Cardiovascular Risk Factors in the Elderly

Sherief Kamel MD FRCPC MEd

NBIMU

April 23, 2021

Disclosures

- Ad Board: Bayer, Servier
- Honorarium: Novartis

Objectives

- Recognize the importance of frailty assessment and use that to individualize treatment goals

- Understand the risk/benefits when it comes to addressing risk factors in the elderly

Elderly Patients

- Highest risk population for cardiovascular disease
- Vascular diseases
    - Coronary artery disease (MI, angina) that can lead to heart failure, atrial fibrillation
    - Cerebrovascular diseases – stroke, vascular dementia
    - Peripheral vascular disease – claudication, limb ischemia, amputation, infections

1 Very Fit – People who are robust, active, energetic and motivated. These people commonly exercise regularly. They are among the fittest for their age.

2 Well – People who have **no active disease symptoms** but are less fit than category 1. Often, they exercise or are very **active occasionally**, e.g. seasonally.

3 Managing Well – People whose **medical problems are well controlled**, but are **not regularly active** beyond routine walking.

4 Vulnerable – While **not dependent** on others for daily help, often **symptoms limit activities**. A common complaint is being "slowed up", and/or being tired during the day.

5 Mildly Frail – These people often have **more evident slowing**, and need help in **high order IADLs** (finances, transportation, heavy housework, medications). Typically, mild frailty progressively impairs shopping and walking outside alone, meal preparation and housework.

6 Moderately Frail – People need help with **all outside activities** and with **keeping house**. Inside, they often have problems with stairs and need **help with bathing** and might need minimal assistance (cuing, standby) with dressing.

7 Severely Frail – **Completely dependent for personal care**, from whatever cause (physical or cognitive). Even so, they seem stable and not at high risk of dying (within ~ 6 months).

8 Very Severely Frail – Completely dependent, approaching the end of life. Typically, they could not recover even from a minor illness.

9. Terminally Ill - Approaching the end of life. This category applies to people with **a life expectancy <6 months**, who are **not otherwise evidently frail**.

## Scoring frailty in people with dementia

The degree of frailty corresponds to the degree of dementia. Common **symptoms in mild dementia** include forgetting the details of a recent event, though still remembering the event itself, repeating the same question/story and social withdrawal.

In **moderate dementia**, recent memory is very impaired, even though they seemingly can remember their past life events well. They can do personal care with prompting.

In **severe dementia**, they cannot do personal care without help.

DALHOUSIE UNIVERSITY *Inspiring Minds*
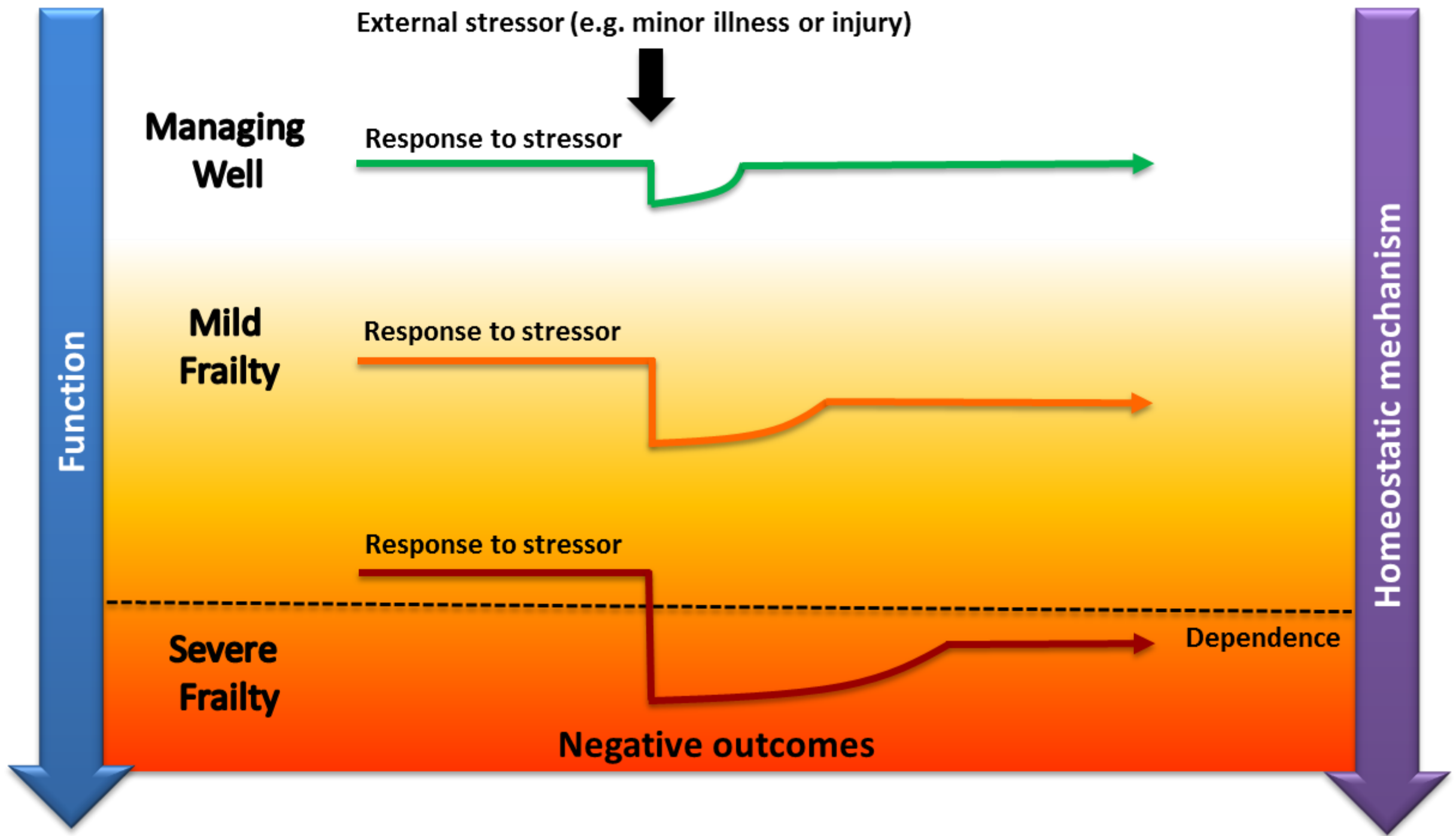
External stressor (e.g. minor illness or injury)

