Supplemental Materials

S1. Natural History Model of lung cancer

Exponential growth of a primary tumor

We developed a natural history model for lung cancer (1); a summary diagram is shown in **Supplemental Figure S1**, in which the x-axis is time, *T,* and the y-axis is a tumor volume, $V(t)$ at time $T = t$. An initial tumor has a size V_0 at $T = 0$ assumed to be 1mm^3, which grows exponentially with $V(t) = V_0 \exp(rt)$, where r is a growth rate parameter with corresponding tumor volume doubling time (TVDT) given as (log2)/*r*. When the tumor size reaches a certain size, V_p, it promotes symptoms that lead to a clinical detection due to the primary tumor; and this V_p and growth rate r are modeled bivariate log-normal distributed, with two mean parameters μ_P, μ_r, and three covariance parameters, σ_1, σ_2 and σ_3.

Growth of metastasis and survival

A metastasis starts growing at time $T = T_{OM}$ and we assume the volume at this time (V_C) is a threshold for cure (cure threshold) so that if the tumor is detected and treated earlier than this point, it can be cured otherwise it is not curable. And this volume is modeled to be Weibull distributed with K_1 and K_2 for shape and scale parameters. So this metastatic burden $B(t)$ grows also proportionally to the primary tumor size with the relation $B(t) = (V(t) - V_C)f$ with unobservable fraction *f* until it reaches a maximum burden size B_D at time $T = T_D$, which is a survival time in case the tumor is not detected and cured before reaching the cure threshold V_C. And this maximum burden divided by the fraction *f*, B_D / f is modeled to be Weibull distributed (with L_1 and L_2 as shape and scale parameters) to avoid non-identifiability.

Staging

If this metastatic burden grows to a certain size, $c_1 B_D$ at time $T = T_{MO}$, which is a fraction of the maximum burden, it becomes an observable metastasis so that if a detection (either clinical detection or screen detection) occurs earlier than this point, it's an early staged tumor otherwise it's an advanced staged tumor.

Clinical detection

When the metastatic burden keeps growing to a certain size, $c_2 B_D$ at time $T = T_M$, it promotes a detection due to metastasis; and whichever comes first—either the detection due to the primary tumor, T_P or due to metastasis, T_M becomes the clinical detection time. In the example shown in **Supplemental Figure S1**, the detection is due to the primary tumor. c_1 and c_2 are regarded as fixed constants across different tumors that need to be estimated from data.

S2. Parameter estimation of natural history model for lung cancer

SEER data

The parameters of the natural history model were estimated using National Cancer Institute Surveillance, Epidemiology and End Results (SEER) survival data for cancer cases diagnosed between 1988 and 2003 (hence in the absence of screening) for each histologic subtype (adenocarcinoma, squamous, large cell and small cell) and gender. The data include 66732 male and 60166 female and provide information on tumor size (D) and stage at clinical detection (A) and survival time (S) up to 15 years. For estimation purposes, tumor diameters at clinical detection were discretized into 6 bins (0-2, 2-2.9, 3- 3.9, 4-4.9, 5-6.9, >7 cm survival times were discretized into 1-year intervals up to 15 years, and stage into early (I-II) or advanced (III-IV).

Maximum likelihood Estimation

We have a total of 11 parameters $\theta = (\mu_r, \mu_P, \sigma_1, \sigma_2, \sigma_3, K_1, K_2, L_1, L_2, c_1, c_2)$ for the natural history model for each histologic subtype and each gender. The parameters were estimated using maximum likelihood approach, with the likelihood function given as:

$$L(\theta) = \left[\prod_{j=0}^{6} \prod_{k=0}^{1} \prod_{l=0}^{14} \Pr(D(\theta) \in [d_j, d_{j+1}), A(\theta) = k, S(\theta) \in [s_l, s_{l+1}))^{N^E_{jkl}} \right] \times \left[\prod_{j=0}^{6} \prod_{k=0}^{1} \prod_{l=0}^{15} \Pr(D(\theta) \in [d_j, d_{j+1}), A(\theta) = k, S(\theta) > s_l)^{N^C_{jkl}} \right]$$

, where $D(\theta)$ is tumor size, $A(\theta)$ is stage, $S(\theta)$ is survival time, and N^E_{jkl} is the count of lung cancer cases who die of lung cancer with tumor size at $[d_j, d_{j+1})$, stage at K and survival time on $[s_l, s_{l+1})$, and N^C_{jkl} is the count of lung cancer cases who were censored due to other cause of morality or loss-to-follow-up until l years with tumor size at $[d_j, d_{j+1})$, stage at K.

