The benefits, harms, and cost-effectiveness of age-based and risk-stratified screening for prostate cancer with MRI

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Abstract

Background

Prostate cancer screening with MRI may lead to lower overdiagnosis by detecting fewer insignificant cancers. However, the balance of benefits and harms, as well as the cost-effectiveness of MRI-based prostate cancer screening under different strategies remains uncertain. The aim of this simulation study was to assess MRI-based prostate cancer screening under both age-based and risk-based screening strategies.

Methods

We used a life-table model to simulate men aged 55 to age 89 under age-based and polygenic risk-based screening strategies using either screening MRI or PSA as the primary screening test. We conducted extensive scenario, threshold, and sensitivity analyses to determine the robustness of conclusions to input parameters. Primary outcomes were prostate cancer deaths, overdiagnosed cancers, resource use, and cost-effectiveness (net health benefit from a healthcare perspective).

Results

MRI screening every 4 years from 55 to 69 years old could reduce overdiagnosis by 42.1% (95% intervals: 19.5%-60.5%) in comparison to a PSA-based screening programme. We estimated that MRI screening would lead to 12 (95% intervals: 7–19) overdiagnosed cancers per 1,000 men screened compared with 21 (95% intervals: 14–29) with PSA screening. All MRI screening strategies generated more quality-adjusted life-years (QALYs) and fewer costs than PSA screening. For age-based MRI screening to have a greater net health benefit (NHB) than no screening would require a willingness-to-pay (WTP) of £119,000 per quality-adjusted life-year (QALY) gained. Risk-stratified MRI screening strategies were more likely to be cost-effective, generate more QALYs, and lead to fewer overdiagnosed cancers than screening all men. At a WTP of £30,000 per QALY gained, MRI screening of men aged 55 with a 10-year absolute risk of prostate cancer of ≥6.4% had a greater NHB than no screening; the most cost-effective strategy at this WTP threshold was MRI screening at a 10-year absolute risk threshold of ≥8.5%. Results were sensitive to assumptions regarding the mean sojourn time – the mean time cancers are screen-detectable but pre-clinical – and the relative mortality benefits of screening strategies.

Conclusion

MRI based screening could reduce overdiagnosis and prove more cost-effective than PSA-based screening. Risk-stratified strategies are likely to be necessary for a prostate cancer screening programme to be considered cost-effective in the UK.

Introduction

Prostate cancer is a leading cause of cancer death in men[1]. Screening for prostate cancer every four years with prostate-specific antigen (PSA) has been shown to reduce prostate-cancer-specific mortality by 13% (95% confidence intervals [5%–20%]) after 23-years follow-up[2]. But the potential harms, particularly overdiagnosis, have hampered the development of a population-based screening programme. Overdiagnosis – the detection of cancers through screening that would not otherwise have been diagnosed[3] – drives overtreatment and subsequent treatment-related harms, reducing the overall benefits of screening[4].

Screening for prostate cancer using magnetic resonance imaging (MRI) may have the potential to mitigate overdiagnosis without a loss of clinical effectiveness. When used following an elevated PSA as a triage test prior to biopsy, MRI (multiparametric or biparametric MRI) reduces the detection of clinically insignificant cancers, defined as Gleason score 6, in both diagnostic[5,6] and screening[7–9] settings without compromising the detection of clinically significant cancer. Preliminary studies using MRI as a first-line test for population screening – the Imperial Prostate 1 Prostate Cancer Screening Trial (IP1-PROSTAGRAM)[10] and ReIMAGINE[11] – suggest that these advantages may also hold in a screening setting. Enriching the screened cohort through prior risk-stratification may further improve the benefit-to-harm profile and cost-effectiveness of prostate cancer screening whilst reducing the resources needed[12].

A prospective, multi-arm, randomised trial of MRI-based screening including polygenic risk has been launched[13]. Modelling can be used to analyse multiple alternative prostate cancer screening approaches under varying assumptions and thus inform strategies for further prospective evaluation. In this work, we aimed to understand the potential impact and cost-effectiveness of screening using MRI, with or without risk-stratification, relative to both PSA screening and no screening.

Methods

Model structure

We simulated cohorts of 1,000 men between the ages of 55 and 89 years. Using a life-table approach, we estimated the age-specific incidence of prostate cancer, deaths from prostate cancer, and deaths from other causes[12,14]. On this background, we superimposed alternative screening approaches both with and without prior risk stratification (see Appendix A for more details).

Modelled scenarios

In our base case, we modelled screening from the age of 55 to 69 at four-yearly intervals. We compared no screening, MRI, and PSA screening approaches, with and without risk stratification. For PSA screening, we assumed that individuals with a positive PSA (≥3ng/ml) would have a multiparametric MRI as a triage test prior to a diagnostic biopsy, as recommended by UK National Institute for Health and Care Excellence (NICE) guidelines[15]. In base case analyses, we considered MRI screening with a single biparameteric MRI (bpMRI) scan followed by diagnostic biopsy if positive (equivalent to Prostate Imaging-Reporting and Data System [PI-RADS] ≥ 3). Different combinations of screening and triage tests impact outcomes by changing the number and profile of cancers detected and ultimately through the relative reduction in mortality that might occur. We consider this explicitly in scenario and sensitivity analyses.

Scenario and sensitivity analyses

Given the uncertainty in key parameters and to allow for the wide number of potential screening pathways that might be used, we ran scenario analyses of the relative mortality reduction with screening, mean sojourn time (MST), episode sensitivity, the cost of a screening MRI, and proportion of screening tests that were positive. The MST is the average time that a cancer is screen-detectable but has not presented clinically[16]. Episode sensitivity describes the sensitivity of the entire diagnostic process, from a positive screening test result through to prostate cancer diagnosis[17]. In each scenario, we re-ran the analyses, holding the parameter of interest constant at a specified value whilst continuing to draw all other parameters from their relevant distributions.

Subsequently, we simultaneously varied the MST, the relative mortality reduction with screening, and the proportion of screening tests positive to analyse the impact of different combinations of these three variables. We then analysed screening from ages 50-69, 50-74, and 55-74. Finally, we performed probabilistic one-way sensitivity analyses of resource use and utility estimates[18].

Polygenic risk-stratified screening

We modelled the impact of stratified screening by centile of the polygenic risk distribution of prostate cancer. Polygenic risk follows a log-normal relative risk distribution[19], whose variance, given known prostate cancer susceptibility loci, is 0.72[20]. Using this distribution, we determined the proportion of prostate cancers, and hence the relative risk of cancer diagnosis amongst those above and below each absolute risk threshold. The average 10-year absolute risk of prostate cancer at age 55 is 2.6% (Figure A.1 in Appendix A). By

multiplying this value by the centile-specific relative risk of cancer (Table A.1 in Appendix A), we determined the 10-year absolute risk by centile of the polygenic distribution.

