Disclosures

Speaker's bureau:	**Servier International, Bayer, Merck Serono, Novartis, Boehringer Ingelheim, Lupin**
Research grant:	**Servier International, Boehringer Ingelheim**
Advisory Board:	**Servier International, Novartis, Amgen Boehringer Ingelheim**

Is our aim to improve quality of life or to increase survival?

Roberto Ferrari

An ideal Health Care System

- Maximizes quality of life and life expectancy for as many people as possible
- Emphasizes health maintanance
- Implements evidence-based prevention, early diagnosis, and treatment

Cardiology: *A story of success!*

- Life expectancy has increased by 10 years
- Cardiology contributed to 7 years!
- Oncology only a couple of months

Why?

- Some (*few*) good ideas
- Tested with (*many*) appropriate clinical trials
- A bit (*a lot!*) of luck

Few ideas

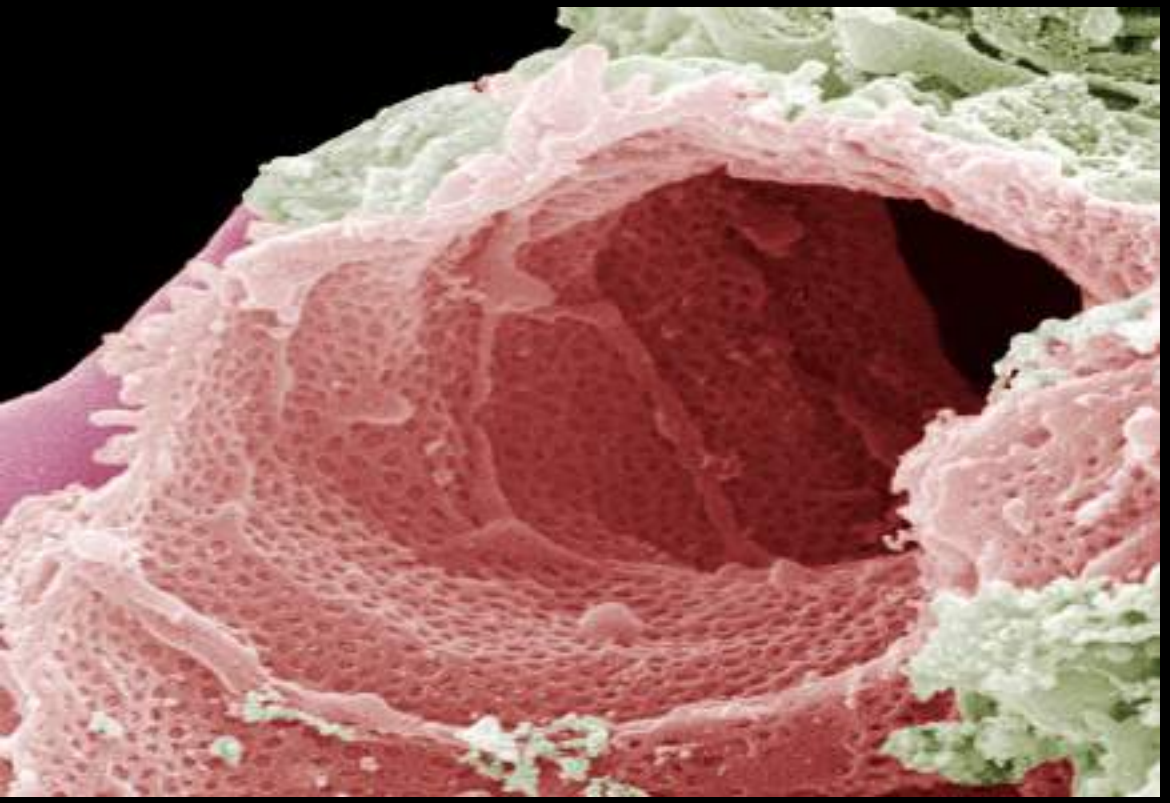
- **The thrombus is the cause and not the consequence of infarction → *thrombolytics first and mechanical reperfusion of AMI***

Here is where we have won!

Few ideas

- **The difference between short term (*good!*) and long term (*bad!*) neuroendocrine response → *ACEi, ARBs, β blockers, MIRNA, and ARNI***
- **Recognition of the deleterious role of cholesterol and LDL in the CV continuum → *statins and all the other classes***

Both reduce apoptosis of the endothelium



Here is where we have won

Few ideas combined to

- **A switch from anecdotes to evidence based therapy**
- **Large simple mortality trial**

Cardiology: *A success……but!*

- A heart attack every 26 seconds
- A death for CV every minute
- 1,9 million deaths per year

Therefore A partial success

- We have not reduced cardiovascular death
- We have postponed it
- We have transformed an “*acute*” pathology into a “*chronic*” one

We have contributed to the ageing of a population (*not always with good quality of life*) and we will continue to do so with a huge increase in public funding

La Salute non ha prezzo!

MA

La Salute costa!

The unsolved problem…

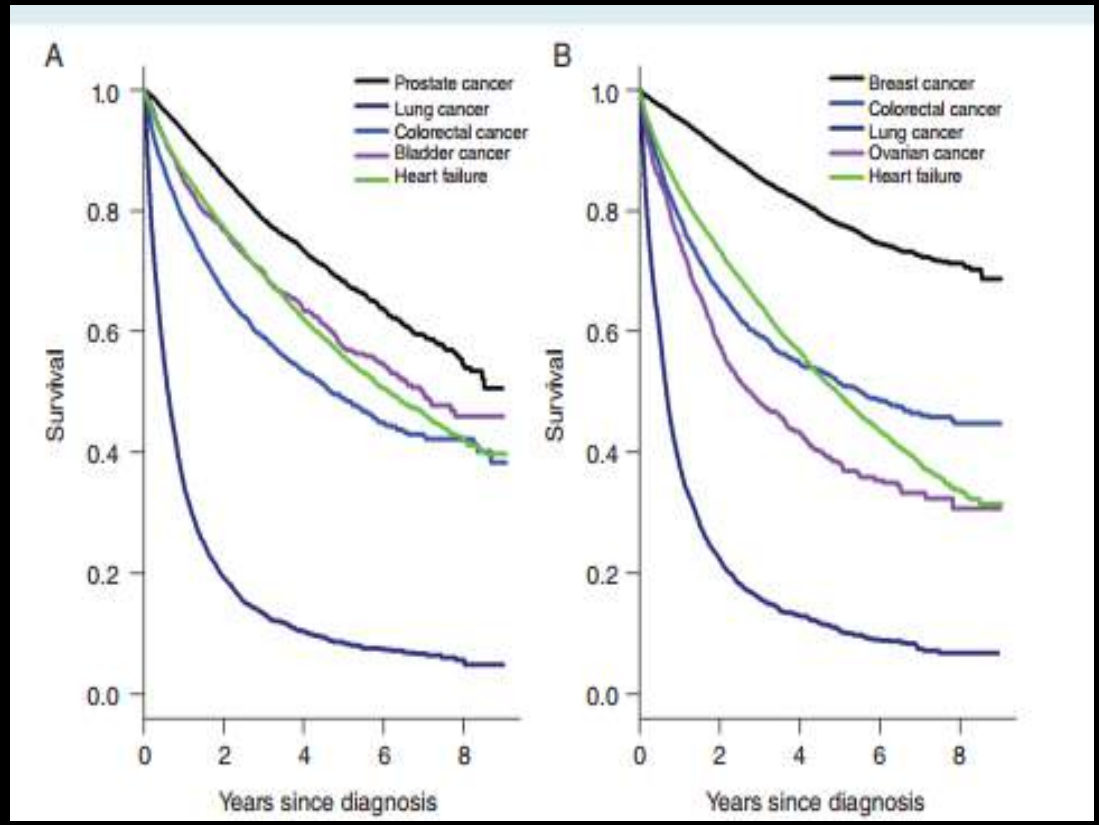
How to spend public funding

It follows that

- Cardiology is a victim of its own success
- The "*Heart Failure paradox*"
- Shift of investments form Cardiology to Oncology
- Despite among 68 new cancer drug indications, only 35 are associated with improvement in survival and quality of life!

Differences between Cardiology and Oncology despite similar mortality

- More success in Cardiology!
- More advocacy in Oncology!
- Quality vs prolongation of life, more relevant in Oncology
- Less successful and more painful treatment in Oncology



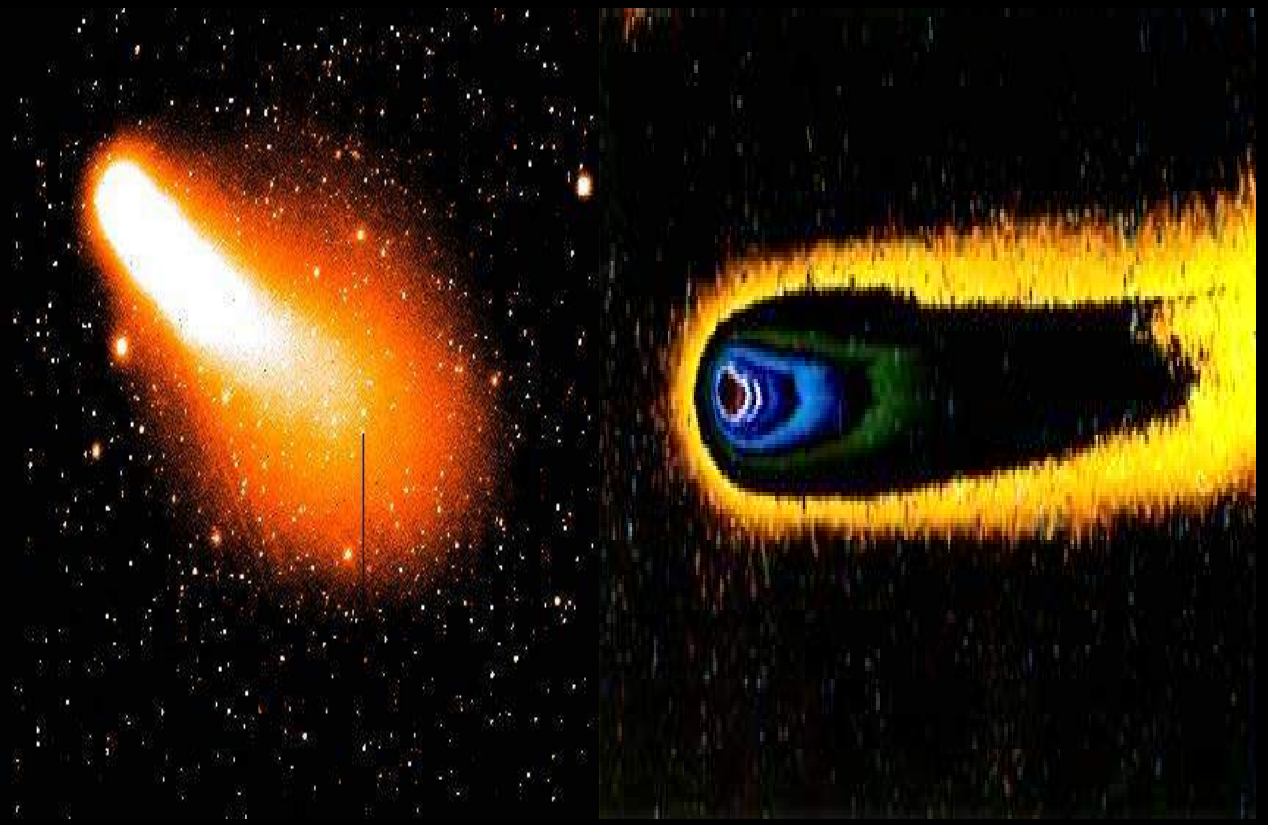
Definition of the goals

- How long do we aim to improve (*CV*) life?
- Should we provide Anni Vita (*years of life*) or Vita agli Anni (*life to years!*)?
- We can beat pathology but not physiology!

- There is no life without death
- Death (*apoptosis*) is an integral part of Nature
- Life (*regeneration*) and death (*apoptosis*) cycle is neither good nor bad: → It is essential!

