CVD Dominates Global NCD deaths < 70 years (2008)

NCD deaths are projected to increase by 15% globally between 2010 and 2020. The greatest increases will be in Africa, the Eastern Mediterranean, and South-East Asia, where they will increase by over 20%.
“The human race has had long experience and a fine tradition in surviving adversity; we now face a task for which we have little experience, the task of surviving prosperity”

Alan Gregg (1890-1957)
Rockefeller Foundation
Modifiable Risk Factors: Prevention Opportunity

9 RFs accounted for 90% of MI in men and 94% in women

Age, Gender, Smoking, BP, Diabetes, Cholesterol

15152 MI patients in 52 countries

INTERHEART Lancet 2004
CVD Prevention Opportunity!

Genetic  Environmental

Clinical Events

Fetus  0  20  40  60  Age (yrs)
The performance of the UK in terms of premature mortality...is below the mean of the EU15+......further progress will require improved public health, prevention, early intervention and treatment activities......and deserves an integrated and strategic response”
Prevalence of Atherosclerosis in the Young

32 Year Old Female

Atherosclerosis (%)

Age (years)

<20  17%
20-29  37%
30-39  60%
40-49  71%
≥50  85%

Tuzcu Circ 2001 103:2075-10
Opportunity for Lifetime Management of CVD Risk

- Exposure to risk factors over time is key
- Early intervention may pay long term dividends
Framingham Heart Study: Lifetime Risk

Adjusted Cumulative Incidence

Attained Age

Men

- 69%
- 50%
- 46%
- 36%
- 5%

Women

- ≥2 Major RFs
- 1 Major RF
- ≥ Elevated RF
- ≥ Not Elevated RF
- All Optimal RFs

8%
27%
39%
50%

Lloyd-Jones Circ. 2006; 113: 791-798
No RCTs to Demonstrate Value of Early Intervention on CV Outcome

“This randomized, double-blind trial involving over 20,000 patients was conducted over a 10 year period. Unfortunately we’ve forgotten why.”
LDL Cholesterol and Coronary Heart Disease among Black Subjects by PCSK9\textsuperscript{142X} or PCSK9\textsuperscript{679X} Allele

No Nonsense Mutation (n=3278)

PCSK9\textsuperscript{142X} or PCSK9\textsuperscript{679X} (N=85)

Coronary Heart Disease (%)

Frequency (%)

LDL Cholesterol in Black Subjects (mg/dl)

P=0.008

88%

Cohen NEJM 2006; 354:1264-72
### CHD Impact of Early vs Late LDL Lowering

Mendelian Randomisation Studies of 9 Polymorphisms in 6 Genes

<table>
<thead>
<tr>
<th>Lower LDL-C (mg/dl)</th>
<th>Meta-Analysis</th>
<th>Sample Size (N)</th>
<th>OR (95% CI)</th>
<th>p (difference)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.0 mmol/L (38.7 mg/dl)</td>
<td>Genetic Studies</td>
<td>312,321</td>
<td>0.46 (0.41-0.51)</td>
<td>8.4x10^{-19}</td>
</tr>
<tr>
<td></td>
<td>Statin Trials</td>
<td>169,138</td>
<td>0.76 (0.74-0.78)</td>
<td></td>
</tr>
<tr>
<td>0.5 mmol/L (19.3 mg/dl)</td>
<td>Genetic Studies</td>
<td>312,321</td>
<td>0.67 (0.64-0.72)</td>
<td>8.4x10^{-19}</td>
</tr>
<tr>
<td></td>
<td>Statin Trials</td>
<td>169,138</td>
<td>0.87 (0.86-0.88)</td>
<td></td>
</tr>
<tr>
<td>0.25 mmol/L (9.7 mg/dl)</td>
<td>Genetic Studies</td>
<td>312,321</td>
<td>0.82 (0.80-0.85)</td>
<td>8.4x10^{-19}</td>
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<tr>
<td></td>
<td>Statin Trials</td>
<td>169,138</td>
<td>0.93 (0.93-0.94)</td>
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</tr>
<tr>
<td>0.125 mmol/L (4.8 mg/dl)</td>
<td>Genetic Studies</td>
<td>312,321</td>
<td>0.91 (0.89-0.92)</td>
<td>8.4x10^{-19}</td>
</tr>
<tr>
<td></td>
<td>Statin Trials</td>
<td>169,138</td>
<td>0.96 (0.96-0.97)</td>
<td></td>
</tr>
</tbody>
</table>

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*Ference J Am Coll Cardiol 2012; 60: 2631–9*
Hazards of Smoking and Benefits of Smoking Cessation

113,752 w and 88,496 m aged ≥25 y in US
Lifetime Risk of Hypertension for Age 30 years

>1m Subjects Without CVD During 5.2 years FU

Lifetime risk for age 30 yrs
63.3 v 46.1%
Average 5 yrs lost

Rapsomaniki Lancet 2014; 383: 1899-1911
Short-term (10-year) risk underestimates lifetime CV risk of young people with hypertension... Lifetime risk with untreated stage 1 hypertension in this age group could be substantial. Lifetime risk assessments may be a better way to inform treatment decisions and evaluate cost effectiveness of earlier drug therapy.
Disenfranchises the young, especially women!

