

Report Supplementary Material 4 (Chapter 6)

1.1. Economic model	3
1.2. References	23
Appendix 2.1: Full regression results	26
Appendix 2.2: Costing tables	29
Appendix 2.3: Model in R	33

List of abbreviations

BCT: Behaviour change technique

DMac: diabetic maculopathy

DR: diabetic retinopathy

DRS: diabetic retinopathy screening

EPOC: Effective Practice and Organisation of Care

HbA1c: Glycated haemoglobin

HCP: Health care professional

HES: Hospital Eye Services

ONS: Office of National Statistics

OR: Odds ratio

QALY: Quality-adjusted life year

QI: Quality improvement

RR: Relative risk

STDR: sight-threatening diabetic retinopathy

SVA: Snellen visual acuity

1.1. Economic model.

It was not necessary to perfectly reproduce the analysis reported in Scanlon and colleagues¹ as our objective was to evaluate the cost-effectiveness of interventions to improve DRS attendance. However, the essential features of the model are the same as are key assumptions and the interested reader is referred back to that report for a detailed description of these. For the same reason, we have not reviewed all the assumptions that underpin the Scanlon model. We rely on sensitivity analyses to explore the significance of substantial changes to the model. The model compares the different BCT and QI components and used evidence from a meta-analysis (and associated estimates of imprecision) to estimate their relative effectiveness and costs. The Scanlon model modelled a cohort of people with diabetes based on a Gloucestershire Diabetic Eye Screening Service cohort of patients. The cohort represented all people within the screening programme. For simplicity, this analysis modelled a cohort of patients with the median values of the cohort modelled in the Scanlon model; the median age was 64. While it is acknowledged that a lot of people will be eligible for a diabetic retinopathy screening programme at much earlier ages, a simple approach is required given the objectives and scope of this study, which is to identify the QIs and BCTs most likely to be cost-effective. As this age was not reflective of people offered DRS it was varied in sensitivity analysis. Diabetic retinopathy disease is considered to consist of different stages affecting one or both eyes, and people with diabetic retinopathy may progress or regress between them.

A pictorial representation of the front-end of the model is presented in Figure 1. If an individual attends DRS there will be the opportunity to receive treatment, which will result in different costs and quality of life than for the individual who did not attend DRS but would have required treatment. An intervention to increase DRS attendance increases the probability that an individual will attend screening and hence change the health service costs and quality of life. Within the model the health outcomes of attending DRS were measured in quality-adjusted life years (QALYs), as this is the standard metric for informing the allocation of resources in the NHS in the UK.

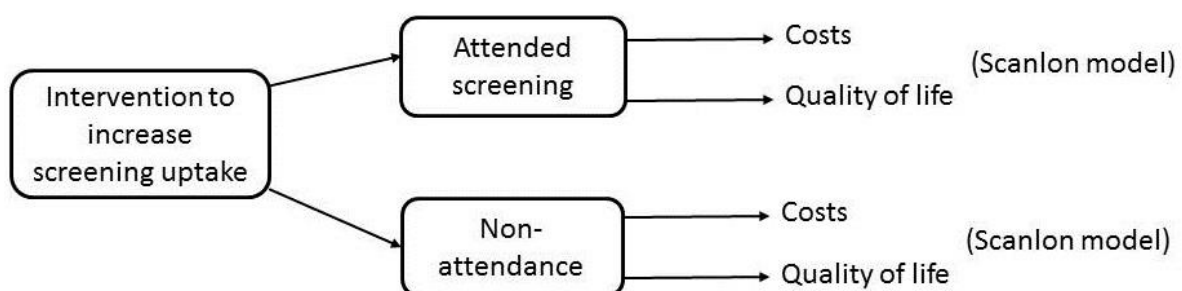


FIGURE 1. Pictorial representation of the initial stages of the economic model.

Model structure and population

People with DM are assumed to transition between DR states over time. The stages of DR are presented in Table 1. Each stage of DR may occur in one eye only or in both eyes. Seven DR states are included in the model. These are presented in Table 2 along with their abbreviations. A state transition cohort (Markov) model modelled the transition of the cohort between the model states every cycle. The cycle length was 6 months. The probabilities of making the transition from one state to another every 6 months are presented in Table 3. In the model these probabilities are adjusted to account for a probability of dying every 6 months. Individuals who have pre-proliferative or proliferative DR in both eyes or diabetic maculopathy in both eyes are assumed to stay in those states unless they die. The dead state is an absorbing state as there is no movement from that state.

The baseline state probabilities and population characteristics are reported in Table 4. The Scanlon model modelled a cohort of people with diabetes based on a Gloucestershire Diabetic Eye Screening Service cohort of patients. The cohort represented all people within the screening programme. For simplicity, this analysis modelled a cohort of patients with then median values of the cohort modelled in the Scanlon model; the median was 64. This was varied in sensitivity analysis. While it is acknowledged that a lot of people will be eligible for a diabetic retinopathy screening programme at much earlier ages, a simple approach is required given the objectives and scope of this study, which is to identify the QIs and BCTs most likely to be cost-effective. Parameters linked to diabetes control and cardiovascular risk (HbA1c and serum cholesterol) are assumed to remain constant throughout our model.

TABLE 1. The stages of diabetic retinopathy and maculopathy disease and their abbreviations.

Diabetic retinopathy stage and maculopathy	Abbreviation
No DR	R0
Background DR (mild non-proliferative DR)	R1
Pre-proliferative retinopathy (moderate to severe non-proliferative DR)	R2
Proliferative retinopathy	R3
Any retinopathy stage	Rx
No diabetic maculopathy	M0
Diabetic maculopathy	M1

DR=Diabetic retinopathy

TABLE 2. The diabetic retinopathy and maculopathy model states and their abbreviations.

State	Abbreviation
No background DR in either eye	R0M0 R0M0
Background DR in one eye	R1M0 R0M0
Background DR in both eyes	R1M0 R1M0
Pre-proliferative or proliferative retinopathy in one eye	R2/3M0 R0/1M0
Pre-proliferative or proliferative retinopathy in both eyes	R2/3M0 R2/3M0
Diabetic maculopathy in one eye	RxM1 RxM0
Diabetic maculopathy in both eyes	RxM1 RxM1

DR=Diabetic retinopathy

TABLE 3. Transition probabilities from one state to another.

From	To						
States	R0M0 R0M0	R1M0 R0M0	R1M0 R1M0	R2/3M0 R0/1M0	R2/3M0 R2/3M0	RxM1 RxM0	RxM1 RxM1
R0M0 R0M0	0.8895	0.11	-	-	-	0.0005	-
R1M0 R0M0	0.12	0.7656	0.11	0.0001	-	0.004	0.0003
R1M0 R1M0	0.01	0.12	0.82	0.01	0.01	0.03	-
R2/3M0 R0/1M0	-	-	-	0.92	0.08	-	-
R2/3M0 R2/3M0	-	-	-	-	1	-	-
RxM1 RxM0	-	-	-	-	-	0.96	0.04
RxM1 RxM1	-	-	-	-	-	-	1

TABLE 4. Baseline state probabilities and population characteristics.

State	Probability
R0M0 R0M0	0.64
R1M0 R0M0	0.188
R1M0 R1M0	0.129
R2-3M0 R0-1M0	0.011
R2-3M0 R2-3M0	0.009
M1 M0	0.04
M1 M1	0.018
Characteristic	Value
Age	64
HbA1c (mmol/mol)	51
Serum cholesterol (mmol/l)	2.4

HbA1c=Glycated haemoglobin

DR screening occurs at regular intervals; currently in the UK, annual screening is recommended. The results of the Scanlon cost-utility analysis identified DRS every three years as the most cost-effective frequency for patients with diabetes and no pre-proliferative DR or PDR or maculopathy. However, the UK National Screening Committee has recommended that the screening for DR should change from one year to two year screening intervals for those at low risk (based on two screening episodes with no detected DR).² One year intervals are recommended for those having any DR in either of two previous screening episodes. The base case model in our analysis assumes annual DRS screening and two-yearly and three-yearly DRS screening as sensitivity analyses.

A positive screening episode is classified as screening positive for pre-proliferative DR, proliferative DR or diabetic maculopathy.

The outcomes of attending DRS and non-attendance are presented in Figure 2. Once an individual attends DRS they receive a positive or negative test result. Individuals with a negative test result from the initial screen and individuals not attending any of their appointments in a given screening period are all invited again a year later. Individuals with a positive test result are referred to the Hospital Eye Services (HES) where appropriate ophthalmic assessment takes place. The HES tests are assumed to

have perfect sensitivity and specificity in the model. Once referred to HES, patients might or might not attend.

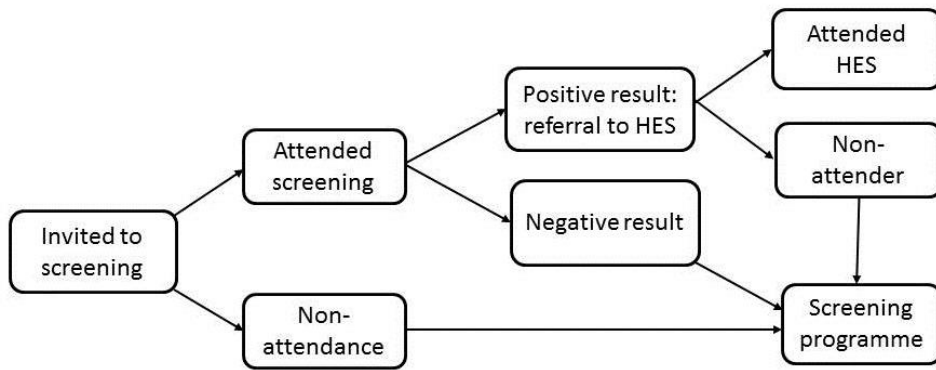


FIGURE 2. Screening pathway for diabetic patients offered diabetic retinopathy screening (reproduced from Figure 15 Scanlon et al.).

The clinical pathway following diagnosis of pre-proliferative or proliferative DR and diabetic maculopathy is presented in Figure 3. An individual who attends the HES and is diagnosed with pre-proliferative DR, proliferative DR or diabetic maculopathy may or may not be offered treatment. An individual who is offered treatment then re-enters the DRS programme and has the opportunity to be screened at the next screening interval. An individual who does not receive treatment is either monitored every 6 months in the HES or re-enters the DRS programme and has the opportunity to be screened at the next screening interval.

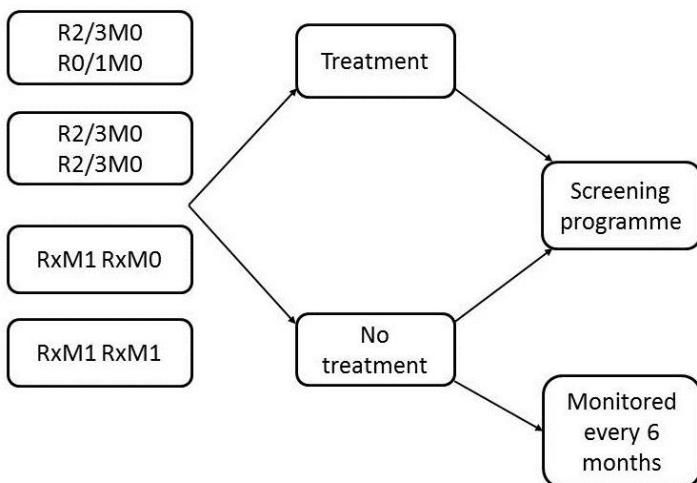


FIGURE 3. Clinical pathways of confirmed cases from HES of pre-proliferative, proliferative retinopathy or diabetic maculopathy (reproduced from Figure 16 in Scanlon et al.).

Screening and treatment

Individuals who receive treatment are assumed to stay with the same stage of DR for the remaining time in the model. It is also assumed that there is a permanent incremental improvement in visual acuity. The improvements in visual acuity for pre-proliferative or proliferative DR (sight-threatening diabetic retinopathy (STDR)) and diabetic maculopathy (DMac) states are reported in Table 5.

TABLE 5. Improvements in visual acuity by treatment combination and state.

Treatment	STDR	DMac
Antiangiogenic	-0.125	-0.146
Antiangiogenic + laser	-0.125	-0.146
Laser	-0.03	-0.016

Individuals are assumed to receive treatment only if they receive a positive diagnosis of pre-proliferative DR, proliferative DR, or diabetic maculopathy in one eye or both eyes after attending the HES referral. Referral to HES can only happen following a positive diagnosis at DRS.

True and false positives are referred to HES. The specificity and sensitivity values used in the model are reported in Table 6.

TABLE 6. The specificity and sensitivity of screening the retinopathy states.

Specificity		Sensitivity of screening relative to true state	
R0M0 R0M0	0.997	R2–3M0 R0–1M0	0.75
R1M0 R0M0	0.978	R2–3M0 R2–3M0	0.96
R1M0 R1M0	0.906	RxM1 RxM0	0.822
		RxM1 RxM1	0.982
Data derived from Scanlon et al. Confidence intervals excluded.			

The probability of attendance of a HES referral and of treatment following attendance of HES depends on the DR stage. The model coefficients used directly in the model are reported in Table 7.

TABLE 7. The results of the logit model for the probability of Hospital Eye Services referral attendance and for the multinomial logit model for the probability of treatment after Hospital Eye Services referral.

Probability of HES referral attendance (logit model)		Probability of treatment after HES referral (multinomial logit model)	
Variable	Coefficient	Variable	Coefficient
Age	-0.01	<i>Antiangiogenic therapy*</i>	
DR grade observed at screening		R2–3M0 R0–1M0 Reference case	
RxM1 RxM0 Reference case		RxM1 RxM1	-0.228
RxM1 RxM1	1.22	R2–3M0 R2–3M0	-3.142
R2–3M0 R0–1M0	0.11	RxM1 RxM0	-1.174
R2–3M0 R2–3M0	0.67	Constant	0.693
Sex: female	-0.19	<i>Both antiangiogenic therapy and laser photocoagulation*</i>	
Constant	1.23	True DR grade diagnosed at HES	
		R2–3M0 R0–1M0 Reference case	
		RxM1 RxM1	0.288
		R2–3M0 R2–3M0	-3.008
		RxM1 RxM0	-0.606
		Constant	-0.693
Data derived from Scanlon et al. Confidence intervals excluded.			
*The third dependent variable category is laser photocoagulation			

Individuals who do not receive treatment at the HES following a positive diagnosis at DRS attendance are either monitored every 6 months or returned to the screening programme. In the base case analysis, it is assumed that 78% of these individuals are monitored. Scanlon and colleagues stated that this was based on expert opinion. This is reduced to 40% in a sensitivity analysis. Those who are monitored are assumed to incur the cost associated with HES assessment. The effect of HES assessment on cost is reported in Table 8 on the log-scale.

