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Public Health England

Protecting and improving the nation's health

Cardiovascular Disease Prevention Return on Investment Tool:

Final Report

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Executive summary

Cardiovascular disease (CVD) prevention is a major public health priority in England. The NHS RightCare Optimal Pathway has highlighted six CVD high-risk conditions that are currently under-diagnosed and insufficiently managed despite a range of available interventions, and therefore represent targets for improvement: hypertension; atrial fibrillation (AF); high cholesterol/high CVD risk including familial hypercholesterolemia (FH); diabetes (type 1 and type 2); non-diabetic hyperglycaemia; and chronic kidney disease (CKD). Public Health England (PHE) identified a need for an integrated single platform return on investment (ROI) CVD prevention tool to support NHS and public health decision makers at both national and local level, based on best available current evidence around CVD prevention in people with the six identified high-risk conditions.

Literature reviews were carried out to identify evidence for effectiveness and cost-effectiveness of interventions that improve the detection and management of the CVD high-risk conditions. Interventions were chosen for inclusion in the tool if they were recommended by NICE for individuals without pre-existing CVD and if there was high quality and recent effectiveness evidence available. Selected detection interventions included NHS Health Checks, annual review in people with a pre-existing condition, cascade testing for FH and opportunistic detection. Selected management interventions included pharmacological interventions (antihypertensives, lipid modification therapy, anticoagulants and blood glucose lowering), lifestyle interventions (NHS DPP, Diabetes structured education, weight management, smoking cessation, nutritional advice for CKD) and interventions that improve adherence to pharmacological interventions (blood pressure self-monitoring, insulin pump and medicines use review). A series of additional reviews were carried out to inform other intervention parameters including costs and duration of effect. Local and national data sources were identified to provide information about current care such as diagnosed prevalence of high-risk conditions and current usage of interventions.

The tool was developed with input from a tool user group who provided information about local priorities for CVD and their requirements for a CVD prevention ROI tool. The tool was based on the pre-existing School for Public Health Research Diabetes Prevention Model, an individual patient simulation model with baseline population characteristics taken from the Health Survey for England 2014. The model was adapted to enable the high-risk conditions and chosen interventions to be included. The tool design enables users to see the potential benefits of either improving detection and/or management of one or more high-risk conditions, or of improving the usage of one or more of the key interventions for people at risk of CVD. The tool is designed to include both the direct costs and benefits of implementing chosen scenarios and the indirect consequences, for example the increased cost of management that will occur as a response to increased diagnosis of high risk conditions.

This document reports the results of a series of exemplar analyses in which detection/management of each condition or usage of each intervention are optimised in turn and compared. These analyses help give some indication to tool users about which interventions or detection and management strategies are likely to provide the most benefit. The results indicate that optimising detection and management of people with QRISK ≥ 10% results in the highest short-term benefits, whereas detection and management of diabetes provides the most benefit in the long-term. Of individual interventions, statins give the most benefits in the short-term and anti-hypertensives or annual review in the long-term. Most lifestyle interventions are not cost-saving within the time horizon of the model, but this does not rule them out from being cost-saving over longer time horizons. Uncertainty analysis is not included in the tool, but it is important to note that there will be some uncertainty around estimates.

Acronyms used in this document

ACEi/ARB: Angiotensin Converting Enzyme Inhibitor/Angiotensin II Receptor Blockers
ACR: Albumin to Creatinine Ratio (measure of kidney function)
AF: Atrial Fibrillation
BMI: Body Mass Index
CCG: Clinical Commissioning Group
CKD: Chronic Kidney Disease
CVD: Cardiovascular Disease
DPP: NHS Diabetes Prevention Programme
FH: Familial Hypercholesterolaemia
HSE: Health Survey for England
HTA: Health Technology Assessment
JBS3: Joint British Societies for the prevention of cardiovascular disease
MI: Myocardial Infarction
NCVIN: National Cardiovascular Intelligence Network
NDH: Non-Diabetic Hyperglycaemia
NICE: National Institute for Health and Care Excellence
NMB: Net Monetary Benefit
ONS: Office of National Statistics
PDF: Portable Document Format
PHE: Public Health England
QALY: Quality Adjusted Life Year
QOF: Quality and Outcomes Framework
QRISK: QResearch Cardiovascular Risk Calculator (score gives 10 year CVD risk)
ROI: Return on Investment
SBP: Systolic Blood Pressure
SPHR: School for Public Health Research
UKPDS: UK Prospective Diabetes Study

Introduction

Cardiovascular disease (CVD) prevention is a major public health priority in England. Currently there are over 2.6 million people in the UK on the Coronary Heart Disease Register and 1.2 million on the Stroke or Transient Ischaemic Attacks Register[1]. CVD mortality varies widely throughout the UK by deprivation, by gender and by regional area, e.g. the highest age-standardised CVD death rates in England are in the North West (320/100,000), compared to only 269/100,000 in the South West[2]. According to a recent European study it is estimated that CVD cost the UK economy €26 billion in 2015 of which €12 billion (46%) came from direct health care costs[3].

Recent declines in mortality mean that more people are living for longer with long-term conditions including CVD and other conditions that increase the risk of CVD. Despite the recent improvements, many CVD cases could be prevented through healthier lifestyles and through better risk factor detection and management[4]. Whilst some risk factors such as smoking have reduced in the population; levels of obesity and diabetes are increasing, and other risk factors such as hypertension and atrial fibrillation remain undiagnosed or poorly managed in many individuals.

The NHS RightCare Optimal Pathway[5] highlighted six CVD high risk conditions that are currently underdiagnosed and insufficiently managed despite a range of available interventions, and therefore represent targets for improvement (**Error! Reference source not found.**):

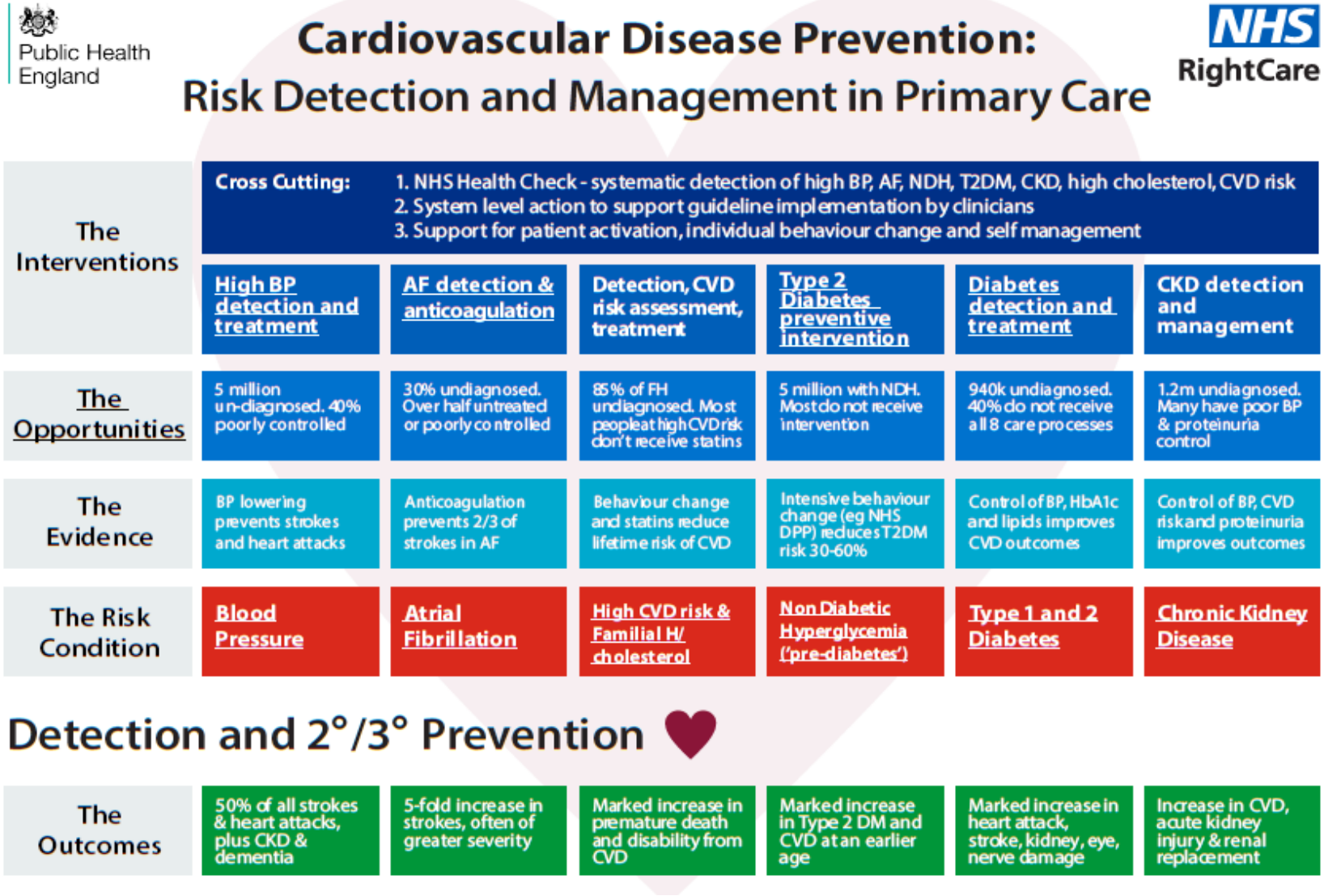
- high blood pressure
- atrial fibrillation (AF)
- high cholesterol/high CVD risk including Familial Hypercholesterolemia (FH)
- Diabetes (Type 2 and Type 1)
- non-diabetic hyperglycaemia
- chronic kidney disease (CKD)

PHE identified that whilst a number of tools pre-existed for assessing return on investment (ROI) for CVD prevention, these used a variety of different evidence sources and assumptions and therefore there was no common platform for the assessment of ROI across different risk conditions and different interventions. There was therefore a need for an integrated, single platform ROI tool to support NHS and public health decision makers at both national and local level.

PHE commissioned a CVD prevention ROI tool focussing on the six high risk conditions from the University of Sheffield. A consistent and up to date evidence review was also required to identify the best quality evidence about the effectiveness and cost-

effectiveness of interventions aimed at detecting and managing each of the risk conditions. The University of Sheffield proposed to develop the ROI tool based on a modification of an existing type 2 diabetes prevention model (The School for Public Health Research (SPHR) Diabetes Prevention Model[6-8]), which has been previously used as the basis of a PHE tool to model the ROI of the NHS Diabetes Prevention Programme (NHS DPP)[9].

Figure 1: NHS RightCare Cardiovascular Disease Prevention Optimal Pathway[5].
Note that data used to inform this may differ from that used in the CVD Prevention ROI Tool, so results may differ.



Evidence reviews

Consultation with the steering group (a project oversight group of internal and external stakeholders. See technical appendix for further information) led to the agreement that interventions that are currently recommended by NICE for detection or management of the six high risk conditions should be prioritised for inclusion in the tool. Whilst of potential interest, the tool would not include policy and structural interventions that improve uptake of and adherence to current NICE guidelines, or novel interventions (not currently NICE recommended) for detection or management of high risk conditions. Selection of interventions for review was therefore guided by recommendations within the relevant NICE guideline documents for the six high risk conditions as follows:

- CG127: Hypertension (last updated 2016)[10]
- CG180: Atrial fibrillation (last updated 2014)[11]
- CG71: Familial Hypercholesterolaemia (last updated 2017)[12]
- CG181: CVD Risk Assessment and Lipid Modification (last updated 2016)[13]
- NG17: Type 1 Diabetes (last updated 2016)[14]
- NG28: Type 2 Diabetes (last updated 2017)[15]
- PH38: Type 2 Diabetes Prevention (includes recommendations for non-diabetic hyperglycaemia; last updated 2017)[16]
- CG182: Chronic kidney disease (last updated 2015)[17]

Selected management interventions were limited to those that specifically contributed to prevention of CVD rather than just control of symptoms; and excluded interventions that were aimed specifically at individuals with pre-existing CVD (e.g. previous stroke or MI), or relevant to only a very small number of individuals with serious disease.

Following selection of intervention topics, a review question was formulated for each included topic, which enabled identification of effectiveness data for each intervention individually or in combination with other included interventions, relating to each relevant high risk group. As an initial step, any existing evidence relating to the effectiveness of recommended interventions was extracted from NICE guideline documentation. If such evidence was relevant to the review question, had been reviewed within the last year and contained outcomes of relevance to the tool then no further reviewing was required. If further evidence was required, searches were designed to identify recent evidence relating to effectiveness of the intervention. Searches were initially aimed at identifying relevant systematic reviews, but if none were found, a second set of searches was carried out to identify relevant randomised controlled trials. A review protocol was designed to enable rapid reviewing for each search topic. In most cases multiple potentially useful studies were identified. Selection of studies for inclusion in the tool was based on an assessment of study quality, relevance to the topic question and input from the steering group. A full description of reviewing methodology and

review reports for each topic are provided in sections 2 & 3 respectively of the accompanying technical appendix.

