Diabetes Professional Care 2019

Cardiovascular Disease Prevention – the MDT Panel

The ABC of CVD Prevention

Declaration of Conflict of Interests

Dr Jim Moore FRCP Edin

GP and GPwSI in Cardiology, Cheltenham

President Elect Primary Care Cardiovascular Society

NICE Guideline Committee member -Chronic Heart Failure 2018

National Heart Failure Audit Steering group

Chair of the GLOS CCG Circulatory Clinical Programme Group

In the last year Honoraria received from AstraZeneca, Bayer and Novartis for various activities including attending and participating in educational events and advisory boards

Primary Care Cardiovascular Society

Primary Care Cardiovascular Society

www.pccsuk.org

Primary Care Cardiovascular Society

How to register for Membership

Annual Subscription

GPs £40

Pharmacists, GP Registrars and Nurses £20

How to Register

To register for membership please follow this link

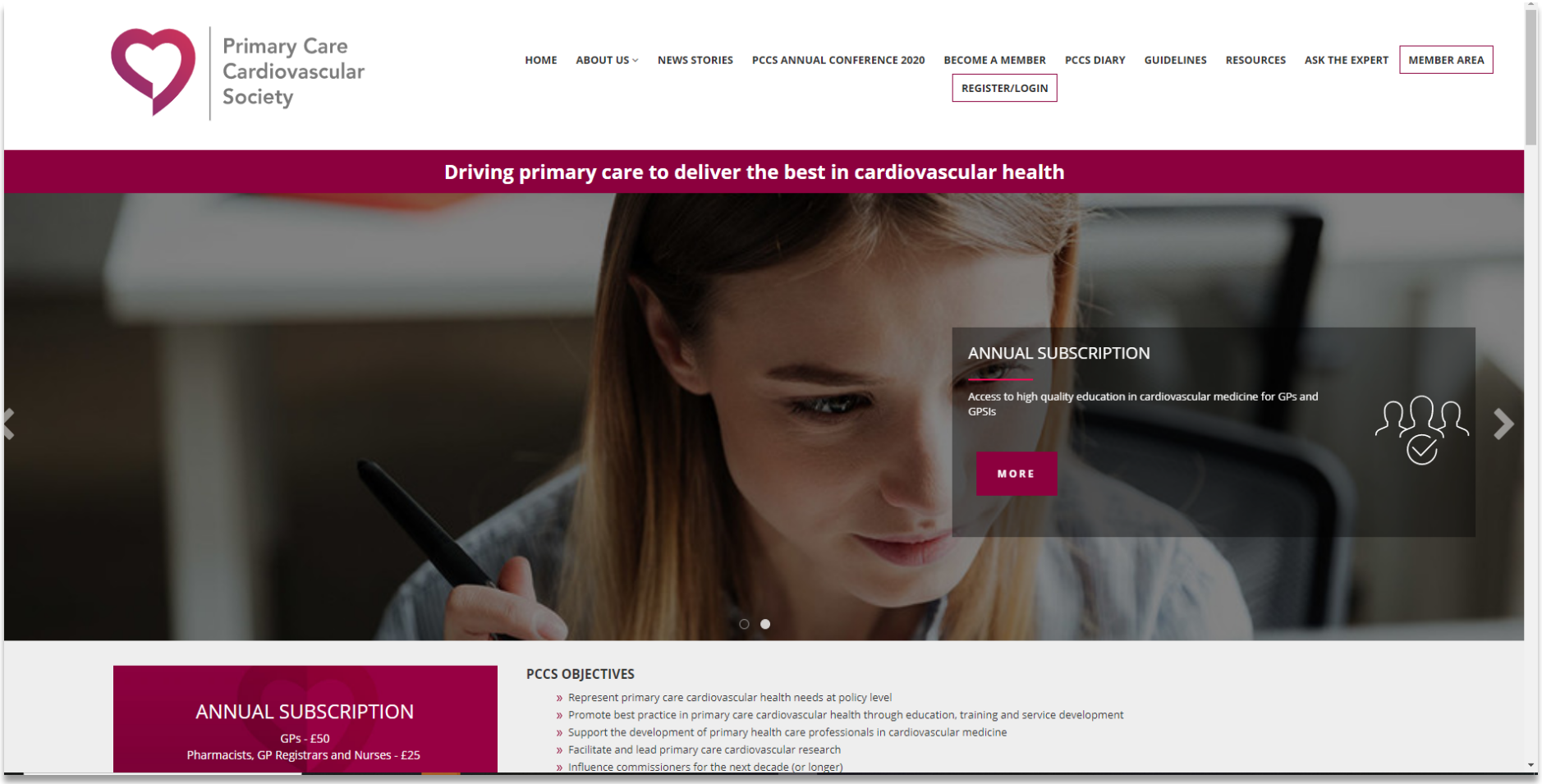
http://pccs.lcwmed.co.uk

Or call 01444 414264

Or email registrations@LCWmed.co.uk

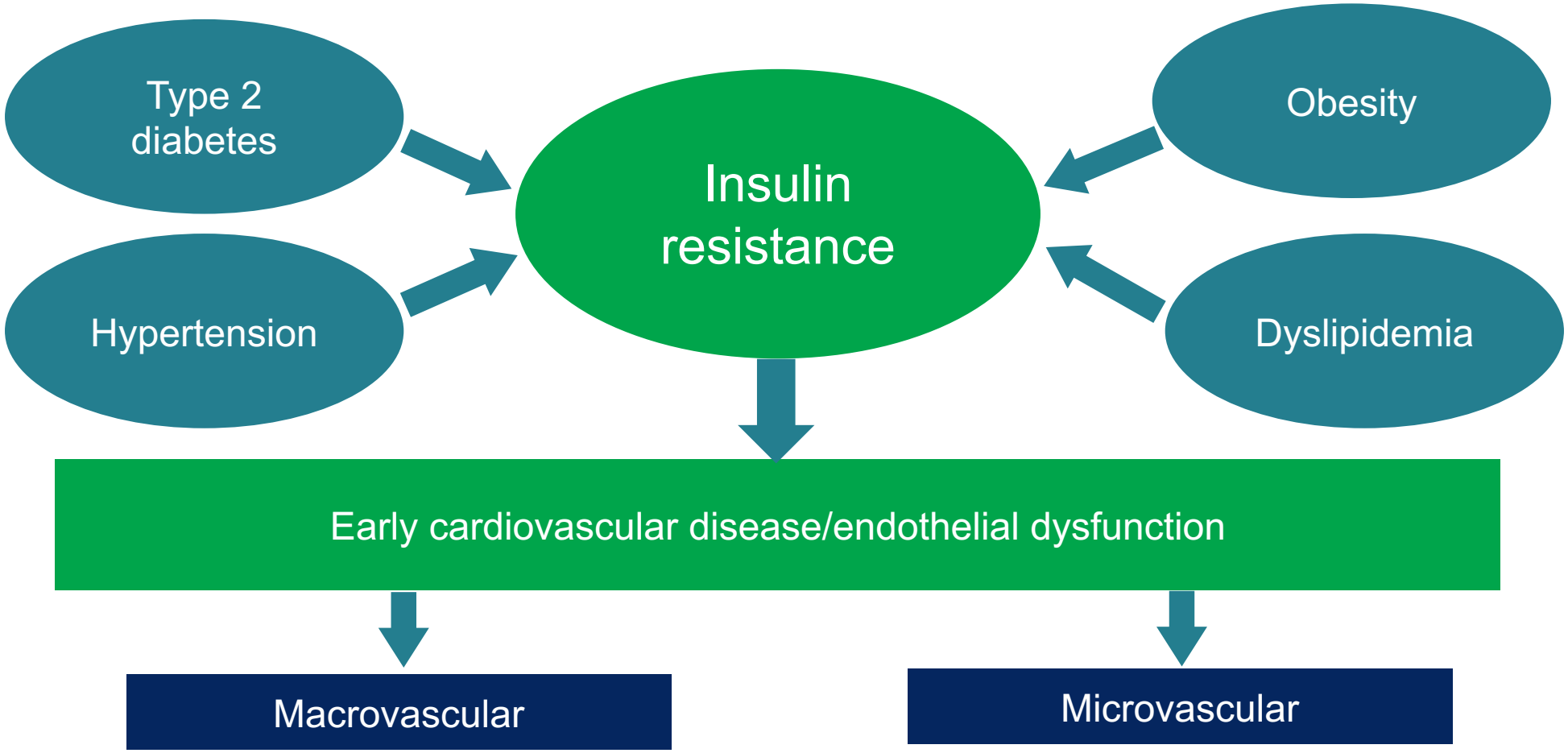
Primary Care Cardiovascular Society

New website



The ABC of CVD Prevention

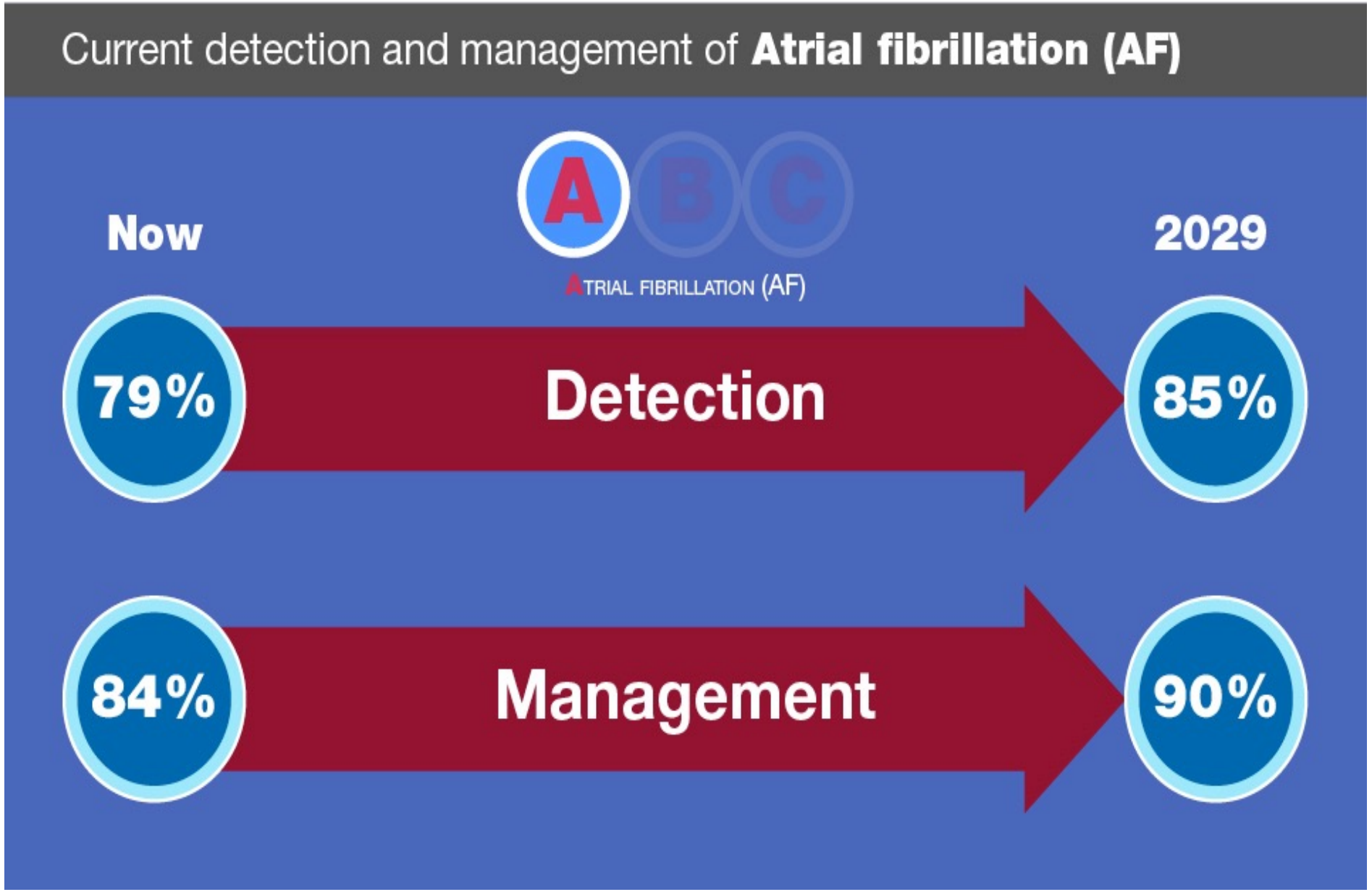
The deadly quartet



DeFronzo RA, et al. *Diabetes Care* 1991;15:173–194

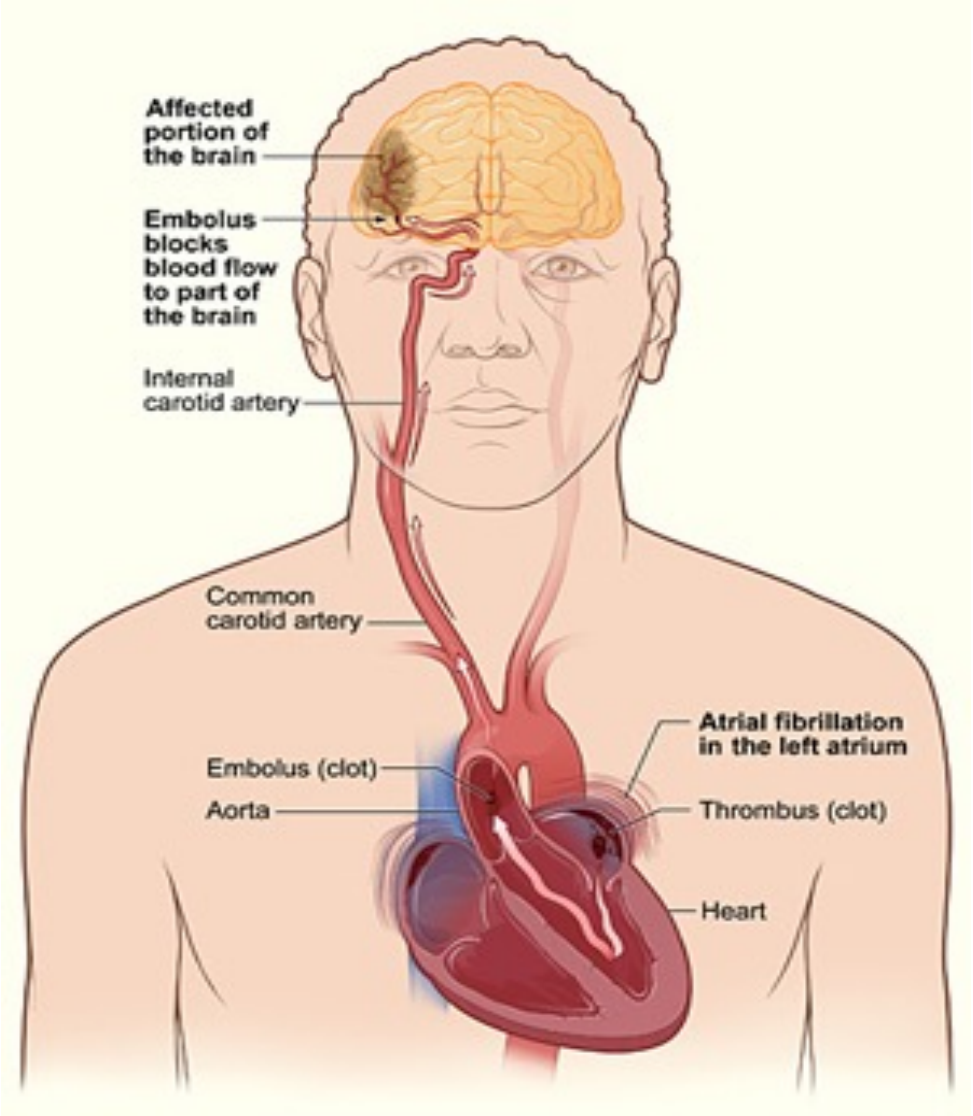
"A"

Atrial Fibrillation


Current detection and management of **Atrial fibrillation (AF)**
A B C
ATRIAL FIBRILLATION (AF)
Now
2029
79%
Detection
85%
84%
Management
90%

The REAL Importance of AF

- Most important preventable cause of stroke
- Emboli from the LA appendage



There is a national programme across England to tackle the issue of AF-related strokes[1]

DETECT

FIND MORE

Awareness campaigns, educate and encourage people to check their pulse rhythm[2]

PROTECT

TREAT MORE

Ensure that all suitable patients with AF receive appropriate treatment[2]

PERFECT

TREAT BETTER

Ensure optimal treatment in all patients[2]

1. The AHSN Network. Available at: https://www.ahsnnetwork.com/about-academic-health-science-networks/national-programmes-priorities/atrial-fibrillation/, accessed December 2018; 2. The AF Toolkit. Available at http://www.londonscn.nhs.uk/wp-content/uploads/2017/06/detect-protect-perfect-london-af-toolkit-062017.pdf, accessed November 2018

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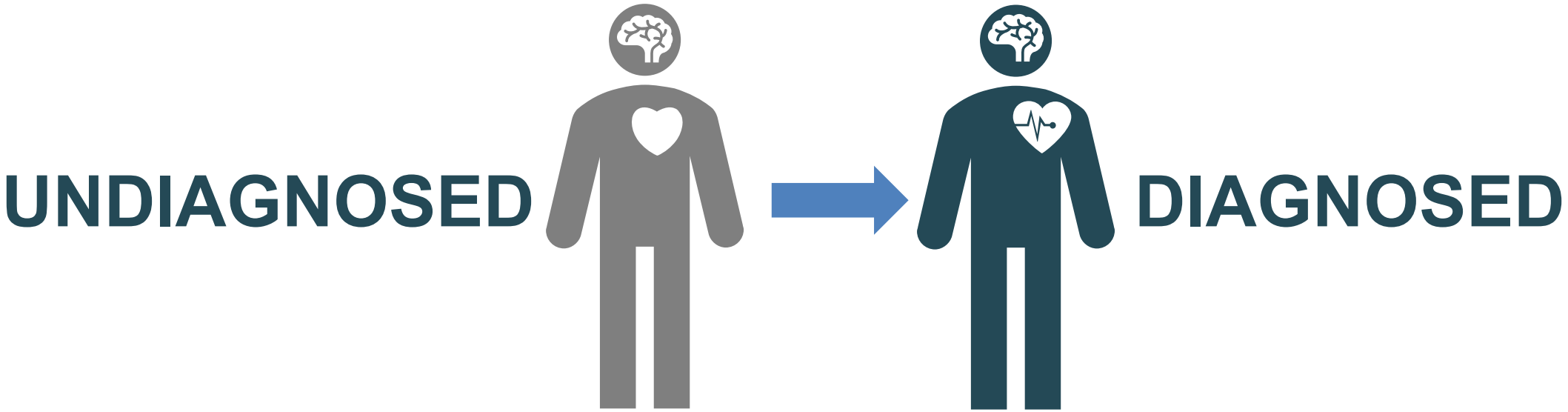
Maximise routine opportunities for case finding to improve AF detection rates

OPPORTUNISTIC
pulse checking

