LOOK AGAIN

EARLY DETECTION
BENEFIT VS RISK
TREATMENT OPTIONS
COST EFFECTIVE TREATMENT
VASCULAR AGE
DIAGNOSIS
MANAGING RISK

LOOK AGAIN at **early detection** and **preventative treatment.**

BAYER ASPIRIN®

This is a Global Toolkit created and reviewed by global medical experts, countries need to localize and validate the content with their LMR team prior to usage and must strictly follow local approved indications.

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CARDIOVASCULAR DISEASE (CVD) IS THE LEADING CAUSE OF DEATH GLOBALLY

ACCOUNTING FOR 17.9 MILLION DEATHS IN 2019[1,2]

Early prevention of CVD still remains a challenge as:

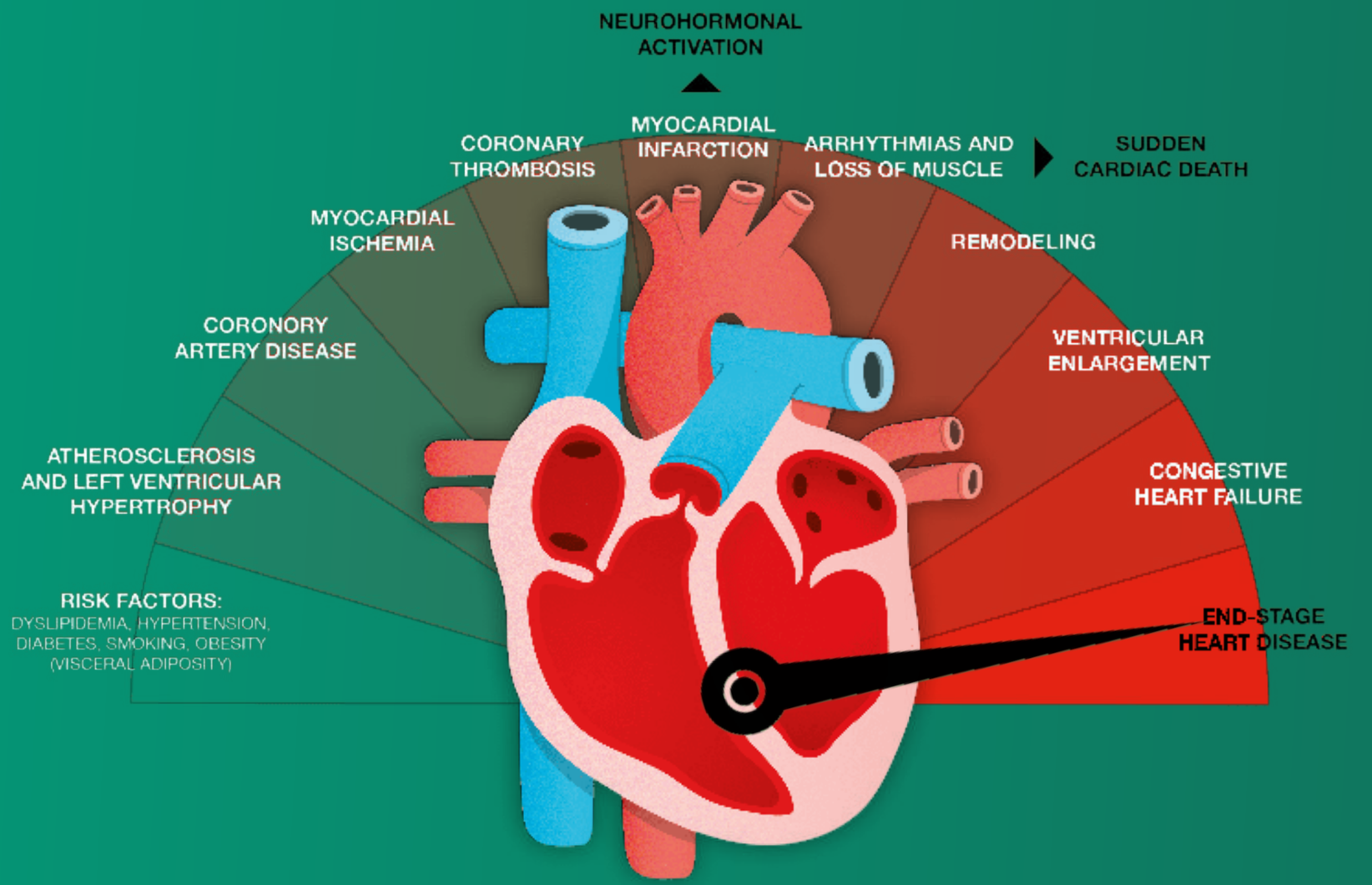
Many patients fall into a "grey area" at the **TREATMENT THRESHOLD**

Lack of availability of diagnostic measures in **LOW-INCOME COUNTRIES**

Some patients lack sufficient information to **PROMOTE COMPLIANCE**

LOOK AGAIN at early intervention in order to prevent potentially fatal end points of CVD

CARDIAC RISK CONTINUUM



ADAPTED FROM DZAU 1991 AND CHRYSANT 2011[3,4]

The cardiac risk continuum is a sequence of events percipitated by a cluster of cardiovascular disease (CVD) risk factors that, if not intervened with early, can lead to end stage heart failure and death.[4]

LOOK BEYOND TRADITIONAL RISK FACTORS

Current focus primarily revolves around traditional chemical physiological risk markers including:[5]

TRADITIONAL RISK FACTORS

SMOKING

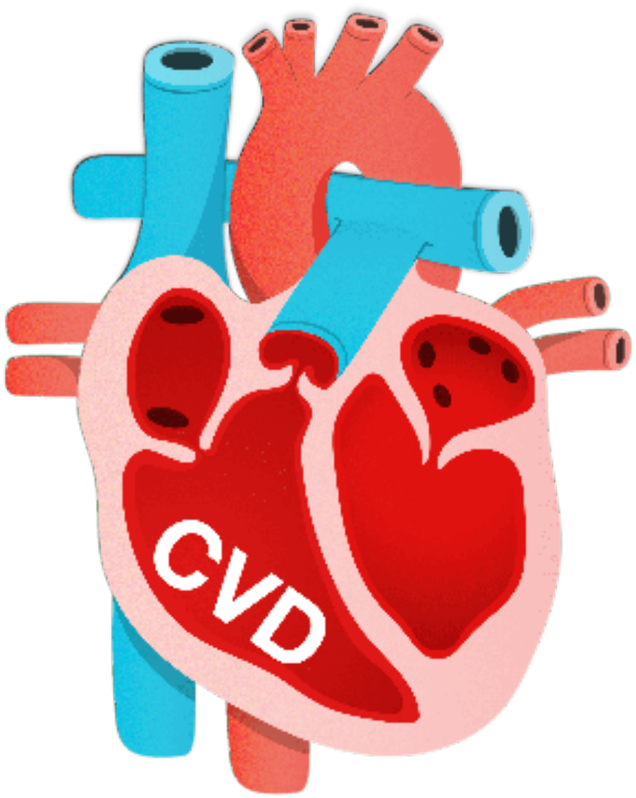
PHYSICAL INACTIVITY

OBESITY

HYPERTENSION

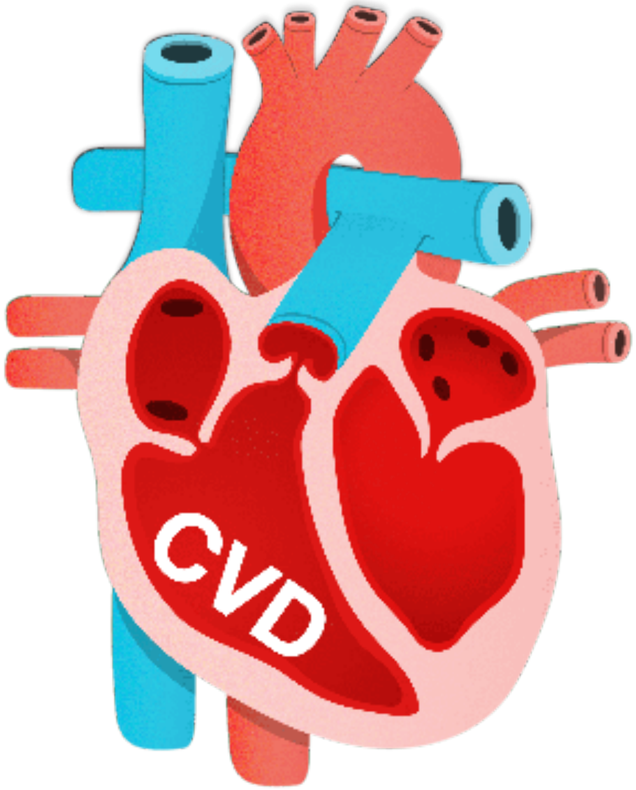
DYSLIPIDEMIA

DIABETES MELLITUS



THE NEW BIOMARKERS

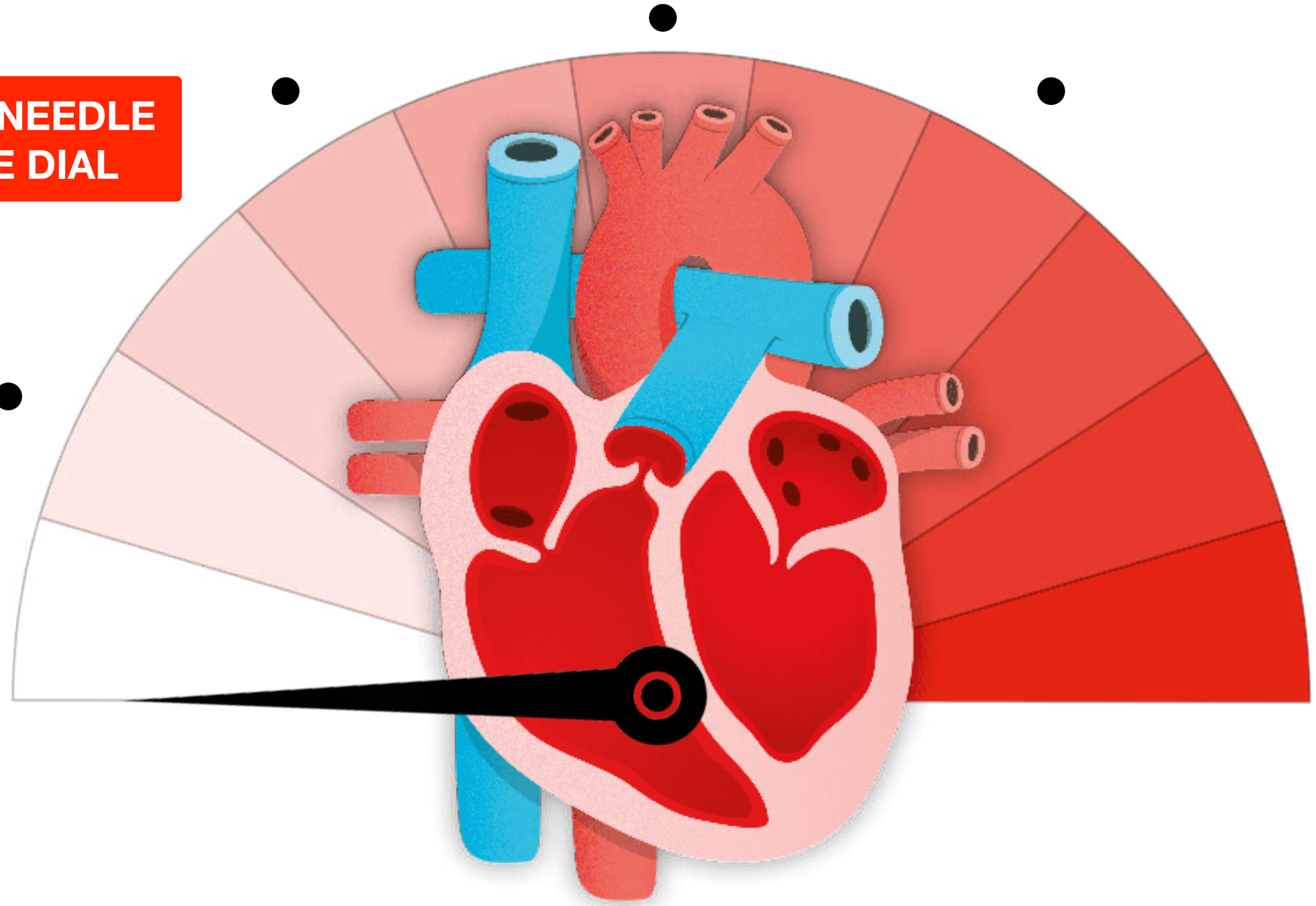
Research has identified additional biomarkers beyond established major risk factors including elevated levels of:[5]



- C-REACTIVE PROTEIN
- ENDOTHELIAL DYSFUNCTION
- LEFT VENTRICULAR HYPER-TROPHY
- MARKERS OF OXIDATIVE STRESS
- INTIMA-MEDIA WALL THICKNESS