Inclusion of interventions within the tool was informed through effectiveness evidence and steering group input. The following interventions are included:

- Lipid Modification Therapy (Atorvastatin 20 mg)
- Anti-hypertensives (Combination Therapy for Hypertension and ACEi/ARB therapy for CKD)
- Anticoagulants for AF
- Blood Glucose Lowering Medication for Type 2 Diabetes
- NHS Diabetes Prevention Programme
- Structured Education Programmes for Diabetes
- Weight Management
- Smoking Cessation
- Individualised Nutritional Advice for CKD
- Continuous Subcutaneous Insulin Infusion (Insulin Pump) for Type 1 Diabetes
- Blood Pressure Self-Monitoring for Management of Hypertension
- Pharmacist Medicines Use Review
- NHS Health Checks
- Cascade Testing for FH
- Opportunistic Detection (variety of methods)
- Annual Review for detection and management

In addition to these interventions, the tool also includes a user-defined intervention on the recommendation of the steering group. This enables users to input details of any other management intervention that they wish to include, providing that they can supply information about its effectiveness (relative risk for CVD), cost, duration of effect and the eligible high risk group.

For several interventions it was not possible to identify relevant effectiveness data. In particular, there were several lifestyle interventions for which behavioural evidence was identified, but no direct evidence for CVD prevention or metabolic change could be found:

- Exercise Referral
- Screening and Brief Intervention for Alcohol
- Brief Advice for Diet and Physical Activity
- Individualised Nutritional Advice for FH

These were not included in the tool as the model framework did not allow behavioural evidence to be incorporated. However, it is important to note that their exclusion from the tool does not mean that such interventions should be discontinued; and they may

be included in future versions of the tool if direct evidence of CVD benefit becomes available. Evidence gaps were also identified relating to intervention combinations, for which little specific effectiveness evidence was found. In order to enable modelling of intervention combinations in the tool, it was therefore assumed that intervention effectiveness estimates were independent (i.e. that there were no interactions between interventions that led to either an increase or a reduction in the effectiveness of one intervention if a second was also applied).

A series of other intervention parameters were also reviewed including cost-effectiveness, intervention costs, and duration of intervention effect. In order to populate the tool input parameters, it was also necessary to find data to inform current levels of detection and management of high risk conditions and usage of interventions (usage defined as the proportion of eligible people undergoing an intervention, comprising proportion offered, uptake and discontinuation). A series of local data sources were identified to inform many of these, including the Quality and Outcomes Framework (QOF)[18], the National Diabetes Audit[19], National Cardiovascular Intelligence Network (NCVIN) prevalence estimates[20 21], and NHS Digital Stop Smoking Services Statistics [22]. Where no local data could be identified, national data sources found through additional searches were used instead. Descriptions of these searches can be found in section 5 of the accompanying technical appendix.
A database of interventions and conditions was made to accompany the tool. This summarises all the evidence for each intervention and for each condition included in the tool.

Modelling and tool development

Tool user group and conceptual modelling

A group of potential tool users was recruited from amongst CCG and local authority public health representatives, PHE regional leads with responsibility for CVD, health professionals with CVD as a special interest and relevant charitable organisations. The tool user group was invited to a one-day workshop to discuss what users would want from an ROI tool. Full details of the tool user group workshop materials and feedback can be found in section 6 of the accompanying technical appendix.

A conceptual model (a plan of the proposed tool detailing what information users would need to input and what information it would produce) was constructed based upon tool user group responses and modelling constraints. Feedback from the tool user group about the conceptual model was obtained through email and an online questionnaire, and changes were made to the conceptual model to incorporate this user feedback. The tool user group were also involved in testing the tool following its development, and their comments were incorporated into the final version of the tool prior to publication.

The tool design enables users to estimate the potential benefits to their local area of either improving detection or management of one or more high-risk conditions, or of improving the usage of one or more of the key interventions for people at risk of CVD. Following input of user-defined targets for detection, management or intervention usage, the underlying model is run and an email is sent to the tool user with a link to their model results. A flexible output page enables tool users to choose which outcomes to see and to download as a PDF.

Model design & development

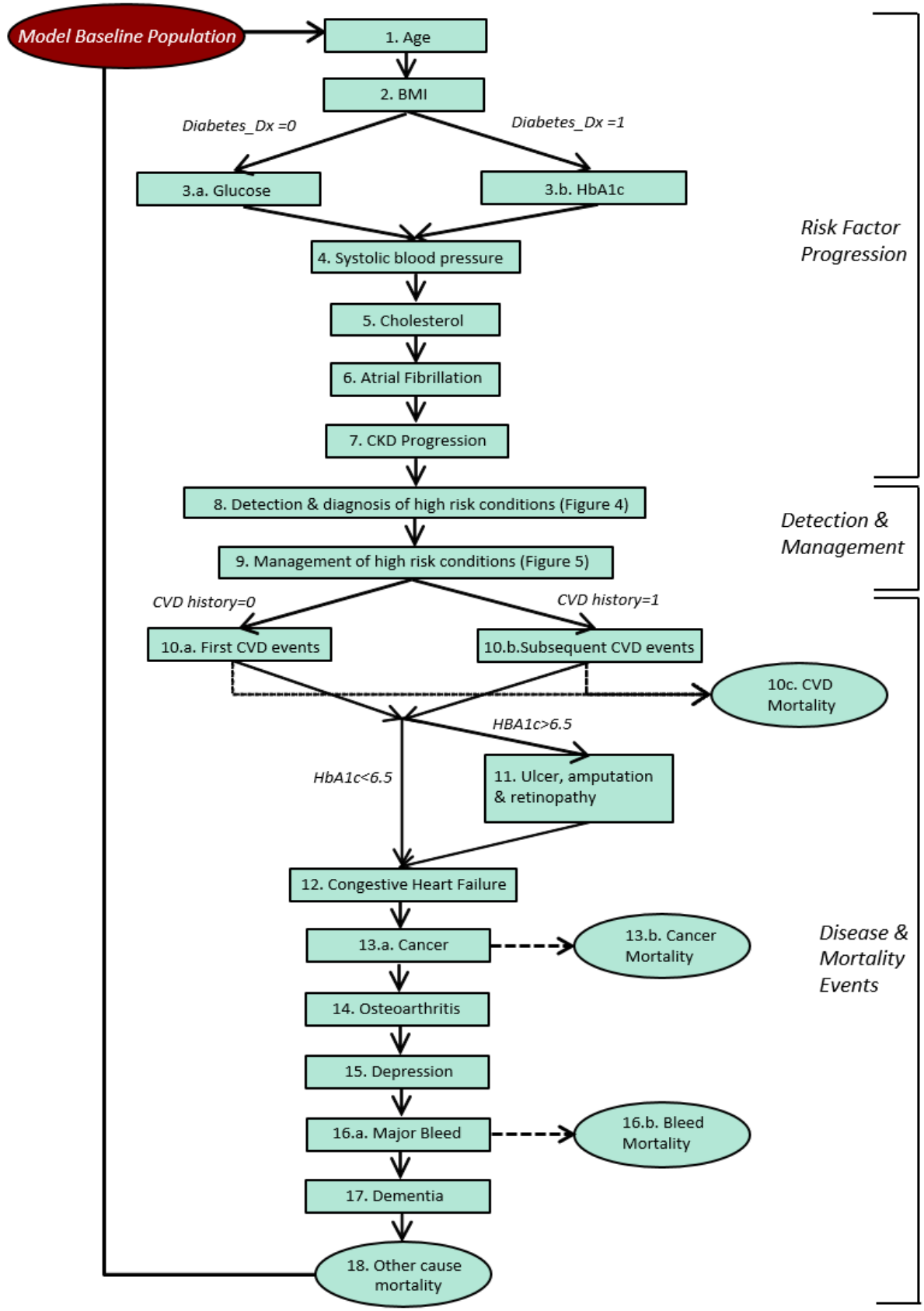
A series of model adaptations were carried out to convert the pre-existing School for Public Health Research (SPHR) Diabetes Prevention model into a CVD Prevention model, which underpins the CVD Prevention ROI tool. Full details of these adaptations can be found in section 8 of the accompanying technical appendix, with just a brief summary presented here.

The SPHR Diabetes Prevention Model is an individual patient simulation model written in R programming code. The baseline population consists of a representative sample of the English population obtained from the Health Survey for England 2014 (HSE 2014)[23], which was chosen for its CVD and diabetes focus. The model simulates the aging of this cohort of people over time, and the changes in their individual metabolic

factors (and therefore disease risk) as they age, including body mass index (BMI), systolic blood pressure (SBP), cholesterol and blood glucose (HbA1c)[6-8].

The model runs in annual cycles (see schematic in Figure 2). For each person, their BMI, cholesterol levels, SBP and HbA1c fluctuate from year to year, representing natural changes as people age and depending upon personal characteristics such as gender, ethnicity and smoking status. Every year in the model, an individual has a risk of undergoing one or more of a range of events including visiting the GP, being diagnosed with and treated for CVD high risk factors, suffering from disease events including cardiovascular disease, and dying; depending upon their personal characteristics. Each condition is associated with a utility decrement and a cost. Outcomes gathered each year include number of clinical events (including CVD and end stage renal failure), new diabetes diagnoses, costs, life years, quality adjusted life years (QALYs) and an estimate of premature mortality.

Figure 2: Model schematic showing the order in which updating of population characteristics takes place in each year of the simulation



The estimated number of individuals in England in each of the high CVD risk groups was ascertained using the national weights available within HSE 2014 (Table 1) and ONS estimates for the total population of England in 2017. This method was also used to obtain the numbers of individuals with two high risk conditions (Table 2).

Table 1: Proportion of individuals from HSE 2014[23] in each high risk group

High Risk Group	No. Individuals (HSE 2014)	Weighted Prevalence in Adult Population (age 16+)	Estimated No. Individuals (England)
QRISK2 ≥10%	3,103	34%	15,149,093
Hypertension	2,622	30%	13,459,209
Familial hypercholesterolaemia	28	0.04%	191,833
Non-diabetic hyperglycaemia	1,186	14%	6,267,794
Diabetes	829	9.5%	4,273,364
of which type 1 diabetes	*50*	*0.6%*	*281,183*
of which type 2 diabetes	*779*	*8.9%*	*4,003,378*
Atrial Fibrillation	280	3.0%	1,354,311
Chronic Kidney Disease (stages 3-5)	577	6.0%	2,706,185
At least one high risk condition	4,334	49%	22,363,307
TOTAL POPULATION*	8,077	100%	45,340,600*
*Total population aged >15 in England according to ONS (2017 estimates)			

Local demographic data (age, sex, deprivation and ethnicity) was used to develop different weights for each local area using the method of iterative proportional fitting (described in more detail in section 8.3 of the technical appendix). This enabled the tool to simulate the population of each local area.

Table 2: The estimated number of individuals in England with two high risk conditions

	QRISK2 ≥10%	Hyper-tension	AF	CKD	Pre-diabetes	Diabetes
QRISK2 ≥10%	15,149,093					
Hypertension	9,717,660	13,459,209				
AF	1,243,777	880,066	1,354,311			
CKD	2,491,019	1,705,808	318,318	2,706,185		
Pre-diabetes	2,928,954	2,626,741	238,025	632,693	6,267,794	
Diabetes	3,568,452	2,802,838	281,483	608,391	NA	4,273,364

Some of the high risk groups including diabetes, non-diabetic hyperglycaemia, hypertension and QRISK ≥ 10% were already adequately modelled in the pre-existing model. Inclusion of type 1 diabetes, AF, FH and CKD required additional modelling work to be carried out; this was informed through a series of reviews of previously published models. Full details of the methodology and findings of these model reviews is available in section 7 of the accompanying technical appendix.

QRISK2 and QStroke algorithms were used to model annual risk of first CVD event[24 25]. Calculation of both risks in each simulated individual enabled a value for cardiac risk to be estimated separately from stroke risk. A series of modifications were applied to cardiac and stroke risk to enable CVD event rate to vary as a result of additional high risk conditions and interventions not included in the original QRISK2 and QStroke algorithms and to normalise against the current incidence of MI and stroke from Hospital Episode Statistics[26]. The type of stroke or cardiac event suffered by each individual was assigned using age and sex dependent probabilities taken from a statins HTA[27]. Following a first event, subsequent CVD events in the same individuals were modelled dependent upon age, sex and prior event only, as QRISK2 and QStroke are not valid for modelling subsequent CVD events. This does mean that the model may underestimate some of the benefit of interventions in preventing subsequent CVD events.

