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Supplementary appendix

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Modelling the utility of polygenic risk scores in UK cancer screening

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SUPPLEMENTARY INFORMATION BOXES

BOX 1: Polygenic Risk Scores: factors to consider in relation to cancer screening

1) Predictive value: The performance of a PRS-tool (model, SNP-set) in distinguishing between those who will develop cancer (cases) from those who will remain unaffected can be quantified by plotting the true positive rate (sensitivity) against the false positive rate (1-specificty) to generate an AUC (area under the curve). More simply, the AUC equates to the likelihood of correctly ascribing an individual as a (future) case versus remaining unaffected, within a population comprising equal proportions of the two. AUC=0.5: no predictive discrimination, AUC=1.0: perfect prediction. Current PRS-tools for common cancers have AUCs of up to 0.70. For an AUC of 0.64, for a threshold that includes 20% of the population, 37% of those who will develop cancer (cases) are included in this "high-risk" group (see below).



Other metrics frequently presented to represent predictive performance of PRS include:

- OR for disease occurrence in PRS-defined top 1%/10% compared to population average
- OR for disease occurrence in PRS-defined top 1%/10% compared to bottom 1%/10%
- the OR for disease per one standard deviation of population PRS distribution
- 2) Genetic ancestry: SNP-sets for current PRS-tools are largely derived from GWAS of European populations. Individuals from non-European populations would be disproportionately misclassified by PRS derived from European populations. To properly redress the ancestral inequity of PRS-tools would require (i) for each different ancestral group a sufficiently large case-control GWAS to generate a PRS which captures a proportionally equivalent heritable cancer risk when compared to that of European populations and (ii) each participant undergoing PRS estimation to undergo an individualised weighting of the different ancestry-specific SNP-sets to reflect their individual ancestry admixture.
- 3) Multimodal PRS-tools: Some PRS-tools incorporate additional 'individual-level' risk factors (family history, breast density, body mass index, lifestyle/physiological factors).(1) In analyses by which PRS-tool predictions are validated against 5 or 10-year cancer incidence in longitudinal cohort data, the AUC presented may also reflect the predictive contribution of age of cancer incidence. Age is a 'population-level' rather than 'individual-level' risk factor, reflected in screening/interventions being offered to pre-specified age-groups.
- 4) Future improvements in PRS: The predictive performance of a PRS-tool is (i) ultimately constrained by the heritability of the disease, which is often comparatively low for many common complex diseases of late onset, (ii) determined by how much of the total heritable risk is captured by the SNPs contributing to the PRS-tool.

BOX 2: Cancer screening: factors to consider regarding PRS-based stratification

Polygenic risk scores are constructed from SNPs exhibiting association with disease in GWAS of disease cases unselected in regard of outcome/lethality (i.e. the PRS will predict cancer incidence but not disease outcome). Risk stratification would potentially differentiate aggressive/lethal cancers only if the underlying GWAS had been restricted to aggressive/lethal cases of disease.(2) It is thus anticipated that stratification using the GWAS-derived PRS will only impact the numeric distribution of cancers across the quantiles; the cancers will not differ systematically between PRS-defined quantiles in their biology, clinical characteristics or clinical behaviour.

- 1) Overdiagnosis (overdetection): Screening detects cancers that otherwise would never have come to medical attention during the person's lifetime (cancers the patient would have "died with" rather than "died from").(3) For example, it is estimated that 11% of breast cancers detected on breast mammography and 42% of prostate cancers detected on PSA screening are "overdiagnoses".(4,5) Aside from substantial costs, if there is concomitant "overtreatment", this can cause harms such as incontinence and impotence. Furthermore, increased rates of suicide and cardiovascular death have been reported immediately after a diagnosis of prostate cancer.(6) As per above, although some studies have reported small differences in overdiagnosis rates, the *proportion* of detected cancers that are overdiagnoses would be predicted to be consistent across PRS-defined strata, i.e. at a rate the same as in unstratified population-based screening.(7,8)
- The impact of cancer screening on survival: Survival benefit from screening is a function of (i) improving stage 2) at diagnosis compared to symptomatic presentation, (ii) this "downstaging" translating into improvement in longterm survival (iii) lead-time bias, where true outcomes are unchanged but appear improved purely on account of earlier detection. For breast cancer, symptomatic presentation is typically at early stage and long-term survival rates are high for stages 1-3 (in part due to improvements in adjuvant therapies) and increasingly stage 4. There is thus limited 'headroom' by which screening might improve survival for such a "good prognosis" cancer. Conversely, over 80% of those diagnosed with stage 1 pancreatic cancer die from their disease within 10 years. For poor-outcome cancers the headroom for improving survival may also be narrow if (i) cancer-specific mortality is high across all disease stages (like pancreatic cancer) and/or (ii) screening only leads to minimal downstagingrelated survival improvement (as recently demonstrated in trials of ovarian cancer screening).(9) There is no rationale to suggest PRS-based risk stratification would influence the impact of a given cancer-screening tool on cancer survival or impact on lead-time bias. Cancer-specific mortality will only account for deaths directly due to the cancer. All-cause mortality is more meaningful evaluation metric, factoring in the deaths consequent from screening, treatment and concurrent morbidities, but requires very substantial power and thus duration of followup.
- **3)** Sensitivity and specificity: Tools screening for presence *today* of a particular cancer must be low-cost, low-harm, convenient, and scalable. Sensitivity is the proportion of all people with cancer that have a positive screening test (true positive rate). Specificity is the proportion of all people without cancer who have a negative result (1- false positive rate). The threshold for defining a cancer screening result as 'positive' will be selected to provide most acceptable balance between sensitivity and specificity. Sensitivity and specificity are essentially innate to the screening tool (when applied to cancers in a specified patient group). Whilst it has been proposed that sensitivity/specificity of some types of tests may differ for contexts in which where disease prevalence varies widely, performance of cancer screening tools is unlikely to differ in meaningful fashion between PRS-defined quantiles. (10)
- 4) Diagnostic tests: Individuals with a positive screening result require a follow-up diagnostic (confirmatory) test, typically involving imaging, endoscopy, and/or biopsy. These diagnostic tests are usually more expensive, invasive, and/or inconvenient than the initial screening test. Limited capacity for these modalities is a key factor in design of screening programs. Some screening protocols involve more complex algorithms of multistage or tiered follow-up. For example, free-to-total prostate-specific antigen (PSA) ratio may be used for follow-up of moderately elevated PSA before proceeding to biopsy.(11)
- 5) Interval cancers: Some cancers will present symptomatically between screens. The periodicity of a screening program (e.g. one-yearly versus two-yearly versus three-yearly) will influence the proportion of cancers diagnosed as interval cancers versus as screen-detected. In the current NHS breast-screening program of 3-yearly mammography aged 50-69, for every 10 breast cancers picked-up on screening, 3 genuine interval breast cancers

arise in screened women.(12) Distinction between imperfect screening sensitivity and interval cancers can be complex.

- 6) Age-specific cancer incidence: For each cancer type the total lifetime likelihood of developing that cancer (e.g. ~1.7% for pancreatic cancer) is unequally distributed across the decades of life. The age window for which screening is offered requires balancing of age-specific cancer incidence versus the life-years gained from a death averted (with UK median life expectancy being ~81 years currently).(13) Most common cancers are diseases predominantly of older age, when life years gained are fewest (>47% of pancreatic and >43% colorectal cancers arise after the age of 75). Risk stratification does nothing to solve this "age paradox".
- 7) Uptake: For current national screening programs, uptake in the UK is typically 65-70%, with variation by region, socio-economic status, and other parameters.(5) Uptake of PRS-profiling when offered as part of a study within the UK NHSBSP (NHS Breast Screening Program) was <20%, but will likely be highly context- and population-specific.(14)</p>

SUPPLEMENTARY METHODS

Cancer Types

Eight solid tumours were selected for inclusion in this analysis based on (i) availability from data generated by Fritsche et al. (2020) of AUC (area under the curve) for validation against UKBiobank of a "PRS-only" risk prediction tool (i.e. AUC without inclusion of age in the prediction) (ii) availability of data generated by Zhang et al. (2020) for projected AUC of "PRS-only" tools based on larger GWAS and totality of common variation (iii) availability of screening tools for which published data on sensitivity/specificity could be identified.

Polygenic Risk Scores

Fritsche et al. (2020) identified from literature and databases, sets of SNPs associated with specified cancers, for which they undertook up to seven approaches to construction of PRS comprising fixed p-value thresholding, LD pruning and thresholding and lassosum. The AUC of the best performing approach on validation against UKBiobank was taken forward for the subsequent analyses and ascribed as the "current" PRS. Zhang et al. used summary-level data from GWAS of European ancestry across multiple cancer sites to estimate the total underlying number of common susceptibility variants (polygenicity) and effect-size distribution. From these they calculate the AUC if the totality of variance due to common variants were captured: this we ascribe as our "optimised" PRS-tool. They also present estimation of AUC for a hypothetical GWAS comprising 4-fold the sample number of the largest GWAS meta-analysis reported to date: this we ascribe as our "future" PRS-tool.

We use the AUC values for the "current, "future" and "optimised" PRS-tools for each cancer type to then derive the related performance metrics inherent to the AUC, which comprise odds ratios (comparing the odds of cancer in the top 50%, 20%, 10%, 5%, and 1% of the PRS to the middle quintile), and the percent of cancers in the population captured by the top 50%, 20%, 10%, 5%, and 1% of the PRS. These metrics are estimated using the assumptions and methods described in detail by Wald and Hingorani et al., and summarised briefly in Supplementary Table 1.(15,16) In brief, these methods rely on the conceptualization of Polygenic Risk Score distributions across a population as two normal distribution curves: one representing those with (or who will develop) cancer (affected), and one representing those without (unaffected).(15) The areas under these curves, represented by the cumulative distribution function (CDF), were used to estimate relative proportions of cases captured at different PRS thresholds, allowing calculation of Odds Ratios (ORs). Calculation of the CDFs for these curves required three parameters: μ_A (the mean of the distribution of the PRS among those affected by cancer), μ_{II} (the mean of the distribution of the PRS among those unaffected by cancer, and $SD(\sigma)$ (the standard deviation of each curve). $SD(\sigma)$ was assumed to be 1 for both curves, μ_{II} was assumed to be 0, and μ_A was determined from the AUC of the PRS as per methods and equations further detailed in the supplementary methods of Hingorani et al.(15)

Lifetime Risks

We then estimated lifetime risk of cancer using a 'current probability' method and period approach.(17,18) This approach accounts for deaths from cancer *and* all other causes and utilises the methods of Cancer Research UK used in their lifetime risk calculations.(18) In brief, for each cancer, we constructed a life table dividing the population into 5-year age bands. To estimate lifetime risks, we started by dividing the population into two groups: the top n% (as represented by the top 50%/20%/10%/5%/1% of the PRS) and the remainder. We estimated the cancer incidence rate in the top n% of the population by splitting the average incidence into two parts (scaled by the relative population size and the OR of the top n% compared to the remainder). We estimated the death rate in

top n% by up scaling the average death rate in the total population according to a ratio of death to incidence rate. Finally, we exposed a 'hypothetical cohort' to the cancer incidence rate in the top n% of the PRS. From each age band to the next, we reduced the cohort size in accordance with competing and cancer risks. We estimated an overall lifetime risk by summing the number of events expected in each age group of the cohort.

Cancers detected by screening

We estimated the number of cancers occurring in the top n% (50%, 20%, 10%, 5%, and 1%) of the PRS, based on our "current", "future", and "optimised" PRS-tools, by application of the percentage of cancers captured within the PRS-defined high risk quantile (Table 1) to CRUK/NDRS data on the number of cancers arising in 5-year age bands. From this, we estimated the number of cancers that would be detected by a hypothetical stratified screening programme using published sensitivity metrics for the cancer-specific "real world" screening tool (Supplementary Table 3, Supplementary Tables 6A-C). To account for potential emergence of improved cancer screening tools, especially for "underserved" cancers, we then repeated the analysis using hypothetical "idealised" screening tool, which we arbitrarily assigned as having a sensitivity of 80% for specificity of 95% (Supplementary Tables 7A-C).

Survival

We modelled the change in 10-year survival that would result from offering various screening programmes to age groups currently falling outside of population screening programmes: women aged 40-49 for breast cancer, men aged 60-69 for prostate cancer, and men and women aged 50 to 59 for colorectal cancer. The approaches evaluated comprised screening within these age-bands i) without restriction (ii) of the PRS-defined high risk 20% (quintile), (iii) of the oldest 20% (iv) of a random 20%.

In brief, these analyses involved re-allocation of cancers across from the routine, urgent (2 week wait) and emergency "routes-to-diagnosis" over to screening. The accordant stage-specific distributions were then re-applied for the updated numbers in each route. The accordant 10-year age-specific, stage-specific net cancer survival figures were then applied.

Within the routes-to-diagnosis datasets utilised, for breast and colorectal cancers small numbers of individuals in these age groups have received screening via age-extension studies. To model 'baseline' survival to there being no screening, we re-allocated these cancers proportionally between the three remaining routes to diagnosis (two week wait, routine and emergency), adjusting baseline figures for survival accordingly. For prostate cancer, where no screening is offered, we used the routes-to-diagnosis data with no changes.

We estimated the proportion of cancers that would be detected by screening by applying published sensitivity and specificity metrics to the expected number of cancers in each pre-specified section of the population (total age band, random quantile of age band, top n% of the PRS, top two years of age band).

- For the total age band, the expected number of cancers was that shown in the CRUK data (Supplementary table 1)
- For the random quintile, it was a scaled version of this total (i.e., we would expect 20% of cancers in 20% of the population).
- For the PRS-defined high-risk 20%, we applied the percentage of cancers captured within the PRS-defined high risk quintile (as per Supplementary Table 4) to CRUK data on the number of cancers arising in respective 5-year age bands (Supplementary Table 1).
- To estimate the number of expected cancers in the top two years of each relevant age band (48-49 for breast, 58-59 for colorectal, and both 58-59 and 60-69 for prostate), we used linear

interpolation across adjacent 5-year age bands to estimate the age-specific incidence rates for each individual year. We then used the age-specific incidence rates for these new 'one-year age bands' in conjunction with population size estimates derived from ONS data to calculate the number of cancers expected across the two years (Supplementary Table 1).

Any remaining cancers (expected to occur in the age band, but not detected by screening) were allocated between three routes of detection (routine, urgent and emergency presentation) in proportion to the distribution shown in the baseline NCRAS routes-to-diagnosis data.

We then estimated the stage distribution of cancers in each age band in proportion to the stage distribution of tumours detected by each route to diagnosis in the NCRAS data. Finally, we estimated the proportion surviving 10-years using 10-year age-specific, stage-specific net survival, using the stage distributions amended on account of addition of screening. We then calculated the annual difference in the number of people surviving 10-years with no screening (baseline) and our modelled screening programmes.

The code and raw data underling these models can be downloaded from GitLab <u>here</u>. https://git.icr.ac.uk/chuntley/modelling-the-utility-of-polygenic-risk-scores-in-uk-cancer-screening

SUPPLEMENTARY TABLES

Supplementary Table 1: Data Sources utilised in analyses

Data Item	Details	Reference/Source
Analysis: Polygenic Risk Scores (Table 1, Sup	Table 4)	
Area under the Curve (AUC) for 'current' polygenic risk scores (PRS) for 8 cancers	PRS constructed using SNPs and GWAS summary statistics from multiple sources via up to seven approaches; AUCs from validation in UKBiobank (best AUC retained)	Fritsche et al., American Journal of Human Genetics(19)
AUC for 'future' PRS for 8 cancers	Projected AUC for a PRS constructed from underlying GWAS with a 4x increased sample size compared to largest published metanalysis	Zhang et al., Nature Communications(20)
AUC for 'perfect' PRS for 8 cancers	Estimate of maximum AUC achievable for PRS capturing variance attributable to all common genetic variants	Zhang et al., Nature Communications(20)
Analysis: Lifetime Cancer Risks, overall and	PRS-defined strata (Table 2, Sup Table 5)	
Age-specific all-cause mortality rates	Estimates for England and Wales, 2018	Office for National Statistics(21)
Age- and sex- specific incidence rates	Estimates for the UK, 2016-2018. Derived by Cancer Research UK (CRUK) from data provided by the National Cancer Registration and Analysis Service (NCRAS), ISD Scotland, the Welsh Cancer Intelligence and Surveillance Unit, Health Intelligence Division, Public Health Wales, and the Northern Ireland Cancer Registry. *Invasive breast cancers (C50) only	Cancer Research UK(22)
Age- and sex- cancer-specific mortality rates for 8 cancers	Estimates for the UK, 2017-2019. Derived by Cancer Research UK (CRUK) from data provided by Nomis mortality statistics, ISD Scotland, the Northern Ireland Cancer Registry, and the Office for National Statistics. *Invasive breast cancers (C50) only	Cancer Research UK(22)
Odds Ratios comparing risk of cancer in top $n\%$ of PRS vs. remainder	Derived from the AUCs for current, future, and optimised PRS for 8 cancers (as described in Polygenic Risk Score section of this table, above)	Fritsche et al., American Journal of Human Genetics(19), Zhang et al., Nature Communications(20)
Analysis: Cancers Detected by Screening PRS (Table 3, Supplementary Tables 6A-D, 7A-D)	-defined strata or age band overall using current or idealised screening tools	
Cancers arising in 5-year age bands	Number of cancers recorded in the UK for each 5-year age band in 2016-2018. Derived by Cancer Research UK (CRUK) from data provided by the National Cancer Registration and Analysis Service (NCRAS), ISD Scotland, the Welsh Cancer Intelligence and Surveillance Unit, Health Intelligence Division, Public Health Wales, and the Northern Ireland Cancer Registry. *Invasive breast cancers (C50) only	Cancer Research UK(22)
Age-specific annual incidence rates per 100,000 for 8 cancers	Estimates for the UK in 2016-2018. Derived by Cancer Research UK (CRUK) from data provided by the National Cancer Registration and Analysis Service (NCRAS), ISD Scotland, the Welsh Cancer Intelligence and Surveillance Unit, Health Intelligence Division, Public Health Wales, and the Northern Ireland Cancer Registry. *Invasive breast cancers (C50) only	Cancer Research UK(22)
Reference size population for each 5-year age band	Average of estimates for the UK for the years 2016-2018. Analysis of population estimates tool, the Office for National Statistics.	Office for National Statistics(23)
Sensitivity estimates for 'real-world' screening tools	Breast cancer (digital mammography),(24) prostate cancer (PSA, 4ng/mL threshold(25) and mpMRI(26)), colorectal cancer (FIT, 20-50 µg/g threshold),(27) pancreatic cancer (CA19-9 20 U/mL threshold),(28) ovarian cancer (MMS (CA-125 + TVU),(9) kidney cancer (USS),(29) lung cancer (low dose CT),(30) and testicular cancer (semen assay).(31)	Published estimates from clinical trials(9,24,25,30,31) and meta-analyses.(26–29)
Sensitivity/sensitivity estimates for hypothetical 'idealised' screening tool	Standard estimate applied across all cancers of sensitivity 80% (for sensitivity 95%).	Hypothetical estimate
Survival analysis (Table 4, Supplementary Ta	bles 8A-E)	
Route-to-diagnosis for breast, prostate, and colorectal cancers in England.	Proportions of cancer diagnoses from (i) screening*, (ii) routine detection**, (iii) urgent symptomatic (two-week wait) and (iv) emergency presentation. Data for England from 2018. Derived by the National Cancer Registration and Analysis Service on request, from the National Cancer Registration Dataset.	National Cancer Registration and Analysis Service (NHSD)(32)

	*National screening programs included small numbers of younger subjects from age-extension trials (e.g. AgeX) **Includes some routine follow-up of high-risk individuals (e.g., those with family history and/or pathogenic variants)	
Stage distribution of breast, prostate, and colorectal cancers according to route of diagnosis in England.	Proportion of cancers of each stage as determined by route to diagnosis. Prostate cancer estimates include routine, urgent symptomatic and emergency routes to diagnosis only. Data for England from 2018. Derived by the National Cancer Registration and Analysis Service on request, from the National Cancer Registration Dataset.	National Cancer Registration and Analysis Service (NHSD)(32)
Stage distribution of prostate cancers diagnosed via screening.	Stage distribution of cancers identified in the screening arm of the European Randomized Study of Screening for Prostate Cancer (ERSPC), conducted across multiple European countries during the 1990s and early 2000s.(33) T and M staging data from the ERSPC trial were mapped onto the '1-4' staging described by CRUK and used by NCRAS.(34)	ERSPC trial(33)
Net 10-year age-specific, stage-specific survival rates for breast, colorectal, and prostate cancers in England.	Estimates for England, 2008-2017 (net 10-year age-specific, all-stage mortality) and 2013-2017 (net 5-year age- specific, stage-specific mortality). Net 10-year age-specific, stage-specific survival was derived from age, site, and stage-specific net 5-year cancer survival, provided by the National Cancer Registration and Analysis Service on request, from the National Cancer Registration Dataset. Overall survival has been adjusted for background age-specific death rates to reflect net cancer-specific mortality.	National Cancer Registration and Analysis Service (NCRAS)(32)
Overdiagnosis rates	Proportion of total cancers detected on screening that would not have been detected without screening on long-term follow-up. Breast cancer: 11%,(5) Colorectal cancer 3.8% (midpoint of reported estimate range),(35) Prostate cancer (PSA screening) 42%.(4,36,37)	Publishes estimates from follow up of national screening programme trials(5).(4,35–37)

Supplementary Table 2: Assumptions utilised in analyses

Assumption	Justification, source, and implications
Polygenic Risk Scores	
Polygenic risk scores show a Gaussian distribution in populations	Support from central limit theorem(15,38)
Polygenic risk score distributions have the same standard deviation in affected and unaffected individuals	Empirical support from previously published scores and mathematical relationships(15,39)
Polygenic risk scores select for disease incidence, not biology or outcome	Polygenic risk scores are constructed from SNP-associations for GWAS of disease cases unselected in regard of outcome/lethality (i.e. the PRS predict cancer incidence). There is minimal evidence to suggest that SNPs associated with cancer incidence will, on case-only GWAS, be associated with disease outcome. Hence, we assume that disease mortality and overdiagnosis rates will not vary by PRS-defined risk quantile.
Lifetime Risks	
A period approach can be applied for the calculation of lifetime risks.	Lifetime risks are calculated through the application of a cross-section of the age-specific incidence and mortality rates in the UK for 2018. These risks represent the risk that would be incurred to a theoretical population living through the cross-section of rates from 2018. This approach is limited by the fact that it does not account for changes in incidence and mortality over time.
Cancer-specific mortality in the top $n\%$ of the PRS is increased in proportion to the change in incidence between the top $n\%$ of the PRS and the remainder.	Cancer-specific mortality in the top $n\%$ of the PRS is expected to increase in comparison to the average mortality, due to the presence of a higher number of cancers in this group. The OR for death in the top $n\%$ of the PRS is unknown, so the average mortality rate can be scaled in proportion to the increase in incidence that occurs in the top $n\%$ of the PRS.
Cancers Arising	
The proportion of cancers expected in the n th percentile of the PRS is equal to the cumulative distribution function at point n of the Gaussian curve describing the distribution of polygenic risk scores in cancer cases.	This is inherent from assumptions and justifications described in Polygenic Risk Scores section above.
Cancers Detected by Screening	
All cancers that are expected to occur within the screening period are present at the time of screening	We model screening programs using a modality of given sensitivity. We assume that all cancers that will develop in that period have already developed at the time of the screen, regardless of screening periodicity. Thus, we over-estimate the impact of the screening, as we discount occurrence of 'interval' cancers (which would not exhibit the shifted stage distribution). We do not explicitly specify screening periodicity; we indicate the capacity requirements of screening two-yearly in regard of screening and diagnostic tests. The assumption is progressively more favourable for longer periodicity of screening.
The sensitivity and specificity of screening tools is constant across PRS-defined risk quantiles.	The sensitivity and specificity of a test is innate to the combination of test, disease, and patient population. It is assumed cancers will not differ systematically in their biology, clinical characteristics or clinical behaviour between the different risk quantiles on account of the underlying GWAS having identified SNP associations from comparison to controls of broad cancer case series, which have been ascertained agnostic to biology and clinical outcome.(10,40)
The sensitivity and specificity of screening tools is constant across age groups	The sensitivity and specificity calculated from screening data in older populations has been applied in our hypothetical analyses of screening in younger populations. In practice it is likely that test performance may be poorer, for example digital mammography in younger women may have poorer sensitivity and specificity on account of higher breast density. In this event, our analyses will overestimate the detection rate and survival benefit for these younger populations.
The cancers detected when screening is introduced are displaced proportionately from the other 3 routes to diagnosis	When modelling introduction of screening, we modelled proportionate shift into screening from across the current routes to diagnosis. In practice, those attending screening are possibly more likely to otherwise present as routine or urgent symptomatic (GP referral routes) than emergency. Accordingly, the predicted survival gain from introduction of screening may be over-emphasised.
The proportion of cancers that are overdiagnoses is constant across PRS-defined risk quantiles.	It is assumed cancers will not differ systematically in their biology, clinical characteristics or clinical behaviour between the different risk quantiles on account of the underlying GWAS having identified SNP associations from comparison to controls of broad cancer case series, which have been

	ascertained agnostic to biology or clinical outcome.(10,40). Accordingly, if trials demonstrate that 42% of cancers detected on unselected population screening are overdiagnoses, we have assumed that 42% of cancers diagnosed in any risk quartile will be overdiagnoses.
Uptake	
There is 100% uptake for SNP-genotyping and screening	This is a deliberate simplification to illustrate maximal theoretical impact for PRS-risk-based screening. In practice, uptake of national screening programs is typically \leq 70% with bias away from population groups at highest cancer risk (relating to their socio-economic and lifestyle factors). Uptake of PRS-SNP genotyping will likely be context- and population-specific; reported uptake of PRS-based stratification when offered as part of a study within the UK NHSBSP (NHS Breast Screening Program) was <20%.(14)
Survival	
Cancer-specific survival has remained static since 2008.	Application of survival data for 2008-2017 for future predictions around screening assumes no change in stage-specific survival. Improvements in stage-specific survival since 2008 will likely mean that survival gains from stage-shift are over-estimated (but would depend on any stage-specific patterns)
The age-stage-specific 10-year survival can be approximated from the age-specific 10-year survival adjusted for the ratio of 5-year stage-specific survival.	For most solid tumours, survival at 10 years post diagnosis typically equates to long-term survival. NCRAS only routinely generated stage-specific survival from 2013. Hence, to obtain stage-specific 10-year survival, we applied established methods of applying the ratio of stage-specific to all stage survival at 5 years (2013-17) to all-stage survival at 10-years (2008-2017).
One-year age specific incidence rates can be estimated from adjacent 5-year age-specific incidence rates using linear interpolation	5-year age-specific incidence rates rise with age across all cancers, but do so in a variable format. Simple linear interpolation allows estimation of one- year age-specific incidence rates within age-bands.
Cancers currently detected by screening in the target age groups would be proportionally detected by other routes to diagnosis in the absence of screening	For breast cancers aged 40-49 and colorectal cancers aged 40-59, a small proportion are currently diagnosed by screening. This is predominantly due to inclusion via an age extension trial (e.g., Age X)*. We model these groups of individuals who are currently having breast screening age 40-49 or colorectal screening age 40-59 as being redistributed into other routes of diagnosis in proportion to the rest of the population. Screening uptake may be higher in individuals of higher socio-economic status, and these individuals may also be less likely to be diagnosed via an emergency presentation. Thus, when redistributing screen-diagnosed individuals proportionally into other routes of diagnosis, we may over-estimate the number of individuals presenting by the emergency route as the baseline. Thus, we are establishing a favourable baseline for comparison in regard of there being absolutely no screening to start, and may even be further lowering the survival rates for this baseline group.
Proportion of cancers of each stage in each route to diagnosis remains constant despite reduction for cancers detected by screening.	It is assumed that subtraction of a group of cancers for detection by screening does not alter the distribution of stage of detection for each of the other three other to diagnosis.

Cancer Site	Screening Tool	Sensitivity	Specificity	Detail	Trial/Source	Reference
	FIT 20 µg/g threshold (CRC)	89	91	20 µg/g threshold (CRC)	Systematic review and meta-analysis	
Colorectal	FIT 20-50 µg/g threshold (CRC)	70	95	20-50 µg/g threshold (CRC)	Systematic review and meta-analysis	Lee J.K. et al. Ann. Intern. Med. (2014).
	FIT >50 µg/g threshold (CRC)	67	96	>50 µg/g threshold (CRC)	Systematic review and meta-analysis	
Dananaaa	CA19-9_20U/mL cut-off	67.8	83	20 U/mL cut-off	Meta-analysis	Zhang Y. et al. Int. J. Clin. Exp.
rancreas	CA19-9_37U/mL cut-off	76.4	72.9	37 U/mL cut-off	Meta-analysis	<i>Med.</i> (2015).
Lung	Low dose CT	84.6	98.6	Three rounds of low-dose CT	NELSON Trial	Herwig N. et al. <i>Lancet Oncol.</i> (2014).
Ducast	Film mammography	66	92	All women, with use of BIRADS Score	DMIST Trial	Pisano E.D. et al. N. Engl. J.
breast	Digital mammography	70	92	All women, with use of BIRADS Score	DMIST Trial	<i>Med.</i> (2005).
Ovary	MMS (CA-125 + TVU)	84	99	First line screening with CA-125 interpreted via ROCA and second-line screening via TVU	UKCTOCS Trial	Jacobs I. L. et al. <i>Lancet</i> (2015)
Ovary	USS	72.9	96.8	First and second line screening via TVU	UKCTOCS Trial	saccos 1.3. et al. Euneer (2015).
	PSA_4ng/mL cut-off	21	91	4ng/mL cut-off	Prostate Cancer Prevention Trial (USA)	Wolf A.M.D. et al. Cancer J
Prostate	PSA_3ng/mL cut-off	32	85	3ng/mL cut-off	Prostate Cancer Prevention Trial (USA)	<i>Clin.</i> (2010).
	mpMRI	89	73	Mend suspected or diagnosed with prostate cancer, with use of PI-RADSv2 score	Meta-analysis	Woo S. et al. <i>Eur. Urol.</i> (2017).
Testis	Semen assay	67	98	automated immunocytochemical staining, scanning microscopy and in silico image analysis	Single Study	Amstrad K. et al. Int. J. Andros. (2011).
Kidney	USS	82	98	Renal ultrasound scan	Literature Review	Rossi S.H. et al. World J. Urol. (2018).