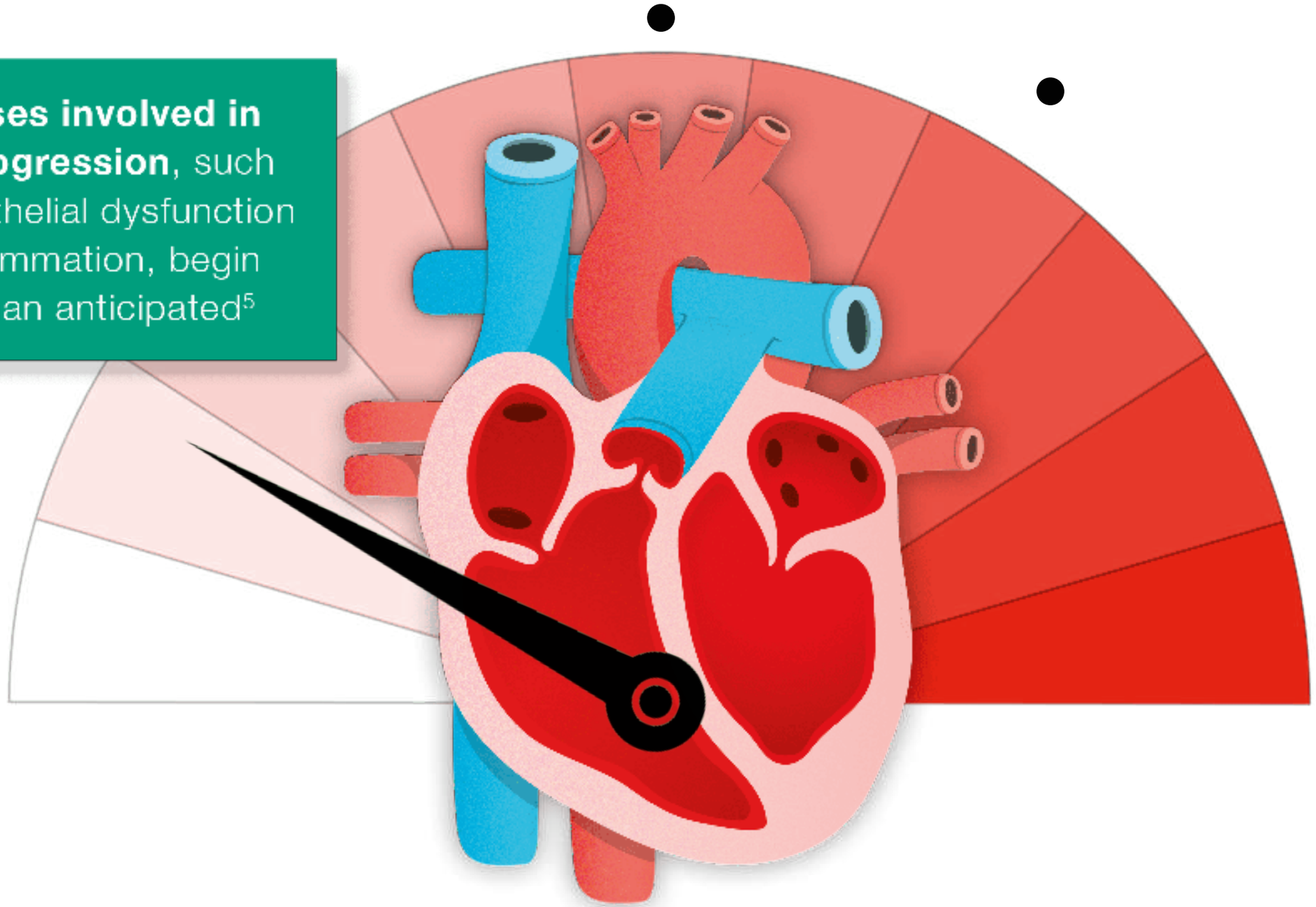
LOOK AGAIN AT EARLY DETECTION AND PREVENTATIVE TREATMENT

SLIDE THE NEEDLE OVER THE DIAL



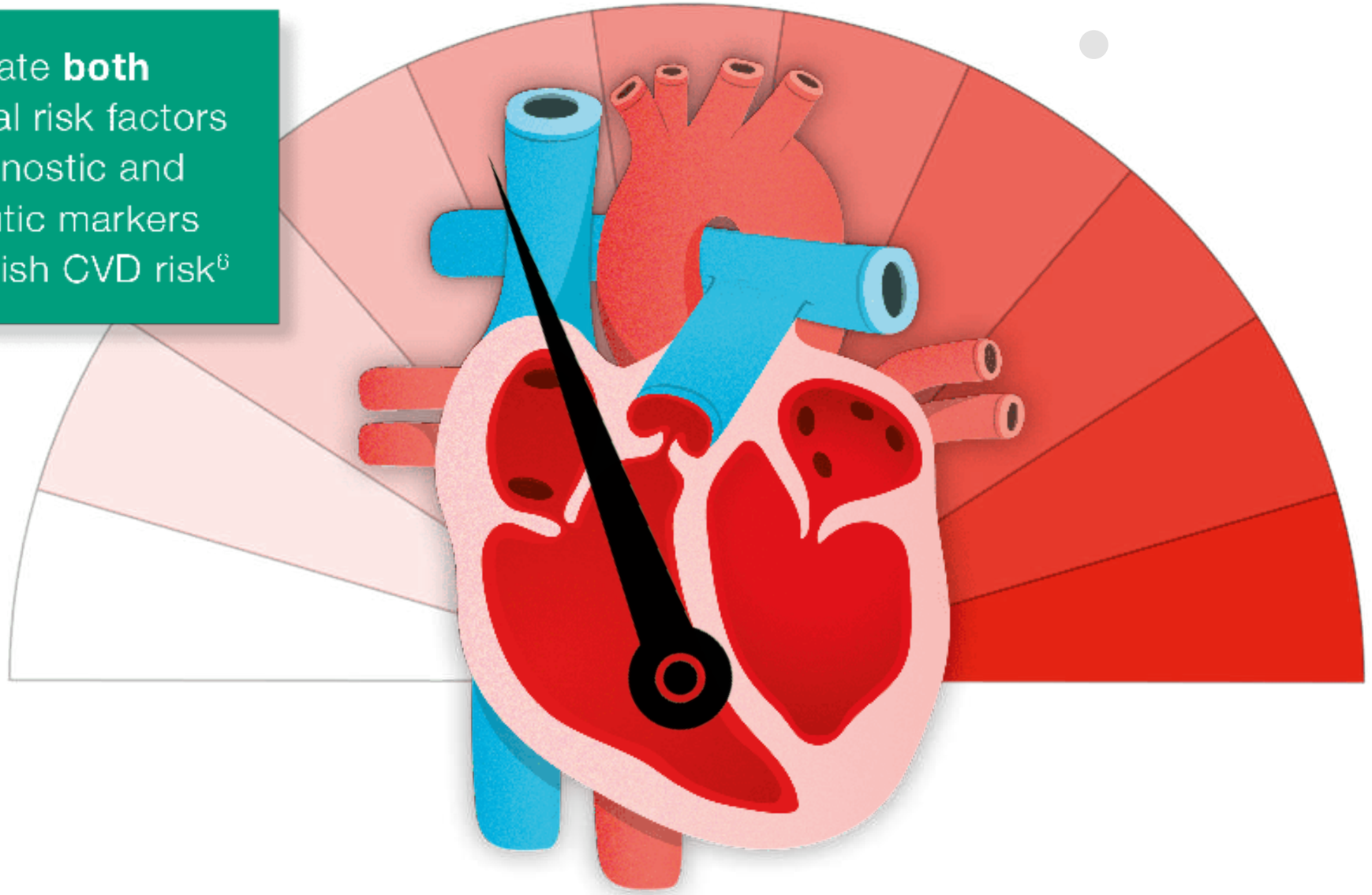
LOOK AGAIN AT EARLY DETECTION AND PREVENTATIVE TREATMENT

Processes involved in CVD progression, such as endothelial dysfunction and inflammation, begin earlier than anticipated[5]



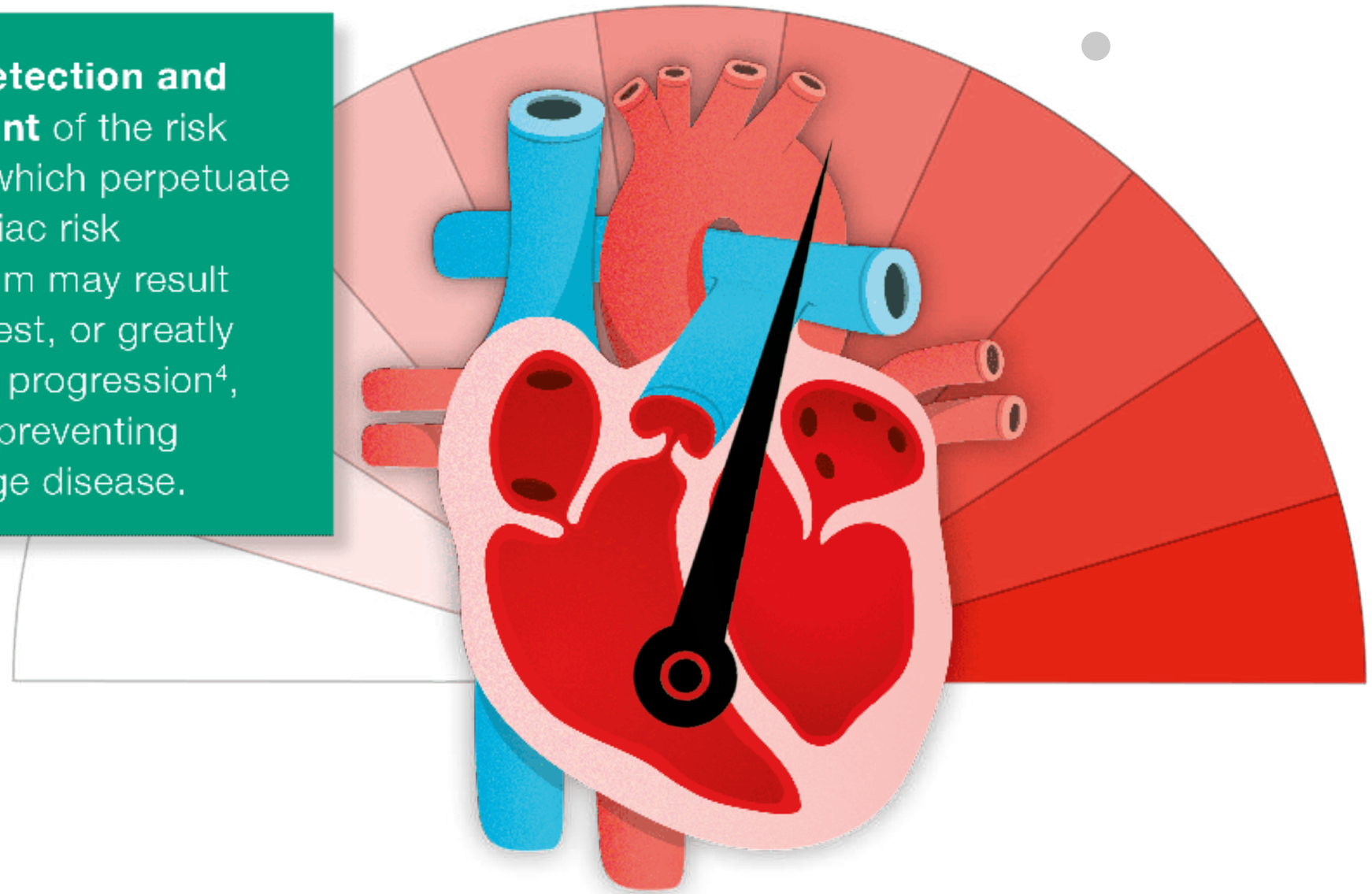
LOOK AGAIN AT EARLY DETECTION AND PREVENTATIVE TREATMENT

Incorporate **both** traditional risk factors and diagnostic and therapeutic markers to establish CVD risk[6]