A range of other conditions were already included in the SPHR Diabetes Prevention model and modelling of these was retained in the CVD Prevention model. This included congestive heart failure; microvascular retinopathy, ulcer and amputation in people with diabetes; breast and bowel cancer, osteoarthritis, depression and dementia. Risk of major bleeding (upper gastrointestinal bleed and intercranial bleed) is increased significantly through usage of anticoagulants and so this was added to the model, together with information about mortality rates following major bleed. Mortality from CVD, cancer and bleed were modelled separately, with other cause mortality modelled through life table information.

The range of detection and management interventions identified as part of the review was added to the model. Detection was modelled through NHS Health Checks, annual review, cascade testing and opportunistic detection. Opportunistic detection was modelled as a process to identify additional individuals following the other three mechanisms, rather than through usage of the specific mechanisms identified as part of the evidence review. This enabled increases in detection through unspecified mechanisms to be included as part of the tool.

The model structure allows the proportion of individuals detected, managed or eligible for an intervention to be maintained at a specific user-defined value over time, despite dynamic changes in the absolute numbers of people eligible. Management for each condition was defined through usage of key management interventions. These included continuous interventions (pharmacological treatments, insulin pump and blood pressure self-monitoring), one-off interventions (lifestyle interventions including NHS DPP, weight management, nutritional advice and educational interventions for diabetes) and repeated interventions (medicines use review and smoking cessation).

All model costs were reviewed and updated, with new costs added where required to model the new health states. Utility scores for each health state were retained from the SPHR Diabetes Prevention model, with new utility decrements added to model major bleed. Following model development, a series of tests and validations were carried out to ensure that the model was behaving as expected.

In the ROI tool, each model run simulates the population twice; firstly, under the assumption of current care and secondly under the assumption of target care (inputted by the tool user), with the difference between these simulations then calculated. All results in the tool are presented as incremental (difference between current care and target care) and cumulative over time.

Exemplar analyses

A set of exemplar analyses has been carried out to demonstrate to tool users which interventions or detection and management strategies are likely to provide the most benefit. Each comparative analysis has been carried out by setting the target detection, management or intervention usage in turn to 100%, whilst keeping targets for all other interventions constant. Some analyses have also been carried out combining optimisation of two or three different interventions. All exemplar analyses have been carried out using England as the selected area. All outcomes are incremental (the difference between current care and target care), and cumulative over time. Presented outcomes for these comparative analyses include total financial cost savings and health benefits measured using CVD events prevented, life years gained, quality adjusted life years (QALYs) gained and net monetary benefit (NMB). The latter measure combines cost-savings and health benefits into a single monetised value as follows:

NMB (£) = (incremental QALYs * value of a QALY) – incremental costs.

Where the value of a QALY has been assumed to be £60,000 as per Department of Health guidelines.

The analyses do not include estimates of uncertainty as probabilistic sensitivity analysis (the gold standard for uncertainty analysis in economic evaluations) is outside of the tool scope. However, it is important for users to note that there will be some uncertainty around these results and that uncertainty is likely to be higher for analyses that apply to small subgroups of the population (i.e. particularly those with FH or type 1 diabetes).

Results summary

A brief summary of the key results is shown here, with more detailed results described in the sections below.

The general trend is that the most beneficial short-term outcomes are obtained by optimising detection and management of people with QRISK ≥10% or through optimising usage of statins, whilst the most beneficial long-term outcomes are obtained through optimising detection and management of people with diabetes, or through optimising usage of antihypertensives or annual review.

Statins are the most cost-saving intervention in the short-term (£216m by year 2), but antihypertensives are most cost-saving in the long-term (£2.3 billion by year 20). Combining the two leads to cost savings of over £4.1 billion by year 20.

Most lifestyle interventions (with the exception of the NHS DPP) are not cost-saving within the 20-year time horizon of the model; however this does not rule them out of being cost-saving beyond this time horizon.

The most cost-saving detection strategy at 20 years is to optimise diabetes detection, whereas the most cost-saving management strategy at 20 years is to optimise management of CKD. However, optimising detection of people with QRISK ≥10% saves costs rapidly (£59m by year 2). Cost savings come from the assumption that additional cases detected will be managed according to current care.

Prevention of the most CVD events and the highest QALY and life year gain is predicted to occur through optimising detection and management of diabetes (1.9m CVD events prevented and 2.5m QALYs and 1.6m life years gained by year 20).

Of single interventions, annual review is predicted to prevent the most CVD events and gain the most QALYs and life years (325k CVD events, 530k QALYs and 424k life years), indicating the importance of diagnosing (and therefore managing) comorbid conditions in people who already have one high risk condition.

Combining optimisation of statins, antihypertensives and anticoagulants is predicted to prevent 553k CVD events, more than any other intervention combination tested.

The greatest net monetary benefit at year 20 would be produced through optimising detection and management of diabetes (£169 billion), with the single interventions antihypertensives and annual review both producing around £33 billion of net monetary benefit, and the combined statins, antihypertensives and anticoagulants scenario producing £62 billion of net monetary benefit.

In the short-term, the greatest net monetary benefit would be produced through optimising detection and management of QRISK ≥10% (£918m at year 2), with statins being the single intervention producing the most net monetary benefit at year 2 (£650m).

Optimising detection of diabetes is hugely cost-saving by 20 years (£31 billion), whilst optimising management of diabetes or usage of blood glucose lowering therapy is not cost-saving by 20 years. This apparent discrepancy is due primarily to the benefits of early diabetes diagnosis in preventing expensive diabetes complications and enabling diabetes to be managed through cheaper first and second line treatments.

Optimising usage of interventions

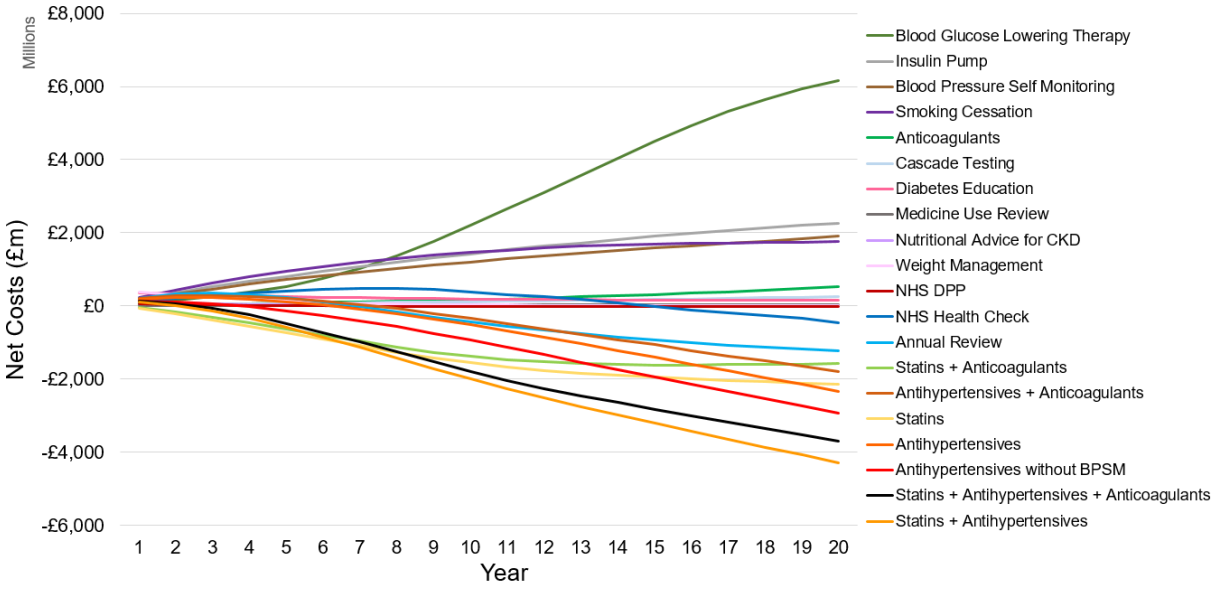
Table 3 shows the intervention costs, total financial savings to the NHS and social care (CVD and non-CVD combined) and net total accrued after 2, 5 and 20 years. Please note that this table does not include the monetised value of health benefits (this is instead shown in Table 8). All interventions are predicted to produce cost-savings, but in many cases these are outweighed by the intervention costs, particularly in the short-term. However, some interventions may be cost-saving beyond the 20-year time horizon of the model. It is also important to note that novel oral anticoagulants will be coming off patent relatively soon, which will reduce the costs of anticoagulation, making it more likely that this intervention will also be cost-saving in the future.

Table 3: Intervention Costs, Total Savings (combined NHS and social care) and Net Total Financial Costs/Savings produced by maximising usage of each intervention.

Costs are positive and savings are negative. Interventions are shown in order with those producing the highest net cost-savings at 20 years at the top of the table.

	Year 2			Year 5			Year 20		
	Intervention Costs	*Total Savings*	Net Total	*Intervention Costs*	*Total Savings*	Net Total	*Intervention Costs*	*Total Savings*	Net Total
Statins + Antihypertensives	*£621,108,601*	*-£603,175,652*	**£17,932,950**	*£1,367,017,855*	*-£1,947,887,566*	**-£580,869,711**	*£4,491,728,707*	*-£8,788,984,240*	**-£4,297,255,533**
Statins + Antihypertensives + Anticoagulants	*£752,023,737*	*-£682,144,575*	**£69,879,162**	*£1,717,446,364*	*-£2,192,697,826*	**-£475,251,462**	*£6,507,597,269*	*-£10,200,355,547*	**-£3,692,758,278**
Antihypertensives without BPSM	*£400,035,818*	*-£282,945,805*	**£117,090,013**	*£832,302,912*	*-£963,257,758*	**-£130,954,846**	*£2,477,025,757*	*-£5,421,286,367*	**-£2,944,260,611**
Antihypertensives	*£528,611,018*	*-£304,248,008*	**£224,363,010**	*£1,143,229,620*	*-£1,029,306,547*	**£113,923,073**	*£3,426,610,823*	*-£5,761,658,824*	**-£2,335,048,000**
Statins	*£100,876,913*	*-£316,576,725*	**-£215,699,812**	*£234,474,239*	*-£971,644,001*	**-£737,169,762**	*£1,097,114,485*	*-£3,235,146,466*	**-£2,138,031,981**
Antihypertensives + Anticoagulants	*£659,856,400*	*-£389,564,202*	**£270,292,197**	*£1,493,646,291*	*-£1,286,930,085*	**£206,716,206**	*£5,434,710,922*	*-£7,230,786,531*	**-£1,796,075,609**
Statins + Anticoagulants	*£232,515,590*	*-£400,347,502*	**-£167,831,912**	*£587,608,820*	*-£1,229,166,469*	**-£641,557,649**	*£3,140,793,856*	*-£4,709,271,081*	**-£1,568,477,224**
Annual Review	*£565,519,863*	*-£236,468,943*	**£329,050,919**	*£1,141,298,540*	*-£916,356,252*	**£224,942,288**	*£2,860,128,232*	*-£4,099,442,146*	**-£1,239,313,913**
NHS Health Check	*£224,765,026*	*-£24,231,154*	**£200,533,872**	*£577,684,193*	*-£167,122,683*	**£410,561,511**	*£1,389,685,190*	*-£1,852,817,079*	**-£463,131,890**
NHS DPP	*£50,146,575*	*-£7,639,660*	**£42,506,915**	*£29,041,171*	*-£24,009,402*	**£5,031,769**	*£35,477,157*	*-£40,822,563*	**-£5,345,406**
Weight Management	*£380,768,418*	*-£64,794,953*	**£315,973,465**	*£309,128,912*	*-£184,914,201*	**£124,214,711**	*£271,982,834*	*-£260,208,524*	**£11,774,310**
Nutritional Advice for CKD	*£121,818,196*	*-£29,864,570*	**£91,953,625**	*£84,611,944*	*-£62,361,111*	**£22,250,833**	*£97,330,981*	*-£80,042,627*	**£17,288,355**
Medicine Use Review	*£13,718,454*	*-£2,476,913*	**£11,241,541**	*£27,885,029*	*-£6,976,183*	**£20,908,846**	*£89,169,301*	*-£44,862,978*	**£44,306,323**
Diabetes Education	*£393,818,707*	*-£52,993,986*	**£340,824,721**	*£403,262,104*	*-£142,160,571*	**£261,101,533**	*£411,463,170*	*-£259,337,957*	**£152,125,213**
Cascade Testing	*£32,761,871*	*-£786,188*	**£31,975,683**	*£73,193,938*	*-£3,022,964*	**£70,170,974**	*£246,815,697*	*£4,241,935*	**£251,057,632**
Anticoagulants	*£132,080,860*	*-£90,356,501*	**£41,724,358**	*£353,367,237*	*-£269,752,365*	**£83,614,872**	*£2,033,165,905*	*-£1,511,754,245*	**£521,411,660**
Smoking Cessation	*£451,923,631*	*-£13,212,199*	**£438,711,432**	*£1,030,344,595*	*-£81,908,949*	**£948,435,646**	*£3,041,364,384*	*-£1,290,798,150*	**£1,750,566,234**
Blood Pressure Self Monitoring	*£374,442,107*	*-£55,503,309*	**£318,938,799**	*£905,552,800*	*-£190,632,881*	**£714,919,919**	*£2,852,811,587*	*-£951,772,265*	**£1,901,039,323**
Insulin Pump	*£358,169,565*	*-£1,071,565*	**£357,098,000**	*£814,426,229*	*-£4,972,803*	**£809,453,426**	*£2,295,771,232*	*-£32,246,185*	**£2,263,525,047**
Blood Glucose Lowering Therapy	*£220,059,088*	*-£72,569,805*	**£147,489,283**	*£812,978,579*	*-£286,604,045*	**£526,374,534**	*£10,009,354,411*	*-£3,852,740,070*	**£6,156,614,341**

Figure 3: Total net costs and savings accrued over time by optimising usage of each intervention. Costs are positive (above the horizontal axis) and savings are negative (below the horizontal axis).