In assessing the value of the likelihood function for a given parameter θ, we use an empirical approach, which is based on simulations; we sample hundreds of thousands of lung cancer patients by sampling parameters from given distributions of natural history parameters (e.g. Weibull or bivariate log-normal distribution). Then to estimate the probability of an event for a given category defined by tumor size, stage and survival time, i.e. $\Pr(D(\theta) \in [d_j, d_{j+1}), A(\theta) = k, S(\theta) \in [s_l, s_{l+1}))$, simply count the number of individuals belonging to the category and divide it by the total number of individuals simulated. Simulation size $N = 100{,}000$ was used for each likelihood value calculation. A stepwise estimation method was used to estimate the parameters based on Nelder-Mead algorithm; a vector of parameters was partitioned in to four sections $\theta = (\mu_r, \mu_P, \sigma_1, \sigma_2, \sigma_3;\ K_1, K_2;\ L_1, L_2;\ c_1, c_2)$ and each section of the parameters was estimated and updated sequentially through optimizations conditioning on the rest of parameters as fixed; the procedure was repeated until the procedure reaches convergence. In order to check convergence, ~700 different initial parameter sets were used that cover the wide range of the whole parameter space. The estimated parameters for each subtype and gender are shown in **Supplemental Table S3** and plots comparing model fits to SEER data (male) are shown in **Supplemental Figure S2**. We note that these are updated estimates compared to the ones previously reported (1).

Low Malignant Potential Tumor (LMP)

In addition to the four major histologic subtypes, we also modeled low malignant potential tumor including bronchioloalveolar cancer, which is commonly detected through LDCT, but not typically detected in the absence of screening. Hence SEER data with patients diagnosed in the absence of screening doesn't include enough information to fit the model for growth and survival of this type of tumor. Hence in order to model low malignant potential tumor, we based it on the natural history parameters of adenocarcinoma, but adjusted its growth rate and cure threshold by fitting the model to NLST data through calibrations that will be described later (See **Section 3.1** and **Supplemental Materials Section S3**); also prediction for its incidence, that is, time for clinical detection in the absence of screening using TSCE was adjusted and estimated through calibrations since predictions by TSCE are based on estimation for the major subtypes, and hence cannot be directly applied for low malignant potential tumor. We note that LMP is a new feature to our model compared to the one used in the previous reports (2, 3).

S3. Calibration

Calibration Method

Specifically, for a given set of calibration parameters, a microsimulation is performed to predict outcomes—such as LC status, detection mode and survival time—for each participant in the NLST. Then study-level outcomes parameters are summarized by counting the LC incidence and mortality among all participants over the study period from year 1 to year 6 (i) by detection mode (screen detection or clinical (interval) detection), (ii) by screening arm (LDCT/CXR) and are compared to the observed outcomes in NLST data. After obtaining study-level outcomes for the given set of calibration, a goodness-of-fit measure is calculated as: $F_i = \sum_{t=1}^{6} \frac{|O_t - E_t|}{E_t}$, where O_t is observed count and E_t is predicted count for time t (t = 1,2,3,4,5,6) for each table for LC incidence or mortality by arms and detection mode; and finally compute $F = \sum_{i=1}^{8} F_i$ for 8 tables defined by (incidence, mortality) x (CT, CXR) x (screen, interval). A set of parameters that minimizes F was chosen as the final parameters to be used for the subsequent analyses.