As the transition probability between DR states depends on treatment and the probability of treatment depends on monitoring, three model states were defined for each DR state: (1) had never had treatment and are not being monitored, (2) have never had treatment and are being monitored, and (3) have had treatment and are not being monitored. With background DR in one eye, background DR in two eyes, no DR and dead states, there were 16 states in the state transition model. See Tables 1 and 2 for a description of these states. As stated above, all individuals who are not being monitored are invited for DRS during a DRS interval. The probability of mortality was derived from life tables from the Office of National Statistics (ONS)³, and this was adjusted using estimates of the relative risk of mortality for people with diabetes compared to the general population.

Costs and utilities of model states

The costs and utilities of the model states are based on the regression coefficients reported in Table 28. The utility regression coefficients come from Lloyd and colleagues.⁴ Both the cost and utility are conditional on logMAR visual acuity. The visual acuity (logMAR) regression coefficients for the model states and baseline characteristics are also reported in Table 28. Utility also depends on responses to the Vision specific patient reported questionnaire, the VFQ-25. LogMAR is mapped to the Snellen visual acuity scale and then the Snellen visual acuity scale is mapped to VFQ-25 at each six month time interval. The data mapping LogMAR to the Snellen visual acuity scale are reported in Table 9. The relationship between logMAR and the Snellen visual acuity scale comes from standard visual acuity tables.⁵ The Snellen visual acuity scale is mapped to VFQ-25 using data from Lloyd and colleagues.⁴ All of the Snellen visual acuity scale (SVA) values in the model cohort are between 6 and 18. SVA scores between 6 and 9 are mapped to 86.3 on VFQ-25, and SVA scores between 12 and 18 are mapped to 61.5 on VFQ-25.

The probability of nursing/residential care admission in the Scanlon model was based on the degree of vision loss. The probability of the level of vision loss was based on an ordered logistic regression. The annual cost of a care home was assumed to be £39,000, which was calculated in Scanlon and colleagues.⁶ In the base case model in our study, the cost of social care was excluded for simplicity. In terms of disease progression, the benefit of screening and treatment is a reduction in progression to pre-proliferative or proliferative DR in both eyes and to diabetic maculopathy in both eyes. Since maculopathy in both eyes had significantly the greatest effect on the probability of vision loss, in sensitivity analysis it was assumed that 10% of people with maculopathy in both eyes were in social care. This was based on the coefficient of maculopathy in both eyes in the ordered logistic regression of impaired vision reported in Table 41 in Scanlon and colleagues.¹

TABLE 8. The results of the ordinary least squares (OLS) model for visual acuity, for the log link model for cost, and the OLS model for the EQ-5D.

Visual acuity (OLS)		Cost (log link)		EQ-5D (OLS)	
Variable	Coefficient	Variable	Coefficient	Variable	Coefficient
Age	0.004	R0M0 R0M0 Reference case		Intercept	0.114
Observed DR grade at screening		R1M0 R0M0	0.105	Gender	-0.043
R0M0 R0M0 Reference case		R1M0 R1M0	0.269	Age	-0.003
R1M0 R0M0	-0.006	R2-3M0 R0-1M0	0.487	VFQ-25	0.01
R1M0 R1M0	-0.005	R2-3M0 R2-3M0	0.625	(LogMAR)	-0.158
R2-3M0 R0-1M0	0.03	RxM1 RxM0	0.444		
R2-3M0 R2-3M0	0.039	RxM1 RxM1	0.423		
M1 M0	0.053	Assessment at HES	0.119		
M1 M1	0.125	Treatment with			
HbA1c	0.001	Photocoagulation	0.271		
Cholesterol	0.002	Antiangiogenic therapy	0.337		
Constant	-0.202	LogMAR (best eye)	1.057		

		HbA1c	0.003		
		Cholesterol	-0.044		
		Constant	5.87		
Data for visual acuity and cost derived from Scanlon et al. Confidence intervals excluded.					
Data for EQ-5D derived from Lloyd and colleagues.					

TABLE 9. The relationship between logMAR and Snellen visual acuity, and between Snellen visual acuity and VFQ-25.

Log MAR	SVA*
-0.3	3
-0.2	3.8
-0.1	4.8
0	6
0.1	7.5
0.2	9.5
0.3	12
*SVA: Snellen visual acuity	

Intervention effect estimates

The effectiveness results reported in the included clinical studies are the effect estimates for the complex interventions studied. This economic analysis investigated the cost-effectiveness of individual components of these complex interventions, and therefore required estimating effect estimates for individual QI components (as defined by the modified EPOC taxonomy) and BCTs by adjusting for other components.⁷ This is in contrast to the analysis in Chapter 3 which sought to estimate mean effects for interventions that included a specific component (versus interventions that did not include it).

The studies varied in their populations and other characteristics. Most studies were conducted outside of the UK. Furthermore, there were insufficient data to model interaction effects between the BCTs and between the QIs. Consequently, the effect estimates were not precise estimates for a specific UK population. The purpose was to provide the parameter estimates for the cost-effectiveness model which evaluates the probability that each QI/BCT is cost-effective accounting for each QI/BCT simultaneously. This can help prioritise further research by identifying the most promising intervention components, and developing interventions utilising them.

A meta-regression analysis, with multiple explanatory variables indicating the different QIs, was conducted for the effects of the QIs on the log-odds ratio of screening attendance. A separate analysis was conducted for the BCTs. Both the patient and HCP-targeted techniques were included in the same regression analyses for both the resource use and effect analyses. While this is a large number of

explanatory variables, there is a pre-defined set of competing interventions, and there is no reason to exclude one over the other. In addition, no statistical tests are conducted as part of this analysis. The purpose is to provide the parameter estimates for the cost-effectiveness model which evaluates the probability that each QI/BCT is cost-effective accounting for each QI/BCT simultaneously. These results should be interpreted as additive, whereas the results in Chapter 3 are not additive.

BCTs or QIs were excluded from the analysis if there were insufficient data to estimate a coefficient, if there were collinearity (overlap of studies between indicator variables), or if there were perfect predictions. As with the meta-analyses reported in Chapter 3, only BCTs and QIs that occurred in at least 10 studies were included in the economic model, and only these results are reported here. These were considered to be less prone to a spurious result. It is likely there is variation in interventions that are coded as a QI or BCT. The greater the number of studies with a particular QI or BCT, the more likely that different approaches to implementing a QI or BCT intervention are present. Random-effect meta-regressions were performed in Stata 15 (StataCorp, Texas).⁸ The dependent variable was the log-odds ratio. There were insufficient data to model interaction effects between the BCTs and between the QIs. Fifty-six studies with a usual care comparator were included in the analyses.

The full set of regression results are presented in Appendix 2.1. The results transformed into relative risks with their 95% confidence intervals for the QIs that occur in at least 10 studies are reported in Table 10. The results transformed into RRs with their 95% confidence intervals for the BCTs that occur in at least 10 studies are reported in Table 11. The ordered resource ranking analysis that appears in Tables 10 and 11 is explained in the resource use and cost estimates section below.

TABLE 10. The EPOC QI component resource use (ordered logit) and effectiveness (meta-regression) results obtained from analyses including all the QIs as explanatory variables.

EPOC QI components	Ordered resource ranking; proportional relative risk [95% CI]	Effect Meta-regression; relative risk [95% CI]
Audit and feedback	1.22 [0.79,1.38]	0.99 [0.78,1.16]
Case management	1.40 [1.28,1.42]	0.87 [0.67,1.05]
Team changes	1.26 [0.97,1.38]	1.14 [1.00,1.24]
Electronic patient registry	0.69 [0.17,1.23]	1.01 [0.74,1.21]
Clinician education	0.89 [0.42,1.24]	1.06 [0.89,1.19]
Clinician reminders	1.26 [0.73,1.40]	1.08 [0.83,1.25]
Patient education	0.80 [0.38,1.18]	1.09 [0.92,1.22]
Promotion of self-management	1.28 [0.85,1.40]	1.12 [0.93,1.26]
Patient reminders	0.64 [0.24,1.09]	1.02 [0.84,1.16]

TABLE 11. The BCT component resource use (ordered logit) and effectiveness (meta-regression) results obtained from analyses including all the BCTs as explanatory variables.

BCT components	Likert resource ranking; proportional RR [95% CI]	Effect Meta-regression; RR [95% CI]
<i>Patient-targeted BCTs</i>		
Problem solving	1.37 [1.03,1.42]	0.95 [0.73,1.13]
Goal Setting (Outcome)	1.27 [0.57,1.41]	1.24 [1.10,1.32]
Feedback on outcomes of behaviour/Biofeedback	0.59 [0.13,1.19]	1.17 [1.02,1.27]
Social Support (unspecified)	0.15 [0.01,0.81]	1.07 [0.87,1.22]
Social Support (practical)	1.29 [0.75,1.41]	0.95 [0.76,1.11]
Instruction on how to perform behaviour	1.38 [1.09,1.42]	0.89 [0.70,1.06]
Information about health consequences	0.17 [0.02,0.76]	1.15 [1.00,1.25]
Prompts/Cues	0.17 [0.02,0.81]	0.91 [0.73,1.07]
Credible source	0.38 [0.01,1.33]	0.85 [0.56,1.10]
Restructuring the social environment	0.80 [0.05,1.40]	0.82 [0.58,1.03]
<i>Healthcare professional-targeted BCTs</i>		
Feedback on outcomes of behaviour/Biofeedback	0.51 [0.12,1.11]	0.85 [0.68,1.01]
Social Support (practical)	1.42 [1.30,1.43]	1.27 [1.10,1.35]
Instruction on how to perform behaviour	0.90 [0.28,1.32]	0.81 [0.61,0.99]
Prompts/Cues	1.34 [0.67,1.42]	0.96 [0.67,1.18]
Credible source	0.89 [0.22,1.34]	0.95 [0.73,1.13]
Restructuring the social environment	1.42 [1.33,1.43]	1.13 [0.94,1.25]
Adding objects to the environment	0.19 [0.02,0.93]	0.98 [0.76,1.15]

In the model, the baseline probability of DRS attendance was based on a minimum standard set by the UK National Screening Committee, not on the probabilities of the usual care arms in the RCTs.⁹ Furthermore, the probability of DRS attendance is varied in sensitivity analysis. Uncertainty in the effect estimate is accounted for in the analysis through probabilistic analysis where values are

sampled from a probability distribution. The probability of DRS attendance following the intervention cannot be greater than one. The following method was followed in the model to ensure this. In the model, a normal distribution is specified for the log-odds ratio using the mean and standard error of the BCT/QI coefficient and the constant of the meta-regression. Values are sampled from this distribution. The exponent is taken of these samples, and converted to a relative risk (RR) as follows

$$RR = \frac{OR}{1 - ACR \times (1 - OR)}$$

where ACR is the baseline risk of DRS attendance.

The relative risk converges to 1 as the baseline risk increases towards 1. An assumption is made that the odds ratio is constant across baseline risk values. This approach recognises that there is greater scope to improve screening uptake when the baseline probability of DRS attendance is lower.

Resource use and cost estimates

The level of the cost of resource use in each included study was of interest for two purposes in this study. Firstly, in the economic analysis, we are interested in estimating the cost of the individual components of the complex interventions included in each study rather than the cost of the complex interventions. This requires a form of multivariable regression with the QI and BCT components as explanatory variables as used in the intervention effectiveness analysis. Secondly, in Chapter 3 the association between resource use and intervention effectiveness was investigated. In Chapter 3 the average effectiveness was calculated at different levels of resource use, and resource use was added as a covariate in a meta-regression.

A measure of the cost of the resource use was needed for each study. As there were 56 studies, an efficient method was required to derive this measure. The approach taken was to design a data abstraction method of recording pre-defined key categories of resource use and the levels of each category. The process of determining the resource categories and levels involved agreement between reviewers on an ordered ranking of resource use for each study. The cost of each level of each resource category was then estimated through random sampling at least three studies with each category and level, costing the resource use associated with the intervention description using national cost estimates, and calculating the average. The total cost of a complex intervention in each study is the product of the resource categories and estimated costs for each category. The cost variable was therefore categorical, and the applicable regression method to estimate the incremental cost of each QI/BCT component was an ordinal logistic regression with the ordered resource use cost ranking as the dependent variable.

The cost analysis for the economic model differs from the work conducted in the review of economic outcomes reported in Chapter 3 in that the economic model utilises unit cost estimates for England and Wales to value the described interventions rather than converting the costs reported in the studies from one currency to another. Arguably, such data would be more transferable as the resources required to provide an intervention may not vary between settings.

It was assumed that all people with DM would be eligible for DRS and that BCT/QI intervention components would target all eligible people. It is noted that some of the evidence on effectiveness of BCT/QI interventions came from studies targeting those most likely not to attend DRS. The meta-regression data has not been able to control for this factor and we have assumed a constant effect. However, we have explored the impact of different baseline uptake rates of DRS to illustrate relative impact of BCT/QI when the baseline uptake was lower.

The ordered ranking score

Different levels of resource use for the main BCT or QI intervention used in each study included in the systematic review were estimated on an ordered scale. This was operationalised by developing categories of resource use with different levels of resource intensity. Two reviewers selected the level of each resource category for each study independently, and disagreements were discussed. As described below, weights were applied to each level of resource use which was used to derive a rank order of resource use for each BCT and QI.

There were two steps in deriving the original ordered ranking score. Firstly, ten studies were selected and two reviewers independently gave a score from 1 to 5 for each main intervention in each study. Notes were recorded for the reasons for the scores. The differences in scores and the reasons for giving the scores were then discussed, and an agreement was reached on the score. The ordered ranking scores given to the 10 studies by the reviewers and the agreed scores are presented in Table 12. The objective was to achieve 9 out of 10 studies scored within 1 point of each other.

TABLE 12. Ordered ranking scores of cost burden of the main intervention in each study (indicated by first author) by each reviewer*.

