



RELY[®]

Study of stroke prevention
in atrial fibrillation

THE RE-LY[®] STUDY RESULTS

Press Briefing

Sunday 30th August 2009, 14:00-15:00



Atrial fibrillation and stroke: The unmet need

Stefan H. Hohnloser, M.D.

J.W. Goethe University
Frankfurt, Germany



AF: a common disease

▶ AF is the most common heart rhythm disturbance

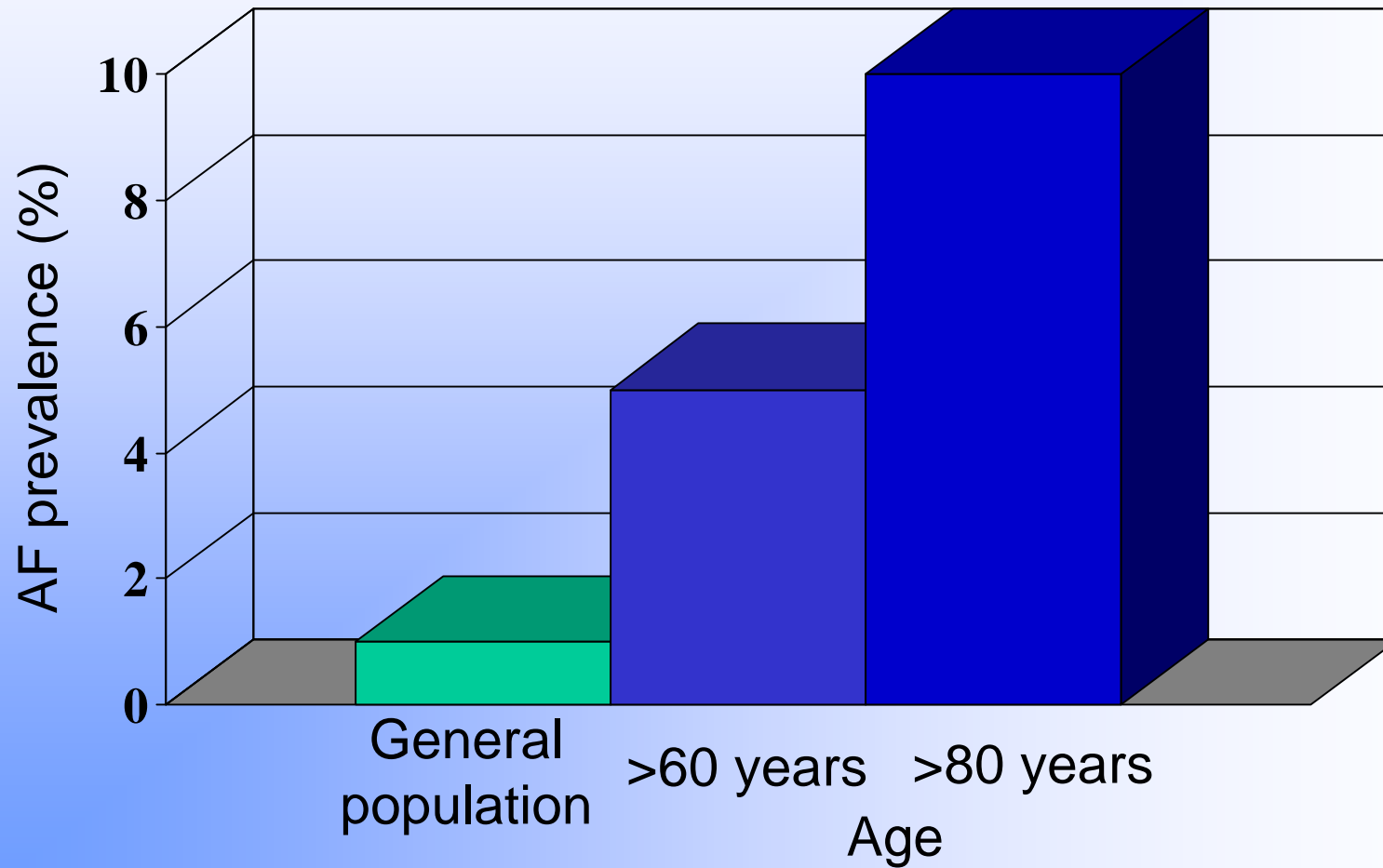
▶ It is estimated that a quarter of 40 year olds will develop AF during their lifetime