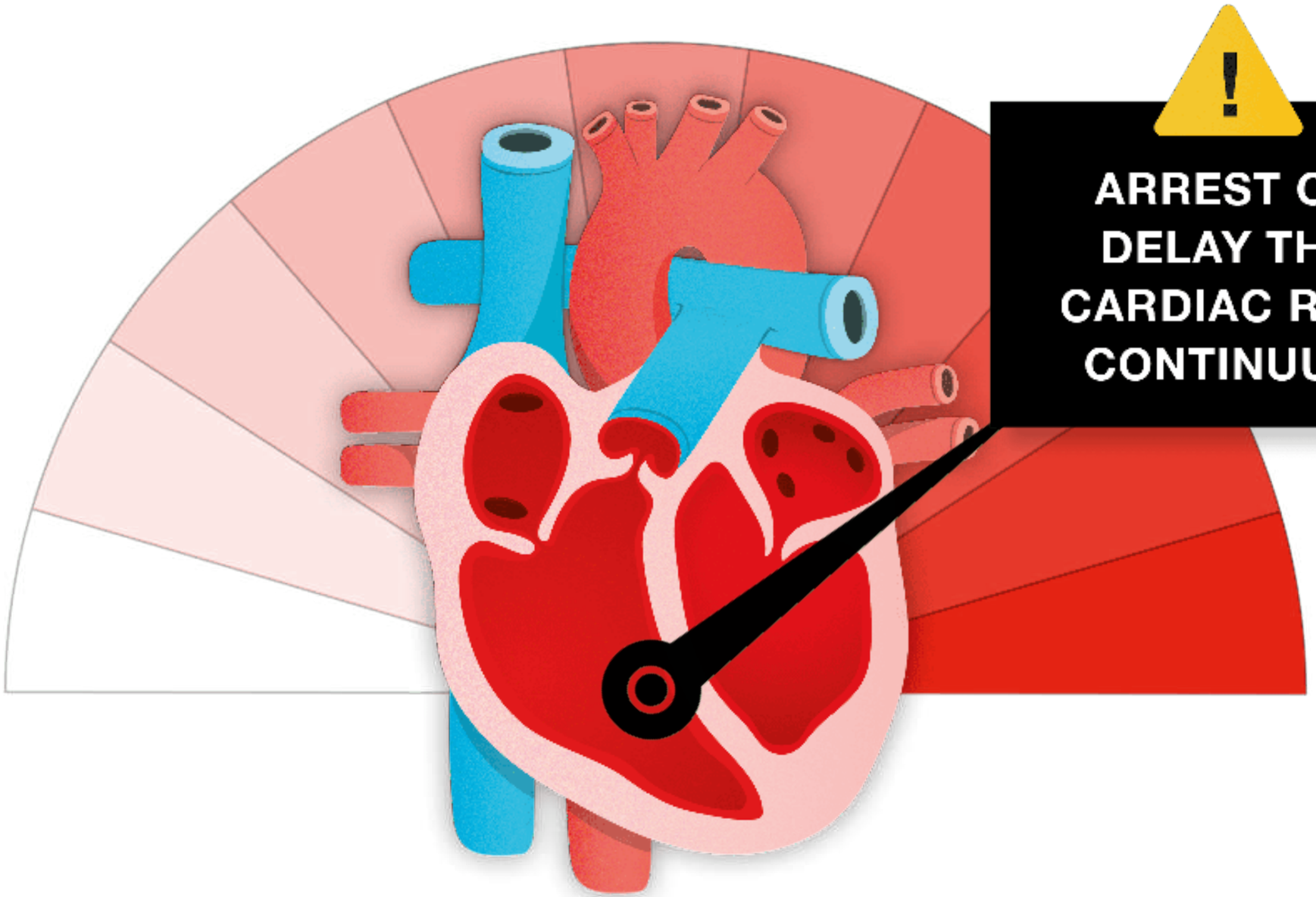


LOOK AGAIN AT EARLY DETECTION AND PREVENTATIVE TREATMENT

Early detection and treatment of the risk factors which perpetuate the cardiac risk continuum may result in its arrest, or greatly delay its progression[4], thereby preventing end-stage disease.

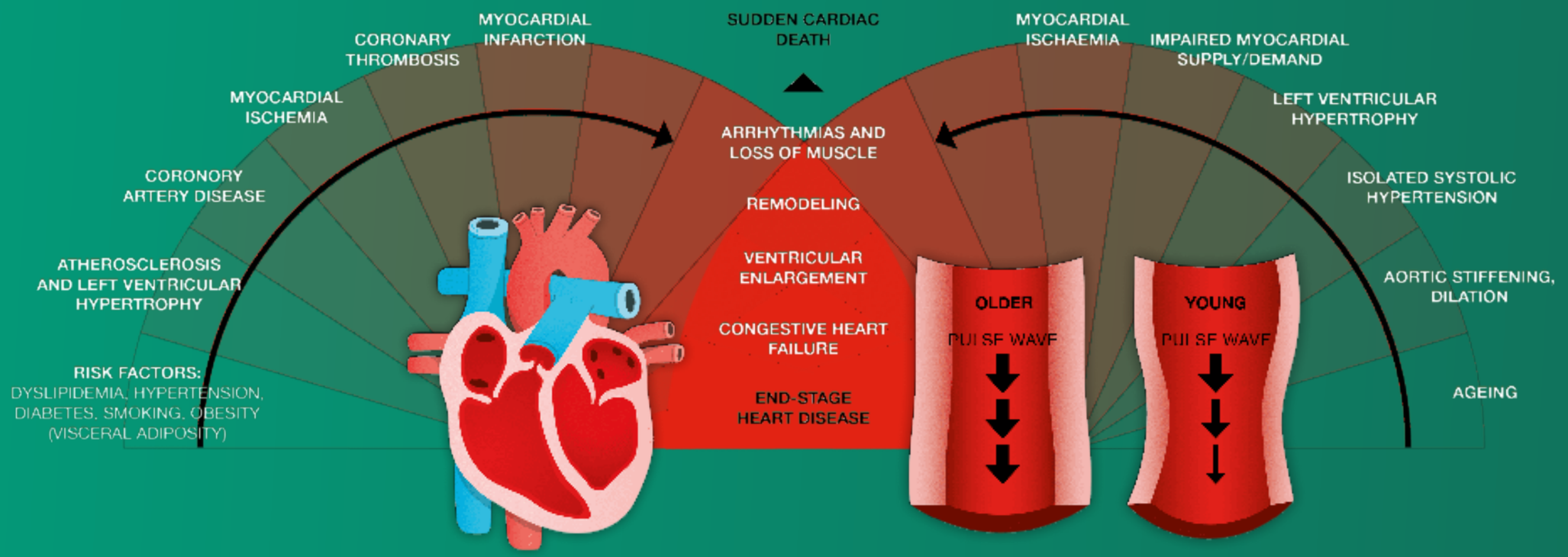


LOOK AGAIN AT EARLY DETECTION AND PREVENTATIVE TREATMENT



VASCULAR AGE

CV ATHEROSCLEROTIC CONTINUUM	INTERACTION OF THE TWO CONTINUA	CV AGING CONTINUUM



ADAPTED FROM O'ROURKE 2010[7]

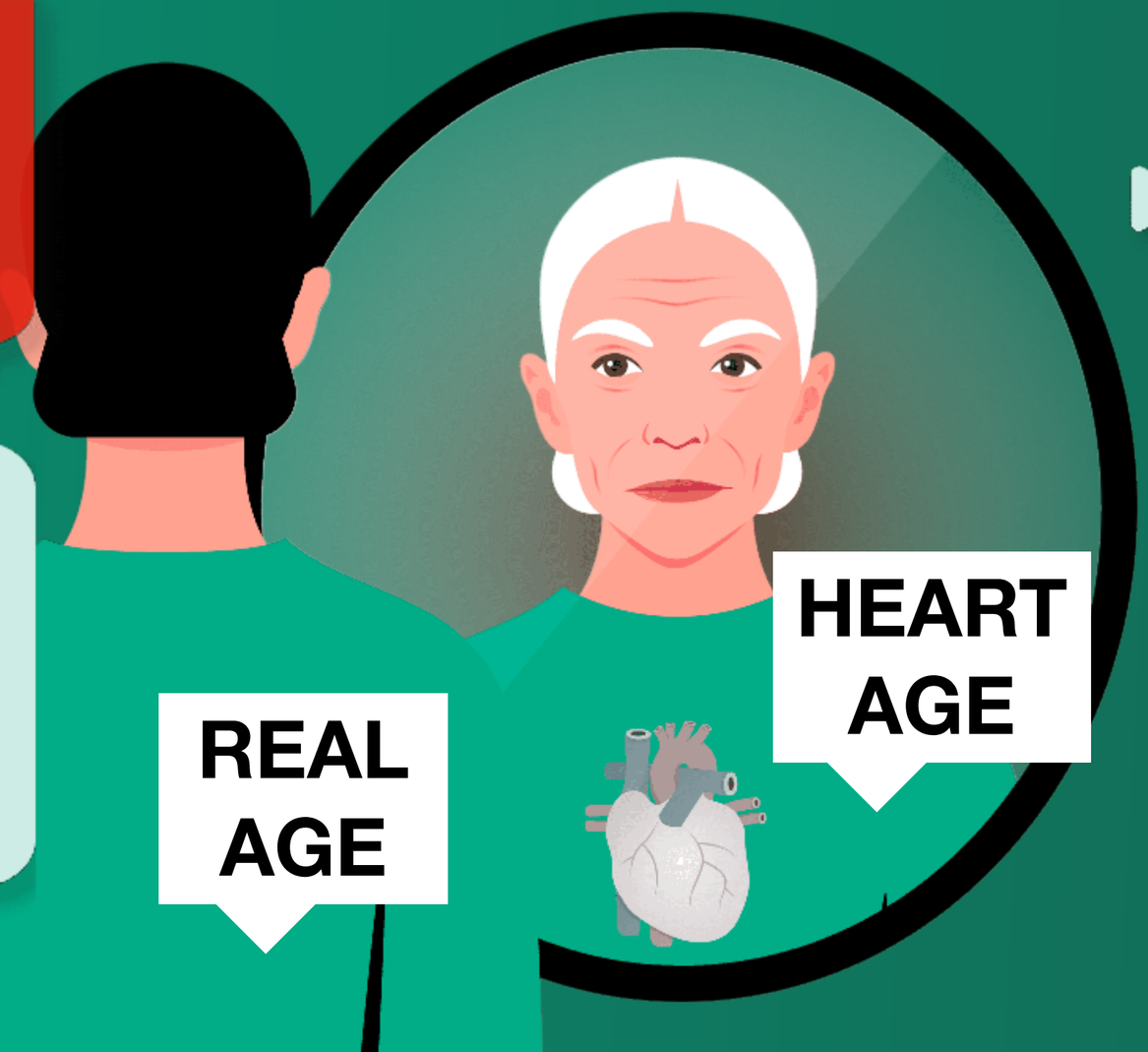
Vascular age is an alternate means of expressing cardiovascular risk in a way that encompasses the complex process occurring with age at cellular levels.[8,9]

VASCULAR AGE CONCEPT

A person's age is the most important determinant of cardiovascular health.[10]

A heart age that is **<u>older</u>** than **current age** indicates elevated risk of CVD, even if the individual's risk of CVD over the next **5-10 YEARS** **is low.**[11]

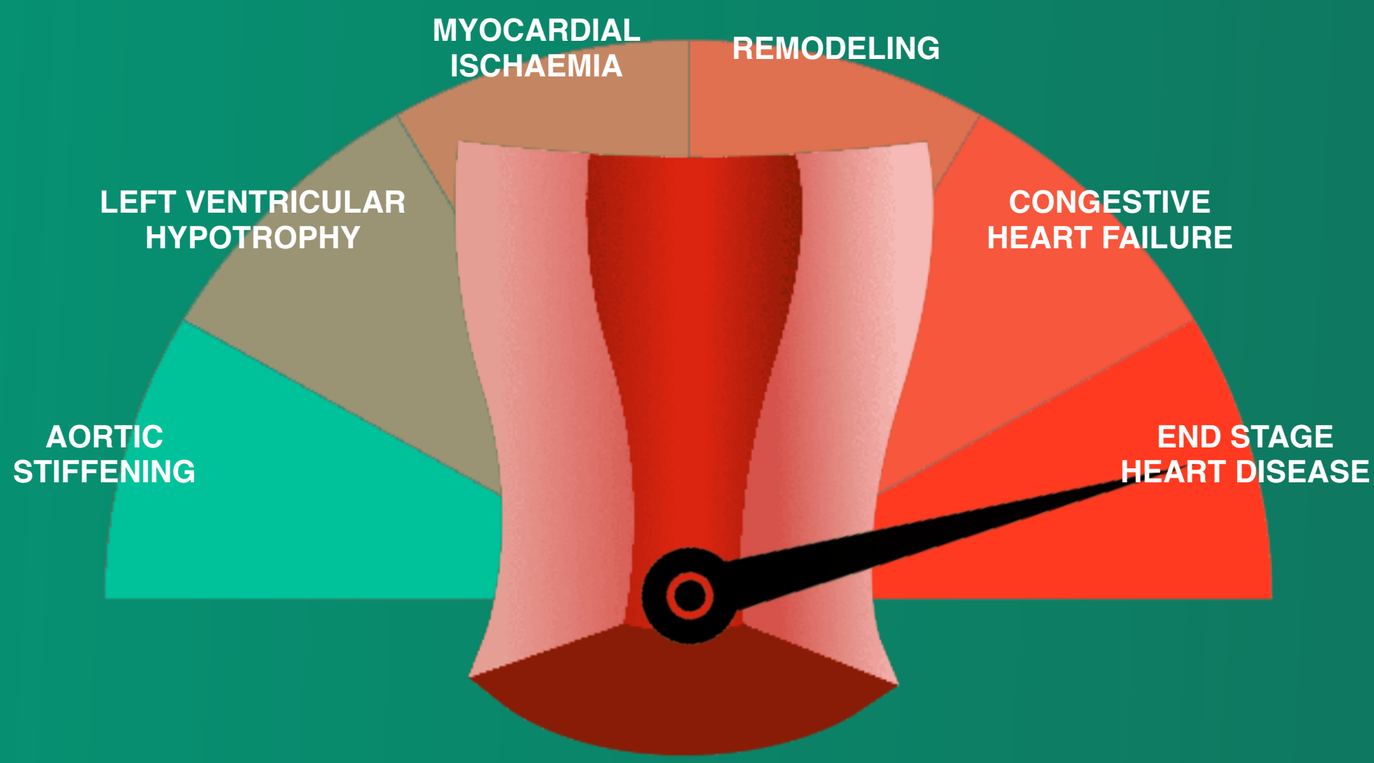
Chronic disease, functional limitations, and cardiovascular mortality increase in complexity, yet significant diversity exists among individuals in the extent to which **age affects outcomes.**[12]



BIOLOGICAL AGEING

Manifests as impairments in the vasculature of the heart including reduced **vascular elasticity**, increased **arterial stiffness**, and dysfunction of the endothelium.[13]

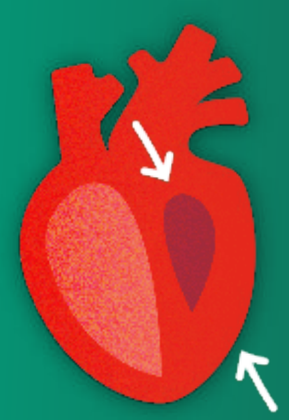
This process can be **accelerated** by the presence of underlying **risk factors**,[13] and can negatively impact a person's quality of life.[12]