Supplementary Table 3. Screening tool characteristics. Description of currently available "real world" screening tools for cancer and their characteristics including sensitivity and specificity.

Supplementary Table 4. Summary of PRS Characteristics

PRS C	haracteristics			Odds Ratios of	f quartile versus	average (middle	quintile)	Percentage o quintile	f cancers cap	tured within t	he PRS-define	ed high risk	
Cancer	Site	Number of Variants	AUC	Тор 50%	Тор 20%	Тор 10%	Тор 5%	Тор 1%	Тор 50%	Тор 20%	Тор 10%	Тор 5%	Тор 1%
	Breast	286,144	0.64	1.59	2.13	2.54	2.96	4.03	70%	37%	22%	13%	4%
	Prostate	178,259	0.70	2.01	2.99	3.83	4.75	7.32	77%	46%	29%	18%	6%
	Colorectal	87	0.62	1.45	1.84	2.12	2.41	3.09	66%	34%	19%	11%	3%
	Pancreas	10	0.58	1.27	1.50	1.65	1.80	2.13	61%	29%	16%	9%	2%
	Ovary	12	0.56	1.19	1.34	1.44	1.53	1.74	58%	26%	14%	8%	2%
PRS	Kidney	12	0.52	1.05	1.09	1.11	1.13	1.17	52%	22%	11%	6%	1%
ent]	Lung	19	0.55	1.17	1.30	1.39	1.47	1.64	57%	26%	14%	7%	2%
Curr	Testis	44	0.70	2.05	3.07	3.95	4.93	7.65	77%	47%	30%	19%	6%
	Breast		0.69	1.91	2.79	3.52	4.32	6.48	76%	44%	28%	17%	5%
	Prostate		0.72	2.16	3.32	4.34	5.49	8.76	79%	48%	32%	20%	6%
	Colorectal		0.64	1.58	2.10	2.50	2.92	3.94	70%	37%	22%	13%	3%
	Pancreas		0.65	1.64	2.22	2.67	3.14	4.33	71%	38%	23%	14%	4%
	Ovary		0.61	1.43	1.81	2.08	2.35	3.00	66%	33%	19%	11%	3%
RS	Kidney		0.65	1.60	2.15	2.58	3.01	4.11	70%	38%	22%	13%	4%
ure P	Lung		0.61	1.41	1.76	2.01	2.26	2.86	65%	33%	19%	11%	3%
Futu	Testis		0.84	4.76	9.20	14.13	20.80	45.55	92%	71%	55%	40%	18%
	Breast	7,599	0.71	2.11	3.22	4.17	5.24	8.28	78%	48%	31%	19%	6%
	Prostate	4,530	0.73	2.33	3.68	4.90	6.30	10.43	81%	51%	34%	22%	7%
	Colorectal	1,484	0.68	1.85	2.65	3.31	4.03	5.94	75%	43%	27%	16%	5%
	Pancreas	1,757	0.71	2.11	3.22	4.17	5.24	8.28	78%	48%	31%	19%	6%
S	Ovary	1,015	0.64	1.57	2.09	2.49	2.89	3.90	69%	37%	22%	13%	3%
d PR	Kidney	2,220	0.70	2.02	3.01	3.86	4.80	7.40	77%	46%	29%	18%	6%
mise	Lung	6,096	0.67	1.77	2.50	3.08	3.70	5.34	73%	41%	25%	15%	4%
Opti	Testis	2,598	0.88	7.35	15.33	25.04	39.15	97.79	95%	79%	65%	51%	25%

PRS	Cancer Site	PRS AUC	Absolute lifetime risk (%)													
			Populatio	on average	top 50%	% of PRS	top 20%	% of PRS	top 10%	% of PRS	top 5%	of PRS	top 1%	of PRS		
			Male	Female	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female		
	Breast	0.64	-	14.3	-	19.5	-	25.3	-	29.5	-	33.7	-	43.4		
	Prostate	0.70	15.2	-	22.6	-	31.9	-	39.1	-	46.4	-	63.2	-		
	Colorectal	0.62	7.6	5.9	10.0	7.7	12.6	9.8	14.4	11.2	16.2	12.7	20.5	16.0		
	Pancreas	0.58	1.8	1.6	2.2	2.0	2.6	2.3	2.8	2.6	3.1	2.8	3.7	3.3		
	Ovary	0.56	-	2.1	-	2.4	-	2.7	-	3.0	-	3.1	-	3.5		
PRS	Kidney	0.52	2.6	1.5	2.7	1.5	2.8	1.6	2.8	1.6	2.9	1.7	3.0	1.7		
rent	Lung	0.55	8.4	7.1	9.6	8.2	10.7	9.1	11.4	9.7	12.0	10.2	13.4	11.4		
Curr	Testis	0.70	0.5	-	0.8	-	1.3	-	1.6	-	2.0	-	3.1	-		
	Breast	0.69	-	14.3	-	20.9	-	29.3	-	35.7	-	42.2	-	57.6		
	Prostate	0.72	15.2	-	23.1	-	33.5	-	41.6	-	49.8	-	66.8	-		
	Colorectal	0.64	7.6	5.9	10.5	8.1	13.7	10.7	16.2	12.6	18.7	14.6	24.7	19.4		
	Pancreas	0.65	1.8	1.6	2.5	2.3	3.4	3.1	4.1	3.8	4.9	4.4	6.7	6.1		
	Ovary	0.61	-	2.1	-	2.8	-	3.5	-	4.0	-	4.5	-	5.7		
RS	Kidney	0.65	2.6	1.5	3.6	2.1	4.8	2.8	5.7	3.3	6.6	3.8	8.9	5.2		
ıre P	Lung	0.61	8.4	7.1	10.9	9.3	13.5	11.5	15.4	13.2	17.3	14.8	21.7	18.5		
Futu	Testis	0.84	0.5	-	1.0	-	1.9	-	2.9	-	4.3	-	9.2	-		
	Breast	0.71	-	14.3	-	21.6	-	31.3	-	39.0	-	46.8	-	65.3		
	Prostate	0.73	15.2	-	23.6	-	34.9	-	43.9	-	53.1	-	74.0	-		
	Colorectal	0.68	7.6	5.9	11.2	8.7	15.8	12.3	19.4	15.2	23.3	18.3	32.9	26.1		
	Pancreas	0.71	1.8	1.6	2.8	2.6	4.3	3.9	5.5	5.0	6.9	6.3	10.9	9.9		
RS	Ovary	0.64	-	2.1	-	2.9	-	3.8	-	4.6	-	5.3	-	7.1		
ld pa	Kidney	0.70	2.6	1.5	3.9	2.3	5.8	3.4	7.4	4.3	9.1	5.3	13.8	8.1		
imis	Lung	0.67	8.4	7.1	12.2	10.4	17.0	14.5	20.9	17.8	24.8	21.3	35.4	30.2		
Opti	Testis	0.88	0.5	-	1.0	-	2.1	-	3.5	-	5.4	-	13.0	-		

Supplementary Table 5. Lifetime risk of eight cancers for the general population, and for the top 50%, 20%, 10%, 5%, and 1% of current, future, and optimised PRS. Lifetime risk is calculated using the current probability method and a period approach, which takes into account competing risks.

Supplementary Table 6a(i). Cancers detected by offering risk stratified screening according to current PRS using sensitivity of current "real world" cancer-screening tools (Cancers of the Breast, Prostate, Colorectum and Pancreas)

		Annual Inciden (per 100,000) for a b and			Annual Incidence per 100,000) for age- band				creening offer 50% of PR:	red to top			S	creening off 20% of Pl	ered to top 6 &S			Se	reening off 10% of PF	fered to top % RS			:	Screening off 5% of Pi	fered to top i RS				1	Screening offer 1% of PR	ed to top	
Cannorr Type	Screening teel	Age Groups	Male	Fenale	Population Size	Cancers arising per year	Number requiring screening in 'high risk' group	Cancers arising in 'high risk' group	Missed cancers arising in f unscreened 'low risk' group ri	Cancers nissed on o creening in 'high- sk' group	Cancers Setected on Percent of screening cancers in 'high- identified risk' group	Number requiring screening in 'high risk' group	Cancers arising in 'high risk' group	Missed cancers arising in snscreened 'low risk' group	Cancers missed on screening in 'high- isk' group	Cancers detected on Percent of screening cancers in 'high- identified risk' group	Number requiring screening in 'high risk' group	Cancers arising in a 'high risk' u group 'i	Missed cancers rising in screened ow risk group	Cancers missed on d screening in 'high- isk' group s	Cancers detected on Percent of screening cancers in 'high- identified risk' group	Number requiring screening in 'high risk' group	Cancers arising in 'high risk' group	Missed cancers arising in unscreened 'low risk' group f	Cancers missed on screening in 'high- isk' group	Cancers detected on P screening in "high- in risk' group	Percent of cancers dentified	Number requiring screening in 'high risk' group	Cancers arising in 'high risk' group	Missed cancers arising in unscreened 'low risk' group	Jancers C issed on det reening so n "high- ir k' group ris	Cancen Lacted on Percent of recening cancens a 'high- identified ik' group
Breast Breast Breast Breast Breast Breast Breast Breast Breast Breast Breast Breast Breast Breast Breast	Digital mammography	40 to 44 45 to 49 50 to 54 55 to 59 60 to 64 65 to 69 70 to 74 70 to 79 Total 40-69 Total 40-69 Total 50-69 Total 50-69 Total 50-69 Total 60-74 Total 60-74	0.0 0.0 0.0 0.0 0.0 0.0 0.0 0.0 0.0 0.0	124.6 214.8 279.8 285.5 338.0 412.3 372.7 403.0 270.9 172.4 282.5 323.9 374.2 291.8 166.0	2,054,223 2,315,479 2,364,638 2,119,637 1,837,174 1,805,190 1,605,610 1,181,645 12,496,922 4,369,703 4,484,325 8,126,689 5,245,974 15,281,647 39,458,052	2,559 4,974 6,616 6,052 6,209 7,443 5,977 4,762 93,853 7,533 12,668 26,320 19,659 44,992 55,545	1,027,112 1,157,740 1,182,319 1,059,844 918,587 902,595 800,805 590,823 6,248,196 2,184,851 2,242,163 4,063,345 2,622,987 7,640,824	1,786 9,471 4,617 4,224 4,393 5,194 4,171 9,323 23,625 5,257 8,841 18,369 9,120	779 1,503 1,999 1,828 1,876 2,249 1,806 1,419 10,228 2,276 3,827 7,952 5,930 13,472	536 1,041 1,385 1,267 1,558 1,251 957 7,088 1,557 2,652 5,510 4,110 9,336	1,250 % 2,430 % 3,252 % 2,956 % 3,636 % 2,930 % 4,538 %4,538 % 4,538 % 4,538 %4,538 % 4,538 % 4,538 %4,538 % 4,538 % 4,538 %4,538 %4,538 % 4,538 %4,538 %4,538 % 4,538 %4,538 % 4,538 %4,538 %4,538 % 4,538 %4,538 %4,538 %4,538 % 4,538 %4,538 %4,538 %4,538 %4,538 %4,538 %4,538 %4,538 %56 %5	0 410,845 0 463,006 0 472,928 0 477,928 0 477,928 0 477,928 0 967,435 0 961,018 0 920,722 2 249,278 2 455,339 0 2,499,278 10,625,545 1,625,318 0 1,049,195 3 3,056,329	955 1,856 2,469 2,259 2,317 2,778 2,231 1,777 12,653 2,811 4,728 9,823 7,926 16,643	1,604 3,118 4,147 3,793 3,892 4,665 3,746 2,985 21,218 4,722 7,940 16,497 12,905 27,949	287 557 741 678 695 833 669 533 9,590 843 1,418 2,947 2,947 2,198 4,993	669 26 1,299 26 1,728 75 1,581 26 1,581 26 1,945 26 1,945 26 1,344 26 2,310 26 3,310 26 5,128 26 5,128 26	205,422 231,548 236,464 211,969 183,717 180,519 160,361 118,165 1,249,639 436,970 448,433 812,669 524,597 1,528,165	570 1,107 1,473 1,548 1,548 1,548 1,548 1,657 1,558 1,657 1,060 7,558 1,677 2,821 5,860 4,370 9,929	1,989 9,867 5,143 4,704 4,827 5,786 4,646 9,702 26,915 5,856 9,847 20,460 15,259 94,663	171 332 442 404 415 497 399 318 2,261 503 846 1,758 1,311 2,979	399 16 775 16 943 16 943 16 952 16 742 16 5,276 16 1,174 16 1,174 16 3,059 16 3,059 16 6,950 16	102,711 115,774 118,232 105,984 91,859 90,260 80,180 59,082 624,820 218,485 228,420 218,485 218,495 218,485 218,495215,495 218,495 218,495 21	333 646 860 787 967 967 777 619 4,400 979 1,646 3,421 2,551 2,551	2,226 4,328 5,786 5,266 5,402 6,478 5,200 4,143 29,453 6,554 6,554 11,022 22,859 17,078 38,797	100 194 258 246 242 290 293 186 1,920 294 494 1,026 765 1,799	233 453 602 551 565 677 544 433 3,080 685 1,152 2,394 1,786 4,057	9 9 9 9 9 9 9 9 9 9 9 9 9 9 9	20,542 23,155 23,646 21,197 18,052 16,036 11,816 124,964 43,697 44,843 81,267 52,460 152,816	90 176 234 219 363 211 168 1,195 266 447 929 693 1,574	2,469 4,798 6,382 5,590 7,180 5,766 4,594 92,658 7,267 12,221 25,991 18,996 43,018	277 53 70 64 66 79 63 50 958 80 194 208 472	63 2 123 2 163 2 150 2 151 2 154 2 154 2 154 2 154 2 154 2 154 2 155 2 154 2 155
Provida Positate Prostate Prostate Prostate Prostate Prostate Prostate Prostate Prostate Prostate Prostate Prostate Prostate Prostate Prostate	PS A_3ng/mL cutoff	40 to 44 45 to 49 50 to 54 55 to 59 60 to 64 65 to 69 70 to 79 Total 40.69 Total 40.69 Total 40.49 Total 60.69 Total 60.69 Total 60.69 Total 60.74 Total 60.74 Total 60.73	4.3 20.5 75.7 201.8 356.1 622.7 759.8 867.2 192.7 12.8 135.4 486.8 291.0 568.1 296.5 183.8	0.0 0.0 0.0 0.0 0.0 0.0 0.0 0.0 0.0 0.0	2,021,385 2,251,680 2,293,479 2,061,919 1,764,828 1,696,999 1,467,965 12,090,277 4,273,065 12,090,277 13,055 12,090,277 14,273,055 12,090,277 14,273,055 12,090,277 14,273,055 14,55,0000 14,55,0000 14,55,0000 14,55,0000000000000000000000000000000000	88 461 1,737 4,160 6,225 10,568 11,153 8,736 23,259 5,897 16,853 22,750 22,750 22,006 43,188 5,254	1,010,692 1,125,840 1,146,736 1,030,959 882,414 848,497 733,983 6,045,139 2,136,532 2,177,696 1,730,911 3,903,605 2,464,893 7,282,804	68 955 1,337 3,202 4,837 8,133 8,583 6,723 17,931 4,538 4,538 4,538 12,970 17,509 21,554 93,238	20 106 400 958 1,448 2,435 2,570 2,013 5,968 126 1,959 9,885 5,241 6,452 9,950	46 241 909 2,177 3,289 5,531 5,837 4,572 12,193 287 9,086 8,820 11,906 14,656 22,602	22 22 114 2 428 2 1,034 2 2,548 2 2,568 2 2,151 2 2,5738 2 165 2 1,450 2 4,150 2 5,603 2 10,636 2	5 404,277 5 450,336 5 412,344 5 352,966 5 399,399 5 293,593 5 201,473 5 2,418,055 5 2,418,055 5 2,418,055 5 2,418,055 5 2,418,055 5 2,418,055 5 2,418,055 5 2,418,055 5 32,448 5 402,364 5 402,364 6 402,464 6 402,464 6 402,464 6 402,464 6 402,464 6 402,464 6 402,4	40 211 797 1,908 2,882 4,846 5,114 4,006 10,684 252 2,704 7,728 10,492 12,842 19,804	48 250 940 2,252 3,403 5,722 6,019 4,750 12,615 297 9,125 12,918 15,164 23,984	27 144 542 1,297 1,960 9,295 9,478 2,724 7,265 171 1,839 5,255 7,694 8,739 19,467	13 15 68 15 255 15 60 15 922 15 1,551 15 1,677 15 3,419 15 5,655 15 2,473 15 3,338 15 4,110 15 6,337 15	202,138 225,168 229,347 206,192 176,443 169,699 146,797 1,00,797 1,209,028 427,306 435,519 946,182 781,721 492,979 1,456,561	25 195 509 1,220 1,843 3,099 3,270 2,562 6,832 161 1,729 4,942 6,671 8,212 12,664	62 926 1,228 2,940 4,442 7,469 7,883 6,174 16,467 9 388 4,168 11,911 16,079 19,794 90,524	18 92 946 829 1,253 2,107 2,224 1,742 4,646 109 1,176 3,360 4,536 5,584 8,611	8 9 43 5 163 5 990 5 990 5 990 5 990 5 900 5 900 5 900 5 900 5 900 5 900 5 1,016 5 5,2 5 5,51 5 2,1381 5 2,628 5 4,052 5	101_069 112_584 114_674 114_674 88_241 84_850 50_368 604_514 213_663 217_770 175_091 90_861 246_489 728_280	16 84 758 1,145 1,925 2,081 1,591 4,243 100 1,074 3,069 4,143 5,101 7,866	72 977 1,421 9,402 5,140 8,645 9,122 7,145 19,056 449 4,823 19,056 4,823 19,784 18,607 22,905 95,922	11 57 215 515 778 1,381 1,082 2,385 68 790 2,087 2,387 3,468 5,349	5 27 101 242 366 616 650 509 1,358 32 344 942 1,355 1,632 2,517	6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6	20,214 22,517 22,935 20,619 17,648 16,970 14,680 10,074 120,903 42,731 43,554 43,618 78,172 49,298 145,656	5 26 97 239 592 592 625 490 1,306 31 391 945 1,275 1,570 2,421	83 4355 1,640 3,997 5,913 9,976 10,552 8,246 21,993 518 5,566 15,908 21,475 26,436 40,767	3 18 66 159 240 403 425 933 888 21 225 642 867 1,067 1,646	2 2 2 8 2 75 2 113 2 150 2 157 2 157 2 100 2 105 2 105 2 105 2 106 2 106 2 106 2 107 2 108 2 109 2 10 10 10 10 10 10 10 10 10 10
Colorestal Colorestal Colorestal Colorestal Colorestal Colorestal Colorestal Colorestal Colorestal Colorestal Colorestal Colorestal Colorestal Colorestal Colorestal Colorestal	FIT 20-50 µg/g threshold (CRC)	40 to 44 45 to 49 50 to 54 55 to 59 60 to 64 65 to 69 70 to 74 76 to 79 Total 40-49 Total 40-49 Total 50.59 Total 50.59 Total 60.74 Total 60.74 Total 60.74 Total 60.74	14.5 24.4 47.1 87.7 151.4 198.3 273.5 351.7 80.8 19.7 66.4 114.2 203.9 119.0 84.5	13.5 21.6 37.1 60.6 91.0 119.1 171.2 234.8 54.1 17.7 48.2 73.6 125.2 80.4 56.5	4,075,608 4,567,159 4,658,111 4,181,606 3,602,002 9,502,183 3,071,575 2,189,011 24,586,669 8,642,767 15,943,902 10,175,760 0,9,847,255 66,041,278	570 1,047 1,958 3,094 4,945 5,516 6,760 6,780 6,318 16,550 16,550 16,550 16,551 16,551 16,621 14,919 16,621 12,9608 42,885	2,037,804 2,283,580 2,329,055 2,090,809 1,801,001 1,751,092 1,595,787 1,094,505 12,299,395 4,321,584 4,419,858 7,971,951 5,087,880 14,925,627	578 694 1,298 2,052 2,881 3,658 4,482 4,189 10,961 10,961 9,889 11,021 11,021	192 953 660 1,042 1,464 1, 853 2,27 8 2,129 5,569 545 1,702 5,024 5,600 9,976	119 208 989 615 864 1,097 1,945 1,257 9,288 922 1,005 2,967 9,306 5,850	265 44 436 44 900 44 1,436 44 2,017 44 2,550 44 2,933 44 2,933 44 2,935 44 2,945 44 7,715 44 13,745 44	5 815,122 5 913,432 5 931,622 5 836,321 5 720,400 5 700,437 5 614,315 5 457,802 5 457,802 5 457,802 5 457,802 5 457,802 5 457,802 5 457,802 5 457,802 5 3,188,780 5 3,188,780 5 3,095,152 5 5,969,451	192 953 660 1,043 1,464 1,859 2,278 2,129 5,570 5,45 1,702 5,025 5,601 9,977	978 694 1,298 2,051 3,657 4,482 4,189 10,960 1,072 3,950 9,888 11,020 19,631	58 106 198 419 558 683 683 683 683 1,671 1,631 1,508 1,508 1,508	134 24 347 24 452 24 750 24 1,025 34 1,031 24 1,935 34 1,450 24 3,859 34 1,512 24 3,513 24 3,513 24 3,512 24 3,513 24 3,514 24 3,512 24 3,513 24 3,514 24 3,512 24 3,513 24 3,514 24	407,561 456,716 465,811 418,161 960,200 950,218 907,157 218,901 2,458,667 864,277 864,277 1,594,390 1,017,576 2,984,725	111 204 381 602 846 1,074 1,516 1,230 3,219 3,15 984 2,904 3,236 5,765	459 8 43 1,577 2,492 9,499 4,442 5,444 5,0 88 19,911 1,502 4,068 12,009 19,385 29, 8 49	39 61 114 254 322 395 369 966 94 295 \$71 971 1,730	78 14 143 14 257 14 402 14 922 14 952 14 861 14 205 14 689 14 203 14 409 14 409 14 200 14 409 14 203 14 203 14 203 14 203 14 203 14 203 14 203 14 203 14 203 14 203 14 203 14 203 14 203 14 14 14 14 14 14 14 14 14 14 14 14 14 14 14	203,740 223,958 253,206 209,040 180,100 175,109 109,451 1,229,933 492,158 441,986 797,195 508,788 1,492,363	63 116 216 342 480 609 747 698 1,826 179 558 1,648 1,648 1,836 3,271	507 931 1,742 2,754 5,845 4,907 6,019 5,550 14,701 1,438 4,494 19,265 14,785 26,337	19 95 66 104 144 183 224 209 548 54 167 494 167 494 551 981	44 81 151 239 396 427 523 489 1,278 125 391 1,153 1,285 2,280	8 8 8 8 8 8 8 8 8 8 8 8 8 8 8 8 8 8 8	40,756 45,672 46,581 41,816 96,020 95,022 90,716 21,890 245,867 86,428 88,997 159,439 101,758 298,473	16 30 56 129 156 192 179 469 46 149 429 471 \$40	554 1,017 1,902 5,906 4,222 5,360 6,568 6,568 16,061 1,571 1,571 1,571 14,490 16,150 16,150 28,768	5 9 17 26 37 47 58 54 141 14 14 14 127 141 252	11 2 21 2 99 2 61 2 100 2 134 2 125 2 932 2 125 2 932 2 100 2 930 2 930 2 938 2
Раноска Раноса Раноса Раноса Раноска Раноска Раноска Раноска Раноска Раноска Раноска Раноска Раноска Раноска Раноска Раноска Раноска Раноска	CA19- 9_20U/mL cutoff	40 to 44 45 to 49 50 to 54 55 to 59 60 to 64 65 to 69 70 to 79 Total 40-69 Total 40-69 Total 50-59 Total 40-79 Total 40-79 Total 40-79 Total 40-78 Total 40-78 Total 40-78	2.6 5.6 10.2 18.3 29.2 47.2 66.4 86.0 17.4 4.2 14.1 24.7 46.5 27.1 19.3	2.0 3.9 7.3 13.6 22.4 34.1 48.8 70.8 13.0 3.0 10.3 18.3 34.5 21.2 15.0	4,075,608 4,567,159 4,658,111 4,181,606 3,502,002 3,502,183 3,071,575 2,189,011 24,586,669 8,642,%7 8,839,717 15,943,902 10,175,%00 29,847,255 66,041,278	94 215 409 666 926 1,417 1,702 9,727 909 1,775 9,418 4,100 7,186 10,452	2,037,804 2,283,580 2,329,055 2,090,803 1,801,001 1,751,092 1,595,787 1,094,505 12,293,335 4,321,984 4,419,858 7,971,951 5,087,880 14,923,627	57 131 250 407 566 866 1,074 1,040 2,277 189 657 2,088 2,505 4,391	97 84 159 259 960 551 662 1,450 120 418 1,310 1,595 2,795	18 42 30 151 182 275 346 595 738 61 211 672 807 1,414	99 41 89 41 169 41 276 41 587 41 728 41 705 41 705 41 705 41 128 41 128 41 128 41 145 42 1,416 41 1,638 41 2,977 4	\$ 15,122 913,432 991,622 \$ 26,321 720,400 700,437 614,315 457,802 4,917,334 1,772,553 1,767,943 3,188,780 2,095,152 5,969,451	27 62 118 192 267 408 506 490 1,073 89 309 984 1,180 2,068	67 153 291 474 659 1,009 1,251 1,212 2,654 2,251 766 2,454 2,920 5,118	9 20 38 62 191 163 151 345 29 100 917 380 666	18 20 42 20 80 20 130 20 181 20 343 20 777 20 727 20 60 20 60 20 667 20 800 20 100 20 100 20 100 20	407,561 456,716 465,811 418,161 960,200 950,218 907,157 218,901 2,458,667 864,277 864,277 883,977 21,594,930 1,017,576 2,984,725	15 34 65 106 147 225 279 270 592 49 171 543 651 1,141	79 181 944 560 779 1,192 1,478 1,492 9,135 260 904 2,875 9,449 6,045	5 11 21 34 47 72 90 87 191 16 55 175 210 967	10 11 25 11 44 11 72 11 100 11 153 11 185 11 185 11 193 11 193 11 116 11 196 11 775 11	203,780 223,958 232,906 209,080 180,100 175,109 153,579 109,451 1,229,933 432,138 441,986 432,138 441,986 1,492,963	8 19 35 58 80 122 152 147 922 27 93 295 295 295 295 295	36 196 374 608 846 1,295 1,595 1,595 3,405 2122 912 912 912 3,123 5,746 6,565	3 6 11 19 285 399 49 47 104 9 30 95 30 95 114 200	6 13 24 99 54 83 103 100 218 83 63 200 240 421	6 6 6 6 6 6 6 6 6 6 6 6 6	40,756 45,672 46,581 41,816 36,020 95,022 90,716 21,850 245,867 86,428 88,397 159,439 101,758 238,473	2 4 8 14 19 29 36 35 76 6 6 22 70 84 147	92 211 401 652 907 1,388 1,721 1,667 3,661 903 1,053 1,053 3,548 4,016 7,099	1 1 3 4 6 9 9 12 11 11 25 2 7 7 23 27 47	1 1 3 1 6 1 9 1 19 1 20 1 24 1 24 1 52 1 47 1 15 1 57 1 100 1

Supplementary Table 6a(ii). Cancers detected by offering risk stratified screening according to current PRS using sensitivity of current "real world" cancer-screening tools (Cancers of the Ovary, Kidney, Lung, Testis)

| | | Annual Incidence
(per 100,000) for age-
band | | | |

 | | s | creening offer
50%
of PRS | red to top | | | s | icreening off
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of Pl | fered to top
%
RS | | | | | | | | | | | | | | | | | | |
 | | S | creening offe
10%
of PR | ered to top
is
RS | | | | Screening offered to t
5%
of PRS | p |
 | | Screening off
1%
of PR | red to top
LS | | | | | | | | | | | | | | | | | | |
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--|---|--|--|---|---|---|--|
| Салонт
Туре | Screening tool | Age Groups | Male | F emale | Population
Size | Cancers
ariting
per year

 | Number
requiring
screening in
'high risk'
group | Cancers
arising in
'high risk'
group | Missed
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unscreened
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group | Cancers
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Supplementary Table 6b(i). Cancers detected by offering risk stratified screening according to future PRS using sensitivity of current "real world" cancer-screening tools (Cancers of the Breast, Prostate, Colorectum and Pancreas)

