillation.aspx

# Annual Risk of Ischemic Stroke

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# Evaluating Bleeding Risk: HAS-BLED Score

- **HAS-BLED**

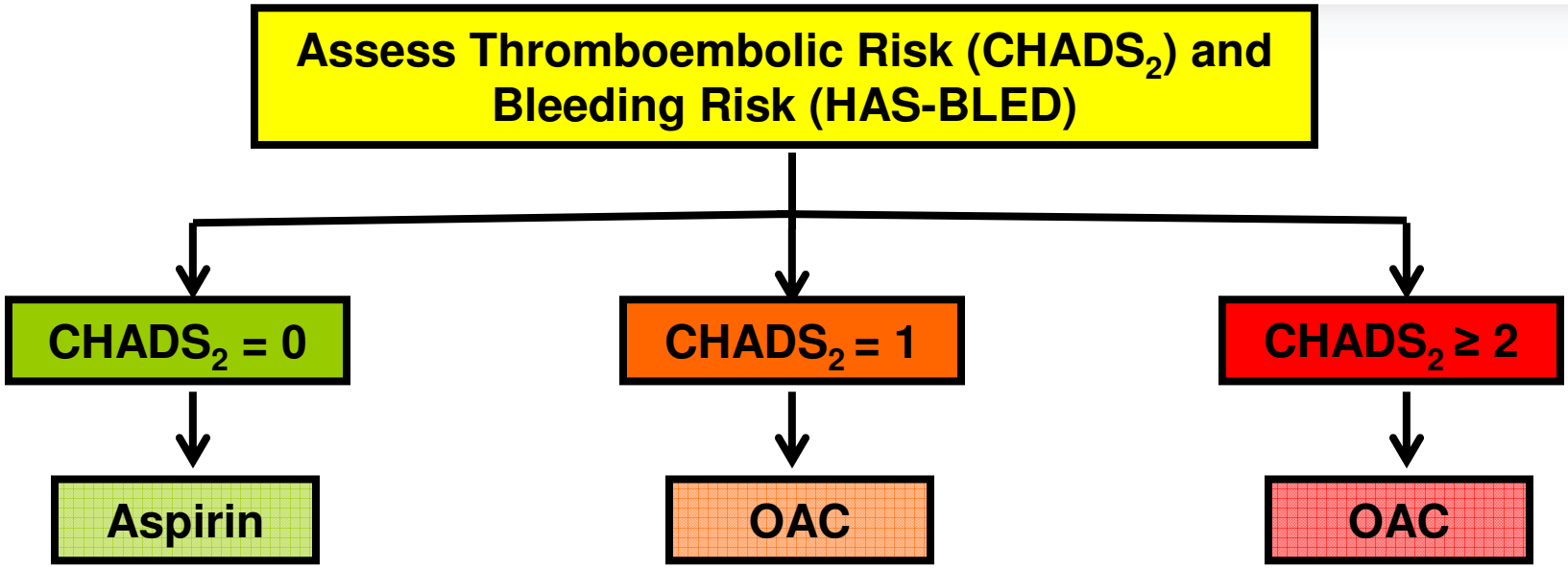
**H**ypertension (systolic ≥ 160 mmHg) = 1 point
**A**bnormal renal or liver function = 1 or 2 points
**S**troke in past = 1 point
**B**leeding = 1 point
**L**abile INRs = 1 point
**E**lderly (age > 65 years) = 1 point
**D**rugs or alcohol = 1 or 2 points

**CAUTION with OAC for score ≥ 3**



Gillis AM et al. Can J Cardiol. 2010;27:74-90.

# Overview of Thromboembolic Therapy




No antithrombotic may be appropriate in selected young patients with no stroke risk factors

Aspirin is a reasonable alternative in some as indicated by risk-benefit

Dabigatran is preferred OAC over warfarin in most patients

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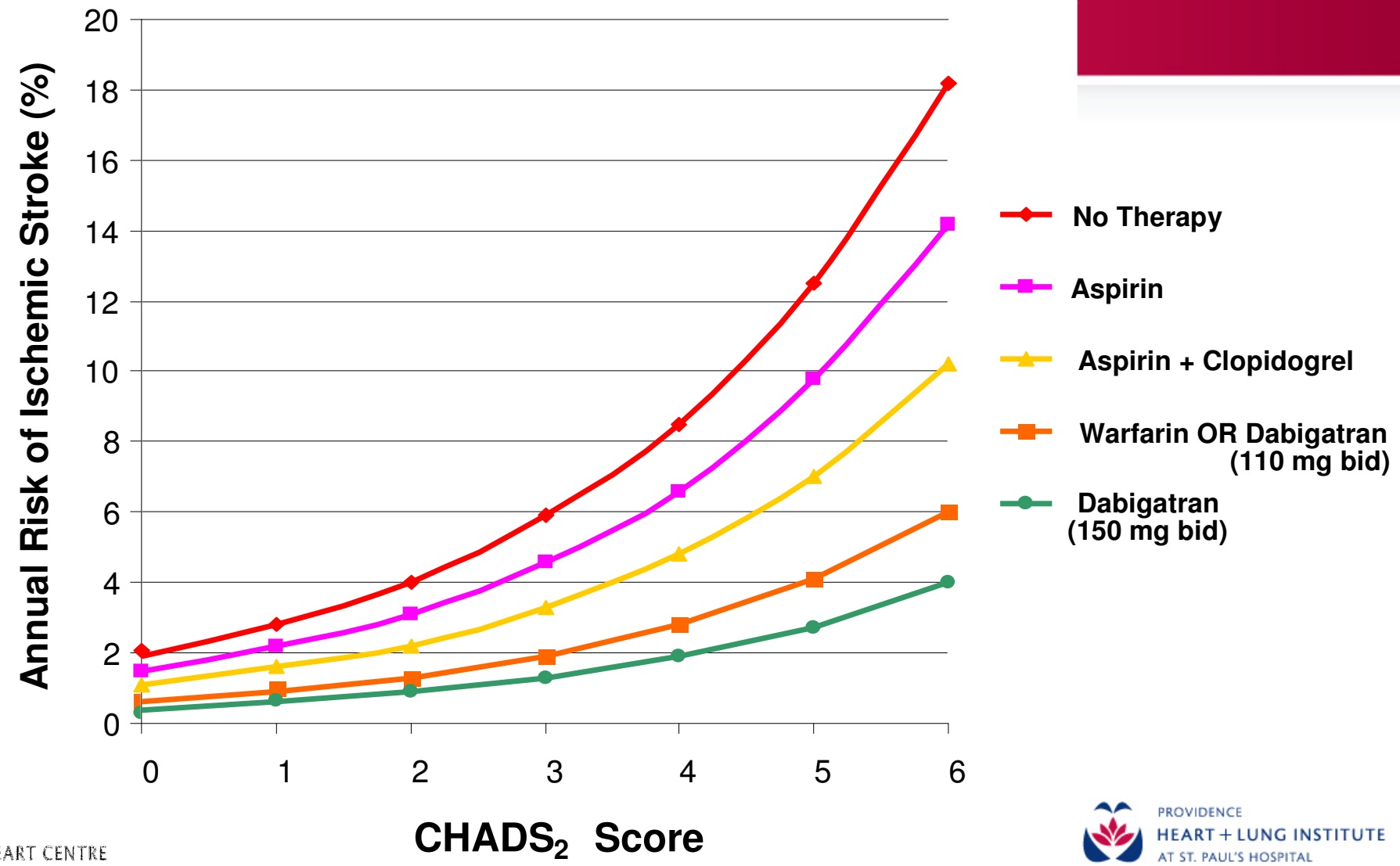
# Managing Stroke Risk: Antithrombotic Agents



# RE-LY:
## Randomized Evaluation of Long-term Anticoagulant TherapY

**Non-valvular AF with $CHADS_2 \geq 1$ or CAD**
(**Excluded**: severe valve disease, CrCl < 30 mL/min, severe liver disease, recent stroke, high bleeding risk)

**44 Countries**
**951 Centres**

**Mean $CHADS_2$ = 2.1**

**Randomized**

**OPEN** | **BLINDED**

| Warfarin | Dabigatran 110 mg bid | Dabigatran 150 mg bid |
|---|---|---|
| (target INR 2 to 3) | | |
| n = 6022 | n = 6015 | n = 6076 |