Model parameters

Age-specific prostate cancer incidence, mortality from prostate cancer and mortality from other causes amongst men in England in the absence of screening were calculated from mean 2017-2019 Office for National Statistics and NHS England data[21,22]. Model inputs and assumptions are presented in Appendix A (Tables A.2-A.6). To validate the reliability of our model's performance, we compared against figures for PSA screening from the European Randomized Study of Screening for Prostate Cancer (ERSPC) (Figures B.1-2 in Appendix B).

Model outputs

We calculated outcomes including prostate cancer diagnoses, deaths from prostate cancer and other causes, PSA tests, biopsies, screening and diagnostic MRI, as well as life-years, quality-adjusted life-years (QALYs) and costs. We used age- and MST-specific estimates of the proportion of screen-detected cancers overdiagnosed[16].

Cost-effectiveness analyses

We calculated the net health benefit (NHB) of different scenarios. NHB considers health gains (QALYs) in the context of the opportunity cost of those foregone in the population by introducing a particular intervention, derived as $NHB_i = QALY_i - (Cost_i / threshold)$, where i is the intervention or strategy and the willingness-to-pay (WTP) threshold for one QALY[23]. We considered thresholds of £20,000 and £30,000 per QALY gained in our main analyses, in line with the UK National Institute for Health and Care Excellence (NICE). Net health benefit is directly proportional to net monetary benefit. The strategy with the highest NHB at a particular willingness-to-pay threshold was considered optimal. Future costs and benefits were both discounted by 3.5%[24]. Utility estimates, resource use, and cost estimates are presented in Appendix A (Tables A.2 and A.7-A.9).

Statistical analyses

We ran 10,000 simulations for each scenario studied, drawing parameters simultaneously from their distributions. For intervals, we present the 2.5th and 97.5th centiles of the sorted probabilistic results.

Code and data availability

All data used in these analyses are openly available. We used Devcan version 6.7.8.5[25] and Julia[26] version 1.11.6 for analyses. The code and underpinning data are available at https://github.com/callta/mri-screening-prostate. We adhered to the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) reporting guideline[27]; a completed checklist is available as an Appendix.

Results

Base case outcomes, resource use, and cost-effectiveness analyses are presented in Table 1, Figures 1-2, and Appendix B (Tables B.1-B.2). Scenario analyses are presented in Figures 3-4 and Appendix B (Figures B.3-B.7 and Tables B.3-B.7).

Outcomes

Age-based MRI screening led to 42.1% (95% intervals: 19.5%–60.5%) fewer overdiagnosed cancers than age-based PSA screening amongst men screened every four years from 55-69. With MRI screening there were 12 (95% intervals: 7–19) overdiagnosed cancers, equating to 21.0% (95% intervals 14.2%–27.4%) of the 58 (95% intervals: 47–70) screen-detected cancers per 1,000 men screened, an 8.7% (95% intervals: 5.0% –13.1%) overall rise in overall prostate cancer incidence, and 2.5 (95% intervals: 1.3–4.1) overdiagnosed cancers per cancer death prevented. By contrast, PSA screening resulted in 21 (95% intervals: 14–29) overdiagnosed cancers, equivalent to 27.9% (95% intervals: 20.5%–34.8%) of the 76 (95% intervals: 65–88) screen-detected cancers per 1,000 men screened, a 15.1% (95% intervals: 10.0%–20.7%) rise in overall prostate cancer incidence, and 4.4 (95% intervals: 2.4–7.4) overdiagnosed per prostate cancer death prevented.

We assumed both MRI and PSA screening could have an equivalent, 20% at its peak before waning, prostate cancer-specific mortality reduction[2]. Under this assumption, if screening from the age of 55, the number needed to screen to prevent a prostate cancer death within a 25-year time horizon (i.e., amongst 55 year olds followed to age 80) was 492, dropping to 295 over a 30-year time horizon.

Resource use

MRI screening led to a 15.1-fold rise in imaging requirements relative to no screening, with the total number of MRI scans rising from 265 (95% intervals: 177-354) to 3,883 (95% intervals: 3,815–3,955) per 1,000 men, and a 3.5-fold increase in the number of biopsies from 177 (95% intervals: 115–248) to 772 (95% intervals 633–923). With PSA screening,

the total number of MRI required rose to 777 (95% intervals: 722-837), a 3.0-fold increase relative to no screening. PSA screening led to fewer biopsies than MRI screening (n=521, 95% intervals: 426-614) in base case analyses.

Cost-effectiveness

By comparison with no screening, MRI screening led to a gain in 6.7 QALYs (95% intervals: -0.5 to 12.5) for an additional £828,826 (95% intervals: £372,128–£1.46M) per 1,000 men. PSA screening led to fewer incremental QALYs (1.1, 95% intervals: -7.6–8.4) but had lower incremental costs (£508,341, 95% intervals: £226,804–£901,892). Both age-based MRI or PSA screening had a probability of ≤1.5% of having a greater net health benefit than no screening at a WTP of £30,000 per QALY (Figure 1). A WTP threshold of £119,000 per QALY gained was necessary for age-based MRI screening to be more cost-effective than no screening, with an equivalent figure of >£200,000 for PSA screening (Figure 1).

The impact of risk-stratified MRI screening

In our main analyses, we present four risk-stratified screening scenarios, broadly reflecting different quartiles of the polygenic risk distribution: screening from the 25th, 50th, 75th, and 90th centiles. These scenarios are equivalent to screening all those at age 55 above 10-year absolute risk thresholds of 3.2%, 4.1%, 5.7%, and 8.0%, respectively (Appendix A Figure A.1 and Table A.1). Amongst the 75% of men above the 25th centile, 94% of prostate cancers occur. The corresponding figures are 80%, 57%, and 33% of prostate cancer cases amongst those above the 50th, 75th, and 90th centiles, respectively.

The full range of outcomes at each centile are presented in Appendix Tables B.1-B.2. Risk-stratified strategies between the 6th and the 74th centile (MRI pathway) and between the 12th and the 98th centile (PSA pathway) of the polygenic risk distribution generated more QALYs and had fewer costs than screening all men (Figure 3). More selective risk-stratified screening strategies were more cost-effective than screening all men (Figure 2), but at the expense of fewer prostate cancer deaths prevented (Table 1 and Appendix B Table B.1-B.2). No screening was the most cost-effective solution at a WTP threshold of £20,000 per QALY, with MRI screening of those above the 92nd centile the most cost-effective solution at a WTP threshold of £30,000 per QALY. At this threshold, MRI screening of those above the 81st centile (≥6.4% 10-year absolute risk at age 55) would have a higher NHB than no screening.