CLOSES THE DIAGNOSIS GAP



Kearney M et al. Br J Gen Pract 2016;66:62–63

Suspected paroxysmal AF undetected by 12L ECG

Event recorder (AliveCor FDA approved)

AF screening in chronic disease management / health promotion

✓*Hypertension*

✓*Heart failure*

✓*CHD*

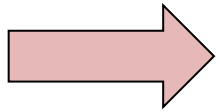
✓*Stroke*

✓*Diabetes*

✓*CKD*

✓*Weight management*

✓*NHS Health Check*



> 90% target population coverage

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What are the perceived barriers to anticoagulation?

Physician's judgement is a major factor in withholding anticoagulation

Why physicians withhold VKAs in patients at risk of stroke ($CHADS_2$ score ≥2)*

Main reason anticoagulant not used	Eligible patients n=2302 [n (%)]
Alcohol misuse	11 (0.5)
Already taking antiplatelet drugs for other medical condition	117 (5.1)
Patient refusal	165 (7.2)
Previous bleeding event	55 (2.4)
Taking medication contraindicated or cautioned for use with VKA	16 (0.7)
Other	239 (10.4)
Unknown	587 (25.5)
Physician's choice	1112 (48.3)

~48% due to physician choice

*Physicians' clinical judgment of stroke risk appears to incorporate factors not included in CHADS2 and CHA2DS2-VASc.Kakkar AK et al. PLoS One 2013;8:e63479

AF Garfield
global anticoagulant registry in the field

Physician's judgement is a major factor in withholding anticoagulation

Why physicians withhold VKAs in patients at risk of stroke ($CHADS_2$ score ≥2)*

Main reason anticoagulant not used	Eligible patients n=2302 [n (%)]
Physician's choice	1112 (48.3)
Bleeding risk	170 (7.4)
Concern over patient compliance	121 (5.3)
Guideline recommendation	32 (1.4)
Fall risk	150 (6.5)
Low risk of stroke	95 (4.1)
Other	544 (23.6)

~48% due to physician choice

*Physicians' clinical judgment of stroke risk appears to incorporate factors not included in CHADS2 and CHA2DS2-VASc.Kakkar AK et al. PLoS One 2013;8:e63479

AF Garfield
global anticoagulant registry in the field

CHA_2DS_2-VASc Score and Stroke Risk?

Risk factor	Points
Prior stroke/ TIA or systemic embolism	2
Age ≥75 years	2
Congestive heart failure*	1
Hypertension	1
Diabetes mellitus	1
Age 65–74 years	1
Female gender	1
Vascular disease	1

Add points together →

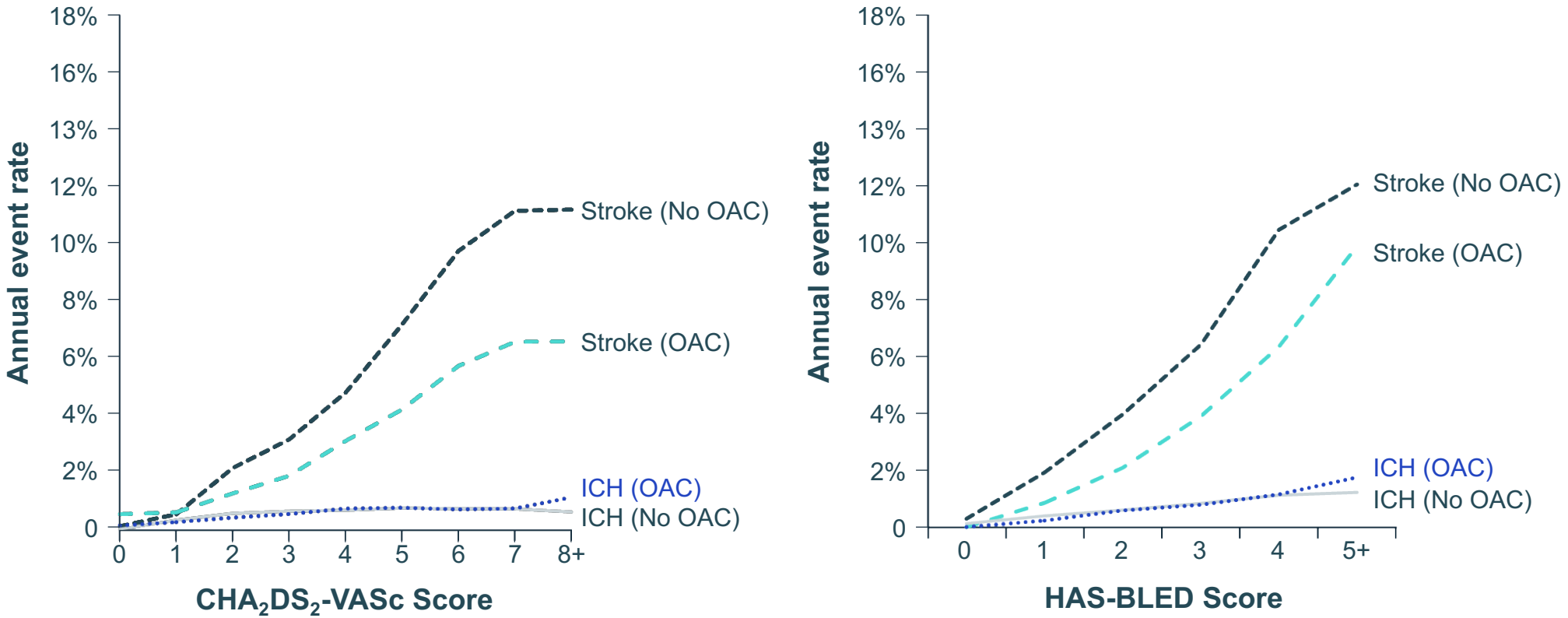
CHA_2DS_2-VASc	Stroke rate events/100 patient-years
9	23.64
8	22.38
7	21.50
6	19.74
5	15.26
4	9.27
3	5.92
2	3.71
1	2.01
0	0.78

*Or moderate-to-severe left ventricular systolic dysfunction (left ventricular ejection fraction ≤40%).