Life and death: a chain of the Universe

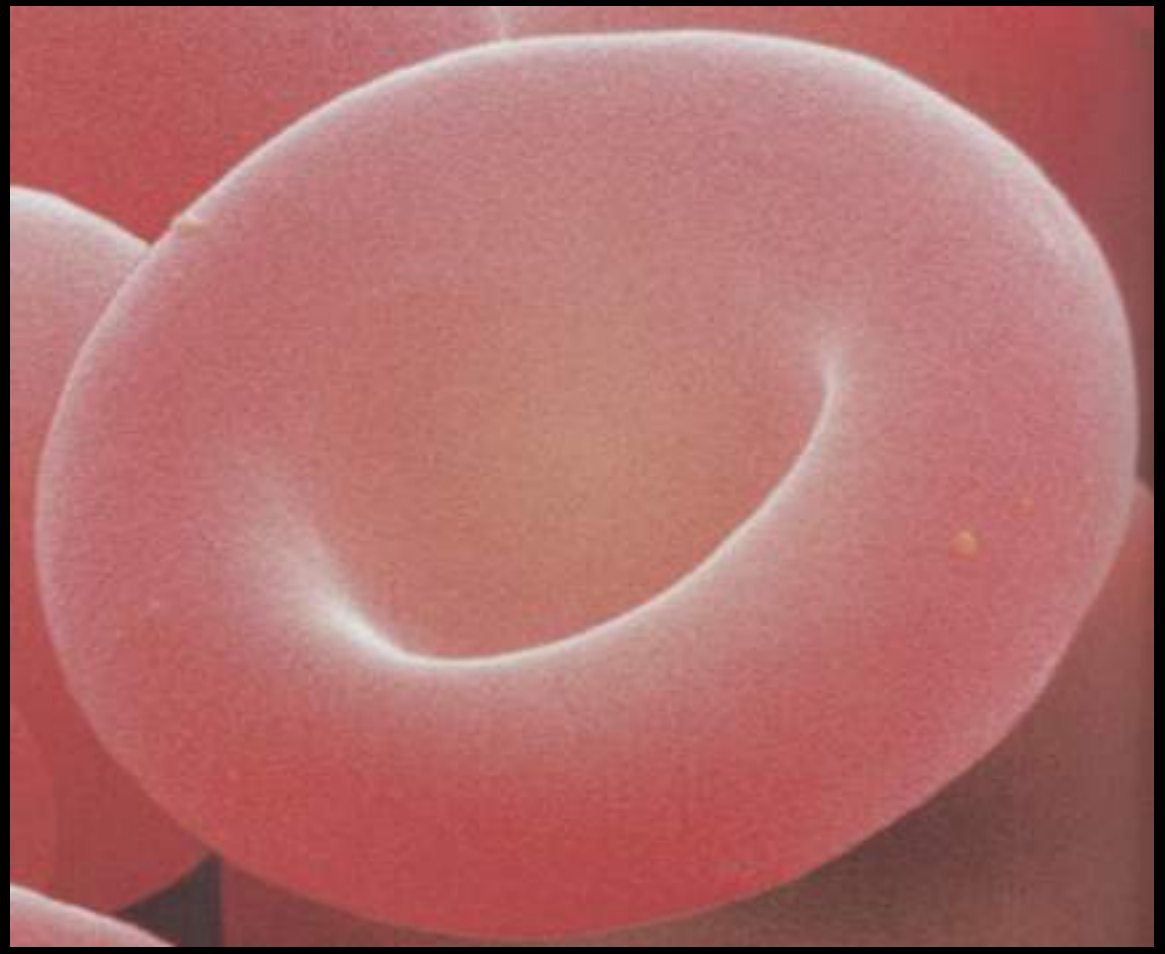
Meteors



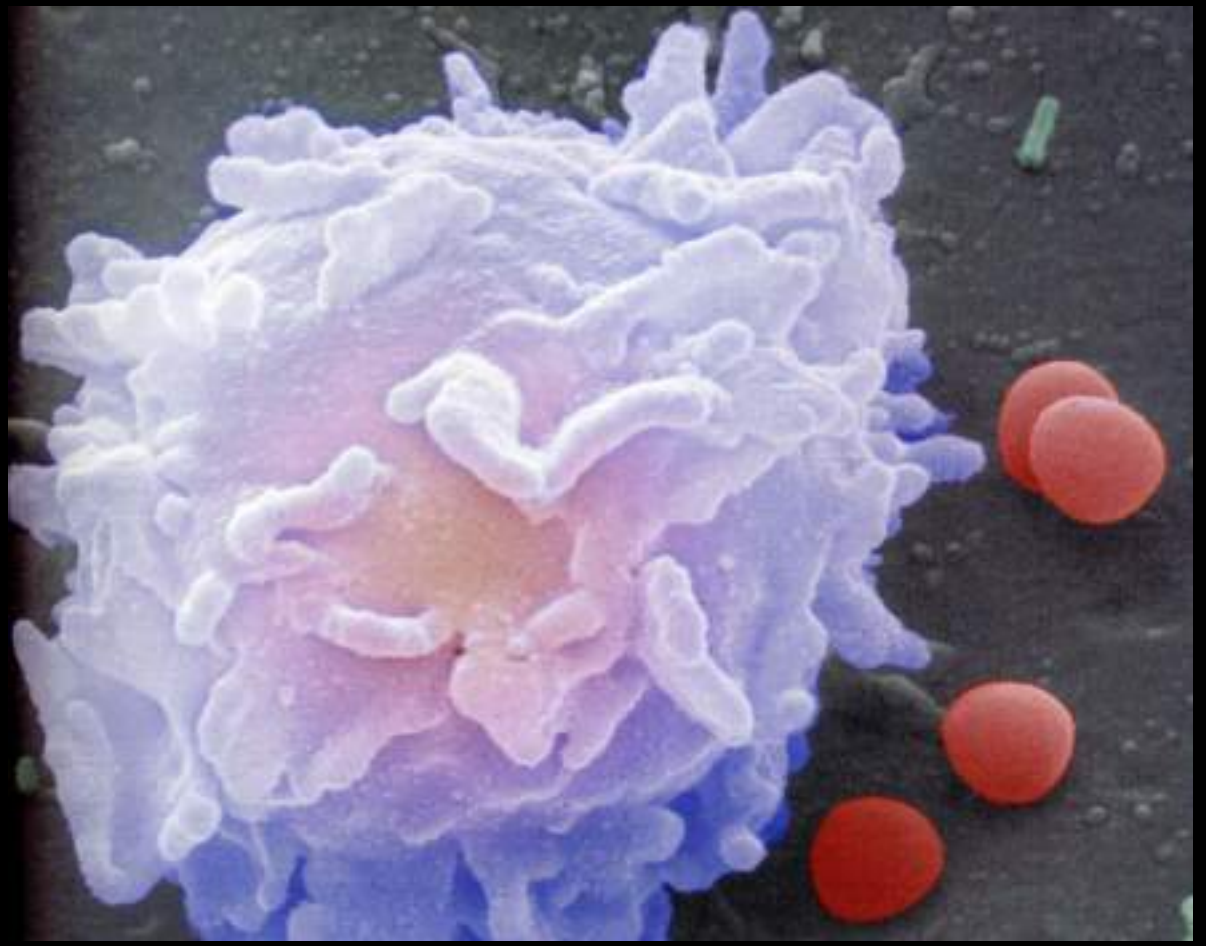
Spring

Fall

Average life: 120 days



Average life: 7 hours



Life and death

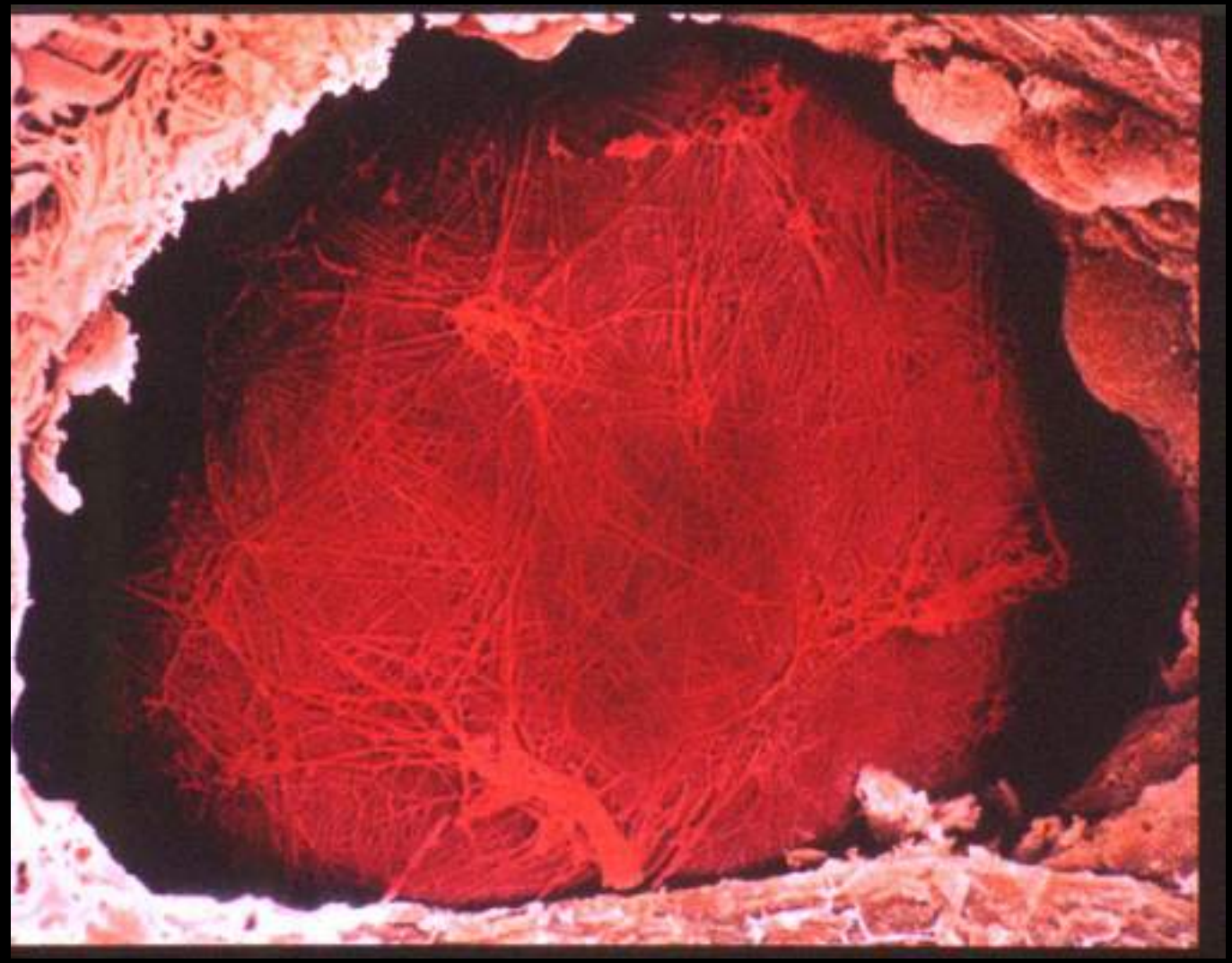
- Life and death are integrating parts of the universe
- Express opposite concepts, but are aspects of the same design
- Two entities programmed from the nuclei

- Life → Reproduction

- Death → Apoptosis

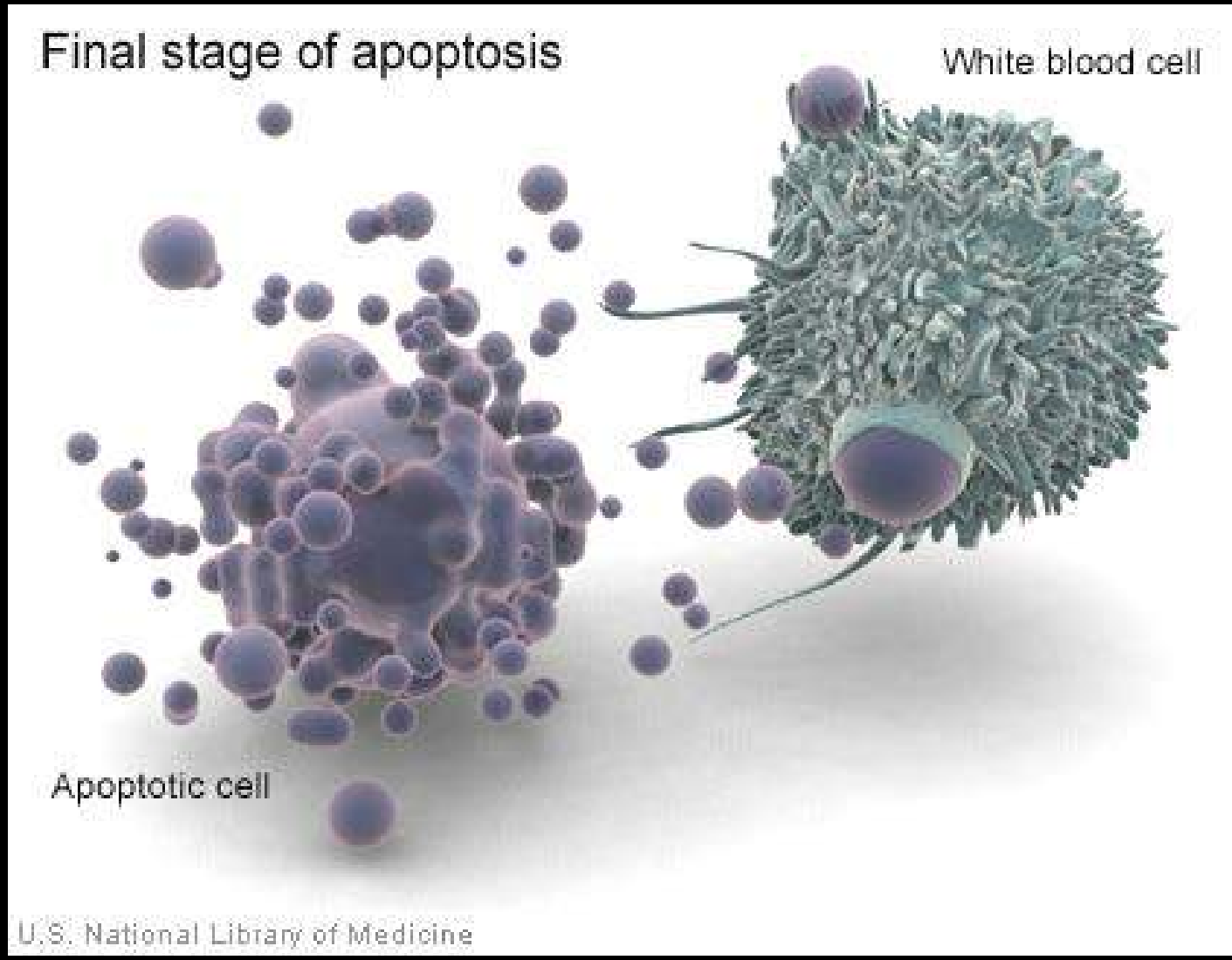
Necrosis = death

- incidental death
- involves millions of cells
- immunological death
- typical of infarction



Apoptosis = death

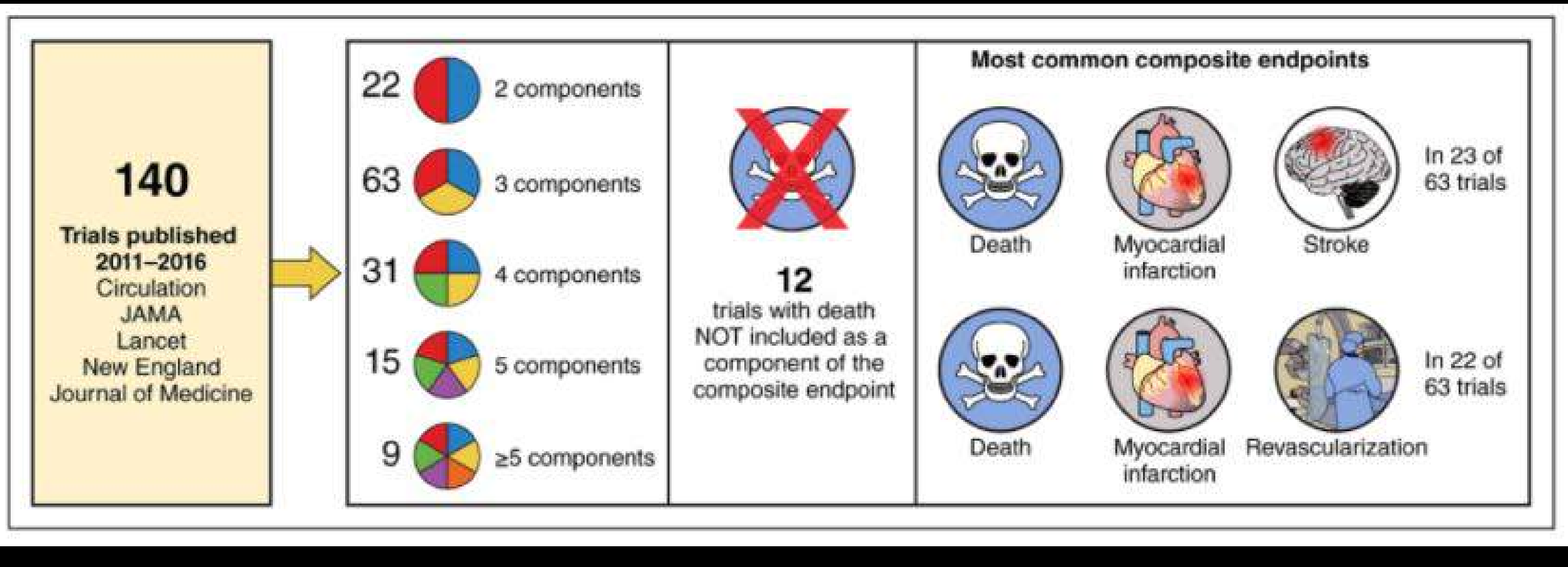
- Programmed death
- Non immunological death
- one cell dies at a time



Quality vs quantity of life: could they be explored in clinical trials?