Author	Reviewer 1	Reviewer 2	Agreed	Algorithm	Reviewer r 3	Reviewer r 4	Reviewer r 5	Reviewer 6
Zwarenstein 2014 ¹²	1	1	1	1	1	1	1	1
Gabbay 2006 ¹³	4	3	4	4	4	5	5	5
Frijing 2002 ¹⁴	4	3	3	3	3	5	3	3
Clancy 2007 ¹⁵	3	2	3	3	4	5	5	3
Glasgow 2005 ¹⁶	2	5	4	4	3	4	4	4
Halbert 1999 ¹⁷	1	2	1	1	1	2	1	1
McDermot 2001 ¹⁸	4	4	4	4	2	3	3	2
Pizzi 2015 ¹⁹	2	2	2	2	3	5	2	2
Steyn 2013 ²⁰	1	2	1	2	2	5	1	2
Zangalli 2016 ²¹	2	3	2	2	2	3	2	2

* A total of six individuals contributed to this, five of these are noted in the acknowledgements, with sixth being SR

The second step involved developing and testing the algorithm and determining the weights applied to the category levels. This approach was chosen over broad descriptions of Likert scores in order to increase consistency. Weights were chosen based on the discussions of the scores. The algorithm was tested twice, first on reviewers 3 and 4, and secondly on reviewers 5 and 6. The descriptions of the resource categories and levels were edited in-between. The results for the other reviewers are also presented in Table 12. The resource categories and levels with their weights are reported in brackets in Table 13. The weights were subsequently revised following a costing exercise (see below).

TABLE 13. The five domains with response options. The weight associated with each response indicated in brackets.

Face to face or care planning minutes/ patient/ 6 months	Phone calls to patients	Additional outreach visits to patients (travel time)	Use of materials/ letters/ software	Training of health professionals other than reading material
None (0)	No (0)	No (0)	None (0)	None (0)
Low 1-40mins (1)	Yes (1)	Yes (2)	Printed materials (1)	Low (1)
Moderate 40-100 (2)			Software (2)	High (2)
High > 100 (3)				

Cost estimates

A few of the included RCTs were selected at random and cost estimates were derived for each of the resource categories until at least three estimates were available for each estimate. While a more precise estimate could be obtained from sampling more studies, this approach was appropriate given the objectives and scope of this study, which is to identify the QIs and BCTs most likely to be cost-effective. This approach is considered sufficient to distinguish between the different levels of resource use identified in the resource categories. The cost analyses for the resource categories are presented in Appendix 2.2. The cost estimates for each resource category for the individual studies are reported in Table 14. This analysis differs from the work conducted in the review of economic outcomes reported in Chapter 3 in that (1) these cost estimates are based on the intervention descriptions in the articles' method's section rather than outcomes, and (2) it utilises unit cost estimates for England and Wales rather than converting costs from one currency to another.

It was assumed that all people with DM would be eligible for DRS and that BCT/QI intervention components would target all eligible people. It is noted that some of the evidence on effectiveness of BCT/QI interventions came from studies targeting those most likely not to attend DRS. The meta-regression data has not been able to control for this factor and we have assumed a constant effect. However, we have explored the impact of different baseline uptake rates of DRS to illustrate relative impact of BCT/QI when the baseline uptake was lower (see section of sensitivity analysis below).

Resources incurred have different units: per patient, per GP, per practice and per country. It was assumed that all software development and design of educational pamphlets would be financed at a higher organisational level than say a general practice, for simplicity taken as the national level. It assumes that a country takes advantage of economies of scale. The total number of people with DM (2,913,538),¹⁰ GP practices (8,151), and GPs (40,265)¹¹ in England were used to derive a cost per

patient for each intervention. The price year was 2016. Salaries were obtained from the Personal Social Services and Resource Unit (PSSRU).²² The cost of a non-mydiatic retinal camera was obtained from BiB Ophthalmology Instruments.²³ The cost of the design of a leaflet was obtained from University Hospitals Birmingham.²⁴ The cost of leaflet production was identified from Birmingham Women’s and Children’s Services.²⁵ The cost of software development was assumed to require one year full time equivalent of a senior programmer (£60,000), four years full time equivalent of junior programmers (£45,000), and 112 hours of GP time. The cost of delivering letters and leaflets was obtained from Royal Mail.²⁶ Fixed costs were annuitized, and the useful life of all fixed costs including equipment, software, educational material design, and health care professional training was assumed to be five years. An annual discount rate of 3.5% was applied.

TABLE 14. Cost estimates for the different resource categories.

Resource category	Average cost (£)	Cost estimates for individual clinical studies (£)				
Printed materials	3.30	3.4	4.0	4.0	3.2	5.0
Software	9.53	7.6	7.6	11.4	11.4	
Low face to face	26.25	22.5	22.5	40.0	20.0	
Medium face to face	76.20	78.8	45.0	104.9		
Low training of health professionals	2.58	2.6	2.6	2.7		
High training of health professionals	8.07	9.4	7.2	7.5		
Phone calls	9.41	6.7	6.7	14.9		

These cost estimates were used to reweight the levels of each resource category. The initial weights did not appear to provide a ranking of interventions that was consistent with the anticipated cost of resources. The main consideration was that insufficient weight was given to patient management and contact time. Therefore, revised weights were produced to better take into account these elements. The revised weights are reported in Table 15 in brackets. A scatter plot of the resource rank score against cost for each study is presented in Figure 4. This shows that the expected cost per patient increases with every unit increase in rank score.

TABLE 15. The five domains with response options with revised weights associated with

each response indicated in brackets.

Face to face or care planning minutes/ patient/ 6 months	Phone calls to patients	Additional outreach visits to patients (travel time)	Use of materials/ letters/ software	Training of health professionals other than reading material
None (0)	No (0)	No (0)	None (0)	None (0)
Low 1-40mins (4)	Yes (2)	Yes (2)	Printed materials (1)	Low (1)
Moderate 40-100 (10)			Software (2)	High (2)
High > 100 (16)				

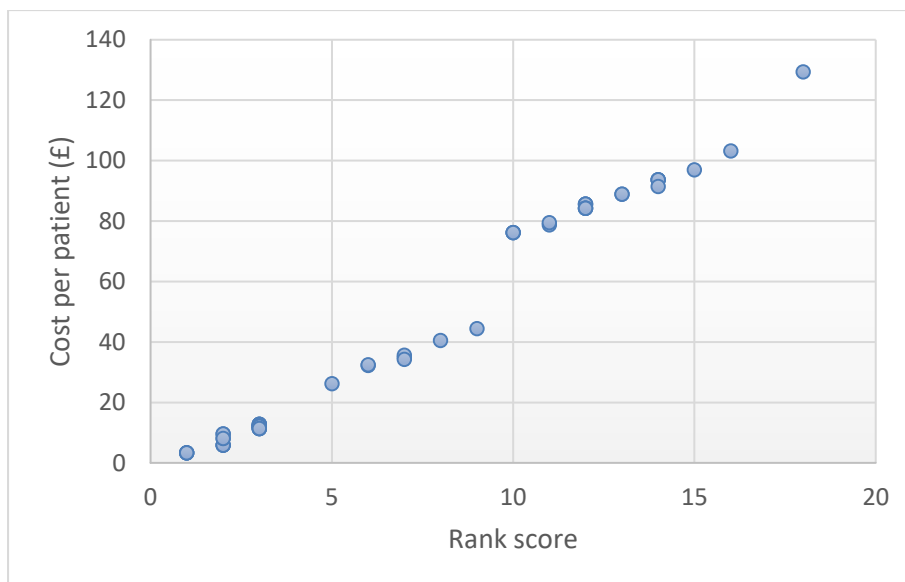


FIGURE 4: Scatterplot of study resource rank scores and cost estimates.

As no study was allocated a rank of 4 or 17, all ranks above these were reduced in order that there be a continuous list of ranks. Cost estimates for each BCT and QI component were then derived by conducting a multiple ordered logit regression. There were insufficient data to model interaction effects between the BCTs and between the QIs. The full analysis results are reported in Appendix 2.1. The transformed coefficients are reported in Table 10 and 11 for all BCTs and QIs which are recorded in at least 10 studies. A transformed coefficient is a proportional odds ratio; the odds ratio that the rank is greater than k for studies including the BCT/QI compared to those that do not, holding all other BCTs/QIs constant. The proportional odds ratio is assumed to true for all k . The coefficients were used in the model to calculate the expected probabilities of each rank, then the expected rank,

and finally the expected rank was assigned a cost estimate according to one of three linear regression models used to describe the relationship between the rank score and cost presented in Figure 4. The coefficients of the three linear regressions are reported in Table 16.

TABLE 16. The effect of resource rank on cost (mean and standard error) for different rank groupings.

	Rank grouping					
	1-3		4-8		9-15	
	Mean	SE	Mean	SE	Mean	SE
Rank	4.38	0.25	4.35	0.29	4.38	0.11
Constant	-1.14		9.52		36.38	

1.2. References

1. Scanlon PH, Aldington SJ, Leal J, Luengo-Fernandez R, Oke J, Sivaprasad S, *et al.* Development of a cost-effectiveness model for optimisation of the screening interval in diabetic retinopathy screening. *Health Technol Assess* 2015;**19**:1-116.
2. Committee UNS. *The UK NSC recommendation on Diabetic Retinopathy screening in adults*. URL: <https://legacyscreening.phe.org.uk/diabeticretinopathy> (Accessed 18/07/2017).
3. Statistics OfN. *National Life Tables*. URL: <https://www.ons.gov.uk/peoplepopulationandcommunity/birthsdeathsandmarriages/lifeexpectancies/datasets/nationallifetablesunitedkingdomreferencetables> (Accessed 18/07/17).
4. Lloyd A, Nafees B, Gavriel S, Rousculp MD, Boye KS, Ahmad A. Health utility values associated with diabetic retinopathy. *Diabet Med* 2008;**25**:618-24.
5. Ophthalmology TRCo. *Snellen and LogMAR acuity testing*. 2015. URL: <https://www.rcophth.ac.uk/wp-content/uploads/2015/11/LogMAR-vs-Snellen.pdf> (Accessed 18/07/2017).
6. Hipwell AE, Sturt J, Lindenmeyer A, Stratton I, Gadsby R, O'Hare P, *et al.* Attitudes, access and anguish: a qualitative interview study of staff and patients' experiences of diabetic retinopathy screening. *BMJ Open* 2014;**4**:e005498.
7. *Cochrane Effective Practice and Organisation of Care (EPoC) Group Taxonomy of Interventions*. 2015. URL: http://epoc.cochrane.org/sites/epoc.cochrane.org/files/public/uploads/epoc_taxonomy_13.12.16.pdf (Accessed 18.7.17).
8. StataCorp. *Stata Statistical Software: Release 14*. In: College Station, TX: StataCorp LP; 2015.
9. UK National Screening Committee. *UK NSC diabetic retinopathy recommendation*; 2016.
10. Diabetes UK. *UK diabetes prevalence*. URL: <http://www.diabetes.co.uk/diabetes-prevalence.html> (Accessed 18/07/2017).

11. Service NH. *General and Personal Medical Services*. 2013. URL: <http://content.digital.nhs.uk/catalogue/PUB09536/nhs-staf-2002-2012-gene-prac-rep.pdf> (Accessed 18/07/2017).
12. Zwarenstein M, Shiller S K, Croxford R, Grimshaw J M, Kelsall D, Paterson J M, *et al*. Printed educational messages aimed at family practitioners fail to increase retinal screening among their patients with diabetes: a pragmatic cluster randomized controlled trial [ISRCTN72772651]. *Implementation Science* 2014;**9**:87-.
13. Gabbay RA, Lendel I, Saleem TM, Shaeffer G, Adelman AM, Mauger DT, *et al*. Nurse case management improves blood pressure, emotional distress and diabetes complication screening. *Diabetes Res Clin Pract* 2006;**71**:28-35.
14. Frijling BD, Lobo CM, Hulscher ME, Akkermans RP, Braspenning JC, Prins A, *et al*. Multifaceted support to improve clinical decision making in diabetes care: a randomized controlled trial in general practice. *Diabet Med* 2002;**19**:836-42.
15. Clancy DE, Huang P, Okonofua E, Yeager D, KM M. Group visits: Promoting adherence to diabetes guidelines. *J Gen Intern Med* 2007;**22**:620-4.
16. Glasgow R E, Nutting P A, King D K, Nelson C C, Cutter G, Gaglio B, *et al*. Randomized effectiveness trial of a computer-assisted intervention to improve diabetes care. *Diabetes Care* 2005;**28**:33-9.
17. Halbert R J, Leung K M, Nichol J M, Legorreta A P. Effect of multiple patient reminders in improving diabetic retinopathy screening. A randomized trial. *Diabetes Care* 1999;**22**:752-5.
18. McDermott RA, Schmidt BA, Sinha A, Mills P. Improving diabetes care in the primary healthcare setting: a randomised cluster trial in remote Indigenous communities. *Med J Aust* 2001;**174**:497-502.
19. Pizzi LT, Zangalli CS, Murchison AP, Hale N, Hark L, Dai Y, *et al*. Prospective randomized controlled trial comparing the outcomes and costs of two eyecare adherence interventions in diabetes patients. *Appl Health Econ Health Policy* 2015;**13**:253-63.
20. Steyn K, Lombard C, Gwebushe N, Fourie JM, Everett-Murphy K, Zwarenstein M, *et al*. Implementation of national guidelines, incorporated within structured diabetes and hypertension records at primary level care in Cape Town, South Africa: a randomised controlled trial. *Global health action* 2013;**6**:20796-.
21. Zangalli CS, Murchison AP, Hale N, Hark LA, Pizzi LT, Dai Y, *et al*. An Education- and Telephone-Based Intervention to Improve Follow-up to Vision Care in Patients With Diabetes: A Prospective, Single-Blinded, Randomized Trial. *Am J Med Qual* 2016;**31**:156-61.
22. University of Kent. PSSRU. *Unit Costs of Health and Social Care*. 2015. URL: <http://www.pssru.ac.uk/project-pages/unit-costs/2015/> (Accessed 18/07/17).
23. Instruments BO. *Ophthalmology Instruments*. URL: <https://www.bibonline.co.uk/> (Accessed 18/07/2017).
24. Birmingham University Hospitals. *Leaflet design*. URL: <http://www.uhb.nhs.uk/graphics-leaflets.htm> (Accessed 18/07/2017).
25. Birmingham Women's and Children's NHS Foundation Trust. *Leaflet production*. URL: <http://www.bch.nhs.uk/node/12593> (Accessed 18/07/2017).
26. Royal Mail. *Delivery prices*. URL: http://www.royalmail.com/sites/default/files/Mar16_Mailmark_Franking_Wallchart_RoyalMail.pdf (Accessed 18/07/2017).
27. Lafata JE, Baker AM, Divine GW, McCarthy BD, Xi H. The use of computerized birthday greeting reminders in the management of diabetes. *J Gen Intern Med* 2002;**17**:521-30.