Calibration Target Parameters

The calibration target parameters and their considered ranges are shown in **Supplemental Table S4**: CT and CXR detection thresholds with ranges 2mm-5mm and 20mm-25mm for CT and CXR respectively; the tumor size threshold for diagnostic follow-up with range 5-10mm; lung cancer incidence time adjustment, i.e. lung cancer clinical detection time adjustment (CDTA1) so that it advances the predicted incidence age using TSCE model by 1-5 years; this was done since TSCE was estimated using NHS/HPF data that include a large proportion of non-smokers and showed discrepancy between observed and predicted outcomes especially for heavy smokers (data not shown); especially the discrepancy became more severe as individuals are heavier smokers (increased smoking duration and intensity). Hence in addition to CDTA1 that is applied for all participants in the simulation, a second adjustment for clinical detection time (CDTA 2) was made only for heavy smokers defined by a given threshold K; the levels of smoking is well summarized in annual hazard estimation (using TSCE) which is the function of mainly smoking (and gender), and hence summation of predicted hazard from age 50 to 100 was used as a measure of threshold K.

The considered range of K was 0.8 to 1.2 which needs to be decided by fits to data through calibration. Lastly, low malignant potential tumor (LMP) related parameters such as tumor growth rate parameter *r* and cure threshold related parameter and clinical detection time adjustment for low malignant tumor (CDTA3), which needs to be delayed this time since the LMP is not symptomatically detected until later in life. See the ranges of these values in **Supplemental Table S4**.

Supplemental Tables

Table S1. Example profiles of individuals with input information and predicted outcomes using our microsimulation model for lung cancer screening

	Input and output variables	Profile 1	Profile 2	Profile 3	Profile 4
Input Variables	Gender	Male	Male	Male	Male
	Smoking Status	Former	Current	Current	Current
	Smoking Start Age	14	18	17	18
	Smoking Quit Age	54	-	-	
	Cig/Day	20	30	30	15
	Age at entry	64	69	60	64
Lung Cancer Incidence	Lung Cancer Case	Yes	Yes	Yes	No
	Age at Clinical Detection of lung cancer	71.78	71.92	62.62	-
Natural history of lung cancer	Histology	AD	SQ	AD	-
	Cure Threshold [1] (mm)	11.82	11.71	10.89	-
	Tumor Volume Doubling Time (days)	187	124	144	-
	Clinical Detection Time from V_0 [2](years)	7.78	2.92	2.62	-
	Time from clinical detection to survival (years)	1.29	1.25	3.03	-
	Tumor Size at Clinical Detection (mm)	84.21	24.29	25.32	-
Screening	Screen Mode	LDCT	LDCT	LDCT	LDCT
	Detection Threshold (mm)	3.1	4.3	4.21	-
	Tumor size at Screen time=0 (mm)	2.97	3.33	5.46	-
	Tumor size at screen time=1 (mm)	4.67	6.57	9.81	-
	Tumor size at screen time=2 (mm)	7.33	-	-	-
Detection	Detection Mode	Screen	Screen	Screen	-
	Tumor Detection Time (year)	1	1	0	-
	Tumor size at detection (mm)	4.67	6.57	5.46	-
Diagnosis	Number of diagnostic follow-ups	3	2	2	-
	Time to diagnosis from randomization (years)	2.75	1.62	1.25	-
	Diagnostic delays (years)	1.75	0.62	1.25	-
	Tumor size at diagnosis (mm)	10.28	10.04	11.36	-
	Tumor Stage at diagnosis	Early	Early	Early	-
	Age at diagnosis	66.75	70.62	61.25	-
Survival /Death	Cured from lung cancer	Yes	Yes	No	-
	Cause of Death	Other	Other	Lung Cancer	Other
	Age for other cause of morality	77.3	88.7	72.5	83.84
	Age of death from lung cancer in the absence of screening	73.06	73.18	65.64	-
	Age of death	77.3	88.7	65.64	83.84

Note:

[1] A tumor volume at the onset of metastasis. If the tumor is detected and treated earlier before reaching this size, it can be cured otherwise it is not curable (See Section S1. Natural History Model of lung cancer for more details)