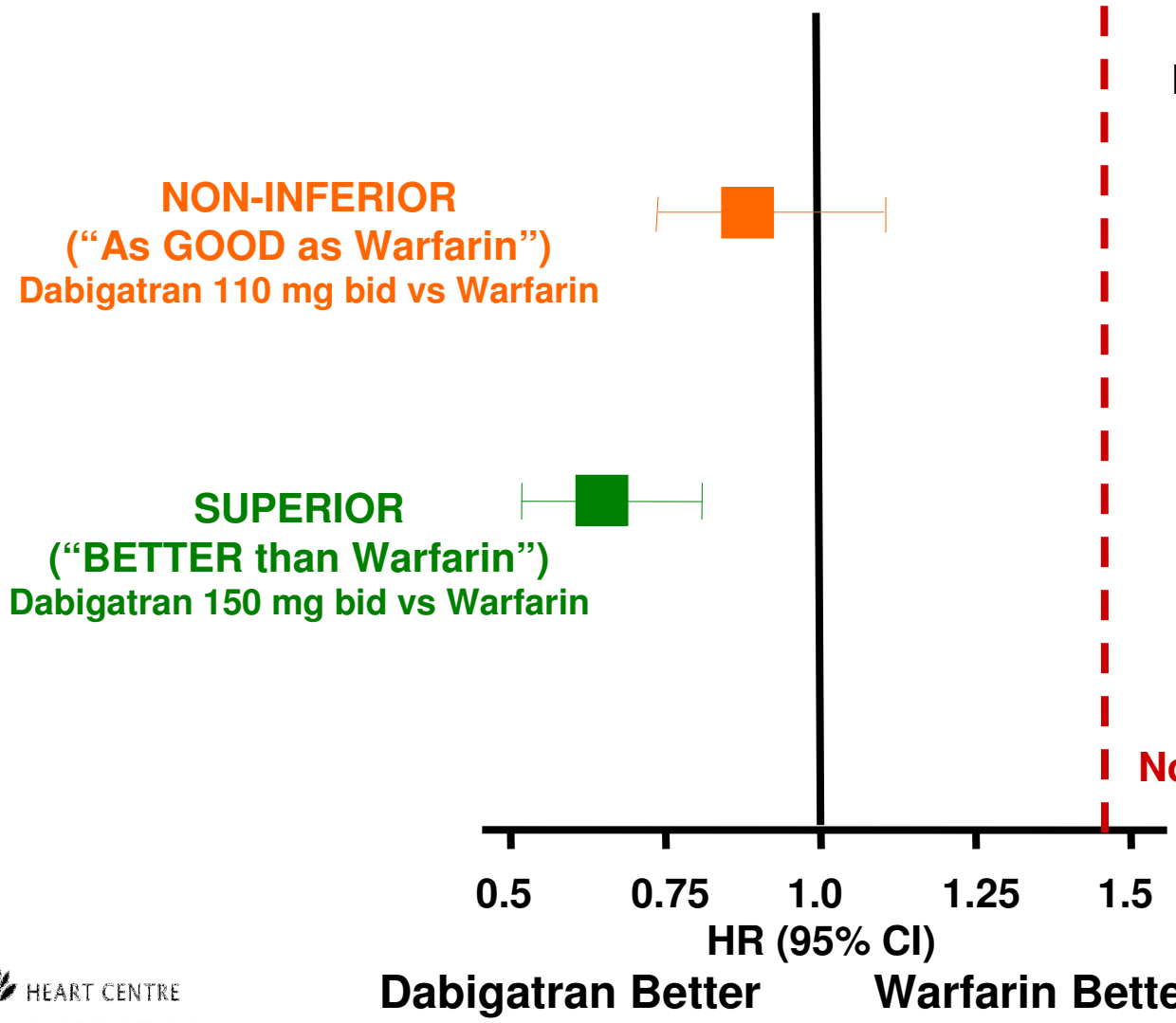
- **Non-inferiority trial**
- **1° Outcome: Composite of stroke or systemic emboli**
- **1° Safety Outcome: Major bleeding**
- **Follow-up median = 2 years**





Connolly SJ et al. N Engl J Med. 2009;361:1139-51.

# RE-LY: Primary Outcome Results
## (Composite of stroke or systemic embolism)




| | Non-Inferiority p-value | Superiority p-value |
|---|---|---|
| NON-INFERIOR ("As GOOD as Warfarin") Dabigatran 110 mg bid vs Warfarin | < 0.001 | < 0.34 |
| SUPERIOR ("BETTER than Warfarin") Dabigatran 150 mg bid vs Warfarin | < 0.001 | < 0.001 |

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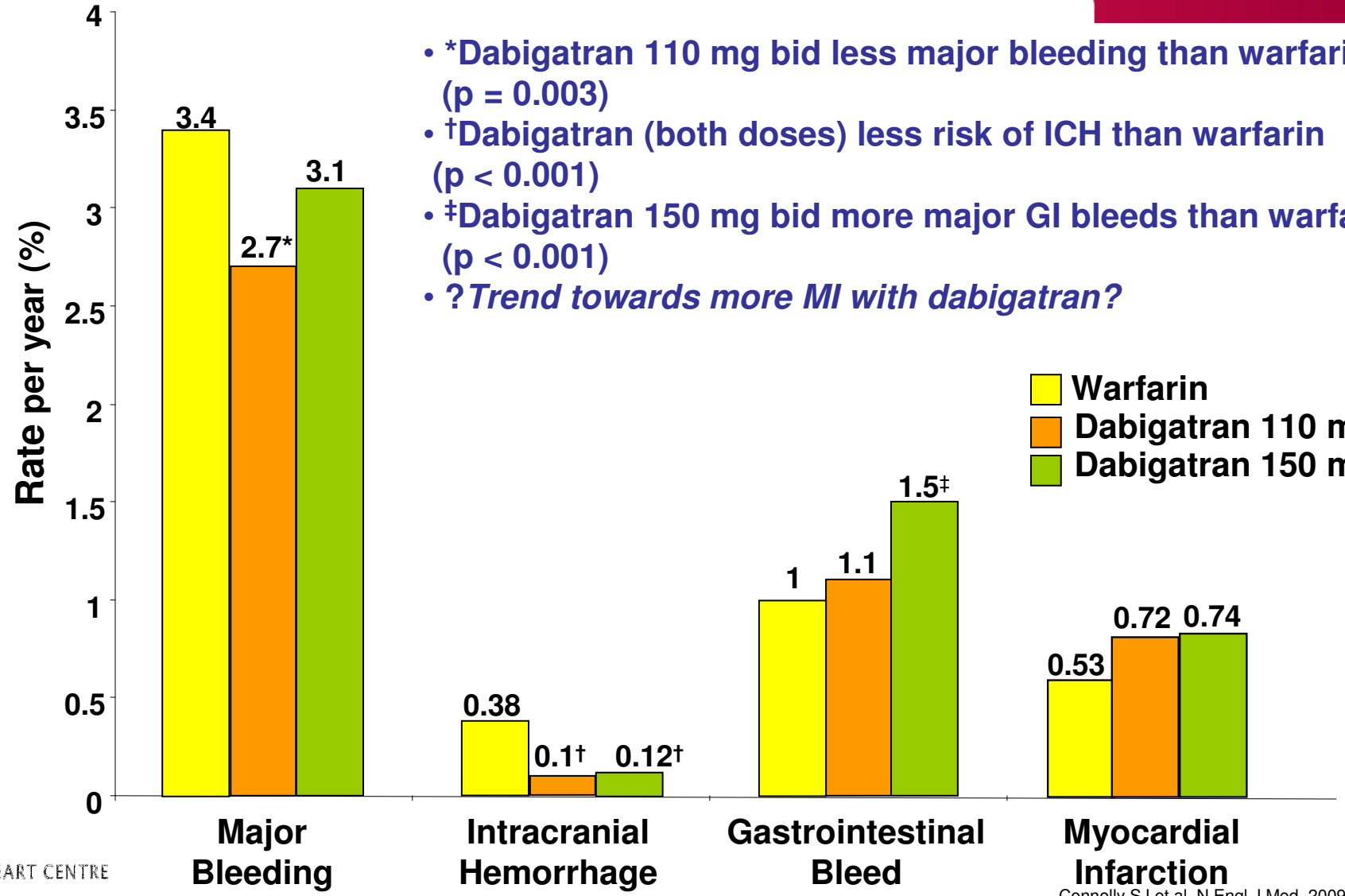
# RE-LY: Primary Safety Outcome Results




- *Dabigatran 110 mg bid less major bleeding than warfarin ($p = 0.003$)
- †Dabigatran (both doses) less risk of ICH than warfarin ($p < 0.001$)
- ‡Dabigatran 150 mg bid more major GI bleeds than warfarin ($p < 0.001$)
- ?*Trend towards more MI with dabigatran?*

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Connolly SJ et al. N Engl J Med. 2009;361:1139-51.

