UCLPartners

Cholesterol

The Size of the Prize for Cardiovascular Disease Prevention

Overview

Background

- The UCLPartners search and stratification tools, part of the UCLPartners Proactive Care Frameworks, stratify patients with high impact conditions so that care can be optimised according to clinical priority and capacity.
- The UCLPartners cholesterol search tool was run in **2 sample Integrated Care Systems (ICSs).** This shows that most patients with pre-existing cardiovascular disease (CVD) need cholesterol optimisation – they are **either on no treatment or suboptimal treatment**.
- Stratification identifies patients who are:
    - On no or suboptimal lipid lowering therapy and so eligible first for statin optimisation, with subsequent titration to second line therapies if needed
    - Immediately eligible for second line therapies because they are on maximal statins but not achieving target cholesterol

Modelling

- UCLPartners has modelled the Size of the Prize for Cholesterol for the 2 pilot ICSs. This gives a trajectory of realistic ambitions for CVD prevention, showing that **large numbers of heart attacks and strokes could be prevented through cholesterol optimisation**.
- CVDprevent has confirmed the UCLP finding that around **20% of people with CVD in England are *not* on statins**. It is likely that there are similar levels of suboptimal dosing and potential population health impact in all ICSs.

CVDACTION

- Note that ***CVDaction*** (a new tool being developed by UCLPartners to complement CVDprevent) will provide every practice in England with patient-level actionable data on opportunities for optimisation in cholesterol and other risk factors for CVD (AF, BP, CKD, diabetes, pre-diabetes).

AHSN Blood Pressure Optimisation Programme

- The AHSN Network BP Optimisation Programme being implemented in all ICSs provides an opportunity for early, targeted action on cholesterol because it focuses on **both blood pressure and lipid optimisation** in people with hypertension.

UCLPartners Cholesterol Stratification in two Integrated Care Systems

- The UCLPartners stratification tool for cholesterol was run in two pilot Integrated Care Systems (one London, one East of England)
- The UCLPartners stratification tool (built for EMIS and SystmOne) stratifies patients with pre-existing CVD into 4 cohorts:
    1. Not on a statin
    2. On statin but suboptimal intensity (ie not atorvastatin or rosuvastatin)
    3. On high intensity statin but suboptimal dose (eg atorvastatin 20/40mg)
    4. On maximal statin dose but non-HDLc* above 2.5 mmol/l (threshold for second line therapies)

- For this Size of the Prize modelling we have combined cohorts 2 and 3 into a single group ('suboptimal statin'). These patients need treatment optimisation with a systematic approach to statin hesitancy and shared decision making,

Please note

- Cohort 4 above only captures patients who have had non-HDLc measured. There may be significant numbers of patients on maximal dose statins who have not had monitoring blood tests (reflecting the historic *Fire-and-Forget* rule) – and hence may be immediately eligible for second line therapies.

The following slides highlight the numbers of cardiovascular events that could be avoided by optimising therapy in all of these patients.

*non-HDLc = non-HDL Cholesterol

ICS 1 (pop 1.7 million) – Cholesterol Size of the Prize Modelling July 2022

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Secondary prevention total population: 49654							
Patient cohort	**No. patients**	**% secondary prevention population**	**Action needed**	**NNT**	**Potential events prevented**	**Note**	**Reference and NNT calculation**
1. Not on statin	10,623	21%	Initiate statin and use second line therapies if inadequate fall in non-HDLc	10	**1062**	CV events (CVD death, MI or strokes) avoided over 5 years	Collins Lancet meta-analysis NNT 10 over 5 years https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(16)31357-5/fulltext
2. On suboptimal statin	29,158	59%	Optimise statin and use second line therapies if inadequate fall in non-HDLc	45	**648**	CV events (CVD death, MI or strokes) avoided over 5 years	TNT study 10mg atrovastatin vs 80mg atorvastatin NNT 45 over 5 years
3. Not at target despite maximal statin	3562	7%	Add second line therapies	54	**66**	CV events (CVD death, MI or strokes) avoided over 2-5 years	No NNT for Inclisiran. NNT for ezetimibe = 42-50 over 5 years; NNT for PCSK9imab = 65 over 2 yrs. Mean NNT = 54 over 2-5 yrs nejm.org/doi/full/10.1056/NEJMoa050461