[2] V_0 is an initial tumor in the natural history model

Table S2. Histologic Subtype Distributions from SEER data

	Female	Male
Adenocarcinoma	0.43	0.35
Squamous	0.23	0.35
Large Cell	0.09	0.09
Small Cell	0.25	0.21

Table S3. Natural History Parameter Estimation

	Female				Male			
Natural History Parameter	Adeno	Squamous	Large Cell	Small Cell	Adeno	Squamous	Large Cell	Small Cell
μ_r	0.38	0.64	0.85	1.40	0.48	0.68	0.99	0.99
μ_P	1.80	1.93	2.34	2.36	2.08	2.04	2.34	2.81
σ_1	1.28	1.38	1.60	1.16	1.35	1.41	1.68	1.31
σ_2	0.80	0.76	0.90	0.72	0.86	0.74	0.79	0.97
σ_3	0.33	0.33	0.39	0.17	0.24	0.22	0.27	0.05
K_1	0.31	0.25	0.25	0.30	0.30	0.23	0.21	0.23
K_2	7.80	7.37	7.06	7.16	7.45	7.22	6.38	6.12
L_1	0.59	0.74	0.71	0.56	0.63	0.79	0.77	0.70
L_2	12.78	13.77	13.22	15.00	12.48	13.71	13.08	13.18
c_1	0.08	0.07	0.12	0.00	0.18	0.14	0.21	0.13
c_2	0.23	0.17	0.20	0.03	0.35	0.20	0.28	0.23
TVDT (days)	173	132	108	62	157	128	94	93
Cure Threshold (cm)	1.09	0.84	0.77	0.88	0.99	0.79	0.56	0.54
Tumor size at clinical detection (cm)	6.04	6.89	6.42	7.03	6.26	7.67	6.69	6.62

Table S4. Calibration Target Parameters and Results of Calibrations

	Calibration Target Parameter	Range	Calibration Results	
			Female	Male
Screening	CT detection threshold	2mm-5mm	2.5mm	2.75mm
	CXR detection threshold	20mm-25mm	21mm	21mm
Diagnostic Follow-up	Tumor size threshold For diagnostic follow-up	5-10mm	8mm	9mm
Adjustment for predictions for lung cancer clinical detection time	Lung cancer clinical detection time adjustment 1 (CDTA1)	0-5 years	1 year	4 year
	Lung cancer clinical detection time adjustment 2 (CDTA 2)	4-5 years	4.25	4.75
	K (hazard threshold for CDTA 2)	0.8-1.2	1	1
Low Malignant Potential Tumor related parameters	TVDT for low malignant potential tumor	1750-2050 days	1850 days	1869 days
	Cure threshold for low malignant potential tumor	9-12cm	11.6cm	9.17cm
	Lung cancer clinical detection time delays for low malignant potential tumor	30-40 years	35 years	35 years