AGING AND ARTERIAL CALCIFICATION

Arterial stiffening occurs with aging and is attributed to the progression of CVD.[14]
As the heart beats, the aorta repeatedly stretches and relaxes, which over time results in the dilation of the aorta and makes the aorta more brittle, wider, and fragile. The aorta then stiffens, increasing the pressure of pulsing blood flow which results in:[14]

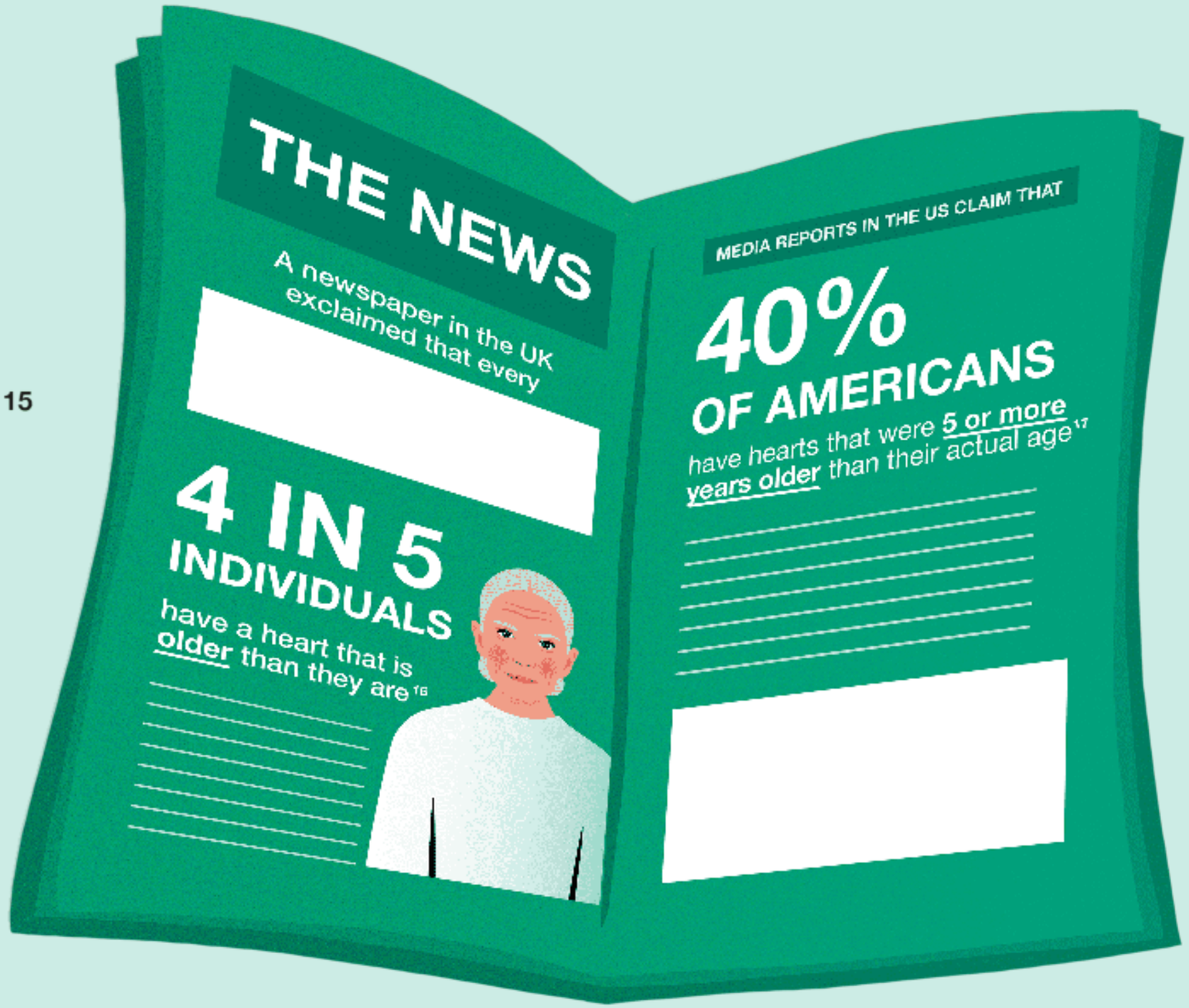
SYSTOLIC HYPERTENSION



LEFT VENTRICULAR HYPERTROPHY

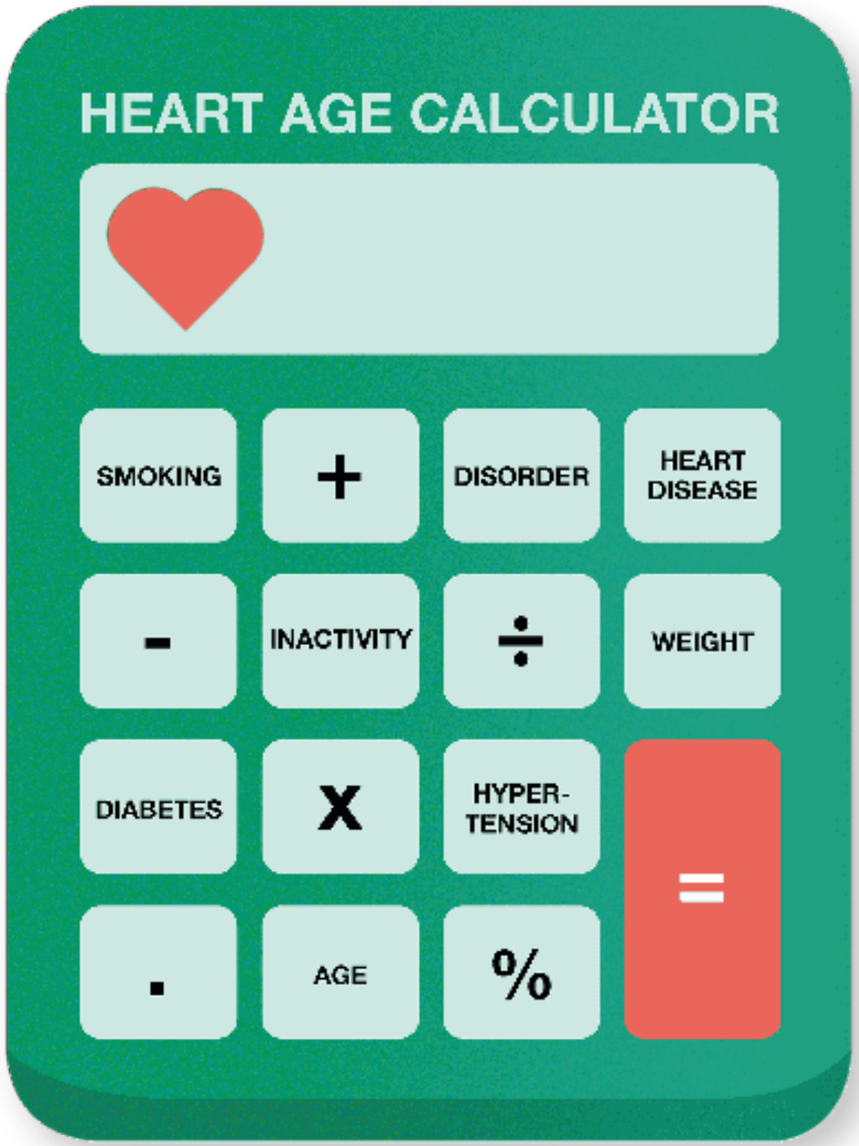
CARDIAC CELL DEATH

VASCULAR AGE CAN BE REFERRED TO AS ‘HEART AGE’[15]



HEART AGE IN PRACTICE

Results from heart age calculators can be used to communicate the long-term consequences of lifestyle choices, prompting appropriate changes and enhancing treatment compliance.[9,15,18,19]



WHAT YOUR PATIENT'S HEART AGE MEANS

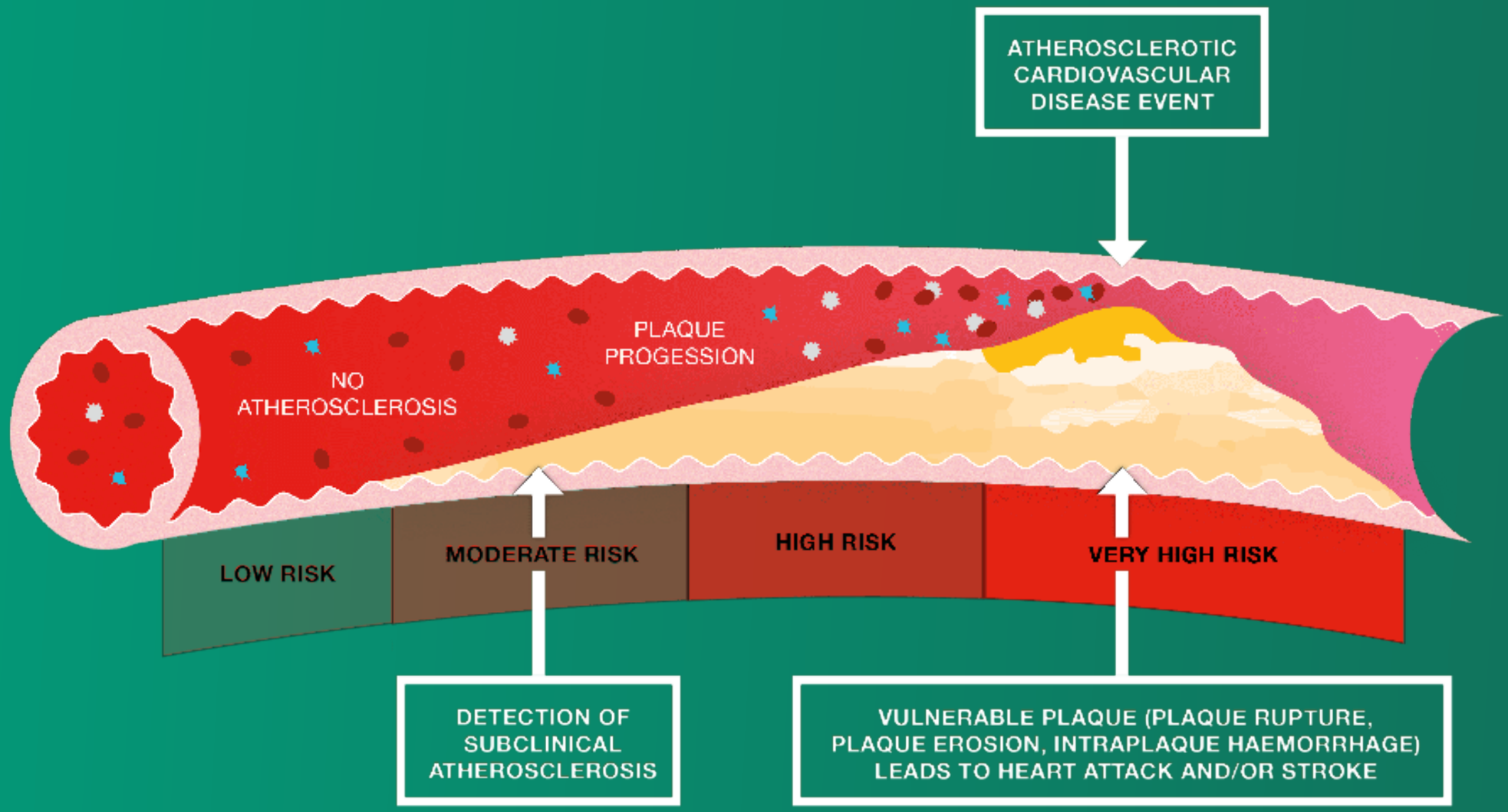
THE CONCEPT OF HEART AGE is easily understood by patients and can elicit better preventative lifestyle modifications.