European Heart Journal 2012; 33: 1635-1701
New Cholesterol Guidelines to a Population-Based Sample

56 million people
Mostly Old Men!!!
Elderly black man
79yr of age
Total cholesterol 150 mg/dl
HDL cholesterol 40 mg/dl
Systolic blood pressure 120 mmHg
Not taking antihypertensive medication
Not diabetic
Nonsmoker
Calculated 10-yr risk of CHD or stroke 13.7%
Comment: Patient qualifies because he has a 10-yr risk of >7.5% but is >75 yr of age.

Moderate-Intensity Statin Therapy Recommended

Kearney NEJM 2014; 370: 275-278
Statin Therapy Not Recommended

White woman with hyperlipidemia and hypertension 46yr of age
Total cholesterol 230 mg/dl
HDL cholesterol 55 mg/dl
Systolic blood pressure 150 mmHg
Taking antihypertensive medication
Not diabetic
Nonsmoker
Calculated 10-yr risk of CHD or stroke 2.0%
Comment: Total cholesterol is high and blood pressure is not controlled, but patient has no other risk factors.

Kearney NEJM 2014; 370: 275-278
Non-smoking men <45yrs
All women <65yrs
<10% 10yr CHD Risk

56% of US adults (87,000,000) have low (<10%) 10yr and high lifetime (≥39%) risk

Marma Circ Cardiothoracic Qual Outcomes 2010;3:8-14
Young Man comes to your Clinic at 25 years

“Waiting for dyslipidemic patients to reach middle age before starting therapy is a failure of prevention”
Hazen 2014
Joint British Societies (JBS)3:
March 26th 2014

Investing in Your Arteries!
JBS3: What’s different? “Investing in Your Arteries”

- **Personalised, lifetime** approach to CVD prevention
- New CVD risk calculator with **understandable risk metrics** linked to interventions. Demonstrate the potential for benefit on a person’s risk over their lifetime.

Empower individuals to take control of their CVD health by promoting lifestyle changes, not just drugs.

Heart March 2014 and www.jbs3risk.com
Established CVD or Familial Hypercholesterolaemia
Diabetes age >40 years
Chronic Kidney Disease

NO

Use JBS3 risk calculator

10 year CVD risk score

BELOW current NICE threshold*:
Examine JBS3 ‘lifetime metrics’
Heart age
Projected CVD risk
To inform discussion on risk modification by:
Lifestyle changes
Drug therapy when indicated

YES

Lifestyle and drug therapy as recommended in JBS3

ABOVE current NICE threshold*:
➢ Lifestyle + Drug therapy

*Current NICE Guidance www.nice.org.uk

Ongoing research on implementation and impact of JBS3 recommendations and risk calculator

www.jbs3risk.com
In addition, it demonstrates some of the disadvantages of using current 10-year absolute risk in young females. Finally, this example demonstrates how the risk calculator can predict optimal time for intervention to achieve the greatest clinical gain and how it might be used to inform the balance of clinical gains versus economic consequences when pharmacological therapy is required in addition to other lifestyle interventions.

Profile of subject 1

A 35-year-old female smoker: Systolic blood pressure of 160 mmHg, Total cholesterol of 7.0 mmol/L, HDL-c of 1.4 mmol/L (non-HDL-c 5.6 mmol/L), Family history of premature CVD.

JBS3 CVD Risk Calculator

35 year old female: adverse risk factors.

Heart March 2014 and www.jbs3risk.com
JBS3 CVD Risk Calculator
35 year old female: adverse risk factors

Predicting an average survival to the age of 71 years without a CVD event, but a 10-year CVD event risk of 1.9% (Figure 3).

Heart March 2014 and www.jbs3risk.com
On average, expect to survive to age 71 without a heart attack or stroke.

Your risk of a heart attack or stroke in the next 10 years is 1.9% assuming you don’t die of anything else.

JBS3 CVD Risk Calculator
35 year old female: adverse risk factors

Heart March 2014 and www.jbs3risk.com
Effect of Risk Factor Modification Intervention in this individual at her current age of 35 years, including stopping smoking and introducing other lifestyle changes and, if necessary, drug therapy to reduce systolic BP to 130 mmHg and TC to 4.0 mmol/L (non-HDL-c 2.6 mmol/L), has the following effect on her risk profile (Figures 5 and 6).
Heart age is reduced from 47 years to 30 years and the average age to first CVD event is increased from age 71 to age 85, gaining 14 years of expected life without a CVD event through risk factor modification.