TIA, transient ischaemic attack

1. Olesen JB, *et al. BMJ* 2011;342:d124; 2. Camm AJ, *et al. Eur Heart J.* 2010;31(19):2369–2429.

The risk of ischaemic stroke ‘without’ OAC exceeds the risk of intracranial bleeding ‘with’ OAC*

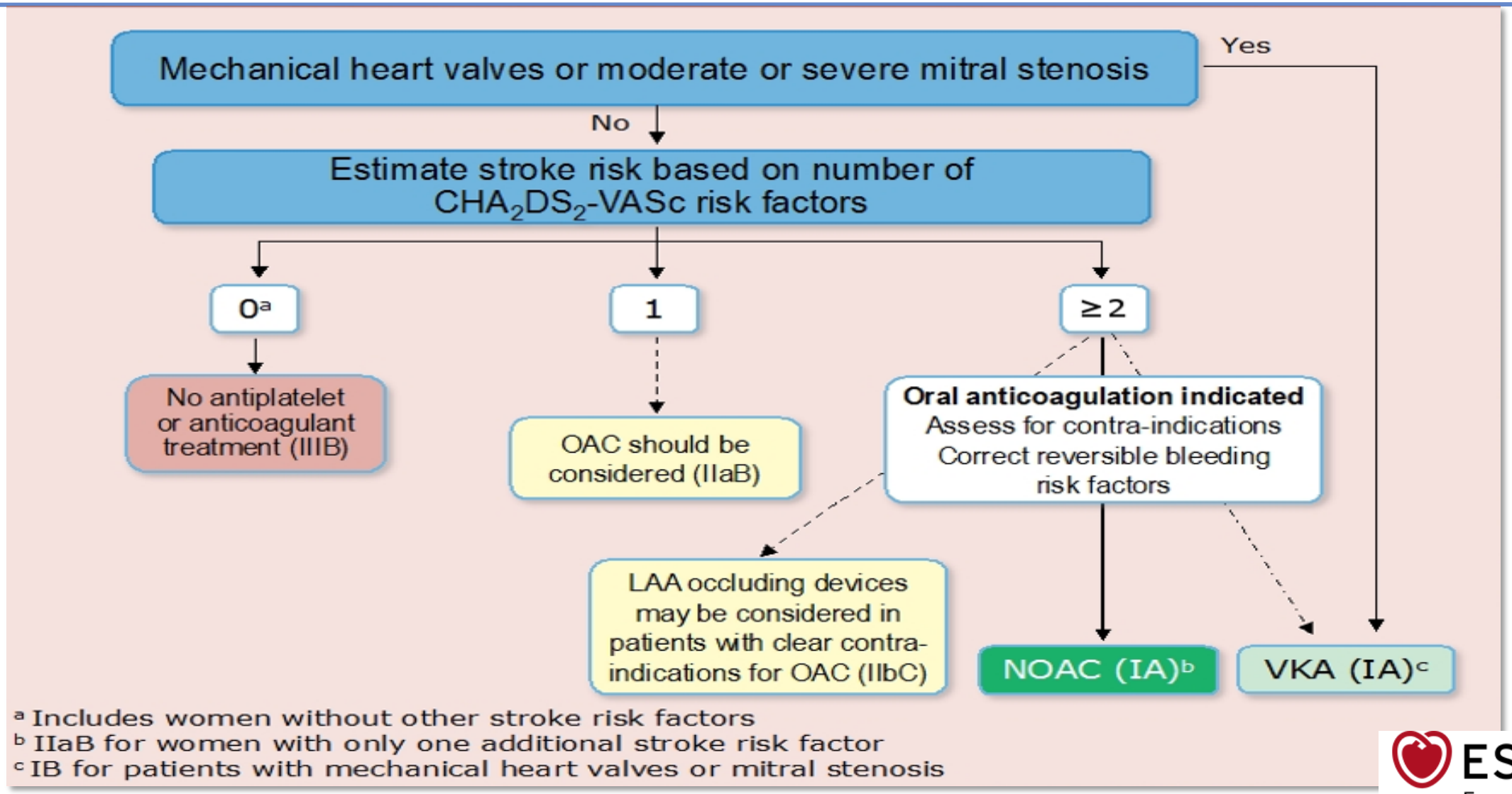


Relation between risk scores and annual event rates of ischaemic stroke and ICH in relation to use of oral anticoagulation in 159,013 Swedish AF patients followed up for 1.5±1.1 years (2005–2008)

*Except those with a very low risk of stroke

Friberg L et al. *Circulation* 2012;125:2298–2307

Who should be anticoagulated? (ESC 2016)



ESC European Society of Cardiology

Adapted from The ESC. 2016 ESC Guidelines for the management of atrial fibrillation. Available at: https://www.escardio.org/Guidelines/Clinical-Practice-Guidelines/Atrial-Fibrillation-Management. Accessed February 2019

NOACs showed a favourable benefit-risk profile versus warfarin

- Meta-analysis of Phase III trials for stroke/SE prevention in non-valvular AF patients on NOACs vs warfarin

19%* reduction in stroke/SE

52%* reduction in ICH

14%† reduction in major bleeding

25%# increase in GI bleeding vs warfarin

NOAC events vs warfarin events	911 vs 1107	204 vs 425	1541 vs 1802	751 vs 591

The relative efficacy and safety profile of NOACs was consistent across a wide spectrum of non-valvular AF patients

Note: 42,411 participants received a new oral anticoagulant and 29,272 participants received warfarin

**P*<0.0001; †*P*=0.06; # *P*=0.04

Ruff CT, et al. *Lancet*. 2014;383:955–962

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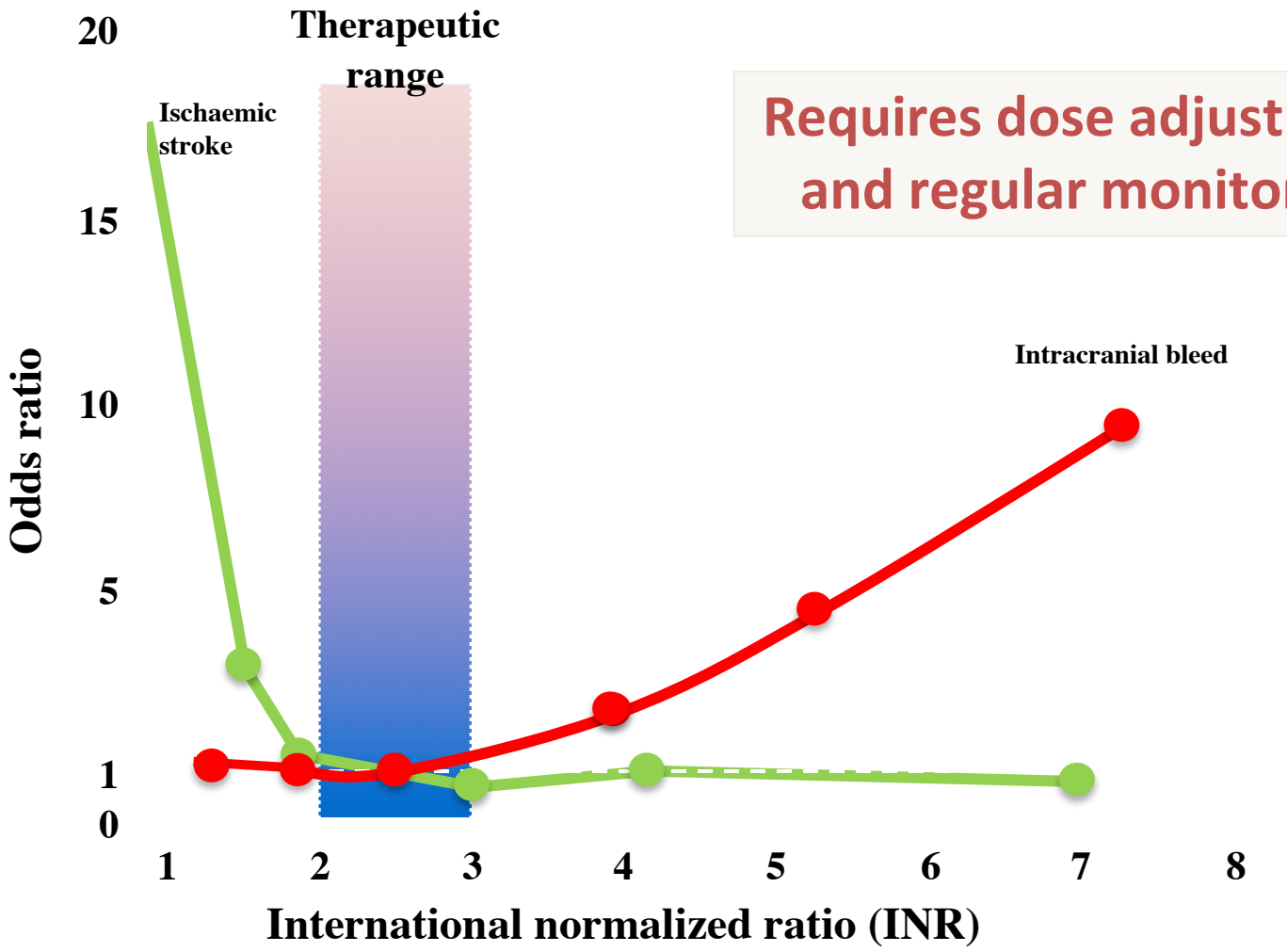
Warfarin and its challenging therapeutic window

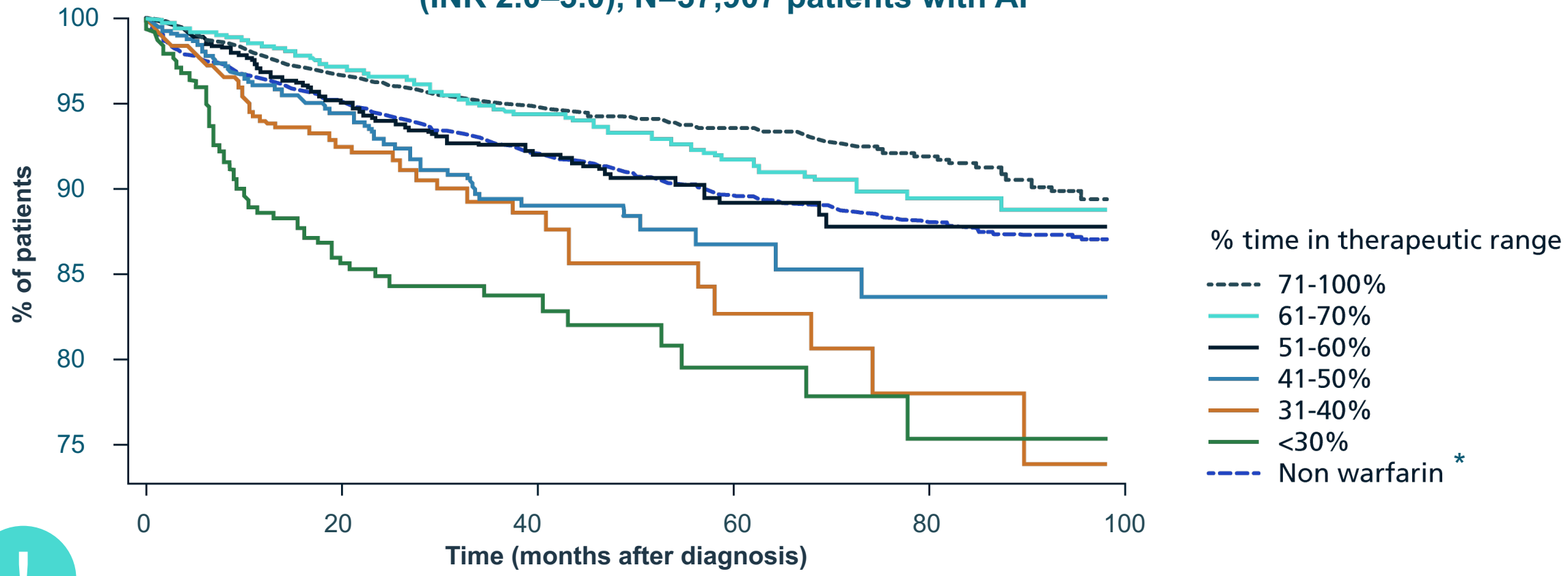


Requires dose adjustment and regular monitoring

ACC/AHA/ESC guidelines: Fuster V *et al*. *Circulation* 2006;114:e257–e354

Time in therapeutic range matters

Proportion of patients without a stroke over time stratified by time spent within therapeutic range (INR 2.0–3.0), N=37,907 patients with AF