Function

Homeostatic mechanism

Managing Well

Response to stressor

Mild Frailty

Response to stressor

Response to stressor

Severe Frailty

Dependence

Negative outcomes

Baumgart et al. Alzheimer's & Dementia 11 (2015) 718

Baumgart et al. Alzheimer's & Dementia 11 (2015) 718
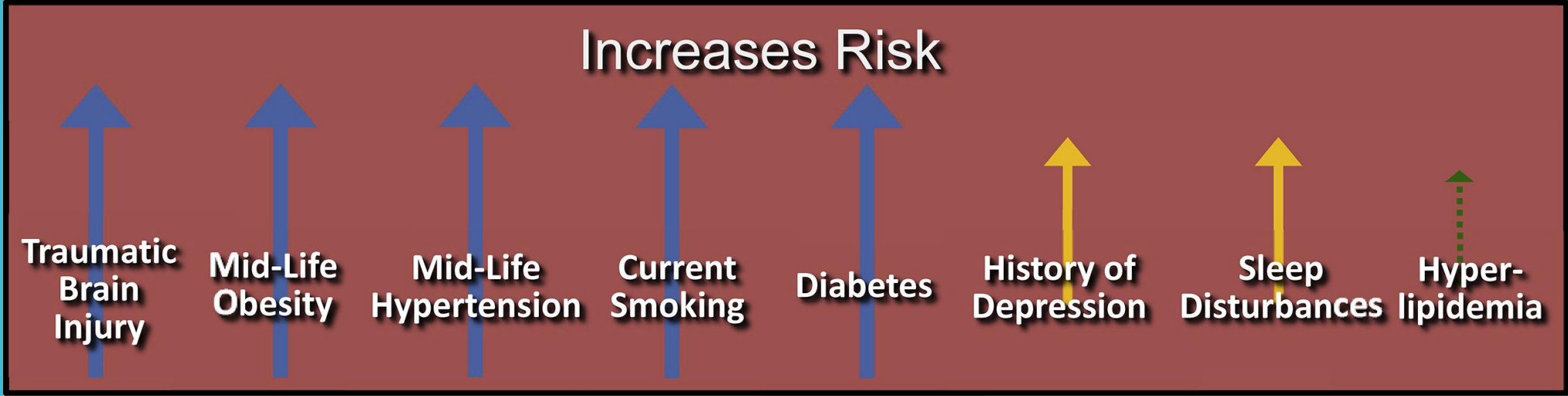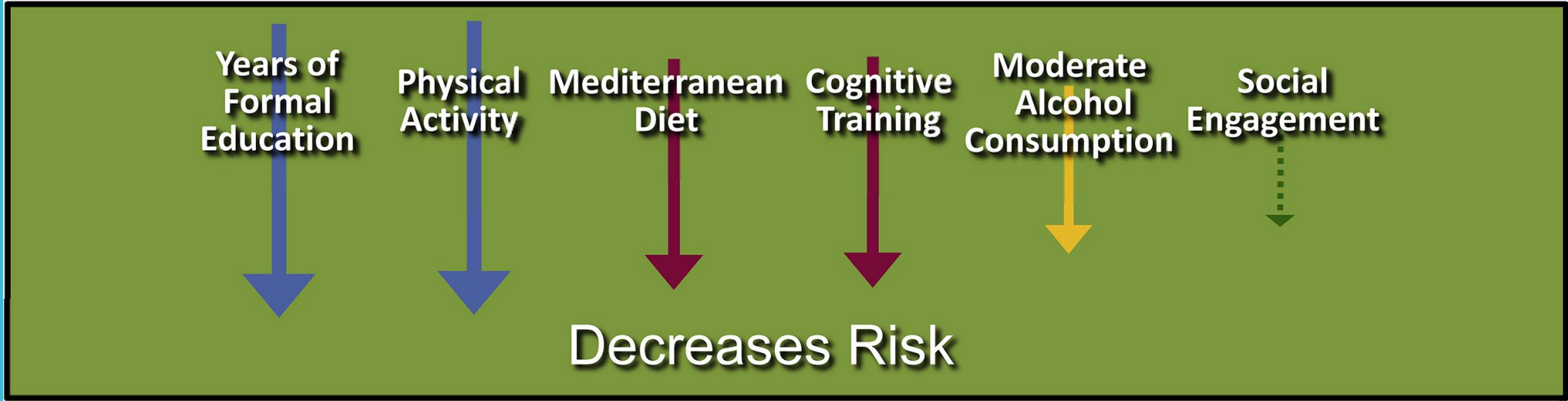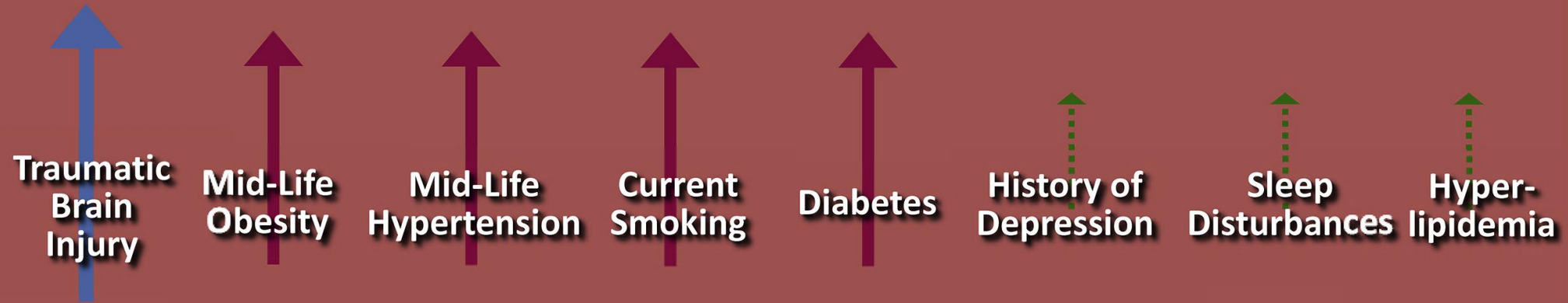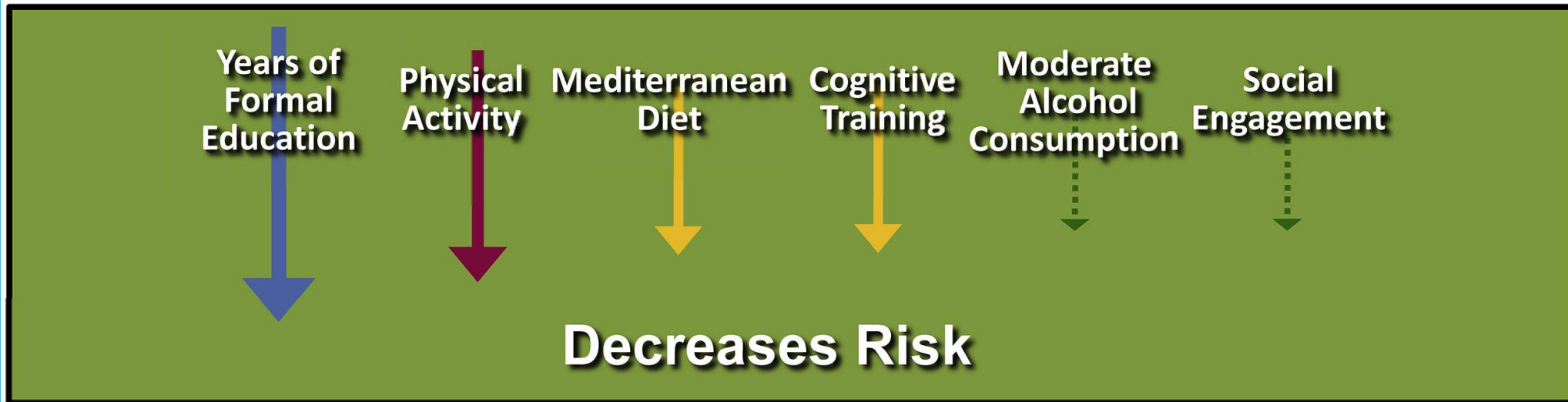
Vascular Risk Factors

- Non-modifiable risk factors include:
  - Age
  - Gender
  - Ethnicity
  - Family history

Modifiable Risk Factors

- Tobacco Use
- Physical Inactivity
- Poor Diet
- Obesity or Overweight
- Excess Alcohol
- Unmanaged Stress
- Lack of Sleep

Manageable Risk Factors

- Hypertension
- Dyslipidemia
- Diabetes
- Metabolic Syndrome

Smoking

WITHIN **20** MINUTES	WITHIN **12** HOURS	WITHIN **2-12** WEEKS	WITHIN **1-9** MONTHS	WITHIN **1** YEAR	WITHIN **5** YEARS	WITHIN **10** YEARS	WITHIN **115** YEARS
Your heart rate and blood pressure drop.	Your carbon monoxide level in the blood drops to normal.	Your circulation improves and your lung function increases.	Your coughing and shortness of breath decrease.	Your risk of coronary heart disease is about half that of a smoker's.	Your risk of stroke is reduced to that of a nonsmoker's.	Your risk of lung cancer falls to about half that of a smoker's, and your risk of cancer of the mouth, throat, esophagus, bladder, cervix, or pancreas decreases.	Your risk of coronary heart disease is that of a nonsmoker's.

Drope J, Schluger NW, editors, The tobacco atlas, 6th edn, Atlanta, GA, American Cancer Society and Vital Strategies, 2018, p. 37
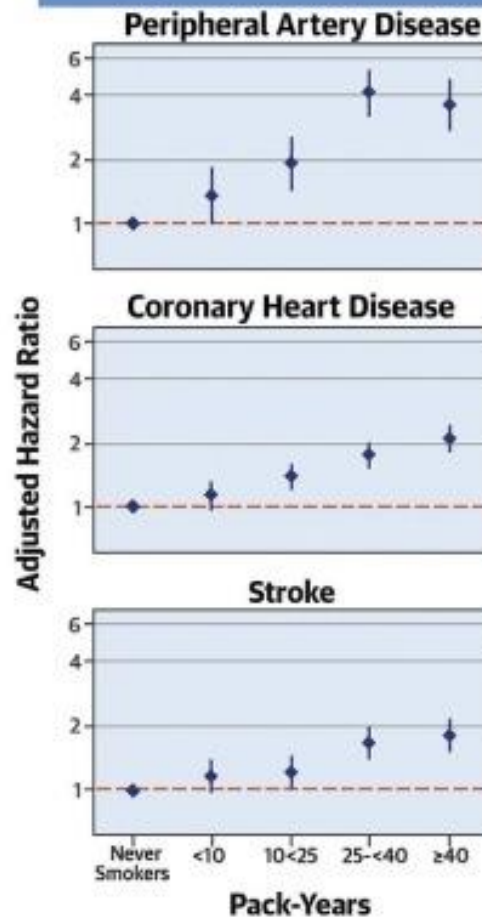
CENTRAL ILLUSTRATION: Smoking Is Associated With Higher Risk of Peripheral Artery Disease Compared With Coronary Heart Disease and Stroke and Longer Residual Risk of Peripheral Artery Disease After Cessation