The single intervention with the highest net total savings in the short term (years 2-5) is to optimise the proportion of people taking statins, which is predicted to save over £700m in England by year five (Table 3 & Figure 3). However, in the long term (20 years), optimising antihypertensive treatment is the single intervention predicted to save the most money (over £2 billion, or almost £3 billion if blood pressure self-monitoring costs are excluded). Other cost saving interventions over the 20-year time horizon include NHS Health Checks and annual review, indicating that detecting high risk conditions is a particularly cost-saving strategy (note that additional detected cases are assumed to be managed through current care, therefore increased detection leads to increased management).

Most of the lifestyle interventions (with the exception of the NHS DPP) are not cost-saving over the 20-year time horizon. It is important to note that the impact of lifestyle interventions in preventing CVD may be under-estimated by the tool due to the lack of direct evidence linking these interventions to CVD. Whilst the CVD benefits have been modelled through the impact of metabolic changes on QRISK (BMI, systolic blood pressure, cholesterol and smoking), any CVD benefits acting independently of these metabolic changes will not be incorporated.

If users wish to look at the benefits of multiple policies (e.g. optimising usage of multiple interventions), then these should be run simultaneously. Some intervention combinations have been analysed to demonstrate the interactions between interventions aimed at treating different high risk conditions. The model assumes that the interventions act independently on their respective risk factors and on CVD risk, as no evidence could be found to support an alternative hypothesis. The most cost-saving

combination analysed here is to combine antihypertensive and statin treatment; predicted to save over £4 billion within 20 years. Note that because the model is an individual patient simulation it includes individuals with multiple comorbidities and therefore does not double count the benefits of two or more interventions given to the same person.

It is important to note that intervention costs relate not only to the selected intervention(s), but also to any changes in the absolute usage of other interventions that may occur as a consequence of keeping the proportion of people eligible for those interventions constant over time. An example of this is shown in Table 4, which focusses in on optimisation of NHS Health Checks. Only about half of the intervention costs in year 1 relate to cost of the NHS Health Check itself, with other costs coming from additional diagnostics to confirm diagnosis in those newly detected and from an increase in usage of management interventions that individuals are eligible for following their diagnosis.

Table 4: Breakdown of Intervention Costs following Optimisation of NHS Health Checks

	NHS Health Checks	
	Year 1	Year 2
NHS Health Check Costs	£53,707,329	£82,584,129
Annual Review Costs	£0	£8,173,516
Cascade Testing Costs	£1,634,835	£2,605,763
Diagnosis Costs	£19,797,798	£35,809,494
Statin Costs	£1,578,785	£5,453,065
Antihypertensive Costs	£9,233,250	£25,134,455
Anticoagulant Costs	£475,575	£252,433
Blood Glucose Lowering Therapy Cost	£1,700,267	£6,454,479
NHS DPP Costs	£10,819,482	£26,302,565
Diabetes Education Costs	£213,579	£465,186
Weight Management Costs	£3,450,484	£9,179,283
Smoking Cessation Costs	£706,871	£1,959,560
Nutritional Advice for CKD Costs	£86,973	£228,737
Medicine Use Review Costs	£5,234,571	£10,736,107
Blood Pressure Self Monitoring Costs	£3,094,873	£9,447,610
Insulin Pump Costs	£0	-£21,356
TOTAL INTERVENTION COSTS	**£111,734,673**	**£224,765,026**

In general, the reasons for changes in the cost of other interventions can be summarised as follows:

Usage of interventions may be increased indirectly if more individuals live for longer as a result of the target change, or if more individuals are diagnosed with high risk conditions as a result of the target change (e.g. if the usage of NHS Health Checks is increased as shown in Table 4).

Usage of interventions may be reduced indirectly if individuals are healthier as a result of the target change (e.g. the NHS DPP reduces the usage of statins and

antihypertensives as the intervention is predicted to reduce blood pressure and cholesterol and therefore reduce the numbers eligible for those treatments).

There are two interventions; blood pressure self-monitoring and medicine use review, which people taking either antihypertensive treatment or any pharmacological intervention are eligible for respectively. If a user chooses to increase usage of pharmacological interventions, this means that there will be a larger pool of people eligible for blood pressure self-monitoring or medicine use review, and therefore usage of these two interventions will increase indirectly. An example of the consequences of this is shown by comparing rows 3 and 4 in Table 3. In row 3, the indirect impact of additional blood pressure self-monitoring as a result of increasing antihypertensive usage has been removed by setting its usage to 0% for both current and target care.

This reduces the intervention costs more than it reduces the total savings, resulting in a higher net total saving at 20 years compared to row 4.

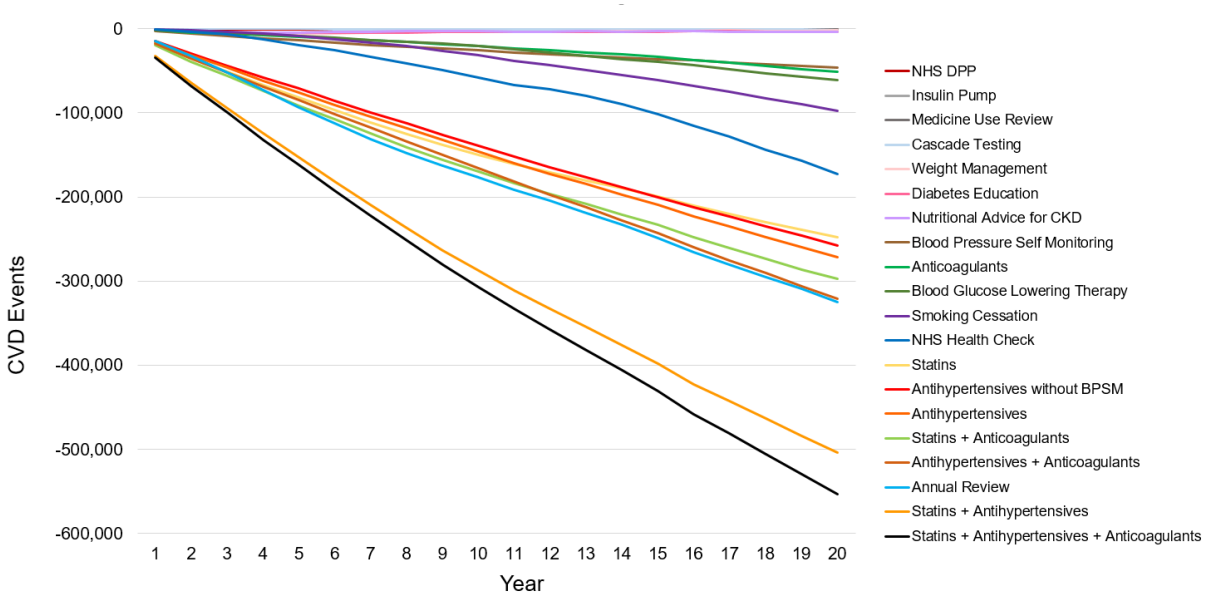
All interventions are predicted to prevent CVD events (Table 5 & Figure 4), with the single intervention preventing most events being annual review. Annual review is used to identify and thereby manage additional high risk comorbidities in people with a pre-existing condition, so this indicates the importance for CVD prevention of intervening in people at very high risk due to multiple comorbidities. The pharmacological treatments tend to perform better than lifestyle interventions in preventing CVD over the short and long-term, with smoking cessation also producing important benefits. Combining pharmacological treatments increases the health benefits produced in a linear way.

Most of the lifestyle interventions have been assumed to have a five-year duration of effect. Optimising usage of these interventions to 100% leads to all eligible individuals receiving it in the first year and only small numbers of newly diagnosed receiving it in subsequent years. This means that most of the benefits of lifestyle interventions in preventing CVD are seen in the first five years of the model, after which some individuals succumb to delayed CVD, thereby reducing the number of cumulative CVD events prevented.

Table 5: CVD Events prevented over time by optimising usage of each intervention. Interventions are shown in order with those producing the highest reduction in events at 20 years at the top of the table.

	Year 2	Year 5	Year 10	Year 20
Statins + Antihypertensives + Anticoagulants	-68,101	-162,369	-307,481	-552,983
Statins + Antihypertensives	-64,298	-153,452	-287,750	-503,737
Annual Review	-32,398	-93,578	-176,450	-325,005
Antihypertensives + Anticoagulants	-35,640	-85,268	-166,153	-321,364
Statins + Anticoagulants	-39,010	-91,543	-170,089	-297,765
Antihypertensives	-31,568	-76,038	-146,360	-271,331
Antihypertensives without BPSM	-29,898	-71,161	-139,352	-257,867
Statins	-34,971	-82,135	-149,583	-247,390
NHS Health Check	-3,337	-19,454	-58,607	-173,242
Smoking Cessation	-1,895	-8,968	-31,801	-97,584
Blood Glucose Lowering Therapy	-3,496	-8,809	-20,817	-61,561
Anticoagulants	-4,358	-9,764	-20,748	-51,228
Blood Pressure Self Monitoring	-5,821	-14,127	-25,721	-46,014
Nutritional Advice for CKD	-4,234	-4,645	-3,099	-4,020
Diabetes Education	-3,326	-5,123	-4,068	-3,353
Weight Management	-4,449	-6,509	-3,896	-2,205
Cascade Testing	-136	-355	-757	-1,455
Medicine Use Review	-129	-284	-618	-1,254
Insulin Pump	-86	-221	-372	-676
NHS DPP	-709	-1,278	-1,271	-502

Figure 4: CVD Events prevented over time by optimising usage of each intervention



All interventions are predicted to increase QALYs and life years with annual review being the single intervention producing the most benefit (see Table 6, Table 7 and Figure 5). Combining statins and anti-hypertensives produces the most QALYs of all combinations tested. It also produces more life years in combination than the sum of optimising the two interventions separately indicating that there is a disproportionate mortality benefit in optimising these two interventions together.

Table 6: QALYs gained over time by optimising usage of each intervention. Interventions are shown in order with those producing the highest QALY gain at 20 years at the top of the table.