Scenario and sensitivity analyses

We used scenario analyses to see how much our results might change given different model parameters (Figure 3-4; Appendix B Figures B.3-B.7 and Appendix B Tables B.3-7). Screening effectiveness is driven by earlier detection of a cancer – governed by the MST and episode sensitivity – coupled with the relative mortality reductions expected. With a shorter MST, screening anticipates fewer years of cancer diagnoses. In turn, this will reduce overdiagnosis and the number of life-years lived with prostate cancer. Greater relative mortality reductions and lower MSTs improved the cost-effectiveness of screening strategies. But, for an age-based screening strategy to be cost-effective within a NICE threshold of £30,000 per QALY, screening would need to reduce deaths by >30%, the MST of screen-detected cancers would need to be 7 years or less, and ≤5% of screening tests would need to test positive (Figure 4). A reduction in deaths amongst all those subject to screening of 30%, assuming 100% uptake, required a >70% reduction in deaths amongst those whose cancer was screen-detected (Appendix Figure B.8).

Reducing the age at which screening starts from 55 to 50, or increasing the age at which it stops from 69 to 74 reduces the cost-effectiveness of screening, whilst screening beyond 70 increases overdiagnosis and thus worsens the benefit/harm profile of screening (Appendix B Table B.7). Our model was insensitive to most costs with the exception of those of biopsies (probabilistic one-way sensitivity analyses shown in Appendix B Figure B.9).

Discussion

In this analysis, we show that the use of MRI as a screening test could reduce overdiagnosis, increase the number of QALYs accrued for a given relative mortality reduction, and improve the cost-effectiveness of formal screening for prostate cancer by comparison with PSA. These benefits are predicated on MRI preferentially detecting clinically significant, Gleason grade ≥7, cancers. Despite these benefits, age-based screening was unlikely to be considered cost-effective in a UK context.

Risk-stratification could improve the cost-effectiveness of prostate cancer screening. In this analysis, we found that screening those men at the 92nd centile of the polygenic risk distribution using an MRI screening pathway would be most cost-effective at the upper range of UK thresholds (£30,000/QALY). The 8% of men above the 92nd centile of the polygenic risk distribution have a 10-year absolute risk of developing prostate cancer of 8.5%, 3.3-fold the 2.6% 10-year average risk of a 55-year old man in England; 29% of prostate cancer cases could be expected amongst these individuals. By restricting eligibility for screening to

those at higher risk of developing prostate cancer, the resource intensity of screening drops and the absolute number of overdiagnosed cancers and therefore quality-adjusted life-years lived with prostate cancer declines. However, fewer prostate cancer deaths will be prevented. And, as risk-stratified eligibility thresholds increase, a growing proportion of prostate cancer diagnoses will occur amongst those not eligible for screening. Further, an organised screening programme targeted at only 8% of men may not be sufficiently clinically valuable even if most cost-effective.

Risk-stratified MRI screening led to the highest number of incremental QALYs relative to no screening when screening men at between the 28th and 53rd centiles, reaching its maximum at the 41st centile. At the 41st centile, 59% of men would be eligible for screening, amongst whom 86% of prostate cancer cases would be expected to occur; the 10-year absolute risk of prostate cancer from the age of 55 in this cohort would be ≥3.7%. By comparison with no screening, we estimate a risk-stratified MRI screening programme using this threshold would reduce prostate cancer deaths by 5 men per 1,000 (14.6%) with 8 overdiagnosed cancers per 1,000 men screened (16.9% of screen-detected cancers). The NHBs of risk-stratified MRI screening strategies from the 82nd centile (47% of prostate cancers amongst these men who are at a 10-year absolute risk of developing prostate cancer of ≥6.5% from age 55) were greater than no screening at a WTP threshold of £30,000 per QALY gained.

We found that MRI strategies in which a positive screening MRI led directly to biopsy might lead to higher biopsy use than PSA screening. This was because biparametric MRI as a screening test led to a similar, if marginally higher, number screening positive in the IP1-PROSTAGRAM (17.6%)[10] study than PSA screening did in ERSPC (16.8%)[28], coupled with the assumption that one-third of biopsies after a positive PSA screen would be avoided through the use of MP-MRI as a triage test[29]. However, biopsy requirements may be overestimated because of the relatively small sample size of IP1-PROSTAGRAM, and could be mitigated with triage testing in an MRI-based programme, for example by using a combination of MRI and PSA tests. Since higher screening test positivity in IP1-PROSTAGRAM was coupled with fewer clinically insignificant cancers, mortality reductions at least as great as with PSA screening in ERSPC are plausible. A greater proportion of the cancers detected with MRI screening were clinically significant than PSA screening, meaning fewer cancers were overdiagnosed and more quality-adjusted life-years were gained for a given mortality reduction.

We based our primary analyses on the ERSPC as the only randomized trial to show evidence of prostate cancer mortality reduction with screening[2]. Extrapolating this to MRI-

based screening required assumptions, of which estimates of sojourn time have proved most important as they underpin the advantages of MRI screening at a given relative mortality reduction. Our estimates of the MST were approximately 10 years for MRI, shorter than the approximately 13 years with a PSA-based programme. This is due to a lower proportion of screen-detected cancers being clinically insignificant, with these Gleason grade 6 cancers estimated to have a more indolent natural history and longer sojourn time than clinically significant cancers. We have not varied the estimated episode sensitivity for clinically significant cancers between PSA and MRI, which will make our analyses more conservative. However, our scenario analyses suggest that our conclusions are robust to a wide range of possible parameter values.

In keeping with the literature on age-based screening with MRI compared to PSA[30], our results suggest that screening all men with an MRI-based approach could increase the number of biopsies required and has a low probability of being cost-effective. However, by contrast with Gulati and colleagues[30], we did not find that overdiagnosis would be higher with MRI than PSA, nor do we feel there are strong grounds to assume that MRI screening will necessarily lead to fewer deaths prevented than an equivalent PSA screening programme. Nevertheless, varying these values in our scenario analyses did not fundamentally change our shared conclusion.

This work has several strengths. We used a transparent simulation approach where key underpinning parameters could be directly inputted. This allowed us to explore a wide range of scenario and sensitivity analyses, particularly in key drivers of the clinical- and cost-effectiveness of any screening programme: relative mortality reduction, mean sojourn time, and episode sensitivity. We do not rely on assumptions of stage shift with regards relative mortality reduction which have been shown to be unreliable in prostate cancer screening[31]. We considered a range of scenarios and MRI pathways, including risk-stratified approaches to screening. We have made the underpinning code open-source.