Table S5. Model calibration results using the NLST data

		CXR arm								CT Arm							
		Screen Detected				Interval Detected				Screen Detected				Interval Detected			
	Time	O	E	E/O.ratio	95%CI	O	E	E/O.ratio	95%CI	O	E	E/O.ratio	95%CI	O	E	E/O.ratio	95%CI
Lung Cancer Incidence	1	135	142	1.05	(0.89-1.24)	52	62	1.19	(0.93-1.53)	266	322	1.21	(1.08-1.35)	22	22	1.00	(0.66-1.52)
	2	63	71	1.13	(0.89-1.42)	66	73	1.11	(0.88-1.39)	163	149	0.91	(0.78-1.07)	17	21	1.24	(0.8-1.88)
	3	65	60	0.92	(0.71-1.18)	63	69	1.1	(0.87-1.39)	178	157	0.88	(0.76-1.03)	27	34	1.26	(0.9-1.76)
	4	14	5	0.36	(0.15-0.86)	117	112	0.96	(0.8-1.15)	33	10	0.3	(0.16-0.57)	71	72	1.01	(0.81-1.28)
	5	1	5	5	(2.08-12.01)	145	148	1.02	(0.87-1.2)	9	0	0		106	94	0.89	(0.72-1.08)
	6	1	0	0		165	177	1.07	(0.93-1.24)	0	0	0		133	137	1.03	(0.87-1.22)
	Total	**279**	**283**	**1.01**	**(0.9-1.14)**	**608**	**642**	**1.06**	**(0.98-1.14)**	**649**	**638**	**0.98**	**(0.91-1.06)**	**376**	**380**	**1.01**	**(0.91-1.12)**
Lung Cancer Mortality	1	21	10	0.48	(0.27-0.9)	14	9	0.64	(0.32-1.21)	23	11	0.48	(0.26-0.85)	5	3	0.6	(0.15-1.75)
	2	30	23	0.77	(0.5-1.13)	40	41	1.02	(0.77-1.41)	45	37	0.82	(0.6-1.14)	11	15	1.36	(0.82-2.26)
	3	32	32	1	(0.71-1.41)	49	47	0.96	(0.71-1.27)	47	49	1.04	(0.79-1.38)	20	16	0.8	(0.49-1.31)
	4	25	32	1.28	(0.9-1.8)	68	65	0.96	(0.76-1.23)	49	51	1.04	(0.8-1.38)	35	25	0.71	(0.47-1.04)
	5	12	25	2.08	(1.41-3.09)	75	85	1.13	(0.92-1.41)	31	45	1.45	(1.09-1.95)	42	44	1.05	(0.78-1.41)
	6	12	17	1.42	(0.91-2.32)	104	101	0.97	(0.8-1.18)	20	34	1.7	(1.22-2.38)	64	65	1.02	(0.79-1.29)
	Total	**132**	**139**	**1.05**	**(0.89-1.24)**	**350**	**349**	**0.99**	**(0.9-1.11)**	**215**	**227**	**1.06**	**(0.93-1.2)**	**177**	**167**	**0.94**	**(0.81-1.1)**

Table S6. Model validation results using the PLCO data for all subjects

	Chest X-ray Arm									**Usual Care Arm**			
	Screen Detected Cases					Interval Detected Cases				Interval Detected Cases			
