Supplementary Material 1: Sensitivity analysis

Influence of assumed cancer prevalence rate in symptomatic patients

We conducted a series of sensitivity analyses in which we tested our assumption about the underlying prevalence of cancer in patients presenting to their GPs.
We thus selected a range of prevalence rates (1.5%, 3% and 4%) and used the reciprocals of these values (66, 33 and 25 respectively) to multiply by the number of cancers to provide estimates of the total number of patients with symptoms possibly indicative of cancer and thus estimate the number of true negatives per practice.

Influence of lower limit of practice size for inclusion in the analysis

We also tested the sensitivity of the results to the lower limit of practice size which was eligible for inclusion in the analysis. In supplementary table 1 we report the sensitivity and specificity of the summary point from a bivariate meta-analysis based on each prevalence rate and lower limit of practice size for inclusion.

Supplementary Table ST1 Sensitivity analysis of influence of (a) lower limit for number of cancers per practice over 5 years and (b) different assumed prevalence of cancer in symptomatic patients on sample size, sensitivity and specificity.

Lower limit of number of cancers	Sample size		Sensitivity[1]	Specificity Assumed prevalence of cancer			
	Practices	Patients		4%	3%	2%	1.5%
None	7630	53,563,589	-	-	-	-	-
5	6705	50,974,927	47.6%	84.1%	88.1%	92.2%	94.2%
30	5960	48,268,374	47.4%	83.9%	87.9%	92.2%	94.1%
50	**5479**	**46,271,734**	**47.4%**	83.7%	**87.8%**	92.1%	94.0%
100	4445	41,198,188	47.3%	83.7%	87.8%	92.1%	94.0%
200	2269	25,878,891	47.5%	84.0%	88.0%	92.2%	94.1%

1. Sensitivity and specificity relate to the summary point from bivariate meta-analysis of all eligible practices.
2. Values in bold indicate the values used and obtained in the primary analysis

Table ST2 Sensitivity analysis of changing assumed cancer prevalence in symptomatic patients on workload for different quintiles of age-standardised referral rate. Data based on 1000 cancers per quintile

	Cancer prevalence = 4% Referral rate quintile		Cancer prevalence =3% Referral rate quintile		Cancer prevalence = 2% Referral rate quintile		Cancer prevalence = 1.5% Referral rate quintile	
	Lowest	Highest	Lowest	Highest	Lowest	Highest	Lowest	Highest
Obtained from data								
Sensitivity	42.8%	50.6%	42.8%	50.6%	42.8%	50.6%	42.8%	50.6%
Specificity	89.4%	76.4%	92.0%	82.4%	94.8%	88.5%	96.1%	91.4%
Application of data to 1000 cancers								
Cancer + fast-track (true positive)	428	506	428	506	428	506	428	506
Cancer, no fast-track (false negative)	572	494	572	494	572	494	572	494
No cancer + fast-track (false positive)	2552	5655	2548	5639	2544	5626	2542	5623
No cancer, no fast track (true negative)	21448	18345	29452	26361	46456	43374	62458	59377
Implications per 1000 cancers								
Total referrals	**2980**	**6161**	**2976**	**6145**	**2972**	**6132**	**2970**	**6129**
Additional fast-track referrals		3181		3169		3160		3159
Additional cancers via fast-track		78		78		78		78

This sensitivity analysis only relates to moving from the lowest quintile to the highest quintile (the leftmost and rightmost data columns in table 4, not the cumulative effect of moving from all quintiles to the highest quintile.