Limitations

Prospective trials with long-term follow-up using MRI as the screening test are not available, such that the model is based on assumptions. We have tried to make these as explicit as possible. We have also undertaken extensive scenario analyses to explore how confident one can be in our conclusions. We constrained the number of screening strategies studied, choosing not to consider multiple different starting/stopping ages and screening intervals, or alternative approaches to risk targeting. Instead, we focussed on a plausible age range and screening interval that closely approximates existing randomised screening evidence, albeit

using PSA rather than MRI as the screening test. This allows for clearer analyses of strategies that are under consideration for prospective evaluation. Importantly, constraining the number of scenarios allows us to minimise, insofar as possible, hidden assumptions, such as relative mortality gains with much longer screening intervals. Alternative approaches to risk targeting and stratification will be the subject of further work.

Conclusion

MRI-based screening for prostate cancer has the potential to reduce overdiagnoses and could generate more QALYs at an equivalent relative mortality reduction than PSA-based screening. Risk-stratified approaches were more likely to be cost-effective and merit further evaluation.

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Contributor statement

TC: conceptualisation, project management, analysis, code development, writing – first draft and further edits. CM: writing – reviewing and editing. EF: writing – reviewing and editing. ME: writing – reviewing and editing. NP: conceptualisation, supervision, methodology, writing – review and editing. TC acts as guarantor.

Data

All data and code used in this analysis are publicly available from https://github.com/callta/mri-screening-prostate.

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Conflicts of interest

ME receives research support from the United Kingdom's National Institute of Health Research (NIHR) UCLH / UCL Biomedical Research Centre. ME has no direct conflict of interest associated with the work presented in this paper. ME acts as an advisor/consultant to SonaCare Inc; Nina Medical; Exact Imaging and Angiodynamics Inc. CM is funded via an NIHR Research Professorship, with additional research funding from Prostate Cancer UK, Cancer Research UK and Movember. CM has received clinical trial funding from SpectraCure, proctor fees for HIFU proctoring from SonaCare and speaker fees from Ipsen in the last three years. TC, EF, and NP have no conflicts of interest to declare.

Figure Legends

Figure 1: Expected costs (blue lines) and QALYs (black lines) relative to no screening when screening men from age 55-69 every four years using either MRI (solid lines) or PSA (dashed lines) pathways.

Figure 2: Net health benefit (NHB) by willingness-to-pay (WTP) threshold. The first row shows (A) the expected incremental NHB of MRI screening relative to no screening, alongside (B) the probability of the incremental NHB being greater than that of no screening. Equivalent figures for PSA screening are shown in the second row. The probability of having an incremental NHB > 0 provides a measure of the spread of outcomes relative to no screening. For example, at a WTP of £30,000 per quality-adjusted life-year (QALY), age-based MRI screening had an incremental NHB of -18.6 QALYs (subfigure A), with a 1.09% probability of being more cost-effective than no screening (subfigure B). At each WTP threshold, the strategy with the highest NHB is the most cost-effective.

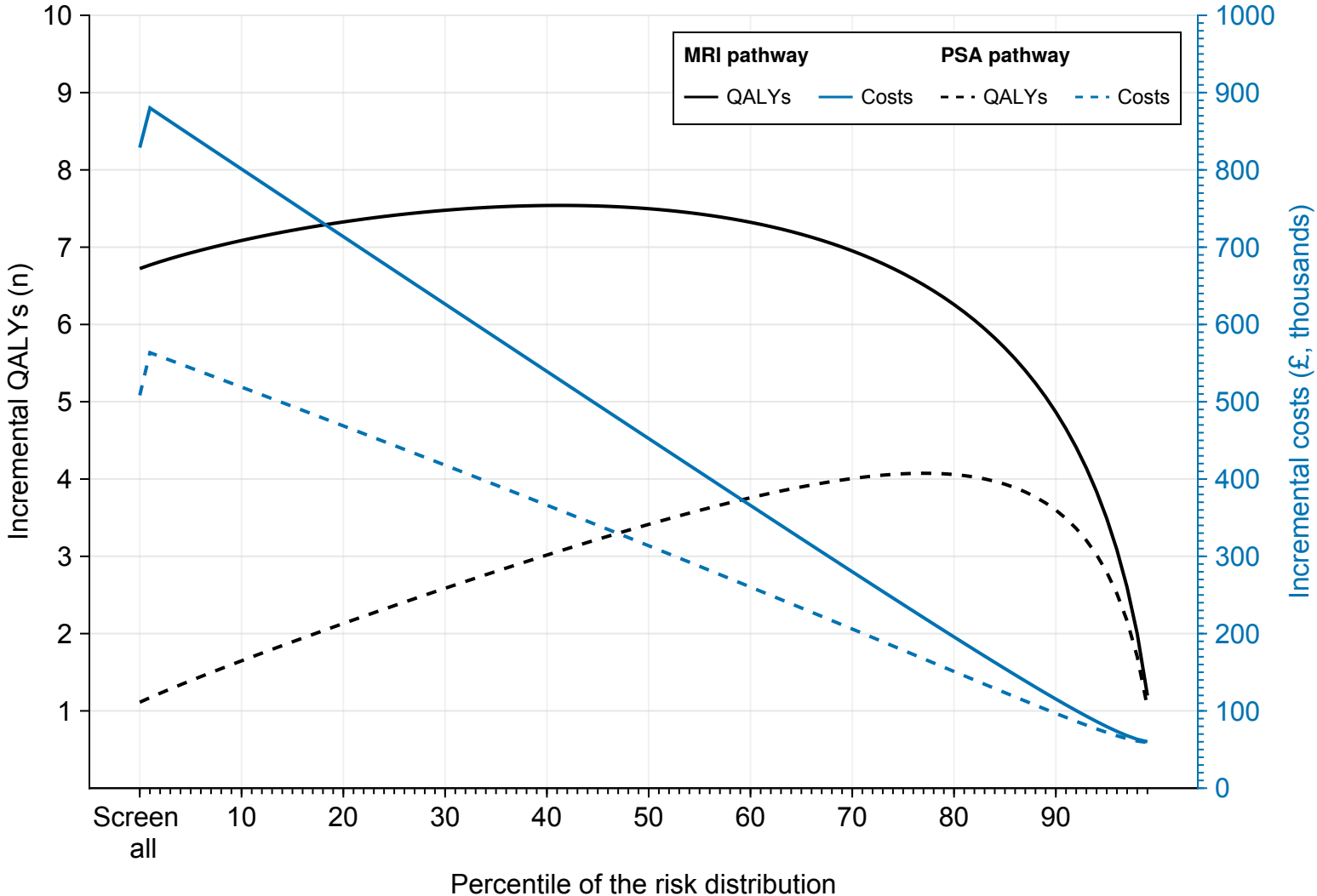
Figure 3: Impact of different relative mortality reductions with screening on the (A) cost-effectiveness of MRI screening (net health benefit at a willingness-to-pay [WTP] threshold of £30,000 per quality-adjusted life-year [QALY]) and (B) the number of prostate cancer deaths prevented relative to no screening.