Peripheral Artery Disease

Myocardial Infarction

Stroke
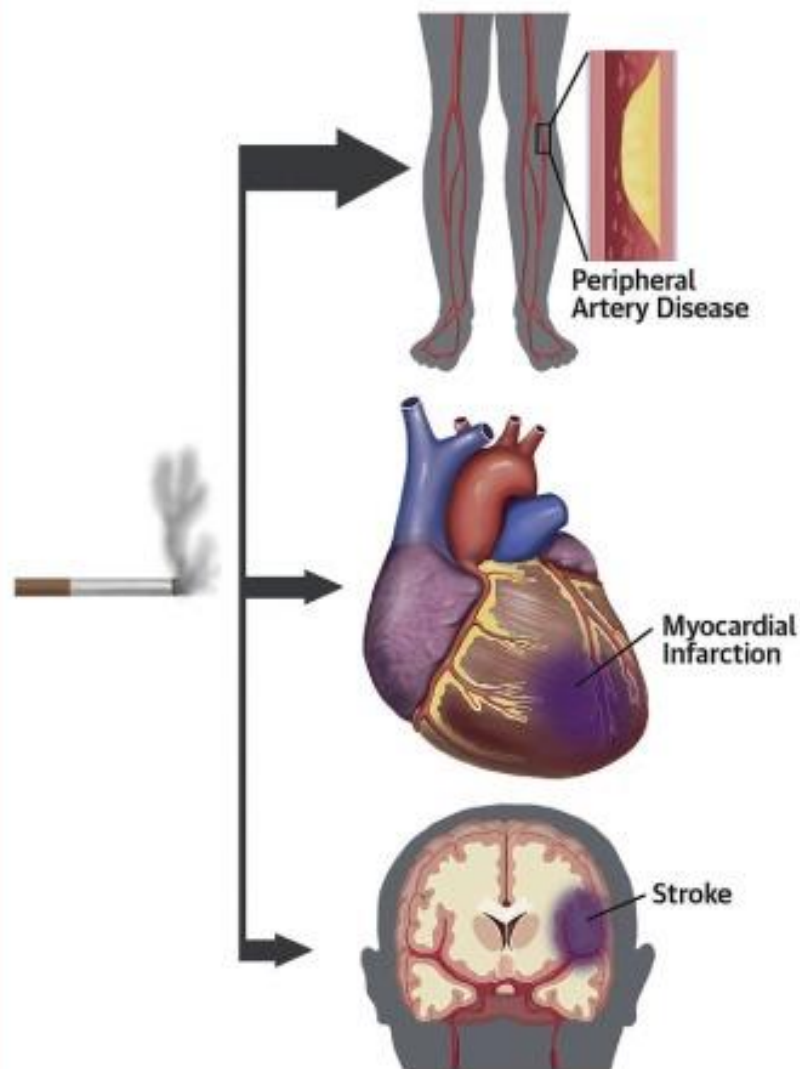
A. Smoking Was Strongly Associated With Major Atherosclerotic Diseases

B. Elevated Risk After Smoking Cessation Prolonged Most For PAD

Peripheral Artery Disease

Coronary Heart Disease

Stroke

Adjusted Hazard Ratio

Pack-Years: Never Smokers, <10, 10<25, 25-<40, ≥40

Years Since Quitting: Never Smokers, ≥30, 20<30, 10<20, 5<10, <5, Current Smokers

Ding, N. et al. J Am Coll Cardiol. 2019;74(4):498–507.
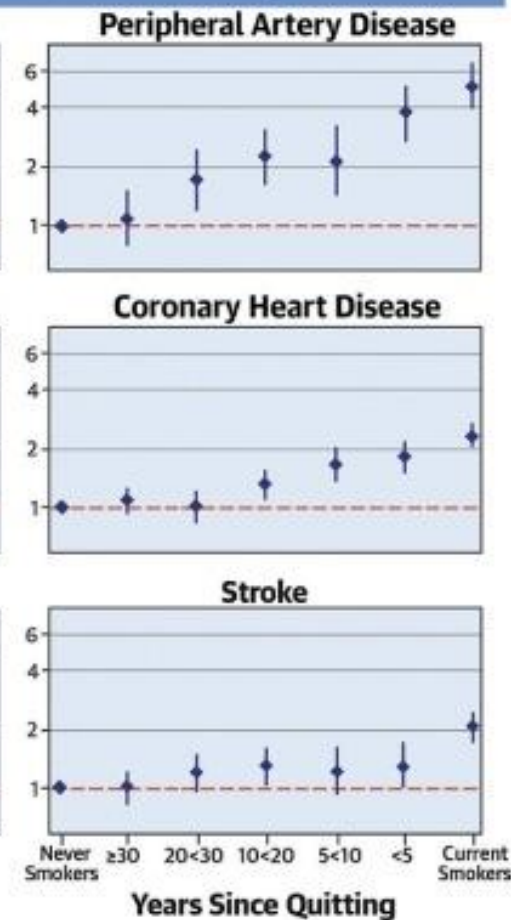
© Randy Glasbergen.

"I'm prescribing a patch to help you quit smoking. Wear it over your mouth."

RISK

BENEFIT

Quantity of life
Quality of life

Polypharmacy
Adverse Drug Reactions

Hypertension

Blood pressure reading just for setting up a home blood-pressure monitor
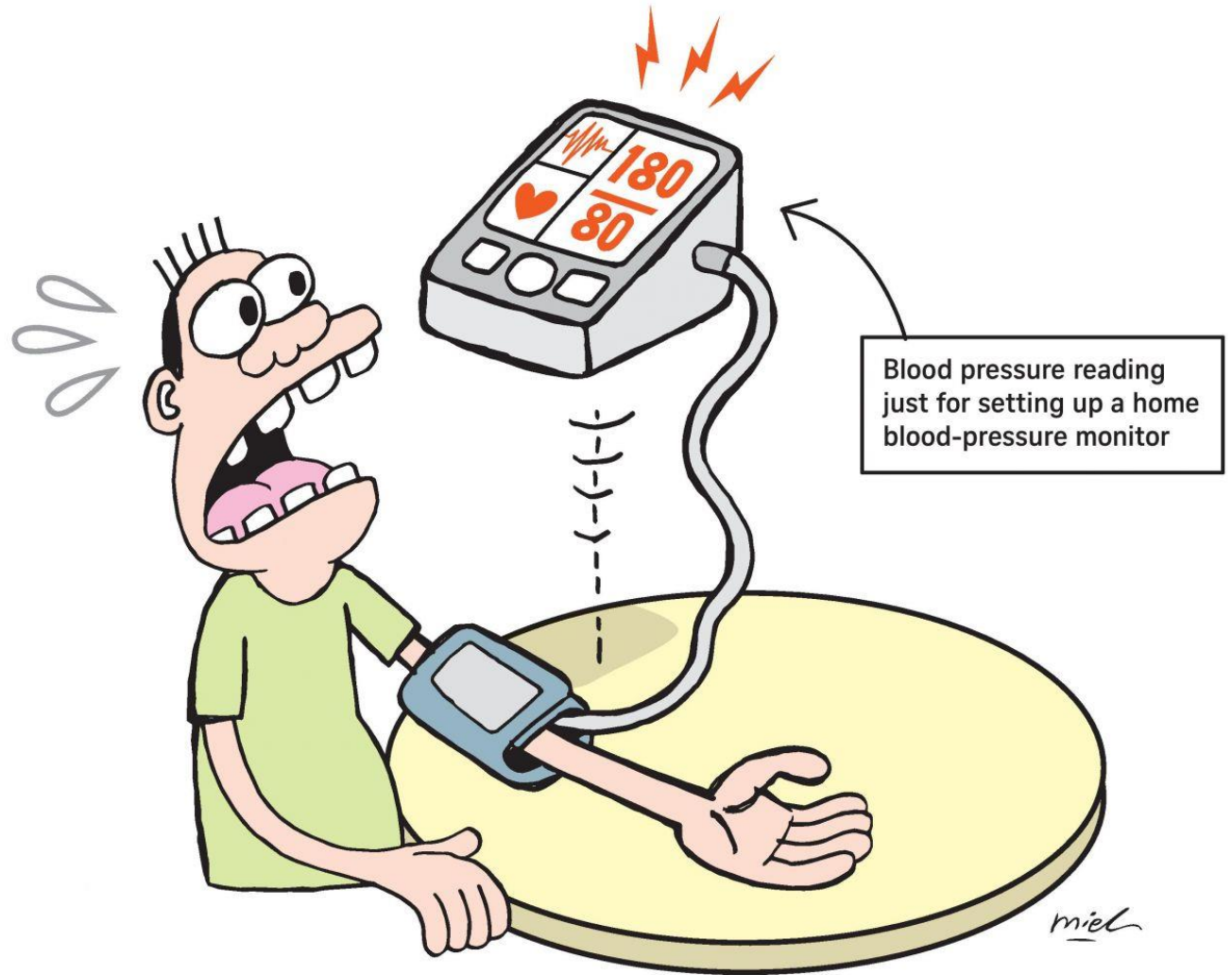
Usual Office BP __Threshold Values__ for Initiation of Pharmacological Treatment