# Managing Stroke Risk: Antithrombotic Agents

| | DOSE | RRR | NOTES |
|---|---|---|---|
| **ASPIRIN** | 80–325 mg qd | 22% | - Cost: $3/month |
| **CLOPIDOGREL** | 75 mg qd | 44%* | - Cost: $90/month; Special Authority required |
| **WARFARIN** | INR 2 to 3 | 66% | - Cost: $15/month<br>- Lab monitoring for anticoagulant effect: INR<br>- Antidote: Vitamin K<br>- Diet modification: consistent vitamin K content<br>- Drug Interactions: numerous; monitor INR |
| **DABIGATRAN** | 110 mg bid | 66% | - Cost: ~$110/month; not a Pharmacare benefit<br>-Twice daily dosing<br>- Contraindicated for CrCl < 30 mL/min<br>- Lab monitoring for anticoagulant effect: ???<br>- Antidote: none<br>- Diet modification: none<br>- Drug Interactions: verapamil, amiodarone--no method of monitoring anticoagulant effect<br>- Storage Issues: 1 month if exposed to air |
| | 150 mg bid | 78% | |

*RRR for combination clopidogrel + aspirin (ACTIVE-A Trial)

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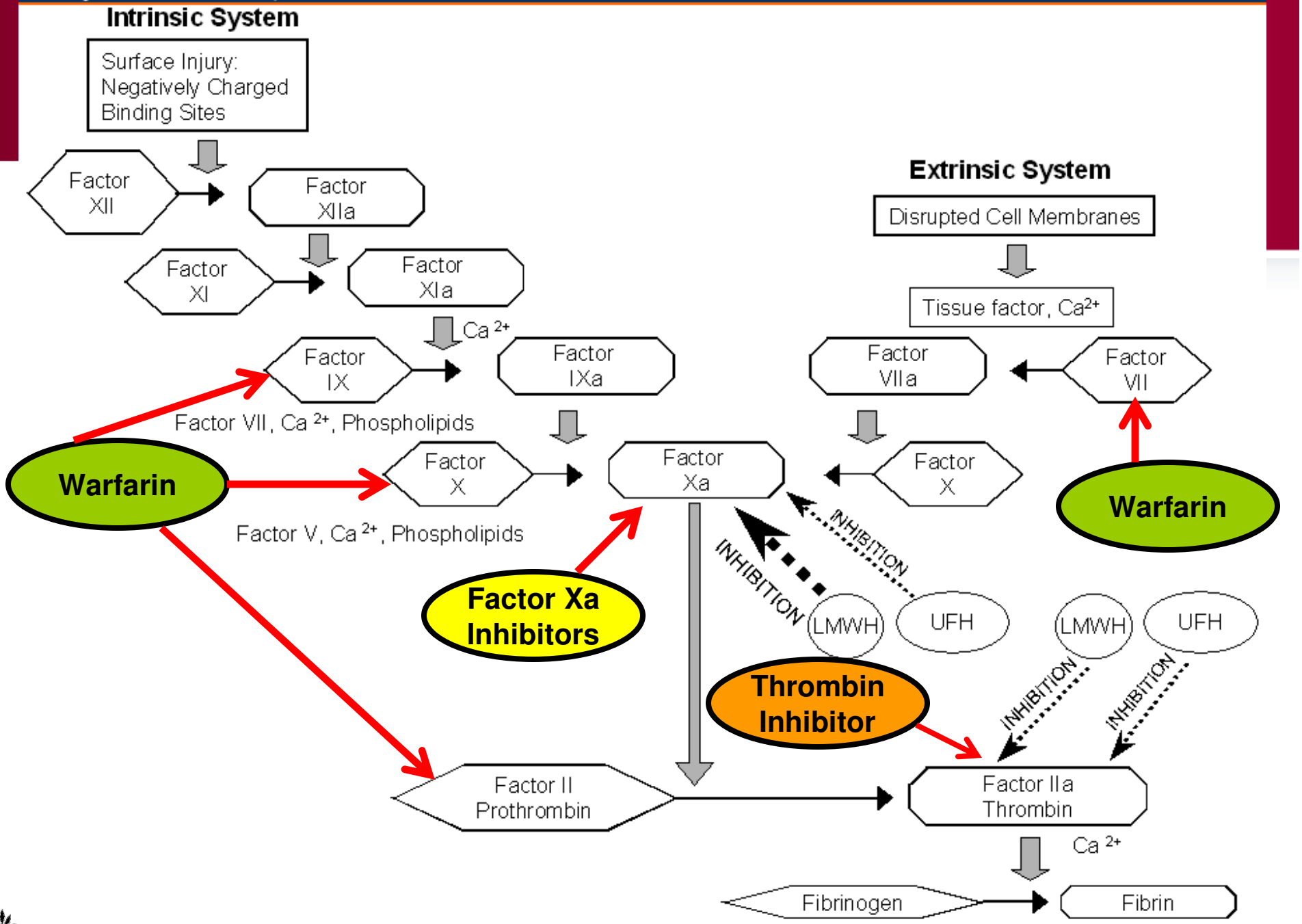
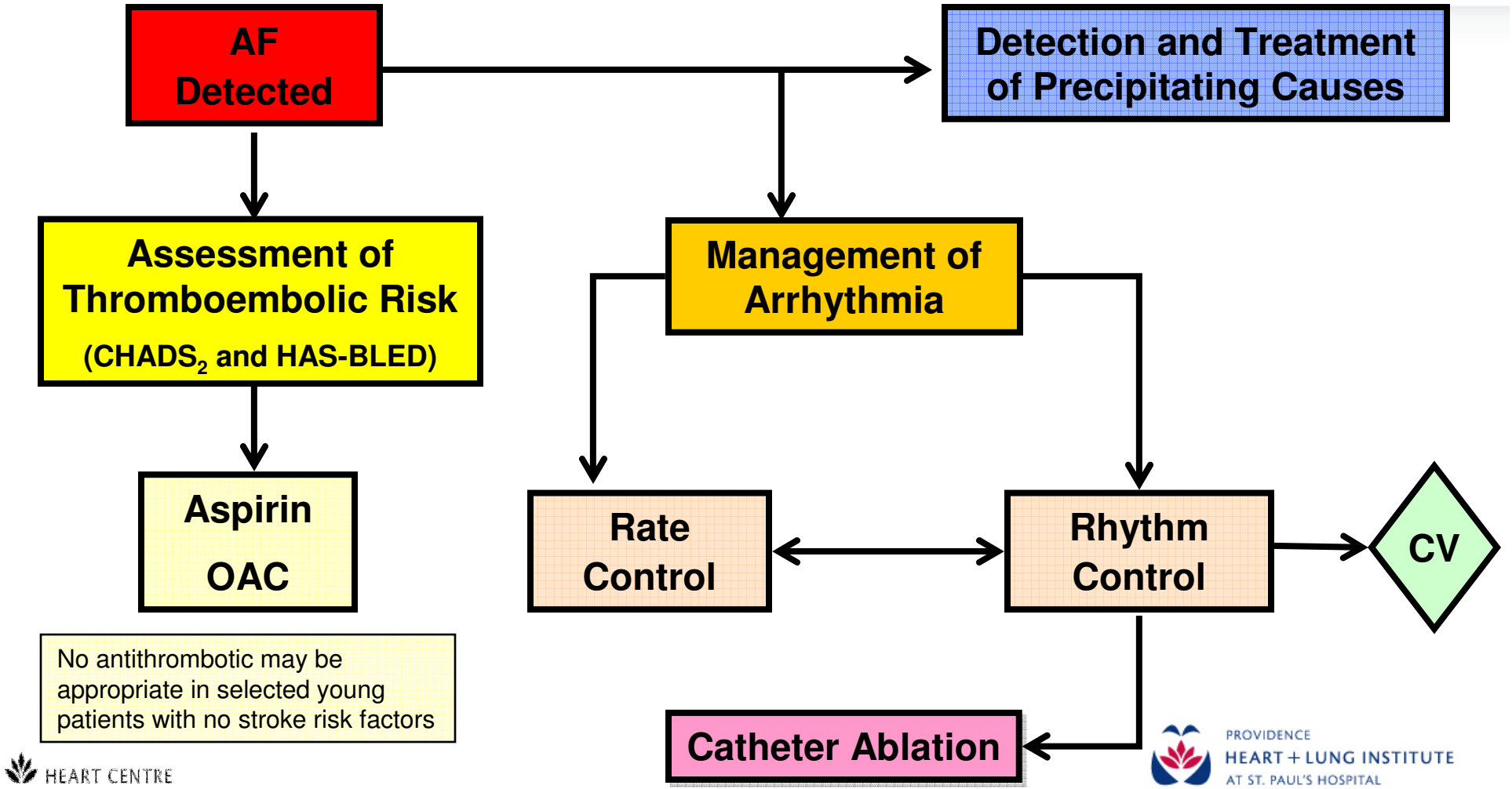
RRR = Relative Risk Reduction



# Antithrombotic Agents:
## Alternatives to Warfarin in the Pipeline

- Factor Xa Inhibitors
  - Rivaroxaban (oral, daily) (ROCKET AF)
  - Apixaban (oral, bid) (AVERROES, ARISTOTLE)
  - Betrixaban (oral, daily) (EXPLORE Xa)
  - Edoxaban (oral, daily) (ENGAGE AF-TIMI 48)
  - Idraparinux (sc injection, weekly) (AMADEUS-stopped early, bleeding risk)
  - Idrabiotaparinux (sc injection, weekly) (BOREALIS AF- terminated)