								S	reening offe	red to top			S	creening off	Fered to top				Sci	reening off	fered to top				Screening off	fered to top			S	reening offer	d to top		_
			Annual In	cidence (per					50 %					209	6					109	6				596					196			
			100,000) ft	or age-band	Popu	lation			ofPR	5				ofPH	RS					ofPl	RS				ofPl	RS				of PRS			
									Missed					Missed						Missed					Missed					Missed			
Cancer	Screening sensitivity	Age Granges					Number	Cancers	cancers	Cancers	Cancers	Number	Cancers	cancers	Cancers	Cancers		Number (Cancers	cancers	Cancers (Cancers	Number	Cancers	cancers	Cancers	Cancers	Number	Cancers	cancers C	ancers C	lan cers	
Type				T	Description Class	Cancers arising	requiring	arising in	arising in "	nissed on d	etected on Percent of	requiring	arising in	arising in 1	missed on (detected on Pe	rcent of	requiring ar	ising in a	arising in	missed on de	tected on Percent of	requiring	arising in	arising in	missed on d	letected on Percent of	requiring	arising in	arising in ^{mi}	ssed on dete	ected on Percer	ent of
			Male	Female	Population Size	per year	screening in	'high risk'	unscreened	creening	screening cancers	screening	'high risk'	unsc reene d	screening	screening c	ancers	screening 'h	igh risk' ur	ins creen ed	screening so	creening cancers	screening	'high risk'	unscreened	screening	screening cancers	screening	'high risk' v	nscreened SC	reening scr	reening canc	cers
							'nign risk'	group	'low risk'	in mign-	in 'nign- identified	in 'nign	group	'low risk'	in 'nign-	in 'nign- 10	entitied	in nign	group '1	low risk'	in 'nign- ii	n mign- identified	in nign	group	'low risk'	in 'nign-	in mign- identified	in 'nign	group	low risk in	'nign- in	inign- identi	.111 80
							Broop		group "	ar group i	in Brook	nak group		group *	nex group	new Brook		new Brook		group '	nak group na	nr Brook	new group		group	isk group i	ter Brook	mak group		group	. group max	r Brook	
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Brent	Digital mammography	40 to 44	0.0	124.6	2,054,223	2,555	1,027,112	1,934	625	580	1,354 53	410,845	1,129	1,430	339	790	31	205,422	712	1,847	214	498 1	9 102,711	437	2,122	BI	306 13	20,542	131	2,428	39	92	- 4
Break	Digital mannugraphy	43 10 49	0.0	214.8	23 15,479	4,9/4	1,157,740	5,700	1,65	1,600	2,052 55	403,090	2,194	7,780	800	2,942	31	231,548	1,984	3,390	415	908 1	9 115,774	849	4,10	100	294 L3 700 11	23,05	400	4,719	102	1/8	
Brand	Digital mannagraphy	55 m 50	0.0	219.0	7 1 10 687	6.057	1,050 844	4 575	1477	1377	3,00 53	473.037	7,660	3,096	801	1.868	31	711.060	1,683	4 3 60	505	1178 11	105 084	1.033	5,010	339	773 13	21 107	310	5 247	03	217	
Bornat	Digital mammigraphy	60 m 64	0.0	338.0	1,837,174	6,205	918,587	4,693	1,516	1,408	3,285 53	367,435	2,738	3,471	821	1,917	я	183,717	1,727	4,482	518	1,209 1	91,859	1,060	5,149	318	742 13	18,372	318	5,891	95	223	- 4
Breat	Digital mammugraphy	65 m 69	0.0	412.3	1,805,190	7,443	902,595	5,626	1,817	1,688	3,938 53	361,038	3,282	4,161	985	2,298	31	180,519	2,070	5,373	621	1,449 19	90,260	1,270	6,173	381	889 13	18,052	381	7,062	114	267	4
Brent	Digital mammugraphy	70 m 74	0.0	372.7	1,603,610	5,977	801,805	4,518	1,459	1,355	3,163 53	320,722	2,636	3,341	791	1,845	31	160,361	1,663	4,314	499	1,164 1	80,180	1,020	4,957	306	714 13	16,036	306	5,671	92	214	- 4
Breat	Digital mammugraphy	75 m 79	0.0	403.0	L18L645	4,762	\$90,823	3,600	1,162	1,080	2,520 53	236,329	2,100	2,662	630	L470	31	118,165	1,325	3,437	397	927 1	9 59,082	813	3,949	244	569 13	11,816	244	4,518	73	171	- 4
Brent	Digital mannugcaphy	Thtal 40-69	0.0	270.9	12,496,392	33,853	6,248,196	25,590	8,263	7,677	17,913 53	2,499,278	14,930	18,923	4,479	10,451	31	1,249,639	9,417	24,436	2,825	6,592 1	624,820	5,777	28,076	1,733	4,044 13	124,964	1,734	32,119	520	1,214	- 4
Breat	Digital mannugraphy	Total 40-49	0.0	172.4	4,369,703	7,533	2,184,851	5,694	1,839	1,708	3,986 53	873,941	3,322	4,211	997	2,326	31	436,970	2,095	5,438	629	1,467 1	218,485	1,285	6,248	386	900 13	43,697	386	7,147	116	270	- 4
is creat	Digen anomicality	mm 50-59	0.0	282.5	4,484,325	12,668	2,242,163	9,5%	3,092	2,875	0,703 53	896,865	3,387	7,081	1,0%	3,911	31	448,433	3,524	9,144	1,057	4407 1	224,216	2,162	10,506	049	1,58 15	44,843	049	12,019	195	454	
D TOM	Digital managegity	Teral 60.74	0.0	323.9	5.745.024	10,320	7 672 1977	14 979	0,424	2,909	10.3927 53	1.040.105	8.657	10.072	3,482	8,60	11	614,009 574 507	5.460	14,162	1,619	3,140 1	400,534	4,491	16.722	1,005	3,144 L3 7,745 L3	81,407	1,005	14,971	404	204	
Breat	Divital managements	Total 40-79	0.0	201.8	15 281 647	44 503	7 640 874	33 709	10.884	10 112	23 596 53	3 056 329	19.666	24 926	5 900	13 766	31	1528165	12 404	32 182	3 721	8 683 1	0 764 (197	7 600	36 087	2 28 7	5 327 13	152 816	2 284	42 308	685	1 599	-1
Breat	Digital mammugraphy	Tatal (all ages)	0.0	166.0	33,458,052	55.543	5				,	,,	_,•						-,		- ,						,	1		-,			
Beartala																																	
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Prostate	PSA_3ng/mL cut-off	40 m 44	4.3	0.0	2,021,385	88	1,010,092	99	19	47	22 25	404,277	43	45	29	14	10	202,138	28	00	10	9 1	0 101,009	18	70	12	° (20,214	0	82	4	2	- 2
Promite -	PSA_Japani. mean	45 B 49 50 m 54	20.5	0.0	2,251,080	101	1,10,840	304	766	077	470 25	450,330	847	438	577	260	16	220,108	540	1199	124	176 1	114,584	91	1 200	77.6	00	22,025	29	134	25	76	
Prostate December a	Par_suput neur	55 m 50	201.8	0.0	7.061.010	4 160	1 010 050	1.297	977	7 7 7 7	1050 25	417 194	2 016	2 144	1 171	64.5	16	206 107	1 716	7 944	305	471 1	107.006	, PL, 97.7	1,129	566	266	20,610	266	7 904	191		
Prostate	PSA 3me/mL cot-off	60 m 64	356.1	0.0	L764.828	6.285	882,414	4,960	1325	3373	1.587 25	352,966	3.047	3.238	2.072	975	16	176.483	1.988	4.297	1.352	636 1	88.241	1.257	5,028	855	402 0	17.648	401	5,884	273	128	2
Prostate	PSA_3op/mL cut-off	65 to 69	62.2.7	0.0	1,696,993	10,561	848,497	8,339	2,229	5,671	2,669 25	339,399	5,123	5,445	3,483	1,639	16	169,699	3,342	7,226	2,273	1,069 1.	84,850	2,114	8,454	1,437	676 0	16,970	675	9,893	4 59	216	2
Prostat e	PSA_3op/mL cot-off	70 m 74	759.8	0.0	1,467,965	11,63	733,983	8,801	2,352	5,985	2,816 25	293,593	5,406	5,747	3,676	1,730	16	146,797	3,527	7,626	2,398	1,129 1	0 73,398	2,231	8,922	L517	714 0	14,680	712	10,441	484	228	2
Prostate	PSA_3op/mL cot-off	75 to 79	867.2	0.0	1,007,365	8,736	503,683	6,894	1,842	4,688	2,206 25	201,473	4,235	4,501	2,880	1,355	16	100,737	2,763	5,973	1,879	884 1	50,368	1,747	6,989	1,188	559 0	10,074	5.58	8,178	379	179	2
Prostate	PSA_3og/mL co+off	Total 40-69	192.7	0.0	12,090,277	23,295	6,045,139	18,386	4,913	12,502	5,883 25	2,418,055	11,294	12,005	7,680	3,614	16	1,209,028	7,368	15,931	5,010	2,358 1	0 604,514	4,661	18,638	3,169	1,491 (i 120,903	1,488	21,811	1,012	476	2
Prostate	PSA_3mg/mL mt-off	Tutal 40-49	12.8	0.0	4,273,065	545	2,136,532	433	116	295	139 25	854,613	266	283	181	85	16	427,306	174	375	118	56 1	213,653	110	439	75	35 0	42,731	35	514	24	 	- 2
Promise December of	PSA 2 to 1 out of	Total 60.60	153.4	0.0	146,000	16.957	1,17,090	4,035	1,64	0.047	4.356	602,764	4,636	5,059	6.665	2614	16	146,152	5 330	4,034	1,494	1 706 1	177.001	1,160	17,00	2 202	1070	74 619	1077	3,540	232	744	
Broatsta	BS& 3mm/mL mLoff	Total 50.60	201.0	0.0	7 817 713	77 750	3 008 606	17.057	4 708	17 208	5 245 25	1 563.443	11.028	11 777	7,400	3 570	16	781 771	7 105	15 555	4 807	7 307 1	1 200 261	4 551	19,100	3 004	1456	38177	1453	71 797	055	465	÷
Prostate	PSA 3mp/mL mt-off	Tatal 60-74	568.1	0.0	4,929,786	28,006	2,464,893	22,100	5,906	15,028	7,072 25	985,957	13,575	14,431	9,231	4,344	16	492,979	8,857	19,149	6,023	2,834 1	246,489	5,602	22,404	3,809	1,793 0	49,298	1,789	26,217	1,217	572	2
Prostate	PSA_3og/mL cot-off	Total 40-79	296.5	0.0	14,565,608	43,188	7,282,804	34,080	9,108	23,175	10,906 25	2,913,122	20,935	22,253	14,236	6,699	16	1,456,561	13,658	29,530	9,288	4,371 1	0 728,280	8,639	34,549	5,875	2,764 0	145,656	2,759	40,429	1,876	83	2
Prostate	PSA_3mg/mL cot-off	Tutal (all ages)	183.8	0.0	32,583,226	52,254	1																										
Coloredal																																	
Colorectal	FIT 20-50 µg/g threshold (CR	40 m 44	14.5	13.5	4.075.608	570	2.037.804	396	174	119	277 49	815,122	211	359	63	148	26	407.561	126	444	38	8 1:	5 203,780	73	497	22	51 9	40,756	20	550	6	H	- 2
Colorectal	FIT 20-50 pp/g threshold (CR)	45 to 49	24.4	21.6	4,567,159	1,045	2,283,580	728	319	218	510 49	913,432	388	659	116	271	26	456,716	231	816	69	162 1	5 228,358	134	913	40	94 5	45,672	36	1,011	11	25	2
Coloectal	FIT 20-50 µg/g threshold (CR	50 to 54	47.1	37.1	4,658,111	1,958	2,329,055	រេះត	597	408	953 49	931,622	725	L233	218	508	26	465,811	432	1,526	129	302 1:	5 232,906	251	1,707	75	176 9	46,581	68	1,890	20	48	2
Colorectal	FIT 20-50 µg/g threshold (CR	55 m 59	\$7.7	60.6	4,181,606	3,094	2,090,803	2,151	943	645	1,506 49	836,321	1,146	1,948	344	802	26	418,161	682	2,412	205	477 1	5 209,080	397	2,697	119	278 5	41,816	107	2,987	32	75	2
Coloe-cal	FTT 20-50 µg/g threshold (CR	60 m 64	151.4	91.0	3,602,002	4,345	5 1,801,001	3,021	1,324	906	2,115 49	720,400	1,609	2,736	483	1,126	26	360,200	958	3,387	287	670 1:	5 180,100	558	3,787	167	390 9	36,020	151	4,194	45	106	2
Colorectal	FIT 20-50 µg/g threshold (CR	65 m 69	198.3	119.1	3,502,183	5,516	1,751,092	3,835	1,681	1,150	2,684 49	700,437	2,043	3,473	613	1,430	26	350,218	1,216	4,300	365	851 1	5 175,109	708	4,808	212	496 5	35,022	191	5,325	57	134	2
Colorectel	FILE AV-20 JUBYE CONSIGNED (C.K. 1977 20-50 a s/s doesdouble (C.K.	75 to 70	2/3.5	234.9	3,071,575	6,761	1 1 004 505	4,700	1,000	1,410	3,020 49	417 802	4,304	4,00	701	1,638	هر بر	307,137	1,490	2,270	447	L043 L	5 100,451	808	5,502	200	5007 L	30,710	235	مرہ 100 6	70	154	
Colorectal	FTT 20-50 a s/s threshold (Call	Total 40-69	80.8	204.8 54.1	24 586 660	16 530	12 293 335	11.497	5.038	3 4 4 8	8044 40	4 917 324	6 127	10.408	1 837	4 285	26	2458 667	3 643	12 887	1 093	2 550 1	5 1 229 333	2177	14 402	637	1485	245 867	574	15 956	172	402	÷
Colorectal	FIT 20-50 µg/g threshold (CR	Tatal 40-49	19.7	17.7	8,642,767	1,617	4,321,384	1,124	493	337	787 49	1,728,553	599	1,018	180	419	26	864,277	356	1,261	107	249 1	432,138	208	1,409	62	145 5	86,428	56	1,561	17	39	2
Coloe-cal	FTT 20-50 µg/g threshold (CR	Total 50-59	66.4	48.2	8,839,717	5,057	4,419,858	3,512	1,540	1,054	2,459 49	1,767,943	1,871	3,181	561	1,310	26	883,972	1,113	3,939	334	779 1.	441,986	649	4,403	195	454 9	88,397	175	4,877	53	123	2
Colorectal	FIT 20-50 µg/g threshold (CR	Tatal 50-69	114.2	73.6	15,943,902	14,913	7,971,951	10,368	4,545	3,110	7,258 49	3,188,780	5,523	9,390	1,657	3,866	26	1,594,390	3,287	11,626	986	2,301 1	5 797,195	1,914	12,999	574	1,340 9	159,439	518	14,395	155	362	2
Coloe-cal	FTT 20-50 µg/g threshold (CR	Total 60-74	203.9	125.2	10,175,760	16,621	1 5,087,880	11,555	5,066	3,467	8,089 49	2,035,152	6,156	10,465	1,847	4,309	26	1,017,576	3,663	12,958	1,099	2,564 1:	5 508,788	2,134	14,487	640	1,494 9	101,758	577	16,044	173	404	2
Colorectal	FIT 20-50 µg/g threshold (CIK	Tutal 40-79	119.0	80.4	29,847,255	29,608	14,923,627	20,584	9,024	6,175	14,409 49	5,969,451	10,966	18,642	3,290	7,676	26	2,984,725	6,526	23,082	1,958	4,568 1	5 1,492,363	3,801	25,807	LH 0	2,661 9	298,473	1,028	28,580	308	719	2
Colorsdal	NT 20-30 µg/g threshold (CK	Total (all ages)	84.5	20.5	60,041,278	47,883	<u></u>																										_
PERMIT																																1	
Panna	CA19-9_20U/mL cutoff	40 m 44	2.6	2.0	4,075,608	94	2,037,804	66	28	21	45 48	815,122	36	58	12	24	26	407,561	22	72	7	15 1	5 203,780	13	81	4	9 5	40,756	4	90	1	2	3
Panna	CA19-9_20U/mL cotoff	45 m 49	5.6	3.9	4,567,159	21.5	5 2,283,580	152	63	49	103 48	913,432	82	133	27	56	26	456,716	50	165	16	34 1	5 228,358	29	186	9	20 9	45,672	8	207	3	5	3
Parama	CA19-9_20U/mL cutoff	50 to 54	10.2	7.3	4,658,111	405	2,329,055	289	120	93	196 48	931,622	157	252	50	106	26	465,811	94	315	30	64 1	6 232,906	55	354	18	38 9	46,581	в	394	5	10	3
Panna	CAL9-9_20U/mL mtoff	55 th 59	18.3	13.6	4,181,606	666	2,090,803	471	195	152	319 48	836,321	255	411	82	173	26	418,161	154	512	49	104 1	209,080	90	576	29	61 <u>1</u>	41,816	25	641	8	17	3
Dama	CAID D 20116mL cutoff	65 10 60	47.0	22.4	3,002,002	910	1 251 002	1.002	414	777	111 18 670 49	740,400	500 507	371	125	269		300,200	111	1.002	105	272 1	s 126,400	100	1 225	10	120	25.000	сı 7	1 264	17	25	
Panna	CA19-9 20U/mL mtoff	70 to 74	66.4	48.8	3,00,183	1 253	1.535.787	1,002	515	400	842 48	614.315	674	1.081	217	457	26	307.157	405	1352	105	275	5 153,579	218	1.510	77	162 9	30,716		1,00	21	45	
Panna	CA19-9 20U/mL cotoff	75 to 79	86.0	70.8	2,189.011	1,707	1,094,505	1,203	499	388	816 48	437,802	652	1,050	210	442	26	218,901	393	1,309	126	266 1	5 109,451	231	L471	74	157 9	21,890	64	1,638	21	43	- 3
Paraman	CA19-9_20U/mL cutoff	Tutal 40-69	17.4	13.0	24,586,669	3,727	12,293,335	2,635	1,092	849	1,787 48	4,917,334	1,429	2,298	460	969	26	2,458,667	860	2,867	277	583 1	6 1,229,333	506	3,221	163	343	245,867	139	3,588	45	95	3
Panna	CA19-9_20U/ml. catoff	Total 40-49	4.2	3.0	8,642,767	305	4,321,384	218	91	70	148 48	1,728,553	118	191	38	80	26	864,277	71	238	23	48 1	432,138	42	267	14	28 9	86,428	12	297	4	8	3
Panna	CA19-9_20U/mL cutoff	Tutal 50-59	14.1	10.3	8,839,717	1,075	4,419,858	760	315	245	51.5 48	1,767,943	412	663	133	279	26	883,972	248	827	80	168 1	6 441,986	146	929	47	99 9	88,397	40	1,035	в	27	3
Panna	CA19-9_20U/ml. cotoff	Tatal 50-69	24.7	18.3	15,943,902	3,418	7,971,951	2,417	1,001	778	1,639 48	3,188,780	1,310	2,108	422	888	26	1,594,390	788	2,630	254	535 1	6 797,195	464	2,954	149	314 9	159,439	128	3,290	41	87	3
Panna	CA19-9_20U/mL cotoff	mm1 60-74	46.5	34.5	10,175,760	4,100	5,087,880	2,899	1,201	934	1,900 48	4,035,152	L 572	2,528	506	1,000	26	1,017,576	946	3,154	305	641 1	508,788	556	3,544	179	377 9	101,758	153	3,947	49	104	
Pannea	CA19-9 2013/ml. mtoff	Total (all arm)	193	15.0	66 041 778	7,180	1 10,913,017	3,081	4,005	1,050	s, m 3 48	5,909,451	4,00	וכקר	ad/	1,000		A. 100 - 100	1,036	هدرد	- 10	.,ue 1	4,794,903	2/2	0,111	314		490,7/3	100	0,917	a,	10.1	

Supplementary Table 6b(ii). Cancers detected by offering risk stratified screening according to future PRS using sensitivity of current "real world" cancer-screening tools (Cancers of the Ovary, Kidney, Lung, Testis)

								S	reening offe	red to top			S	creening offi	ered to top				Screening o	offered to top			5	Screening offe	red to top			S	creening offere	d to top		
			Annual Inc	iden ce (per					50 %					209	6 Č				10	096				596					196			
			100,000) fo	r age-band	Popu	lation			ofPR	S				ofPR	tS				of	PRS				ofPR	S				of PRS			
-							27-04-0		Missed	a	6	22		Missed	a	a	N		Missed	<i>a</i>	a	Number		Missed	o	6	22-11-1		Missed			
Tree	Screening sensitivity	Age Gramps					Number	Cancers	can cers	Cancers sisted on di	Cancers	Number	Cancers	cancers	Cancers niccod on	Cancers fotocted on Decrem	N umber	Cancers	cancers	Cancers missed on d	Cancers storted on Demonster	Number	Cancers	cancers	Cancers nissed on dr	Cancers Notacted on Descant of	Number	Cancers	cancers Ca	ncers Ca	ancers stod on Dor	
.,=			Male	Female	Population Size	Cancers arising	screening in	arising in	arising in	creening 1	creening cancers	screening	arising in	arising in	creening	acreening cancer	a screening	arising in	arising in	screening	screening cancers	screening	arising in	arising in	creening a	creening cancers	acreening	arising in	arising in scr	sec on Gerec	sening ca	ancers
						per year	'high risk'	'high risk'	unscreened	in 'high-	in 'high- identified	in 'high	'high risk'	ansc reened	in 'high-	in 'high- identifi	ed in 'high	'high risk'	uns creen ed	in 'high-	in 'high- identified	in high	'high risk'	unscreened	in 'high-	in high-identified	in 'high	'high risk' v	inscreened in	high- in	'high-ide	entified
							group	group	now risk ri	sk' group ri	isk' group	risk' group	group	now risk.	isk' group	risk' group	risk' grou	p group	TOW fisk	risk' group r	isk' group	risk' group	group	now risk ri	sk' group ri	sk' group	risk' group	group	risk'	group risk	c' group	
									Broob					group					group					Broop					Broob			
Отшу																																
Ovary	MMS (CA-125 + TVU)	40 m 44	0.0	13.2	2,054,223	270	1,027,112	178	92	28	149 55	410,845	90	180	и	76	28 205,47	2 52	218	8	43 1	6 102,711	29	241	5	25	20,542	7	263	1	6	2
Overy	MMS (CA-125 + TVU)	45 to 49	0.0	19.4	2,315,479	448	1,157,740	295	153	47	248 55	463,096	149	299	24	125	28 231,54	8 86	362	- 14	72 1	6 115,774	49	399	8	41	23,155	12	436	2	10	2
Overy	MMS (CA-125 + TVU)	50 to 54	0.0	27.1	2,364,638	64 0	1,182,319	422	218	67	354 55	472,928	213	427	34	179	28 236,46	4 123	517	20	103 1	6 118,232	69	571	11	58	23,646	18	622	3	в	2
Ovary	MMS (CA-125 + TVU)	55 to 59	0.0	34.8	2,119,687	738	1,059,844	486	252	78	409 55	423,937	246	492	39	206	28 211,96	9 141	597	23	119 1	6 105,984	80	658	13	67	21,197	20	718	3	17	2
Overy	MMS (CA-125 + TVD)	65 m 69	0.0	52.3	1 805 100	,	918,585	677	377	100	573 55	361 038	314	63.0	50	264	28 180.51	0 191	763	70	157 1	6 00 260	107	847	16	86	18.057	26	018		77	
Overv	MINS (CA-125 + TVU)	70 m 74	0.0	60.8	1.603.610	975	801,805	643	332	103	540 55	320.722	325	650	52	273	28 160 36	1 187	788	10	157 1	6 80 180	106	869	17	80	16 036	27	948	4	73	2
Overy	MMS (CA-125 + TVU)	75 to 79	0.0	73.8	L18L645	872	590,823	575	297	92	483 55	236,329	290	582	46	244	28 118,16	5 167	705	27	140 1	6 59,082	95	777	15	79	11,816	24	848	4	20	2
Ovary	MMS (CA-125 + TVU)	Tatal 40-69	0.0	30.4	12,496,392	3,804	6,248,196	2,507	1,297	401	2,106 55	2,499,278	1,266	2,538	203	1,064	28 1,249,63	9 729	3,075	117	612 1	6 634,820	412	3,392	66	346	124,964	105	3,699	17	88	2
Ovary	MMS (CA-125 + TVU)	Total 40-49	0.0	16.4	4,369,703	718	2,184,851	473	245	76	397 55	873,941	239	479	38	201	28 436,97	0 138	580	22	116 1	6 218,485	78	640	12	65	43,697	20	698	3	17	2
Ovary	MMS (CA-125 + TVU)	Tatal 50-59	0.0	30.7	4,484,325	1,378	2,242,163	908	470	145	763 55	896,865	459	919	73	385	28 448,43	3 264	1,114	42	222 1	6 224,216	149	1,229	24	125	44,843	38	1,340	6	32	2
Overy	MINIS (CA-LO + 1VU)	Incal 50-69	0.0	58.0	8,1.00,089	3,080	4,003,345	1,749	1,054	20	1,08 55	1 040 105	5,027	4,059	147	303	28 814,00	9 39L 7 514	2,495		49/ L	0 400,334 6 262,200	353	2,00	24	281	81,49/	24	3,001	- 17	<i>1</i> 1	
Overy	MMS (CA-125 + TVD)	Total 40-79	0.0	37.0	15 281 647	5.651	7 640 834	3,724	1922	596	3 128 55	3 056 329	181	3 770	301	1 580	28 1 528 16	5 1083	4 568	173	910 1	6 764 082	ផា	5.038	98	515	152 816	156	5,495	25	131	2
Overy	MMS (CA-125 + TVU)	Total (all ages)	0.0	22.8	33,458,052	7,495		-991			,	1,,	-,	-,,			1	-,						-,								-
x::	1100	40 - 44	10.1	6.0	4.075.608	701	D 077 B04	16			161 0	916 122	116	103		84	77 407 54	1 0	278	10	60 1	4 202 280	40	267		20 1	40.756	<u> </u>				
Linkey	USS	45 m 49	17.7	7.8	4,567,159	507	7 283 580	406	124	110	296 51	013437	718	367	51	159	77 456 71	1 09 6 110	450	15	- 30 L 95 L	6 778 358	76	504	21	56 1	45 677	71	550	6	15	
Kittery	USS	50 m 54	26.8	12.7	4.658.111	913	2.329.055	641	274	174	467 51	931.622	344	571	93	251	27 465.81	1 206	709	56	150 1	6 232,906	120	795	33	8 1	46.581	33	80	9	24	- 3
Kithey	USS	55 to 59	37.1	18.6	4,181,606	1,160	2,090,803	813	347	220	592 51	836,321	436	724	118	318	27 418,16	1 261	899	71	190 1	6 209,080	153	1,007	41	u i	41,816	42	1,118	u	30	3
Kidney	USS	60 m 64	53.7	26.2	3,602,002	1,429	1,801,001	1,001	428	271	730 51	720,400	537	892	146	392	27 360,20	0 321	1,108	87	234 1	6 180,100	188	1,241	51	137 1	36,020	51	1,378	н	37	3
Kidney	USS	65 ta 69	73.9	36.4	3,502,183	1,911	1,751,092	1,339	572	363	976 51	700,437	719	1,192	195	524	27 3 50,21	8 430	1,481	116	313 1	6 175,109	251	1,660	68	183 1	35,022	69	1,842	19	50	3
Kitey	USS	70 to 74	91.2	45.1	3,071,575	2,063	1,535,787	1,445	តាន	392	1,054 51	614,315	776	1,287	210	566	27 307,15	7 464	1,599	126	338 1	6 153,579	271	L,792	74	198 1	30,716	74	1,989	20	54	3
K. altery	USS	75 10 79	110.1	57.2	2,189,011	L,783	10,004,505	1,250	335	339	912 51	437,802	0/1	1,114	642	489	77 718,90	1 401	1,384	109	293 1	6 109,451	235	1,550	04	171 1	21,890	04	6 026	- 17	47	
K interest	USS	Tres 40-09	14.1	10.9	8 647 767	0,907	4 171 194	671	266	1/8	اد مان <u>ہ</u> د 17 17	1 778 551	1,370	557	00	243	27 864.22	7 700	4,663	34	145 1	6 417 119	117	770	123	85 1	86.479	17	9,070	D D	77	
Kidney	USS	Total 50-59	31.7	15.5	8,839,717	2,075	4,419,858	1,454	621	394	1,060 51	1,767,943	780	1,295	211	569	27 883,97	2 467	1,608	126	340 1	6 441,986	273	1,802	74	199 1	88,397	74	2,001	20	54	3
Kitney	USS	Tutal 50-69	45.8	22.6	15,943,902	5,415	7,971,951	3,793	1,622	1,028	2,765 51	3,188,780	2,037	3,378	552	1,485	27 1,594,39	0 1,218	4,197	330	888 1	6 797,195	712	4,703	193	519 1	159,439	194	5,221	53	142	3
Kidney	USS	Total 60-74	71.8	35.5	10,175,760	5,403	5,087,880	3,785	1,618	1,026	2,759 51	2,035,152	2,032	3,371	551	1,481	27 1,017,57	6 1,215	4,188	329	886 1	6 508,788	711	4,692	193	518 1	101,758	194	5,209	53	141	3
Kitney	USS	Tatal 40-79	45.5	23.0	29,847,255	10,150	14,923,627	7,110	3,040	1,927	5,183 51	5,969,451	3,817	6,333	1,035	2,783	27 2,984,72	5 2,283	7,867	619	1,664 1	6 1,492,363	LJ36	8,814	362	974 1	298,473	364	9,786	99	266	3
K. alony	USS	Total (all ages)	29.2	14.8	00,041,7/8	13,323	·										_					_										
Lung																													1	1		
Long	Low dose CT	40 to 44	6.0	5.8	4,075,608	240	2,037,804	157	83	24	132 55	815,122	78	162	12	66	28 407,56	1 45	195	7	38 1	6 203,780	25	215	4	21	40,756	6	234	1	5	2
Long	Low done CT	45 to 49	16.3	14.7	4,567,159	706	2,223,580	460	246	п	390 55	913,432	230	476	35	195	28 456,71	6 132	574	20	աւ	6 228,358	74	632	n	63	45,672	19	687	3	16	2
Long		50 10 54	33.4	31.5	4,058,111	1,512	2,329,055	1 9 80	320	152	834 55	931,022	493	1,019	70	417	78 405,81		1,230	43	239 1	6 232,900	159	1,353	24	24	40,581	40	2,472	- 10	34	
Long	Low dome CT	60 to 64	137.0	124.9	3,602,002	4 711	1,090,203	1,000	1.638	473	7 500 55	720 400	1 517	3 174	217	1300	28 360 20	L .71L 0 879	1,817	115	744 1	6 180 100	495	4 716	76	419	16 020	125	4 586	19	106	
Loog	Low dom: CT	65 m 69	229.5	197.8	3,502,183	7,466	1,751,092	4,870	2,596	750	4,120 55	700,437	2,436	5,030	375	2,061	28 350,21	8 1,394	6,072	215	L179 I	6 175,109	784	6,682	121	663	35,022	198	7,268	30	167	2
Long	Low dom: CT	70 m 74	335.0	278.1	3,071,575	9,178	1,535,787	6,117	3,261	942	5,175 55	614,315	3,060	6,318	471	2,588	28 307,15	7 1,751	7,627	270	1,481 1	6 153,579	985	8,393	152	833	30,716	248	9,130	38	210	2
Long	Low done CT	75 to 79	462.2	340.5	2,189,011	8,680	1,094,505	5,661	3,019	872	4,789 55	437,802	2,832	5,848	436	2,396	28 218,90	1 1,620	7,060	250	L371 I	6 109,451	911	7,769	140	771	21,890	230	8,450	35	195	2
Long	Low dom CT	Tutal 40-69	74.8	68.0	24,586,669	17,531	12,293,335	11,434	6,097	1,761	9,673 55	4,917,334	5,720	11,811	881	4,839	28 2,458,66	7 3,273	14,258	504	2,769 1	6 1,229,333	1,841	15,690	283	1,557	245,867	464	17,067	72	393	2
Long	Low dome CT	Total 40-49	11.4 61.4	10.5	8,042,707	940	4,371,384	017	379	95	377 33	1 262 043	309	037	48	201	28 804,27	7 177	709	7/	149 L 606 1	6 437, 138	99	2 045	21	34	80,428	25	4 201	4	21	- 2
Lang	Low dom: CT	Total 50-69	109.4	98.0	15 043 007	16 58 4	7 071 051	10 817	5 768	1 6 6 6	0151 55	3 188 780	5.411	11 174	833	4 578	28 1 594 30	- 443 0 3,006	13.480	477	2 619 1	6 707 105	1747	14 843	268	1473	159.420	430	16 146	68	372	
Long	Low dom CT	Tutal 60-74	227.8	196.8	10,175,760	21,555	5,087,880	14,059	7,496	2,165	11,894 55	2,035,152	7,032	14,523	1,083	5,949	28 1,017.57	6 4,024	17,531	620	3,404 1	6 508,788	2,263	19,292	349	1,915	101,758	571	20,984	88	483	2
Long	Low dom: CT	Total 40-79	127.8	111.1	29,847,255	35,589	14,923,627	23,212	12,377	3,575	19,637 55	5,969,451	11,611	23,978	1,788	9,823	28 2,984,72	5 6,644	28,945	1,023	5,620 1	6 1,492,363	3,737	31,852	576	3,162	298,473	943	34,646	145	798	2
Long	Low dom: CT	Total (all ages)	90.6	70.1	66,041,278	48,545																										
Teslis																																
Testis	Semen assay	40 m 44	12.3	0.0	2,021,385	248	1,010,692	228	20	75	153 67	404,277	176	72	58	118	48 202.13	8 135	113	45	91 3	7 101,069	100	148	33	67 2	20,214	44	204	н	29	12
Testin	Semen may	45 m 49	9.4	0.0	2,251,680	211	1,125,840	194	17	64	130 67	450,336	150	61	49	100	48 225,16	8 115	96	38	77 3	7 112,584	85	126	28	57 2	22,517	37	174	12	25	12
Testis	Semen any	50 m 54	7.0	0.0	2,293,473	160	1,146,736	147	в	48	98 67	458,695	114	46	37	76	48 229,34	7 87	73	29	58 3	7 114,674	64	96	21	43 2	7 22,935	28	132	9	19	12
Testin	Semen may	55 to 59	5.2	0.0	2,061,919	108	1,030,959	99	9	33	66 67	412,384	77	31	25	51	48 206,19	2 59	49	19	39 3	7 103,096	43	65	14	29 2	7 20,619	19	89	6	в	12
Alexian Tourin	Senen may	00 m 64	3.0	0.0	1,704,828	57	867,414	48	4	10	37 67	332,966	37	15	12	25	48 176,48	3 28 D 77	24	9	19 3	7 88,241	21	31	9	14 2	17,048	9	43	3	0	- 12
Testin	Small may	20 m 24	2.4	0.0	1467.065		711 097	84. 17	3	11	77 67	202.507	29	10	10	10	48 146 20	y 11 7 10	16	4	13 7	7 73,309	14	23	5	0 7	10,970	4	70		3	- 12
Testin	Smen may	75 m 79	1.4	0.0	1,007.365		503,683	л В	í	4	9 67	201,473	10	4	3	7	48 100.73	7 8	6	3	5 3	7 50,368	6	8	2	4 2	10,074	2	12	î	2	12
Testin	Senen may	Total 20-39	16.0	0.0	8,782,738	1,406	4,391,369	1,291	115	4 26	865 67	1,756,548	998	408	329	669	48 878,27	4 766	640	253	513 3	7 439,137	564	842	186	378 2	87,827	247	1,159	82	166	12
Testis	Semen may	Tutal 40-69	6.8	0.0	12,090,277	820	6,045,139	753	67	249	505 67	2,418,055	582	238	192	390	48 1,209,02	8 447	373	147	299 3	7 604, 514	329	491	109	220 2	7 120,903	144	676	48	97	12
Testis	Semen may	Total 40-49	10.7	0.0	4,273,065	459	2,136,532	422	37	139	2872 67	854,613	326	83	108	21.8	48 427,30	6 250	209	83	168 3	7 213,653	184	275	61	123 2	42,731	81	378	27	54	12
Testis	Semen any	Total 50-59	6.2	0.0	4,355,391	268	2,177,696	246	n	81	165 67	871,078	190	78	63	127	48 435,53	9 146	122	48	98 3	7 217,770	108	160	35	72 2	43,554	47	221	16	32	12
Testin	Senen may	Total 50-69	4.6	0.0	7,817,213	361	3,908,606	332	29	109	202 67	1,563,443	256	105	85	172	48 781,72	1 197	164	65	132 3	7 390,861	145	216	48	97 2	78,172	63	298	21	43	12
1440m	Semen may	11121 00-/4	2.6	0.0	4,9 29,780	122	1,404,293	112	10	267	79 67	985,957	91	37	02	01	10 1 456 56	y 70	58	156	4/ 3	7 240,489	51	77	17	34 2	49,298	15	105	7	100	- 12
Testin	Same my	Total (all your)	7.2	0.0	17 583 776	2 354	الم _ح يمير (, 98	74	103		1 4913,004	UL/	191	104	41.5		. 44	- 264		310 3	, , , , , , , , , , , , , , , , , , , ,	349	540		101 1		1.35	, 10		104	