▶ In 2007, 6.3 million people in the US, Japan, Germany, Italy, France, UK and Spain were living with diagnosed AF

▶ **It is estimated that this figure may double within 30 years due to the ageing population**



AF: prevalence increases with age





Consequences of AF

▶ AF doubles the risk of death compared with normal heart rhythm

▶ AF costs the EU approximately €13.5 billion a year; amounting to ~€3,000 per patient

▶ During AF, blood is not completely pumped out of the heart, causing it to pool and clot. If a piece of the clot leaves the heart and travels to a blood vessel supplying the brain with oxygen and nutrients, this leads to stroke.

- AF increases the risk of ischaemic stroke up to 7 times



AF and stroke

▶ AF is responsible for 15% of all strokes

▶ A quarter of patients will have another stroke

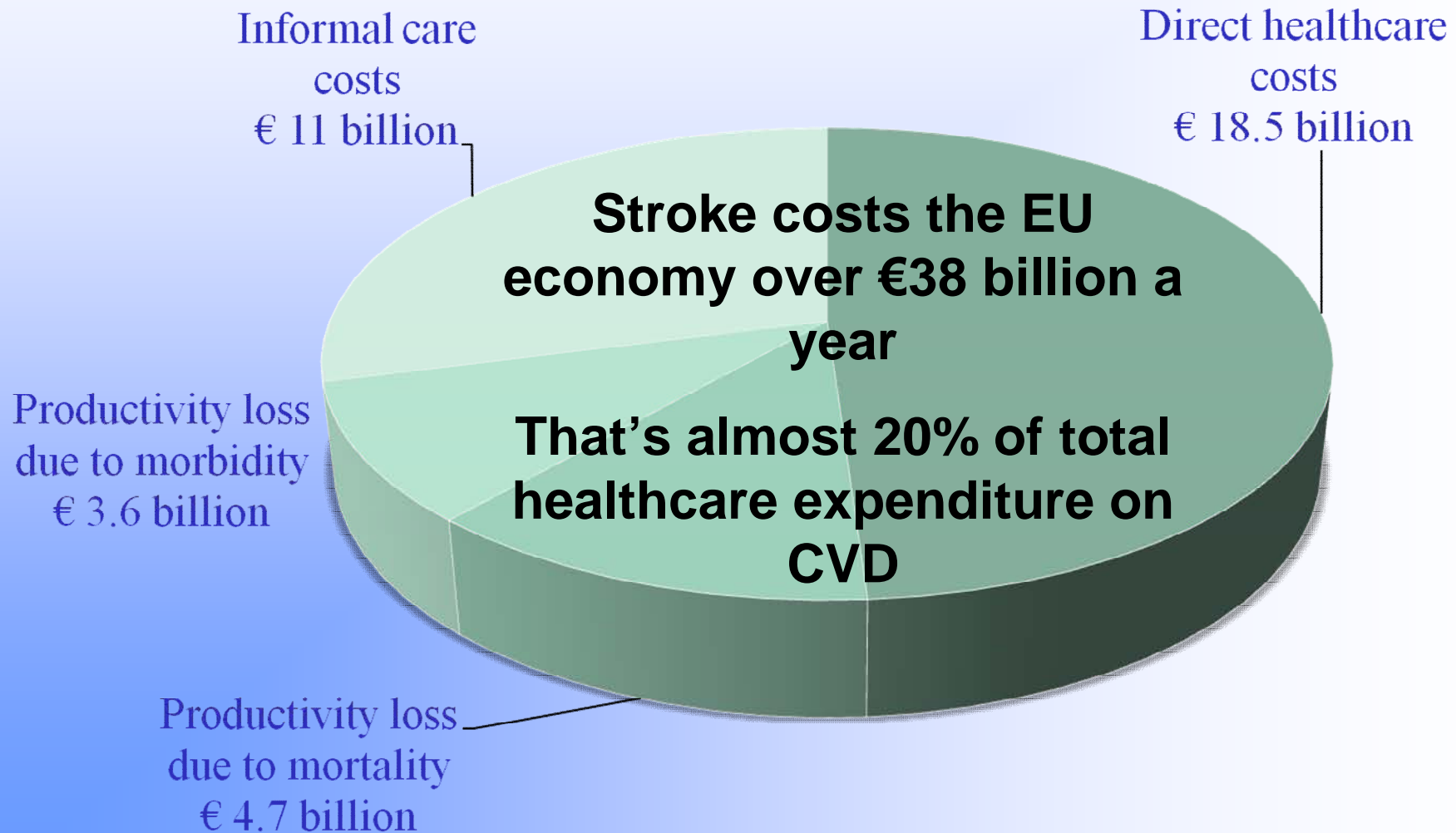
▶ Strokes associated with AF tend to be particularly severe, with increased likelihood of death or disability