	Year 2	Year 5	Year 10	Year 20
Statins + Antihypertensives	13,903	93,828	339,504	966,172
Statins + Antihypertensives + Anticoagulants	12,984	87,775	316,150	883,234
Antihypertensives + Anticoagulants	7,190	50,296	192,003	610,691
Annual Review	5,370	45,270	184,871	529,734
Antihypertensives	6,194	43,879	167,698	523,392
Antihypertensives without BPSM	5,855	41,563	159,950	499,644
Statins + Anticoagulants	8,184	53,086	184,155	479,565
Statins	7,233	46,753	159,143	390,579
NHS Health Check	492	6,647	48,793	222,252
Blood Glucose Lowering Therapy	1,116	7,829	33,329	158,375
Smoking Cessation	300	3,566	23,743	137,796
Anticoagulants	1,032	6,734	25,997	90,771
Blood Pressure Self Monitoring	1,116	8,188	30,439	88,477
Weight Management	1,807	8,678	18,530	26,880
Diabetes Education	981	5,533	12,977	19,964
Nutritional Advice for CKD	700	3,487	6,836	12,004
NHS DPP	201	1,756	5,351	10,164
Medicine Use Review	35	253	818	2,490
Cascade Testing	26	90	521	2,454
Insulin Pump	28	165	611	2,016

Figure 5: QALYs gained over time by optimising usage of each intervention

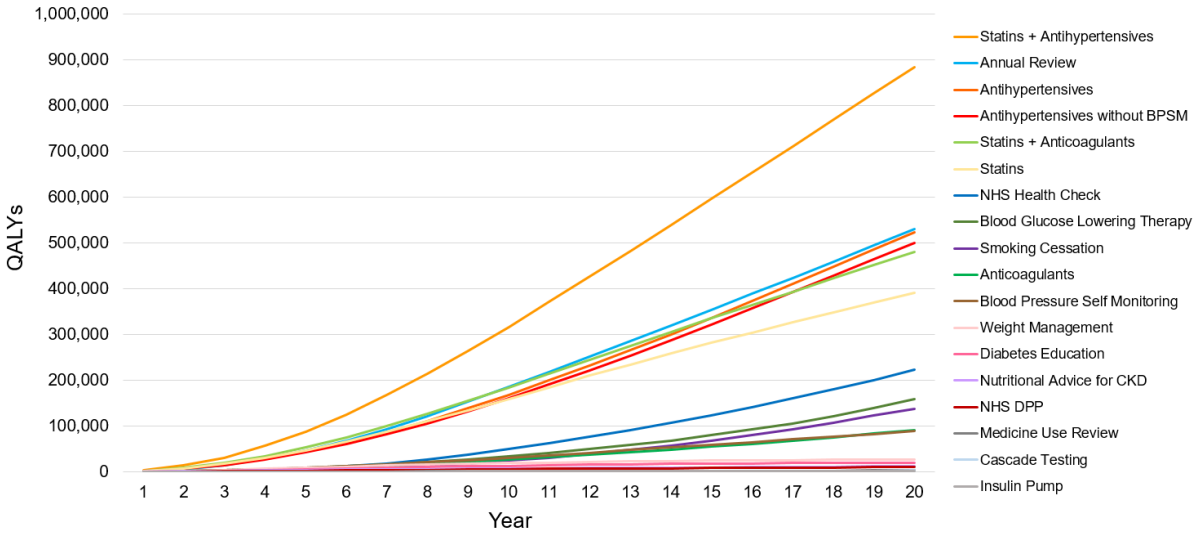


Table 7: life years gained over time by optimising usage of each intervention.
Interventions are shown in order with those producing the highest life year gain at 20 years at the top of the table.

	Year 2	Year 5	Year 10	Year 20
Statins + Antihypertensives	2,450	44,507	214,690	729,079
Statins + Antihypertensives + Anticoagulants	2,327	41,629	198,645	656,991
Antihypertensives + Anticoagulants	1,154	23,695	123,810	479,980
Annual Review	1,166	22,614	123,603	424,213
Antihypertensives	1,035	20,647	106,991	405,114
Antihypertensives without BPSM	942	19,483	102,275	387,369
Statins + Anticoagulants	1,490	25,500	117,025	353,131
Statins	1,371	22,495	99,732	275,724
NHS Health Check	66	2,423	24,617	133,677
Smoking Cessation	54	1,531	13,499	107,890
Anticoagulants	119	3,226	17,969	78,245
Blood Pressure Self Monitoring	197	4,029	20,485	72,275
Blood Glucose Lowering Therapy	140	2,551	13,423	67,915
Diabetes Education	216	2,673	7,810	13,975
Weight Management	92	1,738	6,759	11,793
Nutritional Advice for CKD	115	1,754	5,158	11,293
NHS DPP	19	994	4,419	9,893
Cascade Testing	0	-53	79	2,336
Medicine Use Review	10	161	560	1,463
Insulin Pump	3	33	188	948

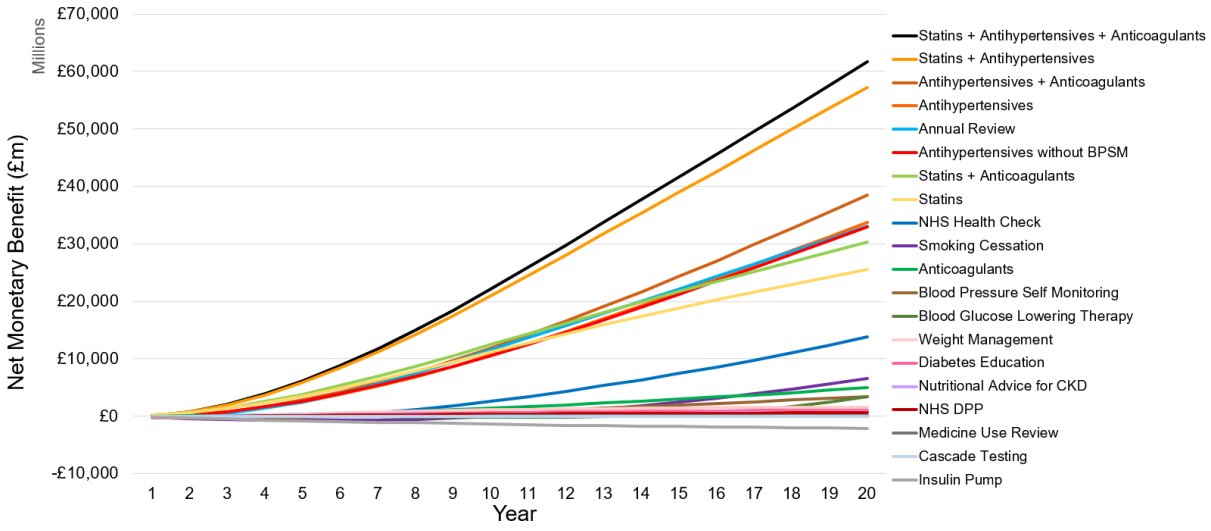
Most interventions are predicted to reduce premature mortality in the long-term, with annual review being the single intervention producing the most benefit (data not shown). However, a small increase in cases of premature mortality is seen with anticoagulants. Although highly effective, anticoagulants are also associated with a relatively small risk of major bleeding, which may be fatal. The magnitude of this effect is subject to considerable uncertainty, and there is a high probability that the modelled effects on premature mortality when running scenarios that increase anticoagulant usage may not be statistically significant. Anticoagulants are recommended by NICE for their overall positive impacts on quality and length of life, as shown by Table 6 and Table 7.

Within the 20 year time horizon, all but two interventions produce positive net monetary benefit (NMB) using £60,000 as the value of a QALY (Table 8 & Figure 6), with anti-hypertensives producing the most NMB of all single interventions. Only a very small number of people in the model have FH or type 1 diabetes and therefore this contributes to high uncertainty around the benefits of Cascade testing and insulin pump.

Table 8: Net Monetary Benefit (value of a QALY = £60,000) obtained over time by optimising usage of each intervention. Interventions are shown in order with those producing the highest NMB at 20 years at the top

	Year 2	Year 5	Year 10	Year 20
Statins + Antihypertensives + Anticoagulants	£764,286,234	£6,104,960,118	£22,162,681,374	£61,663,069,068
Statins + Antihypertensives	£761,079,120	£5,847,360,447	£20,962,312,599	£57,291,288,393
Antihypertensives + Anticoagulants	£161,096,577	£2,811,029,856	£11,856,787,881	£38,437,553,765
Antihypertensives	£147,298,158	£2,518,846,267	£10,584,202,754	£33,738,541,174
Annual Review	-£6,880,037	£2,491,243,318	£11,518,587,355	£33,023,355,479
Antihypertensives without BPSM	£234,214,745	£2,624,723,350	£10,534,778,008	£32,922,905,795
Statins + Anticoagulants	£658,901,150	£3,826,706,357	£12,429,154,289	£30,342,355,774
Statins	£649,652,806	£3,542,320,626	£11,104,021,766	£25,572,753,027
NHS Health Check	-£171,030,828	-£11,722,395	£2,543,494,016	£13,798,246,424
Smoking Cessation	-£420,703,476	-£734,483,758	-£41,604,039	£6,517,222,398
Anticoagulants	£20,211,470	£320,424,984	£1,396,762,646	£4,924,831,828
Blood Pressure Self Monitoring	-£251,952,531	-£223,630,475	£620,360,521	£3,407,583,917
Blood Glucose Lowering Therapy	-£80,505,847	-£56,626,716	-£197,649,576	£3,345,890,789
Weight Management	-£207,537,991	£396,469,483	£1,085,361,572	£1,601,004,366
Diabetes Education	-£281,968,537	£70,875,635	£592,055,784	£1,045,702,367
Nutritional Advice for CKD	-£49,964,503	£186,979,985	£392,036,504	£702,974,613
NHS DPP	-£30,465,161	£100,306,481	£335,114,573	£615,177,498
Medicine Use Review	-£9,126,787	-£5,736,448	£16,023,005	£105,091,991
Cascade Testing	-£30,390,207	-£64,775,666	-£81,873,539	-£103,832,254
Insulin Pump	-£355,436,096	-£799,574,402	-£1,388,033,813	-£2,142,573,933

Figure 6: Net Monetary Benefit obtained over time by optimising usage of each intervention



Optimising detection and management of high risk conditions

Table 9 shows the intervention costs, total savings (CVD and non-CVD combined) and net total accrued after 2, 5 and 20 years when optimising detection and/or management of each condition. Detecting and managing each of the high risk conditions is predicted to produce cost-savings, but in many cases these are lower than the costs of the interventions whose use is increased as a direct or indirect consequence of the additional detection and management.

Additional detection or management of high risk conditions leads directly to increased usage of interventions that NICE guidelines recommend for managing the high risk condition of interest (a full list of these for each condition can be found in the database of interventions). It is assumed that additional detection occurs through opportunistic mechanisms, therefore increased detection does not directly lead to increased usage of NHS Health Check or annual review. However, there may be indirect consequences as outlined above. An additional indirect consequence of increasing the target for detection is that the numbers eligible for NHS Health Check (i.e. with no diagnosed high risk condition) will be reduced and the numbers eligible for annual review (i.e. those with one or more diagnosed high risk condition) will be increased.

In the short term most money is saved by optimising detection and management of CKD (net savings of £802m by year 5) (Table 9 & Figure 7). This is likely to be due to a combination of costs saved through CVD prevention and prevention of end-stage renal failure which is very expensive to manage. Optimising detection of those with QRISK ≥10% is also very cost-saving in the short term (net savings of £59m by year two and £555m by year five). This is likely to be due to two factors; firstly, the current percentage of those diagnosed with QRISK ≥10% is only 10.7% so potential improvements are large, and secondly, the primary management intervention is statins, which are very cost-saving (see the optimising interventions section).

Table 9: Intervention Costs, Total Savings (combined NHS and social care) and Net Total Financial Costs/Savings produced by maximising detection and/or management of each high risk condition. Costs are positive and savings are negative. Conditions are shown in order with those producing the highest net cost-savings at 20 years at the top of each subsection of the table.