ICS 2 (pop 1.1million) – Cholesterol Size of the Prize Modelling July 2022

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Secondary prevention population: 51095 (Data from all but 2 practices included)							
Patient cohort	**No. patients**	**% secondary prevention population**	**Action needed**	**NNT**	**Potential events prevented**	**Notes**	**Reference and NNT calculation**
1. Not on statin	10200	20%	Initiate statin and use second line therapies if inadequate fall in non-HDLc	10	**1020**	CV events (CVD death, MI or strokes) avoided over 5 years	Collins Lancet meta-analysis NNT 10 over 5 years https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(16)31357-5/fulltext
2. On suboptimal statin	31218	61%	Optimise statin and use second line therapies if inadequate fall in non-HDLc	45	**694**	CV events (CVD death, MI or strokes) avoided over 5 years	TNT study 10mg atrovastatin vs 80mg atorvastatin NNT 45 over 5 years
3. Not at target despite maximal statin	Nos not available (local coding anomalies)		Add second line therapies			CV events (CVD death, MI or strokes) avoided over 2-5 years	No NNT for Inclisiran. NNT for ezetimibe = 42-50 over 5 years; NNT for PCSK9imab = 65 over 2 yrs. Mean NNT = 54 over 2-5 yrs nejm.org/doi/full/10.1056/NEJMoa050461

Learnings from the sample populations

National evidence: There is robust evidence that lipid lowering treatment is highly effective at preventing further heart attacks and strokes (ie admissions and deaths) in people with established CVD. Use of drugs to lower non-HDLc is recommended by NICE for all patients with CVD.

Sample Findings:

1. In the two sample ICSs (covering 2.8 million people), a **majority** of individuals with established CVD are ***not*** on recommended lipid lowering therapy:
    - 1 in 5 are on no statin
    - 3 in 5 are on suboptimal dose or intensity of statin
    - Group 3 identifies patients who are on maximal statin therapy but with non-HDLc not at target. These patients will be immediately eligible for second line therapies.
2. There is an additional group of patients with status unknown – patients with existing CVD on maximal dose high intensity statin who have not had non-HDLc checked since commencing statins. A proportion of these will have non-HDLc above target and **will be immediately eligible** for second line therapies

Note

- We have mapped a trajectory of ambition for the first two groups. Group 3 (maximal statins) has not been included in the trajectory because the numbers are relatively small and action (offer second line therapies) would not need to be phased.

The UCLPartners stratification will drive targeted CVD prevention

(See pathway slide 8)

1. Group 1 Patients with CVD not on statin
   - Initiate high dose high intensity statin – support shared decision making and address statin hesitancy
   - After 3 months check non-HDLc. If ≥2.5mmol/l (NICE recommends at least 40% reduction), discuss with patient options for second line therapies (including ezetimibe, inclisiran, PCSK9imab)
2. Group 2 Patients with CVD on statin but suboptimal dose or intensity
   - Titrate to high dose high intensity statin – support shared decision making and address statin hesitancy and / or intolerance
   - After 3 months check non-HDLc. If ≥2.5mmol/l (NICE recommends at least 40% reduction), discuss with patient options for second line therapies (including ezetimibe, inclisiran, PCSK9imab)
3. Group 3 – Patients with CVD on maximum dose high intensity statin but non-HDLc ≥2.5mmol/l (NICE recommends at least 40% reduction)
   - Discuss with patient options for second line therapies (including ezetimibe, inclisiran, PCSK9imab)
4. Status unknown – need blood test
   - Search for patients with CVD on maximal dose high intensity statin who have not had non-HDLc checked since commencing statins.
   - Arrange blood test to identify those whose non-HDLc is ≥2.5mmol/l (NICE recommends at least 40% reduction), and discuss with patient options for second line therapies (including ezetimibe, inclisiran, PCSK9imab)

Optimisation Pathway for Secondary Prevention

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Is patient on high dose, high intensity statin*?
(atorvastatin 80mg or equivalent)

Yes

No

Initiate / increase to high dose high intensity statin **
and re-enforce lifestyle and diet measures

Is non-HDL cholesterol < 2.5mmol/L? ***

Yes

No

Check adherence to statin and lifestyle measures ****

Consider ezetimibe 10mg daily
Reassess after three months. If non-HDL-C remains > 2.5mmol/L; consider injectable therapies arrange a fasting blood test and assess eligibility

Consider injectable therapies
If non-HDL chol > 2.5mmol/L; Arrange fasting blood test to assess eligibility:

- **Inclisiran** - if fasting LDL-C ≥ 2.6mmol/L

OR

- **Refer for PCSK9i (mAB)**⁺ if fasting LDL-C > 4mmol/L (or > 3.5mmol/L if recurrent events)

If eligibility criteria are not met, consider ezetimibe 10mg daily (if not previously considered)

Review annually for adherence to drugs and support for diet and lifestyle measures

Optimal High Intensity Statin for secondary prevention (High intensity statins are substantially more effective at preventing cardiovascular events than low/medium intensity statins)	
Atorvastatin	80mg
Rosuvastatin	20mg

* Dose may be limited if:
- eGFR<30ml/min
- Drug interactions
- Intolerance
- Older age / frailty

** See statin intensity table

*** Current NICE Guidance recommends at least a 40% reduction in non- HDL cholesterol

**** **If statin not tolerated**, follow statin intolerance pathway and consider ezetimibe 10mg daily +/- bempedoic acid 180mg daily. If non HDL-C remains > 2.5mmol/L despite other lipid lowering therapies consider injectable therapies.