# AF Management: Drug Options

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# Rate and/or Rhythm Strategy

| Favors RATE Control | Favors RHYTHM Control |
|---|---|
| Persistent AF | Paroxysmal AF |
| | Newly Detected AF |
| Less Symptomatic | More Symptomatic |
| Over 65 years of age | Less than 65 years of age |
| Hypertension | No Hypertension |
| No History of CHF | CHF clearly exacerbated by AF |
| Previous Antiarrhythmic Drug Failure | No Previous Antiarrhythmic Drug Failure |



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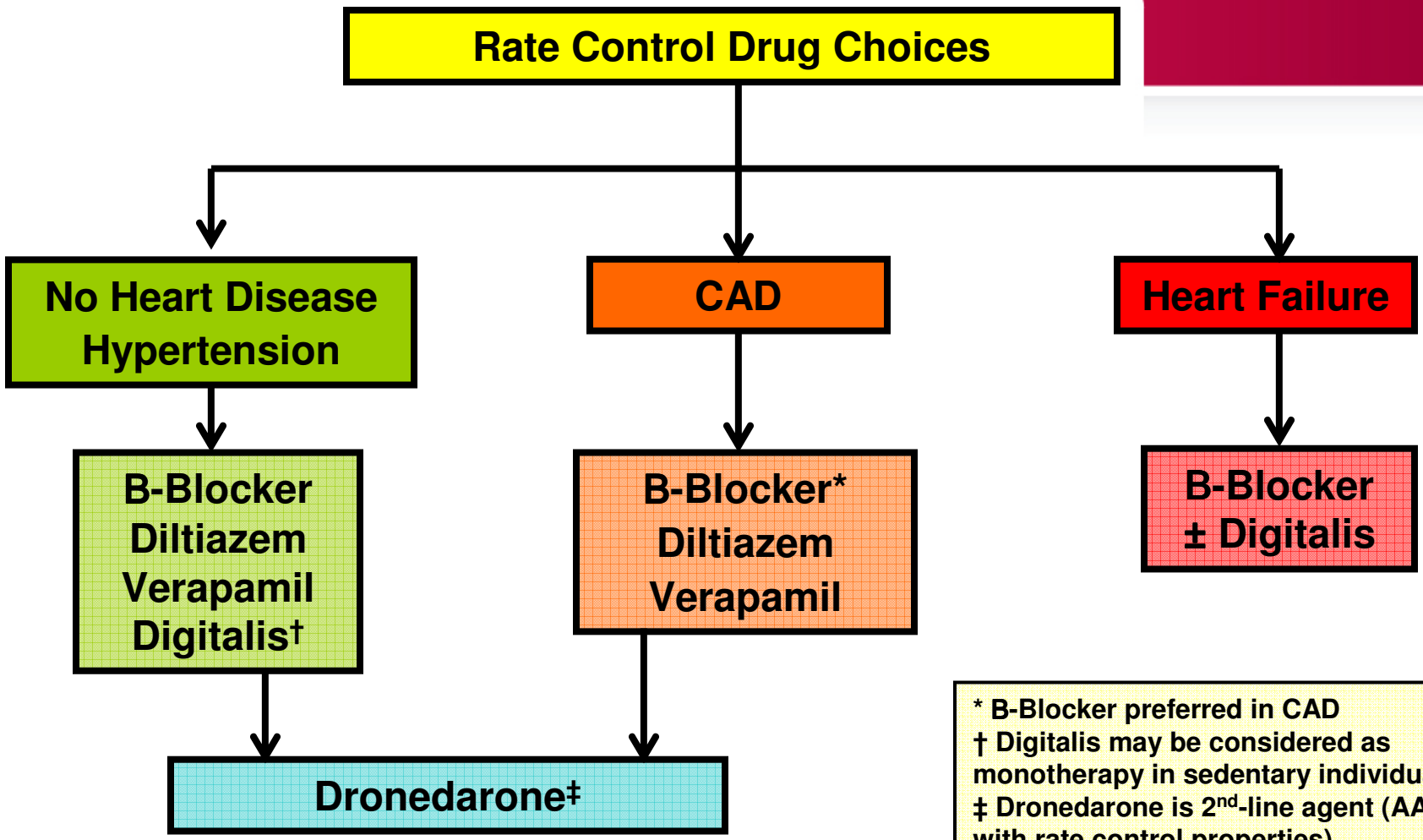
# Rate Control: Drug Choices




* B-Blocker preferred in CAD
† Digitalis may be considered as monotherapy in sedentary individuals
‡ Dronedarone is 2nd-line agent (AAD with rate control properties)

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# Rate Control

- Goals of therapy
  - Improve symptoms and quality of life
  - Prevent deterioration of cardiac function
- Rate control agents do not prevent AF or convert to NSR
- Target resting heart rate less than 100 bpm[1]

| Beta Blockers | Non-Dihydropyridine Calcium Channel Blockers | Cardiac Glycoside |
|---|---|---|
| • Atenolol (Tenormin®)<br>• Bisoprolol (Monocor®)<br>• Carvedilol (Coreg®)<br>• Metoprolol (Lopresor®)<br>• Propranolol (Inderal®)<br><br>**AVOID agents with intrinsic sympathomimetic activity (i.e. acebutolol, pindolol)** | • Diltiazem (Cardizem CD®,Tiazac®)<br>• Verapamil (Isoptin®) | • Digoxin (Lanoxin®) |



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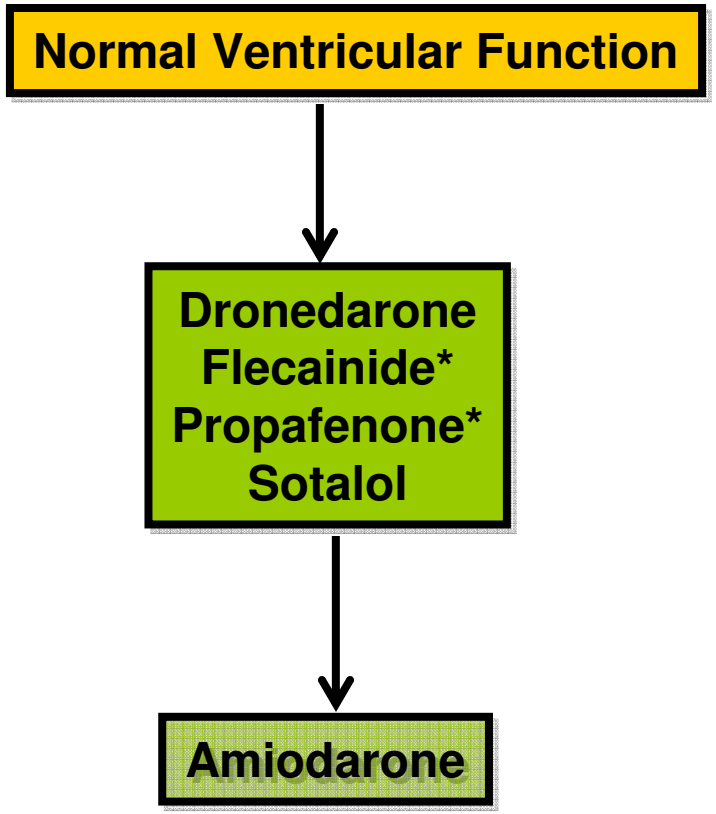
# Rhythm Control Options: Antiarrhythmics in Normal Ventricular Function




* Class I agents should be AVOIDED in CAD
They should be combined with AV-nodal blocking agents



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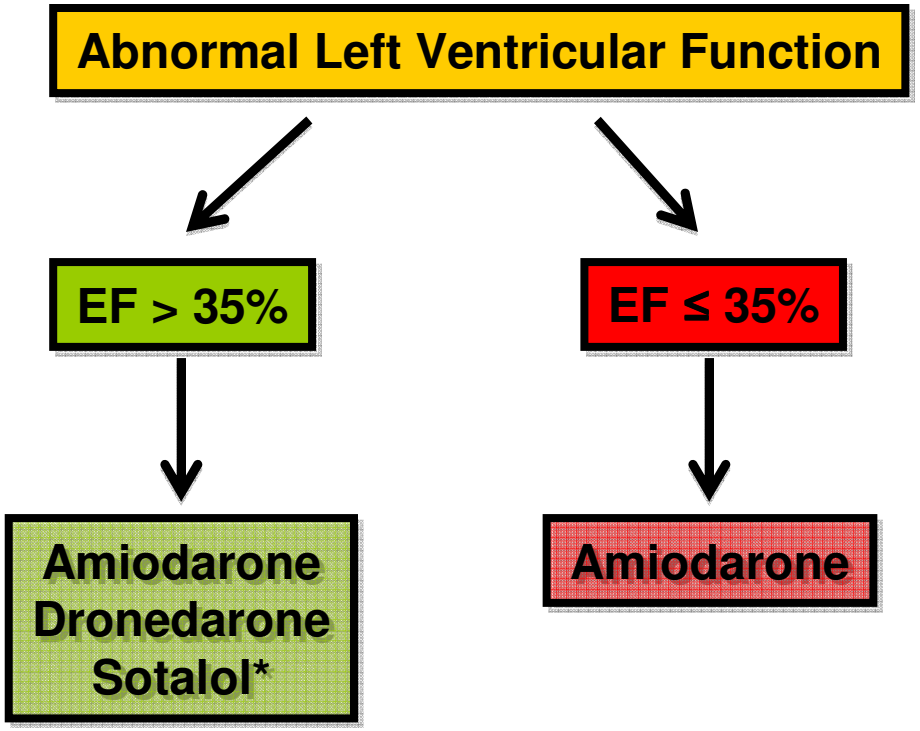
# Rhythm Control Options: Antiarrhythmics in Abnormal LV Function