Heart age scores are recommended to communicate implications of lifestyle to younger people with low absolute risk and high relative risk.[20]

	PATIENT A	PATIENT B
Gender	Male	Female
Real Age	51 years old	45 years old
BMI	26.4	34
Smoke	No	Yes
Hypercholesterolaemia	Yes	Yes
Hypertension	No	Yes
Prediabetic	No	Yes
HEART AGE	**53 YEARS OLD**	**56 YEARS OLD**

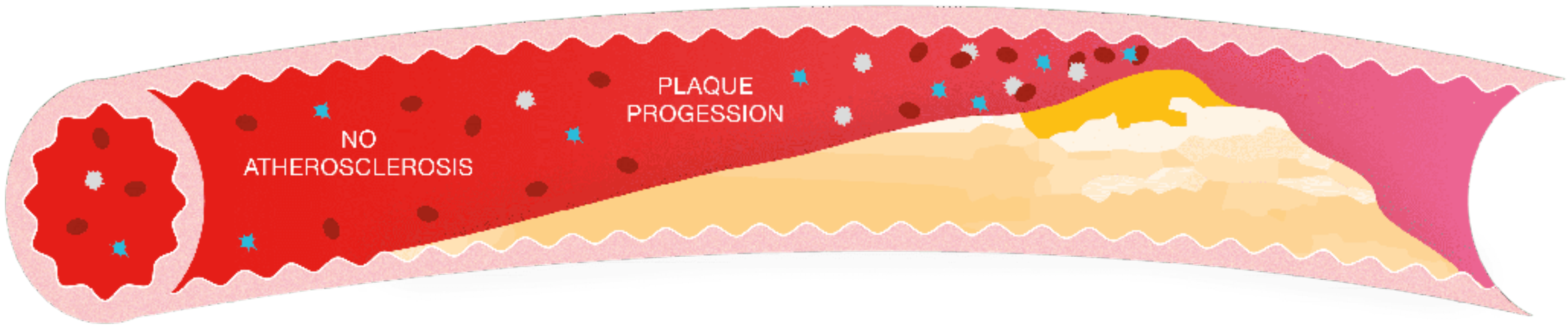
LOOK AGAIN at the pathophysiology of cardiovascular disease

ARTERIAL RISK INDICATES RISK



ADAPTED FROM AHMADI 2019[21]

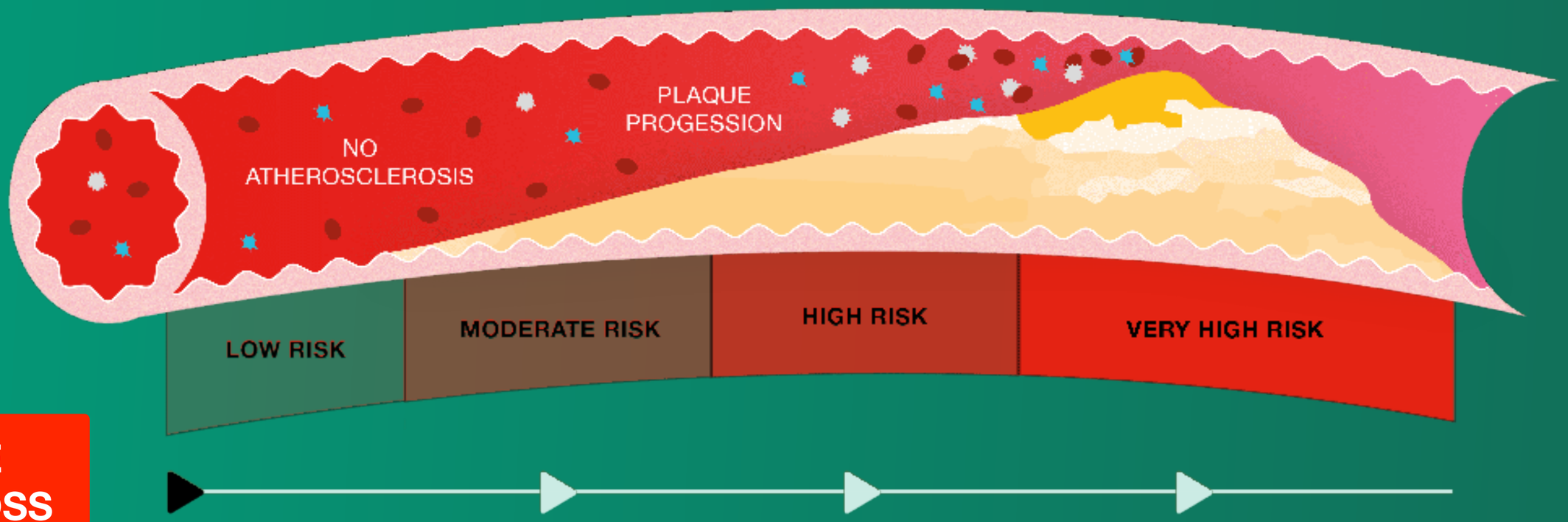
ARTERIAL CALCIFICATION AND CVD RISK



The build-up of coronary calcium (CAC) is a hallmark of atherosclerotic cardiovascular disease (ASCVD)[22]

Increased thickness of the intimal and medial arterial layers is attributed to vascular aging through the same mechanisms responsible for the development and progression of atherosclerosis.[19,23]

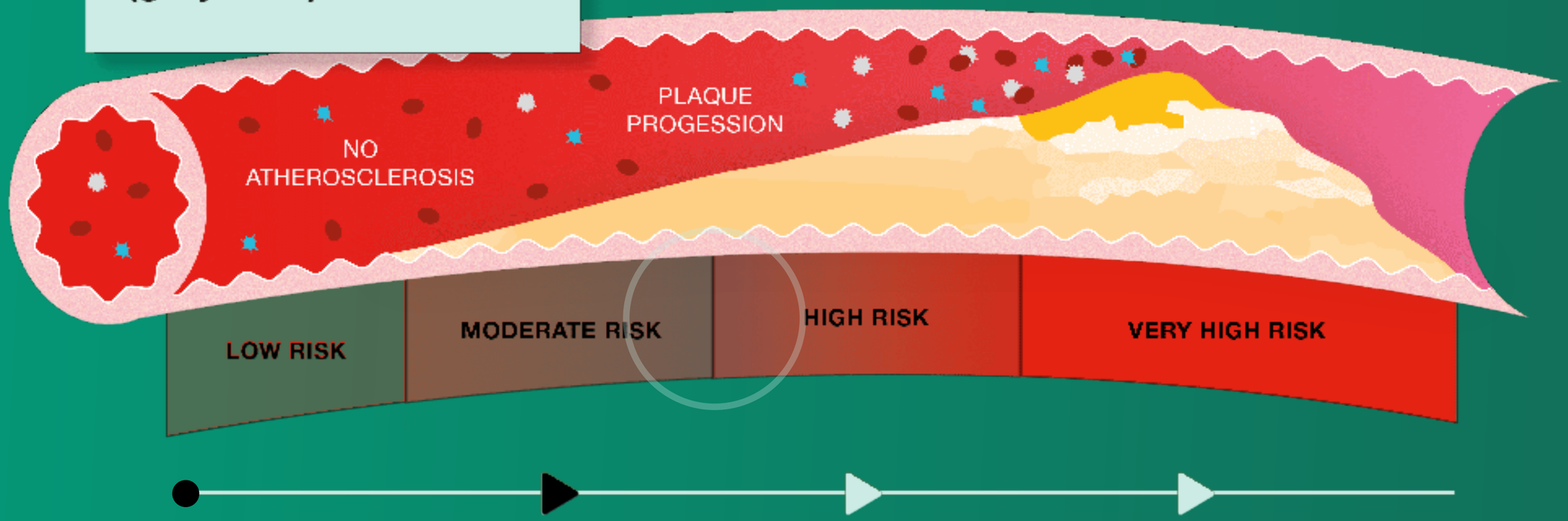
ARTERIAL CALCIFICATION CAN BE CONSIDERED TO IMPROVE RISK PREDICTION[24]



SLIDE ACROSS

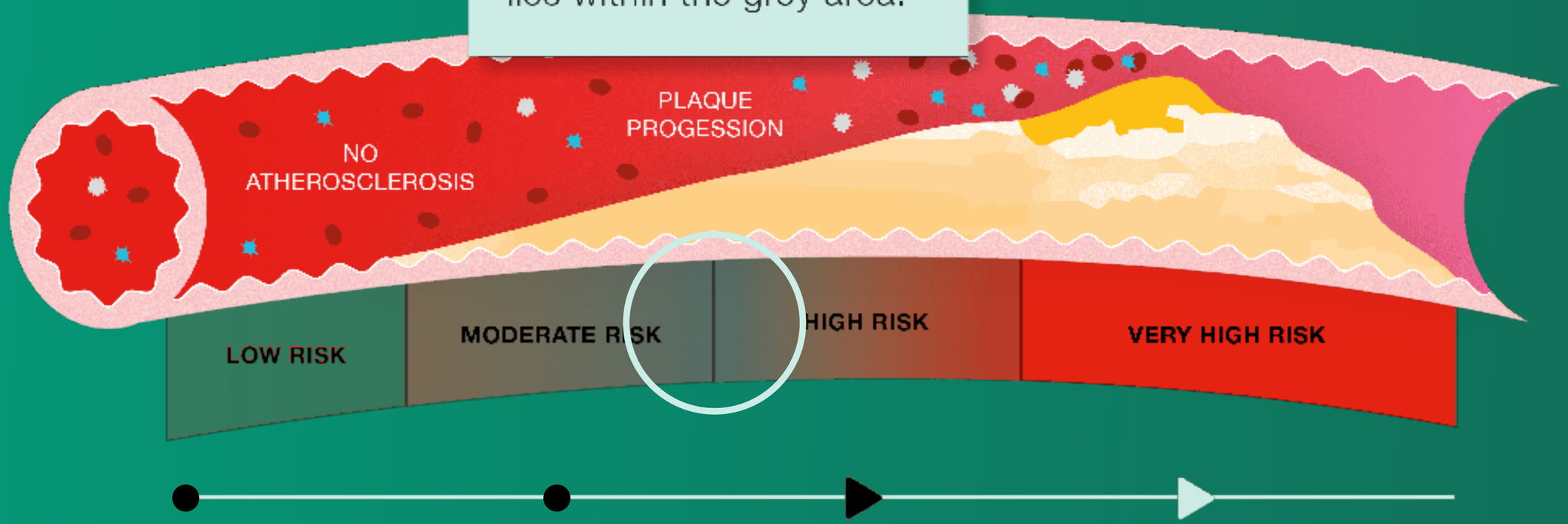
ARTERIAL CALCIFICATION CAN BE CONSIDERED TO IMPROVE RISK PREDICTION[24]

Many cardiovascular risk predictions are calculated as close to a decision threshold (grey area)[24]



ARTERIAL CALCIFICATION CAN BE CONSIDERED TO IMPROVE RISK PREDICTION[24]

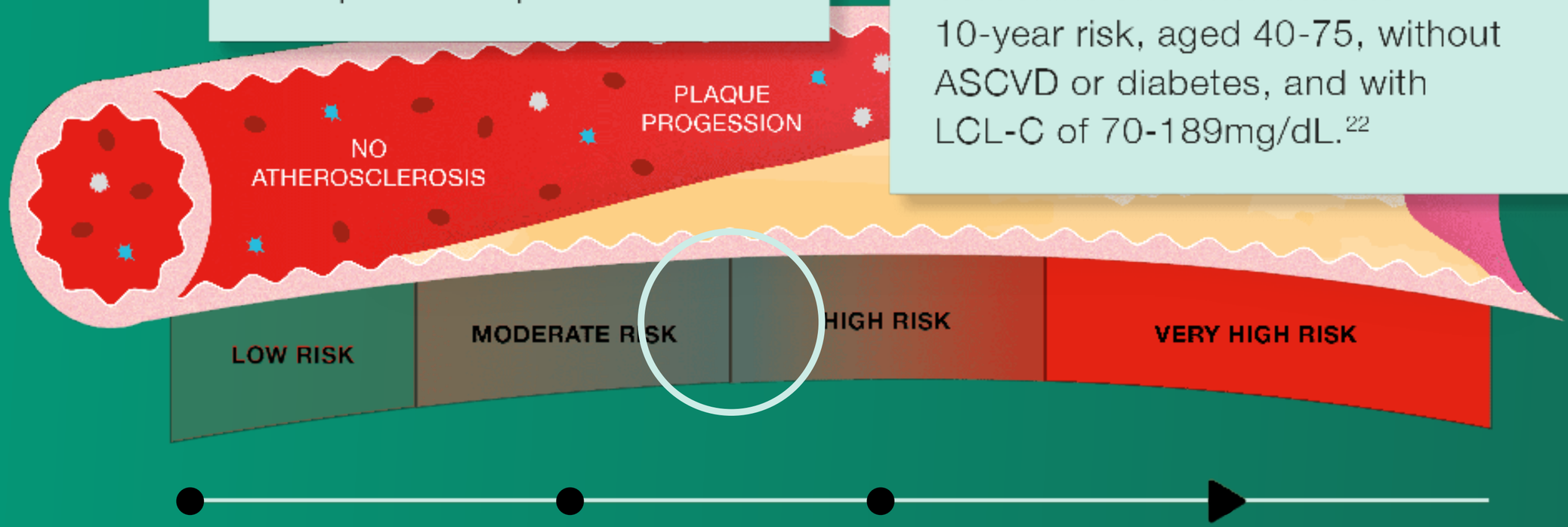
Assessment of CVD risk may seem irrelevant if an individual's therapeutic threshold lies within the grey area.[21]



ARTERIAL CALCIFICATION CAN BE CONSIDERED TO IMPROVE RISK PREDICTION[24]

In these individuals, additional assessment of potential risk modifiers such as arterial calcification can be considered to improve risk prediction.[21]

CAC scoring has been endorsed by several international guidelines to help **improve CVD risk classification in patients** at borderline and intermediate 10-year risk, aged 40-75, without ASCVD or diabetes, and with LCL-C of 70-189mg/dL.[22]



CAC IS A MARKER FOR CVD RISK

Coronary calcium (CAC) scoring is a "robust marker of coronary atherosclerotic plaque burden"[25] and can be used to determine the need for and intensity of preventative therapies.[26]

Studies have shown

17%

of ~7000 people
who with no risk factors
had high CAC scores[27]