Supplementary Table 6c(i). Cancers detected by offering risk stratified screening according to optimised PRS using sensitivity of currently available "real world" screening tools (Cancers of the Breast, Prostate, Colorectum and Pancreas)

								S	creening offer	ed to top			S	creening off	ered to top			S	creening offe	red to top			S	creening of	fered to top			S	creening offe	red to top	
			Annual Incid	lence (per	Dent				50%					209	6 50'				10%					5%) DC'				1%		
			100,000) for	age-band	Popu	lation		_	of PKS	,			_	of Pl	85			_	of PK	5			_	of Pl	KS			_	of PK	<u>,</u>	
Chancer	e						Number	C	Massed (Cancers	Cancers	Number	C	Massed	Cancers	Cancers	Number	C	Missed (Cancers	Cancers	Number	C	Missed	Cancers (Cancers	Number	C	Missed	Cancers C	Cancers
T ype	Second Second Second Second	ulle condita				Cancers arising	requiring	ansing in	ansing in m	issed on d	etected on Percent o	f requiring	arising in	arising in 1	missed on de	etected on Percent o	f requiring	ansing in	arising in m	nissed on d	letected on Percent of	requiring	arising in	anising in	missed on de	tected on Percent of	requiring	arising in	anising in f	issed on det	tected on Percent o
			Male	Fennle	Population Size	per year	screening in	'high risk'	unscreened .	creening a	creening cancers	screening	'high risk' u	unscreened	screening s	screening cancers	screening	'high risk'	unscreened 3	creening	screening cancers	screening	'high risk'	uns creened	screening so	creening cancers	screening	'high risk'	inscreened	creening so	creening cancers
							'high risk'	group	'low risk'	n 'high- i	in 'high- identified	in high	group	'low risk'	in high- i	in high-identified	in high	group	'low risk'	n 'high-	in high-identified	in high	group	'low risk'	in high- is	n 'high- identified	in high	group	low risk	n high- ir	n 'high-id-entifie 12
							group		group ns	k group n	isk group	nsk group		group ^r	isk group n	isk group	risk group		group ni	ac group n	isk group	nsk group		group 1	nak group ris	ik group	nsk group		group n	ic group ris	ac group
Bound																															
Beant	Digital mammography	40 to 44	0.0	124.6	2.054.223	2.559	1.027112	2.004	555	601	1.405 5	5 410.945	1.219	1.940	966	253 9	8 205.422	790	1.769	237	553 22	102.711	457	2.062	149	948 V	4 20.542	157	2.402	47	110
Breant	Digital manuscraphy	45 to 49	0.0	214.8	2,915,479	4,974	1,157,740	9,895	1,079	1,168	2,726 5	5 463,096	2,570	2,604	711	1,659 9	8 291,548	1,537	9,457	461	1,076 22	115,774	966	4,008	290	676 P	4 25,155	905	4,669	92	214
Breant	Digital manageraphy	50 to 54	0.0	279.8	2,964,698	6,616	1,182,919	5,181	1,495	1,554	9,627 5	5 472,928	9,152	9,464	946	2,207 9	8 296,464	2,014	4,572	619	1,491 22	118,292	1,285	5,991	586	900 V	4 23,646	406	6,210	122	2214
Breant	Digital manuscraphy	55 to 59	0.0	285.5	2,119,687	6,052	1,059,844	4,759	1,919	1,422	9,917 5	5 429,997	2,884	5,168	865	2,019 9	8 211,969	1,870	4,182	561	1,909 22	105,984	1,176	4,876	355	825 14	4 21,197	971	5,681	111	250
Baset	Depth scattering appy	60 to 69	0.0	412.3	1,457,174	7443	918,587	4,802	1,397	1,409	4,000 5	5 361,435	3.546	9,997	1 054	2,071 3	8 180519	2 299	5 144	690	1,609 22	91,409	1,446	5,005	302	1012 14	4 18,572	456	6987	114	320
Breat	Digital managerativ	70 to 74	0.0	372.7	1,603,610	5,977	\$01,805	4,680	1,297	1,404	9,276 5	5 920,722	2,848	5,129	854	1,995 9	8 160,961	1,846	4,191	554	1,292 22	30,130	1,161	4,816	948	819 14	4 16,0%	967	5,610	110	257
Breant	Digital manuscraphy	75 to 79	0.0	403.0	1,181,645	4,762	590,828	9,729	1,085	1,119	2,610 5	5 296,329	2,269	2,495	681	1,588 9	8 118,165	1,471	9,291	441	1,090 22	59,002	925	3,897	278	648 l4	4 11,816	292	4,470	88	204
Breant	Digital scattering by	Tatal 40-69	0.0	270.9	12,496,992	35,853	6,248,196	26,509	7,944	7,953	18,556 5	5 2,499,278	16,190	17,729	4,899	11,291 9	8 1,249,639	10,457	29,996	9,197	7,920 22	674,820	6,577	27,276	1,975	4,604 14	4 124,964	2,076	\$1,777	623	1,459
Breant	Digital manusceraphy	Total 40-49	0.0	172.4	4,969,708	7,595	2,184,851	5,899	1,694	1,770	4,129 5	5 8/3,941	3,589	3,944	1,077	2,512 9	8 496,970	2,92/	5,206	658	1,629 22	218,485	1,463	6,070	499	1,024 14	4 43,697	462	7,071	199	\$25
Bennt	Depite examine graphy Depite examine a ratio	Total SIL49	0.0	323.9	1/10/325 \$126.699	26 9 20	4.063.945	20610	5 710	6 189	14.477 5	5 1625 998	12541	19,729	9.262	1,25 3	8 \$12,669	\$ 190	18,190	7,499	5691 22	406 994	5 119	21,207	1.594	1,723 P 9,579 b	4 44,845	1614	34,706	233 ARA	1 190
Broat	Digital manageraphy	Tatal 60-74	0.0	374.2	5,245,574	19,629	2,622,987	15,971	4,258	4,611	10,760 5	5 1,049,195	9,959	10,276	2, 105	6,547 9	8 524,597	6,064	19,565	1,819	4,244 22	262,299	3,819	15,816	1,144	2,669 14	4 52,460	1,204	18,425	961	845
Breant	Digital manusceraphy	Total 40-79	0.0	291.8	15,281,647	44,592	7,640,824	94,919	9,673	10,4%	24,449 5	5 3,056,329	21,247	25,945	6,574	14,875 9	8 1,528,165	19,775	90,817	4,192	9,642 22	764,082	8,663	95,929	2,599	6,064 14	4 152,816	2,795	41,857	\$20	1,914
Breat	Digital managergaby	Total (all ages)	0.0	166.0	35,458,052	55,545																									
Preside																															
Prostate	PSA_3ng/mL cut-off	40 to 44	4.3	0.0	2,021,985		1,010,692	71	17	-48	25 2	6 404,277	45	45	S 1	14 1	6 202,198	90	58	20	10 11	101,069	19	Ð	19	6	7 20,214	6	82	4	2
Presidate	PSA_Sug/mL.cat-off	45 to 49	20.5	0.0	2,251,600	461	1,125,840	\$72	89	253	119 2	6 450,336	295	226	160	75 1	6 225,168	156	905	106	50 11	112,504	101	360	68	92	7 22,517	95	428	25	11
Prostate	PSA_Sug/mL cat-off	50 to 54	75.7	0.0	2,295,475	1,797	1,146,796	1,402	335	953	449 2	6 458,695	886	851	602	248 1	6 229,947	5119	1,148	401	188 11	114,674	579	1,958	258	121	7 22,995	125	1,612	85	40
Peculate	PSA_beg/mil.coll-off DSA_9=stall_out_off	20 to 29 60 to 64	201.8	0.0	1 364 939	4,160	1,030,959	5,007	1 219	9,440	1,0/4 2	6 412,384 6 957.066	\$ 105	3,000	2,190	1036 1	6 176,493	7 191	4 154	1449	451 11	103,056	1 977	3,252	617	150	7 17 649	300	5,880	900	36
Prentate	PSA Sug/mL cat-off	65 to 69	622.7	0.0	1,696,993	10,568	\$48,497	8,528	2,010	5,799	2,729 2	6 999,999	5,990	5,178	3,665	1,725 1	6 169,699	9,584	6,984	2,457	1,147 11	\$4,850	2,906	\$,262	1,568	758	7 16,970	763	9,805	519	244
Prostate	PSA_Sug/mL cat-off	70 to 74	759.8	0.0	1,467,965	11,158	799,943	9,000	2,153	6,120	2,880 2	6 293,593	5,688	5,465	3,868	1,820 1	6 146,797	9,742	7,971	2,572	1,210 11	75,998	2,494	8,719	1,655	779	7 14,680	805	10,948	547	258
Prestate	PSA_Sug/mL cat-aff	75 to 79	867.2	0.0	1,007,965	8,796	503,613	7,019	1,687	4,794	2,256 2	6 201,479	4,455	4,281	3,090	1,426 1	6 100,737	2,962	5,774	2,014	948 11	50,968	1,906	6,890	1,296	610	7 10,074	691	8,105	429	202
Prostate	PSA_Sug/mL cat-off	Tatal 40-69	192.7	0.0	12,090,277	23,299	6,045,199	18,801	4,458	12,784	6,016 2	6 2,418,055	11,882	11,417	8,080	3,802 1	6 1,209,028	7,901	15,998	5,975	2,528 11	604,514	5,064	18,215	3,457	1,627	7 120,908	1,642	21,617	1,144	538
Preside:	PSA_beg/mil.coll-off DSA_Section_cont_off	Tatal 40-49 Tatal 40 59	12.8	0.0	4,275,065	510	2136,532	443	1 190	9,196	142 2	6 871 079	3,007	2,000	2.045	90 1	6 427,306	2,000	9.967	1960	640 11	213,603	1.20	4.5	10	38	7 42,751	40	5470	27	196
Peakate	PSA Sur/nil. cat-off	Tatal 60-69	486.8	0.0	3.461.821	16.853	1,790,911	11.599	9.254	9.247	4.952 2	6 692,964	8.595	8,258	5.844	2,750 1	6 346.182	5,715	11.198	9,886	1829 11	175.091	9.678	19.175	2.501	1177	7 94.618	1.217	15.6%	827	389
Prostate	PSA_Sug/mL cat-off	Total 50-69	291.0	0.0	7,817,219	22,750	1,908,606	18,958	4,992	12,413	5,874 2	6 1,563,443	11,602	11,148	7,889	3,715 1	6 781,721	7,715	15,005	5,246	2,469 11	990,861	4,965	17,785	3,376	1,589	7 78,172	1,642	21,108	1,117	526
Prentate	PSA_Sug/mL.cot-off	Tatal 60-74	568.1	0.0	4,929,786	28,006	2,464,893	22,599	5,407	15,967	7,292 2	6 985,957	14,203	19,729	9,712	4,570 1	6 492,979	9,497	18,509	6,458	9,099 11	346,419	6,112	21,894	4,156	1,956	7 49,298	2,022	25,984	1,975	647
Prostate	PSA_Sug/mL cat-off	Tetal 40-79	296.5	0.0	14,565,608	45,188	7,212,804	94,850	8,998	25,658	11,152 2	6 2,913,122	22,025	21,163	14,977	7,048 1	6 1,456,561	14,645	28,545	9,959	4,687 11	728,280	9,425	99,769	6,409	3,016	7 145,656	3,118	40,070	2,120	998
	ran_agan. mean	TOTAL (ALL NEAL)	100.0	0.0	34,585,425	34,234																									
Calaretal																				1.5											
Colorectal	FIT 20-50 µg/g threshold (CR	40 to 44	14.5	13.5	4,075,608	5%0	2,057,804	425	145	128	258 5	2 815,122	244	\$25	15	171 9	0 407,561	155	417	46	107 15	205,700	99	477	25	65 1.	40,756	2/	545	8	19
Colonetal	FTT 2050 µg/g massicals (CR)	40 to 49	47.1	371	4,567,159	1,047	2,245,540	1.460		234	1022 5	2 913,432	419	1 119	252	519 3	n 465,211	524	1.494	157	967 19	228,238	170	1.699		225 1	1 46,672	94	1364	28	
Colorental	FIT 2050 pg/g threshold (CR)	55 to 59	87.7	60.6	4,181,606	3,094	2,090,808	2,908	786	692	1,615 5	2 \$96,921	1,926	1,768	358	928 9	0 418 161	828	2,266	248	580 15	209,000	508	2,591	151	952 1	1 41,816	148	2,946	45	104
Colorectal	FIT 20-50 µg/g threshold (CR	60 to 64	151.4	91.0	5,602,002	4,945	1,801,001	9,241	1,104	972	2,258 5	2 720,400	1,862	2,415	559	1,908 9	0 960,200	1,163	9,182	949	\$14 15	180,100	707	3,638	212	495 1	1 96,020	208	4,197	63	146
Celerental	FIT 2050 pg/g throhold (CR	65 to 69	198.3	119.1	9,502,183	5,516	1,751,092	4,114	1,402	1,294	2,880 5	2 700,497	2,964	9,152	709	1,655 9	0 950,218	1,476	4,010	449	1,039 15	175,109	1977	4,619	269	628 1	1 95,022	265	5,251	79	185
Colorectal	FTT 20-50 pg/g threshold (CR	70 to 74	273.5	171.2	9,071,575	6,760	1,595,787	5,042	1,718	1,519	3,529 5	2 614,915	2,897	5,863	869	2,028 9	0 907,157	1,809	4,951	545	1,266 19	153,579	1,100	5,660	\$90 800	770 1	1 90,716	924	6,496	97	227
Colorectal	FTT 20-50 pg/g manufald (CR) FTT 20-50 pg/g manufald (CR)	Total 40-69	551.7 80.8	254.8 54.1	2,189,011	6,918]6,590	12 298 995	4,/12	4 201	9,699	3,200 5	2 497,402	7.089	9,447	2 125	4958 9	0 2458667	4.429	4,627	1927	1,140 15 9,096 14	1 229 999	2,634	5,250 19, 24 1	306	120 1	1 245 267	798	15797	298	555
Celerental	FIT 20-50 pg/g threshold (CR)	Total 40-49	19.7	17.7	8,642,767	1,617	4,921,984	1,206	411	962	814 5	2 1,728,559	603	924	208	485 9	0 864,277	435	1,184	190	303 15	492,198	263	1,954	79	184 1	1 86,428	78	1,599	25	54
Colorectal	FIT 20-50 pg/g threshold (CR	Total 50-59	66.4	48.2	\$,\$99,717	5,052	4,419,858	9,768	1,294	1,190	2,638 5	2 1,767,949	2,165	2,887	649	1,515 9	0 \$\$3,972	1,952	9,700	406	946 19	441,986	822	4,290	247	575 1	1 \$8,997	242	4,810	79	170
Celerental	FIT 20-50 pg/g threshold (CE	Total 50-69	114.2	73.6	15,945,902	14,919	7,971,951	11,129	9,790	9,997	7,786 5	2 9,188,780	6,990	8,523	1,917	4475 9	0 1,594,990	9,991	10,922	1,197	2,795 15	797,195	2,426	12,417	728	1,698 1	1 159,499	715	14,198	215	501
Colorectal	FIL 20-50 µg/g Barenhold (CK NTT 10-50 and a thready 11 / 792	10021 60-74 Tatal 40 30	205.9	125.2	10,175,760	16,621	5,067,840	12,396	4,25	5,119	4,6/8 5 15,452 5	2 2,005,152	1,122	9,499	2,157 9,906	4,5460 3	0 1,017,576	4,448	71,005	1,934	5,115 15	306,/86	4,917	13,917 10,707	¥11 1445		1 101,758	19/	15,8,4	139	55% 004
Colorectal	FIT 20-50 pg/g threshold (CE	Total (all ages)	84.5	56.5	66,041 778	42,000	14,943,627	22,063	1,525	0,020	L/06 0	2,303,01	12,067	10,921	3,800	-, I	5 4 58 04,725	1,923	21,085	4,211	دا مەجىر	1,494,963	-1,617	AN, 194	LAND	- 	206,415	1,420	28,106	42.0	304
Fanores																															
Parcesa	CA19-9 20U/mL cutoff	40 to 44	2.6	2.0	4.075.608		2.057.804	74	20	24	50 5	8 \$15,122	45	49	14	90 98	2 407.561	29	65	9	20 21	205.70	12	76	6	12 1	40.76	6		2	4
Pancean	CA19-9_200%mil.contoff	45 to 49	5.6	3.9	4,567,159	215	2,213,510	168	47	54	114 5	8 913,432	102	115	98	69 9	2 456,716	66	149	21	45 21	228,958	42	175	15	28 1	45,672	19	202	4	9
Pancean	CA19-9_200/mil. mioff	50 to 54	10.2	7.3	4,658,111	409	2,329,055	\$20	89	103	217 5	991,622	195	214	63	192 9	2 465,811	126	223	41	86 21	292,906	79	390	26	54 1	46,581	25	984	8	17
Pancean	CA19-9_200/mil. mioff	55 to 59	18.3	13.6	4,181,606	666	2,090,808	522	144	168	954 5	8 \$96,921	917	949	102	215 9	2 418,161	206	460	66	199 21	209,000	129	597	42	\$\$ 19	3 41,816	41	625	19	28
Pancera	CA199_200/mil. mioff	60 to 64	29.2	22.4	5,602,002	926	1,801,001	725	201	299	492 5	3 720,400	441	485	142	299 9	2 960,200	226	640	92	194 21	180,100	180	746	58	122 1	s 96,020	57	869	18	39
Parent	CA19-9_207/mL cmoff	70 to 74	47.2	48.8	3,502,105	1,417	1,751,092	1 976	507	- 27	989 5	5 700,457	877	900	207	456 3	2 907 157	436	1 214	141	962 21	159,570	341	1416	110	291 1	90.716	47 108	1,550	24 95	79
Pancea	CA19-9 200/mil. mioff	75 to 79	86.0	70.8	2,189,011	1,702	1,094,505	1,999	369	429	904 5	8 497,902	\$11	191	261	550 9	2 218,901	526	1,176	169	356 21	109,451	991	1,971	105	224 1	3 21,890	104	1,598	34	71
Pancera	CA19-9_200/ml. mtoff	Total 40-69	17.4	13.0	24,586,669	9,727	12,291,995	2,919	808	940	1,979 5	8 4,917,994	1,776	1,951	572	1,204 9	2 2,458,667	1,151	2,5%	\$71	781 21	1,229,999	724	9,003	295	491 1	3 245,867	229	9,498	74	155
Pancean	CA19-9_200/mail.contoff	Total 40-49	4.2	3.0	\$,642,767	309	4,921,984	242	67	78	164 5	3 1,728,559	147	162	47	100 9	2 \$64,277	95	214	91	65 21	492,198	60	249	19	41 19	3 \$6,428	19	290	6	19
Pancesa	CA199_200/mil.mioff	Lotal 50-59	14.1	10.3	8,899,717	1,075	4,419,858	842	299	2/1	5/1 5	5 1,767,949	512	565	165	947 9	2 1504 972	992	745	10/	225 21	441,586	209	366	6/	142 19	5 88,997	66	1,009	21	45
Parceta	CA199 2076 min	Total 60-74	46.5	34.5	10,175,340	410	5007,000	9,201	209	1 094	2 177 5	8 2095152	1954	2 146	529	1924 9	2 1017576	1,000	2,395	406	859 21	508 788	304	4,7,4 9,909	256	540 1	3 101 752	251	9 249	21	170
Pances	CA19-9 200/mil. mioff	Total 40-79	27.1	21.2	29,847,255	7,196	14,923,627	5,627	1,559	1,812	3,815 5	5,969,451	3,424	3,762	1,102	2,921 9	2 2,984,725	2,220	4,966	715	1,505 21	1,492,963	1,996	5,790	450	947 1	3 294,475	441	6,745	142	299
n	GA100 200 X + 0	T	10.2	15.0	(COU) 77	10.453	1 1 1 1					1					1					1 * * * -					1				

Supplementary Table 6c(ii). Cancers detected by offering risk stratified screening according to optimised PRS using sensitivity of currently available "real world" screening tools (Cancers of the Ovary, Kidney, Lung, Testis)