28. Prael C M, Smilie J G, McInerney M J, Harwell T S, Helgerson S D. Direct mail intervention to increase retinal examination rates in Medicare beneficiaries with diabetes. *Am J Med Qual* 2000;**15**:257-62.
29. Weiss D M, Casten R J, Leiby B E, Hark L A, Murchison A P, Johnson D, *et al.* Effect of behavioral intervention on dilated fundus examination rates in older african American individuals with diabetes mellitus a randomized clinical trial. *JAMA Ophthalmology* 2015;**133**:1005-12.
30. Hermans MP, Elisaf M, Michel G, Muls E, Nobels F, Vandenberghe H, *et al.* Benchmarking is associated with improved quality of care in type 2 diabetes: the OPTIMISE randomized, controlled trial. *Diabetes Care* 2013;**36**:3388-95.
31. Peterson K A, Radosevich D M, O'Connor P, Nyman J A, Prineas R J, Smith S A, *et al.* Improving diabetes care in practice. *Diabetes Care* 2008;**31**:2238-43.
32. Guldberg TL, Vedsted P, Kristensen JK, Lauritzen T. Improved quality of Type 2 diabetes care following electronic feedback of treatment status to general practitioners: a cluster randomized controlled trial. *Diabet Med* 2011;**28**:325-32.
33. Davis R, Fowler S, Bellis K, Pockl J, Al Pakalnis V, Woldorf A. Telemedicine improves eye examination rates in individuals with diabetes: a model for eye-care delivery in underserved communities. *Diabetes Care* 2003;**26**:2476-.
34. Conlin PR, Fisch BM, Cavallerano AA, Cavallerano JD, Bursell SE, Aiello LM. Nonmydriatic teleretinal imaging improves adherence to annual eye examinations in patients with diabetes. *J Rehabil Res Dev* 2006;**43**:733-9.
35. Wagner EH, Grothaus LC, Sandhu N, Galvin MS, McGregor M, Artz K, *et al.* Chronic care clinics for diabetes in primary care: a system-wide randomized trial. *Diabetes Care* 2001;**24**:695-700.
36. Piette JD, Weinberger M, Kraemer FB, McPhee SJ. Impact of automated calls with nurse follow-up on diabetes treatment outcomes in a Department of Veterans Affairs Health Care System: a randomized controlled trial. *Diabetes Care* 2001;**24**:202-8.
37. Gabbay RA, Anel-Tiangco RM, Dellasega C, Mauger DT, Adelman A, Van Horn DHA. Diabetes nurse case management and motivational interviewing for change (DYNAMIC): results of a 2-year randomized controlled pragmatic trial. *J Diabetes* 2013;**5**:349-57.
38. Perria C, Mandolini D, Guerrera C, Jefferson T, Billi P, Calzini V, *et al.* Implementing a guideline for the treatment of type 2 diabetics: results of a cluster-randomized controlled trial (C-RCT). *BMC Health Serv Res* 2007;**7**:79-.
39. Bush K, Thomas R, Raymond N T, Sankar S, Barker P J, O'Hare J P. Cluster randomised controlled trial evaluation of a Link Worker-delivered intervention to improve uptake of diabetic retinopathy screening in a South Asian population. *Diab Vasc Dis Res* 2014;**11**:294-7.

Appendix 2.1.

Full set of regression results

Regression model results for the ordered logit model for the Likert resource ranking analysis, and the meta-regression for the treatment effect estimates. The results of the ordered logit analysis are the proportional log-odds ratios. As the cumulative probability of being at least rank k is modelled, the cut points represent the cumulative log-odds that distinguish rank k_i from k_{i-1} . Since there are 15 ranks, there are 15 cut points.

For the meta-regression, the constant represents the log-odds ratio without any of the listed explanatory variables indicated in a clinical study, and the intervention coefficients represent the difference in log-odds ratio for studies with the intervention compared to studies that do not. The log-odds ratio for an intervention is the sum of the constant and the intervention coefficient.

The EPOC QI component resource use (ordered logit) and effectiveness (meta-regression) results

EPOC QI components	Likert resource ranking (ordered logit)		Effect Meta-regression	
	Mean	SE	Mean	SE
Audit and feedback	0.90	0.79	-0.02	0.33
Case management	2.96	0.85	-0.39	0.29
Team changes	1.19	0.65	0.51	0.27
Electronic patient registry	-0.92	0.98	0.04	0.42
Clinician education	-0.36	0.70	0.21	0.29
Clinician reminders	1.13	0.99	0.28	0.41
Facilitated relay	-0.95	1.02	0.56	0.46
Patient education	-0.60	0.65	0.33	0.30
Promotion of self-management	1.29	0.90	0.45	0.35
Patient reminders	-1.07	0.71	0.06	0.28
Continuous quality improvement	-0.10	1.37	0.63	0.56
Financial incentives	0.74	1.20	0.24	0.52
Constant			0.12	0.29
/cut1	-2.16	0.83		
/cut2	-0.90	0.73		
/cut3	0.92	0.71		
/cut4	1.06	0.72		
/cut5	1.37	0.74		

/cut6	1.84	0.77
/cut7	1.98	0.77
/cut8	2.12	0.77
/cut9	2.56	0.79
/cut10	2.91	0.81
/cut11	4.28	0.93
/cut12	4.69	0.96
/cut13	5.88	1.12
/cut14	6.41	1.23
/cut15	7.18	1.44

The BCT component resource use (ordered logit) and effectiveness (meta-regression) results

BCT components	Ordered resource ranking (ordered logit)		Effect Meta-regression	
	Mean	SE	Mean	SE
	<i>Patient-targeted BCTs</i>			
Problem Solving	2.23	1.08	-0.16	0.31
Goal Setting (Outcome)	1.22	1.27	1.00	0.32
Action Planning	-9.77	3.04	0.63	0.59
Review Behaviour Goals	5.45	3.06	0.18	0.44
Review outcome goals	6.44	3.73	-1.70	0.50
Monitoring of behaviour without feedback	1.64	2.06	-1.15	0.62
Feedback on behaviour	0.14	2.46	0.23	0.57
Self-monitoring of outcomes of behaviour	2.86	2.11	-0.54	0.38
Monitoring of outcomes without feedback	2.53	1.39	0.63	0.28
Feedback on outcomes of behaviour/Biofeedback	-1.20	0.99	0.24	0.33
Social Support (unspecified)	-3.03	1.25	-0.14	0.28
Social Support (practical)	1.36	1.07	-0.34	0.27
Instruction on how to perform behaviour	2.45	1.09	0.54	0.27
Information about health consequences	-2.85	1.09	-0.27	0.26
Prompts/Cues	-2.83	1.15	-0.46	0.39
Credible source	-1.87	1.84	-1.11	0.70
Material incentive (behaviour)	-0.68	2.63	-0.54	0.33
Restructuring the social environment	-0.59	1.80	0.48	0.38
Adding objects to the environment	-0.47	1.36	0.02	0.38
<i>Healthcare professional-targeted BCTs</i>				
Problem Solving	0.75	1.34	0.59	0.40
Goal Setting (Outcome)	-3.28	1.67	-1.06	0.49
Review Behaviour Goals	3.86	2.17	1.57	0.34
Feedback on behaviour	-0.24	1.21	-0.44	0.25
Feedback on outcomes of behaviour/Biofeedback				
Social Support (unspecified)				
Social Support (practical)				
Instruction on how to perform behaviour				

Social comparison				
Prompts/Cues				
Behavioural practice/rehearsal				
Credible source				
Restructuring the social environment				
Adding objects to the environment				
Constant			0.79	0.26
/cut1	-4.04	1.31		
/cut2	-2.01	1.14		
/cut3	1.03	1.09		
/cut4	1.27	1.11		
/cut5	1.71	1.16		
/cut6	2.40	1.22		
/cut7	2.64	1.24		
/cut8	2.89	1.26		
/cut9	3.78	1.35		
/cut10	4.69	1.48		
/cut11	7.09	1.68		
/cut12	7.92	1.78		
/cut13	10.08	2.06		
/cut14	10.81	2.17		
/cut15	12.01	2.41		

Appendix 2.2.

The cost estimates for the resource use categories

The cost estimates for the resource use categories used to record the resource use of the main intervention in the included clinical studies. The total number of people with diabetes (2,913,538), GP practices (8,151), and GPs (40,265) in England were used to derive a cost per patient for each intervention.

The objective was to roughly estimate the cost of interventions based on the intervention descriptions, with assumptions made about the number of patients, GPs and GP practices associated with each cost. This differs from the review of economic-related outcomes reported in the clinical studies which costed the economic outcome data. Different assumptions were made in the different exercises.

Cost per person with diabetes estimates for four studies for the production of education leaflets/pamphlets

Education Printing	Source	Lafata ²⁷	Pizzi ¹⁹	Prela ²⁸	Weiss ²⁹
<i>Fixed</i>					
GP Hourly salary designing leaflets (General GP working hours) £	PSSRU	147	147	147	147
GP Hours of production	Clinical study	14	14	3	21
Leaflet design specialist hourly cost £	University hospitals Birmingham	45	45	45	45
Hours of production	Clinical study	140	140	7	210
Total fixed £		8,358	8,358	756	12,537
Total annuitized £		2,249	2,249	200	3,413
<i>Variable</i>					
Printing cost £		0.6	0.6	0.3	5
HCP time producing feedback hours	Clinical study	0.05	0.05	0.05	
Nurse salary Band 5 including qualifications per hour £	PSSRU	45	45	45	
Delivery cost £	Royal Mail	1.2	1.2	1.2	
Times per year	Clinical study	1.00	1.00	1.00	1.00
<i>Total per person with diabetes £</i>		3.95	3.95	3.20	5.00

Cost per person with diabetes estimates for one study for providing clinician feedback

Clinician feedback	Source	Hermans ³⁰
<i>Variable</i>		
HCP time producing feedback hours	Clinical study	0.2
Nurse salary Band 5 including qualifications per hour £	PSSRU	45
Printing cost £	Birmingham Women's and Children's Hospital	0.6
Up to 100 gram delivery cost £	Royal Mail	0.55
Times per year	Clinical study	3
Total variable/clinician £		29.25
<i>Total variable/person with diabetes £</i>		<i>0.40</i>

Cost per person with diabetes estimates for four studies for the production of patient management software or use of ophthalmic equipment

Software or equipment cost	Source	Peterson ³¹	Guldborg ³²	Davis 2003 ³³	Conlin ³⁴
<i>Fixed</i>					
HCP hours	Assumption	112	112		
HCP hourly cost £	PSSRU	147	147		
Senior programmer cost £	Assumption	60,000	60,000		
Years equivalent	Assumption	1	1		
Junior programmer cost £	Assumption	45,000	45,000		
Years equivalent	Assumption	4	4		
Subtotal £		255,680	255,680		
Installation/GP practice £	Assumption	10,000	10,000		
Cost of equipment/GP practice £	BiB Ophthalmic Instruments			15,000	15,000
Total cost/All GP practices £		81,760,000	81,760,000	122,265,000	122,265,000
Annuitised £		22,259,253	22,259,253	33,286,786	33,286,786
<i>Variable</i>					
Maintenance/GP practice £	Assumption	500	500		
<i>Total cost/person with diabetes £</i>		<i>7.6</i>	<i>7.6</i>	<i>11.42</i>	<i>11.42</i>

Cost per person with diabetes estimates for seven studies for face-to-face or person-specific administration time

Diabetes person face to face clinic contact	Source	Wagner³⁵	Weiss²⁹	Peterson³¹	Piette³⁶	Davis³³	Conlin³⁴	Gabbay³⁷
<i>Variable</i>								
Nurse time (hours)	Clinical study	1.21	0.5	0.5	1			2.33
Nurse salary £	PSSRU	45	45	45	45			45
Hours of clinician time	Clinical study	0.165				0.5	0.25	
Clinician salary £	PSSRU	147				80	80	
<i>Total cost per year £</i>		<i>78.75</i>	<i>22.5</i>	<i>22.5</i>	<i>45</i>	<i>40</i>	<i>20</i>	<i>104.85</i>

Cost per person with diabetes estimates for four studies for training health professionals

Training of health professionals	Source	Perria³⁸	Bush³⁹	Peterson³¹	Guldborg³²	Conlin³⁴	Gabbay³⁷
<i>Fixed</i>							
Health trainer (Band 8a professional staff) hours	Clinical study	4.2				724,770	38847.17333
Health trainer hourly salary £	PSSRU	64				45	45
Health professional hours	Clinical study	16				724,770	1748122.8
Health professional salary £	PSSRU	147				62	45
Total cost/GP £		2,621				77,550,390	80,413,649
Annuitised cost/GP £		683				21,113,182	21,892,708
<i>Per patient group</i>							
Health trainer (Band 5 nurse) hours	Clinical study		14	14	40,265		
Health trainer hourly salary £	PSSRU		45	45	45		
Health professional (Band 5 nurse) hours	Clinical study		42	42	40,265		
Health professional salary £	PSSRU		45	45	147		
Total cost £			2,520	2,520	7,730,880		
Number of people with diabetes	Clinical study		988	988	2,913,538		
<i>Total cost per year £</i>		<i>9.44</i>	<i>2.55</i>	<i>2.55</i>	<i>2.65</i>	<i>7.25</i>	<i>7.51</i>

Cost per person with diabetes estimates for four studies for phone calls to people with diabetes

Phone calls	Source	Bush³⁹	Peterson³¹	Piette³⁶
<i>Variable</i>				
Average phone call £	PSSRU	6.69	6.69	
Hours on phone/person with diabetes	Clinical study			0.33
Hourly wage (Band 5 nurse) £	PSSRU			45
<i>Total cost/person with diabetes £</i>		<i>6.69</i>	<i>6.69</i>	<i>14.85</i>

Appendix 2.3.