Population	SBP	DBP
High Risk (SPRINT population) #	≥ 130	NA
Diabetes	≥ 130	≥ 80
Moderate *	≥ 140	≥ 90
Low risk (no TOD or CV risk factors)	≥ 160	≥ 100

AOBP = automated office blood pressure
TOD = target organ damage
SBP = systolic blood pressure
DBP = diastolic blood pressure

Based on AOBP

*AOBP threshold ≥ 135/85 mmHg

Recommended Office BP Treatment Targets

Treatment consists of health behaviour ± pharmacological management

Population	SBP	DBP
High Risk [#]	≤ 120	NA
Diabetes	< 130	< 80
All others*	< 140	< 90

[#] Based on AOBP
*AOBP threshold ≥ 135/85 mmHg

New Guideline Post-SPRINT

- For high-risk patients, aged ≥ 50 years, with systolic BP levels ≥130 mm Hg, intensive management to target a systolic BP ≤120 mm Hg should be considered

- Intensive management should be guided by automated office BP measurements

- Patient selection for intensive management is recommended and caution should be taken in certain high-risk groups

New Thresholds/Targets for the High-Risk Patient Post-SPRINT: *Who does this apply to?*

Clinical or sub-clinical cardiovascular disease

OR

Chronic kidney disease (non-diabetic nephropathy, proteinuria <1 g/d, *estimated glomerular filtration rate 20-59 mL/min/1.73m^2)

OR

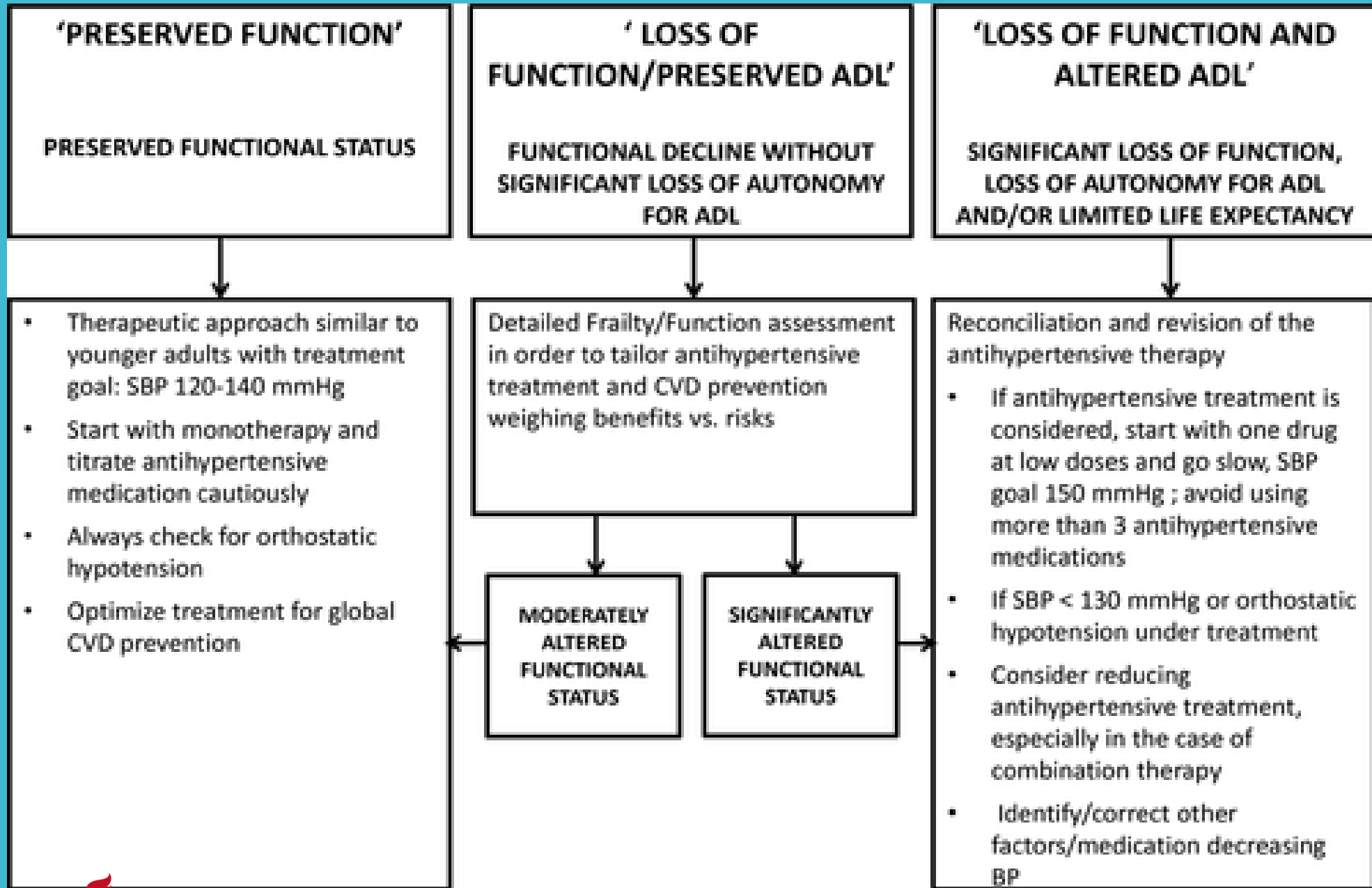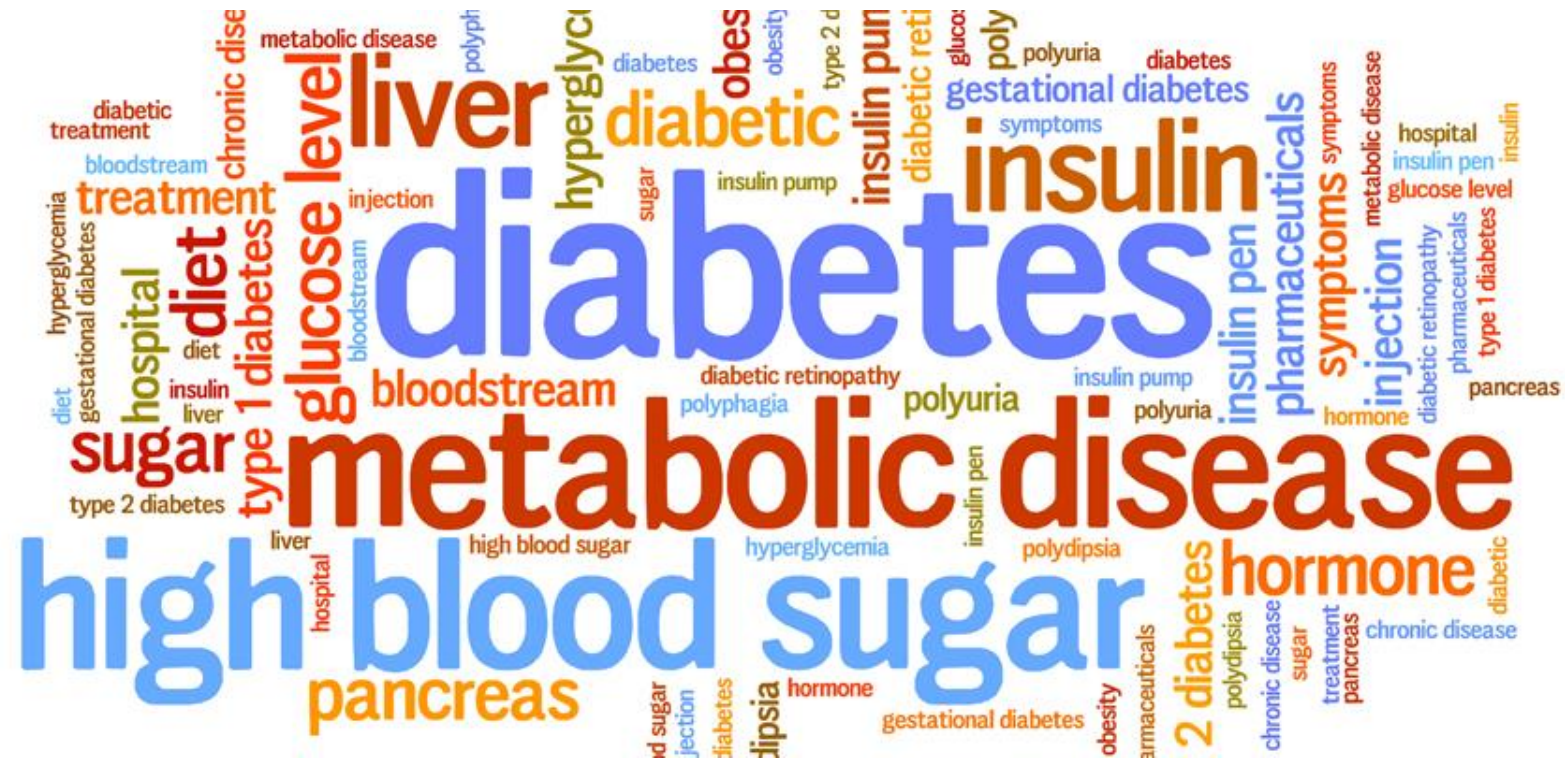[†]Estimated 10-year global cardiovascular risk ≥15%