- Mortality is the standard evaluation for novel therapies
- Rarely quality of life is an endpoint, nor is included in composite endpoints
- Can we measure quality of life in clinical trials?
- Questionnaires (*no matter how good)* are very subjective

Primary composite end points in phase 3 cardiovascular-related clinical trials in the past 5 years



Composite end points in clinical research: *time to reprisal*

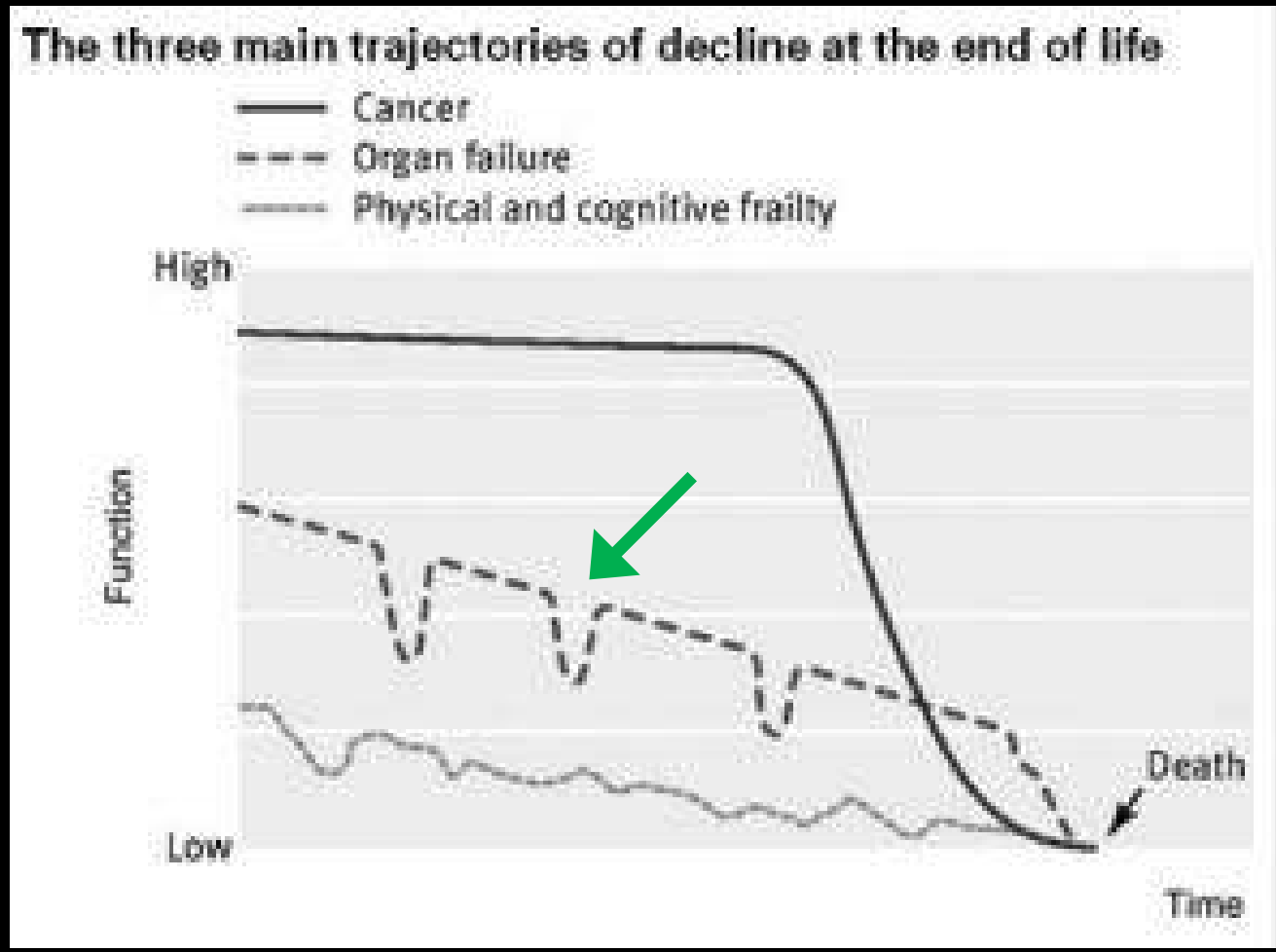
- This approach does not distinguish the relative clinical significance of each composite
- It counts only the first occurrence of any event with the classical "*time to first event analysis*"
- For many trials the result is similar to that of a "*football match*"
- The patients enrolled in trials are not "*real*" and those at the end of their life are not included

The case of heart failure

- NYMA IV or stage D HF has poor prognosis
- Treatment options are:
  - Continue with medications
  - Device interventions
  - Transplantations?
- Patients may decide to forego therapies or procedures
- Deactivate devices implanted earlier
- Refuse for their hospitalization

What to do? *Theoretically*

- Discuss earlier with the patient and the family expectations to establish the goal of care and to shape therapies in accordance
- Easy to say…difficult to do!



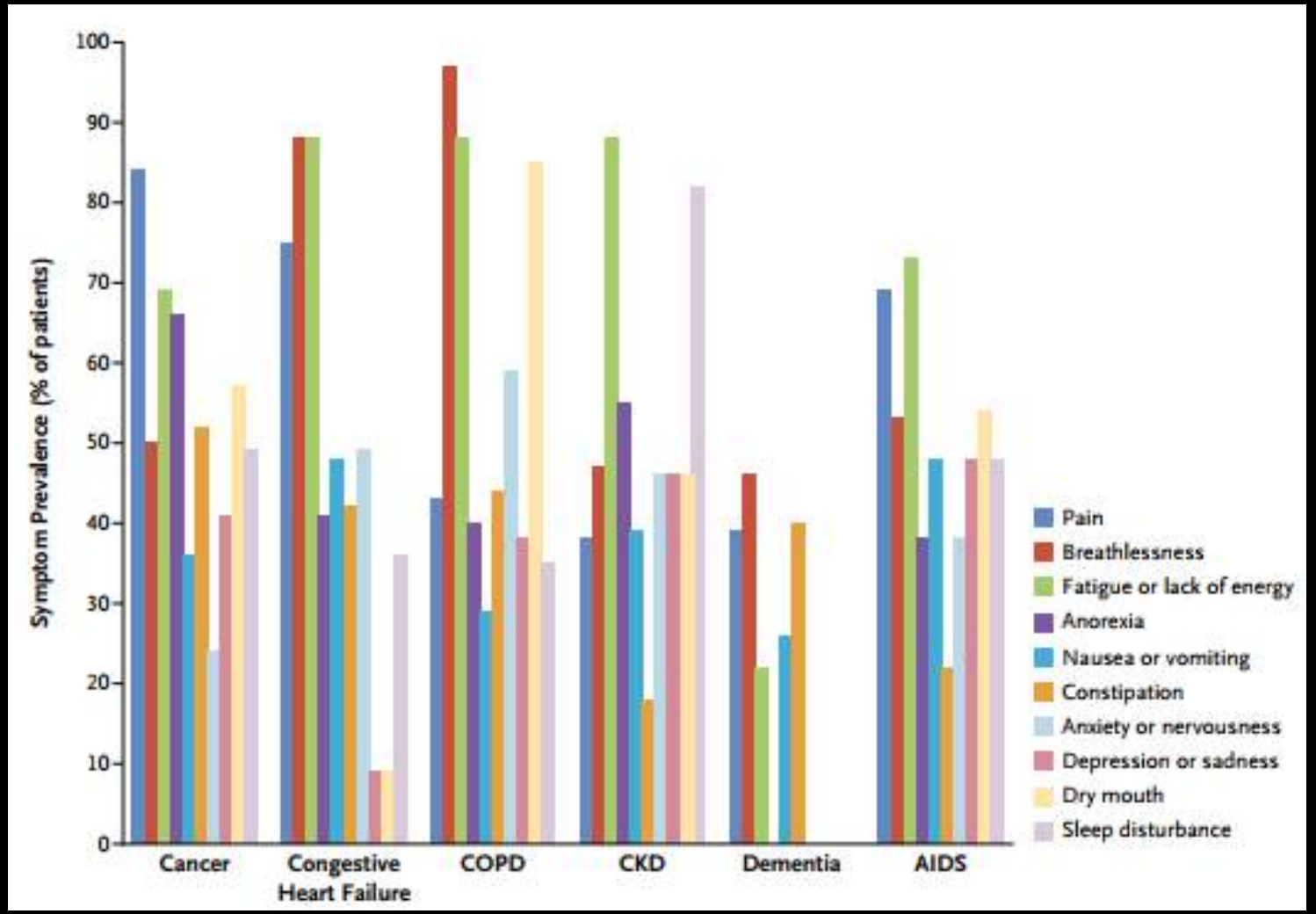
Related problems: predicting prognosis of end stage HF

- Very challenging! Very little data!
- At the moment this is a research priority
- Several algorithms are available…but…

Criteria (Based on Discharge Measurement)	Score if Yes (No = 0)
Age >70 y	1
BUN >40 mg/dL	1
BUN >90 mg/dL	1
6-min walk <300 ft	1
Sodium <130 mEq/L	1
CPR/mechanical ventilation, yes/no	2
Diuretic dose >240 mg at discharge, yes/no	1
No beta-blocker at discharge	1
Discharge BNP >500 pg/mmol	1
Discharge BNP >1,300 pg/mmol	3
Total	0–13

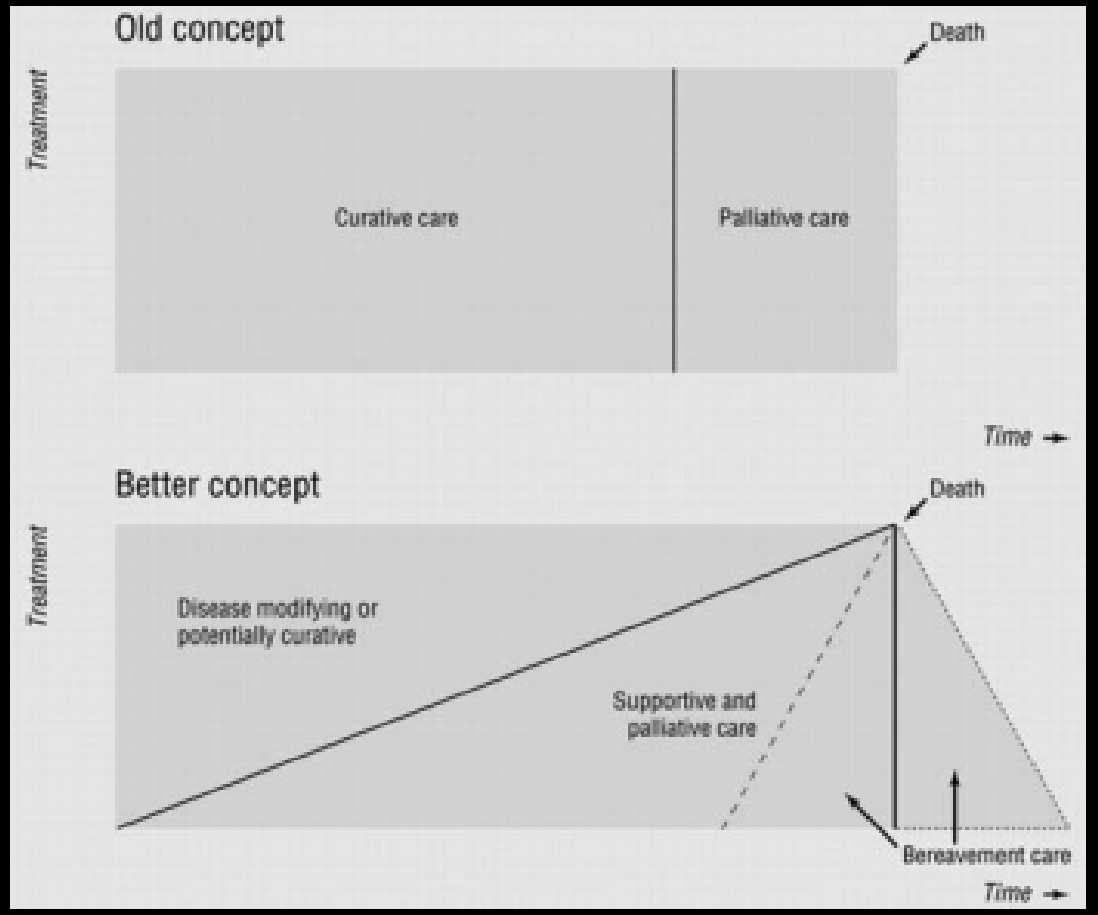
Relieve of symptoms as an improvement of quality of life in advanced illness

Management of symptoms is the best one can do to improve quality of life



Palliative care and hospice

- **Both improve quality of life through symptoms management, using multidisciplinary holistic approach**
- **Psychological, spiritual, emotional, educational care to patient and family**
- **Underutilized in HF (*11,4% in the USA*)**