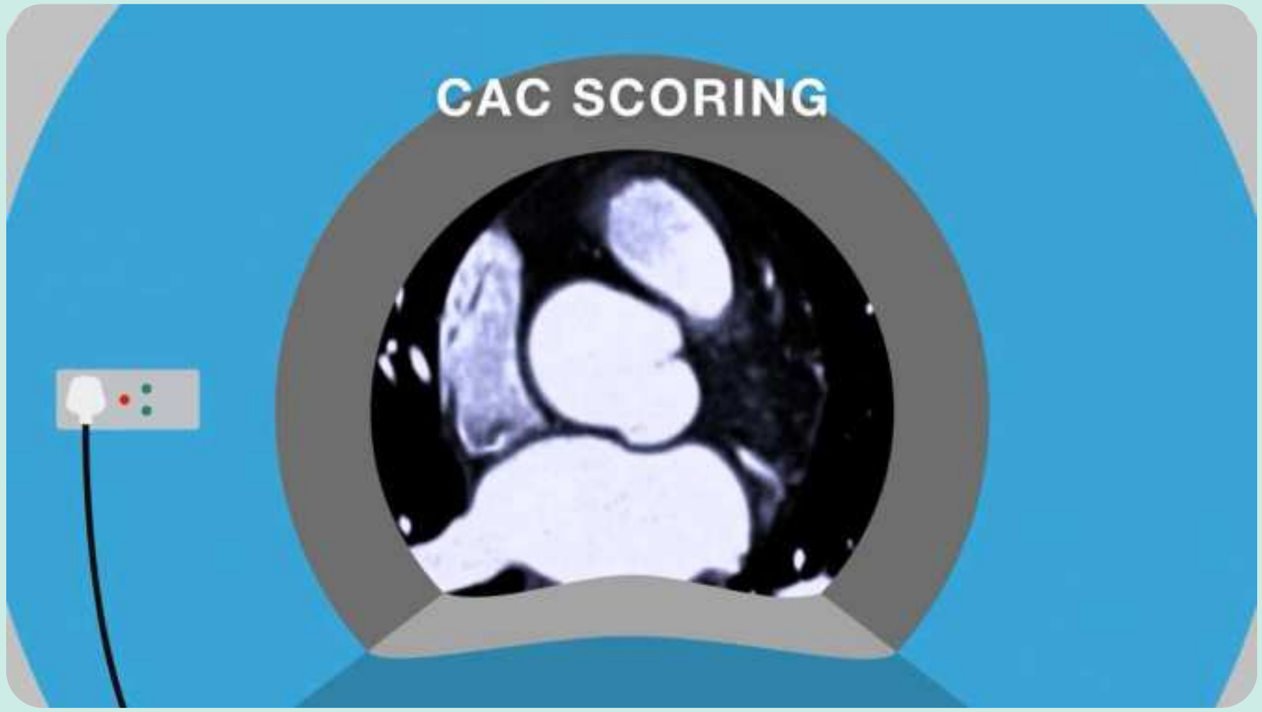
Studies have shown

35%

of ~7000 people
with multiple risk factors
had low CAC scores[27]

DETECTING ARTERIAL CALCIFICATION

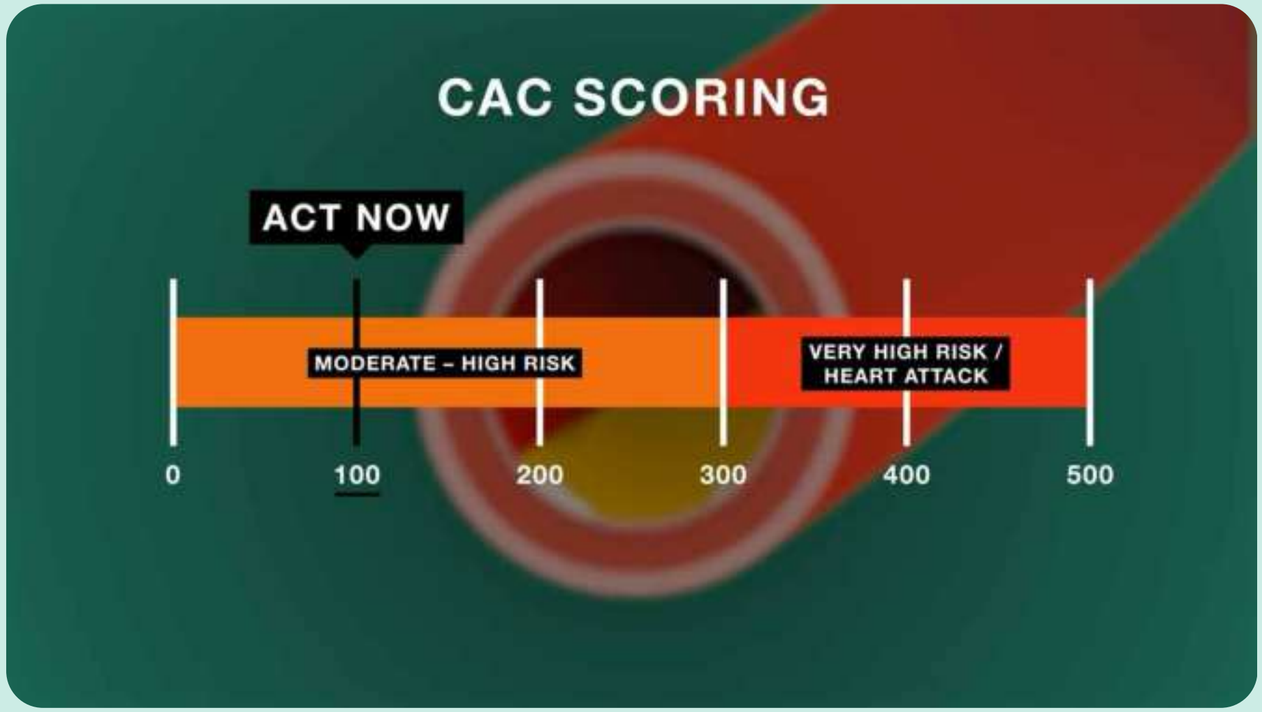
Calcification occurs during the early stages of atherosclerosis and is usually detected using a computerised tomography (CT) scanner with electrocardiogram (ECG) gating abilities.[22,28]



DETECTING ARTERIAL CALCIFICATION

Calcification occurs during the early stages of atherosclerosis and is usually detected using a computerised tomography (CT) scanner with electrocardiogram (ECG) gating abilities.[22,28]

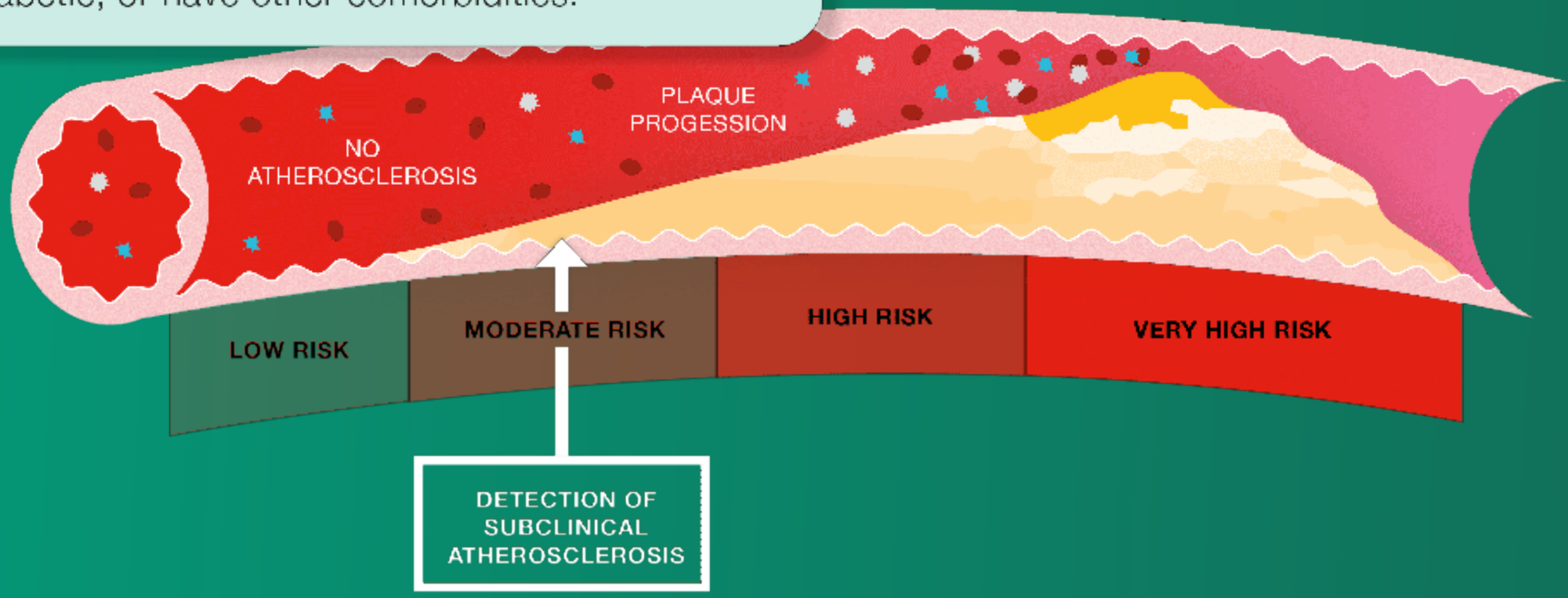
Coronary artery calcification (CAC) scans are evaluated and scored to **determine the extent of coronary calcification**; presence of **CAC score** indicates **plaque burden** which indicates a **higher risk of cardiovascular disease.[28]**



CAC SCORING

CAC scoring is an effective means of assessing the risk of CVD outcomes, especially in asymptomatic people.[22,29]

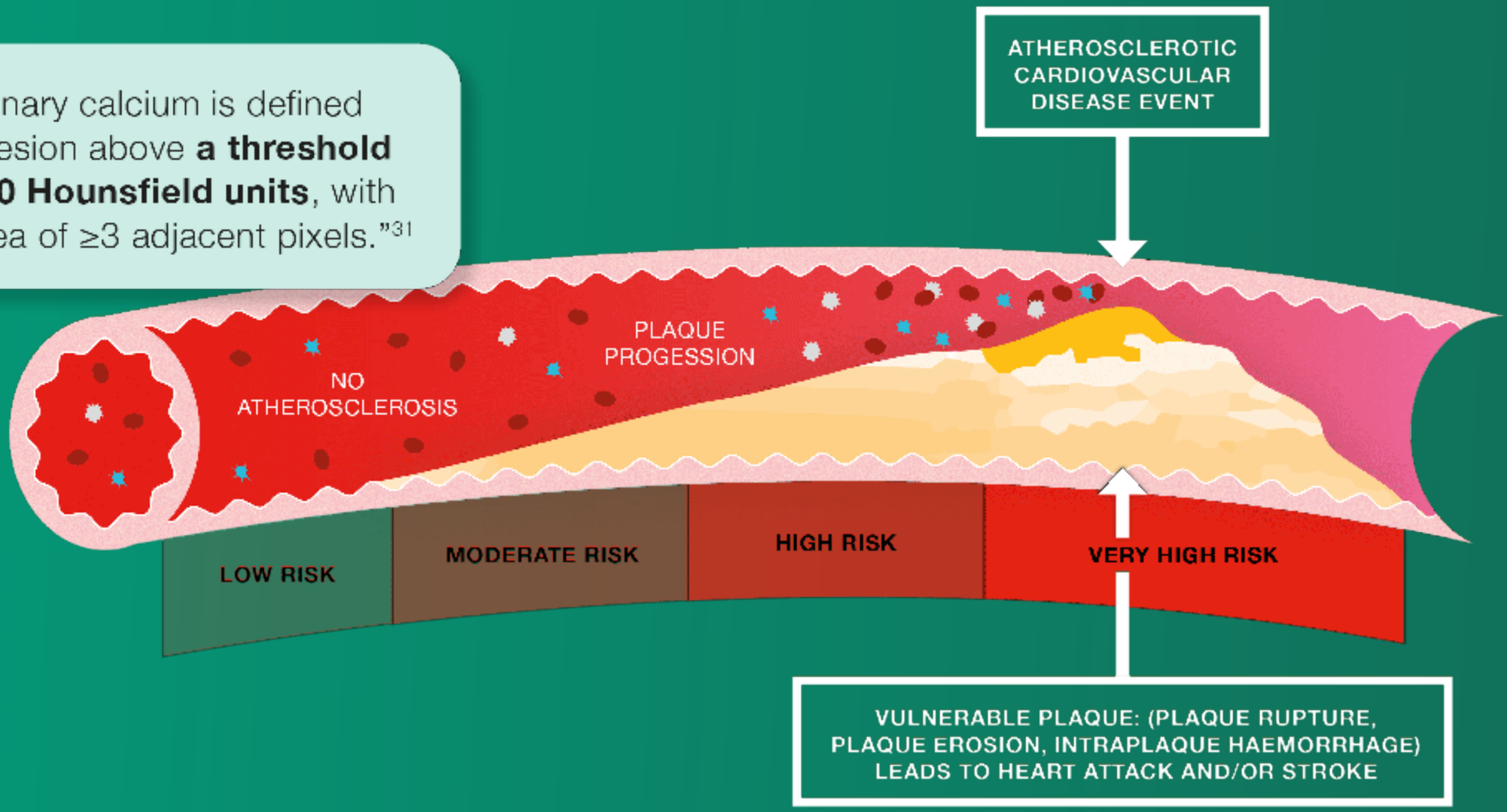
A score of zero indicates a **low risk of having a heart attack** in the next 10 years. This score does not rule out cardiovascular risk in people who smoke, are diabetic, or have other comorbidities.[30]



CAC SCORING

CAC scoring is an effective means of assessing the risk of CVD outcomes, especially in asymptomatic people.[22,29]

"Coronary calcium is defined as a lesion above **a threshold of 130 Hounsfield units**, with an area of ≥3 adjacent pixels."[31]