OR

Age ≥ 75 years

- There was an increased risk of renal deterioration, potassium abnormalities and hypotension with intensified therapy

- Patients with one or more clinical indications should consent to intensive management

[*] Four variable MDRD equation
[†] Framingham Risk Score, D'Agastino, Circulation 2008

'PRESERVED FUNCTION'	'LOSS OF FUNCTION/PRESERVED ADL'	'LOSS OF FUNCTION AND ALTERED ADL'
PRESERVED FUNCTIONAL STATUS	FUNCTIONAL DECLINE WITHOUT SIGNIFICANT LOSS OF AUTONOMY FOR ADL	SIGNIFICANT LOSS OF FUNCTION, LOSS OF AUTONOMY FOR ADL AND/OR LIMITED LIFE EXPECTANCY

- Therapeutic approach similar to younger adults with treatment goal: SBP 120-140 mmHg
- Start with monotherapy and titrate antihypertensive medication cautiously
- Always check for orthostatic hypotension
- Optimize treatment for global CVD prevention

Detailed Frailty/Function assessment in order to tailor antihypertensive treatment and CVD prevention weighing benefits vs. risks

MODERATELY ALTERED FUNCTIONAL STATUS

SIGNIFICANTLY ALTERED FUNCTIONAL STATUS

Reconciliation and revision of the antihypertensive therapy

- If antihypertensive treatment is considered, start with one drug at low doses and go slow, SBP goal 150 mmHg ; avoid using more than 3 antihypertensive medications
- If SBP < 130 mmHg or orthostatic hypotension under treatment
- Consider reducing antihypertensive treatment, especially in the case of combination therapy
- Identify/correct other factors/medication decreasing BP

Diabetes

TABLE 1

Evidence-based guidelines for diabetes management in the elderly[3,4]

Health status/patient characteristics	A1C goal (%)	Treatment considerations
Healthy Few coexisting chronic illnesses Intact cognitive and functional status	<7.5	Metformin is the first-line medication if not contraindicated. Patient-specific factors determine which agents are appropriate for dual or triple therapy, if indicated, to achieve glycemic control.
Complex/intermediate Multiple coexisting chronic illnesses Mild to moderate cognitive impairment 2 or more instrumental ADL impairments	<8	For patients with multiple comorbid conditions or a short life expectancy, evaluate the risks and benefits of using antidiabetic medication. Patient-specific factors dictate the choice of medication therapy (if indicated to achieve glycemic control).
Poor Long-term care or end-stage chronic illnesses Moderate to severe cognitive impairment 2 or more ADL dependencies	<8.5	Less aggressive A1C goals may be appropriate for many, and discontinuation of medication may be the proper course of treatment. This group includes those with severe cardiovascular disease, end-stage chronic diseases in addition to diabetes, and life expectancy <5 years.

A1C, glycated hemoglobin; ADL, activities of daily living.

TABLE 2

# Pharmacotherapy risks and benefits in the elderly[2-4]

Class/drug	Disadvantages	Advantages	A1C-lowering potential	Cost
Metformin	• Gastrointestinal adverse effects • B12 deficiency • Lactic acidosis (rare) in patients with cardiovascular, renal, or hepatic dysfunction	• Minimal hypoglycemia • Likely reduces both microvascular and macrovascular events • Weight loss	1%-1.5%	Low
Sulfonylureas • Glipizide • Glyburide • Glimepiride	• Hypoglycemia (avoid glyburide) • Weight gain	• Good initial efficacy	1%-2%	Low
TZDs • Pioglitazone • Rosiglitazone	• Weight gain • Edema/heart failure • Increased fracture risk • Increased LDL • Increased risk of bladder cancer (pioglitazone)	• Minimal hypoglycemia • Improved HDL • Reduced triglycerides (pioglitazone)	1%-1.5%	Low
DPP-4 inhibitors • Sitagliptin • Saxagliptin • Linagliptin • Alogliptin	• Associated with pancreatitis • Severe joint pain • New or worsening heart failure	• Minimal hypoglycemia • Well tolerated • Once-daily dosing	0.5%-0.9%	High

TABLE 2

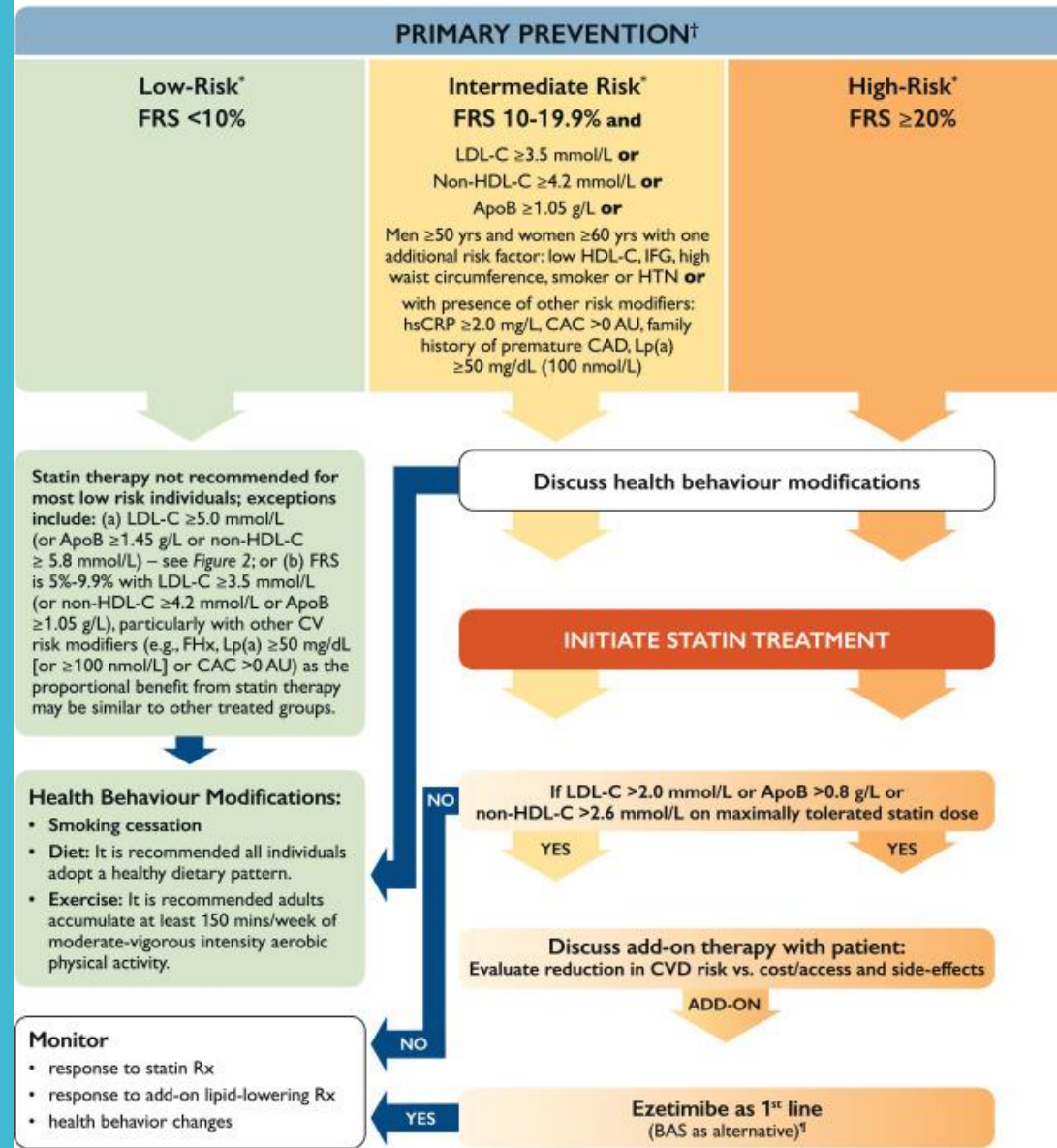# Pharmacotherapy risks and benefits in the elderly[2-4]