* Sotalol should be used with caution with EF 35-40%
Contra-indicated in women >65 yrs taking diuretics



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# Rhythm Control Options

- Convert to NSR
- Choice of drug depends on:
  - Other medical conditions
  - Effectiveness and side effects of past medications and combination treatment

| Class I (Sodium Channel Blockers) | Class II (Beta Blocker) | Class III (Potassium Channel Blockers) |
|---|---|---|
| • Flecainide (Tambocor®)<br>• Propafenone (Rythmol®) | • Sotalol (Betapace®) | • Amiodarone* (Cordarone®)<br>• Dronedarone* (Multaq®)<br>*also effects $Na^+$ and $Ca^{2+}$ channels |


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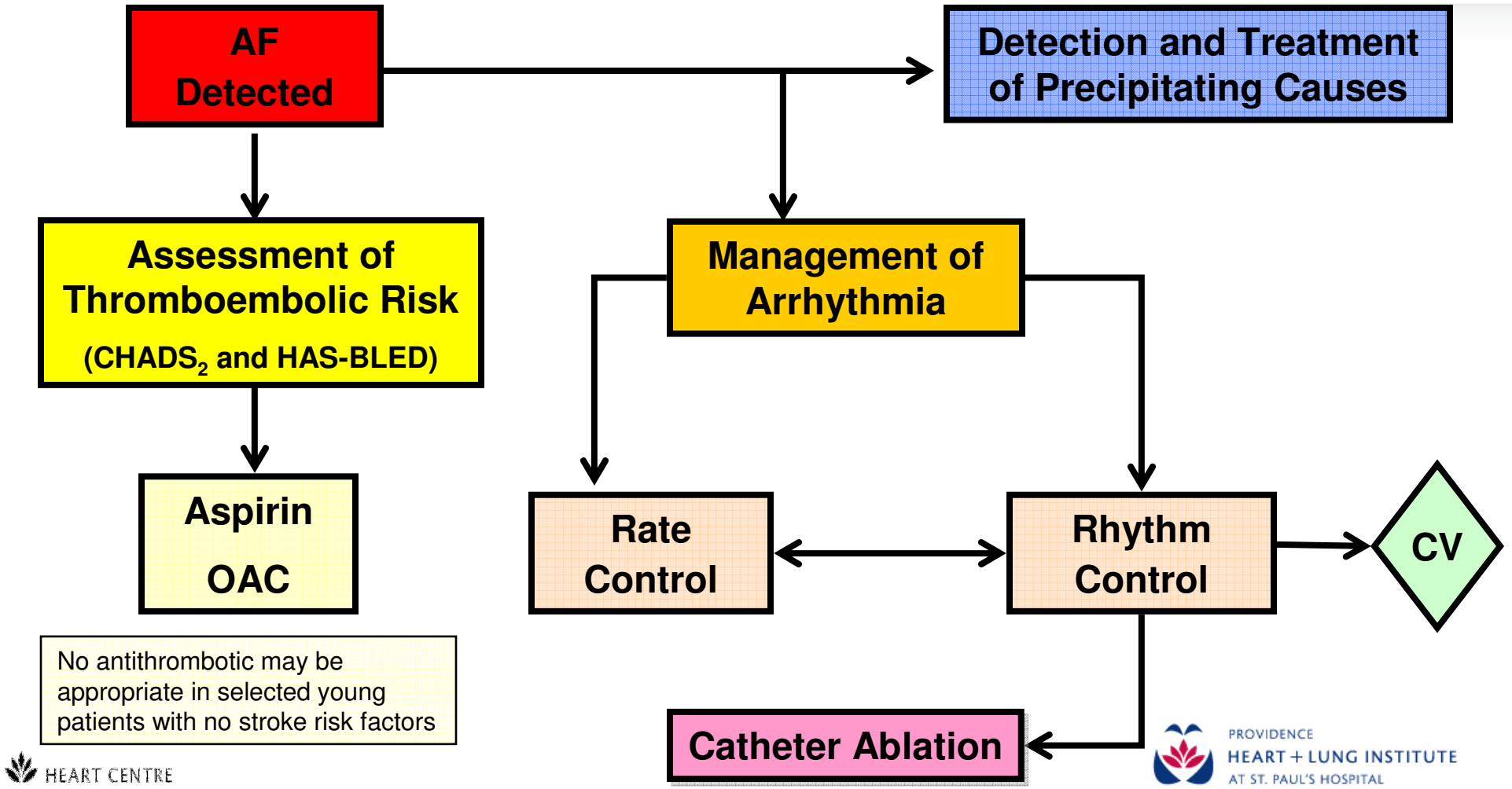
# Rhythm Control Options

| | DOSE | Efficacy at 1 Year | NOTES |
|---|---|---|---|
| **Amiodarone** | 100 - 200 mg daily (after 10 g loading) | 60 – 70% | - Cost: $45/month<br>- Monitoring: liver and thyroid function, PFTs, eye exam<br>- Drug Interactions: warfarin-monitor INR<br>- Toxicity: Liver, Thyroid, Pulmonary, Neuropathy, Photosensitivity |
| **Dronedarone** | 400 mg bid | 40% | - Cost: $145/month<br>- Lab monitoring: liver function<br>- Drug Interactions: no warfarin issues<br>- Toxicity: GI, limited experience- monitor |
| **Flecainide** | 50 – 150 mg bid | 30 – 50% | - Cost: $35 - $70/month (flecainide)<br>- Cost: $45 - $85/month (propafenone)<br>- Contraindicated in CAD or LV dysfunction<br>- 1:1 conduction possible- Rx with AV nodal blocking agent |
| **Propafenone** | 150 – 300 mg tid<br>PIP: 450 - 600 mg prn | 30 – 50% | |
| **Sotalol** | 80 – 160 mg bid | 30 – 50% | - Cost: $30/month<br>- ECG to monitor QT with start, dose changes<br>- Caution with decreased renal function, low EF |

# Dronedarone Summary

| | |
|---|---|
| ↓ **Death** |  |
| ↓ **Hospitalization** |  vs placebo (ATHENA; baseline rate control optimized?) |
| ↓ **AF Recurrence** |  vs placebo (DAFNE, ADONIS/EURIDIS, ATHENA) |
| |  vs amiodarone (preliminary DIONYSOS & indirect comparison meta-analysis by Piccini et al.) |
| ↓ **Adverse Effects** |  vs amiodarone |