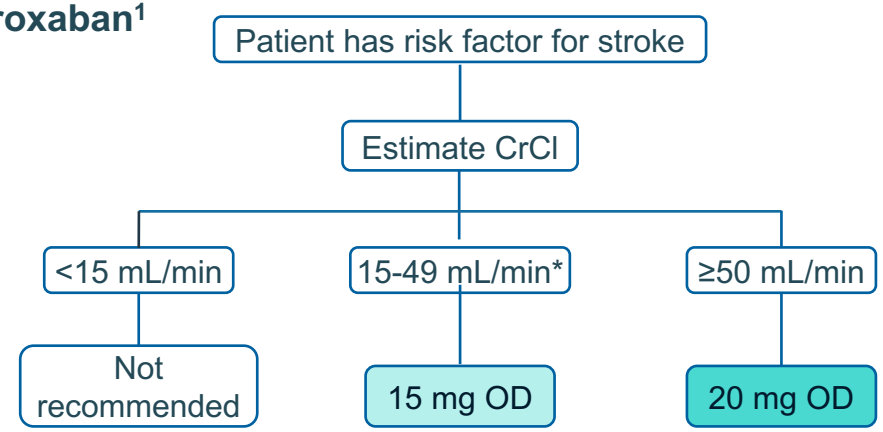
Poor INR control increases the risk of stroke in real-world practice

*The non-warfarin group comprised AF patients not treated with antithrombotic therapy, defined as study patients with no record ever of INR measurements or prescribing of warfarin, aspirin or clopidogrel, or dipyridamole. Warfarin group: study patients with at least one INR measurement in medical history.

Gallagher AM et al. *Thromb Haemost* 2011;106:968–977

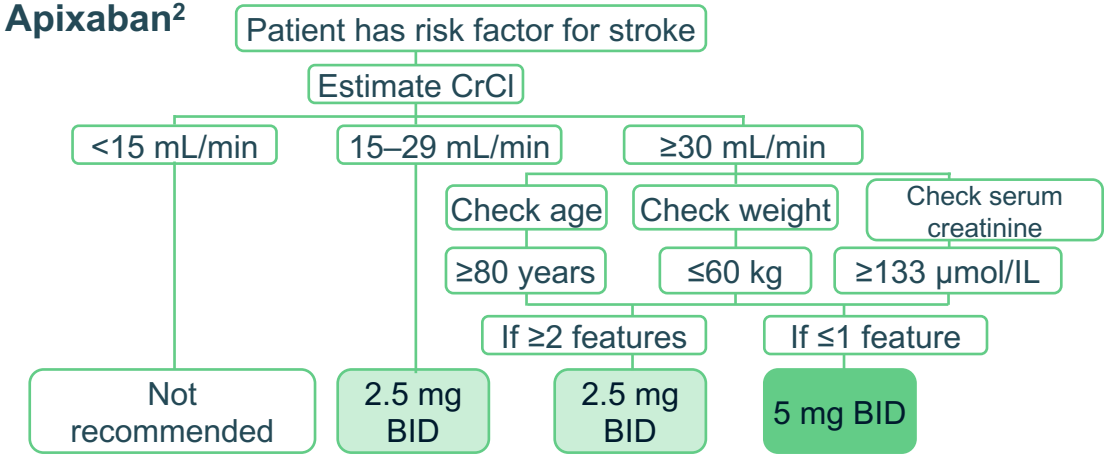
Dose adjustments are required in the presence of renal impairment

Rivaroxaban[1]

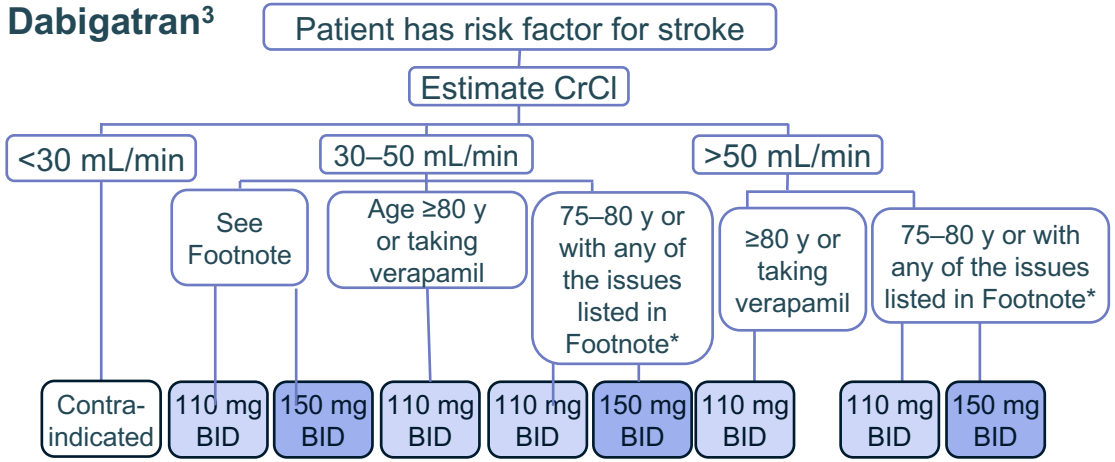


*Rivaroxaban to be used with caution in patients with CrCl 15–29 mL/min

Apixaban[2]

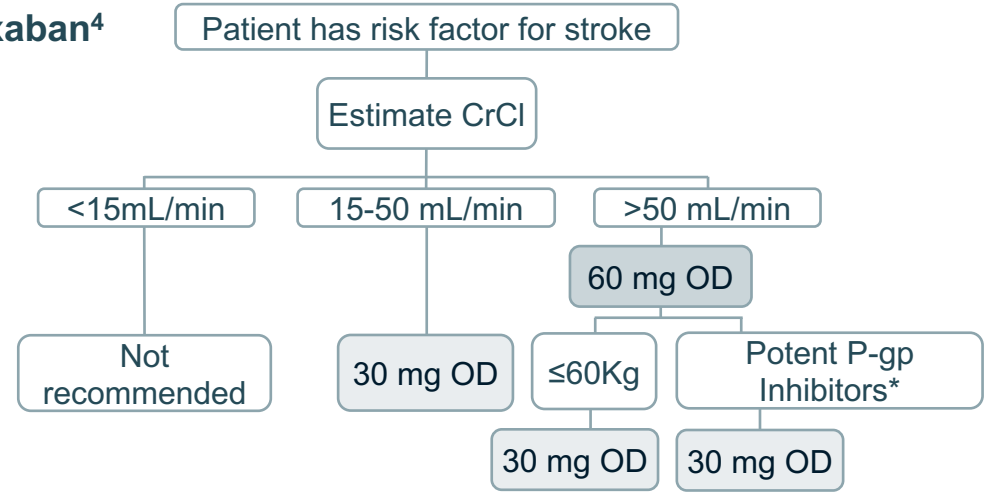


Dabigatran[3]



*Dabigatran dose of 110 mg or 150 mg BID, based on individual assessment of thromboembolic and bleeding risk in patients with gastritis, esophagitis or gastroesophageal reflux, or increased bleeding risk

Edoxaban[4]



*Potent P-gp inhibitors include dronedarone, erythromycin, ciclosporin and ketoconazole

1. Rivaroxaban SmPC; 2. Apixaban SmPC; 3. Dabigatran SmPC; 4. Edoxaban SmPC

Dose adjustments are based on severity of renal impairment, so…

Estimated glomerular filtration rate (eGFR) vs creatinine clearance (CrCl)[1,2]

Category	eGFR (mL/min/1.73m²)	CrCl (mL/min)
Normal	≥90	>80
Mild	60–89	50–80
Moderate	30–59	30–50
Severe	15–29	<30

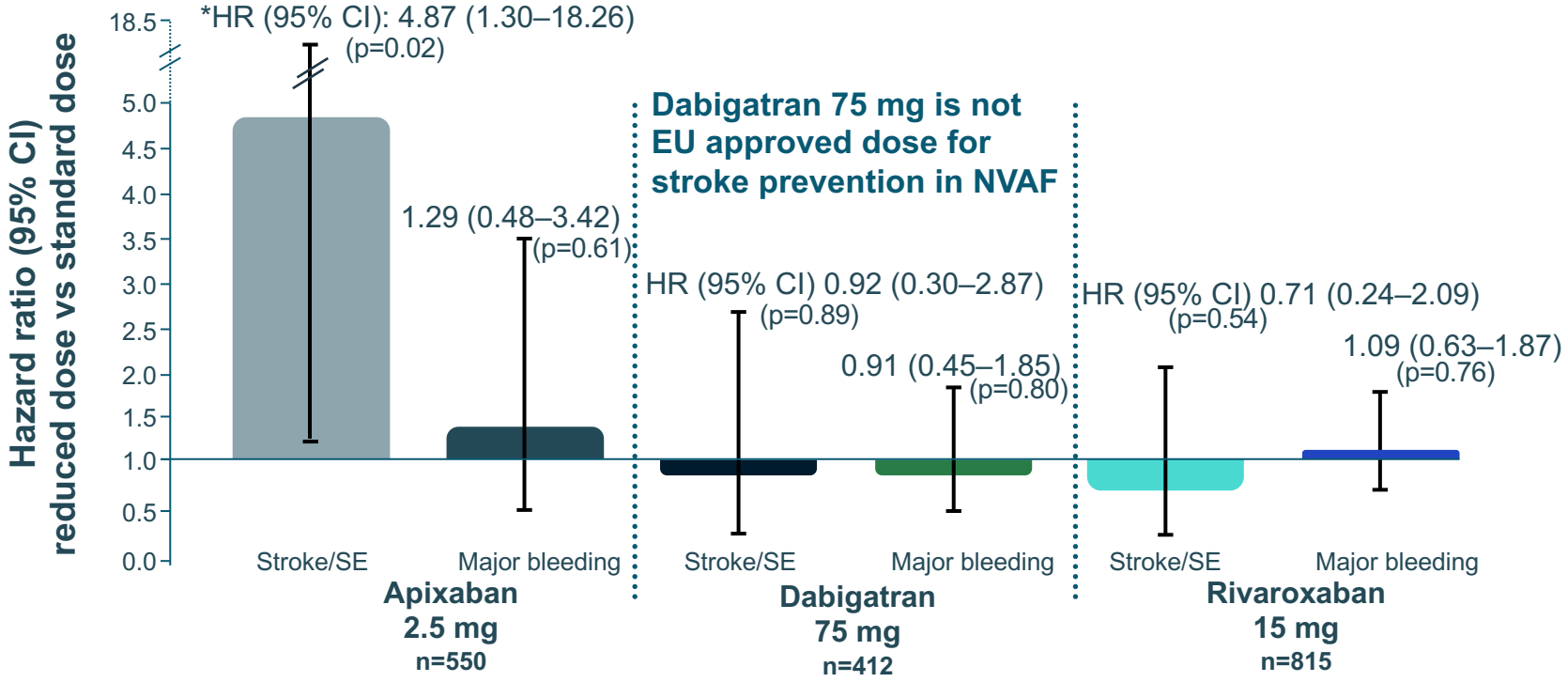
85-year-old woman who weighs 92 kg with serum creatinine 132 has an:
- eGFR 32
- Estimated CrCl 40