Class/drug	Disadvantages	Advantages	A1C-lowering potential	Cost
GLP-1 RAs • Exenatide • Liraglutide • Dulaglutide • Albiglutide	• Injectable • Gastrointestinal adverse effects • Associated with pancreatitis • Avoid in thyroid cancer	• Minimal hypoglycemia • Weight loss • Liraglutide may offer cardiovascular benefit	1%-1.5%	High
SGLT-2 inhibitors • Canagliflozin • Empagliflozin • Dapagliflozin	• Genitourinary infections • Genital yeast infections • Polyuria • Hyperkalemia • Hypotension • Pancreatitis • Increased LDL	• Minimal hypoglycemia • Weight loss • Decreased blood pressure • Once-daily dosing • Empagliflozin may offer cardiovascular benefit	0.5%-1%	High
Insulin	• Injectable • Hypoglycemia • Requires visual, manual, and cognitive skills	• Effective in all patients	Theoretically unlimited efficacy	High

A1C, glycated hemoglobin; DPP-4, dipeptidyl peptidase-4; GLP-1 RA, glucagon-like peptide-1 receptor agonists; HDL, high-density lipoprotein; LDL, low-density lipoprotein; SGLT-2, sodium glucose cotransporter-2; TZDs, thiazolidinediones.
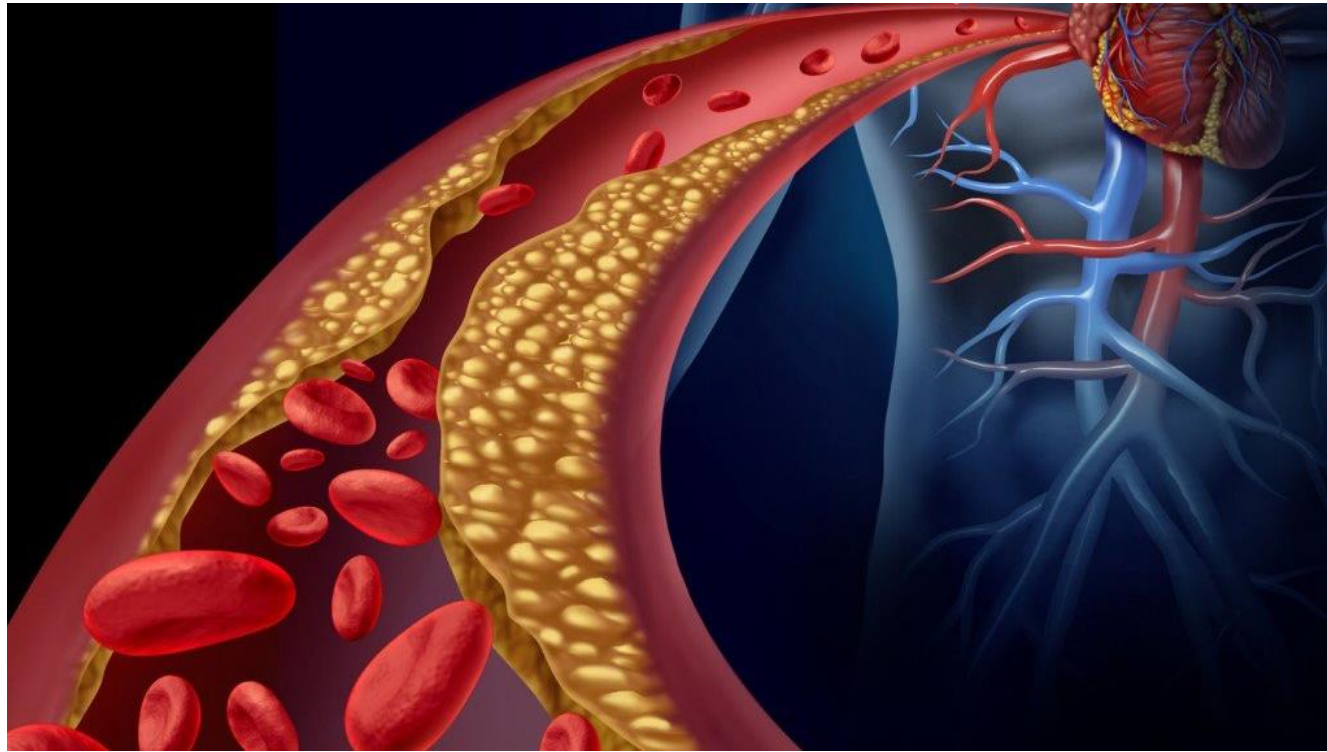
Dyslipidemia

Treatment Approach for Primary Prevention Patients (without a statin indicated condition[‡])

PRIMARY PREVENTION[†]

Low-Risk[*] FRS <10%	Intermediate Risk[*] FRS 10-19.9% and	High-Risk[*] FRS ≥20%
	LDL-C ≥3.5 mmol/L **or** Non-HDL-C ≥4.2 mmol/L **or** ApoB ≥1.05 g/L **or** Men ≥50 yrs and women ≥60 yrs with one additional risk factor: low HDL-C, IFG, high waist circumference, smoker or HTN **or** with presence of other risk modifiers: hsCRP ≥2.0 mg/L, CAC >0 AU, family history of premature CAD, Lp(a) ≥50 mg/dL (100 nmol/L)	

Statin therapy not recommended for most low risk individuals; exceptions include: (a) LDL-C ≥5.0 mmol/L (or ApoB ≥1.45 g/L or non-HDL-C ≥ 5.8 mmol/L) – see *Figure 2*; or (b) FRS is 5%-9.9% with LDL-C ≥3.5 mmol/L (or non-HDL-C ≥4.2 mmol/L or ApoB ≥1.05 g/L), particularly with other CV risk modifiers (e.g., FHx, Lp(a) ≥50 mg/dL [or ≥100 nmol/L] or CAC >0 AU) as the proportional benefit from statin therapy may be similar to other treated groups.

Discuss health behaviour modifications

INITIATE STATIN TREATMENT

Health Behaviour Modifications:
- Smoking cessation
- **Diet:** It is recommended all individuals adopt a healthy dietary pattern.
- **Exercise:** It is recommended adults accumulate at least 150 mins/week of moderate-vigorous intensity aerobic physical activity.

NO — If LDL-C >2.0 mmol/L or ApoB >0.8 g/L or non-HDL-C >2.6 mmol/L on maximally tolerated statin dose

YES   YES

Discuss add-on therapy with patient: Evaluate reduction in CVD risk vs. cost/access and side-effects

ADD-ON

Monitor
- response to statin Rx
- response to add-on lipid-lowering Rx
- health behavior changes

NO

YES — **Ezetimibe as 1st line** (BAS as alternative)[¶]

[‡]Statin indicated conditions consists of all documented ASCVD conditions, as well as other high-risk primary prevention conditions in the absence of ACSVD, such as most patients with diabetes, those with chronic kidney disease and those with a LDL-C ≥5.0 mmol/L.
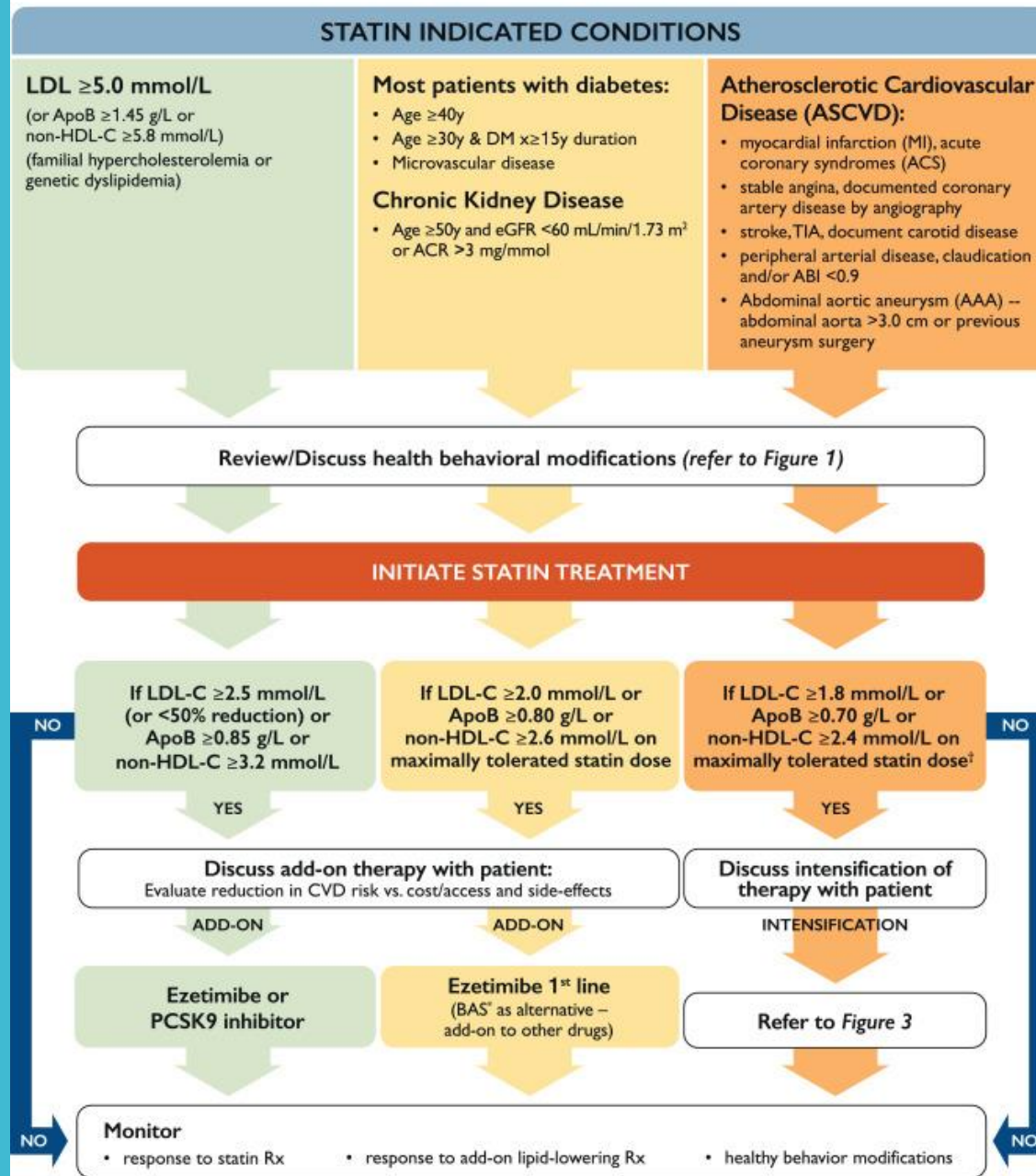
[†]Calculate risk using the Framingham Risk Score (FRS) – refer to the iCCS available on the App Store or on Google Play