	Time	O	E	E/O ratio	95% CI	O	E	E/O ratio	95% CI	O	E	E/O ratio	95% CI
Lung Cancer Incidence	1	116	121	1.04	(0.87-1.24)	44	48	1.09	(0.83-1.46)	96	95	0.99	(0.81-1.21)
	2	55	60	1.09	(0.85-1.41)	63	56	0.89	(0.68-1.15)	117	110	0.94	(0.78-1.14)
	3	65	62	0.95	(0.74-1.22)	71	59	0.83	(0.64-1.07)	133	121	0.91	(0.76-1.09)
	4	63	66	1.05	(0.83-1.34)	74	67	0.91	(0.71-1.15)	121	124	1.02	(0.86-1.22)
	5	6	0			96	100	1.04	(0.85-1.26)	146	134	0.92	(0.77-1.09)
	6	0	0			115	110	0.96	(0.79-1.15)	124	142	1.15	(0.97-1.35)
	7	0	0			166	147	0.89	(0.75-1.04)	128	153	1.2	(1.02-1.40)
	8	0	0			142	154	1.08	(0.93-1.27)	156	161	1.03	(0.88-1.2)
	9	0	0			151	164	1.09	(0.93-1.27)	146	155	1.06	(0.91-1.24)
	10	0	0			149	169	1.13	(0.98-1.32)	130	164	1.26	(1.09-1.47)
	Total	**305**	**309**	**1.01**	**(0.91-1.13)**	**1071**	**1073**	**1.00**	**(0.94-1.06)**	**1297**	**1360**	**1.05**	**(0.99-1.11)**
	Screen Detected Cases					Interval Detected Cases				Interval Detected Cases			
	Time	O	E	E/O ratio	95% CI	O	E	E/O ratio	95% CI	O	E	E/O ratio	95% CI
Lung Cancer Mortality	1	13	5	0.38	(0.17-0.95)	8	8	1	(0.48-1.97)	23	11	0.48	(0.28-0.89)
	2	36	18	0.5	(0.33-0.81)	37	31	0.84	(0.59-1.19)	67	50	0.75	(0.57-0.98)
	3	27	28	1.04	(0.71-1.49)	52	40	0.77	(0.57-1.05)	82	73	0.89	(0.71-1.12)
	4	30	33	1.1	(0.79-1.56)	58	46	0.79	(0.59-1.06)	91	83	0.91	(0.74-1.13)
	5	31	29	0.94	(0.66-1.36)	50	57	1.14	(0.88-1.48)	116	98	0.84	(0.69-1.03)
	6	19	24	1.26	(0.86-1.91)	74	76	1.03	(0.82-1.29)	94	102	1.09	(0.89-1.31)
	7	10	21	2.1	(1.4-3.27)	85	83	0.98	(0.79-1.21)	96	112	1.17	(0.97-1.40)
	8	8	12	1.5	(0.84-2.62)	112	100	0.89	(0.74-1.09)	114	119	1.04	(0.87-1.25)
	9	3	9	3	(1.59-5.83)	127	109	0.86	(0.71-1.03)	121	127	1.05	(0.88-1.25)
	10	3	8	2.67	(1.35-5.35)	100	123	1.23	(1.03-1.47)	98	122	1.24	(1.04-1.49)
	Total	**180**	**189**	**1.05**	**(0.91-1.21)**	**703**	**673**	**0.96**	**(0.89-1.03)**	**902**	**896**	**0.99**	**(0.93-1.06)**