These benefits can also be demonstrated graphically comparing the temporal effects of early sustained intervention versus no intervention (Figures 7 and 8). Note that as the lines diverge, this indicates the optimal time for risk factor modification to obtain maximum clinical benefit.

JBS3 CVD Risk Calculator
35 year old female: adverse risk factors

On average, expect to survive to age 85 without a heart attack or stroke gaining 14 years through interventions

expected life without a heart attack or stroke

Your risk of a heart attack or stroke in the next 10 years is 0.23% assuming you don’t die of anything else

Future smoking category: quit
Systolic Blood Pressure: 160 → 130
Total Cholesterol: 7.0 → 4.0
HDL Cholesterol: 1.4 → 1.4
NonHDL Cholesterol: 2.6
BMI: 25.9

Heart March 2014 and www.jbs3risk.com
The number of potential years gained begins to fall off sharply if intervention is delayed beyond the age of 40 years.

The following additional visual displays can also be used to highlight further the value gained for an individual by early intervention, the various displays enhancing the potential impact on different individuals who often resonate more with one particular display. This first display (Figure 10) demonstrates outcome with and without intervention as compared to the general population, and shows the substantial impact of intervention at an early age.

JBS3 CVD Risk Calculator
35 year old female: adverse risk factors

Heart March 2014 and www.jbs3risk.com
Early Lifestyle Modification

On average, expect to survive to age 76 without a heart attack or stroke, gaining 10 years through interventions.

Expected life without a heart attack or stroke

Your risk of a heart attack or stroke in the next 10 years is 1.1% assuming you don’t die of anything else.

Interventions

- **Future smoking category**: I quit
- **Systolic Blood Pressure**: 158 → 145
- **Total Cholesterol**: 6.8 → 5.9
- **HDL Cholesterol**: 1.2 → 1.2
- **NonHDL Cholesterol**: 4.7
  - **BMI**: 22.2

www.jbs3risk.com
Delayed Intensive Modification

On average, expect to survive to age 73 without a heart attack or stroke, gaining 7.6 years through interventions.

Expected life without a heart attack or stroke:

Your risk of a heart attack or stroke in the next 10 years is 3.2% assuming you don’t die of anything else.

Interventions:

Future smoking category: I quit
Systolic Blood Pressure: 158 → 130
Total Cholesterol: 6.8 → 4.0
HDL Cholesterol: 1.2 → 1.2
NonHDL Cholesterol: 2.8
BMI: 22.2

Reset

www.jbs3risk.com
JBS3: Key Recommendations

- Visualising effects of intervention for patients
- Earlier intervention? Lifestyle first
- New target lipid measure: Non-HDL-c vs. LDL-c
  • Fasting not needed
- Statin intolerance / Statin DM risk: reinforce lifestyle
- Biomarkers or imaging?
- FH / Diabetes / NICE comparisons
JBS3: Start of a new Process

- Changes interactions in primary care
- Personalised approach
- Empowers lifestyle
- Not just a statin conversation!

Implementation and Evaluation challenges!
Next Steps: Formal Evaluation in Primary care

Health Checks

• Understanding
• Behaviour
• Risk factors
• CV events

JBS3
Lifetime CVD Risk Management

Check your heart age

Before you go for your NHS Health Check, you can use this pre-screen tool to get an idea of what your results might show.

Start

Full terms and conditions can be read here

Your results

Your heart age is about 47

Compared to a person of the same age, gender and ethnicity without raised risk factors

You have a 1.8% risk of having a heart attack or stroke in the next 10 years. This means the chance of either of these things happening is low.

Your heart age is higher than your actual age. However, changes to your diet and lifestyle can help lower it.

What affects your heart age?

Smoking

I smoke 20+ a day

Stopping smoking is the single biggest change you can make for your health. One year after stopping, your heart attack risk is half that of a smoker.

You don’t have to go cold turkey alone. There is a wealth of information and support to help you stop.

Get help with quitting

Blood pressure 135 Pre-high

Your blood pressure is described as being pre-high and ideally, it should be below 120/80mmHg. Known as the "silent killer", high blood pressure rarely has obvious symptoms but left untreated, it increases your risk of heart attack or stroke.

The good news is, it can be brought under control through lifestyle changes such as losing weight, reducing the amount of salt you eat, exercising regularly and cutting back on alcohol and caffeine.