RELIABLE ACCESS TO HEALTHCARE IN LOW-MIDDLE INCOME COUNTRIES REMAINS A CHALLENGE[32]

1

Due to its **cost-effectiveness,** low-income countries can

UTILISE ARTERIAL ULTRASOUNDS

to identify at-risk individuals.[23]

2

Very low-income individuals are

LESS LIKELY

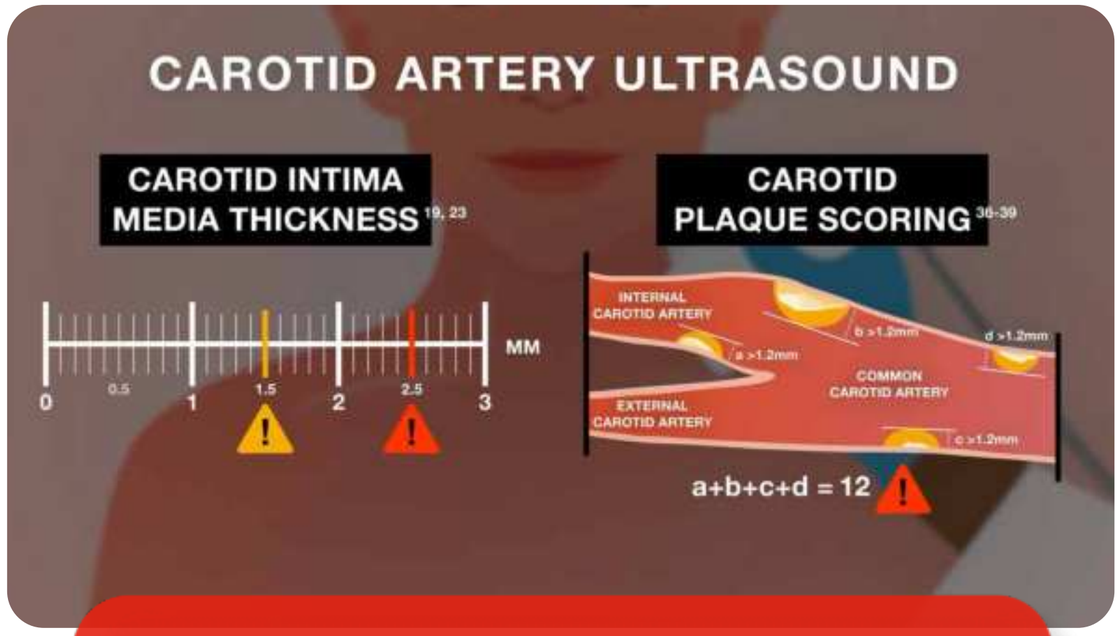
to be screened for CVD or receive preventative care than **high-income** individuals that reside in the same country.[33,34]

ALTERNATIVES TO CAC SCORING

If CAC scoring is inaccessible,

A CAROTID ARTERY ULTRASOUND

can be used to predict CVD events by measuring carotid intima-media thickness (CIMT) or assessing carotid arterial plaques.[24,35]



Carotid ultrasound image-based phenotypes provide a **better understanding of plaque build-up** than conventional risk factors, thereby reflecting a more **comprehensive analysis** of an individual's arterial age.[19]

Carotid plaque is defined as the **presence of focal wall thickening** that is at least **50% greater than that of the surrounding vessel wall** or as a focal region with CIMT greater than 1.5 mm that protrudes into the lumen that is distinct from the adjacent boundary.[35,10]

CARDIAC RISK IMAGING

Communicating an individual's plaque build-up using visual representations:

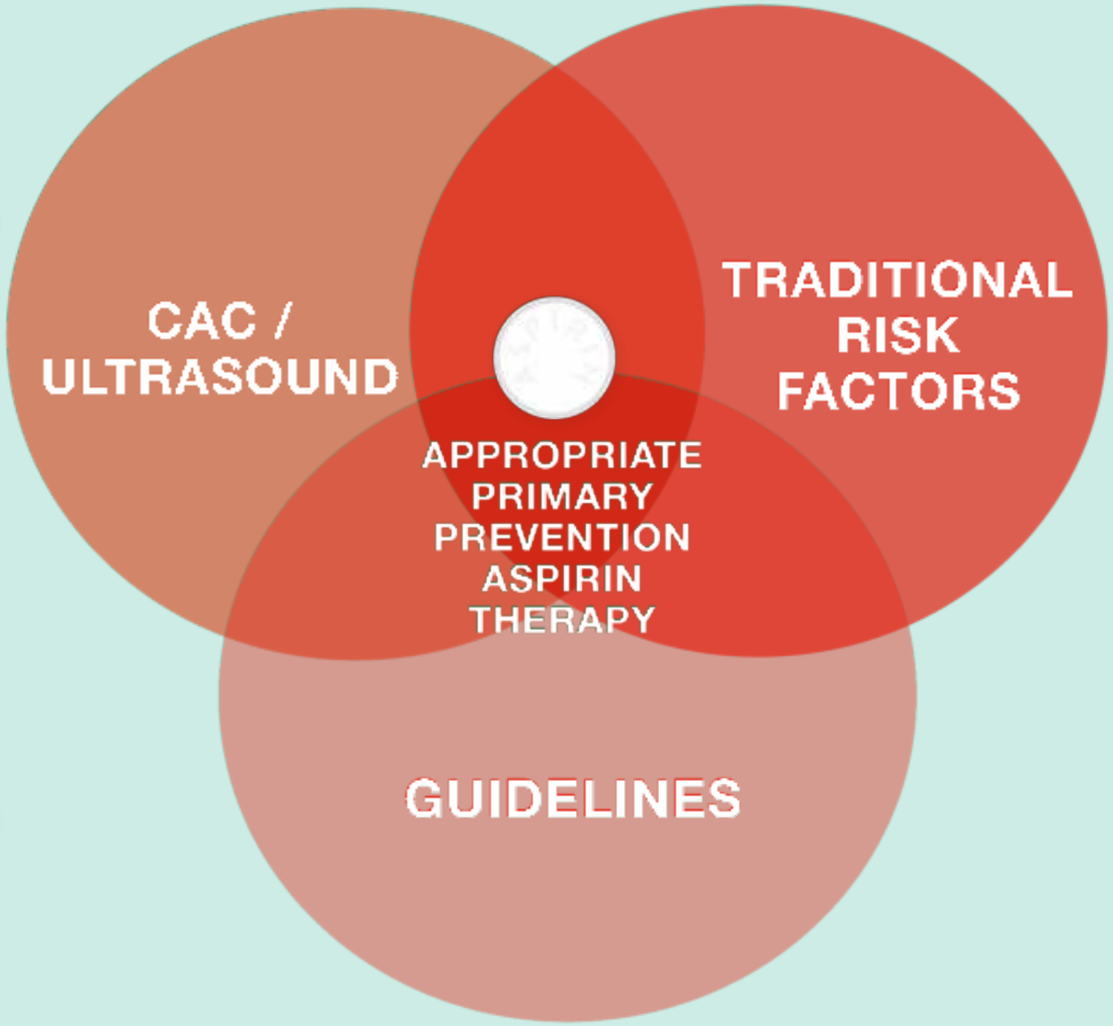
Can **improve motivation for treatment** and **reduce the CVD risk factor burden**[41]

"Was significantly associated with **improved compliance** with cardiovascular risk-reducing behaviors"[42]

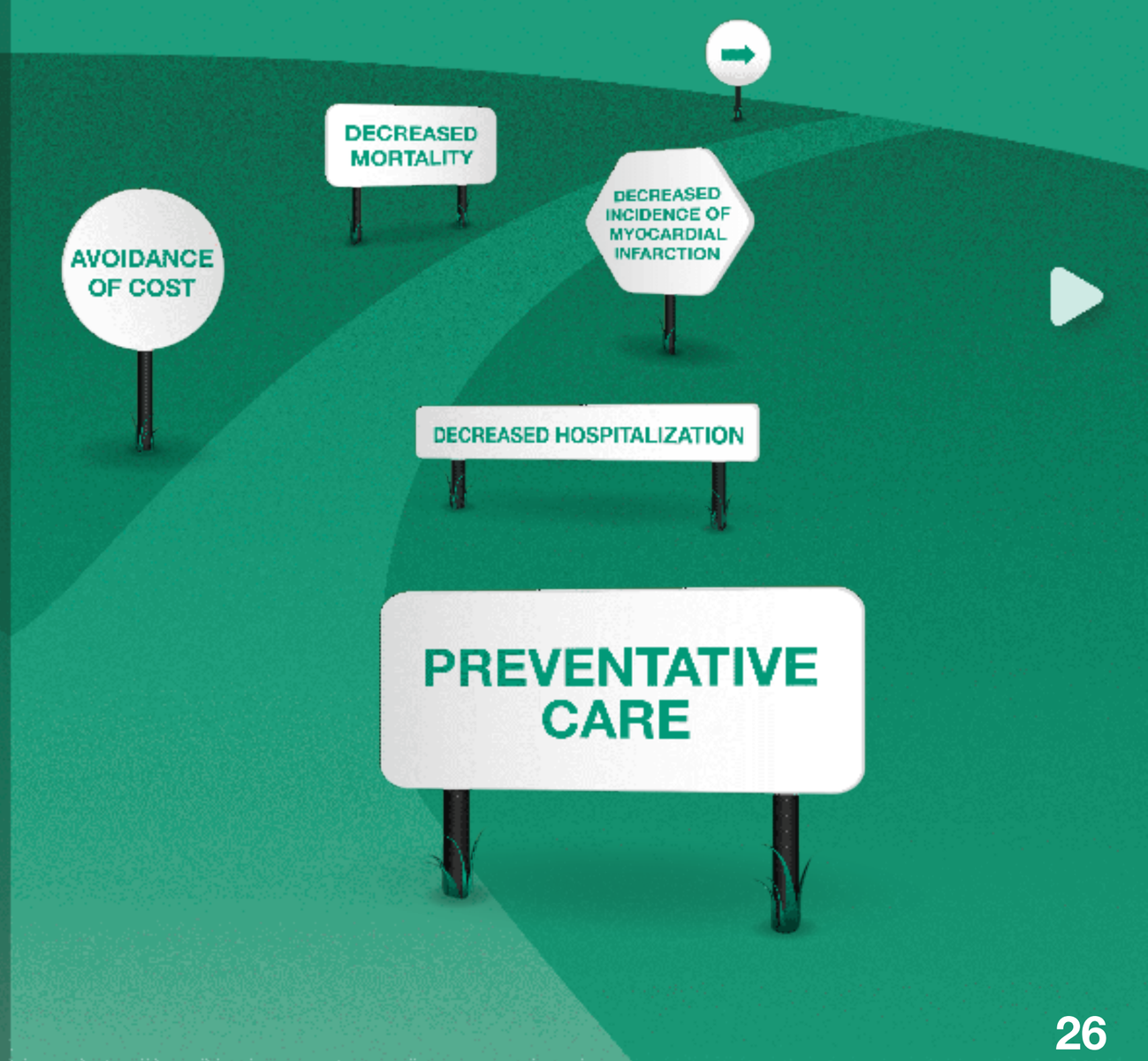
TAILORING ASPIRIN THERAPY WITH CAC

Both **CAC scoring** and **coronary artery ultrasound assessments** can be used to **identify individuals for primary prevention aspirin therapy** where there is lower bleeding risk and risk of atherosclerotic disease is high.[43]

Combining CAC scores with conventional risk factors and guideline recommendations can result in a **more personalized and safer allocation of primary prevention aspirin therapy** particularly in patients with a CAC score of ≥100.[22,25,26]



ASPIRIN IS AN EFFECTIVE AND LOW COST TREATMENT OPTION



ASPIRIN IS A CORNERSTONE FOR CVD PREVENTION

ASPIRIN

LOWERS THE ABSOLUTE-RISK OF CVD EVENTS

substantially in high-risk individuals.[43]

Induced serious vascular events were

8.5% LESS IN THE GROUP TAKING ASPIRIN COMPARED WITH PLACEBO

when perscribed at a dose of 100mg daily for 7.4 years in both, the general population and high-risk groups.[44]

ASPIRIN IS A CORNERSTONE FOR CVD PREVENTION

ASPIRIN

Evidence shows that **prophylactic use of aspirin** for at least **5 years** at a daily dose of **75 and 325mg** **produces more benefit than harm,** which could be influenced by age and patient profile.[45]

but aspirin is underused for the prevention of primary and secondary cardiovascular events.[46]

Appropriate use of aspirin could be both **financially and clinically beneficial**[46]

LONG-TERM ASPIRIN USE SHOWS FAVORABLE BENEFIT-HARM PROFILE[45]

UP TO 50%

non-compliance rates may contribute to suboptimal therapeutic outcomes and an increased risk of major CVD events[47,48]

Reasons for non-compliance include:

- Lack of understanding of the consequences of not taking it[18]
- Lack of awareness of benefits and side effects[47]
- Forgetfulness[17]

ASPIRIN AS PRIMARY PREVENTION IS COST EFFECTIVE

IN THE USA,

primary prevention aspirin therapy has been shown **to save approximately**

$4.2 MILLION OVER 5 YEARS[46]

COST EFFECTIVE

RISK REDUCTION

THE USE OF ASPIRIN

Aspirin is more cost-effective than not using primary prevention aspirin therapy.[49]

REDUCES RISK

Primary prevention aspirin therapy should not be overlooked, particularly in **individuals** with a **HIGH 10-YEAR RISK OF CVD** with low risk of bleeding.[50]