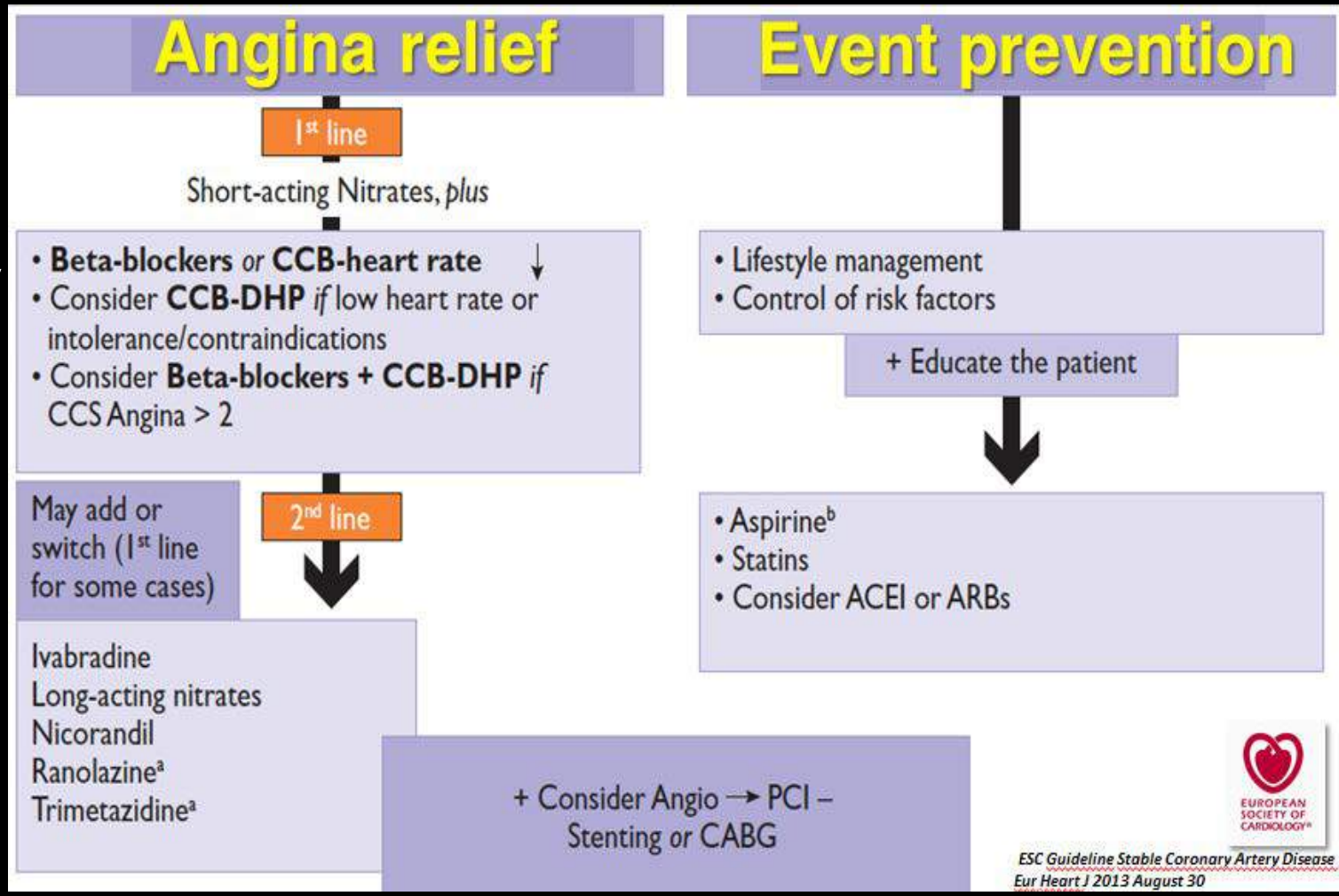


The case of TAVI: *can (utility) or should (futility) it be done?*

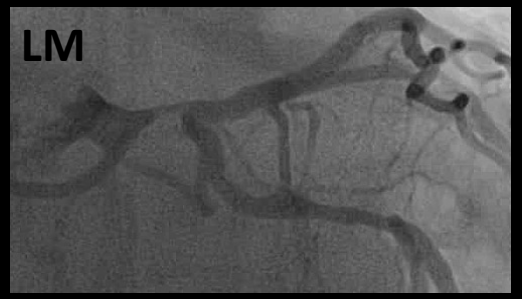
- Dying "*with*" vs "from" aortic stenosis!
- Standard of care for higher surgical risk patients likely to derive 2 years of quantity and quality of life
- Very important frailty assessment
- If treatment is considered futile, patients should be transferred to palliative care
- Of paramount importance is the communication with referring/primary care physicians and families

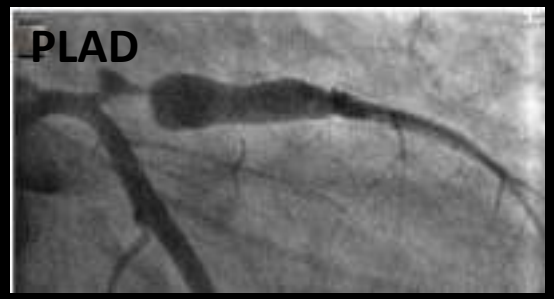
The case of chronic ischaemia

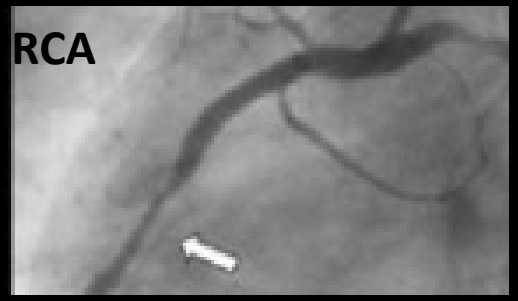
- **The opposite problem: the major goal is an improvement of quality of life**
- ***Role of pharmacotherapy, actual GL suggestions***

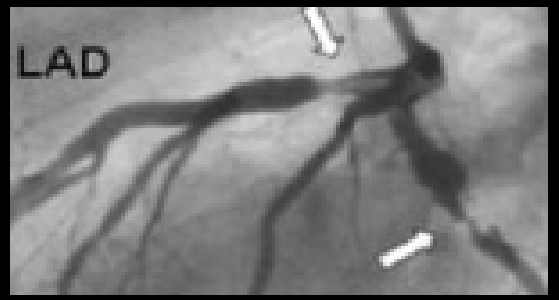


New perspectives in Chronic Angina Treatment: *Role of revascularization*



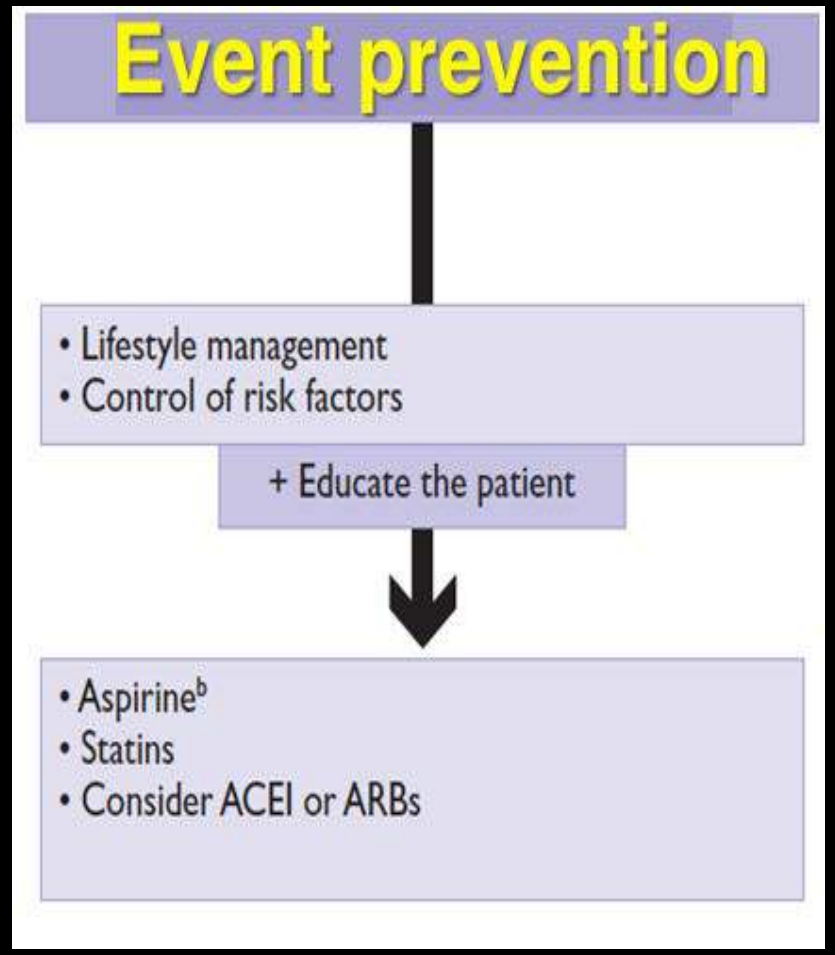






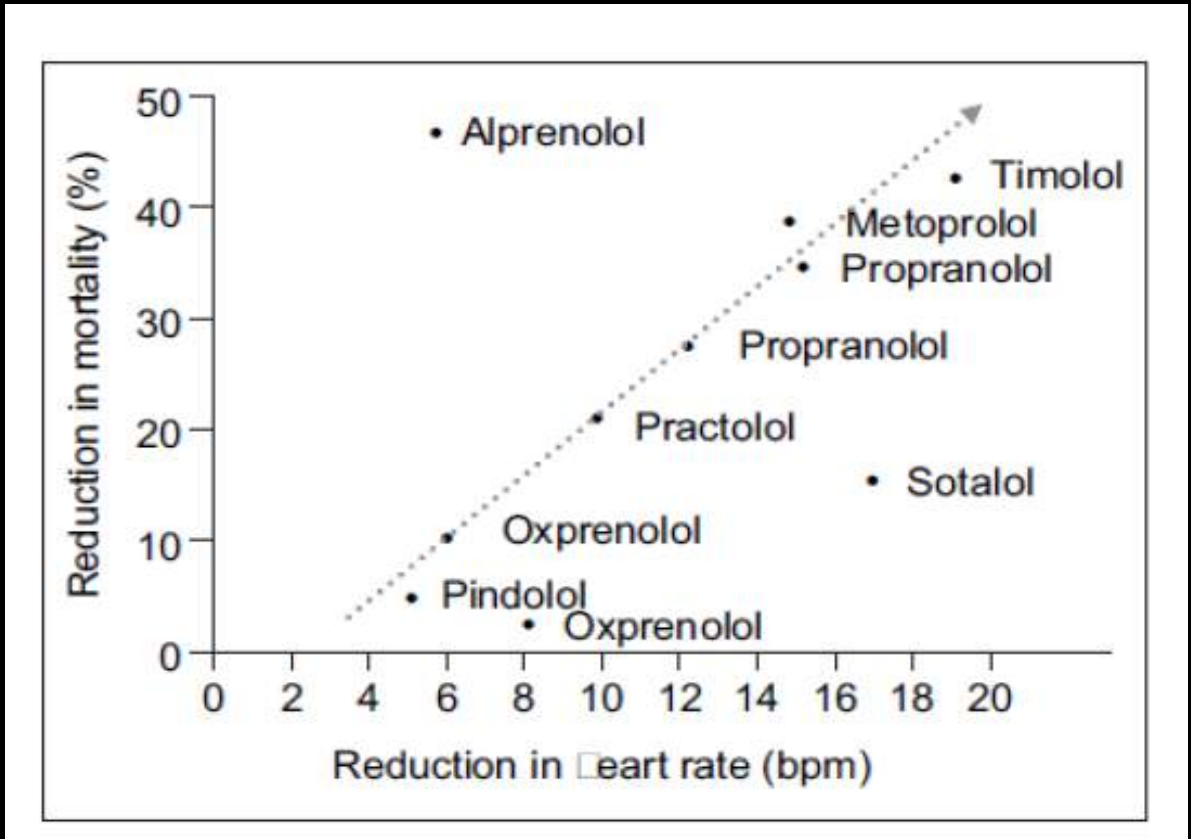
- **Large ischaemic burden(≤10%)**
  - **Left main**
  - **Proximal LAD**
  - **3 vessels disease**
- **When pharmacotherapy has failed**
- **Ischaemia documented by FFR**

New perspectives for increasing life GL on: *Event prevention*



- More attention to preventive programmes and risk factor containment
- Emerging role of inflammation and of HSPCR data from "*CANTOS*" on CANAKINUMAB
- Reduction of progression of atherosclerosis behind BP and cholesterol level
- ACEi better than ARBs
- BB and ivabradine only if LV dysfunction coexists with angina

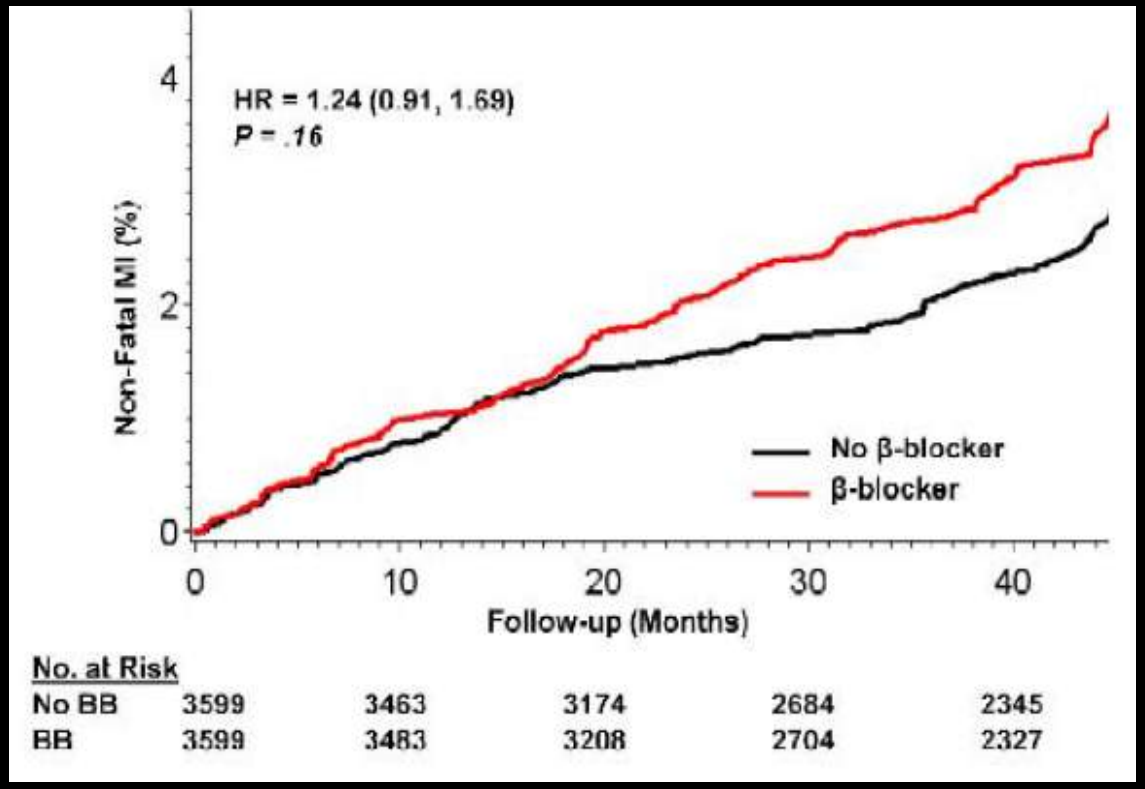
No prognostic role of BB in chronic angina patients but important improvements of quality of life