Table S7. Attendance rate of each screening round in the PLCO data (NLST-eligible). The rate was estimated by calculating the fraction of individuals who attended each round of screening among those who are NLST-eligible.

T*	Attendance Rate
0	0.948
1	0.890
2	0.858
3	0.821

* T is screen time (screening round)

Table S8. Transition probability for compliance to screening estimated using the PLCO data (NLST-eligible)

T*	P_A**	P_{NA}***
0	0.948	0.948
1	0.904	0.673
2	0.913	0.374
3	0.890	0.270

* T is screen time (screening round)

** Prob(Attend screening at T=t given that the individual attended screening at T=t-1) for time t=1,2,3
for T=0, it's Prob (Attend screening at T=0)

***Prob(Attend screening at T=t given that the individual did not attend screening T=t-1) for t=1,2,3
for T=0, it's Prob (Attend screening at T=0)

Supplemental Figures

Figure S1 Natural history model for lung cancer

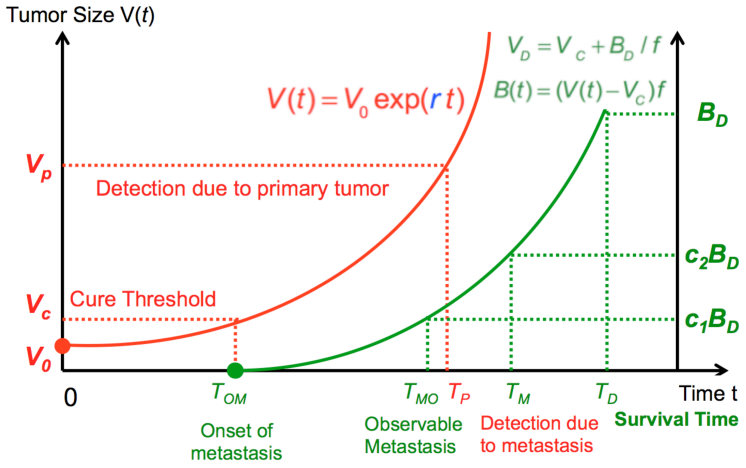
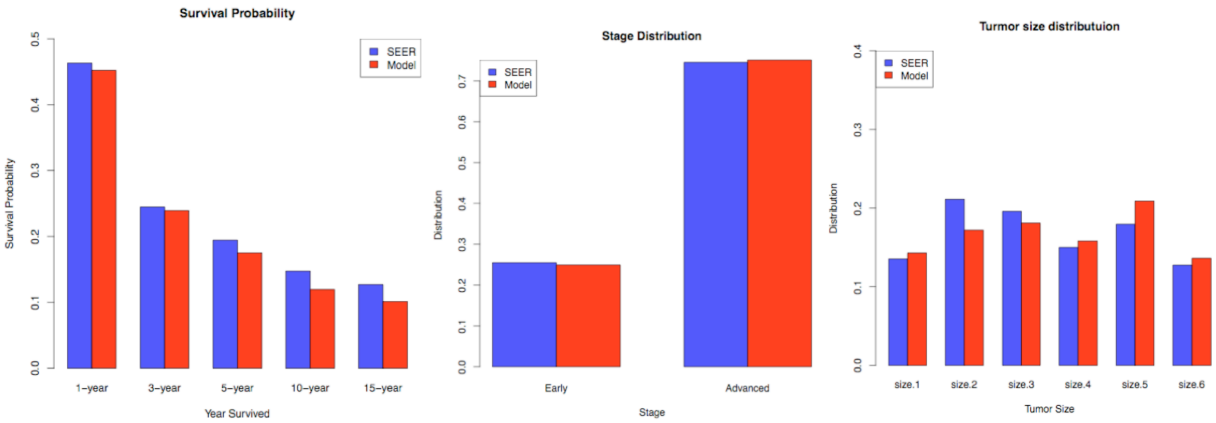
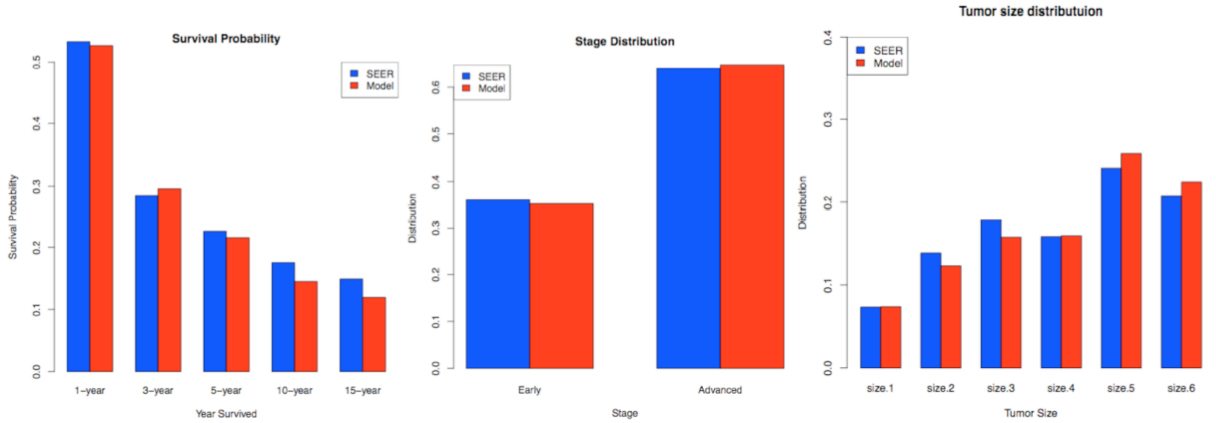


Figure S2 Estimated survival, stage and tumor size distribution using the natural history model comparing to SEER data (male). Blue color represents SEER data and red color shows predictions using the natural history model.