▶ One month after an AF-related stroke up to half of patients are disabled

▶ **After one year up to half of patients are dead**



The financial cost of stroke





Stroke prevention in AF: VKA therapy

VKA therapy is highly effective when well-controlled in clinical trials:

Reduces the
risk of stroke
by 68%

Reduces the
risk of death
by 25%

Two out of three strokes due to AF can be prevented with appropriate anticoagulation



Limitations of VKAs

Unpredictable response

**Narrow therapeutic window
(INR range 2-3)**

Routine coagulation monitoring

Slow onset/offset of action

VKA therapy has several limitations that make it difficult to use in practice

Frequent dose adjustments

Numerous food-drug interactions

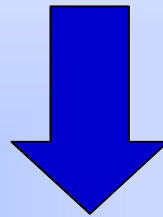
Numerous drug-drug interactions

Warfarin resistance



Limitations of VKAs

Therapeutic range for effective and safe anticoagulation with VKA therapy is difficult to achieve and maintain



VKA therapy is underused

Use of VKA therapy may result in inappropriate INR control



Potential reasons for under-use of VKA therapy and poor INR control

Difficulty in explaining VKA treatment to patients, and their subsequent compliance

Logistics in arranging the subsequent support, education and administration of anticoagulation with VKA treatment

Physician-led resistance over prescribing a drug that is unpredictable



The need for a new oral anticoagulant

Due to the limitations of warfarin, there is a need for new oral anticoagulants that:

Do not require coagulation monitoring

Provide the optimal balance between stroke prevention and bleeding risk

Have predictable and consistent effects

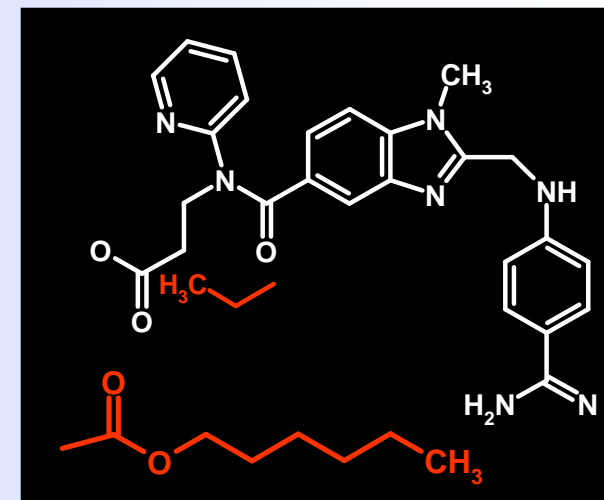
Have fewer drug-drug interactions

Have no drug-food interactions



Dabigatran etexilate

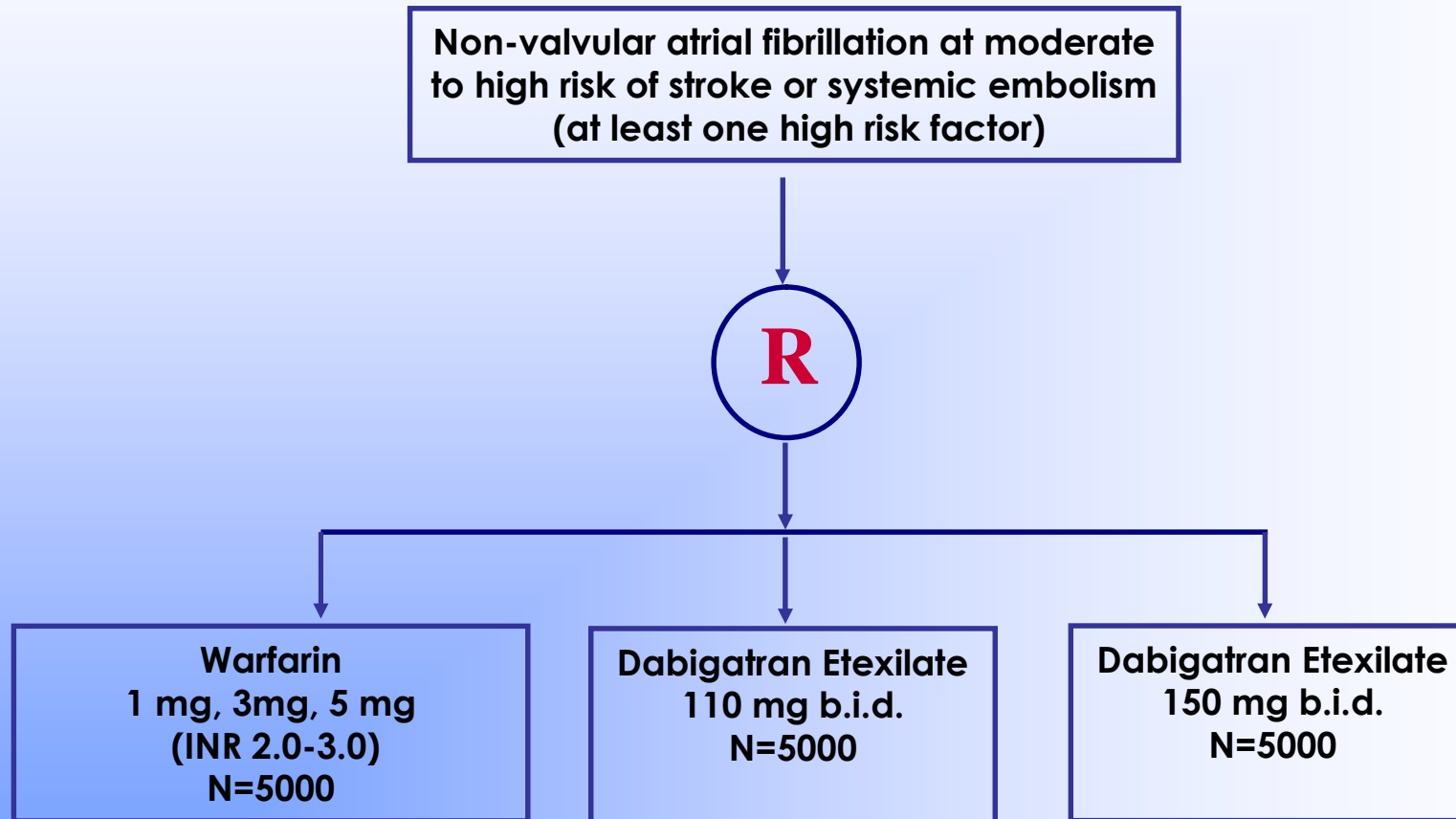
- Dabigatran etexilate is an orally bioavailable *prodrug* of dabigatran
- Oral absolute bioavailability is 6.5%, some pH dependence
- Dabigatran is a *direct thrombin inhibitor*
- Specific for thrombin
- Plasma half-life is 12-17 hours
- *Fixed dosing*, predictable response
- Not metabolized by cytochrome P450 system, thus low drug-drug interactions
- *No need for monitoring*