⁺ NICE Guidance: Evolocumab, Alirocumab

Size of the Prize
For cholesterol optimisation

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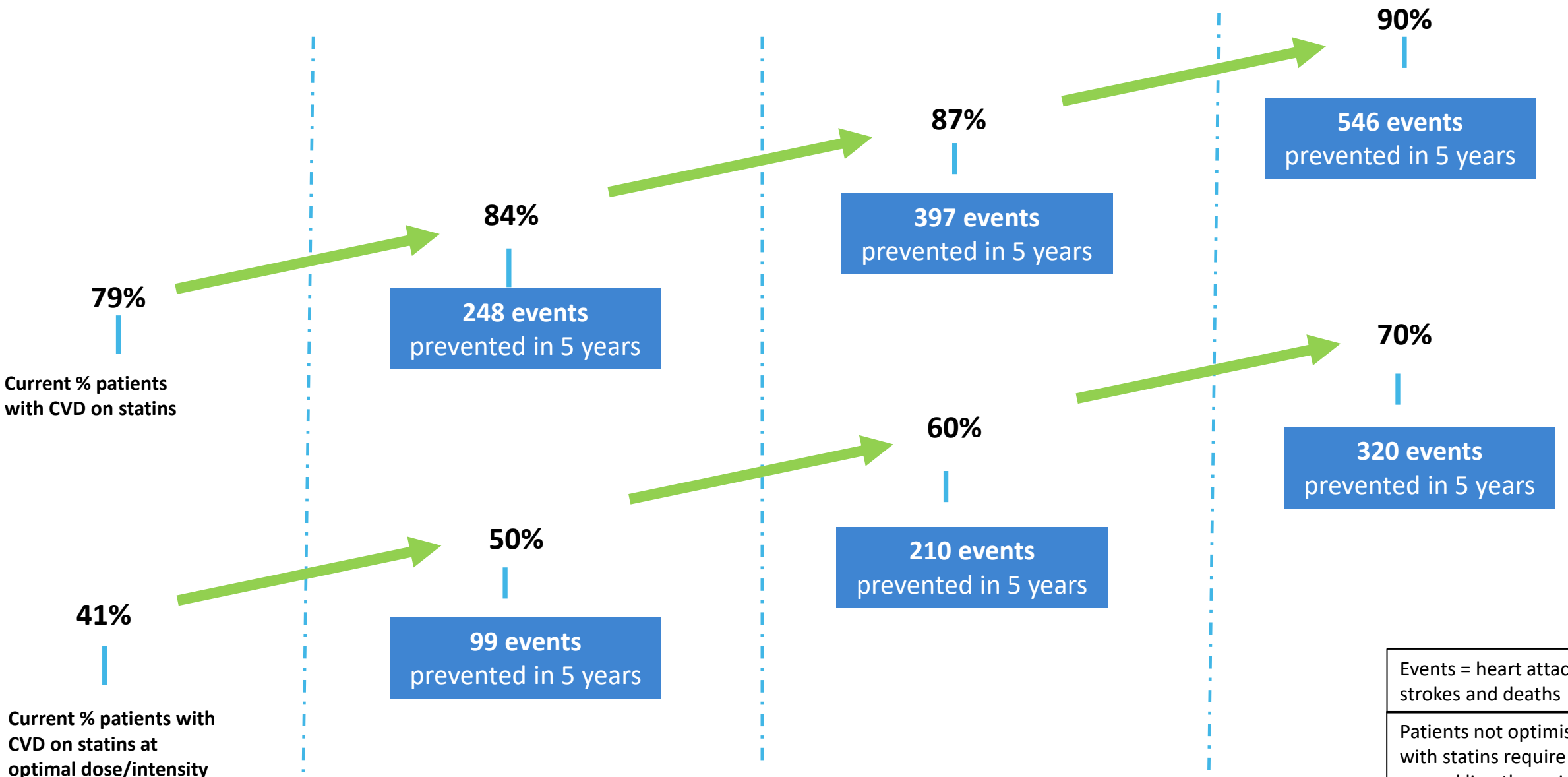
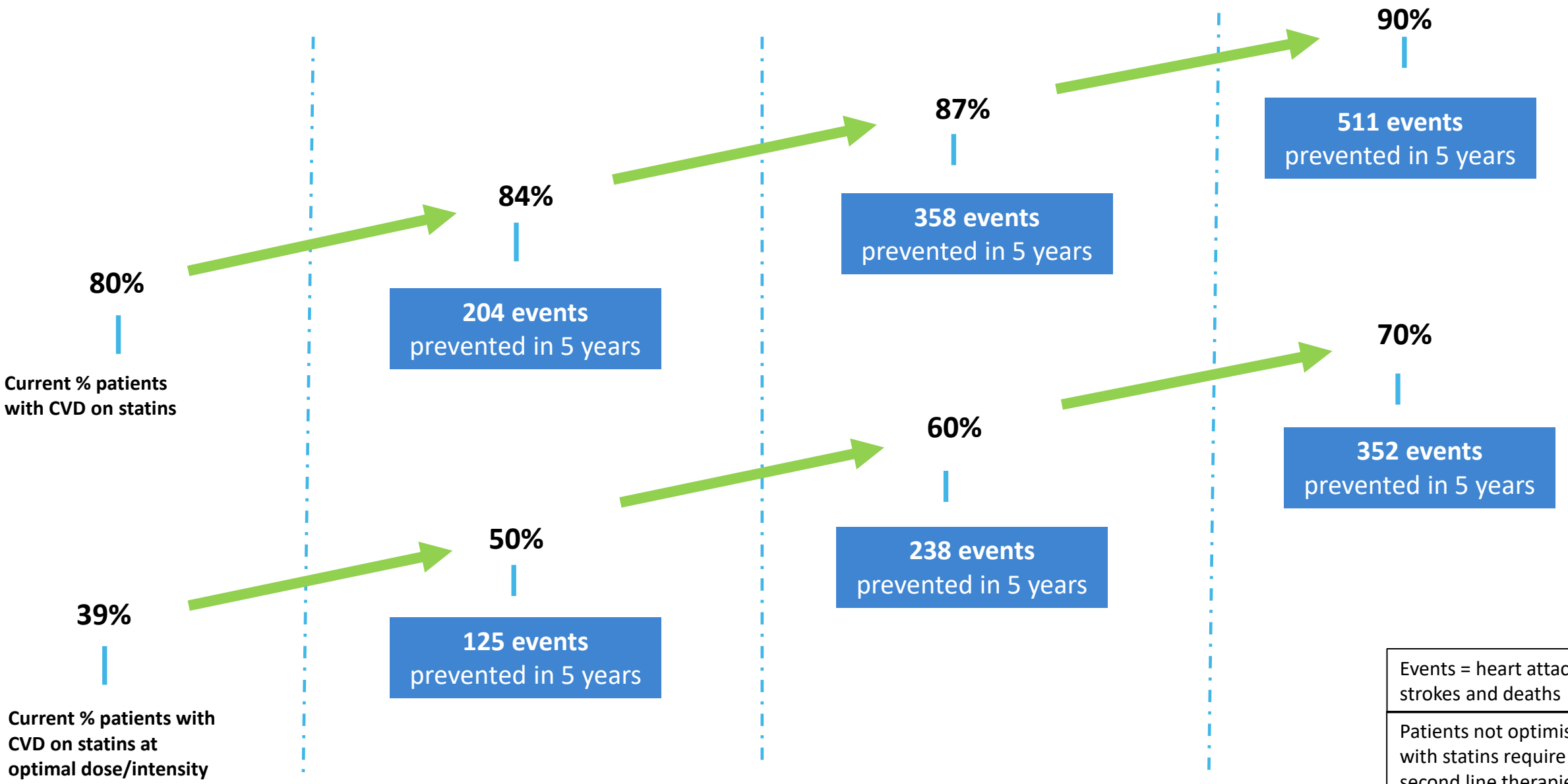
Size of the Prize for Cholesterol – ICS 1 (Pop 1.7 million)
Trajectory of Ambitions for Secondary Prevention



Events = heart attacks, strokes and deaths

Patients not optimised with statins require second line therapies

Size of the Prize for Cholesterol – ICS 2 (Pop 1.1 million)
Trajectory of Ambitions for Secondary Prevention



Events = heart attacks, strokes and deaths

Patients not optimised with statins require second line therapies

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Thank you

For more information please contact:

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