R model

```
tab.dat<-read.csv("wedata.csv",header=TRUE)
tab.datMR<-read.csv("wemort.csv",header=TRUE)

# Model function -----

#####
#####
#DEFINE FUNCTIONS AND PARAMETERS
#####
#####

#Dataframe structure.....
#From 1: Baseline data
#From 101: effect data
#From 201: cost data
#From 601: utility data
#From 301: Initial population distribution then holding population distribution
#From 501: Intermediate clinical data used to populate transition matrix
#From 1001: Transition matrix
#From 2001: Mid-way transition matrix calculation states
#From 3001: Holding states
#From 4001: Trace matrix population
#From 6001: Trace matrix QALYs
#From 8001: Trace matrix costs
#From 10001: Summary results

mod<-function(nSims,det,cpp){

  mStates <- c("A", "IS", "ISR", "M",      "MR",   "B1",   "B2",   "B3",   "B4",   "B5",   "B6", "BS",   "C",
             "CR",   "CCS",
             "E",    "ER",    "ELCS", "EMCS", "EHCS", "ERCS", "TF", "D");

  qcStates <- c("Q1", "Q2", "Q3", "Q4", "Q5", "Q6", "Q7", "Q8", "Q9", "Q10", "Q11", "Q12", "Q13", "Q14", "Q15",
              "Q16", "Q17", "Q18",
              "C1", "C2", "C3", "C4", "C5", "C6", "C7", "C8", "C9", "C10", "C11", "C12", "C13", "C14", "C15",
              "C16", "C17", "C18");

  nTX <- 18

  nStates <- 16;

  cohort <- 1000

  nCycles <- 74;

  mcmcdf <- function (pnStates, n){

    emcmc <- matrix(data=rep(0, (n*(length(pnStates)+1))), nrow=n, ncol=(length(pnStates)+1)); ##SR: creates a matrix of zero values
    ## where the number of rows is the cohort, and the number of columns is the number of states + 1 (not sure yet why there
    ## needs to be a column of 1 to n)
    colnames(emcmc) <- c("ID", pnStates);
```

```

emcmc[,1] <-seq(1,n);
(data.frame(emcmc));
}

rmdf <- function (pnStates, n){

rmd <- matrix(data=rep(0, (n*(length(pnStates)+1))), nrow=n, ncol=(length(pnStates)+1)); ##SR: creates a matrix of zero values
## where the number of rows is the cohort, and the number of columns is the number of states + 1 (not sure yet why there
## needs to be a column of 1 to n)
colnames(rmd) <- c("ID", pnStates);
rmd[,1] <-seq(1,n);
(rmd);
}

df <- function (c, r){

pm <- matrix(data=rep(0, r*c), nrow=r, ncol=c); ##SR: creates a matrix of zero values
## where the number of rows is the cohort, and the number of columns is the number of states + 1 (not sure yet why there
## needs to be a column of 1 to n)
#colnames(pm) <- c(pnStates);

(pm);
}
#####
#####
dft<-df(10500,nSims)
#dft<-MMcreateMatrix2(df, 5389, 10)
df1<-df(10500,nSims)
dfe<-df(10500,nSims)
rmd<-rmdf(qcStates, nSims)
mcmc <- mcmcdf(qcStates, nSims)
#trans<-tab.datTnames(mStates)

#mModel <- MMcreateMatrix(trans, nStates, mStates)

#####
#####
#####
#clinical effectiveness
#####
#####

Comparator_screen <- cpp ##probability of attending screen for comparator
dft[,1]<-Comparator_screen

#####
#####
#Baseline population characteristics
#####
#####
HbA1c <- 51
dft[,2] <- HbA1c

Serum_cholesterol <- 4.3
dft[,3] <- Serum_cholesterol

```

```

Percent_female <- 0.432
dft[,4] <- Percent_female

#####
#Diagnostic accuracy
#####
#####
#Specificity
BDR1 <- 0.997
dft[,5] <- BDR1

BDR2 <- 0.998
dft[,6] <- BDR2

BDR3 <- 0.906
dft[,7] <- BDR3

#Sensitivity
STDR1 <- 0.75
dft[,8] <- STDR1

STDR2 <- 0.96
dft[,9] <- STDR2

DM1 <- 0.822
dft[,10] <- DM1

DM2 <- 0.982
dft[,11] <- DM2

#####
#Transition variables
#####
#prob of treatment following referral to HES
#R2-3M0 R0-1M0
dft[,12]<-0.142460802

#R2-3M0 R2-3M0
dft[,13]<-0.139433873

#RxM1 RxM0
dft[,14]<-0.507499438

#RxM1 RxM1
dft[,15]<-0.69635493

#Prob of monitoring given no treatment following referral to HES
#dft[,16]<-0.78

#basic transition probabilities
preDR1_preDR2<-0.11
dft[,16]<-preDR1_preDR2

preDR1_preDR3<-0
dft[,17]<-preDR1_preDR3

preDR1_DR1<-0

```

```

dft[,18]<-preDR1_DR1

preDR1_DR2<-0
dft[,19]<-preDR1_DR2

preDR1_DM1<-0.0005
dft[,20]<-preDR1_DM1

preDR1_DM2<-0
dft[,21]<-preDR1_DM2

#####
preDR2_preDR1<-0.12
dft[,22]<-preDR2_preDR1

preDR2_preDR3<-0.11
dft[,23]<-preDR2_preDR3

preDR2_DR1<-0.0001
dft[,24]<-preDR2_DR1

preDR2_DR2<-0
dft[,25]<-preDR2_DR2

preDR2_DM1<-0.004
dft[,26]<-preDR2_DM1

preDR2_DM2<-0.0003
dft[,27]<-preDR2_DM2

#####
preDR3_preDR1<-0.001
dft[,28]<-preDR3_preDR1

preDR3_preDR2<-0.12
dft[,29]<-preDR3_preDR2

preDR3_DR1<-0.01
dft[,30]<-preDR3_DR1

preDR3_DR2<-0.001
dft[,31]<-preDR3_DR2

preDR3_DM1<-0.03
dft[,32]<-preDR3_DM1

preDR3_DM2<-0
dft[,33]<-preDR3_DM2

#####
DR1_preDR1<-0
dft[,34]<-DR1_preDR1

DR1_preDR2<-0
dft[,35]<-DR1_preDR2

DR1_preDR3<-0
dft[,36]<-DR1_preDR3

```

DR1_DR2<-0.08
dft[,37]<-DR1_DR2

DR1_DM1<-0
dft[,38]<-DR1_DM1

DR1_DM2<-0
dft[,39]<-DR1_DM2

DR2_preDR1<-0
dft[,40]<-DR2_preDR1

DR2_preDR2<-0
dft[,41]<-DR2_preDR2

DR2_preDR3<-0
dft[,42]<-DR2_preDR3

DR2_DR1<-0
dft[,43]<-DR2_DR1

DR2_DM1<-0
dft[,44]<-DR2_DM1

DR2_DM2<-0
dft[,45]<-DR2_DM2

DM1_preDR1<-0
dft[,46]<-DM1_preDR1

DM1_preDR2<-0
dft[,47]<-DM1_preDR2

DM1_preDR3<-0
dft[,48]<-DM1_preDR3

DM1_DR1<-0
dft[,49]<-DM1_DR1

DM1_DR2<-0
dft[,50]<-DM1_DR2

DM1_DM2<-0.04
dft[,51]<-DM1_DM2

DM2_preDR1<-0
dft[,52]<-DM2_preDR1

DM2_preDR2<-0
dft[,53]<-DM2_preDR2

DM2_preDR3<-0
dft[,54]<-DM2_preDR3

```
DM2_DR1<-0
dft[,55]<-DM2_DR1
```

```
DM2_DR2<-0
dft[,56]<-DM2_DR2
```

```
DM2_DM1<-0
dft[,57]<-DM2_DM1
```

```
#####
```

```
#Treatment probabilities
```

```
#####
```

```
#DR1_ang
```

```
dft[,61]<-0.571380511
```

```
#DR1_anglaser
```

```
dft[,62]<-0.142887182
```

```
#DR1_laser
```

```
dft[,63]<-0.285732307
```

```
#DR2_ang
```

```
dft[,64]<-0.077744196
```

```
#DR2_anglaser
```

```
dft[,65]<-0.022229581
```

```
#DR2_laser
```

```
dft[,66]<-0.900026223
```

```
#DM1_ang
```

```
dft[,67]<-0.326903716
```

```
#DM1_anglaser
```

```
dft[,68]<-0.14426699
```

```
#DM1_laser
```

```
dft[,69]<-0.528829293
```

```
#DM2_ang
```

```
dft[,70]<-0.488499106
```

```
#DM2_anglaser
```

```
dft[,71]<-0.204657457
```

```
#DM2_laser
```

```
dft[,72]<-0.306843437
```

```
#DR1_angtot
```

```
dft[,81]<-dft[,61]+dft[,62]
```

```
#DR1_lasertot
```

```
dft[,82]<-dft[,62]+dft[,63]
```

```
#DR2_angtot
```

```
dft[,83]<-dft[,64]+dft[,65]
```

```
#DR2_lasertot
```

```
dft[,84]<-dft[,65]+dft[,66]
```

```
#DM1_angtot
```

```
dft[,85]<-dft[,67]+dft[,68]
```

```
#DM1_lasertot
```

```
dft[,86]<-dft[,68]+dft[,69]
```

```
#DM2_angtot
```

```
dft[,87]<-dft[,70]+dft[,71]
```

```
#DM2_lasertot
```

```
dft[,88]<-dft[,71]+dft[,72]
```

```
##probability of treatment
```

```
#DR1_pT
```

```
dft[,91]<- 0.142460802
```

```
#DR2_pT
```

```

dft[,92]<- 0.139433873
#DM1_pT
dft[,93]<- 0.507499438
#DM2_pT
dft[,94]<- 0.69635493

#####
#Effect estimates
#####
#constant
dft[,98]<-rnorm(nSims,0.785611,0.2625392)

#blnOR
dft[,101]<- rnorm(nSims,0,1)
#<- blnOR

#bOR
dft[,102]<-exp(0.3123145*dft[,101]-0.158592+dft[,98])
#<- bOR

#bRR
dft[,150]<- dft[,102]/(1-dft[,1]*(1-dft[,102]))
#<- bRR
#b_screen
dft[,170]<- dft[,150]*dft[,1]
#<- b_screen
##

#clnOR
dft[,103]<- rnorm(nSims,0,1)
#<- clnOR

#cOR
dft[,104]<-exp(0.3236347*dft[,103]+1.004057+dft[,98])
#<- cOR

#cRR
dft[,151]<- dft[,104]/(1-dft[,1]*(1-dft[,104]))
#<- cRR
#c_screen
dft[,171]<- dft[,151]*dft[,1]
#<- c_screen
##

#olnOR
dft[,105]<- rnorm(nSims,0,1)
#<- olnOR

#oOR
dft[,106]<-exp(0.2847324*dft[,105]+0.6341538+dft[,98])
#<- oOR

#oRR
dft[,152]<- dft[,106]/(1-dft[,1]*(1-dft[,106]))
#<- oRR
#o_screen
dft[,172]<- dft[,152]*dft[,1]

```

```

#<- o_screen
##

#pInOR
dft[,107]<- rnorm(nSims,0,1)
#<- pInOR

#pOR
dft[,108]<-exp(0.3272442*dft[,107]+0.240764+dft[,98])
#<- pOR

#pRR
dft[,153]<- dft[,108]/(1-dft[,1]*(1-dft[,108]))
#<- pRR
#p_screen
dft[,173]<- dft[,153]*dft[,1]
#<- p_screen
##

#qInOR
dft[,109]<- rnorm(nSims,0,1)
#<- qInOR

#qOR
dft[,110]<-exp(0.2782508*dft[,109]-0.1377803+dft[,98])
#<- qOR

#qRR
dft[,154]<- dft[,110]/(1-dft[,1]*(1-dft[,110]))
#<- qRR
#q_screen
dft[,174]<- dft[,154]*dft[,1]
#<- q_screen
##

#sInOR
dft[,111]<- rnorm(nSims,0,1)
#<- sInOR

#sOR
dft[,112]<-exp(0.2659836*dft[,111]-0.3386256+dft[,98])
#<- sOR

#sRR
dft[,155]<- dft[,112]/(1-dft[,1]*(1-dft[,112]))
#<- sRR
#s_screen
dft[,175]<- dft[,155]*dft[,1]
#<- s_screen
##

#tInOR
dft[,113]<- rnorm(nSims,0,1)
#<- tInOR

#tOR
dft[,114]<-exp(0.2714084*dft[,113]+0.5380853+dft[,98])
#<- tOR

```



```

#tRR
dft[,156]<- dft[,114]/(1-dft[,1]*(1-dft[,114]))
#<- tRR

#t_screen
dft[,176]<- dft[,156]*dft[,1]
#<- t_screen
##

#aalnOR
dft[,115]<- rnorm(nSims,0,1)
#<- aalnOR

#aaOR
dft[,116]<-exp(0.2606318*dft[,115]-0.2692529+dft[,98])
#<- aaOR

#aaRR
dft[,157]<- dft[,116]/(1-dft[,1]*(1-dft[,116]))
#<- aaRR

#aa_screen
dft[,177]<- dft[,157]*dft[,1]
#<- aa_screen
##

#aelnOR
dft[,117]<- rnorm(nSims,0,1)
#<- aelnOR

#aeOR
dft[,118]<-exp(0.392789*dft[,117]-0.4560603+dft[,98])
#<- aeOR

#aeRR
dft[,158]<- dft[,118]/(1-dft[,1]*(1-dft[,118]))
#<- aeRR

#ae_screen
dft[,178]<- dft[,158]*dft[,1]
#<- ae_screen
##

#ajlnOR
dft[,119]<- rnorm(nSims,0,1)
#<- ajlnOR

#ajOR
dft[,120]<-exp(0.3271919*dft[,119]-0.537091+dft[,98])
#<- ajOR

#ajRR
dft[,159]<- dft[,120]/(1-dft[,1]*(1-dft[,120]))
#<- ajRR

#aj_screen
dft[,179]<- dft[,159]*dft[,1]

```

```

#<- aj_screen
##

#balnOR
dft[,121]<- rnorm(nSims,0,1)
#<- balnOR

#baOR
dft[,122]<-exp(0.2469097*dft[,121]-0.4383294+dft[,98])
#<- baOR

#baRR
dft[,160]<- dft[,122]/(1-dft[,1]*(1-dft[,122]))
#<- baRR

#ba_screen
dft[,180]<- dft[,160]*dft[,1]
#<- ba_screen
##

#bcInOR
dft[,123]<- rnorm(nSims,0,1)
#<- bcInOR

#bcOR
dft[,124]<-exp(0.4249868*dft[,123]+1.194787+dft[,98])
#<- bcOR

#bcRR
dft[,161]<- dft[,124]/(1-dft[,1]*(1-dft[,124]))
#<- bcRR

#bc_screen
dft[,181]<- dft[,161]*dft[,1]
#<- bc_screen
##

#bdInOR
dft[,125]<- rnorm(nSims,0,1)
#<- bdInOR

#bdOR
dft[,126]<-exp(0.2708582*dft[,125]-0.5724014+dft[,98])
#<- bdOR

#bdRR
dft[,162]<- dft[,126]/(1-dft[,1]*(1-dft[,126]))
#<- bdRR

#bd_screen
dft[,182]<- dft[,162]*dft[,1]
#<- bd_screen
##

#bilnOR
dft[,127]<- rnorm(nSims,0,1)
#<- bilnOR