The use of aspirin for the primary prevention of CVD has shown an

11% **RELATIVE RISK REDUCTION IN ATHEROSCLEROTIC CARDIOVASCULAR DISEASE (ASCVD) EVENTS**[25]

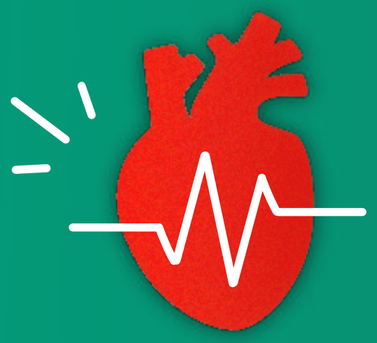
WIDELY AVAILABLE AND AFFORDABLE

Appropriate use of primary and secondary **PREVENTATIVE ASPIRIN THERAPY CAN IMPROVE** patient outcomes with significant **cost savings**.[46]

A SIMPLE AND INEXPENSIVE CVD-PREVENTATIVE MEDICINE that should be considered for at-risk adult patients.[46]

Due to its **LOW COST,** the use of aspirin for CVD prevention can be of **global benefit**, particularly to those **without prior CVD**, and in **low-income countries** where alternative therapies may be unaffordable for most of the population.[51]

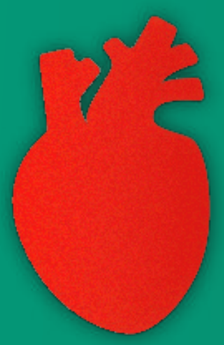
THE FUTURE



A precison approach whereby clinicians can identify individuals

AT RISK OF A PLATELET-MEDIATED EVENT

holds promise to improving CVD outcomes in those who may benefit from **primary prevention aspirin therapy**.[52]



New recommendations show that the decision to initiate

PRIMARY PREVENTION ASPIRIN THERAPY IN ADULTS

aged 40-59 with a 10% or greater 10-year CVD risk and low bleeding risk should be on **individual basis**.[52]

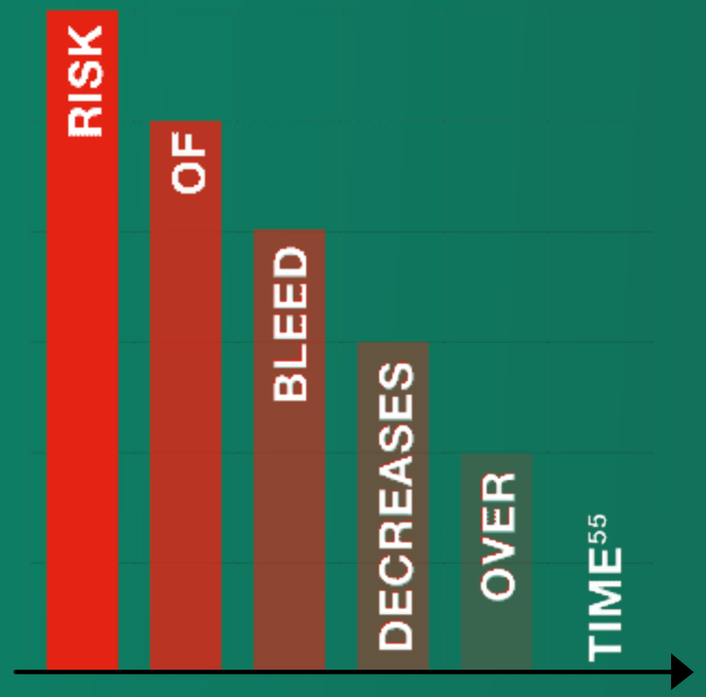
LOOK AGAIN at aspirin as an effective and low cost preventative option

MANAGE RISK OF BLEEDING

5 CASES PER 1000 ASPIRIN USERS[53]

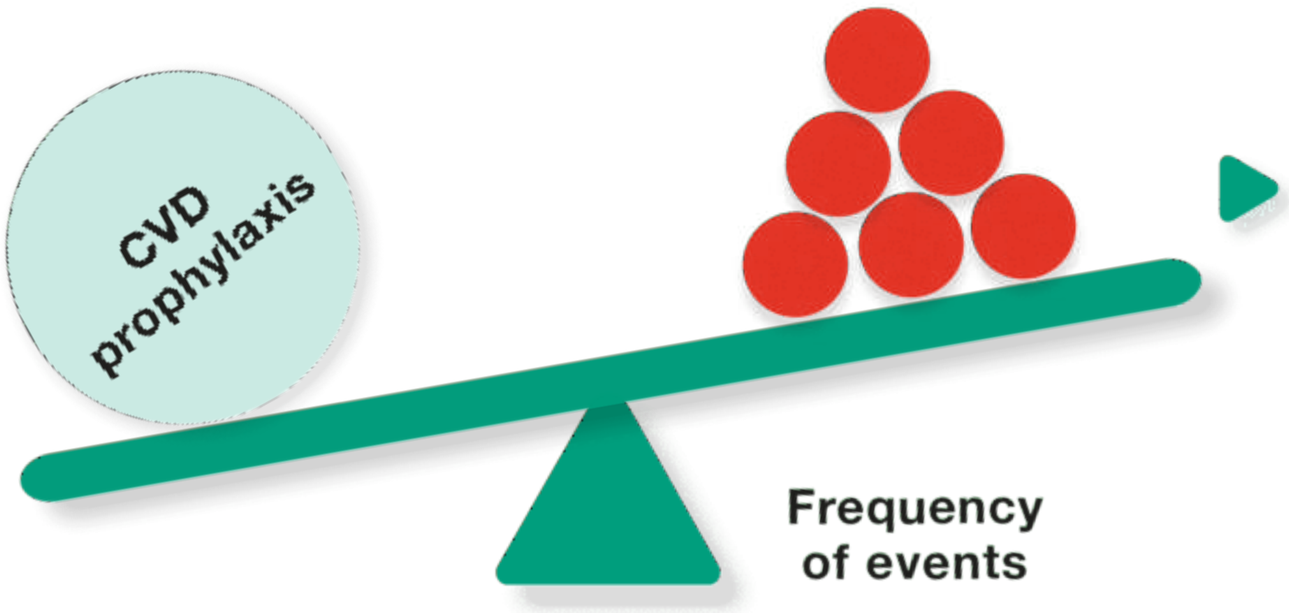
ONLY 50% REQUIRE WITHDRAWAL[54]

"IT'S LIKE COMPARING APPLES WITH ORANGES"



MISCONCEPTIONS AND CONTROVERSY

The **value of aspirin** for primary CVD prevention is limited by **concerns of gastrointestinal (GI) bleeding** that may offset its overall cardioprotective benefits.[55]



"A systemic review of

27 TRIALS AND META-ANALYSES

reported that there is a fine balance between risks and benefits from regular aspirin use in primary prevention of CVD."[56]

PHYSICIANS SHOULD...

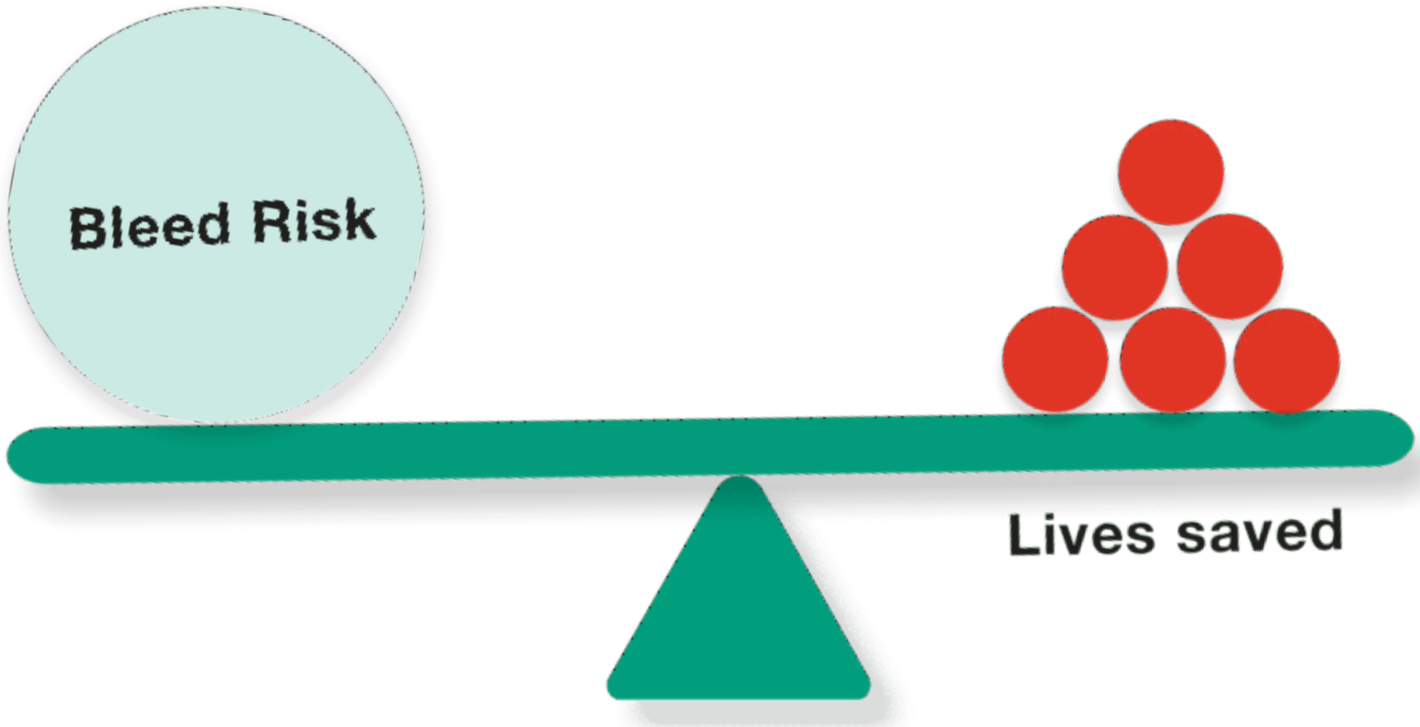
CONSIDER THE SEVERITY OF THE DISEASE

EVENTS PREVENTED

BECAUSE OF INTERVENTION

RATHER THAN SOLEY FOCUSING ON THE FREQUENCY OF EVENTS

BENEFITS IN PATIENTS WITH LOW-RISK OF CARDIOVASCULAR OUTCOME



GI bleeding is attributed to only
1 IN 376 PATIENTS
treated with low-dose aspirin.[57]

For every
160 PATIENTS TREATED, 1 LIFE
could be saved with **low-dose aspirin.**[57]

RELATIVE AND ABSOLUTE RISK

The lowest effective dose should be prescribed to minimise risk.[58,59]

DOSES OF ASPIRIN >100mg DAILY

are associated with a higher risk of GI bleeding than low-dose aspirin.[51]

RELATIVE AND ABSOLUTE RISK

In patients without CVD aspirin **increased absolute risk of a major bleed by**[57]

0.47%
PER YEAR

Although absolute risk of major GI bleeding increases with age the **overall incidence rates decline after**[55,60]

6
MONTHS OF TREATMENT

BENEFIT-HARM RATIO CAN BE IMPROVED

By identifying

HIGH-RISK INDIVIDUALS

and reducing risk prior **to initiating treatment.**[45]

RISK CALCULATORS

can be used to guide physicians in choosing **appropriate personal treatment regimens** for CVD event prevention, based on clinical and laboratory data.[61]

GI BLEEDING ASSOCIATED WITH ASPIRIN THERAPY IS RARE AND CAN MOSTLY BE MANAGED[54]

Those at an increased risk of GI bleed include:

SMOKING

Referring these individuals to smoking cessation programs can inspire a healthier lifestyle and reduce the bleeding risk associated with aspirin therapy.[62]

SMOKING CESSATION

H. PYLORI INFECTION

Commencing *H. pylori* eradication therapy prior to aspirin treatment can greatly reduce the risk of GI bleed.[54]

H. PYLORI ERADICATION

ALCOHOL CONSUMPTION

Lifestyle interventions to help alcohol-dependent individuals on aspirin therapy can reduce GI bleeding risk.[63]

REDUCE ALCOHOL INTAKE

CONCURRENT TREATMENT

Aspirin should be used in caution in those taking other medications that can increase the incidence of GI bleeds such as NSAIDs, certain anticoagulants, and platelet inhibitors.[63,64]

CAUTION WITH OTHER MEDS

ASPIRIN CAN BE CONTINUED IN THE EVENT OF A GI BLEED

In patients who have experienced peptic ulcer bleeding discontinuation of aspirin therapy can increase the risk of

CV EVENTS BY 37%

and increase the risk of death and acute CV events almost 7-fold.[65]

Aspirin therapy should be maintained at **discharge** from hospital.[65]

In patients who **receive low-dose aspirin** and **develop acute ulcer bleeding**, aspirin should be **restarted** as soon as the risk for CV events exceeds the risk of bleeding.[66]

MANAGING GI BLEEDS

THE CONCOMITANT USE OF PROTON PUMP INHIBITORS (PPIS) WITH ASPIRIN CAN

REDUCE ADVERSE GI EFFECTS BY UP TO 31%[67]

and shift the **OVERALL RISK-BENEFIT RATIO** towards overall benefit in **PRIMARY PREVENTION**.[57]

PPIs are effective at **PREVENTING REBLEEDING** after the stabilization of upper GI bleed.[68]

LOOK AGAIN, balance manageable bleed risk against the life altering impairments of CVD events

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