85-year-old woman who weighs 55 kg with a serum creatinine 132 has an:
- eGFR 32
- Estimated CrCl 24

1. National Kidney Foundation. Glomerular Filtration Rate (GFR). 2018. Available at: https://www.kidney.org/atoz/content/gfr, accessed: January 2019; 2. FDA. Guidance for Industry Pharmacokinetics in Patients with Impaired Renal Function — Study Design, Data Analysis, and Impact on Dosing and Labeling. 1998. Available at: https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM072127.pdf, accessed January 2019

Potential under-dosing in AF is associated with higher risk of stroke/systemic embolism

A retrospective claims database analysis of 13,392 patients without renal indication for dose reduction*



No head-to-head clinical trials have been performed between NOACs to evaluate this data

Inappropriate dosing is not recommended. Please refer to relevant NOAC SmPC for appropriate dosing regimen for stroke prevention in patients with NVAF

NVAF: non vualvular atrial fibrillation; SE: systemic embolism. *Excluded: apixaban, serum creatinine ≥1.5 mg/dl; dabigatran, eGFR <30 ml/min/1.73 m2; rivaroxaban, eGFR <50 ml/min/1.73 m2. Propensity score matching used to account for differences in baseline characteristics between patients receiving reduced and standard doses. Yao X et al. *J Am Coll Cardiol* 2017;69:2779–90

Paradigm shift in stroke prevention in AF

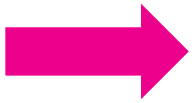
In practice…

Few patients have a CHA_2DS_2-VASc=0

few patients are ineligible for an OAC

Therefore…

The question is not who we should anticoagulate



the question is
who we should <u>not</u> anticoagulate

”B"

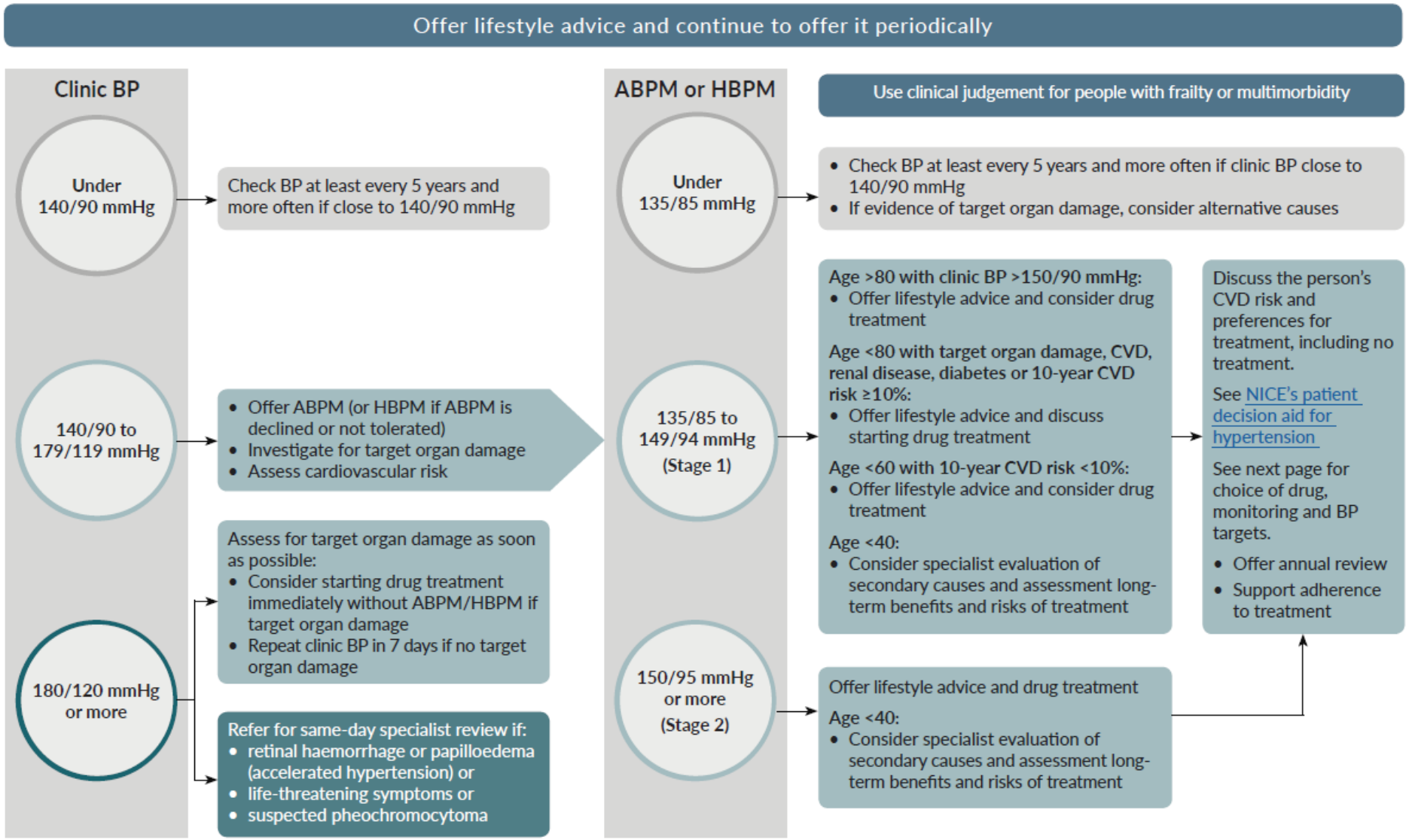
Blood Pressure

Hypertension – what's new?

Beverley Bostock RGN MSc QN
PCCS nurse board member
beverley.bostock@nhs.net

Hypertension in adults: diagnosis and treatment

NICE National Institute for Health and Care Excellence



Abbreviations: ABPM, ambulatory blood pressure monitoring; BP, blood pressure; CVD, cardiovascular disease; HBPM, home blood pressure monitoring.

This is a summary of the recommendations on diagnosis and treatment from NICE's guideline on hypertension in adults. See the original guidance at www.nice.org.uk/guidance/NG136

Diagnosis

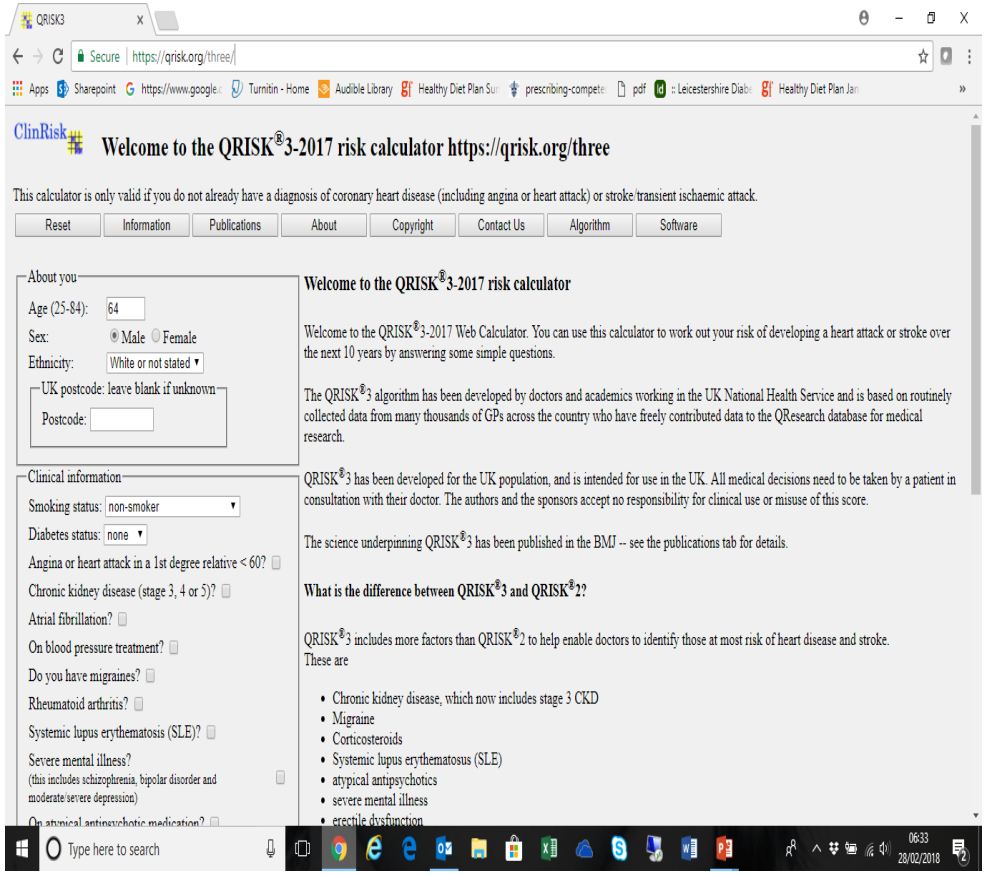
- If clinic BP ≥140/90 – 179/119mm Hg check home readings
- APBM – gold standard, using day time average
- HBPM – if ABPM not available/unsuitable
- BD readings for 4-7 days, losing day 1 before working out the average

Stages

- Stage 1
  - Home: 135/85 – 149/94mm Hg
- Stage 2
  - Home: ≥ 150/95mm Hg

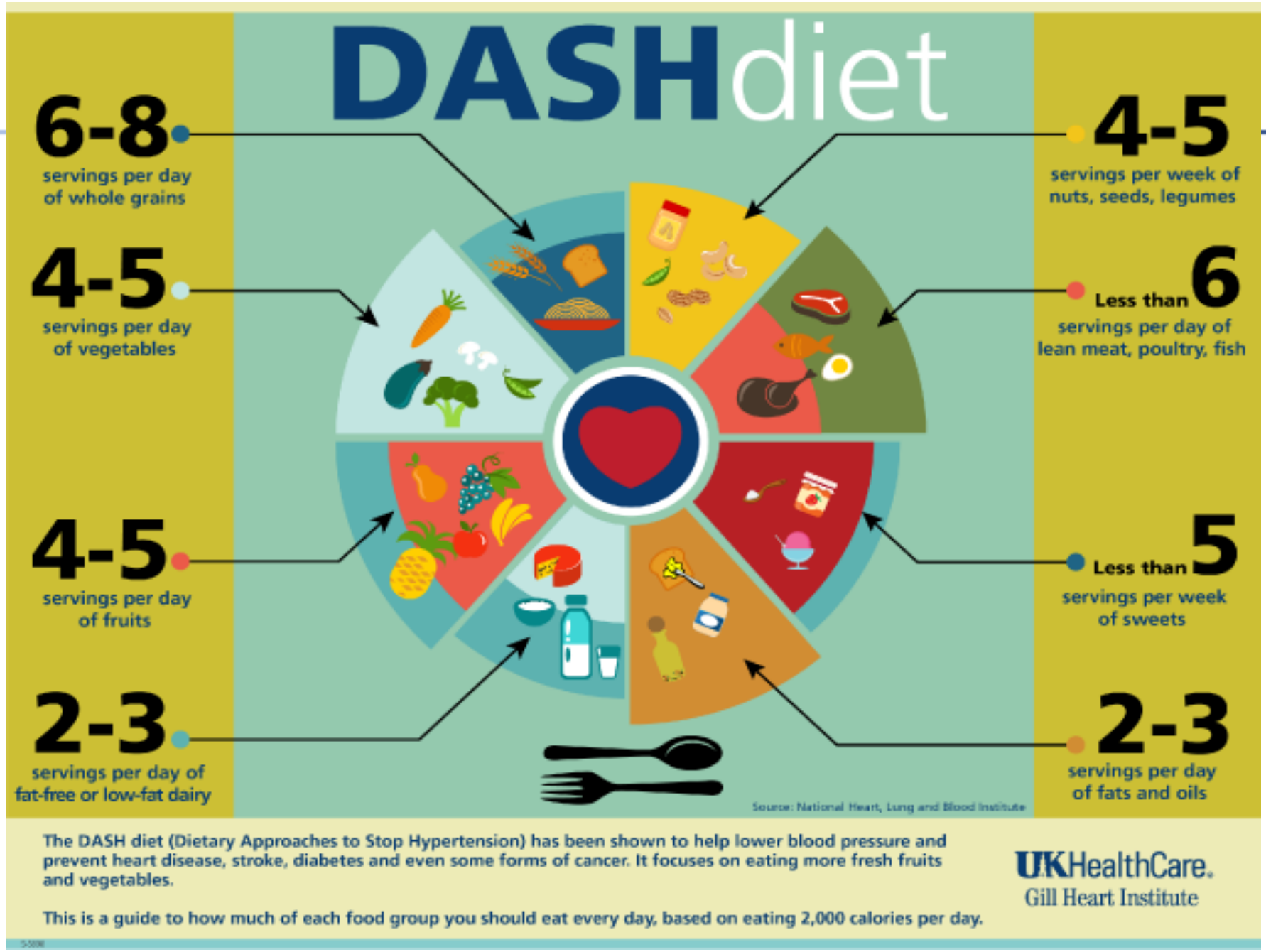
Stage 1

- Treat if CVD risk >10%
- If evidence of CVD, renal problems, diabetes
- Consider treating under 60s anyway as lifetime risk may be underestimated