Figure 4: Impact of simultaneously varying mean sojourn time (MST), the relative mortality reduction with screening, and the proportion of screening tests that are positive on the willingness-to-pay (WTP) threshold per quality-adjusted life-year (QALY) such that an age-based screening programme for men between 55-69 years every 4 years will be cost-effective (i.e., have a net health benefit (NHB) greater than no screening). In each sub-figure screening brings forwards diagnoses by a different number of years (indicated by the MST). For example, in sub-figure A, if the MST of a MRI screening programme were 7 years and 5% of screening tests were positive on average, the relative mortality benefit of the programme would need to be approximately 0.72 to have a ≥50% chance that screening would be cost-effective relative to no screening at a WTP threshold of £30,000 per QALY. For reference, in baseline analyses, the MST was 9.7, 17.6% of screening tests positive (NB., this is test positive, not true positive for cancer), and the RR mortality was 0.8 (see Table A.2 in Appendix A for more details).

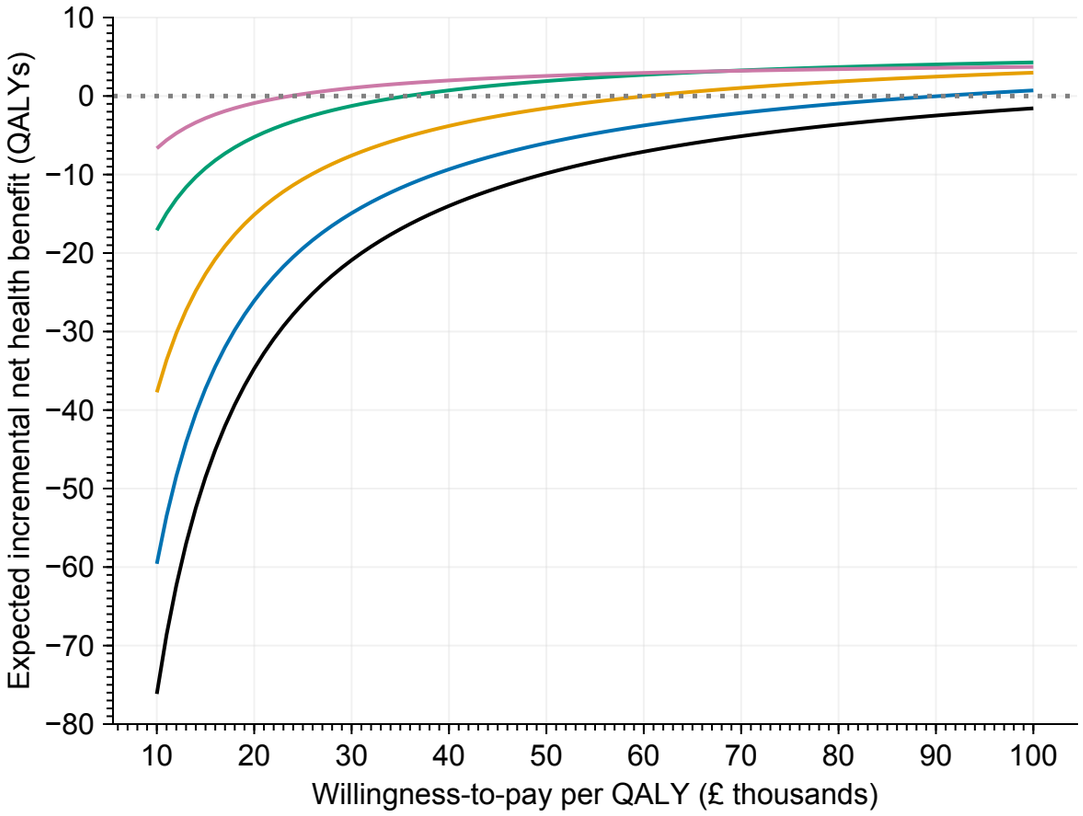
Table 1: Outcomes per 1,000 men screened from age 55 ever 4 years to 69

Strategy	Prostate cancers	Screen-detected cancers	Interval cancers	Overdiagnosed cancers	Deaths from prostate cancer	Screening MRI	Diagnostic MRI	Total MRI	Biopsies	Life-years	QALYs	Costs (GBP £)	NHB (QALYs)
No screening	141	0	0	0	34	0	265	265	177	16,967	14,215	860,616	14,172
PSA screening	162	76	15	18	29	0	777	777	521	16,988	14,216	1,368,958	14,147
Risk-stratified PSA screening													
25th centile	158	70	13	16	29	0	622	622	417	16,987	14,217	1,304,060	14,152
50th centile	153	59	11	14	29	0	477	477	319	16,985	14,218	1,174,306	14,159
75th centile	146	40	8	9	30	0	345	345	231	16,981	14,219	1,039,116	14,167
90th centile	141	22	4	5	31	0	281	281	188	16,976	14,218	957,403	14,171
MRI screening	153	58	16	10	29	3,704	179	3,883	772	16,987	14,222	1,689,443	14,137
Risk-stratified MRI screening													
25th centile	150	54	15	9	29	2,756	181	2,938	606	16,986	14,222	1,530,585	14,146
50th centile	146	45	12	8	29	1,817	190	2,007	447	16,984	14,222	1,313,010	14,157
75th centile	142	31	8	5	30	891	209	1,099	296	16,980	14,221	1,098,208	14,167
90th centile	139	17	4	3	31	346	230	576	215	16,975	14,220	975,925	14,171