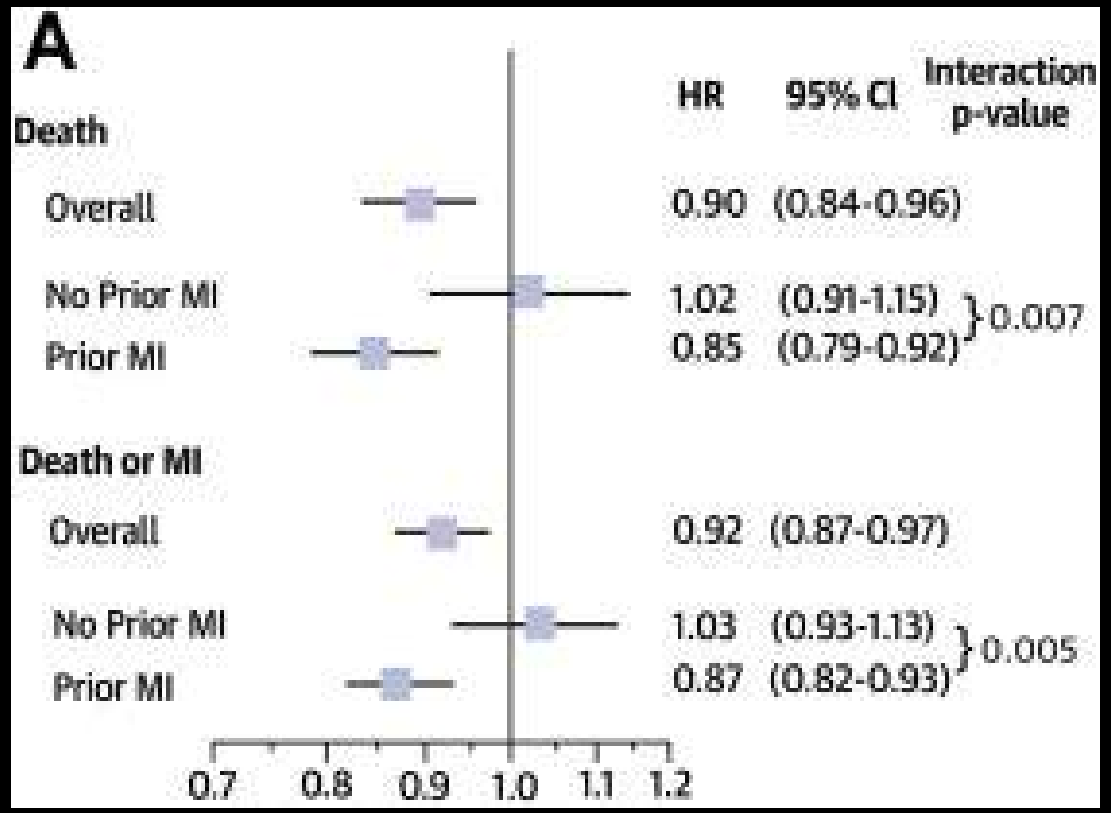
- Data from the 1980s
- In absence of ACEi and statins
- In pre-thrombolytic and primary angioplasty era
- Modern therapy has changed the phenotype of ischaemic myocardium

Contemporary registries: *no prognostic benefits!*

REACH registry: beta blockers in angina without previous MI



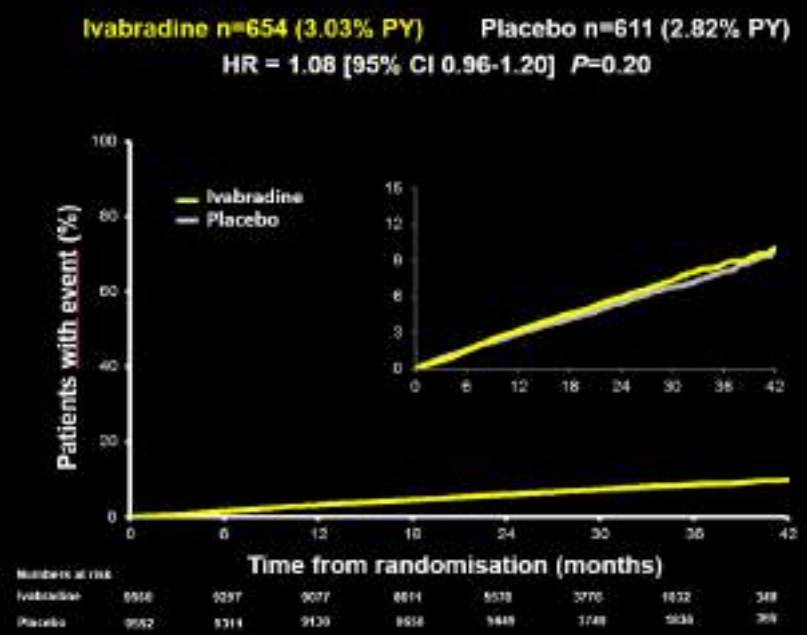
2014 Meta-analysis on 26,793 CAD patients



The same with HR reduction with ivabradine: *data from SIGNIfY*

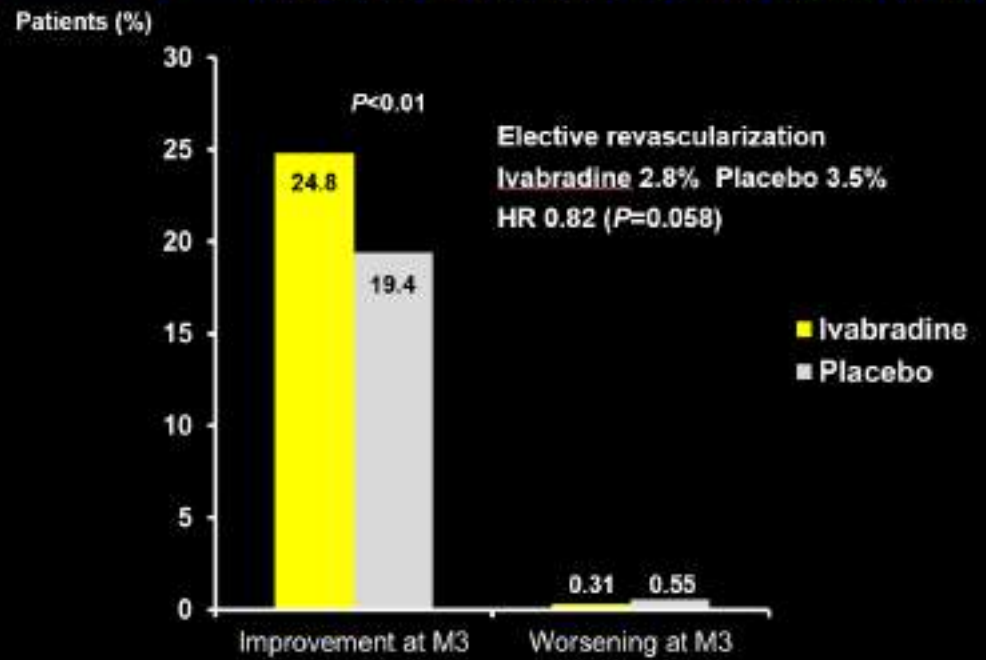
No prognostic benefits

SIGNIfY Primary composite end point

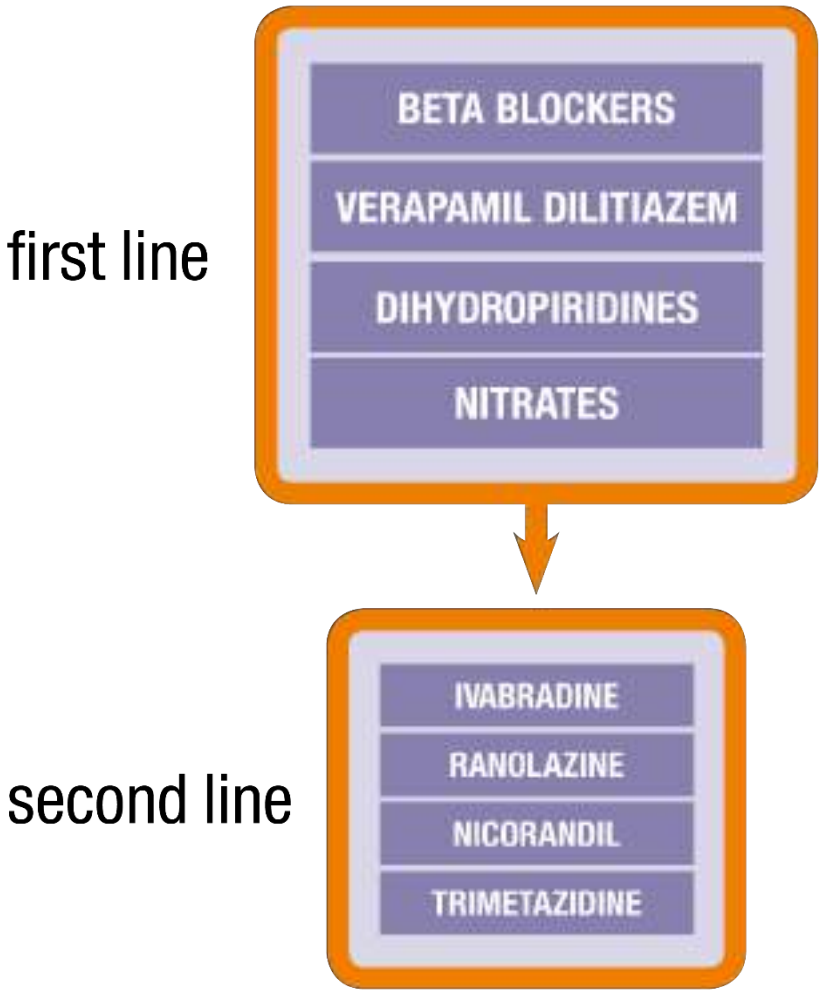


Improvement of quality of life

SIGNIfY Effect of ivabradine on symptoms
(angina population: CCS class ≥II, n=12 049)

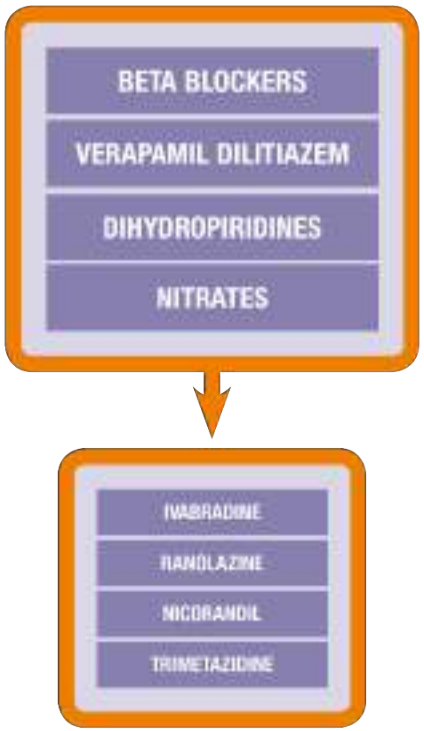


New perspectives for GL on: *angina relief*
Can we do any better?



- Based more on tradition than on evidence
- More evidence-based data and more contemporary ones for second line drugs
- Pathogenesis not considered neither patient's profile nor comorbidities
- **Time to change?**