Dabigatran **etexilate**



The RE-LY Study



- 15,000 patients randomized over a two year period. Minimum 1 year follow-up, maximum of 3 years and mean of 1.5 years of follow-up.
- Patients will be recruited from 1,000 Clinical Centres in 44 countries.



RELY[®]

Study of stroke prevention
in atrial fibrillation

RE-LY trial results

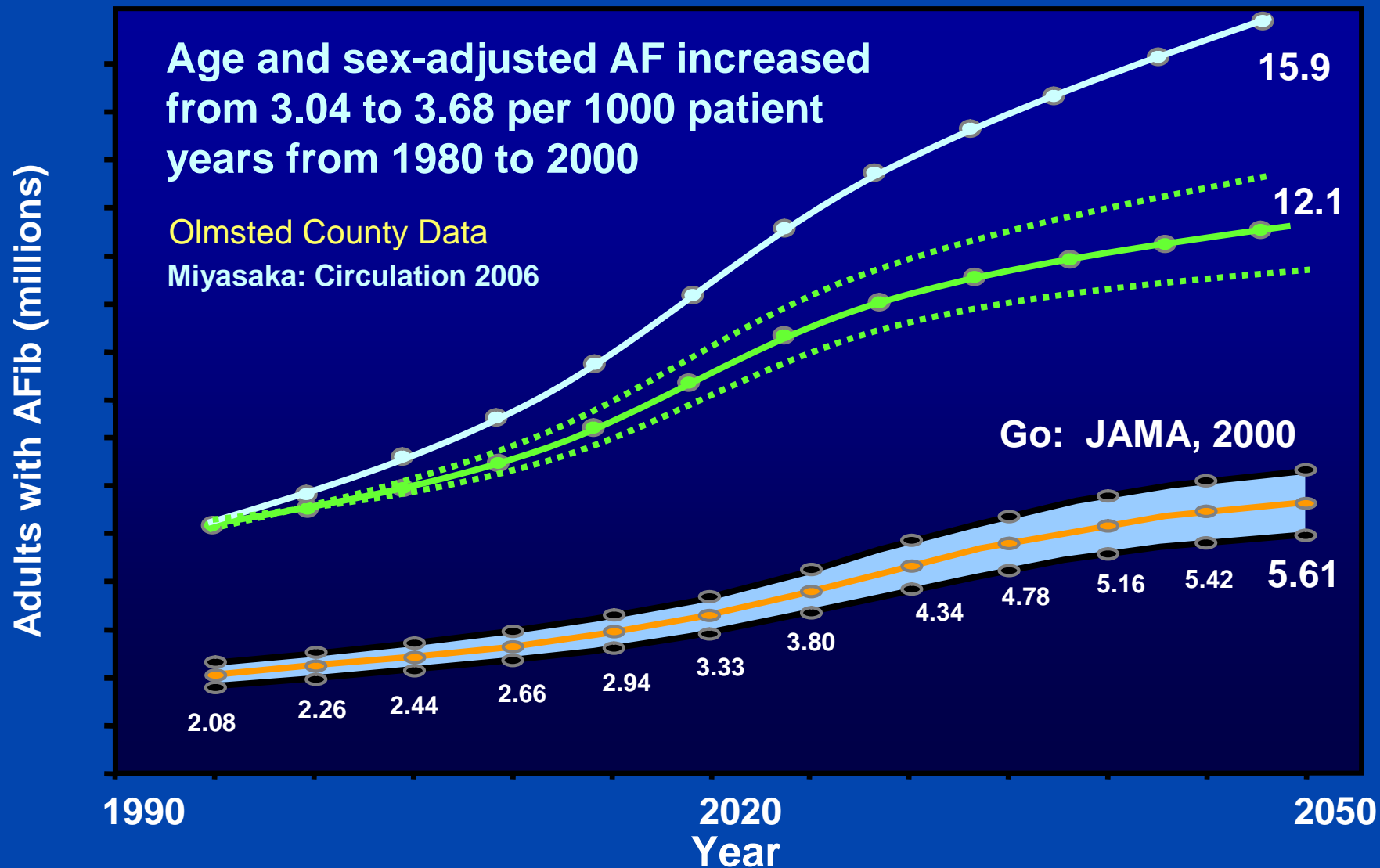
Implications for physicians and patients