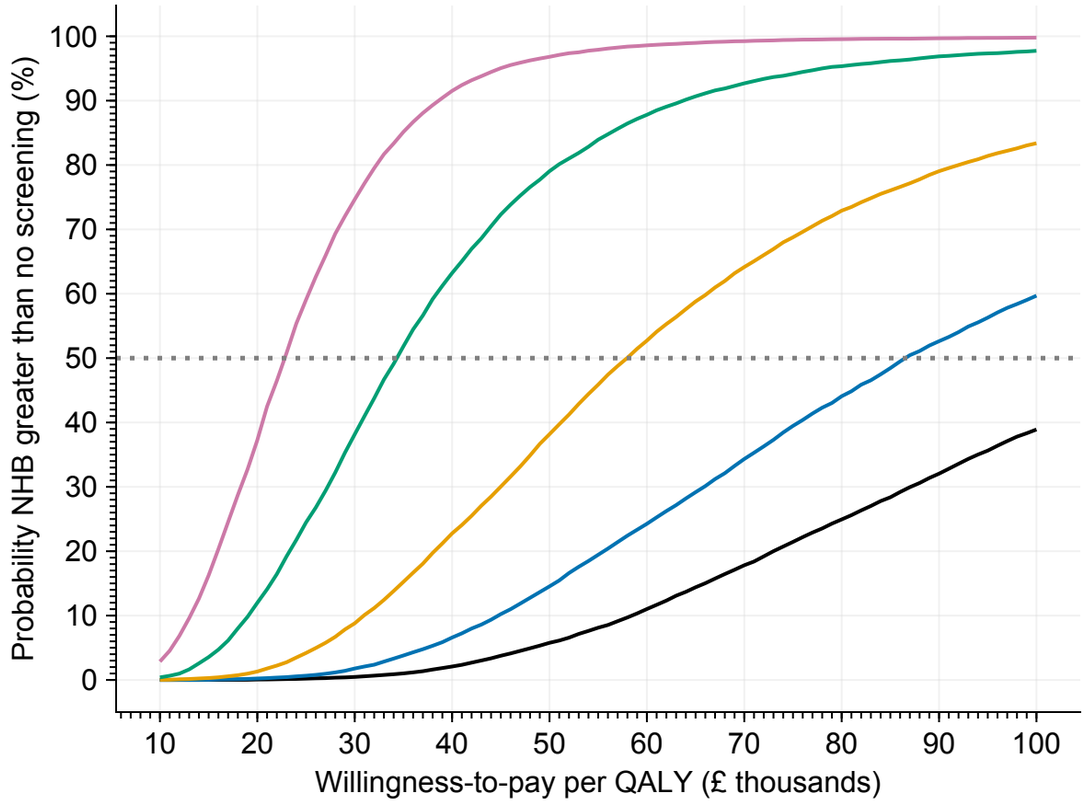
A selection of centiles from the risk distribution are shown to indicate the spread of results (see Appendix B and C for full tables). Net health benefits were calculated at a willingness-to-pay threshold of £20,000 per QALY gained. Net health benefits are calculated as qalys – (costs / threshold). Net health benefits are proportional to net monetary benefit [(threshold * QALYs) – costs]. Abbreviations: PSA, prostate specific antigen; MRI, magnetic resonance imaging; QALYs, quality-adjusted life-years; NHB, net health benefit.


MRI pathway
QALYs
Costs
PSA pathway
QALYs
Costs
Incremental QALYs (n)
Incremental costs (£, thousands)
Screen all
10
20
30
40
50
60
70
80
90
Percentile of the risk distribution

A MRI: Expected iNHB



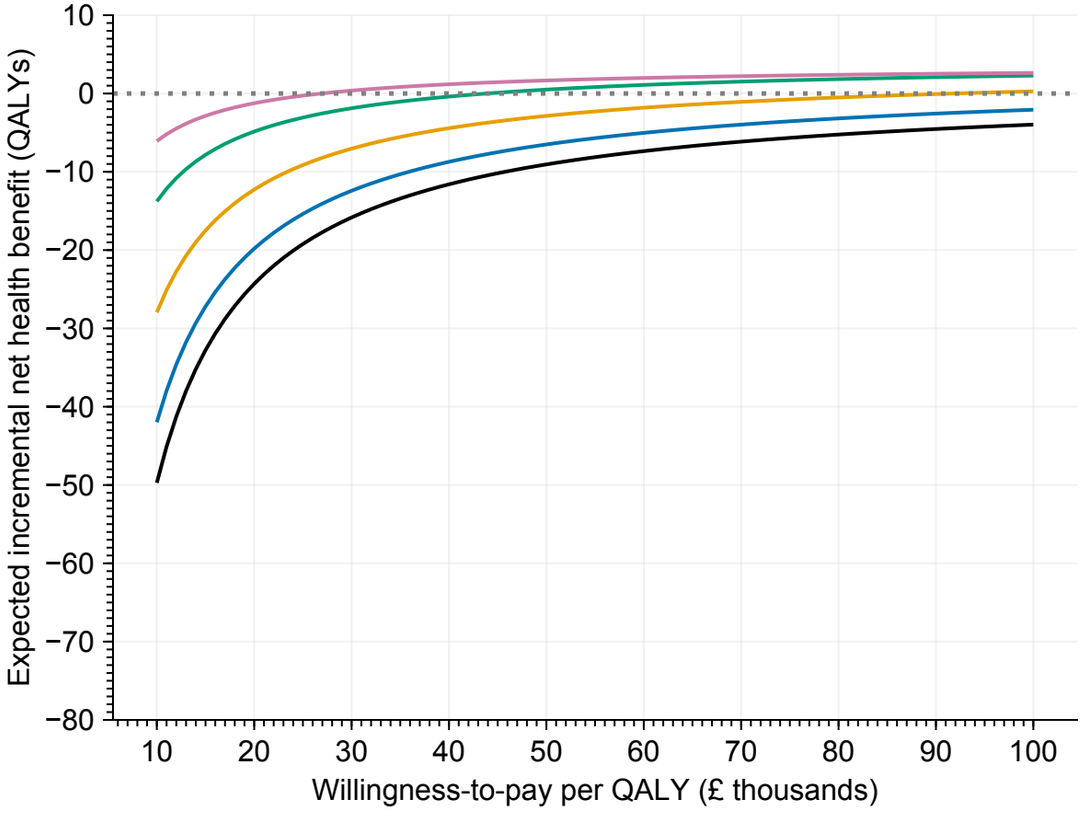
B MRI: Probability iNHB greater than no screening