								Ser	reening offered	to top			Se	reening offe	ared to top			5	Screening offe	ared to top			5	Screening off	ered to top			S	creening off	ared to top		
			Annual Incide	ence (per					50%					20%	i i				10%	•				5%					1%			
			100,000) for a	ge-band	Pop u	lation			of PRS					of PR	s				of PR	s				of Pl	RS				of PF	5		
									Missed _					Missed					Missed					Missed					Missed		_	
Gamer	Screening sensitivity	AgeGroups					Number	Cancers	cancers .	ncers Cancers		Number	Cancers	cancers	Cancers C	ancers	Number	Cancers	cancers	Cancers C	ancers	Number	C ancers	cancers	Cancers	Cancers	Number	Cancers	cancers	Cancers C	ancers	
Lype			Mala	Family	Den ulation Sim	Cancers arising	requiring	arising in a	rising in mis	sed on detected on	Percent of	requiring	arising in a	nising in n	missed on det	ectes on Percent o	requiring	arising in	arising in "	nissed on det	ectes on Percent of	requiring	arising in	arising in	missed on d	setected on Percent of	requiring	arising in	arising in f	assed on det	tected on Per	cent of
			Male	rennie	Population Size	per year	'high rist'	high risk' ur	nscreened in	high in high	identified	in bish	high risk' ur	nscreened	in "high, in	reening cancers bigh, identifie	in 'high	'high risk'	unscreened	in "high in	reening cancers thigh, identified	in 'high	'high risk'	uns creen ed	in 'high-	in high, identified	in high	'high risk'	anscreened	creening so in 'high, it	creening ca n "high-ida	ancers anti-fiad
							Provo	group '1	low risk risk	remo nik' remo	identitied	risk' remo	group '1	ow risk	ak' romo da'	k' moun	risk group	group	'low risk'	sk'renno dil	k' enno	risk' group	group	'low risk'	ist' group a	ni ngn- roannes	risk group	group	'low risk'	al amo cir	ir mgn- 100 ir remo	in nes
							Freeb		group	Brook und Brook		mit groop		group	an groop in	in Brook	the group		group	in group in	a prosp	non Broop		group .	in group i	in prop	non groop		group	a group in	a groop	
Overv																																
Overv	MMS (CA-125 + TVU)	40 to 44	0.0	13.2	2.054.223	270	1 027 112	187	85	90 157	3	410.845	100	170	16	84 3	1 205.422	59	211	9	50 14	102.711	94	2%	6	29 11	20.542	9	261	<u> </u>	1	9
Ovary	MMS (CA-125 + TVU)	45 to 49	0.0	19.4	2,915,479	448	1,157,740	911	157	50 261	58	463,096	165	283	26	199	1 291,548	58	950	16	89 14	8 115,774	57	991	9	48 11	23,155	15	495	2	19	9
Ovary	MMS (CA-125 + TVU)	50 to 54	0.0	27.1	2,964,698	640	1,182,919	444	196	71 575	58	472,928	296	404	98	198 5	1 236,464	140	500	22	118 11	8 118,292	12	558	19	69 11	23,646	22	618	4	19	9
Ovary	MMS (CA-125 + TVU)	55 to 59	0.0	34.8	2,119,687	798	1,059,844	512	226	\$2 490	58	429,997	272	466	44	229	1 211,969	162	576	26	196 14	8 105,984	94	644	в	79 11	21,197	25	719	4	21	9
Ovary	MMS (CA-125+ TVU)	60 to 64	0.0	41.6	1,897,174	764	918,587	530	294	85 445	58	967,495	282	4112	45	257	1 189,717	168	596	27	141 11	8 91,899	97	667	16	\$2 11	18,972	26	738	4	22	9
Ovary	MMS (CA-125 + TVU)	66 to 69	0.0	52.3	1,805,190	944	902,595	655	2319	105 550	58	961,098	948	596	56	295 5	1 180,519	207	757	<u>99</u>	174 11	8 90,260	120	\$24	20	101 11	18,052	92	912		27	9
Ovary	55 (CA-125 + 1VU)	70 to 74	0.0	60.8	1,605,610	90	201,205	6//	258	108 568	38	\$20,722	960	615	38	302	1 160,961	214	761	94	130 13	8 30,130	1244	301	20	104 11	16,0%		941		25	
Ovary		T 4 40 40	0.0	20.4	1,161,640	9.004	594,823	2640	1164	422 2.217	26	236,329	1 409	2.401	716	1170	1 1 240 630	191	2 (77)	199	201 14	a 59,082 a 614,910		10/	14	50 II 409 II	124 064	191	9.679		25	2
Ovary	MMS (CA-125+ TVD)	Total 40.49	0.0	164	4 969 708	718	2124.25	498	220	30 419		173 941	265	453	40	228	496 970	157	4,970	35	192 11	8 718.485		6%	15	77 11	43,607	25	698	4	21	
Overy	MMS (CA.125 + TVD)	Total 50.59	0.0	30.7	4 494 925	1 978	2 242 163	956	472	153 203		396365	508	100	11	477	448.499	902	1076	418	254 11	204 216	176	1 202	21	142 11	44,245	47	1 991		40	9
Ovary	MAG (CA-125+ TVU)	Total 50-69	0.0	38.0	\$,125,689	3.086	4063.945	2.141	945	345 1.799	3	1.625.998	1.199	1.947	182	956	1 \$12.669	677	2,409	106	568 14	8 406.994	394	2.692	65	991 11	\$1,267	106	2.940	17	89	9
Ovary	MMS (CA-125 + TVU)	Tatal 60-74	0.0	51.1	5,245,974	2,613	2,622,987	1,962	\$21	298 1,564	58	1,049,195	990	1,699	158	#91	1 524,597	588	2,095	94	494 11	8 262,299	942	2,941	55	228 11	52,460	92	2,591	15	78	9
Ovary	MMS (CA-125+ TVU)	Total 40-79	0.0	37.0	15,281,647	5,651	7,640,824	9,921	1,790	627 9,294	58	3,056,329	2,085	3,566	994	1,751	1,528,165	1,299	4,412	198	1,041 11	8 764,082	721	4,990	115	606 11	152,816	195	5,456	51	165	9
Ovary	MMS (CA-125 + TVU)	Total (all ages)	0.0	22.8	35,458,052	7,495																										
Kilmey																																
Kidney	USS	40 to 44	10.1	5.0	4.075.608	907	2.057.804	237	70	64 173	56	\$15,122	141	166	38	105	4 407.561	90	217	25	66 21	1 205.780	56	251	ß	41 19	40.756	17	290	5	19	4
Kniney	065	45 to 49	17.7	7.8	4,567,159	580	2,289,580	447	199	121 326	56	915,452	267	SIS	72	195	456,716	171	409	46	125 21	1 228,958	106	474	29	77 19	45,672	95	547	9	24	4
Kidney	USS	50 to 54	26.8	12.7	4,658,111	915	2,329,055	705	210	191 514	56	991,622	421	494	114	907 5	4 465,811	270	645	75	197 21	1 292,906	168	747	45	122 19	46,581	52	863	14	9 8	4
Kniney	USS	55 to 59	37.1	18.6	4,181,606	1,160	2,090,803	894	266	242 652	56	\$\$6,321	594	626	145	949 9	418,161	942	818	99	249 21	1 209,000	219	947	58	155 19	41,816	66	1,094	18	48	- 4
Kidney	OSS	60 to 64	53.7	26.2	3,602,002	1,429	1,801,001	1,102	927	299 805	56	720,400	658	m	178	479 5	14 960,200	421	1,008	114	907 21	1 180,100	262	1,167	71	191 19	96,020	81	1,948	22	59	4
Koney	USS	60 to 69	73.9	36.4	9,502,005	1,911	1,751,092	1,473	498	999 1,074	56	700,457	\$/9	1,042	258	641 5	4 950,218	565	1,948	159	410 21	1 175,109	990	1,561	95	255 19	95,002	106	1,805	29	79	4
Kiney	000	701074	91.2	40.1	2,110,011	2,062	1,004,505	1,976	4/3	401 1,159	20	614,313	949	1,114	207	500	M 307,157	506	1,400	149	443 21	1 100.451	276	1,450	102	2/6 19	21,900	101	1,694	22	85 74	4
Kulmey		Tabl 40.49	34.6	16.9	24,536,649	6902	12 298 995	4 252	1 444	1 516 5 541		4917994	2 900	S.402	76	2114	4 7458667	1 #57	4 445	508	1954 21	1 1 229 333	1155	5147	919	342 19	245,857	956	5946	97	260	
Katary	USS	Tatal 40-49	14.1	6.5	8.642.767	#7	4 921 984	684	203	185 498	56	1728 559	408	479	111	298	4 864,277	261	636	71	191 21	1 492.198	162	725	44	118 19	\$6.428	50	\$57	14	\$7	4
Kidney	USS	Total 50-59	31.7	15.5	8,899,717	2,075	4419,858	1,599	476	495 1,166	56	1,767,943	955	1,120	259	696	4 \$3,972	611	1,464	166	446 21	1 441,906	380	1,695	105	277 19	\$8,997	117	1.958	S2	85	4
Kniney	USS	Tatal 50-69	45.8	22.6	15,945,902	5,415	7,971,951	4,174	1,241	1,191 9,049	56	3,188,780	2,492	2,923	675	1,817 5	1,594,990	1,595	9,820	492	1,163 21	1 797,195	992	4,429	269	725 19	159,499	906	5,109	85	223	4
Kidney	OSS	Total 60-74	71.8	35.5	10,175,760	5,408	5,087,880	4,165	1,238	1,129 9,096	56	2,085,152	2,486	2,917	674	1,815	14 1,017,576	1,592	9,811	491	1,160 21	1 508,788	990	4,419	268	722 19	101,758	905	5,098	\$5	223	4
Kniney	065	Tatal 40-79	45.5	23.0	29,847,255	10,150	14,923,627	7,824	2,326	2,120 5,704	56	5,969,451	4,671	5,479	1,266	9,405	4 2,914,725	2,990	7,160	\$10	2,180 21	1 1,492,963	1,899	8,291	504	1,956 19	298,475	574	9,5%	155	418	4
Kriney	OSS	Total (all ages)	29.2	14.8	66,041,278	19,929																										
Lang																																
Lang	Low dose CT	40 to 44	6.0	5.8	4,075,608	240	2,037,804	176	64	27 149	62	\$15,122	99	141	в	34	6 407,561	61	179	9	52 2.	2 205,780	57	205	6	S1 19	40,756	11	2.29	2	9	4
Long	Low done CT	45 to 49	16.3	14.7	4,567,159	706	2,289,580	518	188	80 498	Q	915,452	292	414	45	247 5	6 456,716	180	526	28	152 22	2 228,958	108	598	17	92 19	45,672	51	675	5	26	4
Long	Low done CT	50 to 54	33.4	31.5	4,658,111	1,512	2329,055	1,108	404	171 998	62	991,622	625	38/	56	5/3	6 465,811	380	1,127		526 Z.	2 212,506	252	1,200	36	196 19	46,581	6/	1,445	10	57	4
Long		20 to 29	/1.4	124.0	4,161,605	4,850	2,090,805	4123	1.067	- 12/ L, 150	0	406,521	1046	2,700	184	1.667	5 416,151	4C1 1.200	4,156	114	624 22	2 209,000	444	4,452	111	10 10	41,816	128	4,500	20	176	4
I mark	Low doile CT	65 to 69	229.5	197.8	\$ 502 185	7466	1,251,092	5409	1,998	345 4 690	60	700497	5 084	4 980	45	2609	5 950218	1,902	5 564	298	1,609 22	2 130,100	1 144	6922	126	958 19	5,002	990	7196	51	779	- 4
Law	Low done CT	70 to 74	335.0	278.1	3,071,575	9,978	1,595,787	6,875	2,508	1,059 5.816	62	614,915	9,874	5,504	597	9.278	5 907,157	2,990	6,988	368	2,022 2.	2 153,579	1,497	7,941	221	1,216 19	90,716	414	8,964	64	950	4
Long	Low done CT	75 to 79	462.2	340.5	2,189,011	8,680	1,094,505	6,969	2,917	980 5,985	Ø	497,902	3,586	5,094	552	3,034	5 218,901	2,212	6,468	941	1,871 22	2 109,451	1,990	7,950	205	1,125 19	21,890	985	\$,297	59	324	4
Lang	Low done CT	Total 40-69	74.8	68.0	24,506,669	17,591	12,299,995	12,851	4,610	1,979 10,872	62	4,917,994	7,249	10,288	1,115	6,127	5 2,458,667	4,467	19,064	688	9,779 2ž	2 1,229,399	2,686	14,845	414	2,272 19	245,867	774	16,757	119	655	4
Long	Low done CT	Total 40-49	11.4	10.5	8,642,767	946	4,921,984	693	253	107 587	Ø	1,728,559	991	555	60	991 9	6 \$64,277	241	705	\$7	204 2	2 492,198	145	\$01	22	125 19	\$6,428	42	904	6	95	4
Lang	Low done CT	Tatal 50-59	51.4	48.4	8,899,717	4,408	4,419,858	9,291	1,177	468 2,754	62	1,767,949	1,821	2,517	220	1,541 5	B 889,972	1,125	9,225	175	950 22	2 441,986	675	9,799	104	571 19	88,997	195	4,219	50	165	4
Long	Low down CT	Total 50-69	227.8	98.9	שפ, פפע, כו חשר אדו חו	16,510 71 444	5.087,890	15,001	4,427	1,8/2 IU,205 7,499 19,949	62	2,095,152	6,802 8,905	9,755	1,005	- 5,191 S	6 1017576	4,25	16,069	846	1,575 Z. 1,647 Y	24 797,195 21 508,799	4,541	14,044	509	2,150 19	109,409	755	20,60%	115	805	- 4
Law	Low done CT	Total 40-79	127.8	111.1	29 \$47 256	95 580	14 923 627	26.089	9 500	4 018 22 077	6	5969.451	14 709	20 886	2.264	12.499	5 2914 775	9 0 69	26 520	1997	7672 2	2 1 492 943	5.4%	90,196	240	4619 19	298.479	1572	94.017	242	1990	- 4
Long	Low done CT	Total (all ages)	90.6	70.1	66,041,278	41,549				.,	.	-,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,	1 9.005					.,			.,	1,00,00	.,		0							Ĩ
T entin											_			_														_				
Tar	Saman 20 9207	40 to 44	12.3	0.0	2 (12) 985	7.42	1.010.692	296	12	78 148	64	404.777	197	51	65	192 4	8 202 199	IE	17		108 44	9 101 049	126	122	41	84 94	20.214	PA -	15	21	42	17
Teri	Semen anay	45 to 49	9.4	0.0	2,251,600	211	1,125,840	201	10	66 195	64	450,396	168	45	55	112	3 225,168	131	74	45	92 4	9 112,504	107	104	-1	72 94	22,517	55	158	18	36	17
Tentin	Semen anay	50 to 54	7.0	0.0	2,295,475	160	1,146,796	152	8	50 102	64	458,695	127	98	42	85	8 229,947	104	56	94	69 49	9 114,674	81	79	27	54 94	22,995	41	119	19	27	17
Testin	Semen anay	55 to 59	5.2	0.0	2,061,919	108	1,030,959	103	5	34 6 9	64	412,984	86	22	28	57 5	3 206,192	70	98	25	47 45	9 105,096	55	53	18	97 94	20,619	27	81	9	18	17
Ter	Semen 2012y	60 to 64	3.0	0.0	1,764,828	52	\$12,414	49	9	16 99	64	952,966	41	11	14	28	8 176,483	94	18	11	29 49	9 \$8,241	26	26	9	18 94	17,648	19	99	4	9	17
Testin	Semen anay	65 to 69	2.4	0.0	1,696,993	41	848,497	99	2	19 26	64	\$19,399	99	1	11	22	8 169,699	27	14	9	18 49	9 \$4,850	21	20	7	14 94	16,970	10	S 1	9	7	17
Terfin	Semen anay	70 to 74	2.4	0.0	1,467,965	95	735,943	99	2	11 22	64	293,593	28	7	9	19	8 146,797	25	12	7	15 49	5 75,998	18	17	6	12 94	14,600	9	26	9	6	17
	Semen 2012	73 10 79	1.4	0.0	1,007,965	14	503,643	13	1	4 9	64	201,4/5	11	200	4	7	5 100,757	9	5	5	6 4	3 50,368 m	7	7	2	5 94	10,074	4	10	117	2	17
Tere	Sense Altay Some way	Total 40.49	6.8	0.0	6,762,796 12,090,777	1,406	6045199	1,296	- 40	-++2 897 258 419	64	2,418,055	651	169	215	496	8 1 209 07*	491	490	175	956 4	9 409,097	/12 A)4	404	197	- 4// 54 - 772 94	120.909	300	612	68	199	17
Ter	Semen and y	Total 40-49	10.7	0.0	4 775 065	450	2196592	497	2	144 269	64	154619	964		120	244	8 427 906	297	167	98	199 49	9 219 659	299	225	77	156 94	42,791	116	949	98	78	17
Terin	Semen anay	Total 50-59	6.2	0.0	4,955,991	268	2,177,696	255	19	\$4 171	64	\$71,078	215	55	70	145	8 485,539	174	94	57	116 4	9 217,770	196	192	45	91 94	45,554	68	200	22	45	17
Teri	Semen anay	Total 50-69	4.6	0.0	7,817,219	961	3,908,606	944	17	119 290	64	1,569,449	227	74	95	192	8 781,721	294	127	77	157 49	990,961	185	178	60	125 94	78,172	91	270	30	61	17
Terlin	Semen 2012y	Total 60-74	2.6	0.0	4,929,786	128	2,464,893	122	6	40 82	64	985,957	102	26	94	68	8 492,979	85	45	27	56 45	9 246,419	65	63	21	49 94	49,298	\$2	96	11	22	17
Ter	Semen 2012y	Total 40-79	6.0	0.0	14,565,608	\$69	7,282,804	\$27	42	275 554	64	2,919,122	690	179	228	462	3 1,456,561	563	906	196	977 49	9 728,280	440	429	145	295 94	145,656	2:20	649	79	147	17
1 enfor	Semen an ray	Lotal (all accu)	1.2	0.0	\$2.585,226	2.954																										

Supplementary Table 7a(i). Cancers detected by offering risk stratified screening according to current PRS using an idealised screening tool with a sensitivity of 0.8 (Cancers of the Breast, Prostate, Colorectum and Pancreas)

Caser Age Group Male Female Population Size Number requiring arising in high high isk group Number screening high group Number arising in high high isk group Number arising in high high isk group Number high high high high high high high high	Number requiring screening in high prop Mines mission mission in high prop Cances mission in high prop Cances mission in high prop Cances mission in high prop Cances mission in high prop Cances mission in high prop Cances mission in high prop Cances mission prop Cances mission mission prop Cances mission mission prop Cances mission mission prop Cances mission mission prop Cances mission prop Cances mission prop </th
Break A A A A A A A A A A A A A A A A A A A	102,711 939 2,226 67 266 10 20,542 90 2,469 18 72 9 115,774 646 4,928 129 517 10 23,155 176 4,798 35 140 9 118,272 860 5,756 172 648 10 23,155 176 4,798 35 140 9 105,984 707 5,265 172 648 10 22,197 214 5,184 43 171 9 9,1859 807 5,402 161 645 10 11,972 2,19 5,950 44 175 9
	102,711 393 2,225 67 266 10 20,242 90 2,469 18 72 9 115,774 646 4,922 129 517 10 23,155 176 4,798 95 M0 9 118,724 646 4,922 129 5,766 172 648 10 23,155 176 4,798 95 M0 9 118,252 860 5,756 172 648 10 23,165 234 6,582 47 187 5 105,594 707 5,265 157 629 10 21,197 214 5,383 43 171 5 91,859 807 5,402 16 646 10 18,172 219 5,590 444 175 5
Breat 40 to 44 0.0 124.6 2,054,223 2,559 1,027,112 1,765 773 957 1,429 56 410,845 955 1,604 191 764 30 205,422 570 1,989 114 455 118	115,7/4 646 4,502 129 517 10 25,155 16 4,708 35 140 3 118,232 860 5,755 172 648 10 23,645 234 6,342 47 187 S 105,984 747 5,265 172 648 10 21,197 214 5,981 43 171 S 91,899 807 5,402 161 646 10 18,972 219 5,990 44 175 S 90,899 807 5,402 161 646 10 18,972 219 5,990 44 175 S
11 meant 10 to 19 0.0 214.8 (2,315,479 4,974 1,57,470 3,471 2,503 694 2,777 56 463,026 1,256 3,118 371 ,435 360 251,548 1,107 3,186 21 2,12 386 18 18 18 18 18 19 19 19	105,984 787 5,265 157 629 10 21,197 214 5,838 43 171 3 91,899 107 5,402 161 646 10 18,972 219 5,990 44 175 9 97,70 577 6,707 10 10 10 10 10 10 10 10 10 10 10 10 10
Breart 55 to 59 0.0 285.5 2,119,687 6,052 1,059,844 4,224 1,828 845 3,379 56 429,957 2,259 3,793 452 1,807 30 211,969 1,948 4,704 270 1,078 18	91,859 807 5,402 161 646 10 18,372 219 5,990 44 175 3
Brezent \$01o 54 0.0 338.0 [1577]74 5,209 915,577 4,939 1176 557 3,466 56 567,457 2,317 3,592 468 1,554 30 183,717 1,942 4,527 276 1,105 18 Brezent 61o 50.9 0.0 4123 1,205 190 7,445 190 7,575 5194 7,249 1,109 4,155 55 56 10518 7,778 4,455 55 72.2 10 105 191 6157 528 931 1926 18	10/20 10/ 54/5 197 //4 UL 18/02/ 207 /18U 27 200 210 2
Brezet 70 to 74 0.0 372.7 1,620,610 5.977 801,805 4,171 1,806 824 3,397 56 320,722 2,231 3,746 446 1,785 30 160,361 1,531 4,646 266 1,045 18	80,180 777 5,200 155 621 10 16,036 211 5,766 42 169 3
Breast 75 to 79 0.0 403.0 []181,645 4,762 590,723 3,523 1,499 665 2,659 56 246,529 []777 2,2985 355 1,422 30 [18,165 1,060 3,702 212 848 18]	59,082 619 4,143 124 495 10 11,816 168 4,594 94 194 9 674,920 4,400 29,453 880 9,520 10 124,954 1,195 97,658 299, 956 9
Breat Total 40-49 0.0 17.21 4 (396) 7558 (21455) 5,57 2,276 1,051 4/206 56 873541 2,411 4/722 562 2,289 30 45570 1,577 5,565 395 1,942 18	218,485 979 6,554 196 783 10 43,697 266 7,267 53 213 5
Breamt Tuda 50.59 0.0 222.5 (4484,325 12,5648) 2,242,163 8,911 9,327 1,768 7,073 56 895,855 4,728 7,940 946 9,782 50 448,479 2,221 9,947 564 2,256 18 Breamt Tuda 50.50 0.0 333 0 915,668 7,940 945 9,969 7,957 9,57 1,768 7,073 56 895,856 4,728 7,940 946 9,785 91 9	224,216 1,616 11,022 329 1,317 10 44,843 447 12,221 89 958 3 406,334 9,471 27,930 684 7,797 10 91,267 979 25,991 195 349 9
mmen 1004 0-97 0.0 22.2 € 1.0.007 0.0 22.2 € 1.0.007 0.0 100 0.0 10,000 0.0 10,000 0.0 10 1000 0.0 1	262,259 2,551 17,078 510 2,041 10 52,460 699 18,996 199 554 3
Breast 10-29 0.0 291.8 5281,647 45.952 7,640,824 91,120 13,472 6,224 24,896 56 3,056,329 16,648 27,949 3,528 13,514 30 1,528,165 9,929 34,668 1,986 7,948 18	764,082 5,795 38,797 1,159 4,636 10 152,816 1,574 46,018 915 1,259 9
Provente 0 to 44 4.3 0.0 2.020,385 88 1.010.692 68 20 14 54 62 404.277 40 48 8 52 57 202.198 26 62 5 21 23	101,069 16 72 3 15 15 20,214 5 13 1 4 4
Prostate 45 to 49 20.5 0.0 2,251,660 461 1,125,440 355 106 71 224 62 450,336 211 250 42 169 37 225,166 135 326 27 106 23	112,584 84 977 17 67 15 22,517 26 495 5 21 4
Provate \$10 to \$4 75.7 0.0 2299,473 1,7371 1,146,716 1,137 40 257 1,069 62 451,695 737 940 199 637 371 229,447 229,447 102 407 23 102 407 23 102 407 23 102 407 23 102 407 23 102 407 23 102 407 23 102 407 23 102 407 23 102 407 23 102 407 23 102 407 23 102 407 23 102 407 102 102 102 102 102 102 102 102 102 102	114,674 916 1,421 69 259 15 22,995 97 1,640 19 78 4 109,096 758 9,402 152 606 15 20,619 299 9,927 47 187 4
Prostate \$0 to 64 356.1 0.0 1.764,822 6.285 882,414 4.887 1.448 967 3,870 62 992,966 2,882 3,403 576 2,306 37 178,483 1.843 4,442 969 1.474 23	28 ,241 1,145 5,140 229 916 15 17,648 952 5,933 70 282 4
Proventing 65 to 69 622.7 0.0 1,656,995 10,5542 444,497 2,135 2,425 1,527 6,507 62 393,999 4,446 5,722 969 3,577 37 169,699 3,099 7,469 520 2,479 23	\$4,850 1,525 \$,643 3 \$ 5 1,540 15 16,970 592 9,976 11 \$ 474 4
Nonate 01017 122-3 03 1440,002 11,122 122,040 4,042 4,111 04007 02 124,111 04007 02 1400 1,011 04007 100 1400 100 1400 140 140 140 140 140 1	50,568 1,591 7,145 918 1,279 15 10,074 490 8,246 98 992 4
Prostate 15:42 10:52 12:02 12:	604,514 4,243 19,056 \$49 9,395 15 120,303 1,306 21,993 261 1,045 4
Product 1043 40-99 12.43 0.01 4,27,005 >>99 2,136,574 4.25 1.26 15 534 6.27 457,615 2.52 297 50 4.01 37 4.27,006 1.61 544 3.2 1.72,65 4.165 544 1.265 2.57 1.57 1.57 1.57 1.57 1.57 1.57 1.57 1	213,553 100 449 20 80 15 42,731 31 518 6 25 4 217,770 1,074 4,823 215 859 15 43,554 331 5,566 66 264 4
Prosente Tand 60.69 485.8 0.0 3.461.021 16.053 1.730.911 12.970 3.003 2.594 10.376 62 692.364 7.720 9.125 1.546 6.102 37 346.102 4.942 11.911 900 3.953 2.3	173,091 3,069 13,784 614 2,455 15 34,618 945 15,908 189 756 4
Provatize 1364/30-99 291.0 00 (217,213) Z2,700 3,9005,606 17,909 5,241 3,502 14,007 621 1,554,43 10,452 12,318 2,006 8,346 37 1701,721 6,671 16,079 1,134 5,357 25 Provatize 1364,074 558.1 0.0 4.923,765 20,006 2,464.893 21,554 6.452 4.311 17,243 62 985,577 12,461 15,164 2,586 10,274 37 492,97 8,212 15,164 2,570 251	990,861 4,143 18,607 829 9,315 15 78,172 1,275 21,475 25 1,020 4 246,489 5.101 22.905 1.020 4.080 15 49.298 1.570 26.496 314 1.256 4
Prostate Table 40.79 2865 0.0 14,555,602 49,182 7,282,804 99,538 9,950 6,648 26,590 62 2,919,122 19,804 29,984 9,961 15,843 37 1,456,561 12,664 90,534 2,533 10,191 29	728,280 7,866 35,322 1,573 6,292 15 145,656 2,421 40,767 484 1,997 4
Hvoatte 15dal (all ages) 183.3 U.0 32,581,228 52,224	
Calenced 0 10 0 4 14 5 13 5 4 075 070 570 12 01/ 100 570 107 76 907 53 915 127 107 570 98 154 77 407 561 111 499 77 99 156	2019 200 69 507 19 50 9 40 256 16 554 9 19 2
Conversal 516 49 24.4 21.6 4.567.16 104 105 106 105 109 555 109 555 51 914.422 353 694 71 262 71 456,76 224 845 41 165 16	228,358 116 991 23 99 9 45,672 90 1,017 6 24 2
Colorental \$0 to \$4 47.1 \$7.1 4(58),111 1,958 2(392,055 1,268 560 260 1,019 59) \$91,522 660 1,258 132 528 27 465,811 \$941 1,577 76 905 16	232,906 216 1,742 43 173 9 46,581 56 1,902 11 44 2
Conversal 3710 77 00.1 131.4 901 131	180,100 480 3,865 96 384 9 36,020 123 4,222 25 99 2
Colorestal 65 to 69 1983 1191 1 5502,185 5516 1 751,092 3,663 1 1558 732 2,926 59 700,497 1 1559 3,657 972 1,447 77 992,018 1074 4,442 215 859 16	175,109 609 4,907 122 448 9 95,022 156 5,960 91 125 2
ucunerate nu ser 2000 114 2 3.011.572 5.0104 5.018 1094 505 4.148 2.129 8.5351 59 45732 2.128 4.180 4.	109,451 698 5,620 140 558 9 21,890 179 6,199 36 143 2
Colorental Tatal 40.69 80.8 54.1 24,556,669 16,530(HWHWHWHW 10,951 5,569 2,192 17,69 39 4,917,934 5,570 10,950 1,114 4,655 27 2,457,667 3,219 13,511 644 2,575 16 1	1,229,338 1,426 14,704 365 1,461 9 245,867 469 16,061 94 575 2
ucionenzi lintari 1949 1977 1977 1977 5022 41,1978 1,1072 549 214 1058 591 1,725 55 549 1,172 109 436 271 1057,291 51,302 61 252 16 Colonenzi lintari 1949 66,4 432 1,238,717 5,052 4,41,928 3,550 1,702 670 2,580 591 1,779,493 1,702 5,350 340 1,352 271 105,772 544 4,068 197 787 16	432,138 179 1,438 36 143 9 86,427 46 1,571 9 37 2 441,986 558 4,494 112 447 9 88,397 143 4,909 29 115 2
Celevental Tuda 50.69 114.2 73.6 15.945,002 14.913 7.971.951 9,389 5,003 1.978 7,911 39 5,3887,780 5,025 9,3888 1,005 4,000 27 1,594,990 2,904 12,009 581 2,323 16	797,195 1,648 13,265 390 1,318 9 159,439 423 14,490 85 338 2
Colorestal Total 60.74 203.9 125.2 10.175,760 16.521 5087,380 11.021 5500 2,204 8,817 591 2,095,152 5,601 11.020 1,120 4,481 271 1,017,576 3,256 113,985 647 2,589 16 Colorestal Total 0.79 119 0 8.04 2987,755 29.662 Meanweave 19 642 9.976 9.926 15.706 51 5.996 51 9.976 19.631 9.995 7.982 721 2,984 725 576 524 642 16 1	508,788 1,836 14,785 967 1,469 9 101,758 471 16,150 94 577 2 1492,963 9.771 26,997 654 2,617 9 298,473 840 28,768 168 672 2
Colorectal Total (all agen) 84.5 56.5 66,041,278 42,285	
Parenta da la companya de	
Panaroma 10 to 44 2.6 2.0 4.075,031 94 2.057,031 57 37 11 46 49 815,122 27 67 5 22 29 407,561 15 79 9 12 19 Panaroma 15, 15, 19 9 12 19	209,780 8 86 2 7 7 40,756 2 92 0 2 2 279 958 19 195 4 15 7 45,572 4 211 1 4 2
Parates 50 16 54 10.2 7.3 4,658,111 409 2,328,055 250 159 50 200 49 59,1522 118 291 24 54 25 46 14 56 544 15 52 15	232,906 35 374 7 28 7 46,581 8 401 2 7 2
Pmanuar 55 to 59 18.3 13.6 (4.118),056 666 (2000,050 407 259 81 326 49 856,521 192 474 38 155 27 418,161 106 560 21 85 19 manuar 2014 (4.119),056 100 100 100 100 100 100 100 100 100 10	209,080 58 608 12 46 7 41,816 14 652 9 11 2 189,000 90 946 16 64 7 96,000 10 907 4 16 2
remitive στιν στι	160,100 e0 e+0 16 64 7 36,020 19 907 4 15 2 175,109 122 1,295 24 98 7 95,022 29 1,988 6 23 2
Parame 70 to 74 664 48.8 3077,575 1,777 1,575,787 1,074 643 225 859 49 64,915 506 1,251 101 405 23 307,575 1,779 1,478 56 223 13	153,579 152 1,605 90 122 7 90,716 96 1,721 7 29 2
pramovani priso /2 90.0 //2.4 (zev.ut.) 1, ///2.1 (294), 200 1, 040 200 2, 207 1, 207 1, 207 2, 201	100,451 147 1,555 29 118 7 21,850 35 1,667 7 28 2 1,229,338 322 3,405 64 258 7 245,867 76 3,651 15 61 2
Panarea Ind 40.49 4.2 3.0 4.642,767 300 4.321,364 189 120 38 151 49 1,722,553 89 220 18 71 29 864,277 49 260 10 99 13	492,138 27 282 5 21 7 85,428 6 909 1 5 2
Prancense 1.642/39/29 14.1 10.3 5ξ.πτρ./17 1.075 4.19.253 657 418 131 525 491 767.943 309 766 62 248 23 553,572 171 904 34 157 154 157 154 156	441,5985 575 5977 4 7 \$82,597 22 1,053 4 18 2 797,195 295 3,123 59 236 7 159,499 70 3,948 14 55 7
Panerea Total 60-74 46.5 34.5 10,175,76 651 3,449 130 5,007,980 2,505 1,595 501 2,004 49 2,035,152 1,180 2,520 226 944 224 1,077,576 651 3,449 130 521 15	508,788 954 9,746 71 284 7 101,758 84 4,016 17 67 2
Pancovan 1564 40-79 27.1 21.2 29267,255 7,1865/#WWWWWW 4,991 2,795 878 5,512 49 5,969,451 2,068 5,118 414 1,655 29 2,988,725 1,141 6,045 228 919 19 1 Pancovan 1564 40 args 19.3 15.0 66,001,778 10,452	1,492,363 621 6,565 124 497 7 298,473 147 7,039 29 118 2