Dr Sarah Jarvis

GP, GP trainer and fellow of the Royal College of
General Practitioners in the UK

Warfarin and the GP

The AF epidemic



Who gets warfarin?

Year	Model	Risk Factors	Event Rate/ Recommendation
2006 ACC/AHA/ESC GLs	CHADS ₂	<u>C</u> HF (1), <u>H</u> TN (1), <u>A</u> ge ≥ 75 yrs (1), <u>D</u> iabetes (1), History of <u>S</u> troke/TIA (2)	Score 0-1: 1.9-2.8% Aspirin Score 2-4: 4.0-5.9% Warfarin Score 5-6: 12.5-18.2% Warfarin

What does it mean to my patients?

Most will have heart disease

Which means a change of lifestyle for many...

They are advised they **MUST** change their diets



Advantage: the Mediterranean diet!!



Which means...

Less meat

More oily fish

Less butter and dairy fat

Substitute mono-polyunsaturates (rape seed oil, olive oil, etc)

Reduce unrefined carbohydrates

More fruit, vegetables and salad

If you're on warfarin, it's not as easy as it looks



“The cat made this look easy”

Breakfast

Bran flakes with semi-skimmed milk

1 piece toast with butter

Orange juice

Coffee with semi-skimmed milk

Mid-morning break

Cup of tea with semi-skimmed milk

2 digestive biscuits



OVERCONFIDENCE

This is going to end in disaster, and you have no one to blame but yourself.

Lunch

Chicken breast shallow-fried with rapeseed oil

Green salad

Grapefruit juice

Piece of fruit

Espresso

But will dinner be such a disaster?



fun100sh.com

Dinner

Feta cheese and walnut salad

Cottage pie with steamed broccoli and cauliflower

Grilled fish with new potatoes and garlic spinach

Roast beef with roast potatoes, peas and brussel sprouts

Glass of wine

Drink of cocoa

“The odd herbal remedy is fine, isn’t it?”

Camomile

Garlic

Ginseng

Co-enzyme Q10

What does it mean to me?

My surgery:

- 11,000 patients
- 108 patients on warfarin
- 1 half-day session per week dedicated to warfarin monitoring
 - 1 nurse and 1 doctor
 - 28 patients per session
 - Every week is a problem for some patients



“What’s my number, doc?”

Average time within therapeutic range – 36%

Too high – risk of haemorrhagic stroke or other major bleed

Too low – not protected against thromboembolic stroke

Longest time between doctor visits – 10 weeks

Average time in our surgery – 3.2 weeks

Which is time consuming for me and very stressful
for my patients

So what could RE-LY[®] mean to me and my patients?

No more food interactions

Very few drug interactions

No more anxiety about the risks of being outside the therapeutic range

No dose adjustments

No more monitoring

Patients attend their GP surgery every 3-6 months rather than every 1-10 weeks

Free to go on holiday

Nurses and doctors freed-up for other work

My patients can face the world with confidence





RELY®

Study of stroke prevention
in atrial fibrillation

Connolly SJ, Ezekowitz MD, Yusuf S *et al.*
Dabigatran versus Warfarin in Patients with Atrial Fibrillation.
N Eng J Med 2009; 361. Published online 30 Aug 2009.