[*]Screening should be repeated every 5 years for men and women aged 40 to 75 years using the modified FRS or CLEM to guide therapy to reduce major CV events. A risk assessment might also be completed whenever a patient's expected risk status changes.

[¶] studies have evaluated the efficacy of BAS for the prevention of ASCVD, but results have been inconclusive.

FRS = Framingham risk score; LDL-C = low-density lipoprotein cholesterol; HDL-C = high-density lipoprotein cholesterol; ApoB = apolipoprotein B; IFG = impaired fasting glucose; HTN = hypertension; hsCRP = high-sensitivity C-reactive protein; CAC = coronary artery calcium; AU – Agatston unit; Rx = prescription; BAS = bile acid sequestrant

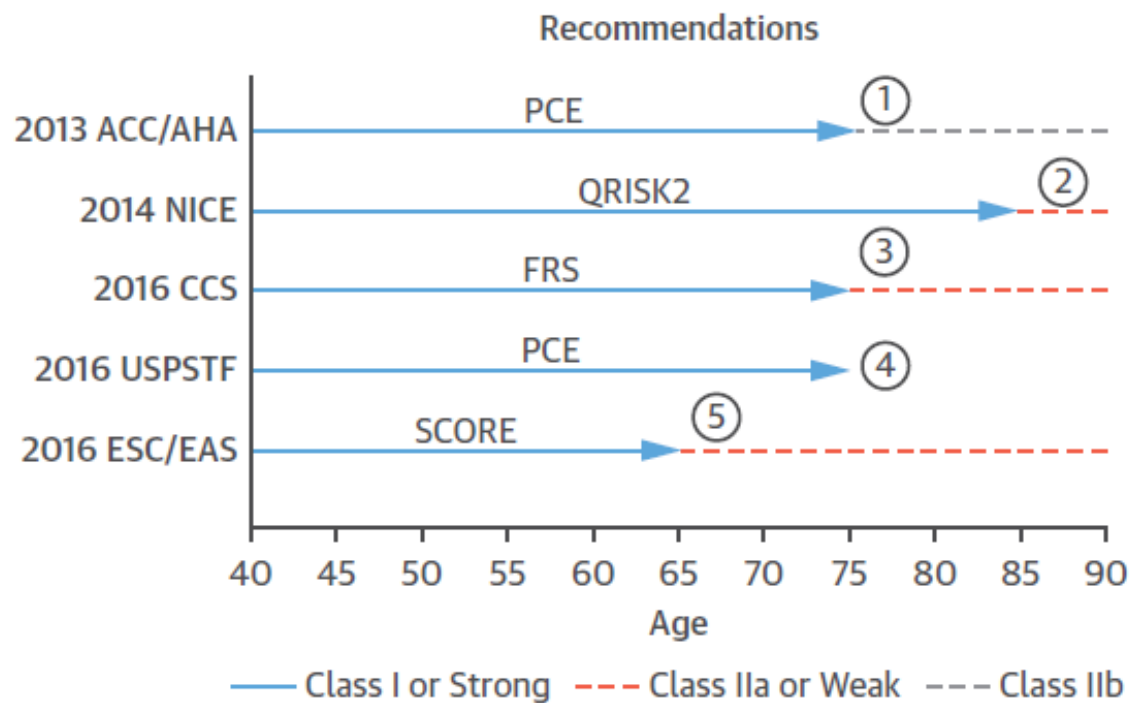# Treatment Approach for Patients with a Statin Indicated Condition

STATIN INDICATED CONDITIONS

LDL ≥5.0 mmol/L

(or ApoB ≥1.45 g/L or non-HDL-C ≥5.8 mmol/L)

(familial hypercholesterolemia or genetic dyslipidemia)

Most patients with diabetes:
- Age ≥40y
- Age ≥30y & DM x≥15y duration
- Microvascular disease

Chronic Kidney Disease
- Age ≥50y and eGFR <60 mL/min/1.73 m³ or ACR >3 mg/mmol

Atherosclerotic Cardiovascular Disease (ASCVD):
- myocardial infarction (MI), acute coronary syndromes (ACS)
- stable angina, documented coronary artery disease by angiography
- stroke, TIA, document carotid disease
- peripheral arterial disease, claudication and/or ABI <0.9
- Abdominal aortic aneurysm (AAA) -- abdominal aorta >3.0 cm or previous aneurysm surgery

---

Review/Discuss health behavioral modifications *(refer to Figure 1)*

INITIATE STATIN TREATMENT

If LDL-C ≥2.5 mmol/L (or <50% reduction) or ApoB ≥0.85 g/L or non-HDL-C ≥3.2 mmol/L

NO — YES

If LDL-C ≥2.0 mmol/L or ApoB ≥0.80 g/L or non-HDL-C ≥2.6 mmol/L on maximally tolerated statin dose

YES

If LDL-C ≥1.8 mmol/L or ApoB ≥0.70 g/L or non-HDL-C ≥2.4 mmol/L on maximally tolerated statin dose[†]

NO — YES

Discuss add-on therapy with patient:
Evaluate reduction in CVD risk vs. cost/access and side-effects

ADD-ON — ADD-ON

Discuss intensification of therapy with patient

INTENSIFICATION

Ezetimibe or PCSK9 inhibitor

Ezetimibe 1st line
(BAS* as alternative – add-on to other drugs)

Refer to Figure 3

Monitor
- response to statin Rx
- response to add-on lipid-lowering Rx
- healthy behavior modifications

NO — NO

FIGURE 1 Recommendations for Primary Prevention With Statins in Apparently Healthy People

Handling of individuals >65 years of age differs substantially among contemporary European and North American guidelines, partly because of the performance (applicability) of the risk model used. ACC/AHA = American College of Cardiology/American Heart Association; CCS = Canadian Cardiovascular Society; ESC/EAS = European Society of Cardiology/European Atherosclerosis Society; FRS = Framingham Risk Score for general cardiovascular disease; NICE = National Institute for Health and Care Excellence; PCE = pooled cohort equation; SCORE = Systematic COronary Risk Evaluation; USPSTF = U.S. Preventive Services Task Force.