```

```

#biOR
dft[,128]<-exp(0.4167135*dft[,127]-0.1361259+dft[,98])
#<- biOR

#biRR
dft[,163]<- dft[,128]/(1-dft[,1]*(1-dft[,128]))
#<- biRR

#bi_screen
dft[,183]<- dft[,163]*dft[,1]
#<- bi_screen
##

#bllnOR
dft[,129]<- rnorm(nSims,0,1)
#<- bllnOR

#blOR
dft[,130]<-exp(0.2898359*dft[,129]-0.1609926+dft[,98])
#<- blOR

#blRR
dft[,164]<- dft[,130]/(1-dft[,1]*(1-dft[,130]))
#<- blRR

#bl_screen
dft[,184]<- dft[,164]*dft[,1]
#<- bl_screen
##

#bolnOR
dft[,131]<- rnorm(nSims,0,1)
#<- bolnOR

#boOR
dft[,132]<-exp(0.3171594*dft[,131]+0.4532762+dft[,98])
#<- boOR

#boRR
dft[,165]<- dft[,132]/(1-dft[,1]*(1-dft[,132]))
#<- boRR

#bo_screen
dft[,185]<- dft[,165]*dft[,1]
#<- bo_screen
##

#bpInOR
dft[,133]<- rnorm(nSims,0,1)
#<- bpInOR

#bpOR
dft[,134]<-exp(0.3109008*dft[,133]-0.062245+dft[,98])
#<- bpOR

#bpRR
dft[,166]<- dft[,134]/(1-dft[,1]*(1-dft[,134]))
#<- bpRR

```

```

#bp_screen
dft[,186]<- dft[,166]*dft[,1]
#<- bp_screen
##

#Probability of monitoring
dft[,99]<-0.78

#####
#####
#Costs
#####
#####

#cost of one screen
dft[,201] <- 33

#Likert standard errors of interventions on log-odds scale

#enter the 15 ologit cut results

dft[,202] <- rmorm(nSims,-4.036502,1.305078)
dft[,203] <- rmorm(nSims,-2.007494,1.135725)
dft[,204] <- rmorm(nSims,1.031078,1.089946)
dft[,205] <- rmorm(nSims,1.26614,1.110955)
dft[,206] <- rmorm(nSims,1.707262,1.155676)
dft[,207] <- rmorm(nSims,2.39646,1.222959)
dft[,208] <- rmorm(nSims,2.636701,1.24124)
dft[,209] <- rmorm(nSims,2.887425,1.259529)
dft[,210] <- rmorm(nSims,3.779752,1.34606)
dft[,211] <- rmorm(nSims,4.686412,1.478103)
dft[,212] <- rmorm(nSims,7.085127,1.675654)
dft[,213] <- rmorm(nSims,7.921756,1.781087)
dft[,214] <- rmorm(nSims,10.07898,2.056043)
dft[,215] <- rmorm(nSims,10.80505,2.171375)
dft[,216] <- rmorm(nSims,12.00981,2.412503)

#enter intervention means

#b
dft[,221] <- 2.227674
#c
dft[,222] <- 1.220926
#o
dft[,223] <- -1.203427
#p
dft[,224] <- -3.025819
#q
dft[,225] <- 1.356444
#s
dft[,226] <- 2.452334
#t
dft[,227] <- -2.845207
#aa
dft[,228] <- -2.831569

```

```
#ae
dft[,229] <- -1.86509
#aj
dft[,230] <- -0.5928834
#ba
dft[,231] <- -1.438731
#bc
dft[,232] <- 4.310422
#bd
dft[,233] <- -0.3034361
#bi
dft[,234] <- 1.864839
#bl
dft[,235] <- -0.3444515
#bo
dft[,236] <- 4.937853
#bp
dft[,237] <- -2.741852

#enter intervention standard errors

#b
dft[,241] <- 1.081678
#c
dft[,242] <- 1.266392
#o
dft[,243] <- 0.9919163
#p
dft[,244] <- 1.254638
#q
dft[,245] <- 1.071337
#s
dft[,246] <- 1.093049
#t
dft[,247] <- 1.089955
#aa
dft[,248] <- 1.146388
#ae
dft[,249] <- 1.836242
#aj
dft[,250] <- 1.799308
#ba
dft[,251] <- 0.9316532
#bc
dft[,252] <- 1.431745
#bd
dft[,253] <- 1.001166
#bi
dft[,254] <- 1.443432
#bl
dft[,255] <- 1.125722
#bo
dft[,256] <- 1.623801
#bp
dft[,257] <- 1.288694

#1-3 rank order Costs
```

```

#cons
dft[,261] <- -1.1271
#mean
dft[,262] <- 4.3750
#standard error
dft[,263] <- 0.2263

#4-8 rank order Costs
#cons
dft[,264] <- 9.5174
#mean
dft[,265] <- 4.3475
#standard error
dft[,266] <- 0.2927

#9-15 rank order Costs
#cons
dft[,267] <- 36.3808
#mean
dft[,268] <- 4.3830
#standard error
dft[,269] <- 0.1125

mr <- tab.datMR
rtrisk<-mr
#as.numeric(mr)

for (b in 1:18){

#####
#Start new dataframe 'dfe' for this inner loop so that the original dataframe 'dft' is preserved for the next loop iteration
#####

dfe<-dft

#####
#Set treatment conditional parameters
#####
if (b==1){
#intevention screening uptake probability
dfe[,502]<-dfe[,1]

} else if (b==2){
#intevention screening uptake probability
dfe[,502]<-dfe[,170]
#Likert result
dfe[,503]<-rnorm(nSims,0,1)

dfe[,511]<- -dfe[,202]+dfe[,221]+dfe[,503]*dfe[,241]*(sqrt(1-(0.095^2)))+0.095*dfe[,101]*dfe[,241]
dfe[,512]<- -dfe[,203]+dfe[,221]+dfe[,503]*dfe[,241]*(sqrt(1-(0.095^2)))+0.095*dfe[,101]*dfe[,241]
dfe[,513]<- -dfe[,204]+dfe[,221]+dfe[,503]*dfe[,241]*(sqrt(1-(0.095^2)))+0.095*dfe[,101]*dfe[,241]
dfe[,514]<- -dfe[,205]+dfe[,221]+dfe[,503]*dfe[,241]*(sqrt(1-(0.095^2)))+0.095*dfe[,101]*dfe[,241]
dfe[,515]<- -dfe[,206]+dfe[,221]+dfe[,503]*dfe[,241]*(sqrt(1-(0.095^2)))+0.095*dfe[,101]*dfe[,241]
dfe[,516]<- -dfe[,207]+dfe[,221]+dfe[,503]*dfe[,241]*(sqrt(1-(0.095^2)))+0.095*dfe[,101]*dfe[,241]
dfe[,517]<- -dfe[,208]+dfe[,221]+dfe[,503]*dfe[,241]*(sqrt(1-(0.095^2)))+0.095*dfe[,101]*dfe[,241]

```



```

dfe[,514]<- -dfe[,205]+dfe[,237]+dfe[,503]*dfe[,257]*(sqrt(1-(0.095^2)))+0.095*dfe[,133]*dfe[,257]
dfe[,515]<- -dfe[,206]+dfe[,237]+dfe[,503]*dfe[,257]*(sqrt(1-(0.095^2)))+0.095*dfe[,133]*dfe[,257]
dfe[,516]<- -dfe[,207]+dfe[,237]+dfe[,503]*dfe[,257]*(sqrt(1-(0.095^2)))+0.095*dfe[,133]*dfe[,257]
dfe[,517]<- -dfe[,208]+dfe[,237]+dfe[,503]*dfe[,257]*(sqrt(1-(0.095^2)))+0.095*dfe[,133]*dfe[,257]
dfe[,518]<- -dfe[,209]+dfe[,237]+dfe[,503]*dfe[,257]*(sqrt(1-(0.095^2)))+0.095*dfe[,133]*dfe[,257]
dfe[,519]<- -dfe[,210]+dfe[,237]+dfe[,503]*dfe[,257]*(sqrt(1-(0.095^2)))+0.095*dfe[,133]*dfe[,257]
dfe[,520]<- -dfe[,211]+dfe[,237]+dfe[,503]*dfe[,257]*(sqrt(1-(0.095^2)))+0.095*dfe[,133]*dfe[,257]
dfe[,521]<- -dfe[,212]+dfe[,237]+dfe[,503]*dfe[,257]*(sqrt(1-(0.095^2)))+0.095*dfe[,133]*dfe[,257]
dfe[,522]<- -dfe[,213]+dfe[,237]+dfe[,503]*dfe[,257]*(sqrt(1-(0.095^2)))+0.095*dfe[,133]*dfe[,257]
dfe[,523]<- -dfe[,214]+dfe[,237]+dfe[,503]*dfe[,257]*(sqrt(1-(0.095^2)))+0.095*dfe[,133]*dfe[,257]
dfe[,524]<- -dfe[,215]+dfe[,237]+dfe[,503]*dfe[,257]*(sqrt(1-(0.095^2)))+0.095*dfe[,133]*dfe[,257]
dfe[,525]<- -dfe[,216]+dfe[,237]+dfe[,503]*dfe[,257]*(sqrt(1-(0.095^2)))+0.095*dfe[,133]*dfe[,257]

```

```

}

```

```

#cumulative probabilities

```

```

dfe[,531]<-1/(1+exp(dfe[,511]))
dfe[,532]<-1/(1+exp(dfe[,512]))
dfe[,533]<-1/(1+exp(dfe[,513]))
dfe[,534]<-1/(1+exp(dfe[,514]))
dfe[,535]<-1/(1+exp(dfe[,515]))
dfe[,536]<-1/(1+exp(dfe[,516]))
dfe[,537]<-1/(1+exp(dfe[,517]))
dfe[,538]<-1/(1+exp(dfe[,518]))
dfe[,539]<-1/(1+exp(dfe[,519]))
dfe[,540]<-1/(1+exp(dfe[,520]))
dfe[,541]<-1/(1+exp(dfe[,521]))
dfe[,542]<-1/(1+exp(dfe[,522]))
dfe[,543]<-1/(1+exp(dfe[,523]))
dfe[,544]<-1/(1+exp(dfe[,524]))
dfe[,545]<-1/(1+exp(dfe[,525]))
dfe[,546]<-1

```

```

#expected probabilities

```

```

dfe[,551]<-dfe[,531]
dfe[,552]<-dfe[,532]-dfe[,531]
dfe[,553]<-dfe[,533]-dfe[,532]
dfe[,554]<-dfe[,534]-dfe[,533]
dfe[,555]<-dfe[,535]-dfe[,534]
dfe[,556]<-dfe[,536]-dfe[,535]
dfe[,557]<-dfe[,537]-dfe[,536]
dfe[,558]<-dfe[,538]-dfe[,537]
dfe[,559]<-dfe[,539]-dfe[,538]
dfe[,560]<-dfe[,540]-dfe[,539]
dfe[,561]<-dfe[,541]-dfe[,540]
dfe[,562]<-dfe[,542]-dfe[,541]
dfe[,563]<-dfe[,543]-dfe[,542]
dfe[,564]<-dfe[,544]-dfe[,543]
dfe[,565]<-dfe[,545]-dfe[,544]
dfe[,566]<-dfe[,546]-dfe[,545]

```

```

#expected ordered ranking

```

```

dfe[,571]<-dfe[,551]*1 + dfe[,552]*2 + dfe[,553]*3 + dfe[,554]*4 + dfe[,555]*5 + dfe[,556]*6 + dfe[,557]*7 + dfe[,558]*8 + dfe[,559]*9 +
dfe[,560]*10 + dfe[,561]*11 + dfe[,562]*12 + dfe[,563]*13 + dfe[,564]*14 + dfe[,565]*15 + dfe[,566]*16

```

```

dfe[,596]<-rnorm(nSims,0,dfe[,263])

```

```

dfe[,597]<-rnorm(nSims,0,dfe[,266])

```

```

dfe[,598]<-rnorm(nSims,0,dfe[,269])

#expected cost
if (b==1){
  dfe[,572]<-0
} else {

  dfe[,572]<-
ifelse(dfe[,571]<4,(dfe[,261]+dfe[,262]*dfe[,571]+dfe[,596]),ifelse(dfe[,571]<9,(dfe[,264]+dfe[,265]*dfe[,571]+dfe[,597]),(dfe[,267]+dfe[,
268]*dfe[,571]+dfe[,598])))

}

#probability of referral to HES
dfe[,581]<-dfe[,502]*(1-dfe[,5])
dfe[,582]<-dfe[,502]*(1-dfe[,6])
dfe[,583]<-dfe[,502]*(1-dfe[,7])
dfe[,584]<-dfe[,502]*dfe[,8]
dfe[,585]<-dfe[,502]*dfe[,9]
dfe[,586]<-dfe[,502]*dfe[,10]
dfe[,587]<-dfe[,502]*dfe[,11]
dfe[,588]<-dfe[,502]*dfe[,8]
dfe[,589]<-dfe[,502]*dfe[,9]
dfe[,590]<-dfe[,502]*dfe[,10]
dfe[,591]<-dfe[,502]*dfe[,11]
dfe[,592]<-dfe[,502]*dfe[,8]
dfe[,593]<-dfe[,502]*dfe[,9]
dfe[,594]<-dfe[,502]*dfe[,10]
dfe[,595]<-dfe[,502]*dfe[,11]

#initial population sequence (cols: 87 to 109)

#preDR1
dfe[,301]<-0.604
#preDR2
dfe[,302]<-0.188
#preDR3
dfe[,303]<-0.129
#DR1
dfe[,304]<-0.011
#DR2
dfe[,305]<-0.009
#DM1
dfe[,306]<-0.04
#DM2
dfe[,307]<-0.018
#MDR1
dfe[,308]<-0
#MDR2
dfe[,309]<-0
#MDM1
dfe[,310]<-0
#MDM2