Blood pressure information
What's good for the Heart is good for the Brain!
Lifetime CVD Risk Management

JBS3 platform applicable to other NCDs such as dementia which share risk factors
CONCLUSIONS AND RELEVANCE  Midlife hypertension and elevated midlife but not late-life systolic BP was associated with more cognitive decline during the 20 years of the study. Greater decline is found with higher midlife BP in whites than in African Americans.
### Brain age calculator Prototype

<table>
<thead>
<tr>
<th>Gender</th>
<th>Male</th>
<th>Female</th>
<th>N/A</th>
<th>N/A</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>58 years</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Total cholesterol</td>
<td>180 mg/dL</td>
<td>180</td>
<td>0%</td>
<td></td>
</tr>
<tr>
<td>HDL cholesterol</td>
<td>45 mg/dL</td>
<td>45</td>
<td>0%</td>
<td></td>
</tr>
<tr>
<td>BP treatment</td>
<td>Yes</td>
<td>No</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Systolic BP</td>
<td>125 mmHg</td>
<td>125</td>
<td>0%</td>
<td></td>
</tr>
<tr>
<td>Smoking</td>
<td>Yes</td>
<td>No</td>
<td>0%</td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td>Yes</td>
<td>No</td>
<td>N/A</td>
<td>N/A</td>
</tr>
</tbody>
</table>

Our cognitive abilities decline as we get older, with the rate of decline accelerating as we age.

Some of this decline can be attributed to vascular risk factors.

Compared to reference risk factor values, your cognitive decline is at a rate which is associated with a 58 year old.
How early should prevention start?
Obesity in the Young

- Tracks to adult obesity
- Accelerates development of Type II DM
- Likely to have cumulative impact

Whincup P and Deanfield J
Childhood Adiposity, Adult Adiposity, and Cardiovascular Risk Factors

BACKGROUND

Obesity in childhood is associated with increased cardiovascular risk. It is uncertain whether this risk is attenuated in persons who are overweight or obese as children but not obese as adults.

Persons who were overweight or obese during childhood but were nonobese as adults had risks of the outcomes that were similar to those of persons who had a normal BMI consistently from childhood to adulthood (P>0.20 for all comparisons).
CVD Prevention: A Long Way to Go!

- JBS3 supports intensive treatment in CVD patients and those at very high risk
- Provides a new personalised prevention framework based on CV risk over lifetime
- ‘Investment in your arteries’ by early lifestyle changes may lead to substantial lifetime health gains
- Empowers people to understand and take control of their CV health
“It should be the function of medicine to have people die young as late as possible”

Ernest L. Wynder M.D.
Opportunity for Lifetime Management of CVD Risk

- Exposure to risk factors over time is key
- Early intervention pays long term dividends
Coronary Heart Disease Mortality in Beijing 1984-1999

1822 Extra deaths Attributable to Risk Factor Changes

- Cholesterol: 77%
- Diabetes: 19%
- BMI: 4%
- Smoking: 1%
- 642 fewer deaths by treatments
  - AMI treatments: 41%
  - Hypertension treatment: 24%
  - Secondary prevention: 11%
  - Heart failure: 10%
  - Aspirin for Angina: 10%
  - Angina: CABG & PTCA: 2%

Critchley J. Circulation, 2004;110:1236-1244
65 year old man

Profile

Date of Birth: 13 4 1949
Gender: male
Ethnic group: White or not stated
Height (m): 1.70 (5'7"
Weight (kg): 65.0
BMI: 22.5

Total Cholesterol: 3.9 mmol/L
HDL Cholesterol: 1.4
NonHDL Cholesterol: 2.5
Systolic Blood Pressure: 150 mm Hg

Do you smoke? No

Have you received blood pressure treatment? 
Do you suffer from diabetes? 
Does a close relative under 60 suffer from CVD? 
Do you have a chronic kidney disease? 
Have you suffered atrial fibrillation? 
Do you have rheumatoid arthritis?

I have never suffered from Cardiovascular Disease ✓
I have read the terms and conditions ✓

Save  Load  Next

Heart March 2014 and www.jbs3risk.com
On average, expect to survive to age 83 without a heart attack or stroke.

Expected life without a heart attack or stroke.

Your risk of a heart attack or stroke in the next 10 years is 10% assuming you don’t die of anything else.

Interventions:
- Future smoking category: No
- Systolic Blood Pressure: 150
- Total Cholesterol: 3.9
- HDL Cholesterol: 1.4
- NonHDL Cholesterol: 2.5
- BMI: 22.5

Heart March 2014 and www.jbs3risk.com
On average, expect to survive to age 83 without a heart attack or stroke gaining 0.40 years through interventions.

Your risk of a heart attack or stroke in the next 10 years is 8.5% assuming you don't die of anything else.