	Year 2			Year 5			Year 20		
	Intervention Costs	*Total Savings*	Net Total	*Intervention Costs*	*Total Savings*	Net Total	*Intervention Costs*	*Total Savings*	Net Total
Detection Diabetes	*£267,052,390*	*-£86,455,367*	**£180,597,023**	*£763,207,582*	*-£223,639,635*	**£539,567,948**	*£2,931,207,158*	*-£34,562,907,341*	**-£31,631,700,183**
Detection QRISK ≥10%	*£361,078,532*	*-£420,105,604*	**-£59,027,072**	*£934,653,688*	*-£1,490,015,971*	**-£555,362,283**	*£4,553,716,479*	*-£5,284,571,117*	**-£730,854,638**
Detection CKD	*£83,790,677*	*-£123,643,108*	**-£39,852,431**	*£178,068,011*	*-£384,112,540*	**-£206,044,529**	*£596,411,091*	*-£1,108,681,352*	**-£512,270,261**
Detection Hypertension	*£838,113,811*	*-£171,530,791*	**£666,583,021**	*£1,606,452,179*	*-£681,358,798*	**£925,093,381**	*£4,003,447,327*	*-£4,059,032,556*	**-£55,585,229**
Detection FH	*£177,279,002*	*-£15,254,092*	**£162,024,909**	*£250,152,093*	*-£50,612,307*	**£199,539,786**	*£502,530,477*	*-£194,983,261*	**£307,547,216**
Detection AF	*£167,765,061*	*-£95,635,665*	**£72,129,396**	*£478,863,544*	*-£325,575,775*	**£153,287,769**	*£2,535,998,574*	*-£1,680,814,247*	**£855,184,327**
Detection NDH	*£1,315,546,693*	*-£59,065,079*	**£1,256,481,614**	*£2,793,277,997*	*-£381,441,991*	**£2,411,836,006**	*£4,008,346,672*	*-£373,653,471*	**£3,634,693,200**
Management CKD	*£422,264,750*	*-£370,660,437*	**£51,604,313**	*£586,362,425*	*-£1,025,697,868*	**-£439,335,444**	*£1,618,763,597*	*-£2,721,000,961*	**-£1,102,237,363**
Management QRISK ≥10%	*£329,972,849*	*-£155,236,499*	**£174,736,350**	*£634,302,076*	*-£540,256,061*	**£94,046,015**	*£2,650,276,975*	*-£2,877,236,971*	**-£226,959,996**
Management FH	*£2,430,124*	*-£306,626*	**£2,123,498**	*£4,799,062*	*-£599,966*	**£4,199,096**	*£12,537,464*	*£8,285,673*	**£20,823,138**
Management NDH	*£93,088,880*	*-£9,815,830*	**£83,273,050**	*£101,534,337*	*-£31,934,864*	**£69,599,473**	*£195,692,686*	*-£122,892,131*	**£72,800,555**
Management Hypertension	*£1,214,385,911*	*-£219,250,999*	**£995,134,913**	*£2,292,514,047*	*-£809,023,256*	**£1,483,490,791**	*£5,692,531,716*	*-£5,174,655,013*	**£517,876,703**
Management AF	*£209,203,419*	*-£100,345,301*	**£108,858,118**	*£491,502,190*	*-£301,160,852*	**£190,341,338**	*£2,444,596,071*	*-£1,716,794,476*	**£727,801,595**
Management Diabetes	*£2,000,160,461*	*-£247,628,140*	**£1,752,532,321**	*£4,233,862,590*	*-£864,311,820*	**£3,369,550,770**	*£19,107,347,160*	*-£6,365,028,365*	**£12,742,318,795**
Detection & Management Diabetes	*£2,511,109,639*	*-£371,424,526*	**£2,139,685,112**	*£5,350,568,725*	*-£1,216,930,832*	**£4,133,637,893**	*£19,111,104,478*	*-£40,244,416,033*	**-£21,133,311,555**
Detection & Management CKD	*£717,238,622*	*-£658,377,581*	**£58,861,042**	*£1,086,406,307*	*-£1,889,265,617*	**-£802,859,309**	*£3,233,433,812*	*-£5,026,641,056*	**-£1,793,207,243**
Detection & Management QRISK ≥10%	*£2,916,175,029*	*-£1,625,897,041*	**£1,290,277,988**	*£6,081,164,840*	*-£5,324,133,133*	**£757,031,707**	*£21,451,032,324*	*-£21,491,797,878*	**-£40,765,554**
Detection & Management FH	*£200,559,642*	*-£18,645,297*	**£181,914,344**	*£295,053,289*	*-£62,049,485*	**£233,003,803**	*£608,959,517*	*-£243,273,177*	**£365,686,340**
Detection & Management AF	*£437,531,566*	*-£228,963,313*	**£208,568,253**	*£1,117,755,113*	*-£723,512,672*	**£394,242,441**	*£5,728,676,411*	*-£3,942,779,279*	**£1,785,897,131**
Detection & Management Hypertension	*£2,987,927,895*	*-£519,754,274*	**£2,468,173,621**	*£5,846,167,218*	*-£1,953,171,505*	**£3,892,995,713**	*£14,990,522,795*	*-£12,189,692,463*	**£2,800,830,333**
Detection & Management NDH	*£2,896,826,961*	*-£177,368,132*	**£2,719,458,829**	*£4,915,371,352*	*-£805,002,049*	**£4,110,369,303**	*£7,477,060,976*	*-£2,025,645,089*	**£5,451,415,887**

In the long-term, optimising detection of those with diabetes is estimated to save the most money (almost £32 billion), which is far higher than detection or management of any other condition (Table 9, Figure 7, Figure 8 & Figure 9). This is likely to be partially due to the fact that the proportion of people thought to have undiagnosed diabetes is high (about 30% of the total), and partially due to the high costs of treating diabetes and its complications. Perhaps counterintuitively, optimising management of diabetes in those already detected does not produce net cost savings within 20 years. The reason for this discrepancy between optimising management and detection of diabetes is likely to be due to the benefits of early detection of diabetes. By optimising detection, individuals are diagnosed within a year after getting diabetes, when their HbA1c is only just over 6.5%. These people are known to have much better outcomes than people diagnosed at higher HbA1c (UKPDS study[28]), and within a 20 year time horizon tend to only require treatment with the relatively cheap first and second line glucose lowering therapies such as metformin. Conversely, optimising management of those who are already detected, but who are not being treated adequately, is likely to require the much more expensive third line therapies including insulin. Note that optimising both detection and management together for any of the high risk conditions does not produce additive effects.

Figure 7: Total net costs and savings accrued over time by optimising detection of each high risk condition. Costs are positive (above the horizontal axis) and savings are negative (below the horizontal axis).

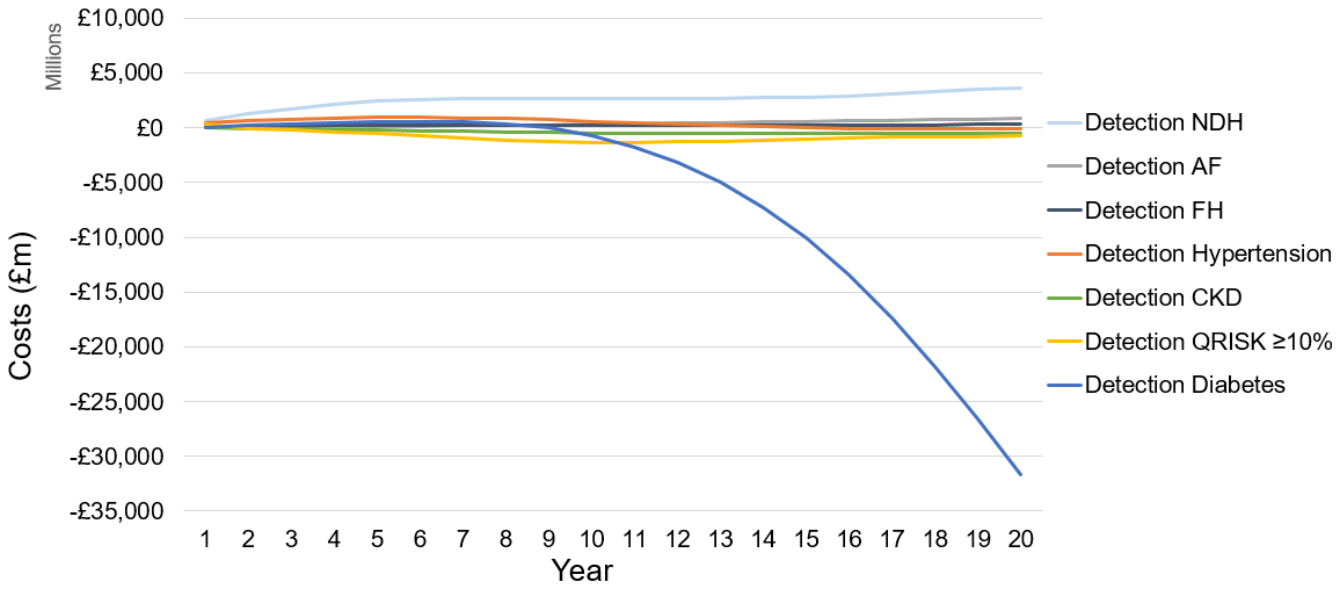


Figure 8: Total net costs and savings accrued over time by optimising management of each high risk condition. Costs are positive (above the horizontal axis) and savings are negative (below the horizontal axis).

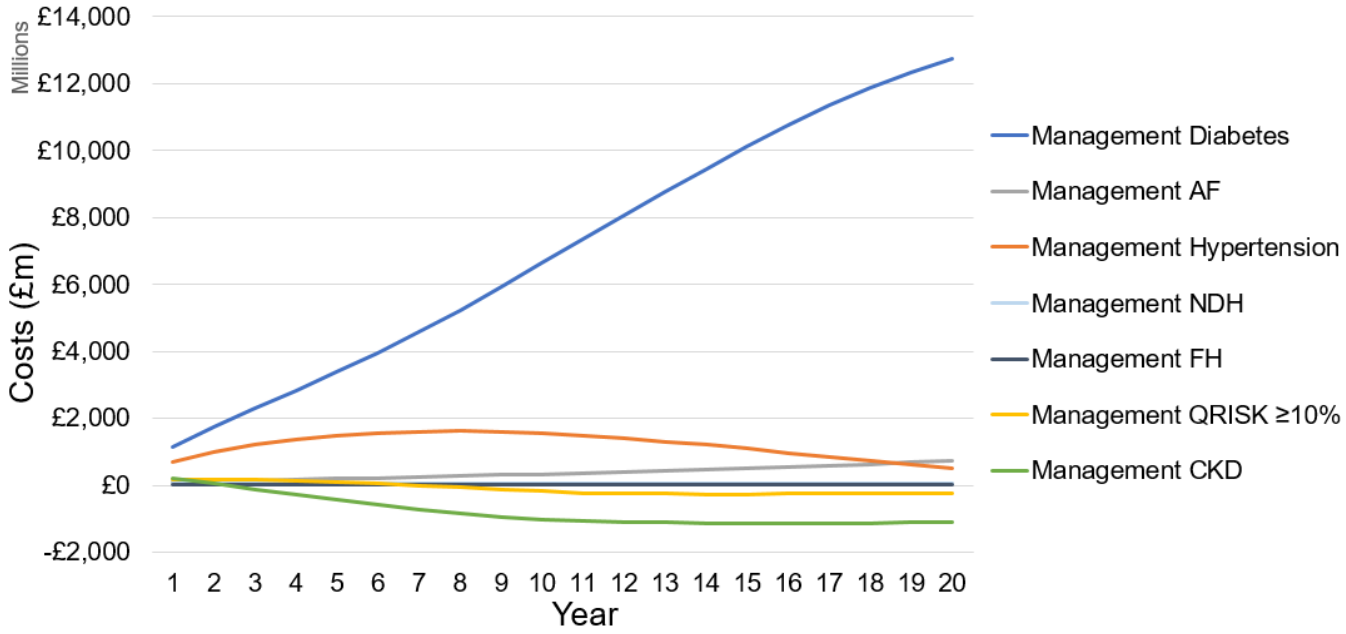
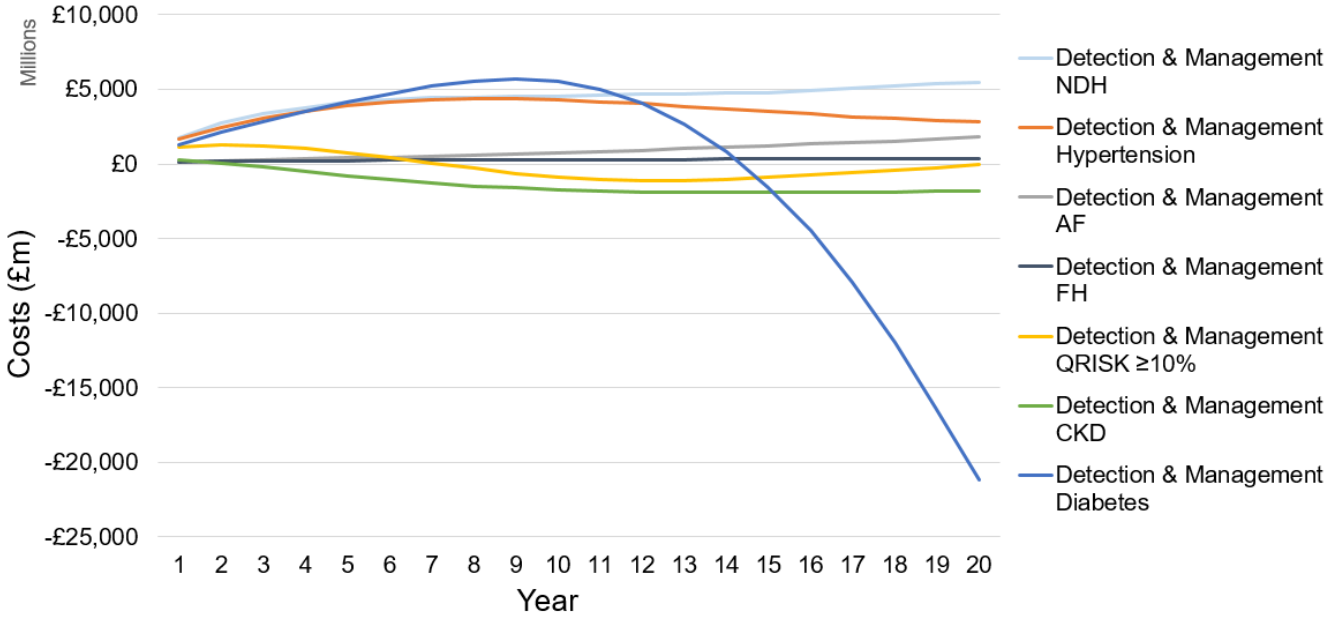


Figure 9: Total net costs and savings accrued over time by optimising detection & management of each high risk condition. Costs are positive (above the horizontal axis) and savings are negative (below the horizontal axis).