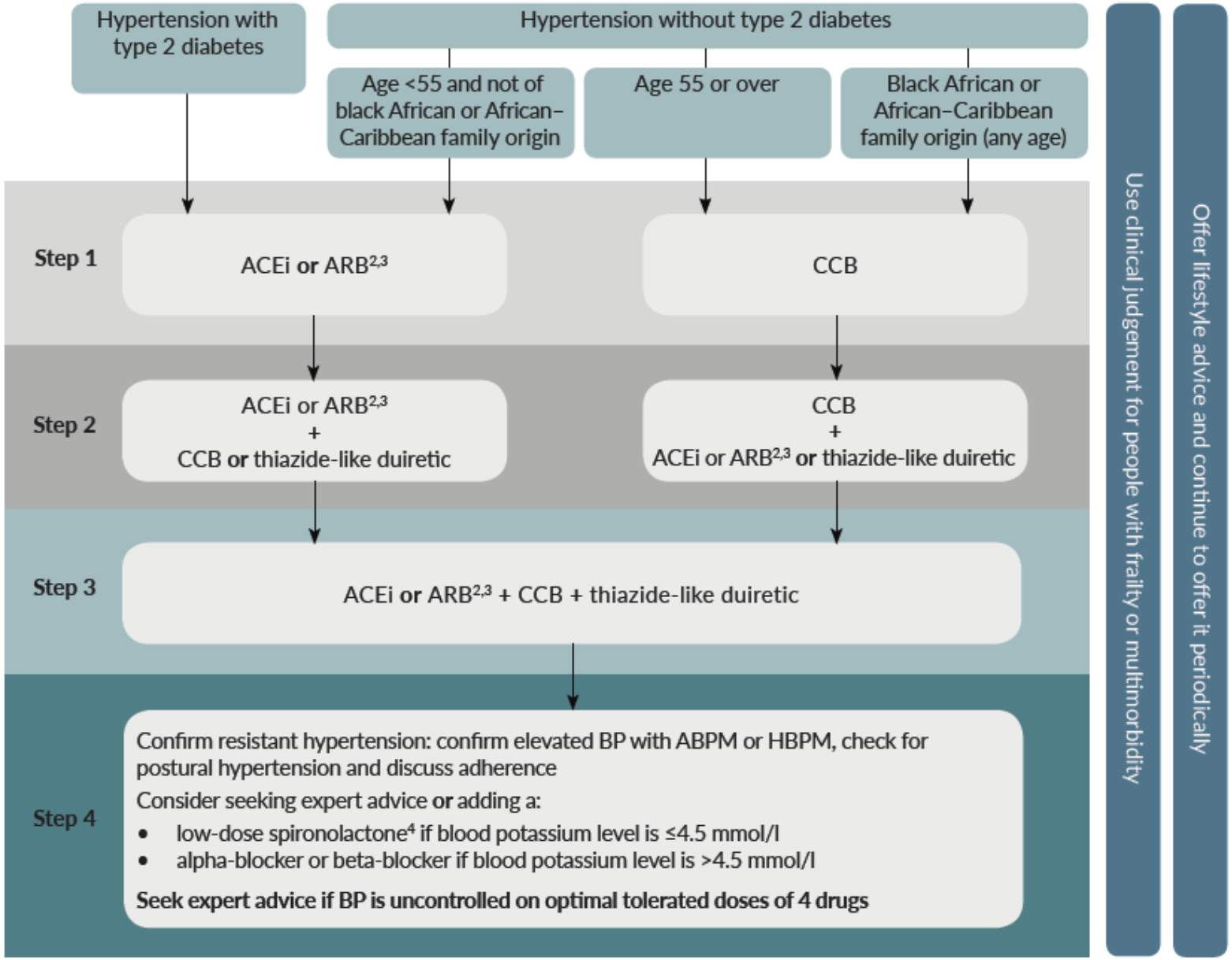


Stage 2

Treatment


DASHdiet
6-8
servings per day
of whole grains
4-5
servings per day
of vegetables
4-5
servings per day
of fruits
2-3
servings per day of
fat-free or low-fat dairy
4-5
servings per week of
nuts, seeds, legumes
Less than 6
servings per day of
lean meat, poultry, fish
Less than 5
servings per week
of sweets
2-3
servings per day
of fats and oils
Source: National Heart, Lung and Blood Institute
The DASH diet (Dietary Approaches to Stop Hypertension) has been shown to help lower blood pressure and prevent heart disease, stroke, diabetes and even some forms of cancer. It focuses on eating more fresh fruits and vegetables.
This is a guide to how much of each food group you should eat every day, based on eating 2,000 calories per day.
UKHealthCare
Gill Heart Institute

Choice of antihypertensive drug[1], monitoring treatment and BP targets



Monitoring treatment

Use clinic BP to monitor treatment.

Measure standing and sitting BP in people with:

- type 2 diabetes **or**
- symptoms of postural hypotension **or**
- aged 80 and over.

Advise people who want to self-monitor to use HBPM. Provide training and advice.

Consider ABPM or HBPM, in addition to clinic BP, for people with white-coat effect or masked hypertension.

BP targets

Reduce and maintain BP to the following targets:

Age <80 years:

- Clinic BP <140/90 mmHg
- ABPM/HBPM <135/85 mmHg

Age ≥80 years:

- Clinic BP <150/90 mmHg
- ABPM/HBPM <145/85 mmHg

Postural hypotension:

- Base target on standing BP

Frailty or multimorbidity:

- Use clinical judgement

[1]For women considering pregnancy or who are pregnant or breastfeeding, see NICE's guideline on hypertension in pregnancy. For people with chronic kidney disease, see NICE's

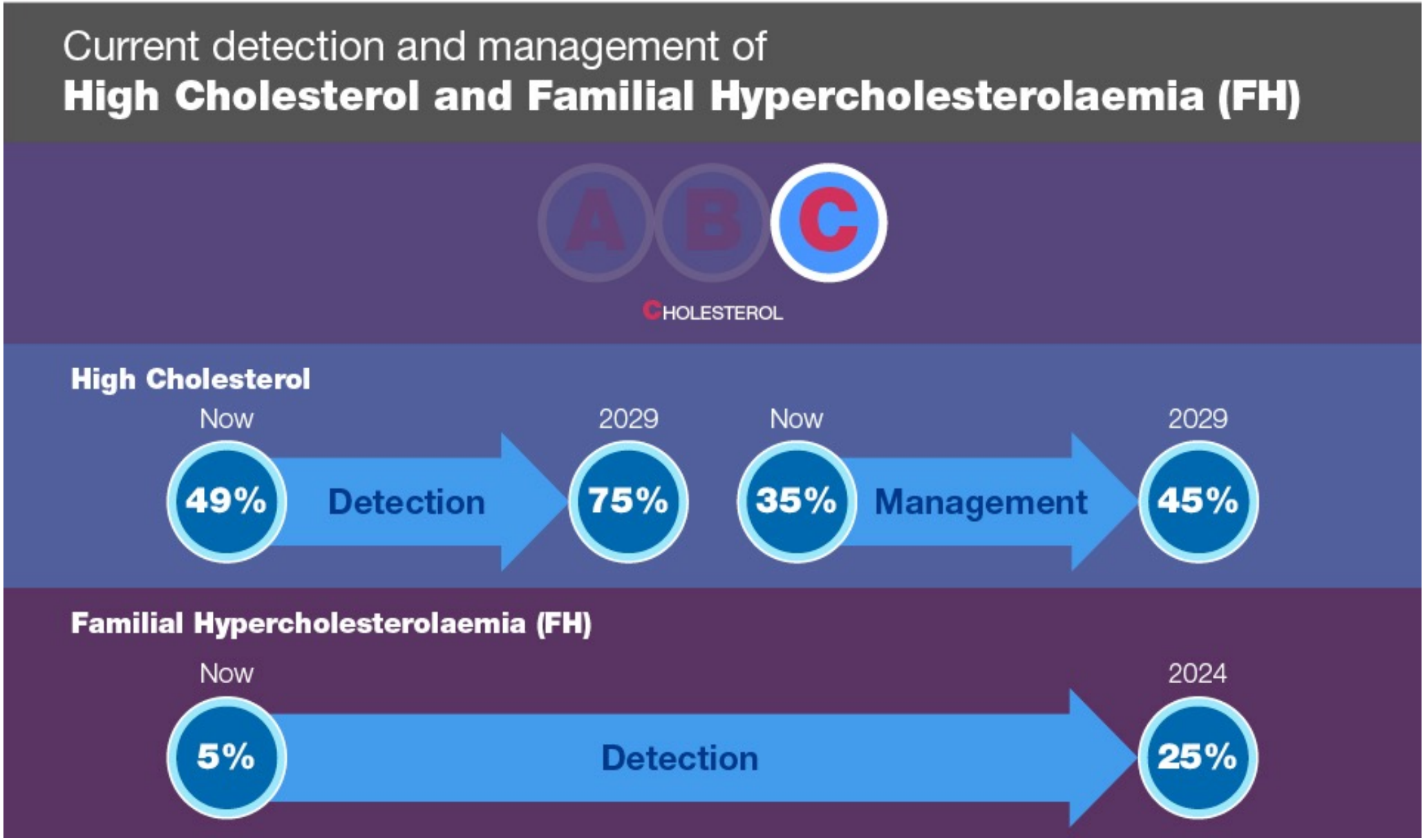
In a nutshell

- Under 55 and/or diabetes? ACEi or ARB
- 55+ or African-Caribbean? CCB
- Step 2 – add the other one OR thiazide-like diuretic
- Before step 3 – check adherence to meds and lifestyle
- Step 3 means all three

”C"

Cholesterol

Current detection and management of **High Cholesterol and Familial Hypercholesterolaemia (FH)**