```

```

dfe[,311]<-0
#TDR1
dfe[,312]<-0
#TDR2
dfe[,313]<-0
#TDM1
dfe[,314]<-0
#TDM2
dfe[,315]<-0
#Dead
dfe[,316]<-0

dfe[,4001:4016]<-dfe[,301:316]

# write.csv(df1, file = "df1.csv")

##utilities
dfe[,601]<- tab.dat[1,"Utility_preDR"]/2
dfe[,602]<- tab.dat[1,"Utility_preDR"]/2
dfe[,603]<- tab.dat[1,"Utility_preDR"]/2
dfe[,604]<- tab.dat[1,"Utility_nTx_DR1"]/2
dfe[,605]<- tab.dat[1,"Utility_nTx_DR2"]/2
dfe[,606]<- tab.dat[1,"Utility_nTx_DM1"]/2
dfe[,607]<- tab.dat[1,"Utility_nTx_DM2"]/2
dfe[,608]<- tab.dat[1,"Utility_nTx_DR1"]/2
dfe[,609]<- tab.dat[1,"Utility_nTx_DR2"]/2
dfe[,610]<- tab.dat[1,"Utility_nTx_DM1"]/2
dfe[,611]<- tab.dat[1,"Utility_nTx_DM2"]/2
dfe[,612]<- tab.dat[1,"Utility_Tx_DR1"]/2
dfe[,613]<- tab.dat[1,"Utility_Tx_DR2"]/2
dfe[,614]<- tab.dat[1,"Utility_Tx_DM1"]/2
dfe[,615]<- tab.dat[1,"Utility_Tx_DM2"]/2
dfe[,616]<- 0

##probability of HES assessment
dfe[,621]<- tab.dat[1,"Attend_preDR"]*dfe[,581]
dfe[,622]<- tab.dat[1,"Attend_preDR"]*dfe[,582]
dfe[,623]<- tab.dat[1,"Attend_preDR"]*dfe[,583]
dfe[,624]<- tab.dat[1,"Attend_DR1"]*dfe[,584]
dfe[,625]<- tab.dat[1,"Attend_DR2"]*dfe[,585]
dfe[,626]<- tab.dat[1,"Attend_DM1"]*dfe[,586]
dfe[,627]<- tab.dat[1,"Attend_DM2"]*dfe[,587]

dfe[,628]<- 1
dfe[,629]<- 1
dfe[,630]<- 1
dfe[,631]<- 1

dfe[,632]<- tab.dat[1,"Attend_DR1"]*dfe[,588]
dfe[,633]<- tab.dat[1,"Attend_DR2"]*dfe[,589]
dfe[,634]<- tab.dat[1,"Attend_DM1"]*dfe[,590]
dfe[,635]<- tab.dat[1,"Attend_DM2"]*dfe[,591]

##log costs

```

```

dfe[,751]<- 0.119*dfe[,621]+1.057*tab.dat[1,"Va_preDR"]+0.153+-0.1892+5.87
dfe[,752]<- 0.119*dfe[,622]+1.057*tab.dat[1,"Va_preDR"]+0.153+-0.1892+5.87+0.105
dfe[,753]<- 0.119*dfe[,623]+1.057*tab.dat[1,"Va_preDR"]+0.153+-0.1892+5.87+0.269
dfe[,754]<- 0.119*dfe[,624]+1.057*tab.dat[1,"Va_nTx_DR1"]+0.153+-0.1892+5.87+0.487
dfe[,755]<- 0.119*dfe[,625]+1.057*tab.dat[1,"Va_nTx_DR2"]+0.153+-0.1892+5.87+0.625
dfe[,756]<- 0.119*dfe[,626]+1.057*tab.dat[1,"Va_nTx_DM1"]+0.153+-0.1892+5.87+0.444
dfe[,757]<- 0.119*dfe[,627]+1.057*tab.dat[1,"Va_nTx_DM2"]+0.153+-0.1892+5.87+0.423
dfe[,758]<- 0.119*dfe[,628]+1.057*tab.dat[1,"Va_nTx_DR1"]+0.153+-0.1892+5.87+0.487
dfe[,759]<- 0.119*dfe[,629]+1.057*tab.dat[1,"Va_nTx_DR2"]+0.153+-0.1892+5.87+0.625
dfe[,760]<- 0.119*dfe[,630]+1.057*tab.dat[1,"Va_nTx_DM1"]+0.153+-0.1892+5.87+0.444
dfe[,761]<- 0.119*dfe[,631]+1.057*tab.dat[1,"Va_nTx_DM2"]+0.153+-0.1892+5.87+0.423
dfe[,762]<-
0.119*dfe[,628]+1.057*tab.dat[1,"Va_Tx_DR1"]+0.271*dfe[,81]*dfe[,91]*dfe[,628]+0.337*dfe[,82]*dfe[,91]*dfe[,628]+0.153+-
0.1892+5.87+0.487
dfe[,763]<-
0.119*dfe[,629]+1.057*tab.dat[1,"Va_Tx_DR2"]+0.271*dfe[,83]*dfe[,92]*dfe[,629]+0.337*dfe[,84]*dfe[,92]*dfe[,629]+0.153+-
0.1892+5.87+0.625
dfe[,764]<-
0.119*dfe[,630]+1.057*tab.dat[1,"Va_Tx_DM1"]+0.271*dfe[,85]*dfe[,93]*dfe[,630]+0.337*dfe[,86]*dfe[,93]*dfe[,630]+0.153+-
0.1892+5.87+0.444
dfe[,765]<-
0.119*dfe[,631]+1.057*tab.dat[1,"Va_Tx_DM2"]+0.271*dfe[,87]*dfe[,94]*dfe[,631]+0.337*dfe[,88]*dfe[,94]*dfe[,631]+0.153+-
0.1892+5.87+0.423

```

##state specific costs

```

dfe[,771]<-exp(dfe[,751])
dfe[,772]<-exp(dfe[,752])
dfe[,773]<-exp(dfe[,753])
dfe[,774]<-exp(dfe[,754])
dfe[,775]<-exp(dfe[,755])
dfe[,776]<-exp(dfe[,756])
dfe[,777]<-exp(dfe[,757])
dfe[,778]<-exp(dfe[,758])
dfe[,779]<-exp(dfe[,759])
dfe[,780]<-exp(dfe[,760])
dfe[,781]<-exp(dfe[,761])
dfe[,782]<-exp(dfe[,758])
dfe[,783]<-exp(dfe[,759])
dfe[,784]<-exp(dfe[,760])
dfe[,785]<-exp(dfe[,761])

```

##total costs

```

dfe[,701]<-dfe[,771]/2+dfe[,502]*(1-dfe[,5])*33
dfe[,702]<-dfe[,772]/2+dfe[,502]*(1-dfe[,6])*33
dfe[,703]<-dfe[,773]/2+dfe[,502]*(1-dfe[,7])*33
dfe[,704]<-dfe[,774]/2+dfe[,502]*dfe[,8]*33
dfe[,705]<-dfe[,775]/2+dfe[,502]*dfe[,9]*33
dfe[,706]<-dfe[,776]/2+dfe[,502]*dfe[,10]*33
dfe[,707]<-dfe[,777]/2+dfe[,502]*dfe[,11]*33
dfe[,708]<-dfe[,778]/2
dfe[,709]<-dfe[,779]/2
dfe[,710]<-dfe[,780]/2
dfe[,711]<-dfe[,781]/2
dfe[,712]<-dfe[,782]/2+dfe[,502]*dfe[,8]*33
dfe[,713]<-dfe[,783]/2+dfe[,502]*dfe[,9]*33
dfe[,714]<-dfe[,784]/2+dfe[,502]*dfe[,10]*33

```



```

dfe[,715]<-dfe[,785]/2+dfe[,502]*dfe[,11]*33
dfe[,716]<-0

##Define new initial population- first row of trace matrix
dfe[,6001:6016]<-dfe[,4001:4016]*dfe[,601:616] #QALYs
dfe[,8001:8016]<-dfe[,4001:4016]*dfe[,701:716] #Costs

#Sum the QALYs across the states for each cycle
dfe[,10001]<-rowSums(dfe[,6001:6016])

#Sum the costs across the states for each iteration
dfe[,10101]<-rowSums(dfe[,8001:8016])

#write.csv(df1, file = "df1.csv")

#i<-3
df1<-dfe

for (i in 2:74){

##utilities
df1[,601]<- tab.dat[i,"Utility_preDR"]/2
df1[,602]<- tab.dat[i,"Utility_preDR"]/2
df1[,603]<- tab.dat[i,"Utility_preDR"]/2
df1[,604]<- tab.dat[i,"Utility_nTx_DR1"]/2
df1[,605]<- tab.dat[i,"Utility_nTx_DR2"]/2
df1[,606]<- tab.dat[i,"Utility_nTx_DM1"]/2
df1[,607]<- tab.dat[i,"Utility_nTx_DM2"]/2
df1[,608]<- tab.dat[i,"Utility_nTx_DR1"]/2
df1[,609]<- tab.dat[i,"Utility_nTx_DR2"]/2
df1[,610]<- tab.dat[i,"Utility_nTx_DM1"]/2
df1[,611]<- tab.dat[i,"Utility_nTx_DM2"]/2
df1[,612]<- tab.dat[i,"Utility_Tx_DR1"]/2
df1[,613]<- tab.dat[i,"Utility_Tx_DR2"]/2
df1[,614]<- tab.dat[i,"Utility_Tx_DM1"]/2
df1[,615]<- tab.dat[i,"Utility_Tx_DM2"]/2
df1[,616]<- 0

##probability of HES assessment
df1[,621]<- tab.dat[i,"Attend_preDR"]*df1[,581]
df1[,622]<- tab.dat[i,"Attend_preDR"]*df1[,582]
df1[,623]<- tab.dat[i,"Attend_preDR"]*df1[,583]
df1[,624]<- tab.dat[i,"Attend_DR1"]*df1[,584]
df1[,625]<- tab.dat[i,"Attend_DR2"]*df1[,585]
df1[,626]<- tab.dat[i,"Attend_DM1"]*df1[,586]
df1[,627]<- tab.dat[i,"Attend_DM2"]*df1[,587]

df1[,628]<- 1
df1[,629]<- 1
df1[,630]<- 1
df1[,631]<- 1

df1[,632]<- tab.dat[i,"Attend_DR1"]*df1[,588]
df1[,633]<- tab.dat[i,"Attend_DR2"]*df1[,589]
df1[,634]<- tab.dat[i,"Attend_DM1"]*df1[,590]
df1[,635]<- tab.dat[i,"Attend_DM2"]*df1[,591]

```

```

##log costs
df1[,751]<- 0.119*df1[,621]+1.057*tab.dat[i,"Va_preDR"]+0.153+-0.1892+5.87
df1[,752]<- 0.119*df1[,622]+1.057*tab.dat[i,"Va_preDR"]+0.153+-0.1892+5.87+0.105
df1[,753]<- 0.119*df1[,623]+1.057*tab.dat[i,"Va_preDR"]+0.153+-0.1892+5.87+0.269
df1[,754]<- 0.119*df1[,624]+1.057*tab.dat[i,"Va_nTx_DR1"]+0.153+-0.1892+5.87+0.487
df1[,755]<- 0.119*df1[,625]+1.057*tab.dat[i,"Va_nTx_DR2"]+0.153+-0.1892+5.87+0.625
df1[,756]<- 0.119*df1[,626]+1.057*tab.dat[i,"Va_nTx_DM1"]+0.153+-0.1892+5.87+0.444
df1[,757]<- 0.119*df1[,627]+1.057*tab.dat[i,"Va_nTx_DM2"]+0.153+-0.1892+5.87+0.423
df1[,758]<- 0.119*df1[,628]+1.057*tab.dat[i,"Va_nTx_DR1"]+0.153+-0.1892+5.87+0.487
df1[,759]<- 0.119*df1[,629]+1.057*tab.dat[i,"Va_nTx_DR2"]+0.153+-0.1892+5.87+0.625
df1[,760]<- 0.119*df1[,630]+1.057*tab.dat[i,"Va_nTx_DM1"]+0.153+-0.1892+5.87+0.444
df1[,761]<- 0.119*df1[,631]+1.057*tab.dat[i,"Va_nTx_DM2"]+0.153+-0.1892+5.87+0.423
df1[,762]<-
0.119*df1[,628]+1.057*tab.dat[i,"Va_Tx_DR1"]+0.271*df1[,81]*df1[,91]*df1[,628]+0.337*df1[,82]*df1[,91]*df1[,628]+0.153+-
0.1892+5.87+0.487
df1[,763]<-
0.119*df1[,629]+1.057*tab.dat[i,"Va_Tx_DR2"]+0.271*df1[,83]*df1[,92]*df1[,629]+0.337*df1[,84]*df1[,92]*df1[,629]+0.153+-
0.1892+5.87+0.625
df1[,764]<-
0.119*df1[,630]+1.057*tab.dat[i,"Va_Tx_DM1"]+0.271*df1[,85]*df1[,93]*df1[,630]+0.337*df1[,86]*df1[,93]*df1[,630]+0.153+-
0.1892+5.87+0.444
df1[,765]<-
0.119*df1[,631]+1.057*tab.dat[i,"Va_Tx_DM2"]+0.271*df1[,87]*df1[,94]*df1[,631]+0.337*df1[,88]*df1[,94]*df1[,631]+0.153+-
0.1892+5.87+0.423

##state specific costs
df1[,771]<-exp(df1[,751])
df1[,772]<-exp(df1[,752])
df1[,773]<-exp(df1[,753])
df1[,774]<-exp(df1[,754])
df1[,775]<-exp(df1[,755])
df1[,776]<-exp(df1[,756])
df1[,777]<-exp(df1[,757])
df1[,778]<-exp(df1[,758])
df1[,779]<-exp(df1[,759])
df1[,780]<-exp(df1[,760])
df1[,781]<-exp(df1[,761])
df1[,782]<-exp(df1[,758])
df1[,783]<-exp(df1[,759])
df1[,784]<-exp(df1[,760])
df1[,785]<-exp(df1[,761])

##total costs

#screening state

if (i==3 | i==5 | i==7 | i==9 | i==11 | i==13 | i==15 | i==17 | i==19 | i==21 | i==23 | i==25 | i==27 | i==29 | i==31 | i==33 | i==35 |
i==37 | i==39 | i==41 | i==43 | i==45 | i==47 | i==49 | i==51 | i==53 | i==55 | i==57 | i==59 | i==61 | i==63 | i==65 | i==67 |
i==69 | i==71 | i==73){

df1[,701]<-df1[,771]/2+df1[,502]*(1-df1[,5])*33+df1[,572]
df1[,702]<-df1[,772]/2+df1[,502]*(1-df1[,6])*33+df1[,572]
df1[,703]<-df1[,773]/2+df1[,502]*(1-df1[,7])*33+df1[,572]
df1[,704]<-df1[,774]/2+df1[,502]*df1[,8]*33+df1[,572]