ACTUAL AND....
FUTURE GL
FOR ANGINA



BETA BLOCKERS

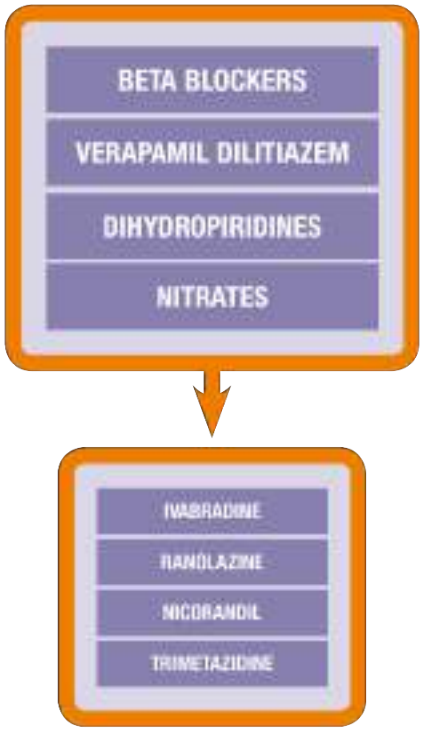
IVABRADINE

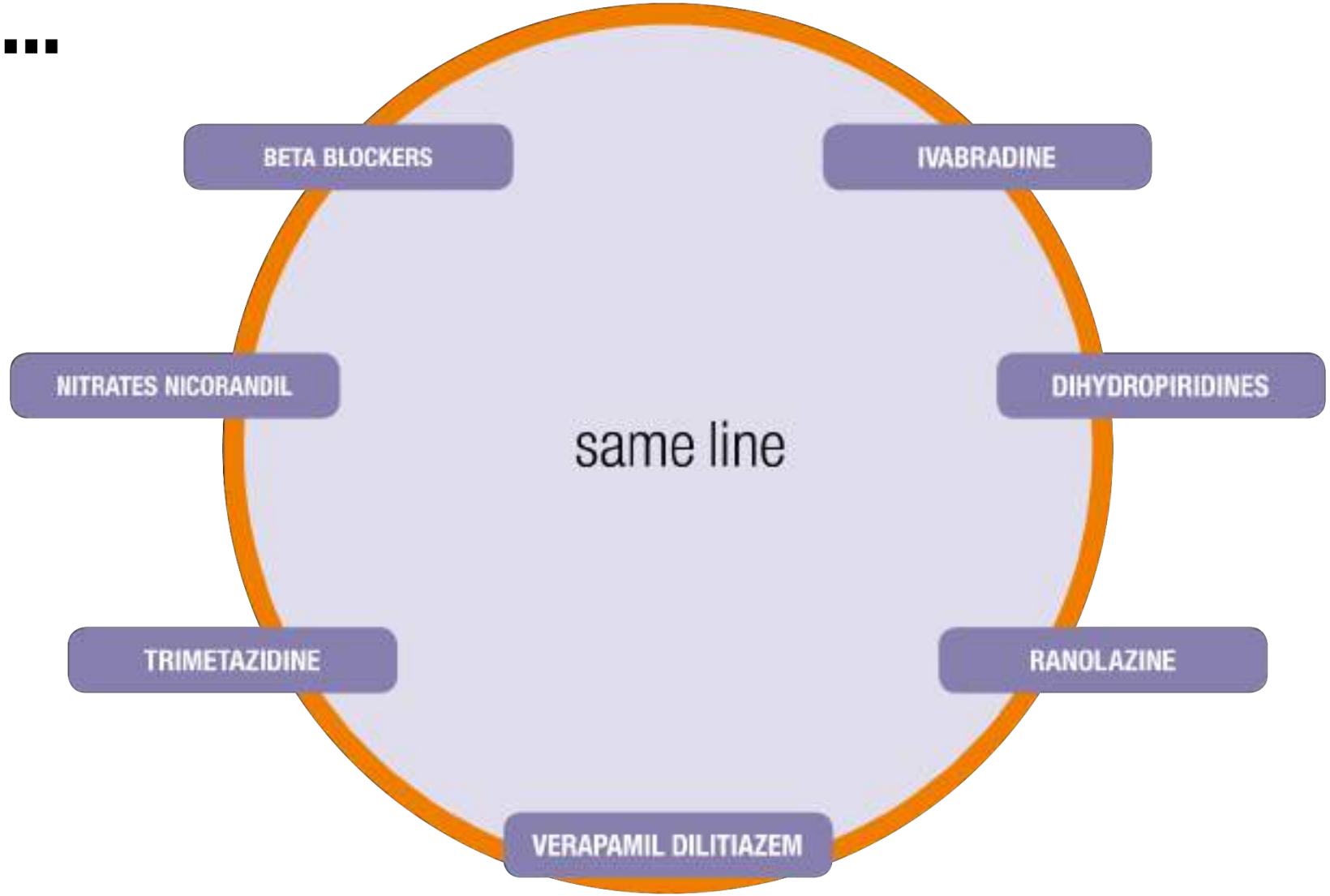
NITRATES NICORANDIL

RANOLAZINE

VERAPAMIL DILITIAZEM

ACTUAL AND.... FUTURE GL FOR ANGINA





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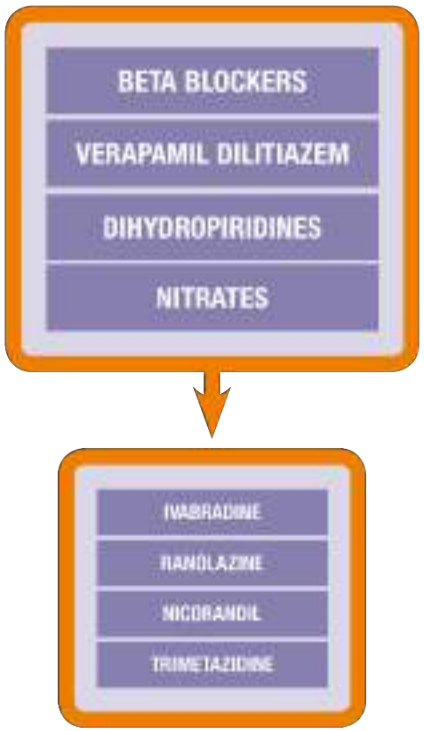

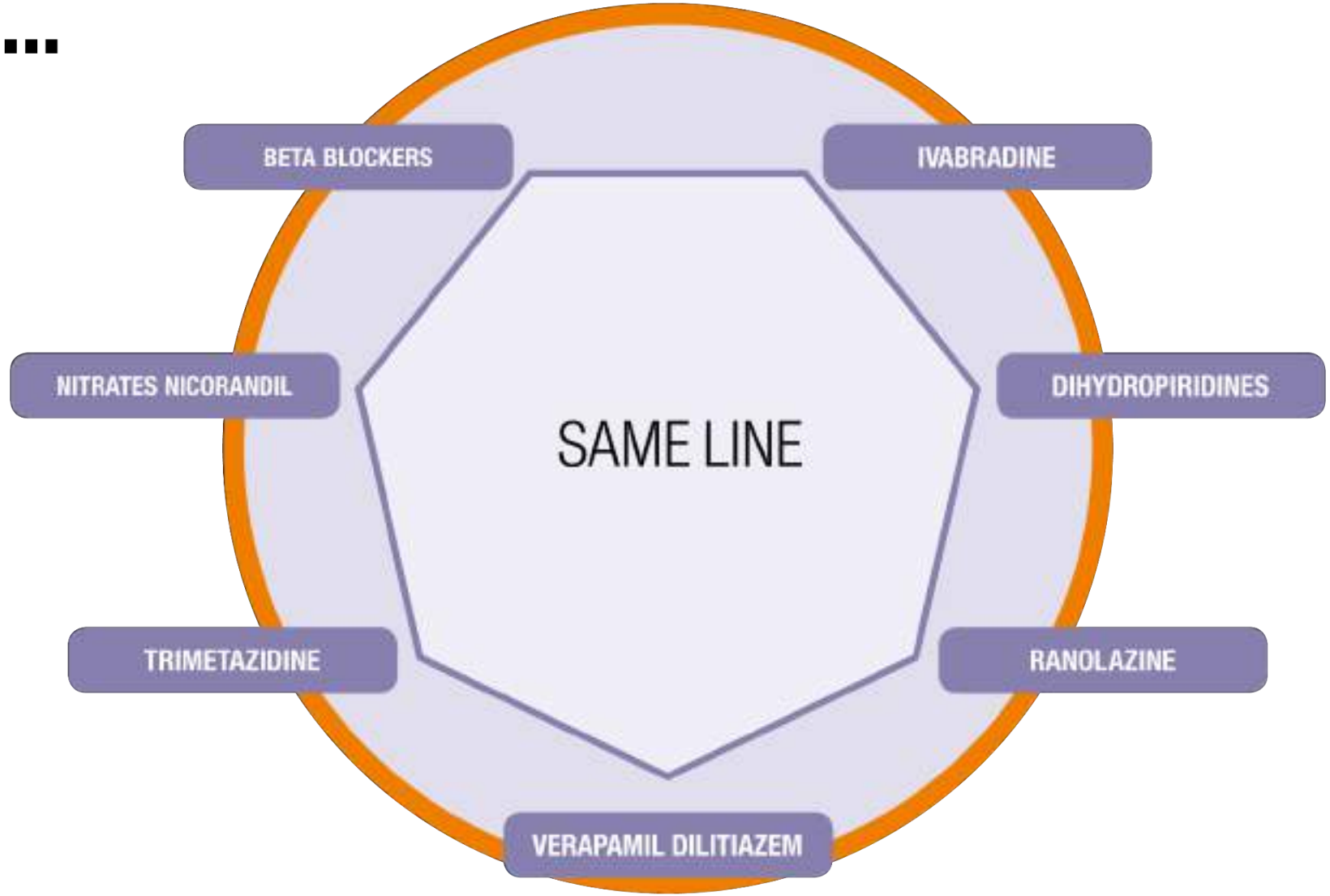

ACTUAL AND.... FUTURE GL FOR ANGINA

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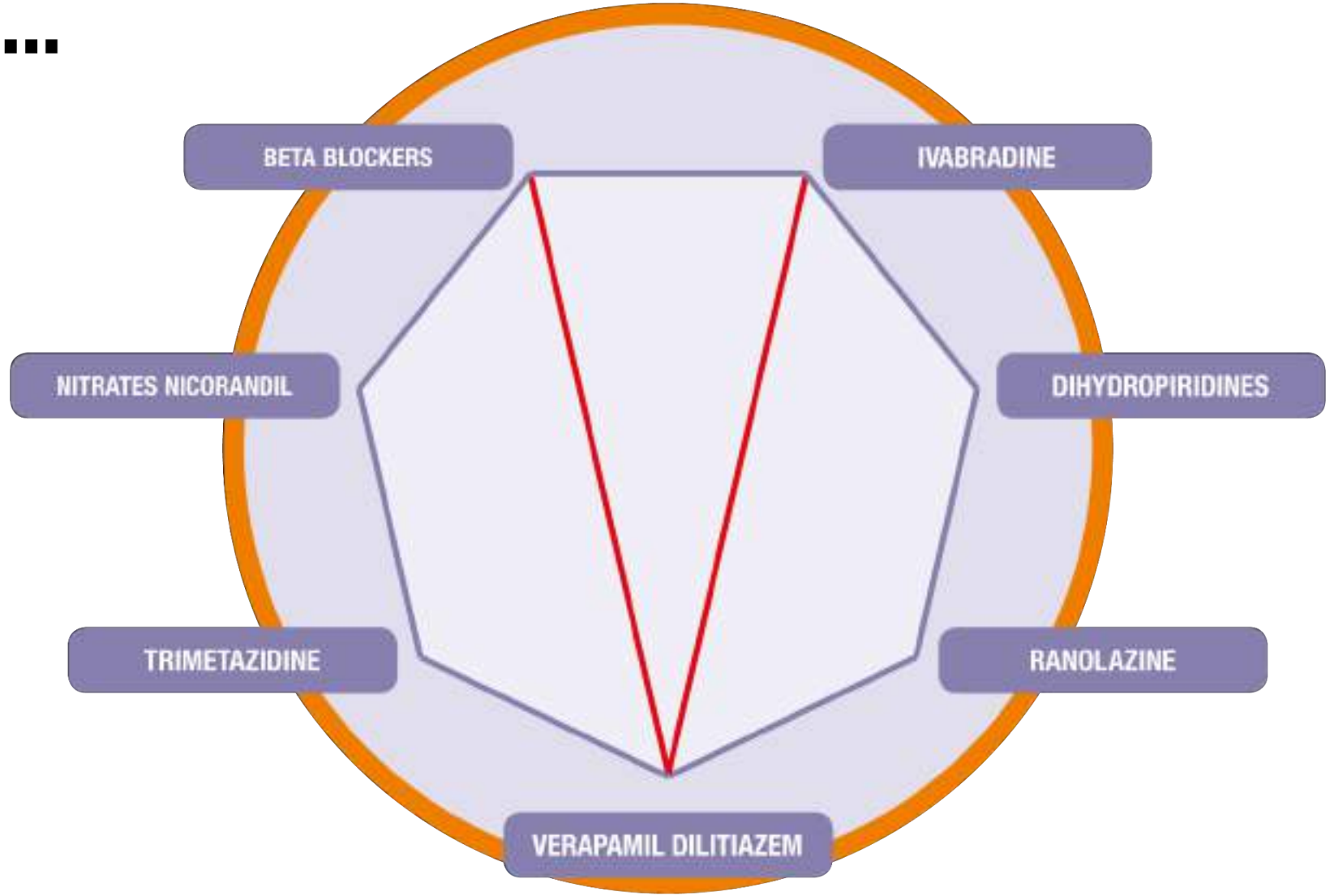

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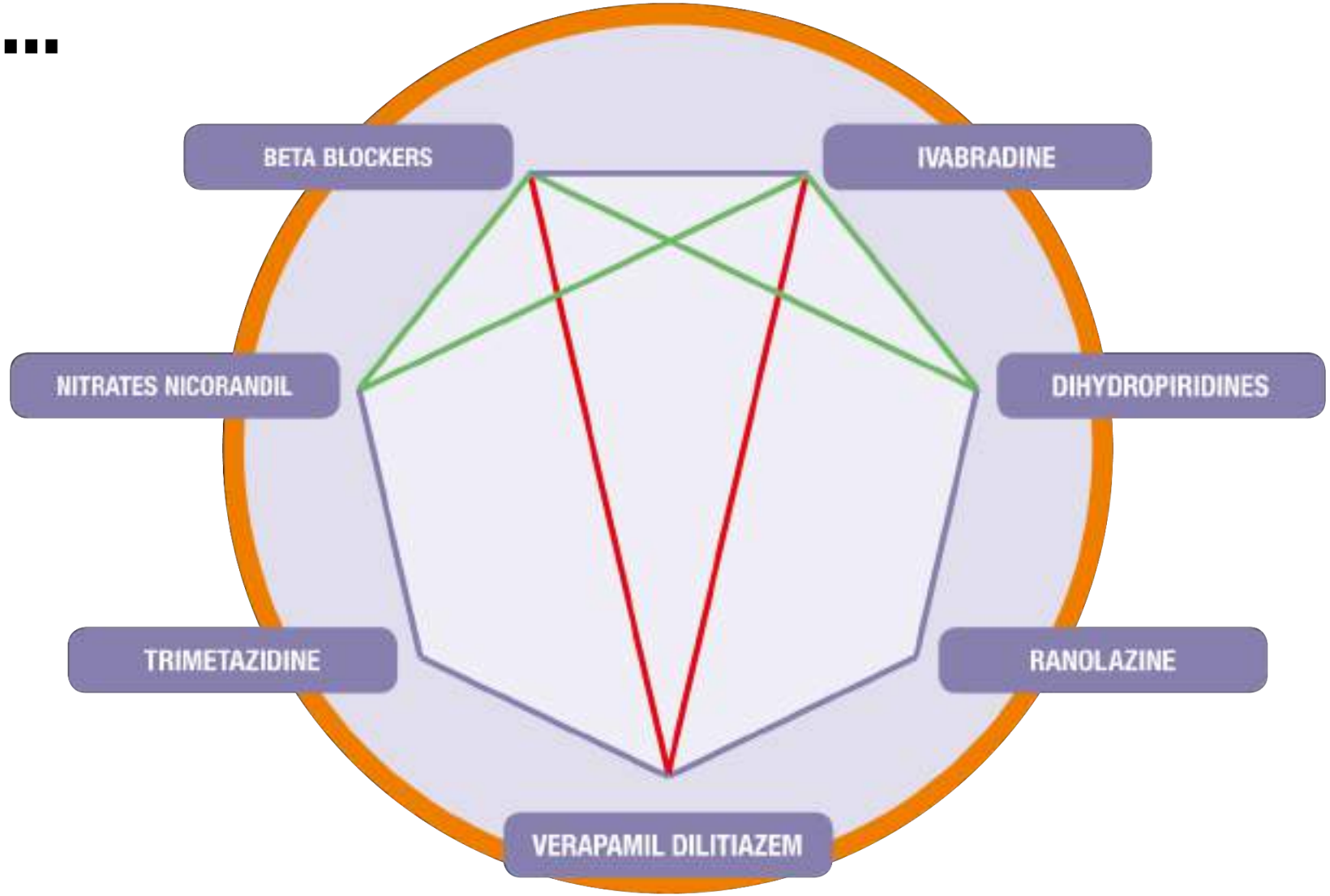