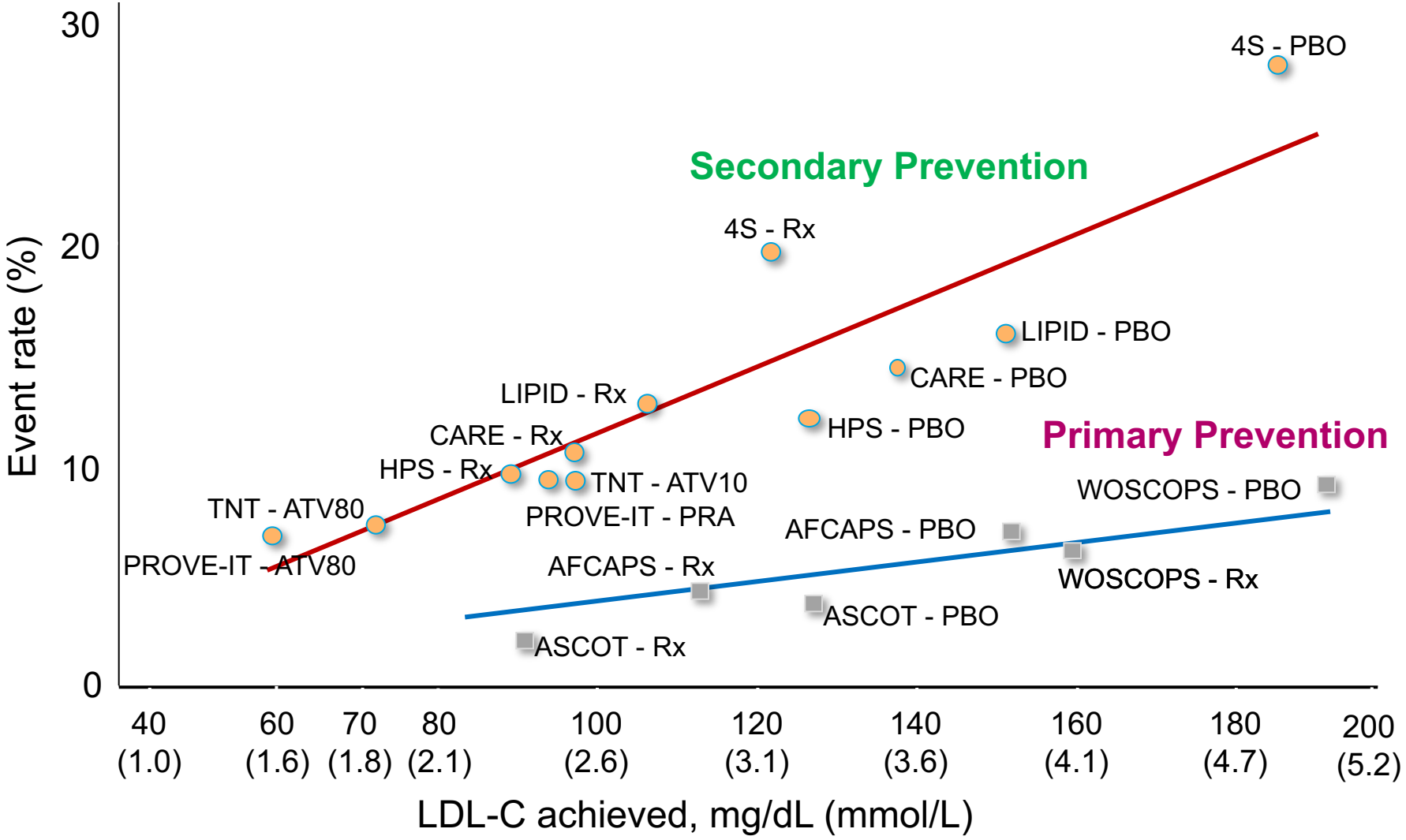
Lipoproteins HDL … LDL and non HDL

- **High Density (Highly desirable) Lipoprotein or HDL**
  - is inversely related to CHD risk….the higher the better!
  - average HDL value in the UK is 1.2 for men and 1.4 for women.
  - TC/HDL ratio greater predictive value for CHD than LDL .

- **Low Density (Less desirable) Lipoprotein**
  - is directly related to CHD risk….the lower the better

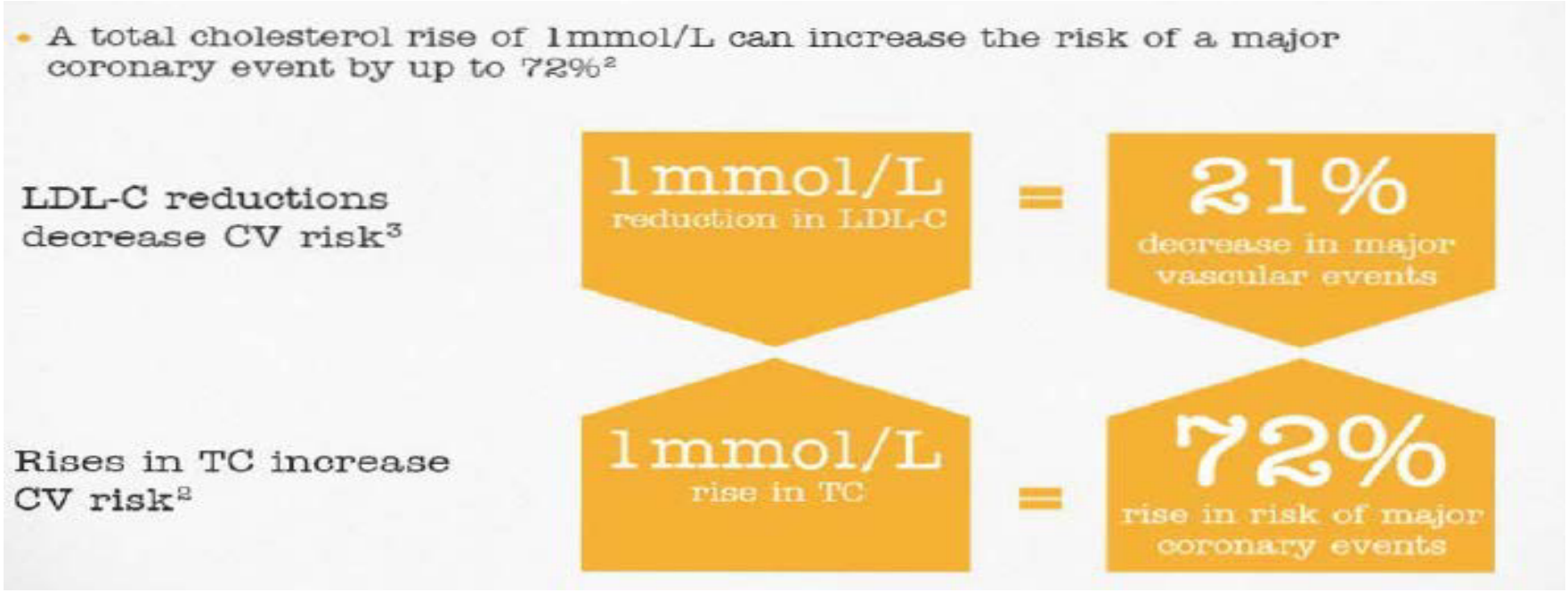
- **Non-HDL cholesterol (Not desirable) ….TC minus HDL**
  - is directly related to CHD risk….the lower the better
  - calculated by subtracting HDL from the total cholesterol
  - has a greater predictive value for CHD than LDL
  - is a surrogate for Apolipoprotein B

On-Treatment LDL and CHD Events in Statin Trials



Adapted from Rosenson RS. *Expert Opin Emerg Drugs*. 2004;9:269-279.
LaRosa JC et al. *N Engl J Med*. 2005;352:1425-1435.

Non-adherence can lead to poor cholesterol management thereby increasing CV risk



1. Jacobson TA. *Mayo Clinic Proc* 2008; 83: 687–700.
2. NICE clinical guideline 67 for lipid modification. Available at: www.nice.org.uk Last accessed November 2014
3. Baigent C, et al. *Lancet* 2005; 366:1267–1278.

Lipid profiles …… the BIGGER picture

- Patient A - Tot Chol 5.5 : HDL 2.4, LDL 2.6, Non-HDL 3.1 ,
  TG 1.9, TC/HDL 2.3

- Patient B - Tot Chol 5.5 : HDL 0.7, LDL 4.0, Non-HDL 3.8, TG 4.9, TC/HDL 7.8

- 95% confidence limits on a single cholesterol measurement are around ± 14% of the true value

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Cardiovascular disease: risk assessment and reduction including lipid modification (CG181)

Published July 2014

Primary prevention
Identifying people for a full formal risk assessment

Use a systematic strategy to identify those likely to be at high risk of CVD

- estimate CVD risk and prioritise those with a 10 year CVD risk of 10% or more for a full formal risk assessment

- Review risk in over 40's on an ongoing basis

Do not use opportunistic assessment as the main strategy to identify CVD in unselected people

Primary prevention

Offer atorvastatin 20mg to

- Up to age 84 years with *10% or greater risk of CVD over 10 years*
- CKD
- Type 1 Diabetes
  - over 40 years old
  - for 10 years or not
  -concomitant nephropathy or CVD risk factors

Consider atorvastatin 20mg

- all adults with Type 1 Diabetes
- over 85 years old

GDG on…..”Why atorvastatin 20mg”

- QALY £4125
- **“most clinically and cost effective option for Primary Prevention”**

Lipid modification therapy

- Use evidence based therapies that reduce CVD morbidity and mortality
- Statins lower LDL
- If using statins then choose one of high intensity and low acquisition cost

Reduction in low-density lipoprotein cholesterol

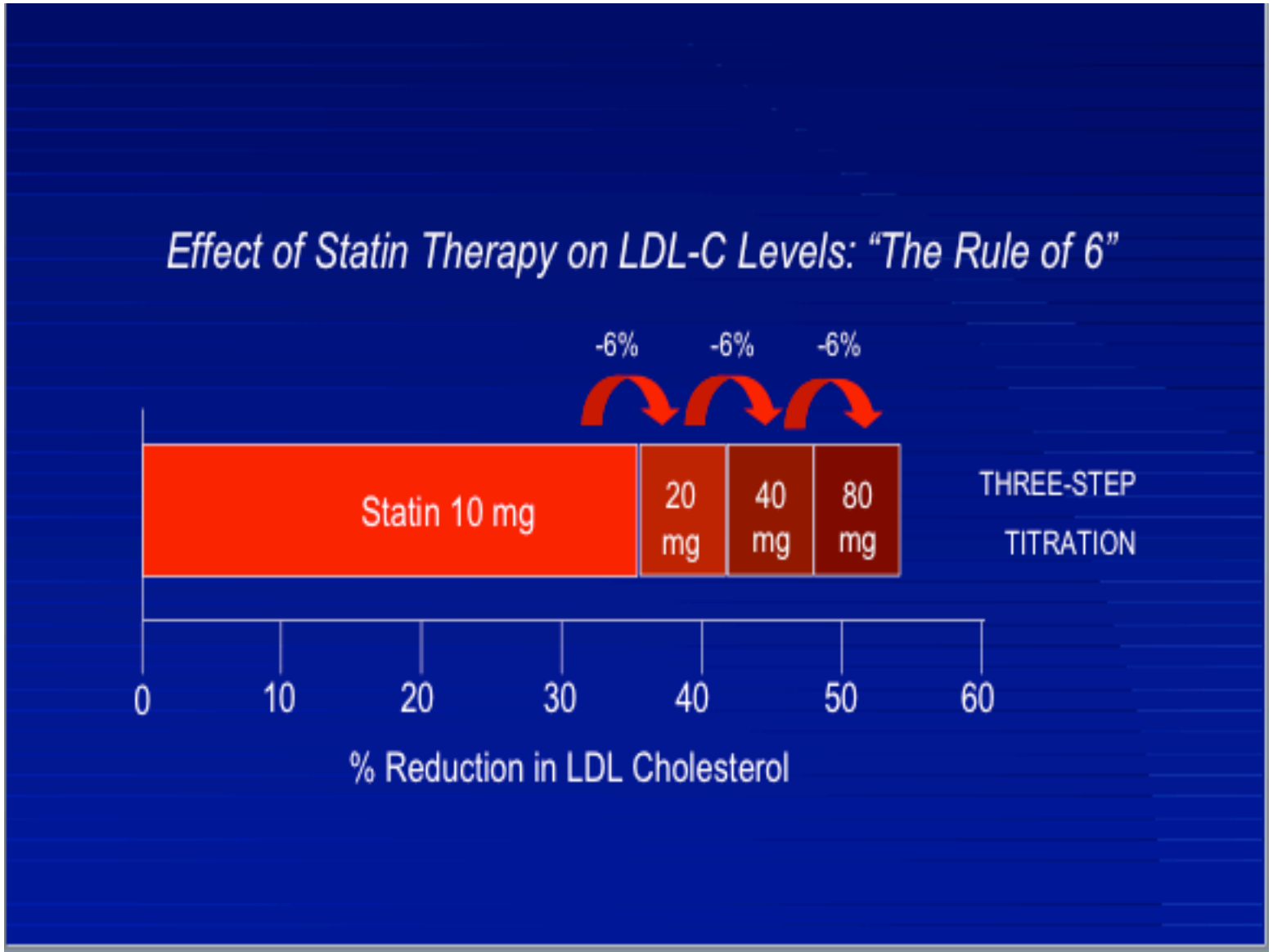
Dose (mg/day)	5	10	20	40	80
Fluvastatin	-	-	21%[1]	27%[1]	33%[2]
Pravastatin	-	20%[1]	24%[1]	29%[1]	-
Simvastatin	-	27%[1]	32%[2]	37%[2]	42%[3,4]
Atorvastatin	-	37%[2]	43%[3]	49%[3]	55%[3]
Rosuvastatin	38%[2]	43%[3]	48%[3]	53%[3]	-

1. 20–30%: low intensity
2. 31–40%: medium intensity
3. Above 40%: high intensity
4. Note advice from the MHRA about the increased risk of myopathy associated with high-dose (80 mg) simvastatin (Drug Safety Update May 2010)

Choose statin of high intensity and low acquisition cost

Adapted from NICE Guideline CG181. Available at: https://www.nice.org.uk/guidance/cg181/resources/cardiovascular-disease-risk-assessment-and-reduction-including-lipid-modification-pdf-35109807660997. Last accessed: 20 February 2019.