```

```

df1[,705]<-df1[,775]/2+df1[,502]*df1[,9]*33+df1[,572]
df1[,706]<-df1[,776]/2+df1[,502]*df1[,10]*33+df1[,572]
df1[,707]<-df1[,777]/2+df1[,502]*df1[,11]*33+df1[,572]
df1[,708]<-df1[,778]/2
df1[,709]<-df1[,779]/2
df1[,710]<-df1[,780]/2
df1[,711]<-df1[,781]/2
df1[,712]<-df1[,782]/2+df1[,502]*df1[,8]*33+df1[,572]
df1[,713]<-df1[,783]/2+df1[,502]*df1[,9]*33+df1[,572]
df1[,714]<-df1[,784]/2+df1[,502]*df1[,10]*33+df1[,572]
df1[,715]<-df1[,785]/2+df1[,502]*df1[,11]*33+df1[,572]
df1[,716]<-0

```

```

} else {

```

```

df1[,701]<-df1[,771]/2+df1[,502]*(1-df1[,5])
df1[,702]<-df1[,772]/2+df1[,502]*(1-df1[,6])
df1[,703]<-df1[,773]/2+df1[,502]*(1-df1[,7])
df1[,704]<-df1[,774]/2+df1[,502]*df1[,8]
df1[,705]<-df1[,775]/2+df1[,502]*df1[,9]
df1[,706]<-df1[,776]/2+df1[,502]*df1[,10]
df1[,707]<-df1[,777]/2+df1[,502]*df1[,11]
df1[,708]<-df1[,774]/2
df1[,709]<-df1[,775]/2
df1[,710]<-df1[,776]/2
df1[,711]<-df1[,777]/2
df1[,712]<-df1[,778]/2+df1[,502]*df1[,8]
df1[,713]<-df1[,779]/2+df1[,502]*df1[,9]
df1[,714]<-df1[,780]/2+df1[,502]*df1[,10]
df1[,715]<-df1[,781]/2+df1[,502]*df1[,11]
df1[,716]<-0
}

```

```

MORT <- rtrisk[i,"mort"]

```

```

df1[,801]<-MORT

```

```

df1[(1000+15*16+1):(1000+15*16+15)]<-df1[,801]

```

```

#ALIVE <- 1-MORT

```

```

df1[,802] <- 1-df1[,801]

```

```

##Transition probabilities grouped by original state, excluding transition to the next treatment and mortality

```

```

#Dead to dead

```

```

df1[(1000+15*16+16)]<-1

```

```

#####

```

```

#Transition variables

```

```

#####

```

```

#basic transition probabilities

```

```

#preDR1_preDR2<-0.11

```

```

df1[(1000+1*16+1)]<-df1[,16]*df1[,802]

```

```

#preDR1_preDR3<-0

```

```

df1[(1000+2*16+1)]<-df1[,17]*df1[,802]

```

```

#preDR1_DM1<-0.0005

```

```

df1[(1000+5*16+1)]<-df1[,20]*df1[,802]

#preDR1_preDR1<-
df1[(1000+0*16+1)]<-1-df1[(1000+1*16+1)]-df1[(1000+2*16+1)]-df1[(1000+5*16+1)]-df1[,801]

#####
#preDR2_preDR1<-0.12
df1[(1000+0*16+2)]<-df1[,22]*df1[,802]

#preDR2_preDR3<-0.11
df1[(1000+2*16+2)]<-df1[,23]*df1[,802]

#preDR2_DR1<-0.0001
df1[(1000+3*16+2)]<-df1[,24]*df1[,802]

#preDR2_DM1<-0.004
df1[(1000+5*16+2)]<-df1[,26]*df1[,802]

#preDR2_DM2<-0.0003
df1[(1000+6*16+2)]<-df1[,27]*df1[,802]

#preDR2_preDR2<-
df1[(1000+1*16+2)]<-1-df1[(1000+0*16+2)]-df1[(1000+2*16+2)]-df1[(1000+3*16+2)]-df1[(1000+5*16+2)]-df1[(1000+6*16+2)]-
df1[,801]

#####
#preDR3_preDR1<-0.001
df1[(1000+0*16+3)]<-df1[,28]*df1[,802]

#preDR3_preDR2<-0.12
df1[(1000+1*16+3)]<-df1[,29]*df1[,802]

#preDR3_DR1<-0.01
df1[(1000+3*16+3)]<-df1[,30]*df1[,802]

#preDR3_DR2<-0.001
df1[(1000+4*16+3)]<-df1[,31]*df1[,802]

#preDR3_DM1<-0.03
df1[(1000+5*16+3)]<-df1[,32]*df1[,802]

#preDR3_preDR3<-
df1[(1000+2*16+3)]<-1-df1[(1000+0*16+3)]-df1[(1000+1*16+3)]-df1[(1000+3*16+3)]-df1[(1000+4*16+3)]-df1[(1000+5*16+3)]-
df1[,801]

if (i==3 | i==5 | i==7 | i==9 | i==11 | i==13 | i==15 | i==17 | i==19 | i==21 | i==23 | i==25 | i==27 | i==29 | i==31 | i==33 | i==35 |
    i==37 | i==39 | i==41 | i==43 | i==45 | i==47 | i==49 | i==51 | i==53 | i==55 | i==57 | i==59 | i==61 | i==63 | i==65 | i==67 |
    i==69 | i==71 | i==73){

#####
#DR1_DR2<-0.08
df1[(1000+4*16+4)]<-df1[,37]*(1-df1[,624])*df1[,802]+df1[,37]*df1[,624]*df1[,802]*(1-df1[,12])*(1-df1[,99])

#DR1_MDR2<-0.08
df1[(1000+8*16+4)]<-df1[,37]*df1[,624]*(1-df1[,12])*df1[,99]*df1[,802]

```

```

#DR1_TDR2<-0.08
df1[(1000+12*16+4)]<-df1[,37]*df1[,624]*df1[,12]*df1[,802]

#DR1_MDR1<-
df1[(1000+7*16+4)]<-(1-df1[,37])*df1[,624]*(1-df1[,12])*df1[,99]*df1[,802]

#DR1_TDR1<-0.08
df1[(1000+11*16+4)]<-(1-df1[,37])*df1[,624]*df1[,12]*df1[,802]

#DR1_DR1<-
df1[(1000+3*16+4)]<-(1-df1[(1000+4*16+4)]-df1[(1000+8*16+4)]-df1[(1000+12*16+4)]-df1[(1000+7*16+4)]-
df1[(1000+11*16+4)]-df1[,801])

#####
#DM1_DM2<-0.04
df1[(1000+6*16+6)]<-df1[,51]*(1-df1[,626])*df1[,802]+df1[,37]*df1[,626]*df1[,802]*(1-df1[,14])*(1-df1[,99])

#DM1_MDM2<-0.04
df1[(1000+10*16+6)]<-df1[,51]*df1[,626]*(1-df1[,14])*df1[,99]*df1[,802]

#DM1_TDM2<-
df1[(1000+14*16+6)]<-df1[,51]*df1[,626]*df1[,14]*df1[,802]

#DM1_MDM1<-
df1[(1000+9*16+6)]<-(1-df1[,51])*df1[,626]*(1-df1[,14])*df1[,99]*df1[,802]

#DM1_TDM1<-
df1[(1000+13*16+6)]<-(1-df1[,51])*df1[,626]*df1[,14]*df1[,802]

#DM1_DM1<-
df1[(1000+5*16+6)]<-(1-df1[(1000+6*16+6)]-df1[(1000+10*16+6)]-df1[(1000+14*16+6)]-df1[(1000+9*16+6)]-
df1[(1000+13*16+6)]-df1[,801])

#####
#DR2_TDR2
df1[(1000+12*16+5)]<-df1[,625]*df1[,13]*df1[,802]

#DR2_MDR2
df1[(1000+8*16+5)]<-df1[,625]*(1-df1[,13])*df1[,99]*df1[,802]

#DR2_DR2
df1[(1000+4*16+5)]<-(1-df1[(1000+12*16+5)]-df1[(1000+8*16+5)]-df1[,801])

#DM2_TDM2
df1[(1000+14*16+7)]<-df1[,627]*df1[,15]*df1[,802]

#DM2_MDM2
df1[(1000+10*16+7)]<-df1[,627]*(1-df1[,15])*df1[,99]*df1[,802]

#DM2_DM2
df1[(1000+6*16+7)]<-1-df1[(1000+14*16+7)]-df1[(1000+10*16+7)]-df1[,801]

} else {

#####

```

```

#DR1_MDR2<-0.08
df1[(1000+8*16+4)]<-0

#DR1_TDR2<-0.08
df1[(1000+12*16+4)]<-0

#DR1_MDR1<-
df1[(1000+7*16+4)]<-0

#DR1_TDR1<-0.08
df1[(1000+11*16+4)]<-0

#DR1_DR2<-0.08
df1[(1000+4*16+4)]<-df1[,37]*df1[,802]

#DR1_DR1<-
df1[(1000+3*16+4)]<-(1-df1[(1000+4*16+4)]-df1[,801])

#####

#DM1_MDM2<-0.04
df1[(1000+10*16+6)]<-0

#DM1_TDM2<-
df1[(1000+14*16+6)]<-0

#DM1_MDM1<-
df1[(1000+9*16+6)]<-0

#DM1_TDM1<-
df1[(1000+13*16+6)]<-0

#DM1_DM2<-0.04
df1[(1000+6*16+6)]<-df1[,51]*df1[,802]

#DM1_DM1<-
df1[(1000+5*16+6)]<-(1-df1[(1000+6*16+6)]-df1[,801])

#####

#DR2_TDR2
df1[(1000+12*16+5)]<-0

#DR2_MDR2
df1[(1000+8*16+5)]<-0

#DR2_DR2
df1[(1000+4*16+5)]<-1-df1[,801]

#DM2_TDM2
df1[(1000+14*16+7)]<-0

#DM2_MDM2

```

```

df1[(1000+10*16+7)]<-0

#DM2_DM2
df1[(1000+6*16+7)]<-1-df1[,801]

}
#####

#TDR1_TDR1
df1[(1000+11*16+12)]<-1-df1[,801]

#TDR2_TDR2
df1[(1000+12*16+13)]<-1-df1[,801]

#TDM1_TDM1
df1[(1000+13*16+14)]<-1-df1[,801]

#TDM2_TDM2
df1[(1000+14*16+15)]<-1-df1[,801]

#####
#MDR1_MDR2<-0.08
df1[(1000+8*16+8)]<-df1[,37]*(1-df1[,12])*df1[,802]

#MDR1_TDR2<-0.08
df1[(1000+12*16+8)]<-df1[,37]*df1[,12]*df1[,802]

#MDR1_TDR1<-0.08
df1[(1000+11*16+8)]<-(1-df1[,37])*df1[,12]*df1[,802]

#MDR1_MDR1<-0.08
df1[(1000+7*16+8)]<-1-df1[(1000+8*16+8)]-df1[(1000+12*16+8)]-df1[(1000+11*16+8)]-df1[,801]

#####
#MDR2_TDR2<-0.08
df1[(1000+12*16+9)]<-df1[,13]*df1[,802]

#MDR2_MDR2<-0.08
df1[(1000+8*16+9)]<-1-df1[(1000+12*16+9)]-df1[,801]

#####
#MDM1_MDM2<-0.08
df1[(1000+10*16+10)]<-df1[,51]*(1-df1[,14])*df1[,802]

#MDM1_TDM2<-0.08
df1[(1000+14*16+10)]<-df1[,51]*df1[,14]*df1[,802]

#MDM1_TDM1<-0.08
df1[(1000+13*16+10)]<-(1-df1[,51])*df1[,14]*df1[,802]

#MDM1_MDM1<-0.08
df1[(1000+9*16+10)]<-1-df1[(1000+10*16+10)]-df1[(1000+14*16+10)]-df1[(1000+13*16+10)]- df1[,801]

#####
#MDM2_TDM2<-0.08
df1[(1000+14*16+11)]<-df1[,15]*df1[,802]

```

```

#MDM2_MDM2<-0.08
df1[(1000+10*16+11)]<-1-df1[(1000+14*16+11)]-df1[,801]

##initial population cols: 87 to 109
for (j in 1:16){

  ##define holding intermediate states: 1001:763 transition matrix; 789:1413 for intermediate states
  df1[(3001+(j-1)*16):(3016+(j-1)*16)]<-df1[,301:316]*df1[(1001+(j-1)*16):(1001+15+(j-1)*16)]#A
}

for (j in 1:16){

  ##cols 89 to 113 becomes the holding vector for the initial population
  df1[(301+(j-1))]<-rowSums(df1[(3001+(j-1)*16):(3016+(j-1)*16)])
}

##derive the population distributions from the second cycle onwards
df1[(4001+(i-1)*16):(4016+(i-1)*16)]<-df1[,301:316]

##derive the QALYs from the second cycle onwards
df1[(6001+(i-1)*16):(6016+(i-1)*16)]<-df1[(4001+(i-1)*16):(4016+(i-1)*16)]*df1[,601:616]/(1+0.017655865)^(i-0.5);

##derive the Costs from the second cycle onwards
df1[(8001+(i-1)*16):(8016+(i-1)*16)]<-df1[(4001+(i-1)*16):(4016+(i-1)*16)]*df1[,701:716]/(1+0.017655865)^(i-0.5);

#Sum the QALYs across the states for each cycle
df1[(10001+(i-1))]<-rowSums(df1[(6001+(i-1)*16):(6016+(i-1)*16)])

#Sum the costs across the states for each iteration
df1[(10101+(i-1))]<-rowSums(df1[(8001+(i-1)*16):(8016+(i-1)*16)])

} #END OF i in 2:12 loop

#write.csv(df1, file = "df1.csv")

#Sum the QALYs across the cycles
df1[,10201]<-rowSums(df1[,10001:10074])

#Sum the Costs across the cycles
df1[,10202]<-rowSums(df1[,10101:10174])

rmd[(1+b)]<-df1[,10201]
rmd[(19+b)]<-df1[,10202]

}#end intervention loop

mcmc<-rmd

(mcmc);
}

```