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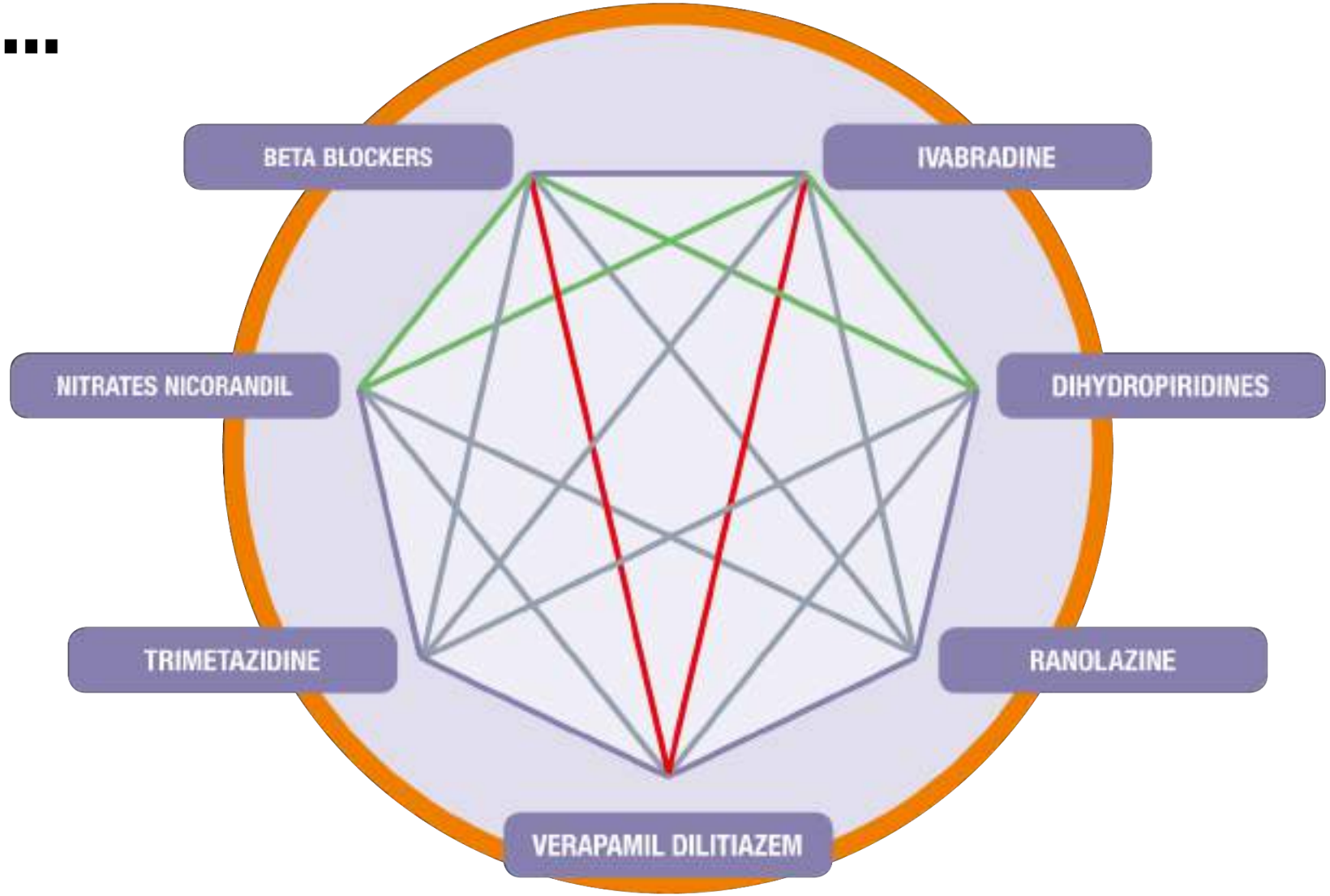

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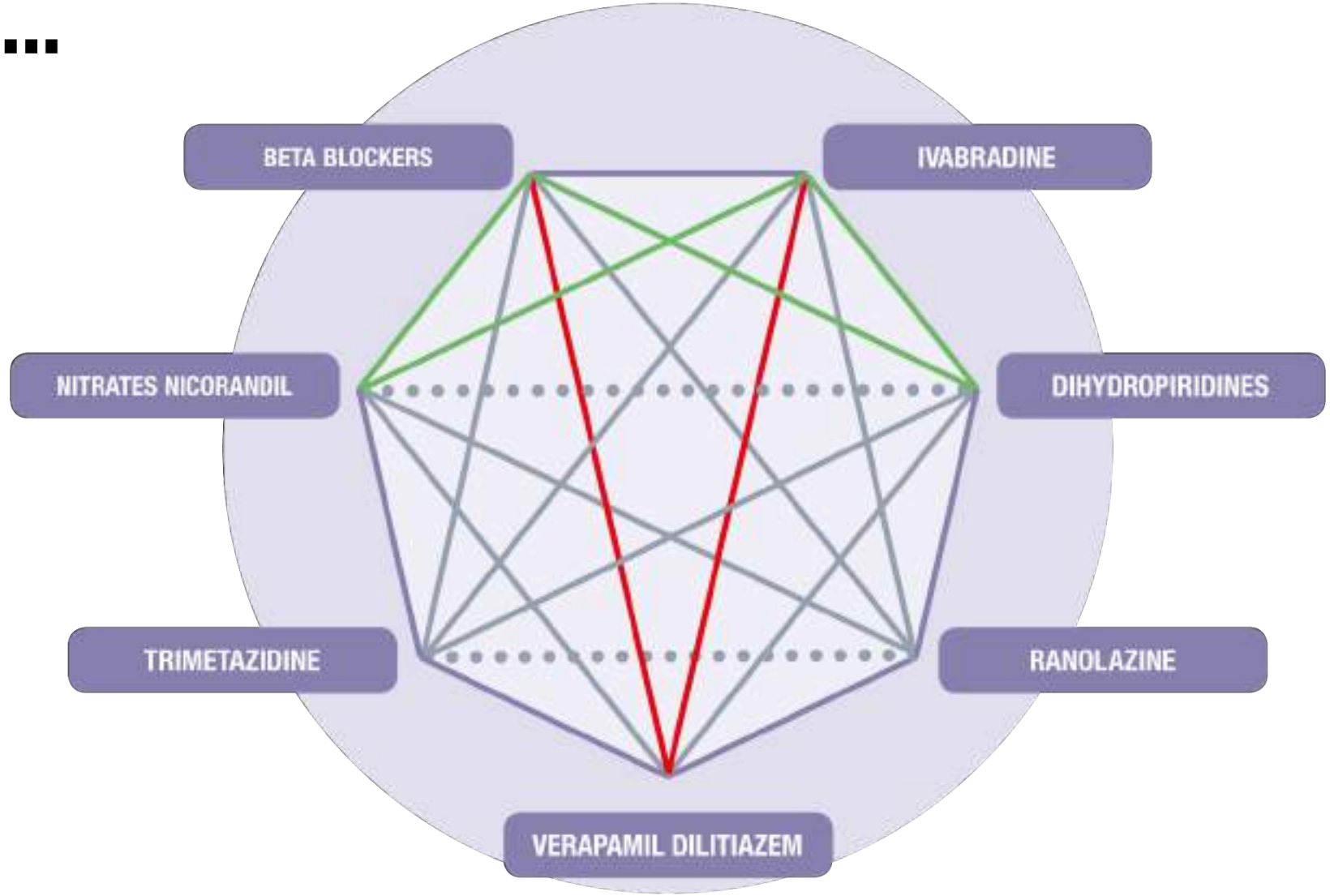
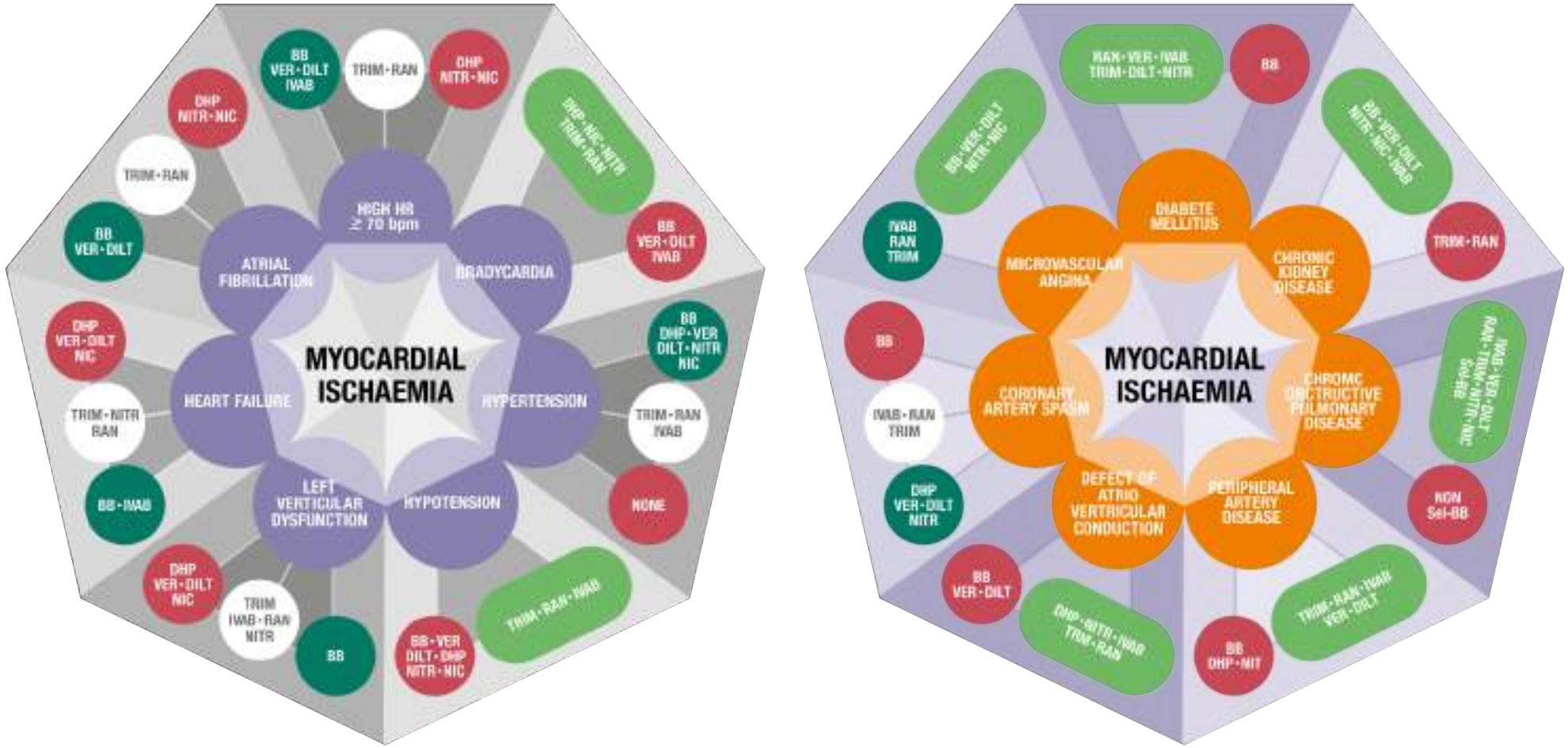


FLEXYBILITY OF THE DIAMOND APPROACH ACCORDING
to patient features and comorbilities



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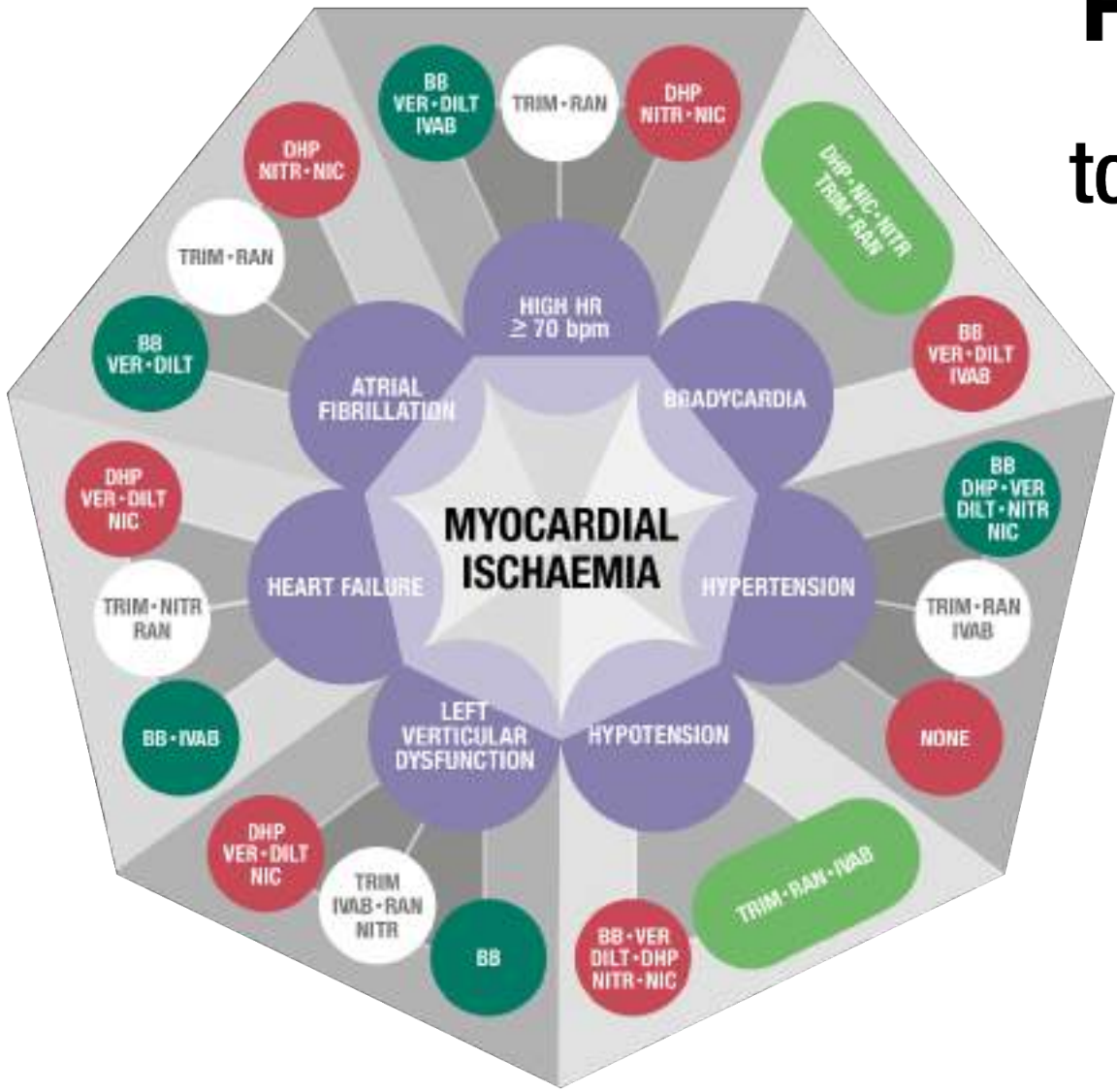