Statin therapy –”the rule of 6”



NICE Primary Prevention Decision Aid

Cardiovascular risk 10% over 10 years: no treatment

If 100 people at this level of risk take no statin, over 10 years on average:

- 90 people will not develop CHD or have a stroke (the green faces)
- 10 people will develop CHD or have a stroke (the red faces).

Cardiovascular risk 10% over 10 years: taking atorvastatin

If all 100 people take atorvastatin for 10 years, over that time on average:

- 4 people will be saved from developing CHD or having a stroke (the yellow faces)
- 90 people will not develop CHD or have a stroke, but would not have done anyway (the green faces)
- 6 people will still develop CHD or have a stroke (the red faces).

Follow up & targets in Primary and Secondary prevention

- Measure TC, HDL and non-HDL at 3 months
- ***Aim for a greater than 40% reduction in non-HDL cholesterol***
- Consider annual reviews for all patients thereafter

If not achieved non-HDL target

- optimise lifestyle measures(if not already achieved)
- Consider titrating dose of atorvastatin to 80mg where not already taking
- Consider combination therapy with ezetimibe

- **…still not achieved non-HDL target**
- Consider alternative (higher potency) statin
- ***Consider combination therapy with ezetimibe***

- *Discuss with patients (at medication review) on low/medium intensity statins the benefits/risks of high intensity statins*

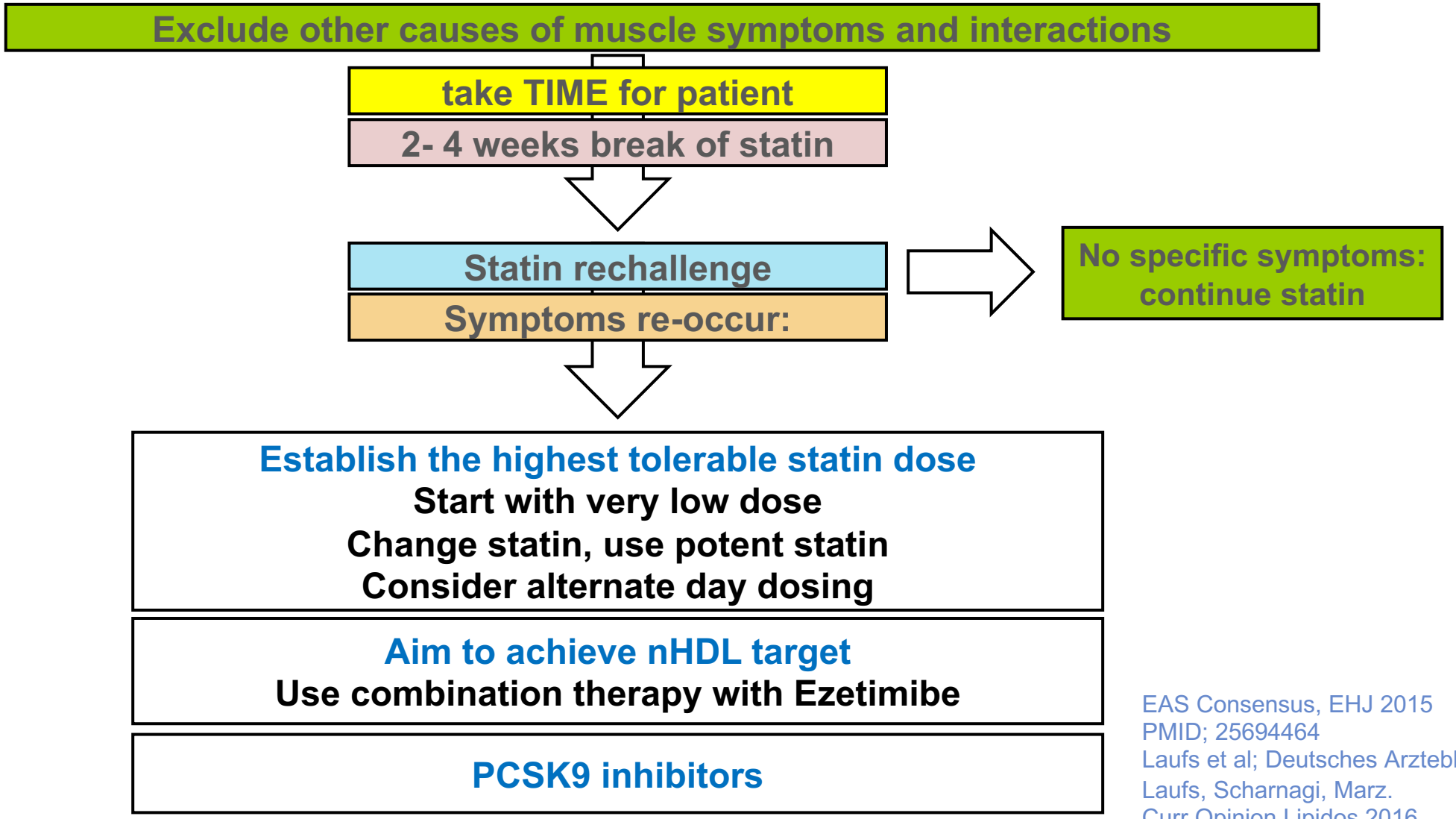
	Blinded randomised phase (ASCOT-LLA)		Non-blinded non-randomised phase	
	Placebo (n=5079)	Atorvastatin (n=5101)	Atorvastatin non-user (n=3490)	Atorvastatin user (n=6409)
Muscle related				
Patients (n)	283	298	124	161
AE rate (% per annum)	2·00%	2·03%	1·00%	1·26%
HR (95% CI)	1	1·03 (0·88–1·21)	1	1·41 (1·10–1·79)
p value	..	0·72	..	0·006
Erectile dysfunction				
Patients (n)	302	272	99	88
AE rate (% per annum)	2·14%	1·86%	0·80%	0·68%
HR (95% CI)	1	0·88 (0·75–1·04)	1	0·89 (0·66–1·20)
p value	..	0·13	..	0·44
Sleep disturbance				
Patients (n)	210	149	82	72
AE rate (% per annum)	1·46%	1·00%	0·66%	0·56%
HR (95% CI)	1	0·69 (0·56–0·85)	1	0·87 (0·63–1·20)
p value	..	0·0005	..	0·40
Cognitive impairment				
Patients (n)	32	31	36	22
AE rate (% per annum)	0·22%	0·20%	0·29%	0·17%
HR (95% CI)	1	0·94 (0·57–1·54)	1	0·59 (0·34–1·02)
p value	..	0·81	..	0·06

First event only in each phase reported; definite and probable AEs reported; number of patients with at least one event reported. AE=adverse event. HR=hazard ratio.

Table 2: **Risk of adverse events of interest**

The ”NOCEBO effect”

Management of patients with possible statin related muscle symptoms



EAS Consensus, EHJ 2015
PMID; 25694464
Laufs et al; Deutsches Arzteblatt 2015
Laufs, Scharnagi, Marz.
Curr Opinion Lipidos 2016

The statin-associated risk of developing diabetes is low in absolute terms when compared with the reduction in coronary events[1]

- Results of a meta-analysis of 13 trials show that statins, as a class, slightly increase the risk of diabetes[1]
- In pre-diabetic patients (FPG 5.6–6.9 mmol/L), rosuvastatin has been associated with an increased risk of diabetes[2]
- Additional factors hypertension, ↑ Triglycerides, ↑BMI
- The risk, however, is outweighed by the reduction in vascular risk with statins and therefore should not be a reason for stopping statin treatment[1-3]

NNH: number needed to harm – 1 additional case of diabetes for every 498 patients treated per year[4]

NNT: number needed to treat – 155 patients treated with a statin to prevent 1 CV event per year[4]

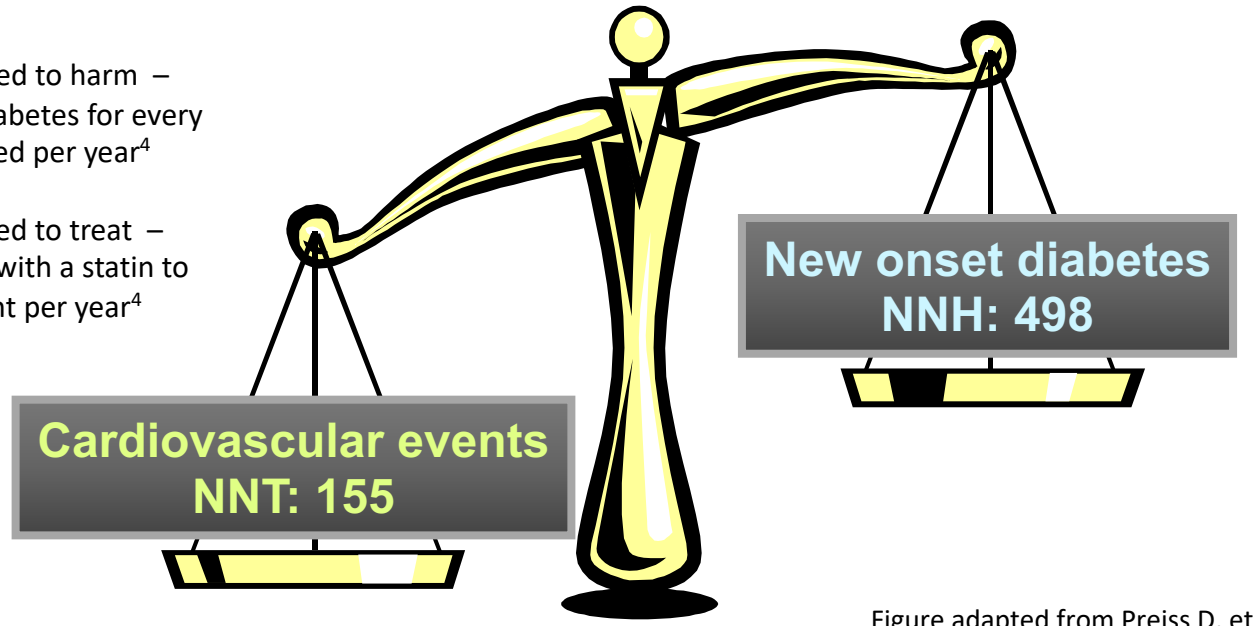


Figure adapted from Preiss D, et al. 2011[4]

1. Sattar N, et al. *Lancet* 2010; 375: 735–742.
2. CRESTOR. Summary of Product Characteristics. Nov 2014.
3. Lipitor. Summary of Product Characteristics. Nov 2014
4. Preiss D, et al. *JAMA.* 2011; 305: 2556–2564.

Thank you …any questions?

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