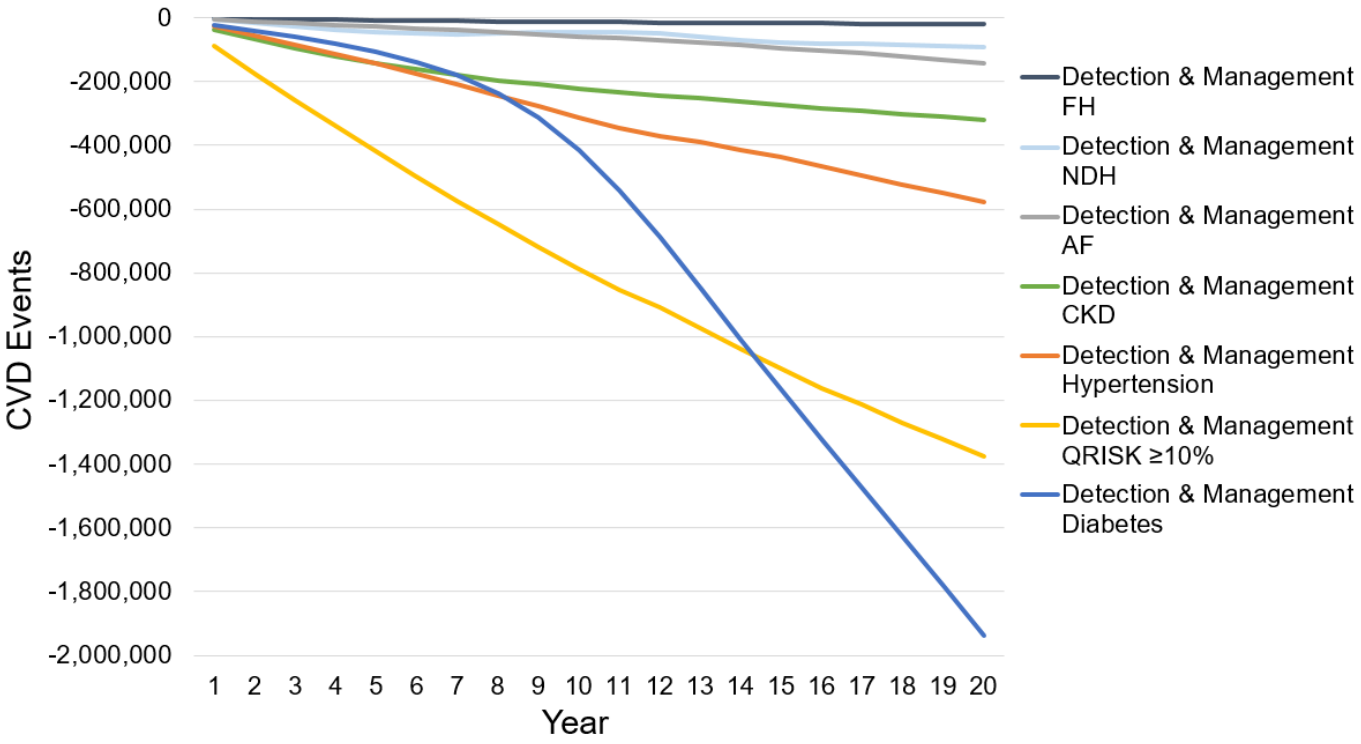
CVD events are prevented when detection and management is optimised for all high risk conditions (Table 10 & Figure 10). In line with cost savings, most CVD events are prevented in the short-term by improving detection of QRISK ≥10%, and in the long-term by improving detection of diabetes, with even more events prevented if management is optimised at the same time.

Optimising detection of NDH actually causes a slight increase in the number of CVD events by year 20. This is likely to be due to the fact that people identified with NDH are primarily eligible for the DPP, a one-off intervention which has only a five-year duration of effect. Although this delays the onset of diabetes and CVD, and reduces mortality, individuals will eventually succumb to these conditions after the DPP effectiveness wears off, thereby reducing the number of cumulative CVD events prevented in the long-term. This indicates the importance of also optimising the management of NDH, and the detection and management of diabetes if long-term benefits are to be seen.

Table 10: CVD Events prevented over time by optimising detection and/or management of each high risk condition. Conditions are shown in order with those producing the highest reduction in CVD events at 20 years at the top of each subsection of the table.

	Year 2	Year 5	Year 10	Year 20
Detection Diabetes	-15,478	-47,362	-299,906	-1,691,096
Detection QRISK ≥10%	-51,780	-137,702	-251,802	-488,946
Detection Hypertension	-19,074	-51,796	-116,539	-190,798
Detection CKD	-13,144	-31,637	-51,482	-65,809
Detection AF	-4,650	-12,366	-25,074	-59,946
Detection FH	-3,031	-6,614	-9,780	-15,232
Detection NDH	-6,093	-23,684	-9,123	1,271
Management Hypertension	-21,757	-58,071	-126,344	-249,658
Management Diabetes	-21,568	-50,494	-102,791	-222,240
Management CKD	-38,327	-78,377	-126,060	-192,929
Management QRISK ≥10%	-16,228	-41,530	-89,611	-166,276
Management AF	-5,300	-11,662	-24,565	-60,861
Management NDH	-824	-1,725	-2,907	-5,475
Management FH	-34	-78	-121	48
Detection & Management Diabetes	-40,311	-105,713	-415,380	-1,936,938
Detection & Management QRISK ≥10%	-175,238	-419,835	-788,389	-1,375,369
Detection & Management Hypertension	-54,353	-144,166	-313,980	-576,808
Detection & Management CKD	-68,447	-143,888	-221,106	-322,066
Detection & Management AF	-11,527	-27,475	-57,700	-141,071
Detection & Management NDH	-16,527	-46,206	-44,222	-90,699
Detection & Management FH	-3,610	-7,959	-12,628	-20,294

Figure 10: CVD Events prevented over time by optimising detection and management of each high risk condition



QALYs and life years are gained over time when detection and/or management of each high risk condition is optimised (Table 11 and Table 12). Initially a slight reduction in QALYs (but not life years) is seen when detection of diabetes is optimised. This is likely to be due to the increase in depression which occurs when individuals are diagnosed with diabetes. However, in subsequent years, this is overwhelmed by a huge gain in QALYs as diabetes complications are prevented through early diagnosis and treatment, meaning that by 20 years, optimising diabetes detection is much more beneficial than optimising detection of any other condition. Management of hypertension produces more QALYs and life years than any other management strategy, whilst detection and management of diabetes is the most beneficial strategy overall.

Table 11: QALYs gained over time by optimising detection and/or management of each high risk condition. Conditions are shown in order with those producing the highest QALY gain at 20 years at the top of each subsection of the table.

	Year 2	Year 5	Year 10	Year 20
Detection Diabetes	-585	-4,619	84,002	2,038,833
Detection QRISK ≥10%	9,832	72,575	266,224	698,805
Detection Hypertension	3,696	28,791	125,916	394,946
Detection NDH	1,493	20,703	97,784	199,114
Detection CKD	2,718	18,337	60,767	126,207
Detection AF	1,126	8,146	32,853	105,330
Detection FH	562	3,692	12,594	34,177
Management Hypertension	4,700	33,942	136,621	467,671
Management Diabetes	5,115	32,836	117,882	401,293
Management CKD	7,931	48,721	153,636	346,061
Management QRISK ≥10%	3,421	23,562	89,435	264,988
Management AF	1,269	8,185	30,817	106,960
Management NDH	249	2,135	7,363	19,240
Management FH	6	70	207	513
Detection & Management Diabetes	5,369	34,268	220,337	2,464,418
Detection & Management QRISK ≥10%	36,820	240,969	839,065	2,249,825
Detection & Management Hypertension	11,265	84,025	346,858	1,151,729
Detection & Management CKD	14,189	89,055	277,468	608,245
Detection & Management NDH	4,417	46,052	177,328	402,106
Detection & Management AF	2,827	19,109	74,074	251,452
Detection & Management FH	662	4,441	15,080	40,854

Figure 11: QALYs gained over time by optimising detection and management of each high risk condition

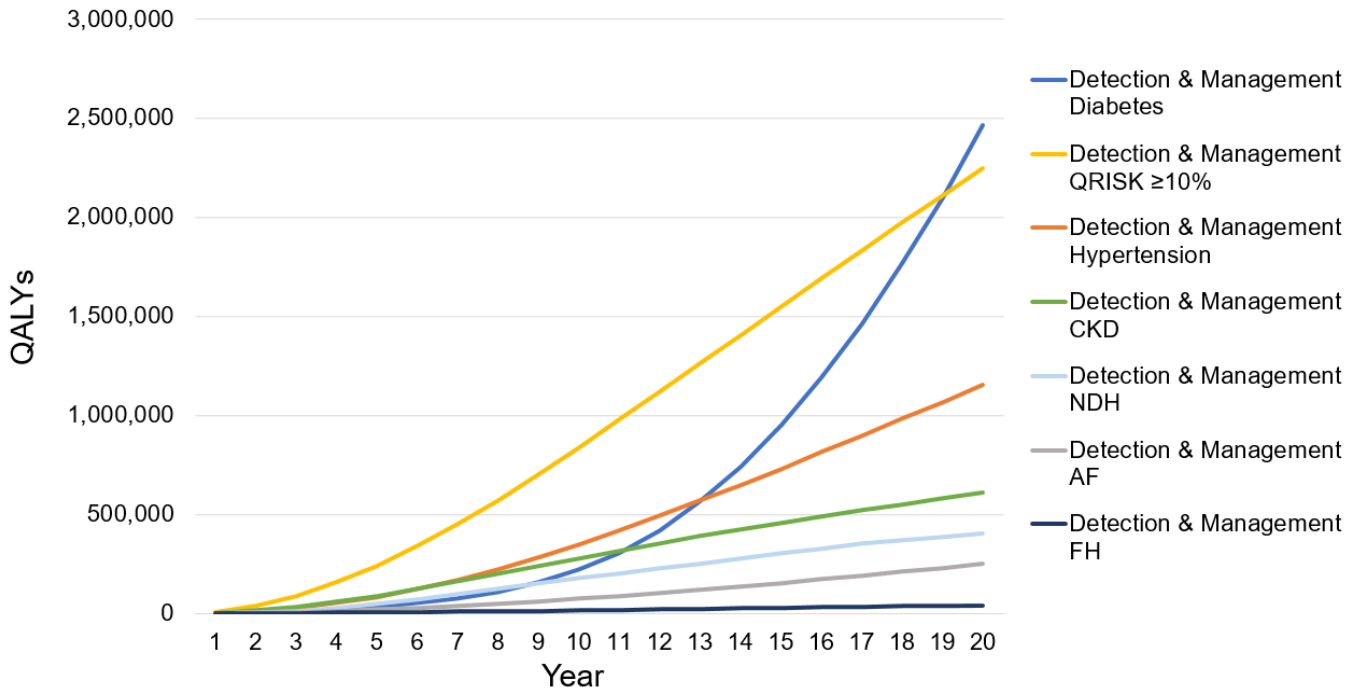


Table 12: Life years gained over time by optimising detection and/or management of each high-risk condition. Conditions are shown in order with those producing the highest life year gain at 20 years at the top of each subsection of the table.