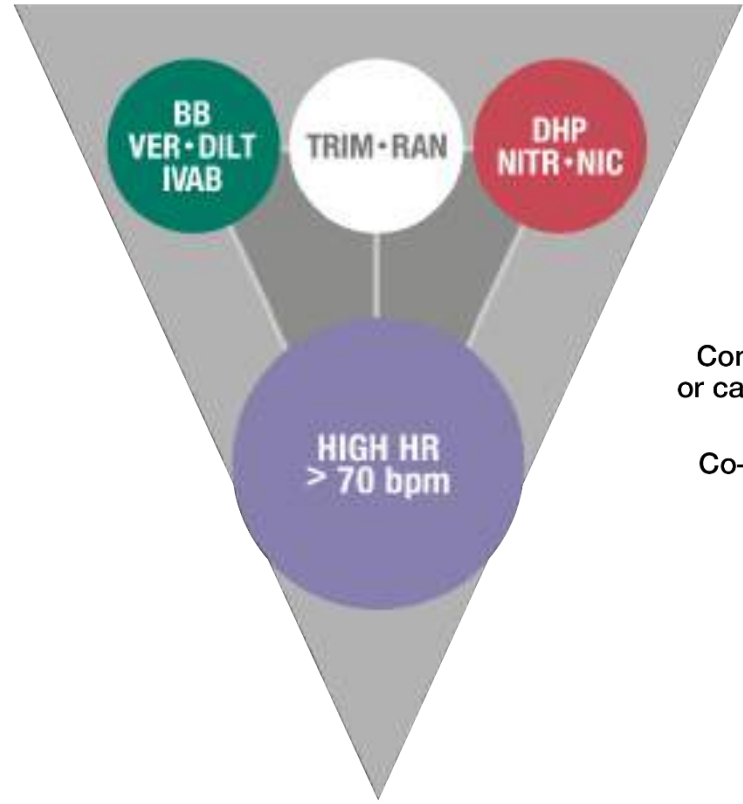

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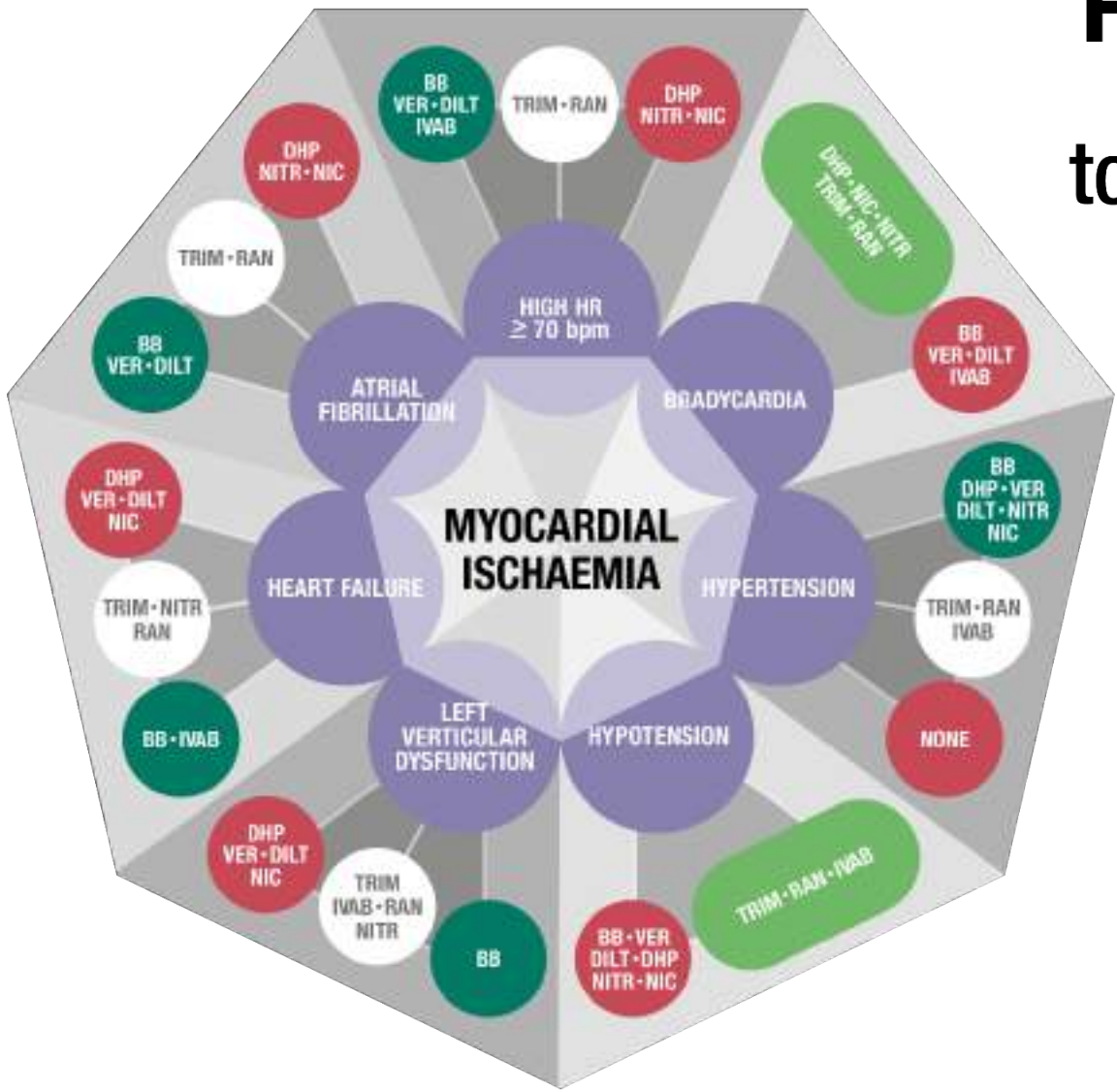

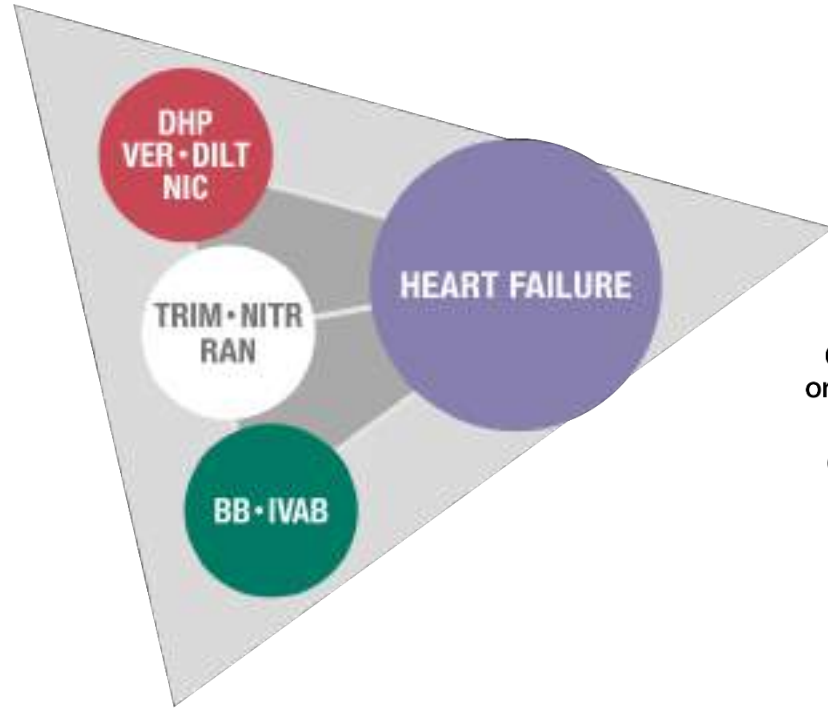

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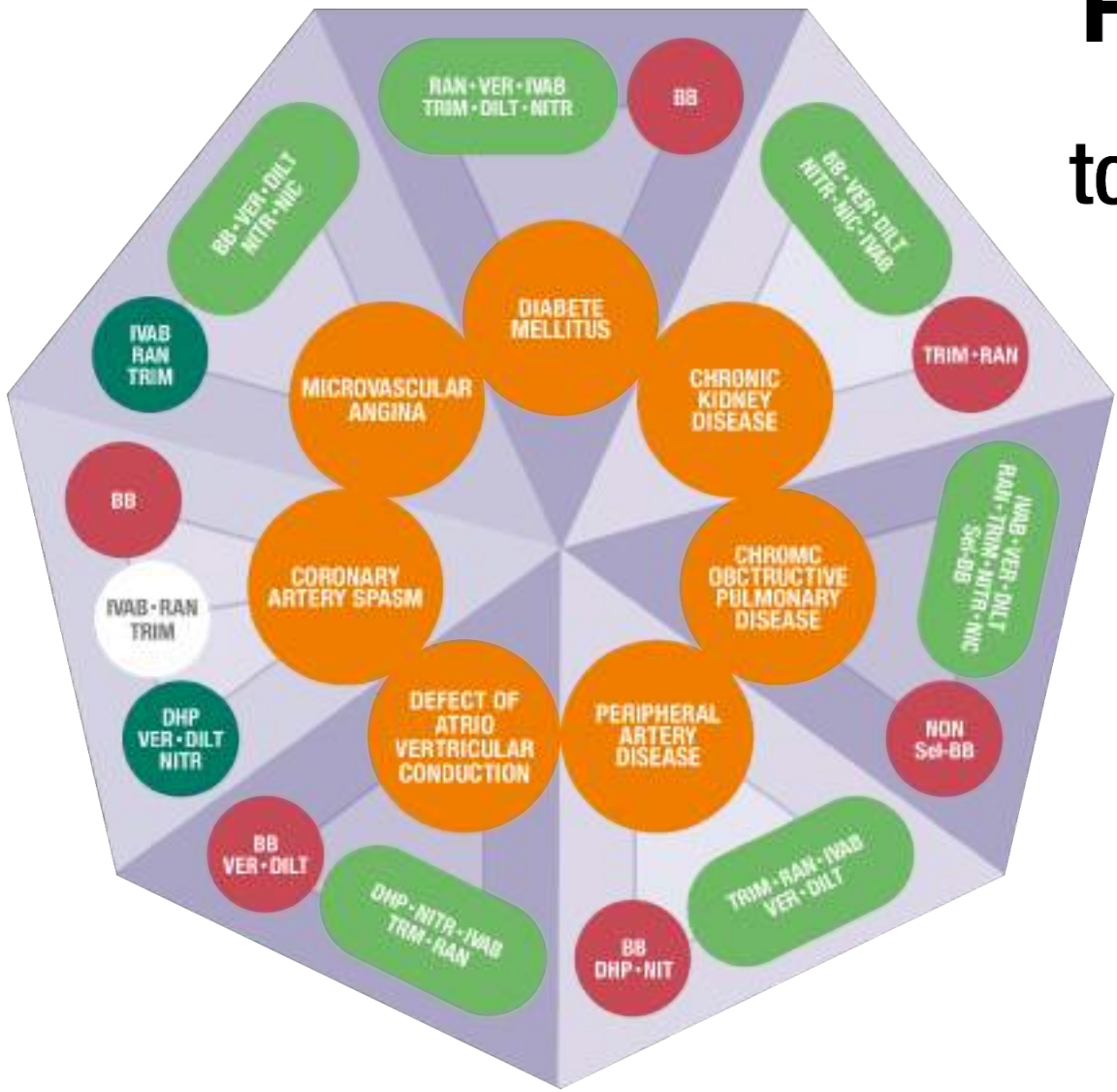

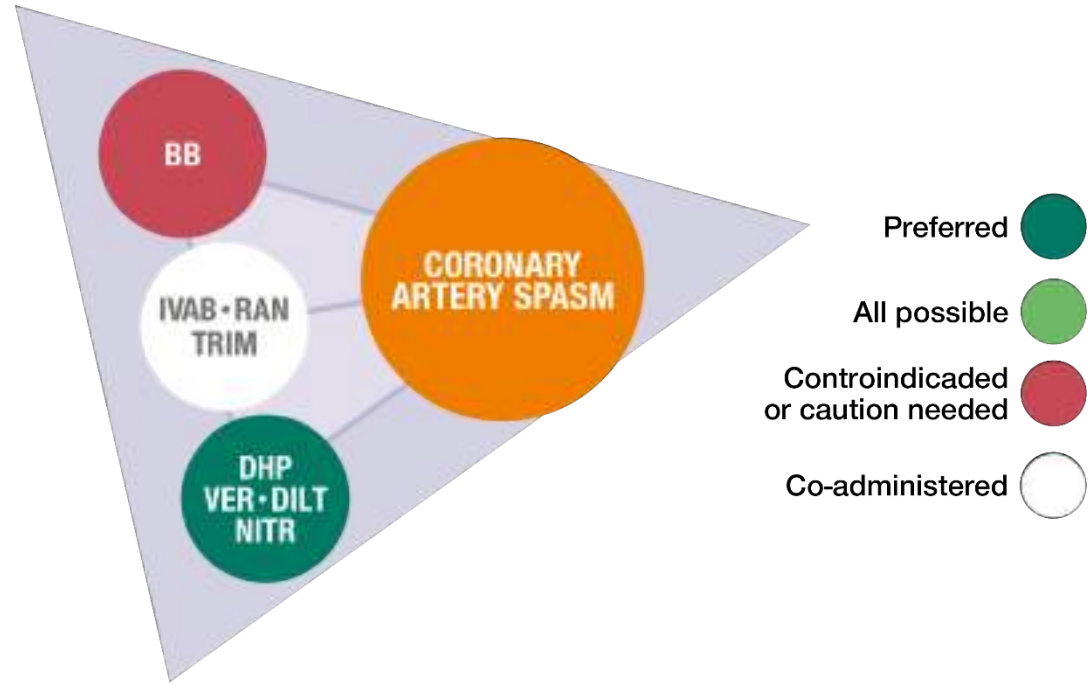

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Is our aim to improve quality of life or to increase survival?

- Of course we should pursue them both
- The important is to have common sense and professionalism
- In Cardiology these goals are normally achieved