Supplementary Table 7a(ii). Cancers detected by offering risk stratified screening according to current PRS using an idealised screening tool with a sensitivity of 0.8 (Cancers of the Ovary, Kidney, Lung, Testis)

		Annual (per 100,0	Incidence 00) for age-				5	Screening of 509	Fered to top %			s	creening of 20	fered to top %				5	creening of 109	fered to top				s	creening of 5%	Fered to top				Ser	eening offe 1%	red to top		
Салаат Туре	Аде Стоция	ba Male	Female	Popul Population Size	Cancers arising	Number requiring screening in 'high risk' group	Cancers arising in 'high risk' group	of P. Missed cancers anising in unscreened 'low risk'	Cancers missed on screening in 'high- risk' group	Cancers detected on Percent of screening cancers in 'high- identified risk' group	Number requiring screening in 'high risk' grown	Cancers arising in 'high risk' group	of P Missed cancers arising in susceened 'low risk'	Cancers missed on screening in "high- risk" group	Cancers detected on P screening in 'high- it risk' group	ercent of cancers dentified	Number requiring screening in 'high risk' group	Cancers arising in 'high risk' group	of P Missed cancers arising in unscreened 'low risk'	Cancers missed on screening in 'high- nisk' grown	Cancers detected on Pero screening can in 'high- iden nisk' group	Notent of requirements and requirements	iumber (quiring a reening 'h h 'high k' group	Cancers ising in igh risk'u group	of P Missed cancers arising in anscreened 'low risk'	Cancers missed on screening in 'high- risk' grown	Cancers detected on Percer screening canc in 'high- identi nisk' group	Nur requirs screet ied in t	nber Canc ning arising ning 'high s tigh group	bers c g in ari risk' un up 'lo	of PR dissed cancers rising in screened iscreened iow risk'	S Cancers hissed on d creening n 'high- sk' group r	Cancers letected on F screening in 'high- i risk' group	Percent of cancers identified
						mar group		group	ing Broob	The Proop	non Stoop		group	ing group			Int Broop		group		mar Broop		a 5100p	_	group	ing Broob	nac groop			1	group	in group i	on Broop	
Ovary Osary	40 to 44	0.0	13.2	2 054 225	270	1 027 112	157	119	91	126 45	410 845	71	199	14	57	21	205 422	98	292		90	- 11 - 1	102 711	20	250	4	16	6 2	1542	5	265	1	4	
Ovany	45 to 49	0.0	19.4	2,915,479	448	1,157,740	261	187	52	208 47	463,096	118	990	24	94	21	251,548	63	S 8 5	19	51	11 1	115,774	94	414	7	27	6 2	155	8	440	2	6	1
Ovany Ovany	50 to 54 55 to 59	0.0	27.1 34.8	2,964,698 2,119.687	640 798	1,182,919	972 429	268	74	298 47 343 47	472,921	168	472	94 99	194	21 21	296,464 211.969	90 104	550 634	18	72	11 1	118,232	48	592 683	10	98 44	6 2	3,646 1.197	11	629 725	2	9	1
Ovany	60 to 64	0.0	41.6	1,897,174	764	918,587	444	\$20	89	356 47	967,495	201	563	40	161	21	185,717	108	656	22	86	11	91,859	57	707	11	46	6 1	,972	19	751	5	10	i
Ovany Ovany	65 to 69 70 to 74	0.0	52.3 60.8	1,805,190	944	902,595 201 205	549	995 408	110	499 4	961,094 920 722	248	696 719	50	198	21	180,519	199	\$11 \$57	27	107	11	90,260 30 130	71	875	14	57	6 1	1,052 5 056	16	928	9	19	
Overy	75 to 79	0.0	73.8	1,181,645	\$72	590,825	507	365	101	406 47	236,925	229	643	46	185	21	118,165	125	749	25	98	11	59,042	66	\$06	19	52	6 1	1,816	15	857	5	12	î
Ovany	Total 40-69 Total 40-49	0.0	30.4	12,496,992	5,804 71 e	6,248,196	2,215	1,591	445	1,770 47	2,499,271	999	2,805	200	799	21	1,249,639	597	9,267	107	490	11 6	624,820	2266	9,518	57	229	6 12	1,964	65	9,799 706	15	52	1
Ovany	Total 50-59	0.0	30.7	4,484,925	1,978	2,242,163	802	576	160	641 47	896,865	362	1,016	72	290	21	448,499	194	1,184	39	156	11 2	224,216	104	1,274	21	89	6 4	1,8 45	29	1,955	5	19	1
Overy	Total 50-69	0.0	38.0	8,125,689	9,086	4,063,945	1,795	1,291	959	1,496 47	1,625,994	\$10	2,276	162	648	21	\$12,669	496	2,650	\$7	948	11 4	406,334	292	2,854	46	186	6 8	,267	52	9,094	10	42	1
Ovany Ovany	Total 40-79	0.0	37.0	5,245,974	5,651	7,640,824	3,287	2,964	657	2,690 47	3,056,325	1,494	4,167	297	1,187	21	1,528,165	379 798	4,855	160	638	11 7	764,0 8 2	425	5,226	40 \$5	340	6 15	2,460 2,816	-16 96	5,555	19	36	1
Ovany	Total (all ages)	0.0	22.8	33,458,0 52	7,495							_																						
Kilney																																	_	
Kidney Kidney	40 to 44 45 to 49	10.1	5.0	4,075,608	907 580	2,037,804	161 904	146	32 61	129 40	\$15,122 919,491	67 136	240 454	19	55	17	407,561	94 64	275	7	57	9 1	209,780 278 958	17	290 547	9	14	5 4	0,756	4		1	5	1
Kidney	50 to 54	26.8	12.7	4,658,111	915	2,929,055	479	496	96	584 40	981,622	199	716	40	159	17	465,811	102	815	20	81	9 1	292,906	52	865	10	41	5 4	5,581	11	904	2	9	1
Kidney Kidney	55 to 59 61 to 64	37.1	18.6	4,181,606	1,160	2,090,805	60 8 749	552	122	486 42	\$36,921 720,400	252	908	50 67	202	17	418,161	129	1,091	26	105	9 2	209,040	66	1,094	19	52	5 4	1,816 5.020	14	1,146	9	11	1
Kidney	65 to 69	73.9	36.4	3,502,183	1,911	1,751,092	1,001	910	200	801 40	700,497	415	1,496	83	352	17	350,218	212	1,699	42	170	9 1	175,109	108	1,805	22	86	5 9	5,022	22	1,889	4	18	i
Kidney	70 to 74	91.2	45.1	3,071,575	2,069	1,535,787	1,081	982	216	365 40	614,915	448	1,615	90	959	17	907,157	229	1,894	46	185	9 1	159,579	117	1,946	25	95	5 9	0,716	24	2,099	5	19	1
Kidney	Total 40-69	34.6	16.9	24,586,669	6,302	******	905 9,902	8,000	660	2,642 42	4,917,994	1,369	4,993	274	1,096	17	2,458,667	699	5,608	140	560	9 1,2	229,393	356	5,946	71	285	5 24	5,867	74	6,228	15	59	
Kidney	Total 40-49	14.1	6.5	8 642 767	887	4,921,984	465	422	93	972 40	1,728,559	199	694	99	154	17	864,277	98	719	20	79	9 4	492,198	50	\$97	10	40	5 8	5,428	10	877	2	8	1
Kidney Kidney	Total 50-59 Total 50-69	31.7	15.5	8,839,717 15.943.902	2,075	4,419,858	2.898	2.577	217	2.270 42	9,188,780	451	1,624	90 295	961	17	885,972 1.594.990	250	4,814	120	184	9 4	441, 536 797.195	306	1,958	25 61	94 245	5 15	1,997 2,499	24 63	2,051	15	51	1
Kidney	Total 60-74	71.8	35.5	10,175,760	5,409	5,087,880	2,891	2,572	566	2,265 40	2,085,152	1,174	4,229	295	999	17	1,017,576	600	4,805	120	480	9 5	508,788	305	5,098	61	244	5 10	,758	ങ	5,940	15	51	1
Kidney Kidney	Total 40-79 Total (all arm)	45.5	23.0	29,847,255 66.041.278	10,150	******	5,919	4,831	1,064	4,255 42	5,969,451	2,206	7,944	441	1,764	17	2,984,725	1,127	9,025	225	901	9 1,4	492,969	574	9,576	115	459	5 29	54 79	119	10,031	24	95	1
Long					,																													
Long	40 to 44	6.0	5.8	4,075,608	240	2,037,804	198	102	28	110 44	815,122	61	179	12	49	20	407,561	99	207	7	26	11 2	209,780	17	225	9	14	6 4	0,756	4	296	1	5	1
Long	45 to 49	16.3	14.7	4,567,159	706	2,283,580	405	901 645	\$1 179	324 46 604 46	919,492	181	525	96 77	144	20	456,716	96	610	19	77	11 2	228,958	51	655	10	41	6 4	5,672	11 7M	695	2	9	1
Long	55 to 59	71.4	67.1	4,181,606	2,896	2,090,803	1,660	1,296	992	1,928 46	\$36,321	740	2,156	148	592	20	418,161	395	2,501	79	316	11 2	209,080	209	2,687	42	167	6 4		47	2,849	9	97	1
Long	60 to 64	137.0	124.9	3,602,002	4,711	1,801,001	2,701	2,010	540	2,161 46	720,400	1,204	3,507	241	964	20	960,200 960,200	645	4,068	129	514	11 1	180,100	940	4,971	68	272	6 9	5,020	76	4,695	15	61	1
Long	70 to 74	335.0	278.1	3,071,575	9,978	1,535,787	5,977	4,001	1,075	4,301 46	614,915	2,998	6,980	490	1,527	20	30,210	1,279	8,099	256	1,023	11 1	159,579	677	8,701	195	541	6 9	0,716	151	9,227	30	121	1
Long	75 to 79	462.2	340.5	2,189,011	8,680	1,094,505	4,977	9,709	995	3,981 46	497,802	2,219	6,461	444	1,775	20	218,901	1,184	7,496	297	947	11 1	109,451	626	8,054	125	501	6 2	1,890	140	8,540	28	112	1
Long	Total 40-69	/4.8	68.0 10.5	24,586,669 8,642,767	946	4,921,984	542	404	108	494 46	1,728,559	4,442	15,049 704	836 -48	3,586 199	70 20	2,458,667 864,277	129	15,140	4/8	105	11 4	492,198	1,265	16,266	14	55	6 8	5,428	2 8 3	991	57	12	1
Long	Total 50-59	51.4	48.4	8,899,717	4,408	4,419,858	2,527	1,881	505	2,022 46	1,767,949	1,127	3,281	225	902	20	883,972	601	9,807	120	481	11 4	441,986	S18	4,090	64	254	6 8	1,997	71	4,997	14	57	1
Long	Lotal 50-69 Total 60-74	227.8	98.9 196.8	15,945,902	16,585 21,555	7,971,951 5,087,880	9,509 12,958	7,076 9,197	1,902	7,607/ 46 9,887 46	2,035,152	4,240	12,945	848 1,102	9,992 4,409	20 20	1,594,990	2,262	14,525	452	2,952	11 1	797,195 508,788	1,197/ 1,555	15,988	239	957 1,244	6 15	9,439 1,75 8	267 947	16,518	53 69	214	1
Long	Total 40-79	127.8	111.1	29,847,255	35,589	жжныйны	20,404	15,185	4,081	16,323 46	5,969,451	9,099	26,490	1,820	7,279	20	2,944,725	4,854	90,795	971	3,883	11 1,4	492,363	2,568	39,02 1	514	2,054	6 29	475	574	95,015	115	459	1
Long	Total (all ages)	90.6	70.1	66,041,278	48,549																	_									_		_	
Lentin Territo	40 to 44	12.2	0.0	2 021 995	748	1.010.692	102	56	a e	154 5	404 277	115	199	743	97	97	202.19*	74	174	16	40	24	101.069	AF	302		97	15 2	1 214	14	294	a		-
Terfi	45 to 49	9.4	0.0	2,251,600	248	1,125,840	163	48	99 89	191 6	450,336	98	115	23	78	57	225,168	63	148	15	50	24 1	112,584	-+o 99	172			15 2 15 2	ç517	12	199	2	10	5
Terfin Terfin	50 to 54	7.0	0.0	2,295,475	160	1,146,796	124	96	25	99 6	458,695	74	86	15	60	97	229,947	48	112	10	98 74	24 1	114,674	90	190	6	24	15 2	2,935	9	151	2	7	5
Terfi	50 to 64	5.2	0.0	2,061,919	108	1,030,959	84 40	24 12	17	92 6	412,384	5U 24	>8 28	10 5	40	57 57	200,192	52	76 36	6	25 12	24 1	105,096 88,241	ری 10	42	4	10	B 2 B 1	,619 /,648	5	49	1	2	- 5
Terfin	65 to 69	2.4	0.0	1,696,993	41	\$48,497	92	9	6	25 6	399,999	19	22	4	15	97	169,699	12	29	2	10	24	\$4,850		99	2	6	1 1	5,970	2	39	0	2	5
Terfin Terfin	70 to 74 75 to 79	2.4	0.0	1,467,965	95 14	793,949	27	8 9	5	22 6	299,599	16	19	9	19	97 97	146,797	10	25 jn	2	8	24	79,998 50.968	7	28	1	5	15 1	1,640 0.074	2		0	2	- 5
Terfin	Total 20-99	16.0	0.0	8,782,798	1,406	4,991,969	1,089	917	218	\$71 6	1,756,541	654	752	191	525	97	\$78,274	420	986	84	996	24 4	499,197	262	1,144	52	210	в 8	1,827	81	1,925	16	65	5
Terlin Terlin	Total 40-69 Total 40-49	6.8	0.0	12,090,277 4 773,045	\$20	6,045,199	635	185	127	508 6	2,418,055	981 219	499	76	905 171	97 97	1,209,028	245	575	49	196	24 e	604,514	159	667 979	91 17	122	15 12	0,903 2.791	47	779	9	98 21	5
Terfi	Total 50-59	6.2	0.0	4,955,991	-1.59	2,177,696	208	60	42	166 6	\$71,071	125	145	-0	100	37	495,599	80	188	16	64	24 2	217,770	50	218	10	40	15 4	1,554	16	252	3	12	5
Terfin Terfin	Total 50-69	4.6	0.0	7,817,219	361	3,908,606	280	\$ 1	56	224 6	1,569,449	168	193	94	194	97 97	781,721	104	255	22	86	24 9	390,861	67	294	19	54	15 7	172	21	940	4	17	5
Terfi	Total 40-79	6.0	0.0	14,565,608	128	7,282,804	573 673	29 196	20 195	598 60	2,919,122	404	ыя 465	12 \$1	48	37	1,456,561	34 260	50 609	52	208	24 7	210,189 728,280	162	707	5 92	190	15 14	7,276 5,656	50	\$19	10	40	- 5
Terfin	Total (all ages)	7.2	0.0	32,583,226	2,954																													

Supplementary Table 7b(i). Cancers detected by offering risk stratified screening according to future PRS using an idealised screening tool with a sensitivity of 0.8 (Cancers of the Breast, Prostate, Colorectum and Pancreas)

		Annual Inc 100,000) fo	idence (per rage-band	Popul	ation		S cree	ning offered	to top 50% of	PRS		\$ cre	aning offered (to top 20% o	of PRS			S creer	ning offered t	to top 10% of	f PRS			S cree	ening offered t	o top 5% of I	PRS			S cree	ning offered t	o top 1% of	PRS	
Cancer Type	Age Groopa	Male	Female	Population Size	Cancers arising	Number requiring screening in 'high risk' group	Cancers arising in 'high risk' group	Missed cancers arising in unscreened 'low risk' group	Cancers missed on screening in "high- risk" group	Cancers detected on Percen screening cance in 'high- identif risk' group	of screening in 'high risk' grou	Cancers arising in "high risk" group	Missed cancers arising in unscreened 'low risk' group	Cancers missed on screening in 'high- nisk' group	Cancers detected on screening in 'high- risk' group	Percent of cancers identified	Number requiring screening in 'high risk' group	Cancers arising in 'high risk' group	Missed cancers arising in unscreened 'low risk' group	Cancers missed on screening in "high- risk" group	Cancers detected on 1 screening in 'high- risk' group	Percent of cancers identified	Number requiring screening in 'high nisk' group	Cancers arising in 'high risk' group	Missed cancers arising in unscreened 'low risk' group	Cancers missed on screening in 'high- risk' group	Cancers detected on screening in 'high- risk' group	Percent of cancers identified	Number requiring screening in 'high risk' group	Cancers arising in 'high risk' group	Missed cancers arising in unscreened 'low risk' group	Cancers missed on screening in 'high- risk' group	Cancers detected on screening in 'high- risk' group	Percent of cancers identified
Breast																																		
Breat	40 to 44	0	125	2,054,229	2,559	1,027,112	1,994	625	987	1,548 60	410,845	1,129	1,490	226	905	95	205,422	712	1,847	142	569	22	102,711	457	2,122	87	949	14	20,542	191	2,428	26	105	4
Breat	45 ID 49 50 Io 54	0	215	2,515,479	6,616	1,157,740	5,760	1,615	1.000	4,001 60	403,090	2,194	3,780	419	2,05	35	251,546	1,344	4.776	968	1,107	22	115,774	1 129	4,125 5,417	226	905	14	25,155	235 999	6,777	68	204	4
Breat	55 to 59	0	236	2,119,687	6,052	1,059,844	4,575	1,477	915	3,660 60	429,987	2,669	3, 383	594	2,195	35	211,969	1,683	4,969	357	1,947	22	105,984	1,039	5,019	207	\$26	14	21,197	310	5,742	62	248	4
Breat	60 to 64	0	338	1,897,174	6,209	918,587	4,693	1,516	989	3,755 60	367,435	2,798	3,471	548	2,191	35	1\$3,717	1,727	4,482	\$45	1,982	22	91,859	1,060	5,149	212	848	14	18,572	S18	5,891	64	254	4
Breat	65 to 69	0	412	1,805,190	7,449	902,595	5,626	1,817	1,125	4,501 60	361,058	9,282	4,161	656	2,626	95	180,519	2,070	5,979	414	1,656	22	90,260	1,270	6,173	254	1,016	14	18,052	581	7,062	76	305	4
Breat	70 to 74	0	\$75	1,603,610	5,977	\$01,305	4,518	1,459	904	5,614 60	\$20,722	2,696	9,941	527	2,109	95	160,961	1,663	4,914	S 35	1,990	22	\$0,1\$0	1,020	4,957	204	\$16	14	16,086	306	5,671	61	245	4
Breat	75 16 79	0	403	1,181,645	4,762	590,825	3,600	1,162	720	2,880 60	296,929	2,100	2,662	420	1,680	95	118,165	1,925	9,497	265	1,060	22	59,082	819	3,949	163	650	14	11,816	244	4,518	49	195	4
Brownt	Total 40-69	0	177	12,490,392	7 599	2 184 851	5 604	4,203	1,190	4 555 60	\$79.041	9.977	4 211	2,960	7.659	35	1,2/49,609	3,417	5 498	410	1,555	22	218 495	3,111	6 748	1,155	4,621	14	12/4,304	1,739	32,119	347	900	4
Breat	Total 50-59	0	212	4.484.925	12.668	2,242,163	9.576	9,092	1,135	7,661 60	\$96,865	5.587	7.081	1.117	4.469	95	448.495	3.524	9.144	705	2.819	22	224 216	2,162	10.506	492	1,729	14	44.849	649	12.019	190	519	4
Breat	Total 50-69	0	924	8,126,689	26,920	4,063,945	19,896	6,424	3,979	15,917 60	1,625,99	11,608	14,712	2,922	9,226	35	\$12,669	7,921	18,999	1,464	5,857	22	406,334	4,491	21,829	898	3,598	14	\$1,267	1,948	24,972	270	1,079	4
Breat	Total 60-74	0	574	5,245,974	19,629	2,622,987	14,838	4 791	2,968	11,870 60	1,019,19	5 8,657	10,972	1,791	6,925	95	524,597	5,460	14,169	1,092	4,968	22	262,299	3,950	16,279	670	2,610	14	52,460	1,005	18,624	201	804	4
Breat	Total 40-79	0	292	15,281,647	44,592	7,640,824	35,708	10,884	6,742	26,966 60	3,056,32	9 19,666	24,926	3 ,9 55	15,799	95	1,528,165	12,404	92,188	2,481	9,923	22	764,042	7,609	96,983	1,522	6,088	14	152,816	2,284	42,508	457	1,827	4
Breat	Total (all ages)	0	166	99,45 8 ,052	55,545						_																							
Prostate	40 + 44		0	2 021 995		1.010.602	60	10	14	<u> </u>	404 777	49	-	0	94	90	202.19*	70	60	6	m	ж	101.065	1.	70		14	16	20.214		*7	1		-
Prostate	40 10 44	- 4	0	2,021,585	40	1,010,692	964	19	14	26 63	404,277	45	40	45	179	99	202,198	276	915	ъ 10	117	<u>15</u> 15	101,069	18	70	4	14	16	20,014	- 6 - 70	82	1 6	4 24	5
Prostate	50 to 54	76	ō	2,293,473	1.797	1,146,796	1.971	966	274	1.097 63	458.695	\$42	895	168	674	39	229.947	549	1.1#	110	499	25	114,674	947	1.990	69	278	16	22,995	111	1.626	22	89	5
Prostate	55 to 59	202	0	2,061,919	4,160	1.050.959	3,283	\$77	657	2,626 63	412,984	2,016	2,144	405	1,619	39	206,192	1,916	2,844	263	1,052	25	103,096	832	9,928	166	666	16	20,619	266	9,894	59	219	5
Prostate	60 to 64	956	0	1,764,828	6,285	\$\$2,414	4,960	1,925	992	5,968 65	352,966	9,047	3,238	609	2,497	99	176,485	1,988	4,297	398	1,590	25	\$8,241	1,257	5,028	251	1,006	16	17,648	401	5,884	\$0	921	5
Prostate	65 to 69	623	0	1,696,993	10,568	848,497	8,999	2,229	1,668	6,671 63	\$\$9,999	5,129	5,445	1,025	4,098	39	169,699	9,942	7,226	668	2,674	25	\$4,850	2,114	8,454	429	1,691	16	16,970	675	9,895	195	540	5
Prostate	70 16 74	760	0	1,467,965	11,155	755,985	8,801	2,952	1,760	7,041 63	299,599	5,406	5,747	1,081	4,925	99	146,797	9,527	7,626	705	2,822	25	79,998	2,231	\$,922	446	1,785	16	14,680	712	10,441	142	570	5
Prostate Doustate	75 10 79 T-4-1 40 40	86/	0	12 090 777	8,736	503,683	6,894	4,019	1,579	5,515 63	201,4/3	4,295	4,501	34/	3,366	399	100,757	7,969	3,973	555	5 905	15 16	50,368	1,147	6,989	349	4,739	16	10,074	338	8,178	112	446	5
Prostate	Total 40-49	195	0	4 273 065	549	2 196 592	499	116	\$7	947 69	\$54.619	266	289	59	219	99	427 906	174	975	95	199	25	219 659	110	499	22	1,728	16	42 791	95	514	7	28	5
Prostate	Total 50-59	195	0	4,955,991	5,897	2,177,696	4,659	1,244	991	3,729 69	\$71,075	2,858	3,099	572	2,287	39	435,599	1,865	4,032	\$75	1,492	25	217,770	1,180	4,717	236	944	16	49,554	\$77	5,520	75	301	5
Prostate	Total 60-69	487	0	9,461,821	16,853	1,750,911	15,299	3,554	2,660	10,699 68	692, 964	\$,169	8,684	1,694	6,585	39	946,182	5,990	11,525	1,066	4,264	25	179,091	9,971	19,482	674	2,697	16	94,618	1,077	15,776	215	\$61	5
Prostate	Total 50-69	291	0	7,817,219	22,750	3,908,606	17,952	4,798	3,590	14,962 69	1,569,44	11,028	11,722	2,206	8,822	39	781,721	7,195	15,555	1,499	5,756	25	390,861	4,551	18,199	910	9,64 1	16	78,172	1,459	21,297	291	1,163	5
Prostate	Total 60-74	568	0	4,929,786	28,006	2,464,893	22,100	5,906	4,420	17,610 63	945,957	19,575	14,491	2,715	10,\$60	<u>99</u>	492,979	8,857	19,149	1,771	7,086	25	246,499	5,602	22,404	1,120	4,482	16	49,298	1,789	26,217	358	1,491	5
Prostate	Total 40-79	297	0	14,565,608	49,188	7,282,804	94,080	9,108	6,816	27,264 69	2,919,12	2 20,995	22,259	4,187	16,748	99	1,4%,%1	19,658	29,590	2,792	10,927	25	728,280	8,699	94,549	1,728	6,911	16	145,656	2,759	40,429	552	2,207	5
Coloractal	1042 (20 200)	1.01		32,763,220	34,4.54																													
Colorectal	40 to 44	15	14	4.075.608	570	2.087.804	996	174	79	317 56	\$15,122	211	359	42	169	90	407.561	126	444	25	101	18	209.780	75	497	15	59	10	40.756	20	550	4	16	9
Colorectal	45 to 49	24	22	4,567,159	1,047	2,283,580	728	\$19	146	582 56	919,482	388	659	78	\$10	30	456,716	291	\$16	46	185	18	228,358	194	919	27	108	10	45,672	36	1,011	7	29	9
Colorectal	50 to 54	47	\$ 7	4,658,111	1,958	2,929,055	1,961	597	272	1,089 56	991,622	725	1,299	145	580	30	465,811	492	1,526	86	945	18	292,906	251	1,707	50	201	10	46,581	68	1,890	14	54	9
Colcrectal	55 to 59	88	61	4,181,606	3,094	2,090,803	2,151	943	490	1,721 56	\$36,321	1,146	1,948	229	917	30	418,161	682	2,412	196	546	18	209,040	997	2,697	79	918	10	41,816	107	2,987	21	\$6	9
Colorectal	60 to 64	151	91	9,602,002	4,945	1,801,001	3,021	1,924	604	2,417 56	720,400	1,609	2,796	922	1,287	50	960,200	958	9,987	192	766	18	180,100	558	5,787	112	446	10	96,020	151	4,194	90	121	
Colorectal	20 to 24	196	170	3,502,185	6 760	1, 51,092	3,835	1,661	267	3,068 36	614 915	2,045	3,475	409	2,009	30	907.157	1,216	4,300	2/0	1 107	18	175,109	106	4,808	142	566	10	35,022	191	5,325	38	155	с е
Colorectal	75 to 79	352	295	2,189,011	6,918	1,094,505	4,992	1,926	\$78	3,514 56	497,802	2,940	3,978	468	1,872	30	218,901	1,999	4,925	279	1,114	18	109,451	\$11	5,507	162	649	10	21,890	219	6,099	44	175	9
Colorectal	Total 40-69	\$ 1	54	24,586,669	16,590	12,298,995	11,492	5,068	2,298	9,194 56	4,917,99	6,122	10,408	1,224	4,898	30	2,458,667	9,649	12,887	729	2,915	18	1,229,399	2,122	14,408	424	1,698	10	245,867	574	15,956	115	459	9
Colorectal	Total 40-49	20	18	8,642,767	1,617	4,921,984	1,124	493	225	899 56	1,728,55	599	1,018	120	479	30	\$64,277	356	1,261	71	285	18	492,198	206	1,409	42	166	10	\$6,428	56	1,561	11	45	5
Colorectal	Total 50-59	66	48	8,899,717	5,052	4,419,858	9,512	1,540	702	2,810 56	1,767,94	3 1,871	9,181	974	1,497	30	\$\$3,972	1,119	3,939	223	891	18	441,986	649	4,403	190	519	10	\$1,997	175	4,877	95	140	9
Colorectal	Lotal 50-69 Total 60.74	204	14	15,943,902	14,915	1,9/1,951	10,368	4,045	2,074	8,294 56 9.744 54	3,188,78	J 5,525	9,390	1,105	4,419	UK NP	1,594,390	3,257	11,626	65/ 799	2,629	18	191,195	7 194	12,999	3103	1,551	10	159,439	518	14,395	104	414	2 9
Colorectal	Total 40-79	119	80	29.847.255	29.608	14.923.627	20,584	9.024	4.117	16,467 56	5,969.45	1 10,966	18,642	2.193	1,523	30	2.944.725	6,526	23.012	1.305	5.221	18	1,492,969	5.801	25,807	760	3.041	10	294,475	1.028	28,580	206	\$22	3
Colorectal	Total (all ages)	85	57	66,041,278	42,885	1-1-1-01		-,	.,	,	-,, (5		,				,,	-,		-,	-,			-,						-,	-,			
Pancreas																																		
Pancrean	40 to 44	3	2	4,075,608	94	2,087,804	66	28	15	59 57	\$15,122	36	58	7	29	\$1	407,561	22	72	4	17	18	209,780	15	81	9	10	11	40,756	4	90	1	9	9
Panorem	45 to 49	6	4	4,567,159	215	2,223,580	152	63	30	122 57	915,482	\$2	199	16	66	91	456,716	50	165	10	40	18	228,958	29	186	6	25	11	45,672	8	207	2	6	9
Pancrean	50 to 54	10	14	4,658,111	409	2,929,055	2009	120	58	251 57	951,622	157	252	51	125	91	465,811	94 154	512	19	129	18	292,906	55 90	354 576	11	44 77	11	46,581	15	994 641	5	12	9 9
Panorea	50 to 64	29	22	3 602 002	926	1 201 001	655	271	191	524 57	720.400	955	571	71	204	\$1	960 200	214	712	49	171	18	180 100	126	300	25	101	11	96 020	45 95	391	7	28	
Pances	65 to 69	47	54	3,502,189	1,417	1,751,092	1,002	415	200	802 57	700,487	549	874	109	495	\$1	950,218	927	1,090	65	261	18	175,109	192	1,225		154	11	95,022	59	1,964	11	42	
Pancrea	70 to 74	66	49	3,071,575	1,757	1,595,787	1,242	515	248	994 57	614,915	674	1,0415	195	599	\$1	907,157	405	1,952	81	\$24	18	159,579	238	1,519	48	191	11	90,716	66	1,691	19	53	9
Pancrea	75 to 79	86	71	2,189,011	1,702	1,094,505	1,203	499	241	963 57	497,802	652	1,050	190	522	S 1	218,901	39 3	1,309	79	\$14	18	109,451	231	1,471	46	185	11	21,890	64	1,638	19	51	9
Ранстен	Total 40-69	17	19	24,586,669	9,727	12,298,995	2,695	1,092	527	2,108 57	4,917,99	1,429	2,298	236	1,149	91	2,458,667	860	2,867	172	688	18	1,229,989	506	9,221	101	405	11	245,867	199	9,588	28	112	9
Panorem	Lotal 40-49 Total 40-49	4	3	\$,642,767	1.075	4,321,384	218	91	44	1/0 5/	1,128,55	5 118 1 412	191	1/4	52	91	464,217 1119,977	2/1	218	14	5/	18	452,138	42	261 979	8 79	34	11	85,428	12	1.095	2	97	<u>لا</u> ۹
Panores	Total 50-69	25	18	15,943,902	5,418	7,971,951	2.417	1.001	483	1.999 57	3,188 78	1.310	2.10	262	1.048	51	1.594,990	788	2,630	158	691	18	797,195	464	2.954	93	971	11	159,499	128	3,290	26	102	3
Pancrea	Total 60-74	46	94	8,881,257	4,100	4,440,628	2,899	1,201	580	2,519 57	1,776,25	1 1,572	2,528	\$14	1,257	\$1	888,126	946	9,154	119	757	18	444,063	556	9,544	m	445	11	88,815	159	3,947	91	125	9
Panoren	Total 40-79	27	21	29,847,255	7,186	14,923,627	5,081	2,105	1,016	4,065 57	5,969,45	1 2,755	4,491	551	2,204	91	2,944,725	1,658	5,528	992	1,326	18	1,492,963	975	6,211	195	780	11	298,475	269	6,917	54	215	9
Pancrea	Total (all ages)	19	15	66,041,278	10,452																													