	Year 2	Year 5	Year 10	Year 20
Detection Diabetes	659	5,677	73,536	1,275,450
Detection QRISK ≥10%	1,812	32,325	155,700	425,350
Detection Hypertension	530	11,650	68,453	292,805
Detection NDH	116	8,410	63,864	219,736
Detection CKD	534	9,354	39,619	95,592
Detection AF	166	4,013	23,741	88,581
Detection FH	85	1,481	6,828	24,447
Management Hypertension	603	13,757	79,918	354,536
Management CKD	1,371	24,750	107,223	284,219
Management Diabetes	754	12,853	62,216	249,252
Management QRISK ≥10%	620	10,400	50,733	182,081
Management AF	146	3,721	20,466	88,731
Management NDH	27	1,152	5,593	17,277
Management FH	0	50	166	690
Detection & Management Diabetes	1,478	20,887	146,099	1,554,567
Detection & Management QRISK ≥10%	6,508	104,598	474,479	1,479,572
Detection & Management Hypertension	1,475	33,545	194,000	841,181
Detection & Management CKD	2,567	45,334	190,051	484,239
Detection & Management NDH	383	20,537	117,097	358,676
Detection & Management AF	391	9,372	51,794	213,355
Detection & Management FH	100	1,831	8,084	27,625

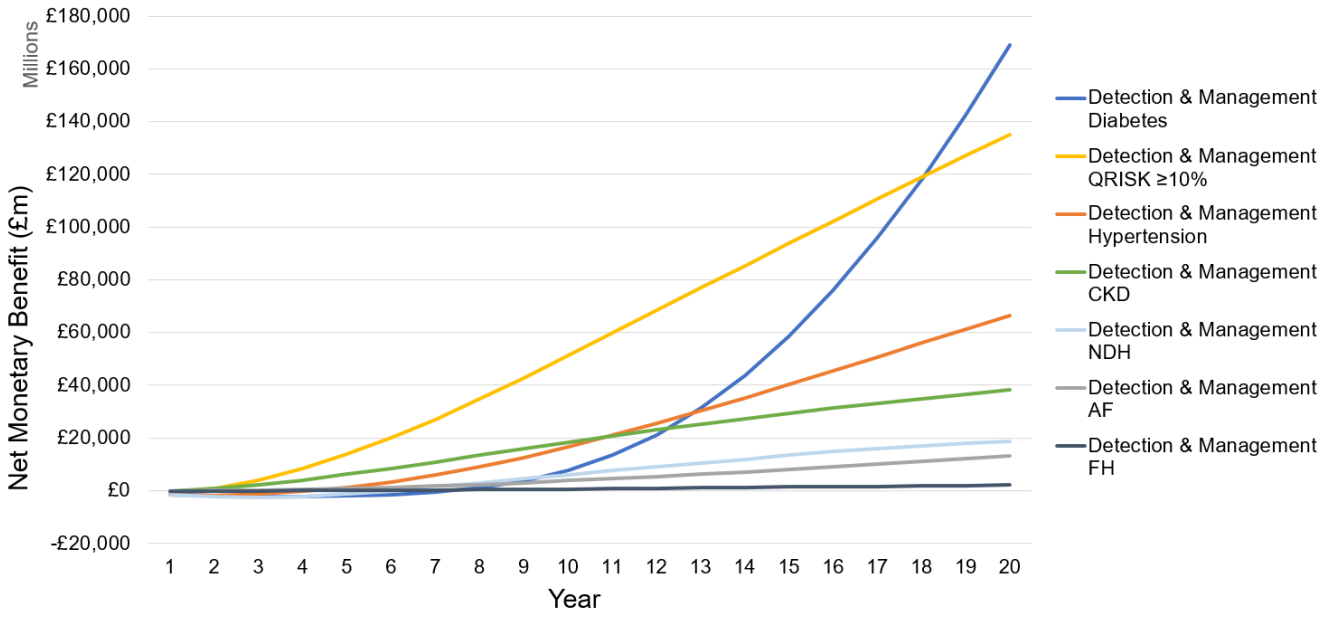
Premature mortality is predicted to be generally reduced through improving detection and management of all high risk conditions apart from AF, with highest reduction of premature mortality produced through optimising detection and management of diabetes (data not shown). Detection and management of AF involves increasing usage of anticoagulants. Although highly effective, anticoagulants are also associated with a relatively small risk of major bleeding, which may be fatal. The magnitude of this effect is subject to considerable uncertainty, and the modelled effects on premature mortality with increased AF detection or management may not be statistically significant. Anticoagulants are recommended by NICE for their overall positive impacts on quality and length of life' the where optimising detection and/or management.

Optimising detection and management of all conditions produces net monetary benefit by year 20 (Table 13 & Figure 12). Detection and management of people with QRISK ≥ 10% produces the highest NMB in the short-term (£919m at year 2), whilst in the long-term, detection and management of new diabetes cases produces much higher NMB than any of the other options (£169 billion at year 20).

Table 13: Net Monetary Benefit (value of a QALY = £60,000) obtained over time by optimising detection and/or management of each high risk condition. Conditions are shown in order with those producing the highest NMB at 20 years at the top of each subsection of the table.

	Year 2	Year 5	Year 10	Year 20
Detection Diabetes	-£215,686,751	-£816,736,646	£5,740,840,219	£153,961,707,765
Detection QRISK ≥10%	£648,972,188	£4,909,853,727	£17,311,547,582	£42,659,145,554
Detection Hypertension	-£444,836,935	£802,378,421	£6,958,557,107	£23,752,373,801
Detection NDH	-£1,166,913,386	-£1,169,668,186	£3,171,098,116	£8,312,152,074
Detection CKD	£202,953,473	£1,306,275,443	£4,123,998,623	£8,084,690,453
Detection AF	-£4,571,880	£335,478,855	£1,651,979,024	£5,464,605,875
Detection FH	-£128,319,261	£21,990,156	£512,507,152	£1,743,070,804
Management Hypertension	-£713,135,231	£553,047,479	£6,653,080,203	£27,542,400,433
Management CKD	£424,265,101	£3,362,577,726	£10,230,052,775	£21,865,904,347
Management QRISK ≥10%	£30,493,806	£1,319,679,547	£5,548,905,145	£16,126,241,892
Management Diabetes	-£1,445,628,535	-£1,399,407,702	£436,474,331	£11,335,261,001
Management AF	-£32,707,672	£300,774,658	£1,517,934,215	£5,689,782,613
Management NDH	-£68,330,332	£58,480,427	£376,258,567	£1,081,587,955
Management FH	-£1,769,102	£7,774	£5,631,907	£9,978,450
Detection & Management Diabetes	-£1,817,520,758	-£2,077,568,207	£7,707,450,839	£168,998,385,363
Detection & Management QRISK ≥10%	£918,932,098	£13,701,106,307	£51,235,394,709	£135,030,263,040
Detection & Management Hypertension	-£1,792,285,183	£1,148,499,313	£16,499,555,075	£66,302,937,291
Detection & Management CKD	£792,450,218	£6,146,183,825	£18,377,589,590	£38,287,894,145
Detection & Management NDH	-£2,454,409,009	-£1,347,248,301	£6,080,729,875	£18,674,951,427
Detection & Management AF	-£38,952,465	£752,294,535	£3,718,753,468	£13,301,235,703
Detection & Management FH	-£142,222,304	£33,431,297	£613,369,886	£2,085,523,960

Figure 12: Net Monetary Benefit obtained over time by optimising detection and management of each high risk condition.



Further information

The accompanying technical appendix contains full details of the reviewing methodology and findings, the modelling adaptations and the tool user group input.

The database of interventions and conditions (linked through the tool) summarises all the information about the values and data sources used in the model for each of the interventions and high risk conditions.

The PHE CVD Prevention ROI tool can be found at the following link: https://cvd-prevention.shef.ac.uk/

The tool user guide (linked through the tool) provides information on how to use the tool including a worked example and explanation of the results.

If you have any further questions about the tool, please email: healtheconomics@phe.gov.uk.

References

1. Cardiovascular Disease Statistics 2017: British Heart Foundation; 2017 [Available from: https://www.bhf.org.uk/research/heart-statistics/heart-statistics-publications/cardiovascular-disease-statistics-2017 accessed 10th January 2018.
2. Bhatnagar P, Wickramasinghe K, Williams J, et al. The epidemiology of cardiovascular disease in the UK 2014. *Heart* 2015;101(15) doi: doi:10.1136/heartjnl-2015-307516
3. European Cardiovascular Disease Statistics: European Heart Network; 2017 [Available from: http://www.ehnheart.org/cvd-statistics/cvd-statistics-2017.html accessed 10th January 2018.
4. Cardiovascular Disease Outcomes Strategy: Improving outcomes for people with or at risk of cardiovascular disease: DH Cardiovascular Disease Team; 2013 [Available from: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/217118/9387-2900853-CVD-Outcomes_web1.pdf accessed 10th January 2018.
5. Cardiovascular Disease Prevention: Risk Detection and Management in Primary Care: NHS Rightcare; 2016 [Available from: https://www.england.nhs.uk/rightcare/wp-content/uploads/sites/40/2016/09/cvd-pathway.pdf accessed 10th January 2018.
6. Breeze PR, Thomas C, Squires H, et al. Cost-effectiveness of population-based, community, workplace and individual policies for diabetes prevention in the UK. *Diabetic Medicine* 2017;34:1136-44. doi: DOI: 10.1111/dme.13349
7. Breeze PR, Thomas C, Squires H, et al. The impact of Type 2 diabetes prevention programmes based on risk-identification and lifestyle intervention intensity strategies: a cost-effectiveness analysis. *Diabetic Medicine* 2017;34:632-40. doi: 10.1111/dme.13314
8. Thomas C, Sadler S, Breeze P, et al. Assessing the potential return on investment of the proposed UK NHS diabetes prevention programme in different population subgroups: an economic evaluation. *BMJ Open* 2017;7:e014953. doi: doi:10.1136/bmjopen-2016-014953
9. Sadler S, Thomas C, Brennan A, et al. NHS Diabetes Prevention Programme Return on Investment Tool V1.0: Public Health England & University of Sheffield; 2016 [Available from: https://dpp-roi-tool.shef.ac.uk/.
10. NICE Guideline CG127: Hypertension; The clinical management of primary hypertension in adults: National Institute for Health and Care Excellence, 2011.
11. NICE Guideline CG180: Atrial Fibrillation; The management of atrial fibrillation: National Institute for Health and Care Excellence, 2014.
12. NICE Guideline CG71: Identification and management of familial hypercholesterolaemia (FH): National Institute for Health and Care Excellence, 2008 (update 2017).
13. NICE Guideline CG181: Lipid modification; Cardiovascular risk assessment and the modification of blood lipids for the primary and secondary prevention of cardiovascular disease: National Institute for Health and Care Excellence, 2014.
14. NICE Guideline NG17: Type 1 diabetes in adults; Diagnosis and management: National Institute for Health and Care Excellence, 2015.
15. NICE Guideline NG28: Type 2 diabetes in adults; Management: National Institute for Health and Care Excellence, 2015.
16. NICE Public Health Guideline PH38: Type 2 diabetes; prevention in people at high risk: National Institute for Health and Care Excellence, 2012 (update 2017).
17. NICE Guideline CG182: Chronic Kidney Disease in adults; Assessment and management: National Institute for Health and Care Excellence, 2014.
18. Quality and Outcomes Framework: NHS Digital; 2017 [Available from: http://content.digital.nhs.uk/qof accessed 16th January 2018.

19. National Diabetes Audit: NHS Digital; 2017 [Available from: http://content.digital.nhs.uk/nda accessed 16th January 2018.
20. CKD prevalence estimates for local and regional populations. National Cardiovascular Intelligence Network: Public Health England; 2015 [Available from: https://www.gov.uk/government/publications/ckd-prevalence-estimates-for-local-and-regional-populations accessed 18th May 2018.
21. Atrial fibrillation prevalence estimates for local populations. National Cardiovascular Intelligence Network: Public Health England; 2017 [Available from: https://www.gov.uk/government/publications/atrial-fibrillation-prevalence-estimates-for-local-populations accessed 18th May 2018.
22. Statistics on NHS Stop Smoking Services in England - April 2016 to March 2017: NHS Digital; 2017 [Available from: https://digital.nhs.uk/data-and-information/publications/statistical/statistics-on-nhs-stop-smoking-services-in-england/statistics-on-nhs-stop-smoking-services-in-england-april-2017-to-december-2017 accessed May 18th 2018.
23. Health Survey for England 2014: NHS Digital; 2014 [Available from: https://data.gov.uk/dataset/health_survey_for_england.
24. Hippisley-Cox J, Coupland C, Vinogradova Y, et al. Predicting cardiovascular risk in England and Wales: prospective derivation and validation of QRISK2. *BMJ Open* 2008;336:a332. doi: doi:10.1136/bmj.39609.449676.25
25. Hippisley-Cox J, Coupland C, Brindle P. Derivation and validation of QStroke score for predicting risk of ischaemic stroke in primary care and comparison with other risk scores: a prospective open cohort study. *BMJ* 2013;346:f2573 doi: doi: https://doi.org/10.1136/bmj.f2573
26. Hospital Episode Statistics: Hosptial Admitted Patient Care Activity: NHS Digital; 2017 [accessed 21st May 2018.
27. Ward S, Lloyd JM, Pandor A, et al. A systematic review and economic evaluation of statins for the prevention of coronary events. . *Health Technol Assess* 2007;11(14):1-iv.
28. Clarke PM, Gray AM, Briggs A, et al. A model to estimate the lifetime health outcomes of patients with type 2 diabetes: the United Kingdom Prospective Diabetes Study (UKPDS) Outcomes Model (UKPDS no. 68). *Diabetologia* 2004;47(10):1747-59.