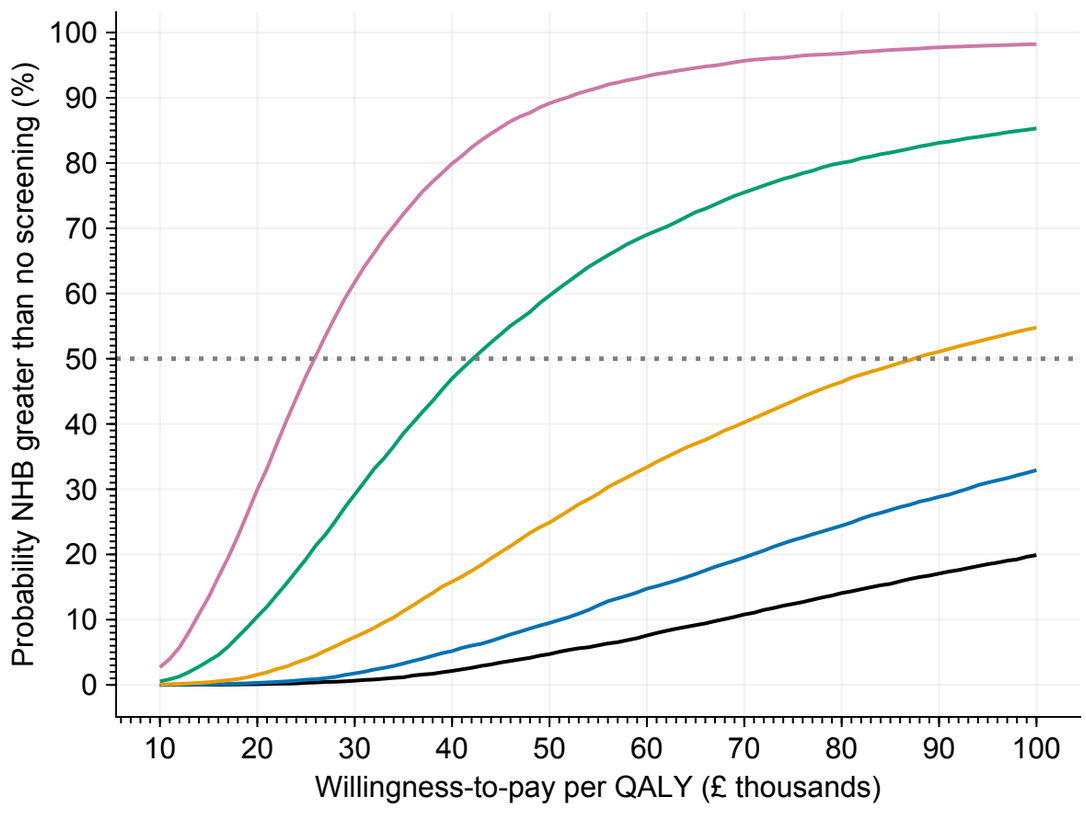
Strategy

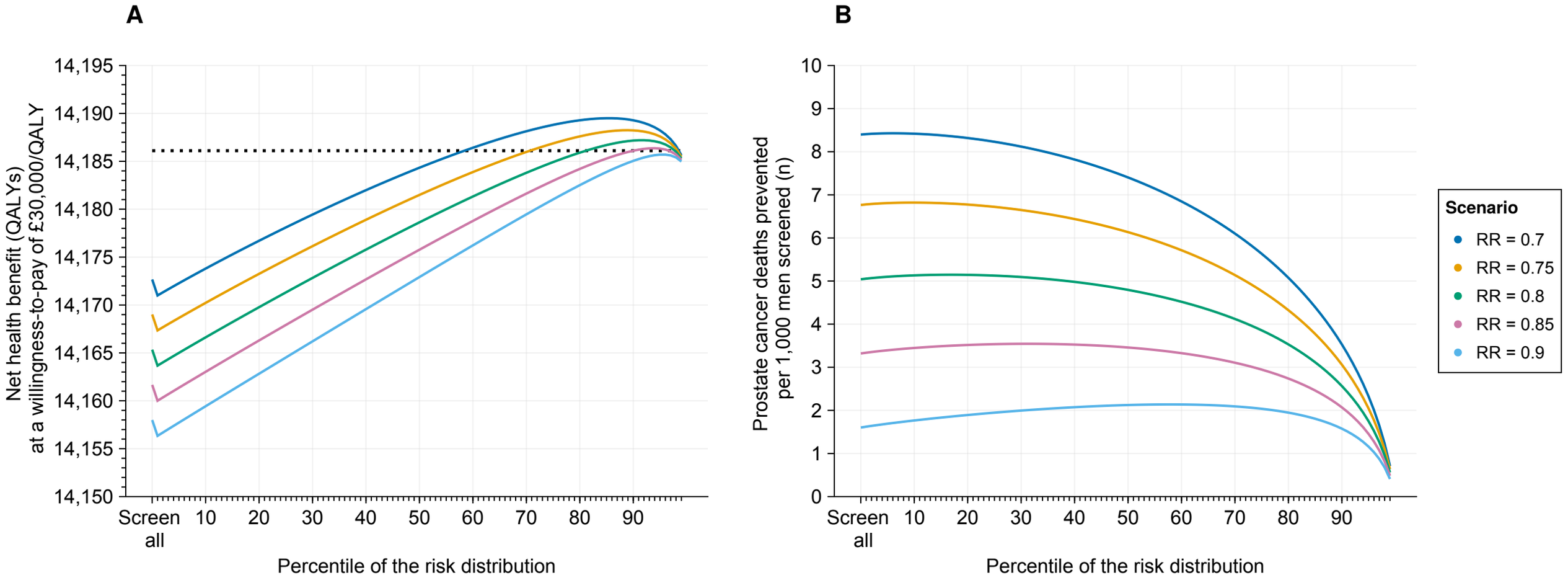
- Screen all
- 25th percentile
- 50th percentile
- 75th percentile
- 90th percentile