Supplementary Table 7b(ii). Cancers detected by offering risk stratified screening according to future PRS using an idealised screening tool with a sensitivity of 0.8 (Cancers of the Ovary, Kidney, Lung, Testis)

		Annual In (per 100,00	ncidence 0) for age-				s	creening off 50%	ered to top			S	creening of 20	ffered to top					Screening o 10	offered to top 0%				5	Screening off 5%	ered to top			1	Screening of 19	fered to top		
Canor Type	Age Groups	Male	Female	Population Size	Cancers arising	Number requiring screening in 'high risk' group	Cancers arising in 'high risk' group	of PH Missed cancers arising in unscreened 'low risk' group	Cancers missed on o screening in 'high- risk' group	Cancers letected on Percent of screening cancers in 'high- identified isk' group	Number requiring screening in 'high risk' group	Cancers arising in high risk' group	of F Missed cancers arising in inscreened 'low risk' group	Cancers missed on screening in 'high- nisk' group	Cancers detected on screening in 'high- risk' group	Percent of cancers identified	Number requiring screening in 'high risk' group	Cancers arising in 'high risk' group	Missed cancers arising in unscreened 'low risk' group	Cancers missed on screening in 'high- risk' group	Cancers detected on Pe screening of in 'high- id risk' group	ercent of s cancers s dentified ri	Number requiring screening 'h in 'high isk' group	Cancers rising in igh risk' group	of PF Missed cancers arising in unscreened 'low risk' group	Cancers missed on d screening in 'high- isk' group 1	Cancers letected on Percent of screening cancers in 'high- identified risk' group	Number requiring screening in 'high risk' group	Cancers arising in high risk' group	of P Missed cancers arising in unscreened 'low risk' group	Cancers missed on screening in 'high- nisk' group	Cancers detected on 1 screening in 'high- risk' group	Percent of cancers identified
Ormy																																	
Overy	40 to 44	0.0	13.2	2,054,223	270	1,027,112	178	92 157	36	142 53	410,845	90 140	180	18	72	27	205,422	52	218	10	41	15	102,711	29	241	6	23	20,542	7	263	1	6	2
Ovancy	50 to 54	0.0	27.1	2,364,638	640	1,182,319	422	218	375 84	337 53	472,928	213	427	43	170	27	236,464	123	517	25	98	15	118,232	69	571	14	56	23,646	12	622	4	14	2
Overy Overy	55 to 59 60 to 64	0.0	34.8	2,119,617	738	1,059,844	486	252	97 101	319 53	423,937	246	492	49	197	27	211,969	141	597	28	113	15	105,984	\$0 \$3	658	16	64 66	21,197	20	718	4	16	2
Overy	65 to 69	0.0	52.3	1,805,190	944	902,595	622	322	124	498 53	361,058	314	630	63	251	21	180,519	181	763	36	145	15	90,260	102	\$42	20	\$2	18,052	26	918	5	21	2
Overy Overy	70 to 74 75 to 79	0.0	60.8 73.8	1,603,610	975	\$01,\$05 590,\$23	643	332	129	514 53 460 53	320,722	325	660	65 58	260	77	160,361	197	788	37	150	15	\$0,1\$0 59.0\$7	106	869 777	21	85 76	16,036	27	948 848	5	22	2
Overy	Total 40-69	0.0	30.4	12,496,392	3,804	6,248,196	2,507	1,297	501	2,006 53	2,499,278	1,266	2,538	253	1,013	27	1,249,639	729	3,075	146	583	15	624,820	412	3,392	\$2	330	124,964	105	3,699	21	84	2
Osary Osarv	Total 40-49 Total 50-59	0.0	16.4 30.7	4,369,703	718	2,184,851	473	245	95	379 53	\$73,941 \$96.\$65	239	479 919	48	191 367	27	436,970	138	580	28	211	15	218,485 224,216	78	640 1.229	16 30	62 120	43,697	20	698 1.340	4	16 30	2
Overy	Total 50-69	0.0	38.0	\$,126,689	3,086	4,063,345	2,034	1,052	407	1,627 53	1,625,338	1,027	2,059	205	\$22	27	\$12,669	591	2,495	118	473	15	406,334	335	2,751	67	268	\$1,267	85	3,001	17	68	2
Osary Osary	Total 60-74 Total 40-79	0.0	51.1 37.0	5,245,974	2,683	2,622,987	1,768	915	354	1,415 53 2,979 53	1,049,195	1.993 1.991	1,790	179	715	21	524,597 1.528.165	514	2,169	103	411 \$66	15	262,299 764.092	291 613	2,392	58	233	52,460	74 156	2,609	31	59	2
Owny	Total (all ages)	0.0	22.8	33,458,052	7,495		-					-,																		-1			
Kilney																										-						-	
Kidney Kidney	40 to 44 45 to 49	10.1	5.0 7.8	4,075,608	307	2,037,004	215	92 174	43	172 56 325 56	\$15,122 913,432	218	192 362	23	92 175	30 30	407,561	69 130	238	14	55 104	12	203,780	40	267	15	32 1 61 1	40,756	11 21	296	2	9 17	3
Kidney	50 to 54	26.8	12.7	4,658,111	915	2,329,055	641	274	128	513 56	931,622	344	571	69	25	30	465,811	206	709	41	165	18	232,906	120	795	24	96 1	46,581	33	882	7	26	3
Kadmey Kidmey	55 to 59 60 to 64	37.1 53.7	18.6 26.2	4,181,605 3.602.002	1,160	2,090,003	\$13 1.001	347	163 200	650 56 \$01 56	136,321 720.400	436	724 1892	\$7	349 430	30 30	418,161 360,200	261	1106	52	209	15	209,080	153	1,007	31 38	122 1	41,816 36.020	42	1,118	10	33	3
Kidney	65 to 69	73.9	36.4	3,502,183	1,911	1,751,092	1,339	572	268	1,071 56	700,437	719	1,192	144	575	30	350,218	430	1,481	\$ 6	344	18	175,109	251	1,660	50	201 1	35,022	69	1,842	14	55	3
Kadaney Kadaney	70 to 74 75 to 79	91.2 110.1	45.1 57.2	2,189,011	2,063	1,535,717	1,445	535	250	1,136 36	614,315 437, 9 02	671	1,207	134	537	30 30	218,901	464	1,399	93	371 321	18	153,579 109,451	271 235	1,792	54 47	188 1	30,716	74 64	1,989	15	59 51	
Kidney	Total 40-69	34.6	16.9	24,586,669	6,302	12,293,335	4,415	1,887	883	3,532 56	4,917,334	2,370	3,932	474	1,896	30	2,458,667	1,417	4,815	203	L134	18	1,229,333	\$29	5,473	166	663 1	245,867	226	6,076	45	181	3
Kidney	Total 50-59	31.7	0.5	\$,\$39,717	2,075	4,521,584	1,454	621	291	1,163 56	1,767,943		1,295	156	624	30	\$13,972	467	1,608	93	373	18	452,158	273	1,802	55	218 1	\$6,428 \$1,397	74	2,001	15	60	3
Kidney	Total 50-69	45.8	22.6	15,943,902	5,415	7,971,951	3,793	1,622	759	3,035 56	3,188,780	2,037	3,378	407	1,629	30	1,594,390	1,218	4,197	244	974	18	797,195	712	4,703	142	570 1	159,439	194	5,221	39	155	3
Kidney	Total 40-79	45.5	23.0	29,847,255	10,150	14,923,627	7,110	3,040	1,422	5,688 56	5,969,451	3,817	6,333	763	3,054	30	2,984,725	2,213	7,867	457	1,826	18	1,492,363	1,336	4,692 8,814	267	1,061 1	298,473	364	9,786	73	291	3
Kidney	Total (all ages)	29.2	14.8	66,041,278	13,323																												_
Lung	40 40 44	6.0	5.8	4 075 608	240	2.037.004	157	9 3	31	115 57	\$15.172	78	167	16	63	76	407.561	6	195	0	36	15	203 200		715	5	70	40.756	6	734		5	
L	45 to 49	16.3	14.7	4,567,159	706	2,283,580	460	246	92	368 52	913,432	230	476	46	194	76	456,716	132	574	26	105	15	228,358	74	632	15	59	45,672	19	617	4	15	2
	50 to 54 55 to 59	33.4	31.5	4,658,111	1,512	2,329,055	986	526	197	789 52	931,622	493	1,019	99	395 756	26	465,811	242	1,230	56	226	15	232,906	159 304	1,353	32	127	46,581	40	1,472	15	32	2
Lang	60 to 64	137.0	124.9	3,602,002	4,711	1,101,001	3,073	1,638	615	2,458 52	720,400	1,537	3,174	307	1,230	26	360,200	\$79	3,832	176	704	15	180,100	495	4,216	99	396	36,020	125	4,586	25	100	2
	65 to 69 70 to 74	229.5 335.0	197.8 278.1	3,502,183	7,466	1,751,092	4,870	2,596	974	3,896 52	700,437	2,436	5,060 6 31 8	487	1,949 7.448	26	350,218	1,394	6,072	279	1,115	15	175,109	784	6,682	157	627 788	35,022	198 748	7,268	40	158	2
L	75 to 79	462.2	340.5	2,189,011	8,680	1,094,505	5,661	3,019	1,132	4,529 52	437,802	2,132	5,848	566	2,265	36	218,901	1,620	7,060	324	1,296	15	109,451	911	7,769	182	729	21,890	230	8,450	46	184	2
	Total 40-69 Total 40-49	74.8	68.0 10.5	24,586,669	17,531	12,293,335	11,434	6,097	2,287	9,147 52 494 52	4,917,334	5,720	11,\$11 637	1,144	4,576	76 76	2,458,667	3,273	14,250	655	2,618	15	1,229,333 432,138	1,841 99	15,690 847	368	1,473	245,867	464	17,067	93	372	2
L	Total 50-59	51.4	48.4	8,839,717	4,408	4,419,858	2,875	1,533	575	2,300 52	1,767,943	1,438	2,970	288	1,150	76	\$13,972	\$23	3,515	165	658	15	441,986	463	3,945	93	370	88,397	117	4,291	23	93	2
	Total 50-69 Total 60-74	227.8	98.9 196.8	10,175,760	21,555	5,087,880	14,059	7,496	2,165	8,004 52 11,247 52	2,035,152	7,032	14,523	1,062	4,329	20 76	1,017,576	4,034	15,449	\$05	3,219	15	508,788	2,263	14,845	453	1,811	101,758	439	20,984	114	352 457	2
	Total 40-79 Total (dl ana)	127.8	111.1	29,847,255	35,589	14,923,627	23,212	12,377	4,642	18,570 52	5,969,451	11,611	23,978	2,322	9,289	26	2,984,725	6,644	28,945	1,329	5,315	15	1,492,363	3,737	31,852	747	2,990	291,473	943	34,646	189	754	2
Tatis	rown (wr wiger)	50.0	/0.1	00,011,278	46,349																												
Testis	40 to 44	12.3	0.0	2,021,385	248	1,010,692	228	20	46	182 73	404,277	176	72	35	141	57	202,138	135	113	27	108	44	101,069	100	148	20	80 3	20,214	44	204	9	35	14
Testis Testis	45 to 49 50 to 54	9.4	0.0	2,251,680	211	1,125,840	194	17	39	155 73	450,336	150	61	30	120 or	57	225,168	115	96	23	92 70	44	112,584	15 44	126	17	68 3 51 7	22,517	37	174	7	30	14
Testis	55 to 59	5.2	0.0	2,061,919	100	1,030,959	99	9	20	79 73	412,384	77	31	15	61	57	206,192	59	49	17	47	44	103,096	43	65	9	35 3	20,619	19	89	4	15	14
Testis Testis	60 to 64 65 to 69	3.0	0.0	1,764,828	52	2 882,414 848,407	48	4	10	38 73 30 73	352,966	37	15	7	30 74	57	176,483	201	3M 10	6	23	44	\$\$,241 \$4,\$50	21	31	4	17 3	17,648 16,970	9	43	2	7	14
Testis	70 to 74	2.4	0.0	1,467,965	35	733,913	32	3	6	26 73	293,593	25	12	5	25 20	57	146,797	19	16	4	15	44	73,398	14	21	3	11 3	14,680	6	29	1	5	14
Testis Testis	75 to 79 Tobal 20 30	1.4	0.0	1,007,365	14	503,683	13	1	3	10 73	201,473	10	4	2	\$ 700	57	100,737	344	6	2	6	44	50,368 439 137	6 564	8	113	4 3	10,074	2	12	0	2	14
Testis	Total 40-69	6.8	0.0	12,090,277	\$20	6,045,139	753	67	151	603 73	2,418,055	5112	238	116	466	57	1,209,028	447	373	195	358	44	604,514	329	491	66	263 3	120,903	144	676	-13	115	14
Testis Testis	Total 40-49 Total 50-59	10.7	0.0	4,273,065	459	2,136,532	422	37	84 49	337 73	\$54,613 \$71.07#	326 190	133	65 38	261	57	427,306	250	209	50 70	200	44	213,653	184	275	37	147 3	42,731	\$1 47	378	16	65 38	14
Testis	Total 50-69	4.6	0.0	7,\$17,213	361	3,908,606	332	29	66	265 73	1,563,443	256	105	51	205	57	781,721	197	164	39	157	44	390,861	145	216	29	116 3	78,172	63	298	13	51	14
Testis Testis	Total 60-74 Total 40-79	2.6	0.0	4,929,786 14,565,608	128	2,464,893	118	10	24 160	94 73 639 73	985,957	91 617	37	18	73 494	57	492,979	70	58 305	14	56 379	44	246,489 728 280	51 340	77 520	10 70	41 3	49,298	23	105	31	18	14
Testis	Total (all ages)	7.2	0.0	32,583,226	2,354					13	,,					51	,	,,,,	545	15							21						

Supplementary Table 7c(i). Cancers detected by offering risk stratified screening according to optimised PRS using an idealised screening tool with a sensitivity of 0.8 (Cancers of the Breast, Prostate, Colorectum and Pancreas)

		Annual II (per 100,0	ncidence 000) for	Popul	ation		Sci	reening offer 50%	red to top			Sc	reening offe 20%	er ed to top				Sc	reening offe 10%	red to top				Sc	reening offe 5% of PR	ered to top			s	creening offer 1%	red to top		
Cancer Type	Age Group s	Male	Female	Pop ulation Size	Cancers arising	Numb er in 'high risk' screening group	Cancers arising in high risk group	PRS false negative (missed cancers arising in low' risk	false d egatives	Total Percent of letected cancers by detected reeening	Number C in 'high au risk' hi screening group	F Cancers rising in igh risk group a	rk S false negative (missed cancers urising in low' risk	creening false d legatives sc	Total Pe etected c by d reening	rcent of ancers etected	Number (in 'high au risk' h screening group	F Cancers rising in igh risk group	PRS false negative (missed cancers arising in 'low' risk	reening false d egatives sc	Total P letected by creening	Percent of cancers detected	Number (in 'high risk' a screening group	P Cancers p rising in igh risk group a	PRS false negative (miss ed cancers nrising in low' risk	creening false legatives s	Total detected cancers by detected creening	Numb er f in 'high risk' screen ing group	Cancers arising in high risk group	PRS false negative (missed cancers arising in 'low' risk	reening de false de egatives scu	Fotal Per stected ca by d reening	rcent of ancers etected
Brast																																	
Breast	10 to 44 15 to 49	0.0	124.6	2,054,223	2,559	1,027,112	2,004	555	401	1,603 63	410,845	1,219	1,340	244	975	38	205,422	790	1,769	158	632	25	102,711	497	2,062	99	398 1	5 20,542	157	2,402	31	126	5
Breast	50 to 54	0.0	279.8	2,364,638	6,616	1,182,319	5,181	1,435	1,036	4,145 63	472,928	3,152	3,464	630	2,522	38	236,464	2,044	4,572	409	1,635	25	118,232	1,285	5,331	257	1,028 1	5 23,646	406	6,210	\$1	325	5
Breast	55 to 59	0.0	285.5	2,119,687	6,052	1,059,844	4,739	1,313	948	3,791 63	423,937	2,884	3,168	577	2,307	38	211,969	1,870	4,182	374	1,496	25	105,984	1,176	4,876	235	941 1	5 21,197	371	5,681	74	297	5
Breast Breast	50 to 64 55 to 69	0.0	412.3	1,837,174	6,209 7.443	918,587	4,862	1,547	1,166	3,890 63 4,663 63	367,435	2,958	3,251	592 709	2,367	38 38	183,717 180,519	2,299	5,144	384	1,534	25	91,859	1,446	5,003	241	1.157 1	5 18,372	456	6.987	91	365	- 5
Breast	70 њо 74	0.0	372.7	1,603,610	5,977	\$01,505	4,620	1,297	936	3,744 63	320,722	2,848	3,129	570	2,278	38	160,361	1,846	4,131	369	1,477	25	\$0,1\$0	1,161	4,816	232	929 1	5 16,036	367	5,610	73	293	5
Breast	75 to 79 T-++1 40 40	0.0	403.0	1,181,645	4,762	590,823	3,729	1,033	746	2,983 63	236,329	2,269	2,493	454	1,815	38	118,165	1,471	3,291	294	1,177	25	59,082	925	3,837	185	740 1	5 11,816	292	4,470	58	234	5
Breast	Total 40-69	0.0	172.4	4,369,703	7,533	2,184,851	5,899	1,634	1,180	4,719 63	\$73,941	3,589	3,944	718	2,871	38	436,970	2,327	23,390 5,206	465	1,862	25	218,485	1,463	6,070	293	1,171 1	5 43,697	462	7,071	92	370	5
Breast	Fotal 50-59	0.0	282.5	4,484,325	12,668	2,242,163	9,920	2,748	1,984	7,936 63	\$96,\$65	6,036	6,632	1,207	4,829	38	448,433	3,913	8,755	783	3,131	25	224,216	2,461	10,207	492	1,969 1	5 44,843	177	11,891	155	621	5
Breast Breast	Total 50-69 Total 60-74	0.0	323.9	5 745 974	26,320	4,063,345	20,610	5,710	4,122	16,411 63	1,625,338	9353	13,779	2,508	10,033	38 38	\$12,669	\$,130 6.064	13,565	1,626	6,504	25	406,334	3,113	21,207	1,023	4,091 1 3.051 1	5 57,460	1,614	24,705	323	963	5
Breast	Total 40-79	0.0	291.8	15,281,647	44,592	7,640,824	34,919	9,673	6,984	27,935 63	3,056,329	21,247	23,345	4,249	16,997	38	1,528,165	13,775	30,817	2,755	11,020	25	764,082	8,663	35,929	1,733	6,930 1	5 152,816	2,735	41,857	547	2,188	5
Breast	Fotal (all ages)	0.0	166.0	33,458,052	55,545																												
Prostate	10 m 44	4.3	0.0	2 021 395		1 010 697	71	17	14	57 65	404 277	45	43	9	36	41	202.138	30	58	6	74	72	101.069	19	69	4	15 1	7 20 214	6	n	1	5	6
Prostate	15 to 49	20.5	0.0	2,251,680	461	1,125,840	372	89	74	298 65	450,336	235	226	47	188	41	225,168	156	305	31	125	27	112,584	101	360	20	1 0 1	22,517	33	428	7	27	6
Prostate	50 to 54	75.7	0.0	2,293,473	1,737	1,146,736	1,402	335	280	1,121 65	458,695	\$\$6	\$51	177	709	41	229,347	589	1,148	118	471	27	114,674	379	1,358	76	303 1	7 22,935	125	1,612	25	100	6
Prostate	50 to 64	356.1	0.0	1,764,828	6,285	1,050,959	5,072	1,213	1,014	4,057 65	352,966	3,205	3,080	424 641	2,564	41	176,483	2,131	4,154	426	1,129	27	88,241	1,372	4,913	274	1,097 1	7 17,648	454	5,800	91	363	6
Prostate	55 to 69	622.7	0.0	1,696,993	10,568	\$48,497	8,528	2,040	1,706	6,822 65	339,399	5,390	5,178	1,07\$	4,312	41	169,699	3,584	6,984	717	2,867	27	\$4,\$50	2,306	\$,262	461	1,845 1	16,970	763	9,805	153	610	6
Prostate Prostate	70 to 74 75 to 79	759.8	0.0	1,467,965	11,153	733,983	9,000 7 049	2,153	1,800	7,200 65	293,593	5,688	5,465	1,138	4,550	41	146,797	3,782	7,371	756	3,026	27	73,398	2,434	\$,719 6,930	487	1,947 1	7 14,680	805 631	10,348	161	644 504	6
Prostate	Total 40-69	192.7	0.0	12,090,277	23,299	6,045,139	18,801	4,498	3,760	15,041 65	2,418,055	11,882	11,417	2,376	9,506	41	1,209,028	7,901	15,398	1,580	6,321	27	604,514	5,084	18,215	1,017	4,068 1	120,903	1,682	21,617	336	1,345	6
Prostate	Total 40-49	12.8	0.0	4,273,065	549	2,136,532	443	106	89	354 65	\$54,613	280	269	56	224	41	427,306	186	363	37	149	27	213,653	120	429	24	96 1	42,731	40	509	1	32	6
Prostate	Total 50-59 Total 60-69	486.8	0.0	4,355,391 3,461,821	5,897	1,730,911	4,758	3,254	2,720	3,807 65	692,364	3,007	8,258	1,719	6,876	41	435,539 346,182	5,715	3,897	400	4,572	27	173,091	3,678	4,610	736	2,942 1	7 43,554 7 34,618	4.26	5,471	243	973	6
Prostate	Total 50-69	291.0	0.0	7,817,213	22,750	3,908,606	18,358	4,392	3,672	14,686 65	1,563,443	11,602	11,148	2,320	9,282	41	781,721	7,715	15,035	1,543	6,172	27	390,861	4,965	17,785	993	3,972 1	78,172	1,642	21,108	328	1,314	6
Prostate	Total 60-74 Total 40-79	568.1 296.5	0.0	4,929,786	28,006	2,464,893	22,599	5,407	4,520	18,079 65	985,957	14,283	13,723	2,857	11,426	41	492,979	9,497	18,509 78,543	1,899	7,598	27	246,489	6,112	21,894	1,222	4,889 1	7 49,298	2,022	25,984	404	1,617	6
Prostate	Total (all ages)	183.8	0.0	32,583,226	52,254	1,000,000	51,050	•,	0,510		1,713,111		11,105	1,105	11,010		1,150,501	11,015			11,110			3,115	55,165	1,000	1,510	115,050	3,110	10,010	0		, in the second se
Colorectal																																	
Colorectal	40 to 44	14.5	13.5	4,075,608	570	2,037,804	425	145	85	340 60	\$15,122	244	326	49	195	34	407,561	153	417	31	122	21	203,780	93	477	19	74 1	3 40,756 45,670	27	543	5	22	4
Colorectal	50 to 54	47.1	37.1	4,658,111	1,958	2,329,055	1,460	498	292	1,168 60	931,622	\$39	1,119	168	671	34	465,811	524	1,434	105	419	21	232,906	319	1,639		255 1	3 46,581	94	1,864	19	75	- 4
Colorectal	55 to 59	87.7	60.6	4,181,606	3,094	2,090,803	2,308	786	462	1,846 60	\$36,321	1,326	1,768	265	1,061	34	418,161	828	2,266	166	662	21	209,080	503	2,591	101	403 1	3 41,816	148	2,946	30	119	4
Colorectal	50 to 64 55 to 69	151.4	119.1	3,602,002	4,345	1,751,092	4,114	1,104	\$23	3.291 60	700,400	2.364	3,152	473	1,489	54 34	350,200	1,163	3,182	233	930	21	180,100	107	3,638 4.619	141	718 1	3 36,020	265	4,137	42	212	4
Colorectal	70 њо 74	273.5	171.2	3,071,575	6,760	1,535,787	5,042	1,718	1,00\$	4,033 60	614,315	2,897	3,863	579	2,317	34	307,157	1,209	4,951	362	1,447	21	153,579	1,100	5,660	220	88 0 1	30,716	324	6,436	65	259	4
Colorectal Colorectal	75 to 79 Total 40–69	351.7	234.8 54.1	2,189,011 24 586 669	6,31 8 16 530	1,094,505	4,712	1,606	942 2.466	3,770 60 9863 60	437,802	2,707	3,611	541	2,166	34	218,901	1,691	4,627	338	1,352	21	109,451	1,028	5,290 13,841	206	\$22 1 2152 1	3 21, 890 3 245 8 67	303	6,015	159	242	4
Colorectal	Total 40-49	19.7	17.7	8,642,767	1,617	4,321,384	1,206	411	241	965 60	1 728 553	693	924	139	554	34	\$64,277	433	1,184	\$7	346	21	432,138	263	1,354	53	210 1	86,428	71	1,539	16	62	4
Colorectal	Total 50-59 Total 50-69	66.4	48.2	\$,\$39,717 15.043.002	5,052	4,419,858	3,768	1,284	754	3,014 60	1,767,943	2,165	2,887	433	1,732	34	\$\$3,972 1.594.390	1,352	3,700	270	1,081	21	441,986	\$22 7.476	4,230	164	658 1	3 \$\$,397	242	4,810	48	194	4
Colorectal	Total 60-74	203.9	125.2	10,175,760	16,621	5,087,880	12,396	4,225	2,479	9,917 60	2,035,152	7,122	9,499	1,424	5,698	34	1,017,576	4,448	12,173	890	3,558	21	508,788	2,420	13,917	541	2,163 1	3 101,75 8	797	15,824	159	638	4
Colorectal	Total 40-79	119.0	80.4	29,847,255	29,608	14,923,627	22,083	7,525	4,417	17,666 60	5,969,451	12,687	16,921	2,537	10,150	34	2,984,725	7 ,92 3	21,685	1,585	6,338	21	1,492,363	4,817	24,791	963	3,854 1	3 298,473	1,420	28,188	284	1,136	4
Colorectal	Fotal (all ages)	84.0	56.5	66,041,278	42,880																	-									_	_	_
Pancreas	40 to 44	2.6	2.0	4,075,608	94	2,037,804	74	20	15	59 63	\$15,122	45	49	9	36	38	407,561	29	65	6	23	25	203,780	18	76	4	15 1	5 40,756	6		1		
Pancreas	15 ю 49	5.6	3.9	4,567,159	215	2,283,580	168	47	34	135 63	913,432	102	113	20	\$2	38	456,716	66	149	13	53	25	228,358	42	173	8	33 1	5 45,672	13	202	3	11	5
Panciezs Panciezs	50 to 54	10.2	7.3	4,658,111	409	2,329,055	320	\$9 144	64 104	256 63 417 63	931,622	195 317	214	39	156	38	465,811	126	283	25	101	25	232,906	179	330 537	16	64 1 104 1	46,581 5 41,816	25	384	5	20	5
Panciezs	50 to 64	29.2	22.4	3,602,002	926	1,\$01,001	725	201	145	510 63	720,400	441	415	11	353	38	360,200	2005	640	57	229	35	180,100	180	746	36	144 1	5 36,020	57	\$69	11	45	5
Pancreas	55 to 69 70 to 74	47.2	34.1	3,502,183	1,417	1,751,092	1,110	307	222	\$\$\$ 63	700,437	675	742	135	540	38	350,218	438	979	SS	350	25	175,109	275	1,142	55	220 1	5 35,022	\$7	1,330	17	70	5
Panciezs	75 to 79	86.0	70.8	2,189,011	1,702	1,094,505	1,333	369	267	1,066 63	437,802	\$11	\$20	167	649	38	218,901	526	1,214	105	424	25	109,451	331	1,410	66	2/5 1	5 21,890	104	1,598	21	\$4	5
Pancreas	Fotal 40-69	17.4	13.0	24,586,669	3,727	12,293,335	2,919	\$0\$	584	2,335 63	4,917,334	1,776	1,951	355	1,421	38	2,458,667	1,151	2,576	230	921	25	1,229,333	724	3,003	145	579 1	5 245,867	229	3,498	46	183	5
Panciezs Panciezs	Total 40-49 Total 50-59	4.2	3.0 10.3	1,642,767 1 139 717	309 1.075	4,321,384	242	67 233	48	194 63 673 63	1,728,553	147 512	162	29 102	410	38 31	\$64,277 \$\$3.977	95 332	214 743	19	76	25	432,138	60 209	249	12	48 1	5 86,428	19	290	4	15 53	5
Pancreas	Total 50-69	24.7	18.3	15,943,902	3,418	7,971,951	2,677	741	535	2,141 63	3,188,780	1,629	1,789	326	1,303	38	1,594,390	1,056	2,362	211	845	25	797,195	664	2,754	133	531 1	5 159,439	210	3,208	42	168	5
Panciezs	Fotal 60-74 Fotal 40-20	46.5	34.5	10,175,760	4,100	5,087,880	3,211	889	642	2,568 63	2,035,152	1,954	2,146	391	1,563	38	1,017,576	1,267	2,833	253	1,013	25	508,788	797	3,303	159	637 1	5 101,758	251	3,849	50	201	5
Panciezs	Fotal (all ages)	19.3	15.0	66,041,278	10,452	14,723,021	3,021	ענקי	1,120		7,707,431	3,424	3,102	36.9	4,139	24	a,709,12J	4,620	4,900		1,110	23	1,476,303	סאכיי	5,00	713	1,117 1	478,913	441	0,743			,