# Overview of AF Management

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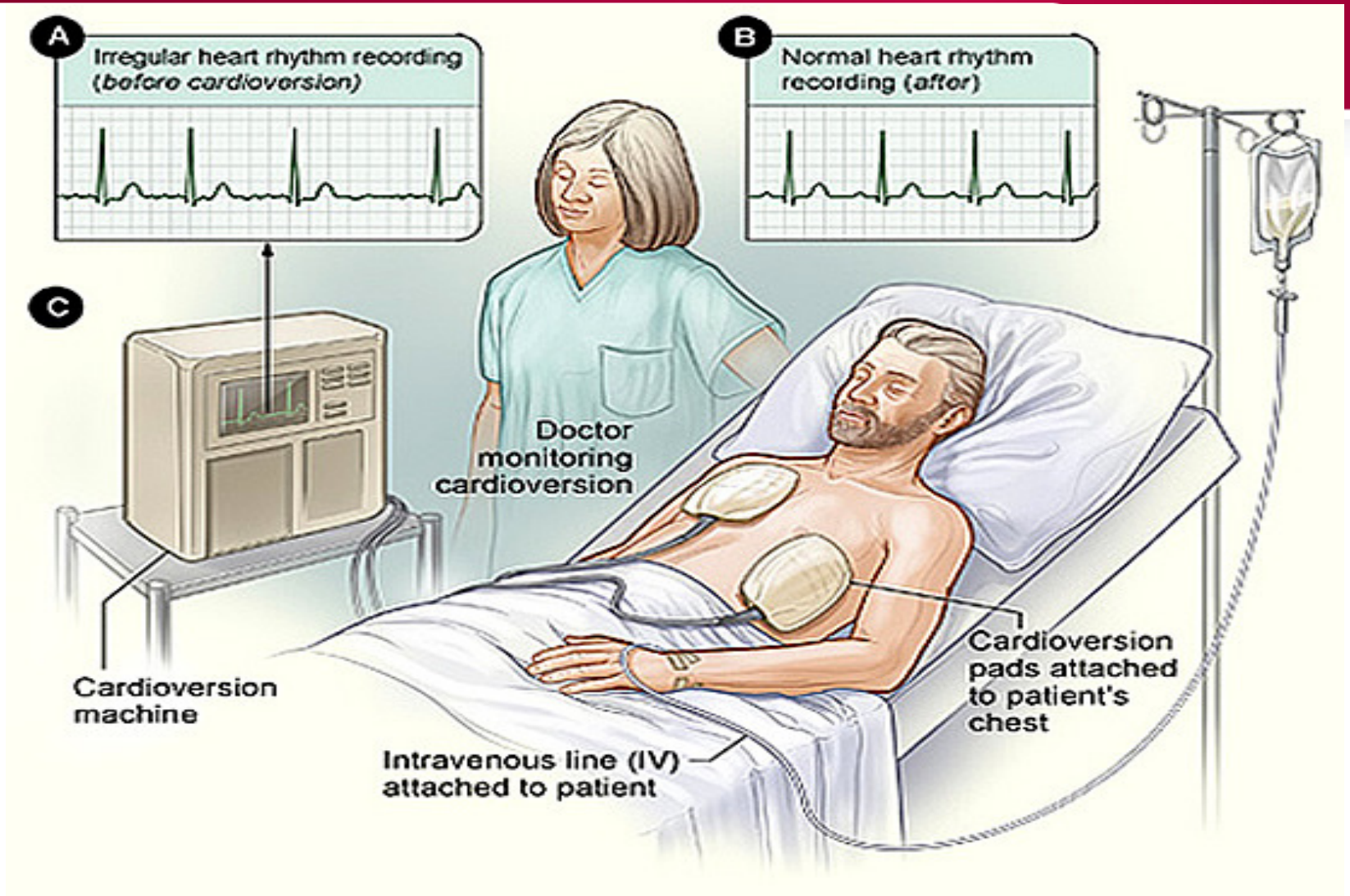
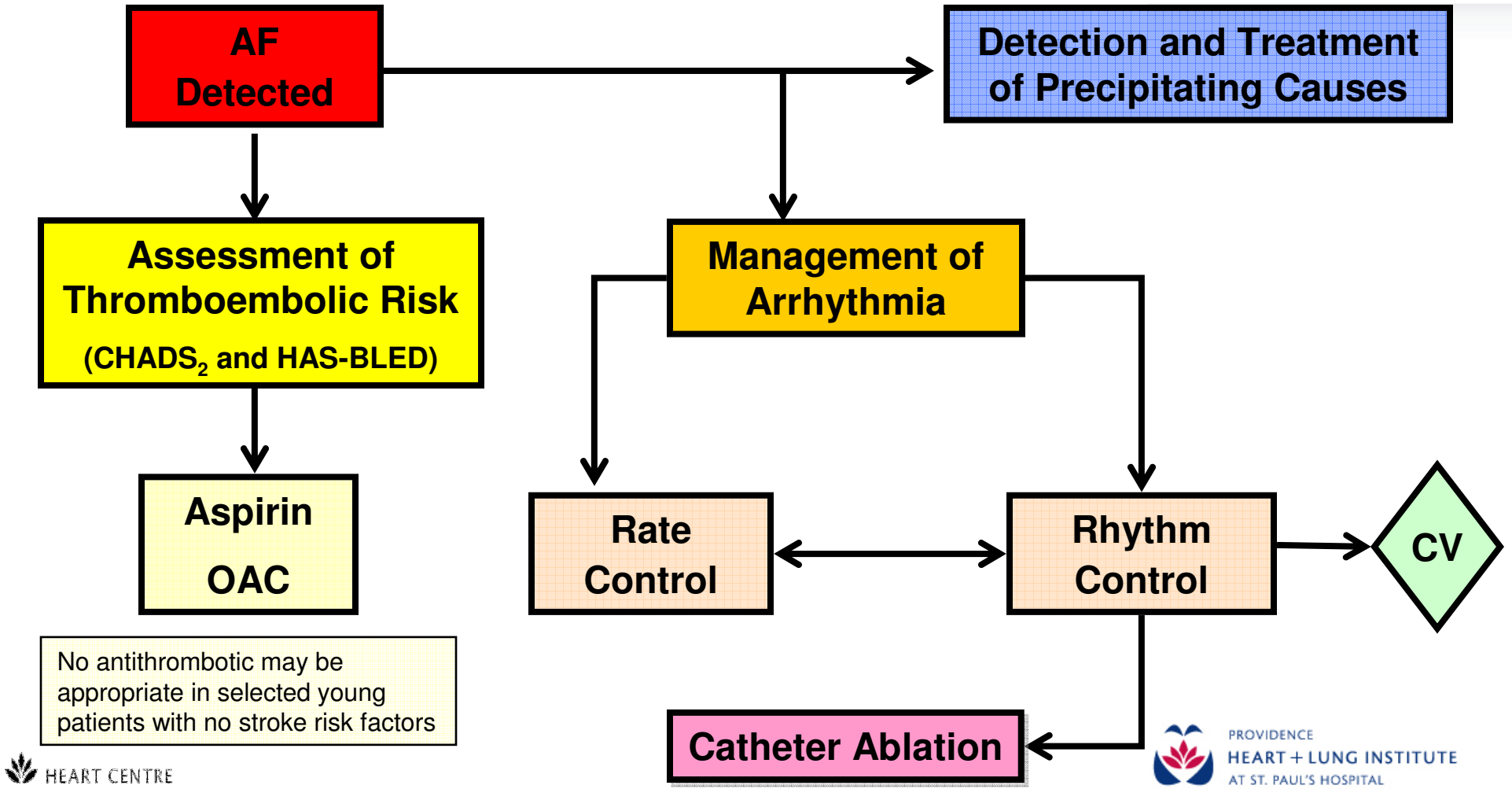
# Restoring Normal Sinus Rhythm: Direct Current Cardioversion






http://www.heartrhythmspecialistsla.com/services-cardioversion-los-angeles-ca.html