Research Evidence for Statins

Practical Geriatric Care Considerations

Lack of RCTs: Statin in Primary Prevention

Suboptimal Risk Prediction Model Approaches

Statin Associated Muscle Symptoms

Cost Effectiveness

Disasbility/Competing Risk Assessment
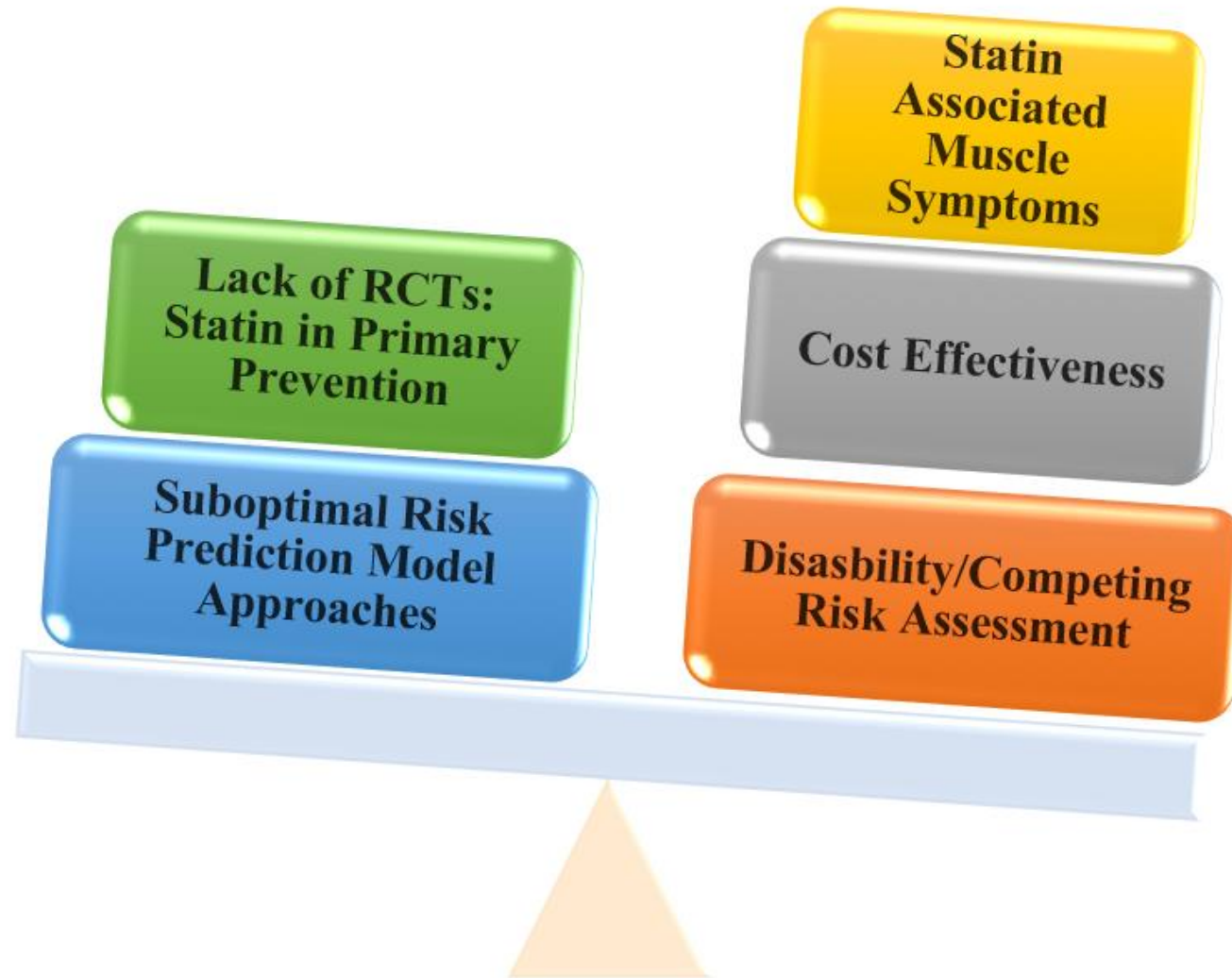
ESC/EAS 2016 Guidelines.
Treatment of dyslipidemia in older adults[a]

	Class	Level
Statin treatment is recommended for older adults with *established CVD* similarly to that for younger patients	I	A
Since older patients often have co-morbidities and altered drug pharmacokinetics, *lipid-lowering medication should be started at a lower dose* and then titrated with caution to achieve goals in serum lipid concentrations which are the same as in younger patients	IIa	C
Statin therapy should be considered in *older adults without CVD*, in the presence of hypertension, smoking, diabetes and dyslipidemia.	IIa	B

CVD: cardiovascular disease. Class of recommendation. Level of evidence.
[a]Catapano AL et al. European Heart Journal 32: 1769-818, 2016.

Primary Prevention

Favouring statin therapy	Not generally speaking against statin therapy	Discouraging from statin therapy	Evidence particularly unclear and urgently needed
Diabetes mellitus Expected drug adherence Absence of end-of-life situation Patient preference	Advanced age Mild to moderate renal insufficiency	Difficulty adhering to current therapies (Multiple) interacting co-medication Serious adverse statin events in the past Competing non-vascular conditions likely limiting life expectancy	Frailty

Future

- The results of three trials are anticipated with great interest:

- A Clinical Trial of STAtin Therapy for Reducing Events in the Elderly (STAREE): atorvastatin 40 mg compared in healthy elderly people (≥70 years)

- Statins In The Elderly (SITE): RCT on statin cessation in people ≥75 years

- Pragmatic Evaluation of Events And Benefits of Lipid-lowering in Older Adults (PREVENTABLE) (Recruiting expected to start in September 2020)
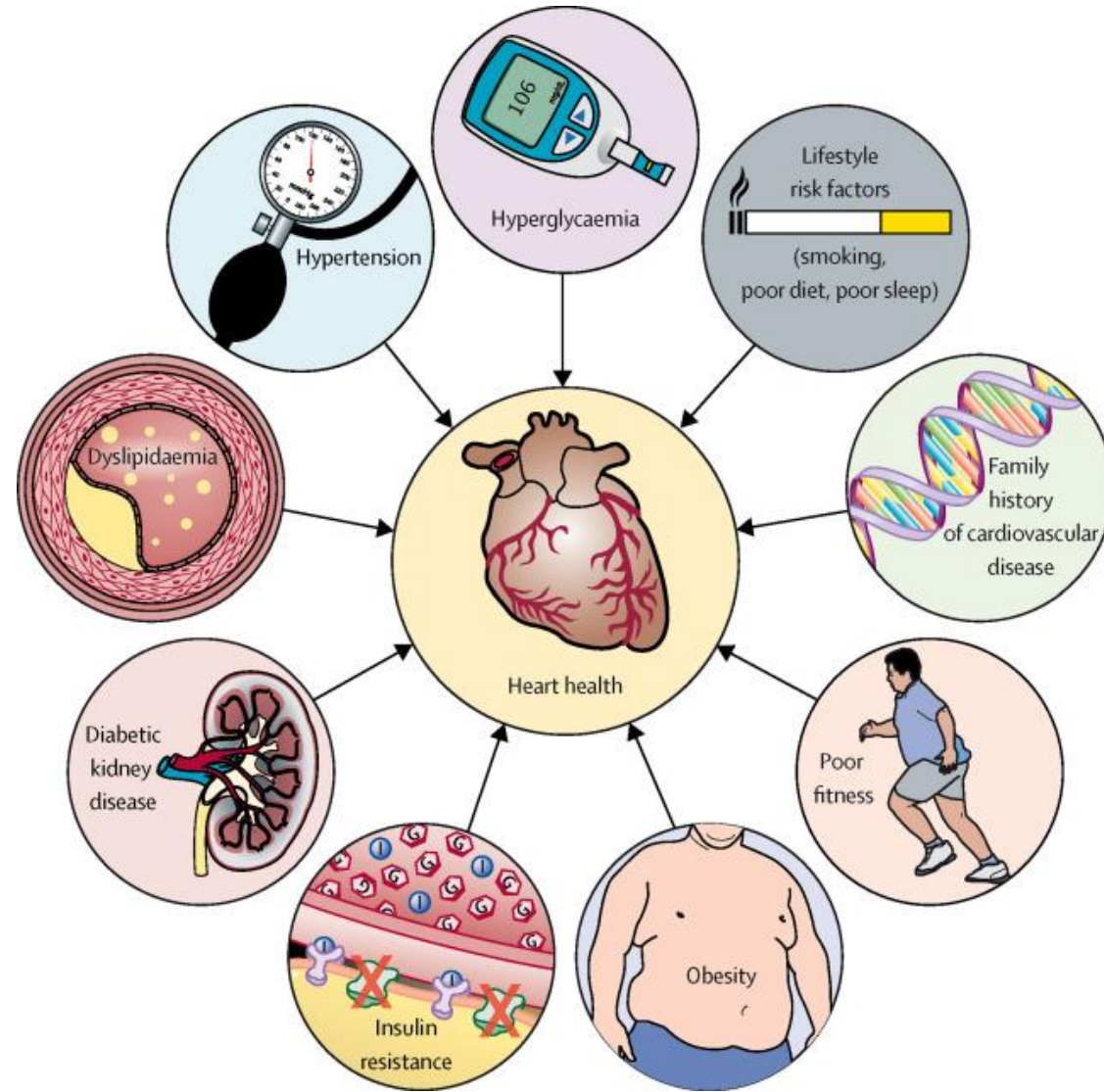
Conclusions

- Elderly are the highest risk population for cardiovascular disease with potential treatment that may improve quality of life and possibly survival

- Personalized medicine is essential

- Treatment of vascular risk factors can help cognitive health as well as cardiovascular health

- If frail, consider different treatment goals when it comes to pharmacotherapy

- Data specific to this population is still lacking and hopefully future trials will provide some further direction

Thank you