Supplementary Table 7c(ii). Cancers detected by offering risk stratified screening according to optimised PRS using an idealised screening tool with a sensitivity of 0.8 (Cancers of the Ovary, Kidney, Lung, Testis)

		Annual In (per 100,0	cidence 00) for	Popp	lation		Sc	reening offer 50%	ed to top			Sc	reening off 20%	ered to top				s	creening offer 10%	ed to top				Sc	reening offe 5%	ered to top				Sc	reening offer 1%	ed to top		
Сансег Туре	Age Groups	Male	F emale	Pop ulation Size	Cancers arising	Numb er in 'high risk' screening group	Cancers arising in high risk group	PRS false negative (missed cancers arising in 'low' risk	reening false egatives s	Total Percent of letected cancers by detected creening	Numb er in 'high risk' screening group	Cancers arising in high risk group	rising in bw'risk	creening false d negatives sc	Total etected by reening	Percent of cancers detected	Number in 'high risk' screening group	Cancers trising in high risk group	PRS false negative (missed cancers arising in 'low' risk	reening false d gatives so	Total Pe detected o by d screening	ercent of cancers letected	Number in 'high risk' au screening group	P Cancers rising in iigh risk group a	rkS false negative (miss ed cancers nrising in low' risk	creening false uegatives	Total detected by screening	Percent of cancers detected	Number C in 'high au risk' hi screening group	ancers ising in igh risk group	rRS false negative scr (missed cancers ne rising in low' risk	eening T alse det gatives scre	otal Perc ected car by det eening	cent of ncers tected
Orary	10 - 11	0.0	13.2	2 054 222	77	102711	1977	•2	27	150 56	410 845	100	1.20	20	*0	20	205.422	50	211	12	17	1.	102 711	24	726	7		10	20.542	0	261			- 2
Ovay	15 16 49	0.0	19.4	2,034,223	441	1,157,74	2 1er D 311	137	62	249 56	463,096	165	283	33	132	30	231,548		350	20	79	18	115,774	57	391	11	46	10	23,155	15	433	3	12	3
Ovary	50 to 54	0.0	27.1	2,364,638	640	1,182,31	9 444	196	89	355 56	472,928	236	404	47	189	30	236,464	140	500	28	112	18	118,232	\$2	558	16	65	10	23,646	22	618	4	18	3
Ovmy C	55 to 59	0.0	34.8	2,119,687	731	1,059,84	512	226	102	410 56	423,937	272	466	54	218	30	211,969	162	576	32	129	18	105,984	94	644	19	75	10	21,197	25	713	5	20	3
Ovay	55 to 69	0.0	52.3	1,805,190	944	902,59	5 655	234	131	524 56	361,038	348	596	70	279	30	180,519	207	737	41	154	18	90,260	120	\$24	24	96	10	18,052	32	912	6	26	3
Ovmy	70 њо 74	0.0	60.8	1,603,610	975	5 \$01,\$0	5 677	298	135	541 56	320,722	360	615	72	288	30	160,361	214	761	43	171	18	\$0,1\$0	124	851	25	100	10	16,036	34	941	7	27	3
Ovary	75 to 79 F-+1 40 60	0.0	73.8	1,1\$1,645	\$72	2 590,82	3 605 C 3 640	267	121	484 56	236,329	322	550	64	257	30	118,165	191	6\$1	38	153	18	59,082	111	761	22	89	10	11,816	30	842	6	24	3
Ovay	Total 40-09	0.0	16.4	4,369,703	5,404	2,184,85	5 2,040 I 4918	220	100	399 56	\$73,941	265	453	53	212	30	436,970	157	561	31	126	18	218,485	92	626	18	73	10	43,697	25	693	20	20	3
Ovmy	Fotal 50-59	0.0	30.7	4,484,325	1,37	2,242,16	3 956	422	191	765 56	\$96,\$65	508	\$70	102	407	30	448,433	302	1,076	60	242	18	224,216	176	1,202	35	141	10	44,843	47	1,331	9	38	3
Ovmy O	Total 50-69	0.0	38.0	8,126,689	3,004	5 4,063,34	5 2,141	945	428	1,713 56	1,625,338	1,139	1,947	228	911	30	\$12,669	677	2,409	135	541	18	406,334	394	2,692	79	315	10	\$1,267	106	2,980	21	85	3
Ovary	Total 40-74	0.0	37.0	15 281 647	5,651	7640 \$2	4 3 921	1 730	784	3 1 37 56	3 056 329	2085	3 566	417	1668	30	1 528 165	1 239	4 412	248	991	13	764 082	542 721	4 930	144	577	10	52,460 152,816	195	5456	39	156	3
Ovmy	Fotal (all ages)	0.0	22.8	33,458,052	7,49	5	-,	-1		-,			-,		-,		-,,	-,	-3												-1			
Kidney																																		
Kidney	40 to 44	10.1	5.0	4,075,608	307	7 2,037,90	4 237	70	47	189 62	\$15,122	141	166	28	113	37	407,561	90	217	18	72	24	203,780	56	251	11	45	15	40,756	17	290	3	14	5
Kidney	50 to 54	26.8	12.7	4,567,159	915	2,22,5,54	5 705	210	141	564 62	931.622	421	494	84	337	37	436,716	270	645	54	216	24	232,906	108	747	34	134	15	45,672	52	\$63	10	41	- 5
Kidney	55 to 59	37.1	18.6	4,181,606	1,160	2,090,80	894	266	179	715 62	\$36,321	534	626	107	427	37	418,161	342	\$1\$	68	273	24	209,080	213	947	43	170	15	41,816	66	1,094	13	52	5
Kidney	50 to 64	53.7	26.2	3,602,002	1,425	9 1,801,00	1,102	327	220	\$\$1 62 1.129 63	720,400	658	771	132	526	37	360,200	421	1,008	84	337	24	180,100	262	1,167	52	209	15	36,020	81	1,348	16	65	5
Kidney	70 to 74	91.2	45.1	3,071,575	2,063	1,731,09. 3 1,535,78	2 1,475 7 1,590	476	318	1,178 62	614,315	949	1,032	190	759	37	307,157	608	1,5%	122	436	24	153,579	378	1,685	76	302	15	30,716	117	1,805	22	93	- 5
Kidney	75 њ 79	110.1	57.2	2,189,011	1,78	5 1,094,50	5 1,376	409	275	1,101 62	437,802	\$21	964	164	657	37	218,901	526	1,259	105	421	24	109,451	327	1,458	65	262	15	21,890	101	1,684	20	\$1	5
Kidney	Total 40-69	34.6	16.9	24,586,669	6,302	2 12,293,33	5 4,858	1,444	972	3,886 62	4,917,334	2,900	3,402	580	2,320	37	2,458,667	1,857	4,445	371	1,485	24	1,229,333	1,155	5,147	231	924	15	245,867	356	5,946	71	285	5
Kidney	Total 50-59	31.7	15.5	\$,839,717	2.07	5 4,419, 8 5	1.599	476	320	1,280 62	1,767,943	955	1,120	191	764	37	\$\$3,972	611	1,464	122	489	24	432,134	380	1,695	76	304	15	\$\$,397	117	1.958	23	94	5
Kidney	Total 50-69	45.8	22.6	15,943,902	5,415	5 7,971,95	1 4,174	1,241	835	3,339 62	3,188,780	2,492	2,923	498	1,993	37	1,594,390	1,595	3,820	319	1,276	24	797,195	992	4,423	198	794	15	159,439	306	5,109	61	245	5
Kidney	Total 60-74	71.8	35.5	10,175,760	5,403	3 5,087,88	4,165	1,238	\$33	3,332 62	2,035,152	2,486	2,917	497	1,989	37	1,017,576	1,592	3,811	318	1,273	24	508,788	990	4,413	198	792	15	101,758	305	5,098	61	244	5
Kidney	Total (all ages)	29.2	14.8	66,041,278	13,323	3 14,925,62	1 1,824	2,520	1,365	6,239 62	5,969,451	4,071	3,4 79	994	5,151	51	2,984,725	2,990	7,100	398	2,392	24	1,492,303	1,839	\$,291	512	1,488	15	254,415	D /4	9,5 (0	115	439	,
Lung																																		
Lang	10 њ.44	6.0	5.8	4,075,608	240	2,037, 80	1 176	64	35	141 59	\$15,122	99	141	20	79	33	407,561	61	179	12	49	20	203,780	37	203	7	29	12	40,756	11	229	2	8	4
Lung Lung	15 16 49 50 in 54	16.3 33.4	14.7 31.5	4,567,159	1 513	5 2,2103,510 7 3 7 9 05	D 518 S 1.108	188	104	414 59	913,432	292	414	58 175	233	33	456,716	180	526	36	144 308	20 70	228,358	108	598 1780	22	185	12	45,672	31 67	675	6	25 53	4
Lung	55 to 59	71.4	67.1	4,1\$1,606	2,896	5 2,090,80	3 2,123	773	425	1,698 59	\$36,321	1,196	1,700	239	957	33	418,161	738	2,158	148	590	20	209,080	444	2,452	89	355	12	41,816	128	2,768	26	102	4
Lung	50 to 64	137.0	124.9	3,602,002	4,711	1,\$01,00	3,454	1,257	691	2,763 59	720,400	1,946	2,765	389	1,557	33	360,200	1,200	3,511	240	960	20	180,100	722	3,989	144	577	12	36,020	208	4,503	42	166	4
Lang	50 16 69 70 in 74	229.5	278 1	3,502,183	9 375	1,751,09.	2 5,413 7 6,875	2 503	1,095	4,378 39	614 3 15	3,084	4,382	775	3,468	33	307 157	7,902	5,364	38U 478	1,522	20	153 579	1,144	7 941	219	1 150	12	35,022	330	1,136	00 #3	331	4
Lung	75 to 79	462.2	340.5	2,189,011	8,680	1,094,50	5 6,363	2,317	1,273	5,090 59	437,802	3,586	5,094	717	2,869	33	218,901	2,212	6,468	442	1,769	20	109,451	1,330	7,350	266	1,064	12	21,890	383	8,297	77	307	4
Lang	Total 40-69	74.8	68.0	24,586,669	17,531	12,293,33	5 12,851	4,680	2,570	10,2\$1 59	4,917,334	7,243	10,288	1,449	5,794	33	2,458,667	4,467	13,064	\$93	3,574	20	1,229,333	2,686	14,845	537	2,149	12	245,867	774	16,757	155	619	4
Lang	Total 50-59	51.4	48.4	\$ \$39.717	4.40	4,521,50	3.231	1.177	646	2.585 59	1,767,943	1.\$21	2.587	364	1.457	33	\$\$3.972	1.123	3.285	225	195	20	452,158	675	3.733	135	540	12	\$0,428 \$1,397	195	4.213	39	156	4
Lung	Fotal 50-69	109.4	98.9	15,943,902	16,58	7,971,95	12,158	4,427	2,432	9,726 59	3,188,780	6,852	9,733	1,370	5,481	33	1,594,390	4,226	12,359	845	3,381	20	797,195	2,541	14,044	508	2,033	12	159,439	733	15,852	147	586	4
Lung	Total 60-74	227.8	196.8	10,175,760	21,555	5 5,087,88	0 15,801	5,754	3,160	12,641 59	2,035,152	\$,905	12,650	1,781	7,124	33	1,017,576	5,492	16,063	1,098	4,394	20	508,788	3,303	18,252	661	2,642	12	101,758	952	20,603	190	762	4
Lung	Total (all ages)	90.6	70.1	66,041,278	48,549	9 14,923,62	20,049	9,00	9,210	20,811 39	10,909,431	14,703	20,6 60	2,941	11,702		2,7 0 9,723	9,009	20,920	1,814	وديري	20	1,492,903	5,455	90,190	r,ost	4,302	12	238,413	1,572	94,017	514	1,476	4
Testis																																		
Testas	10 16 44	12.3	0.0	2,021,385	241	1,010,69	2 236	12	47	189 76	404,277	197	51	39	158	64	202,138	161	\$7	32	129	52	101,069	126	122	25	101	41	20,214	63	185	13	50	20
Testis	10 ko 49 50 ko 54	9.4	0.0	2,251,680	211	1,125,84	J 201 5 152	10	40 30	161 76	450,336	168	43	34	134	64 64	225,168	137	74	27	109	52	112,584	107	104	21	\$ 6	41	22,517	53 41	158	11	43 37	20
Tesus	55 to 59	5.2	0.0	2,061,919	10	1,030,95	9 103	5	21	\$2 76	412,384	\$6	22	17	69	64	206,192	70	38	14	56	52	103,096	55	53	11	44	41	20,619	27	\$1	5	22	20
Testis	50 to 64	3.0	0.0	1,764,828	52	2 \$\$2,414	4 49	3	10	40 76	352,966	41	11	8	33	64	176,483	34	18	7	27	52	\$\$,241	26	26	5	21	41	17,648	13	39	3	11	20
Testis Tastis	50 to 69 70 to 74	2.4	0.0	1,696,993	41	1 848,49 5 733.08	/ 39 3 22	2	8	31 76	339,399	33	1	7	26	64 64	169,699	27	14	5	21	52	\$4,\$50 73,309	21	20	4	17	41	16,970	10	31	2		20
Testis	75 ю 79	1.4	0.0	1,007,365	14	503,68	3 13	1	3	11 76	201,473	11	3	2	9	64	100,737	25	5	2	7	52	50,368	7	7		6	41	10,074	4	10	1	3	20
Testas	Fotal 20-39	16.0	0.0	\$,7\$2,73\$	1,406	5 4,391,36	1,338	68	268	1,070 76	1,756,548	1,116	290	223	8 93	64	\$78,274	911	495	182	729	52	439,137	712	694	142	570	41	\$7,\$27	356	1,050	71	285	20
Testis	Total 40-69	6.8 10.7	0.0	4,273,065	\$20	2,136.53	7 /300) 2 437	40	136	0.24 76 349 76	2,418,000	601 364	169	130	521 292	64 64	427 306	251 297	2019	106	4.D 731	52	213,653	416 233	404	83 47	55Z 185	41	42,731	2046	51Z 343	42	93	20
Testis	Total 50-59	6.2	0.0	4,355,391	264	2,177,69	5 255	13	51	204 76	\$71,078	213	55	43	170	64	435,539	174	94	35	139	52	217,770	136	132	27	109	41	43,554	68	200	14	54	20
Testás	Total 50-69	4.6	0.0	7,817,213	361	3,908,60	5 344	17	69	275 76	1,563,443	287	74	57	229	64	7\$1,721	234	127	47	187	52	390,861	183	178	37	146	41	78,172	91	270	18	73	20
Testas	1 otal 60-74 Total 40-79	2.6	0.0	4,929,786	121	2,464,89 7,282,90	s 122 4 127	6 42	24	97 76	985,957 2 913 122	102	179	20	¥1 552	64 64	492,979	13 563	45	117	66 451	52 52	246,489 728,280	65 440	63 429	13	52 357	41	49,298	32	96 649	6 44	176	20
Testis	Fotal (all ages)	7.2	0.0	32,583,226	2,35	4		•••	100	10		•,•	1.5	150		- 1	,						,						,==					

Supplementary Table 8. Outcomes including 10-year survival from screening offered to PRS-defined high risk 20% (current and future), oldest 20% and random 20%.

Impact of screening for cancers of the breast (40-49 years), colorectum (50-59 years) and prostate (50-59, 60-69 years). Presented are modelled outcomes for screening of the full population, a PRS-defined high-risk quintile (20%), the oldest quintile (20%), a randomly-selected fifth of the population and the full population. Metrics presented are modelled for the UK population (~66 million) for annual cancers arising and deaths averted. These are maximal estimates based on several favourable assumptions, which include (i) that all cancers arising in the screening interval are present at time of screen (i.e. no interval cancers) (ii) full population uptake for PRS and for screening (see methods).

	be	odlaity	pr		Population	-	10 ye	ear survival	ival	(%)	deaths	er one
	Cancer T.	Screening mo	Age -baı	Population size	Cancers arising annually	Size of screened Group	Total	Deaths averted	Ten year surv (%)	Survival Improvement	Reduction in (%)	Individuals so for 10 years p death averted
ng 1e)	Breast		40 to 49	4,369,703	7,533		6,839		90.8%			
lo eni elir	Prostate		50 to 59	4,355,391	5,897		5,385		91.3%			
rcre bas	Prostate		60 to 69	3,461,821	16,853		15,591		92.5%			
s (j	Colorectal		50 to 59	8,839,717	5,052		3,337		66.1%			
d o	Breast	Digital mammography	40 to 49	4,369,703	7,533	873,941	6,941	102	92.1%	1.4%	14.7%	854
r Tc	Prostate	PSA_3ng/mL cut-off	50 to 59	4,355,391	5,897	871,078	5,443	58	92.3%	1.0%	11.4%	1,495
ing % nt F	Prostate	PSA_3ng/mL cut-off	60 to 69	3,461,821	16,853	692,364	15,748	158	93.4%	0.9%	12.5%	439
een 2(rrei	Prostate	mpMRI	50 to 59	4,355,391	5,897	871,078	5,547	162	94.1%	2.7%	31.7%	537
Scr (cu	Prostate	mpMRI	60 to 69	3,461,821	16,853	692,364	16,029	438	95.1%	2.6%	34.7%	158
	Colorectal	FIT 20-50 µg/g threshold (CRC)	50 to 59	8,839,717	5,052	1,767,943	3,525	188	69.8%	3.7%	11.0%	940
<u>c</u> .	Breast	Digital mammography	40 to 49	4,369,703	7,533	873,941	6,959	121	92.4%	1.6%	17.4%	723
To RS)	Prostate	PSA_3ng/mL cut-off	50 to 59	4,355,391	5,897	871,078	5,447	62	92.4%	1.0%	12.0%	1,414
ing % e PJ	Prostate	PSA_3ng/mL cut-off	60 to 69	3,461,821	16,853	692,364	15,757	167	93.5%	1.0%	13.2%	416
een 20 tur	Prostate	mpMRI	50 to 59	4,355,391	5,897	871,078	5,556	171	94.2%	2.9%	33.5%	508
Scre (fu	Prostate	mpMRI	60 to 69	3,461,821	16,853	692,364	16,054	463	95.3%	2.7%	36.7%	149
01	Colorectal	FIT 20-50 µg/g threshold (CRC)	50 to 59	8,839,717	5,052	1,767,943	3,544	207	70.1%	4.1%	12.0%	856
est up	Breast	Digital mammography	40 to 49	4,369,703	7,533	937,850	6,919	80	91.8%	1.1%	11.6%	1,166
gro	Prostate	PSA_3ng/mL cut-off	50 to 59	4,355,391	5,897	786,032	5,427	42	92.0%	0.7%	8.2%	1,872
ige og	Prostate	PSA_3ng/mL cut-off	60 to 69	3,461,821	16,853	702,786	15,686	95	93.1%	0.6%	7.5%	738
enir in a	Prostate	mpMRI	50 to 59	4,355,391	5,897	786,032	5,502	117	93.3%	2.0%	22.8%	673
sree %	Prostate	mpMRI	60 to 69	3,461,821	16,853	702,786	15,855	265	94.1%	1.6%	21.0%	265
Sc 20	Colorectal	FIT 20-50 µg/g threshold (CRC)	50 to 59	8,839,717	5,052	1,596,060	3,492	155	69.1%	3.1%	9.0%	1,030
ly-	Breast	Digital mammography	40 to 49	4,369,703	7,533	873,941	6,893	55	91.5%	0.7%	7.9%	1,594
0%	Prostate	PSA_3ng/mL cut-off	50 to 59	4,355,391	5,897	871,078	5,410	25	91.7%	0.4%	5.0%	3,427
and 5 d 2	Prostate	PSA_3ng/mL cut-off	60 to 69	3,461,821	16,853	692,364	15,659	69	92.9%	0.4%	5.4%	1,007
n ra sete	Prostate	mpMRI	50 to 59	4,355,391	5,897	871,078	5,456	71	92.5%	1.2%	13.8%	1,232
ree sele	Prostate	mpMRI	60 to 69	3,461,821	16,853	692,364	15,782	191	93.6%	1.1%	15.1%	362
Sc	Colorectal	FIT 20-50 µg/g threshold (CRC)	50 to 59	8,839,717	5,052	1,767,943	3,449	112	68.3%	2.2%	6.5%	1,584
u	Breast	Digital mammography	40 to 49	4,369,703	7,533	4,369,703	7,113	274	94.4%	3.6%	39.5%	1,594
atic	Prostate	PSA_3ng/mL cut-off	50 to 59	4,355,391	5,897	4,355,391	5,512	127	93.5%	2.2%	24.8%	3,427
hul	Prostate	PSA_3ng/mL cut-off	60 to 69	3,461,821	16,853	3,461,821	15,934	344	94.5%	2.0%	27.2%	1,007
od	Prostate	mpMRI	50 to 59	4,355,391	5,897	4,355,391	5,738	353	97.3%	6.0%	69.0%	1,232
ull (Prostate	mpMRI	60 to 69	3,461,821	16,853	3,461,821	16,546	956	98.2%	5.7%	75.7%	362
Щ	Colorectal	FIT 20-50 µg/g threshold (CRC)	50 to 59	8,839,717	5,052	8,839,717	3,895	558	77.1%	11.0%	32.5%	1,584

Supplementary Table 9: Impact on AUC of incorporation of multimodal parameters into risk prediction model.

Adapted from Kachuri et al, Nature Communications 2020 Nov 27;11(1):6084. PRS_{IV} are calculated from inverse variance (IV) weights. AUC values were estimated at 5 years of follow-up using UKBiobank. Sex is only included in the predictive model for cancers of the colon/rectum, lung, kidney, and pancreas. Family history and other predictors are included where on univariate analysis they have been demonstrated to improve the model for prediction of cancer incidence.

			AUC for	predictive	model inclu	ıding				
Cancer site	Cases in UK-Biobank	Variants in PRS	(A) Age [+ sex]	(B) Age [+ sex] + family history	(C) Age [+ sex] + PRS _{IV} (instead of family history)	(D) Age [+ sex] + other predictors	(E) Age [+ sex] + family history + other predictors	(F) Age [+ sex] + family history + PRS _{IV}	(G) Age $[+ sex]$ +other predictors + PRS _{IV}	(H) Age [+ sex] + family history + other predictors + PRS _{IV}
Prostate	4740	161	0.713	0.720	0.766			0.769		
Testis	52	52	0.658		0.787					
Breast	4760	162	0.548	0.562	0.626		0.573			0.637
Ovary	445	36	0.620	0.622			0.643			0.660
Colon/rectum	2725	103	0.680	0.681	0.708		0.688			0.716
Lung	1541	109	0.704	0.714	0.710		0.843			0.846
Kidney	612	19	0.687			0.713			0.722	
Pancreas	493	22	0.695				0.715	0.745		

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