# Overview of AF Management

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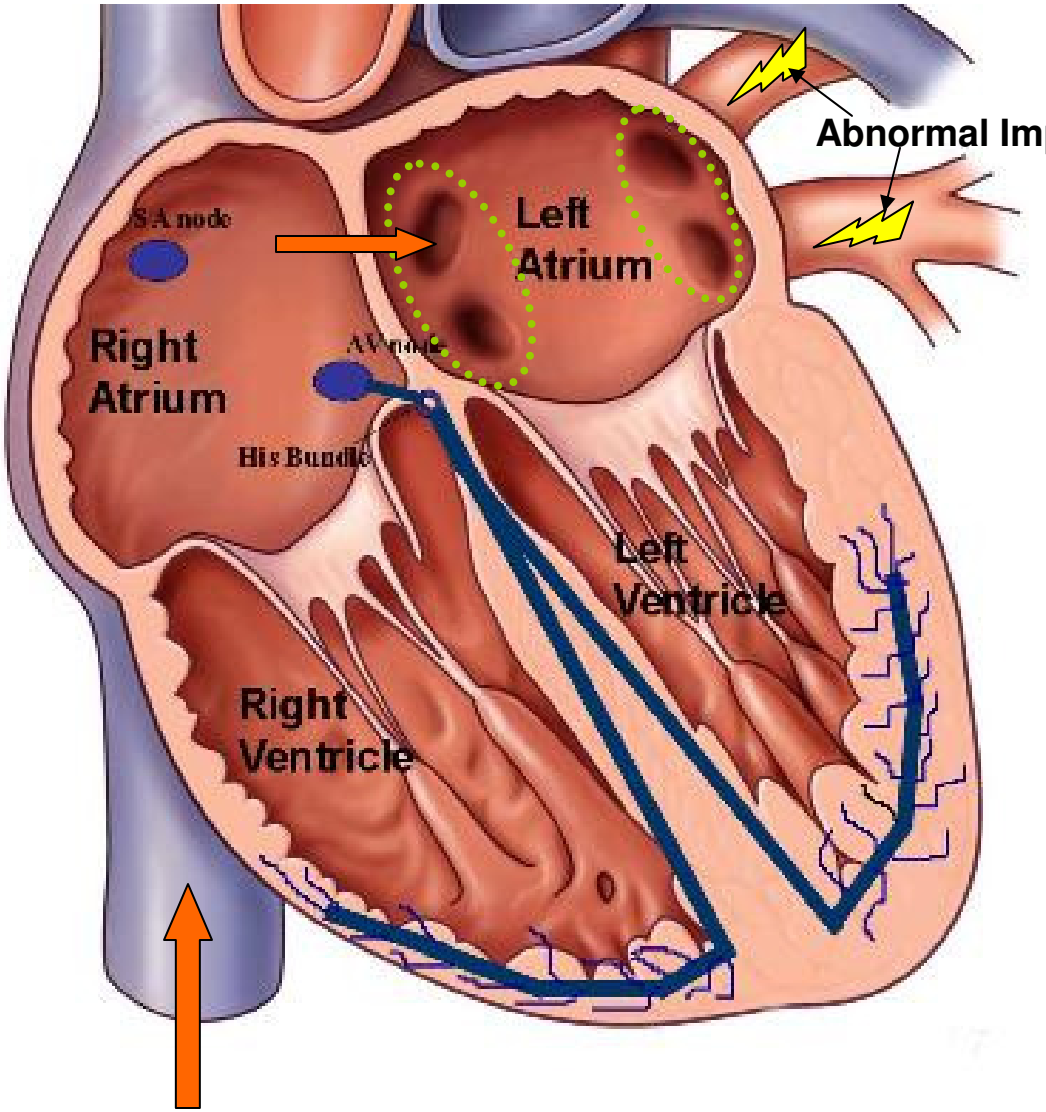
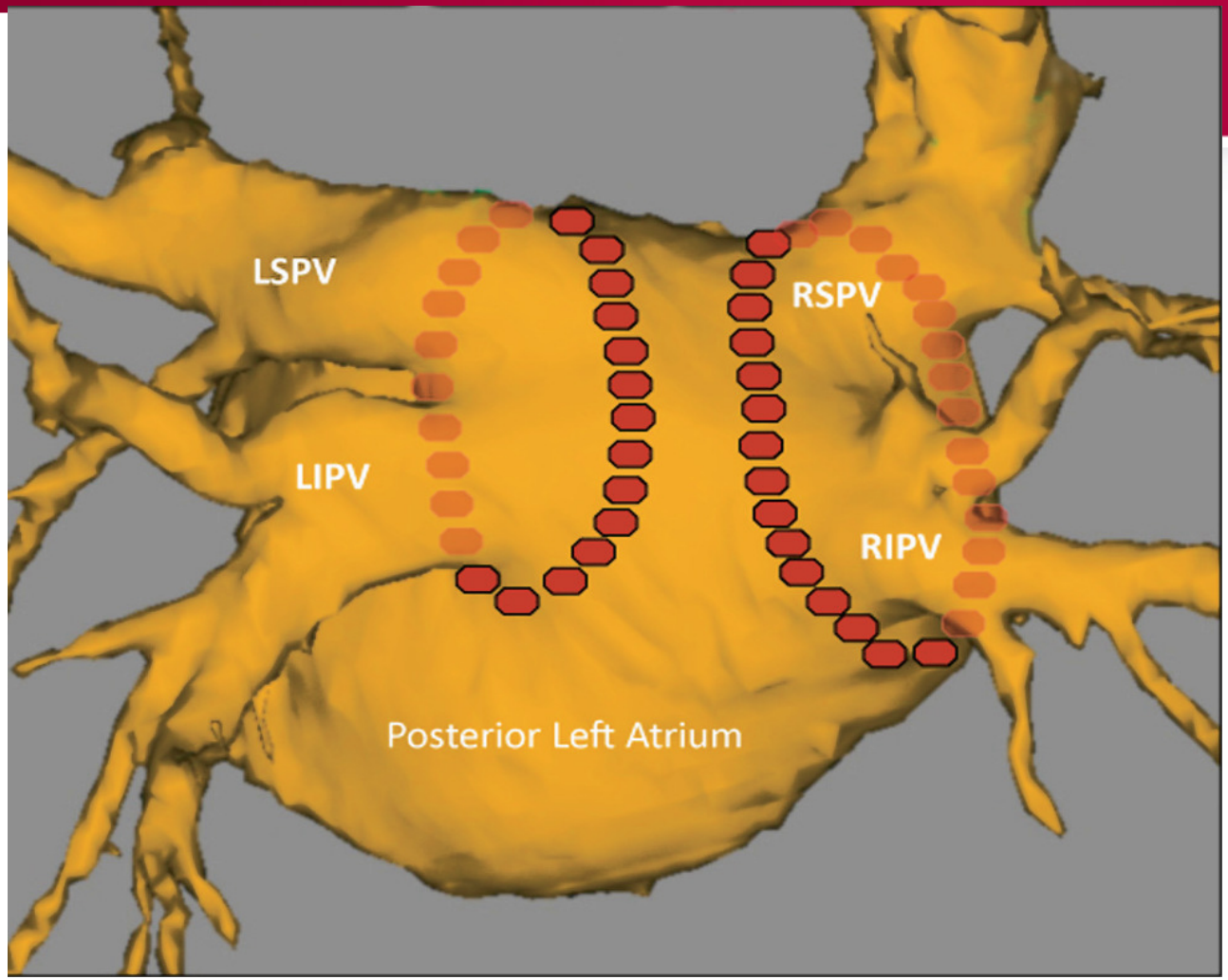
Gillis AM et al. Can J Cardiol. 2010;27:47-59.

# Atrial Fibrillation Ablation



# AF Ablation Using NavX Mapping System






Gillis AM et al. Can J Cardiol. 2010;27:60-66.

# Factors to Consider About Ablation

- Anticoagulation
- Success rates ~ 70%
- Factors associated with reduced outcomes
- 20% repeat procedure
- May take up to 3 months for stability
- Definition of success

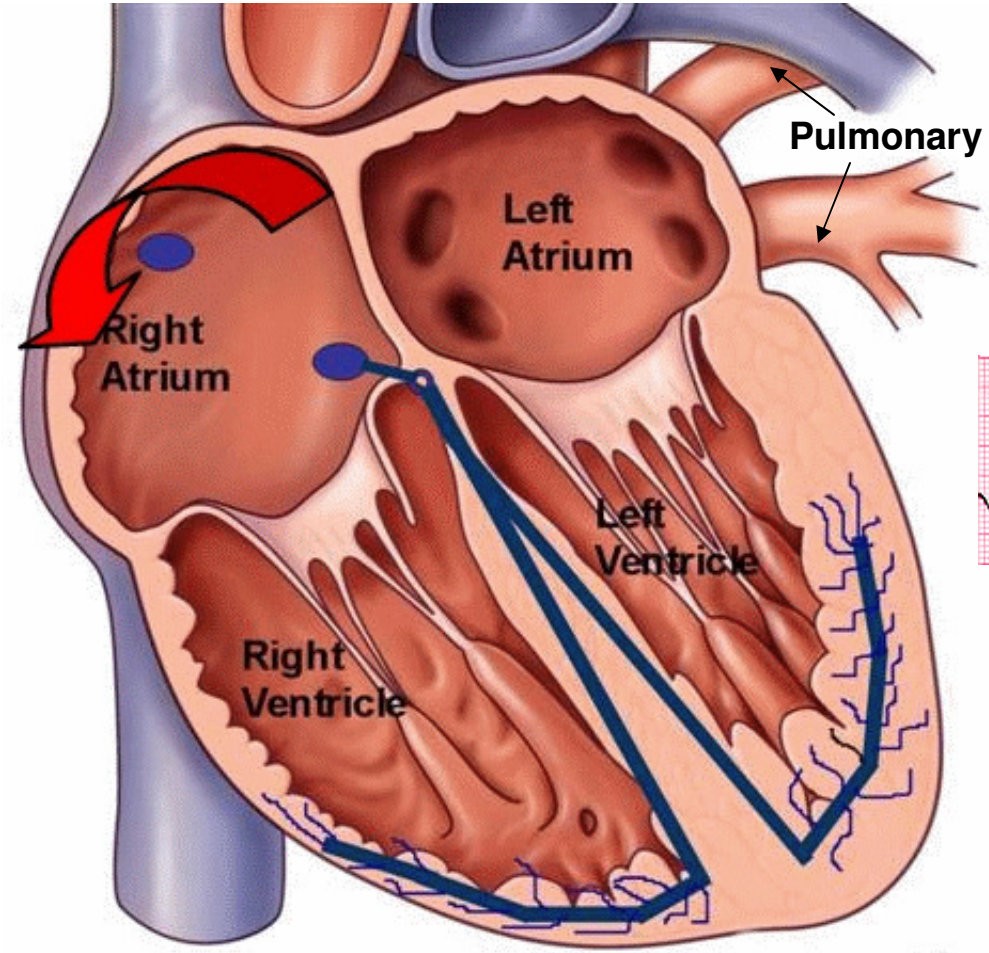
# Potential Risks of AF Ablation

- Bleeding
- Pericarditis
- Increased palpitations
- Cardiac tamponade
- AV node block requiring pacemaker
- Stroke
- Infection
- Pulmonary vein stenosis
- Esophageal fistula
- Phrenic nerve damage
- Heart valve, wall, or vessel injury
- Risk to life