C PSA: Expected iNHB

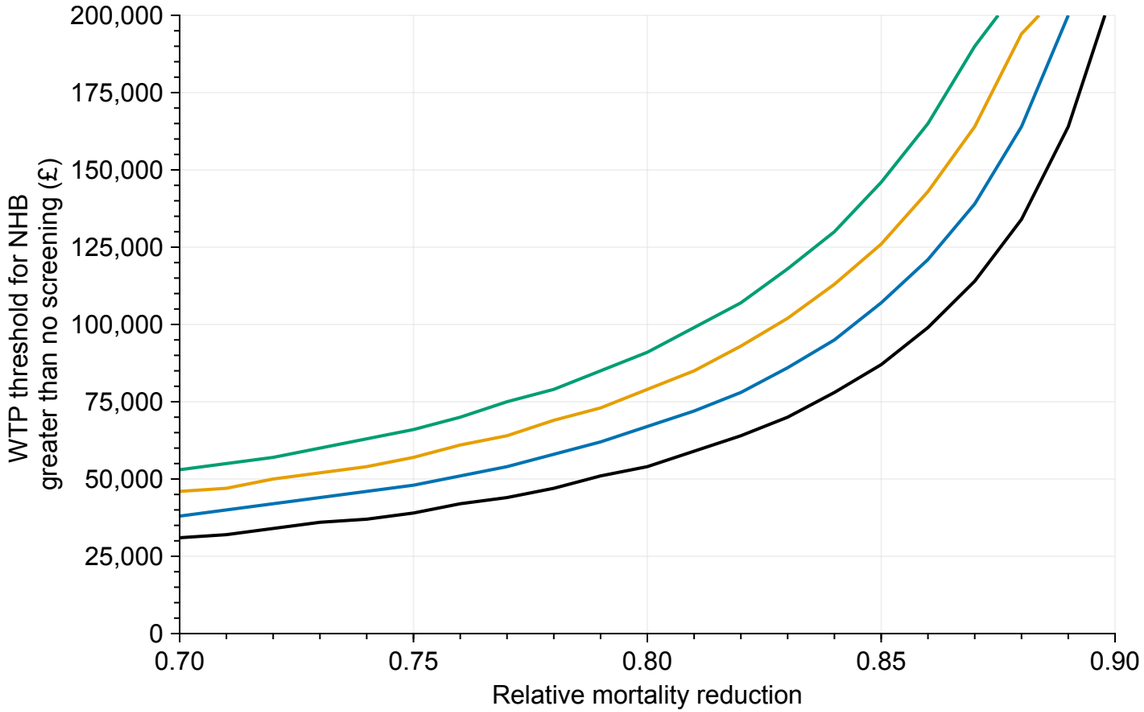


D PSA: Probability iNHB greater than no screening

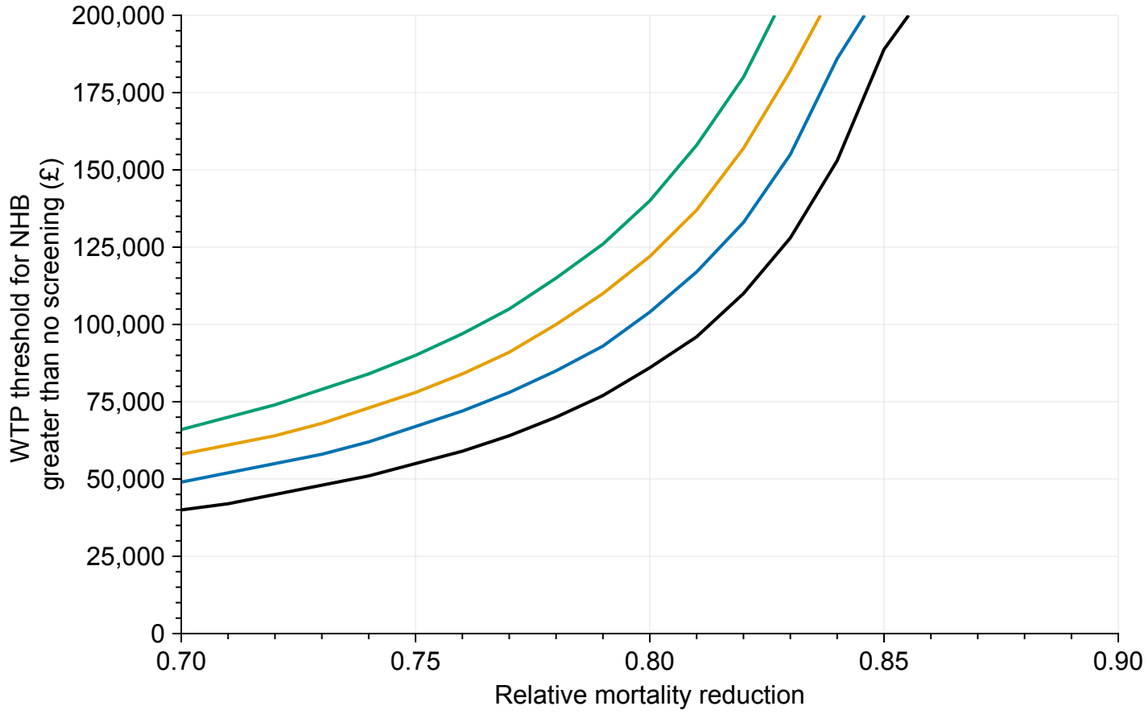



A
B
Net health benefit (QALYs)
at a willingness-to-pay of £30,000/QALY
14,195
14,190
14,185
14,180
14,175
14,170
14,165
14,160
14,155
14,150
Screen all
10
20
30
40
50
60
70
80
90
Percentile of the risk distribution
Prostate cancer deaths prevented
per 1,000 men screened (n)
10
9
8
7
6
5
4
3
2
1
0
Screen all
10
20
30
40
50
60
70
80
90
Percentile of the risk distribution
Scenario
RR = 0.7
RR = 0.75
RR = 0.8
RR = 0.85
RR = 0.9

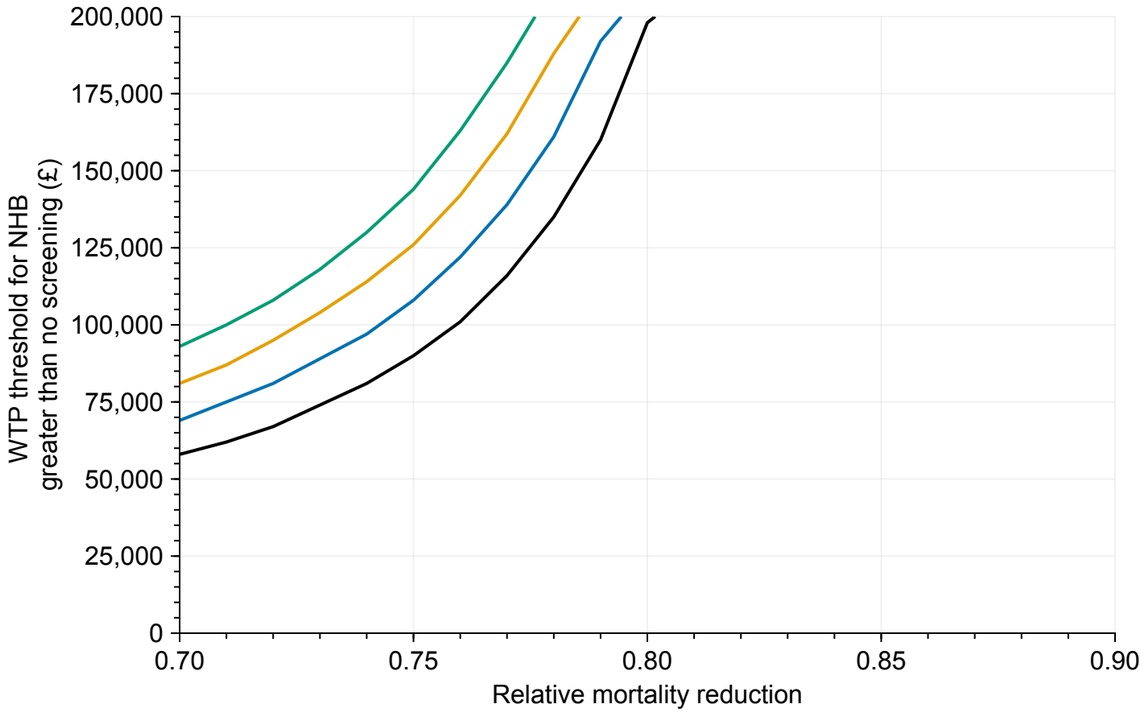
A MST = 7 years



B MST = 9 years



C MST = 11 years



D MST = 13 years