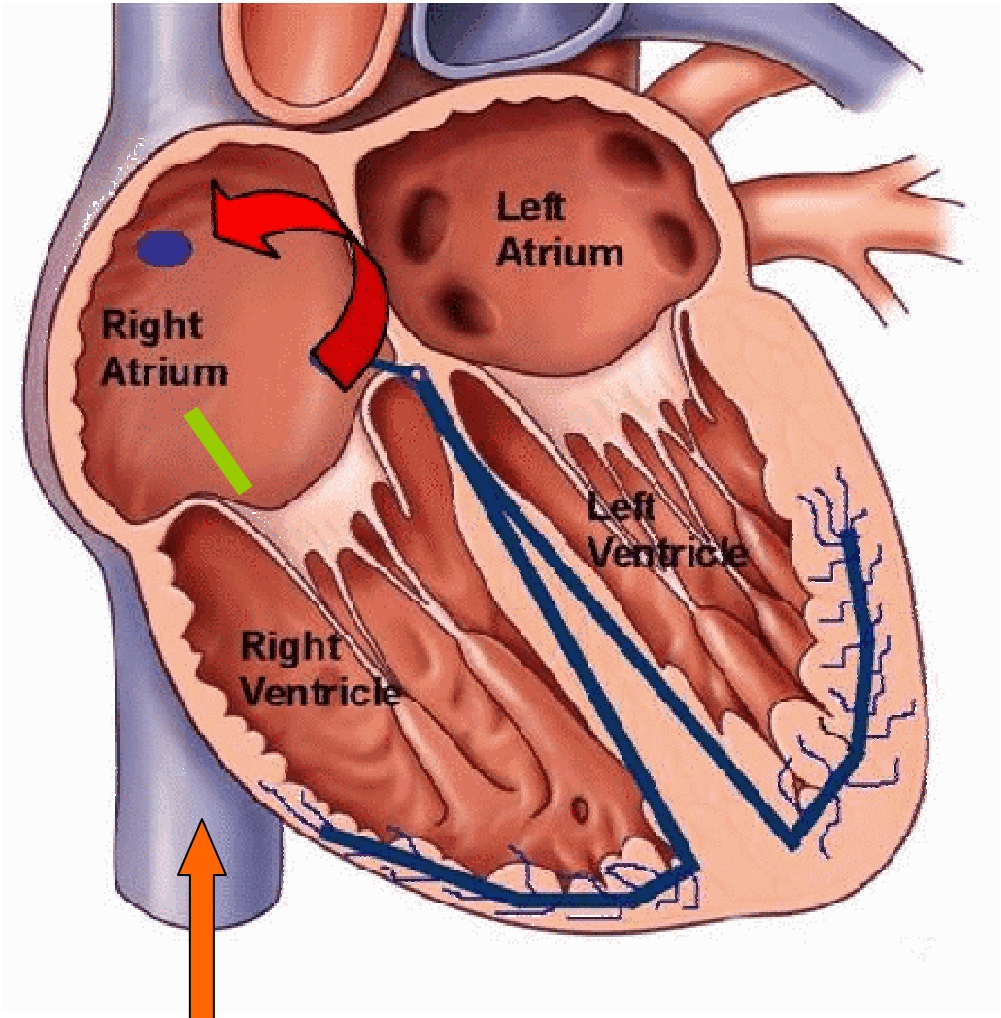
# Goals of AF Ablation

- Decrease symptom burden
- Improve quality of life
- Improve exercise tolerance
- Minimize drug therapy
    - ALWAYS require anti-thrombotic medication

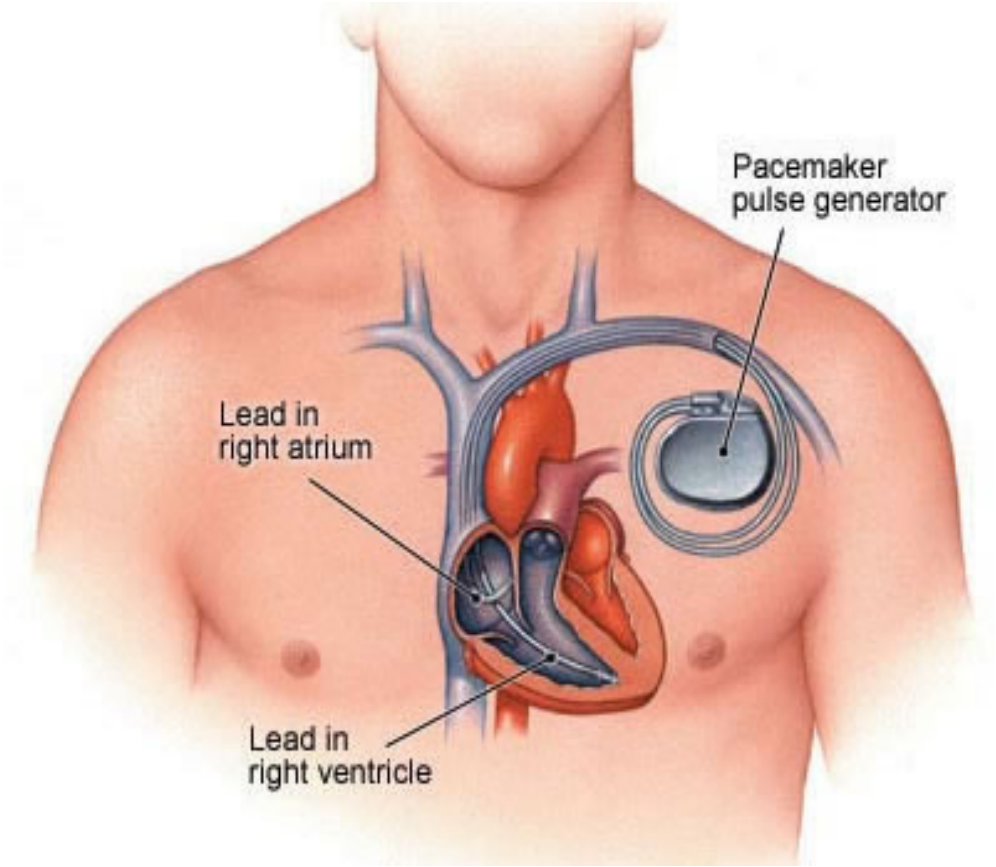
# Atrial Flutter




# Atrial Flutter Ablation



# Pacemaker and AV Node Ablation



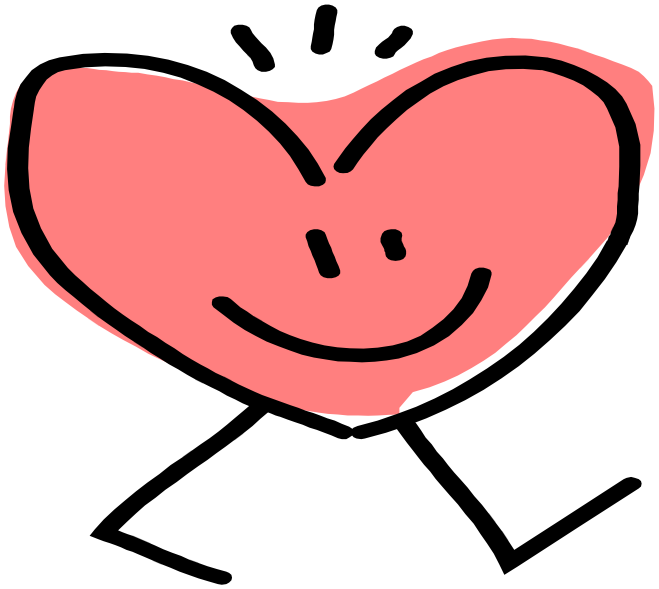



http://www.chrsonline.ca/patients/pacemakers.htm

# Take Home Messages

- Stroke prevention
- Reduction of symptom burden and improve QOL
- Ablation:
  - Option for failed anti-arrhythmic
  - Option for highly symptomatic
- Patient and medical team partnership

# Questions?



**Atrial Fibrillation Clinic**
**604-806-9475**

# Resources

## Canadian Cardiovascular Society

- www.ccsguidelineprograms.ca

## Heart Rhythm Society

- www.hrsonline.org

## Heart and Stroke Foundation

- www.heartandstroke.bc.ca

# AF Ablation: Extra Information

- Patient is under general anaesthetic for duration of procedure (~3 hours)
- Catheter introduced into upper leg and advanced to the heart
- Left-sided procedure requires catheter being placed into the left atrium under x-ray and echo guidance (trans-septal puncture)
- Intracardiac electrograms from catheter tip are evaluated by the physician
- Radiofrequency energy is used to burn heart tissue in target area
- “Burning” disrupts the electrical flow in the heart that is causing the abnormal rhythm, allowing the natural heart rhythm to dominate