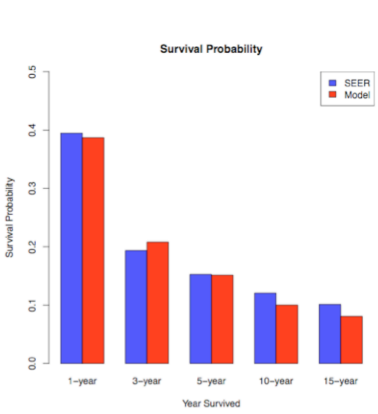
Adenocarcinoma

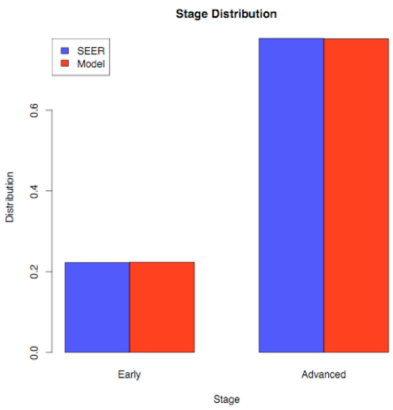


Squamous



Large Cell


Survival Probability
SEER
Model
Survival Probability
0.0
0.1
0.2
0.3
0.4
0.5
1−year
3−year
5−year
10−year
15−year
Year Survived


Stage Distribution
SEER
Model
Distribution
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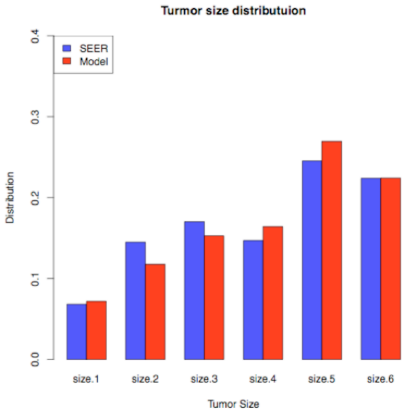
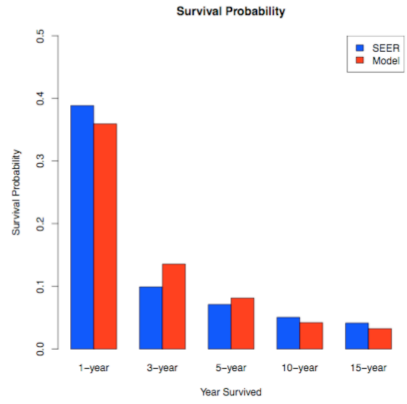
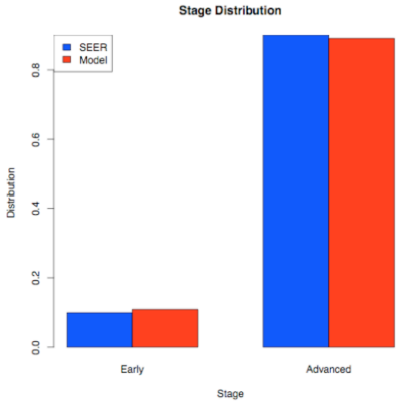
0.2
0.4
0.6
Early
Advanced
Stage


Turmor size distributuion
SEER
Model
Distribution
0.0
0.1
0.2
0.3
0.4
size.1
size.2
size.3
size.4
size.5
size.6
Tumor Size

Small Cell


Survival Probability
SEER
Model
Survival Probability
0.0
0.1
0.2
0.3
0.4
0.5
1−year
3−year
5−year
10−year
15−year
Year Survived


Stage Distribution
SEER
Model
Distribution
0.0
0.2
0.4
0.6
0.8
Early
Advanced
Stage

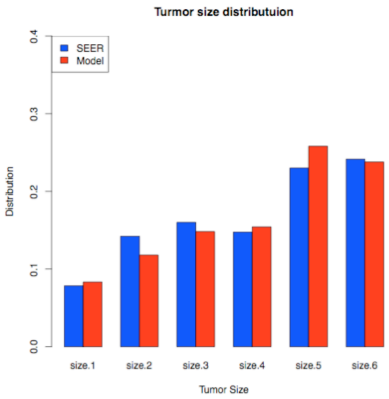

Turmor size distributuion
SEER
Model
Distribution
0.0
0.1
0.2
0.3
0.4
size.1
size.2
size.3
size.4
size.5
size.6
Tumor Size

Figure S3 Model calibration results using NLST data for CXR arm. Cumulative lung cancer incidence and mortality over study time. Observed data is in blue and predicted data is in red. Dotted lines are 95% confidence interval. First row is for lung cancer incidence and second row is for lung cancer death.

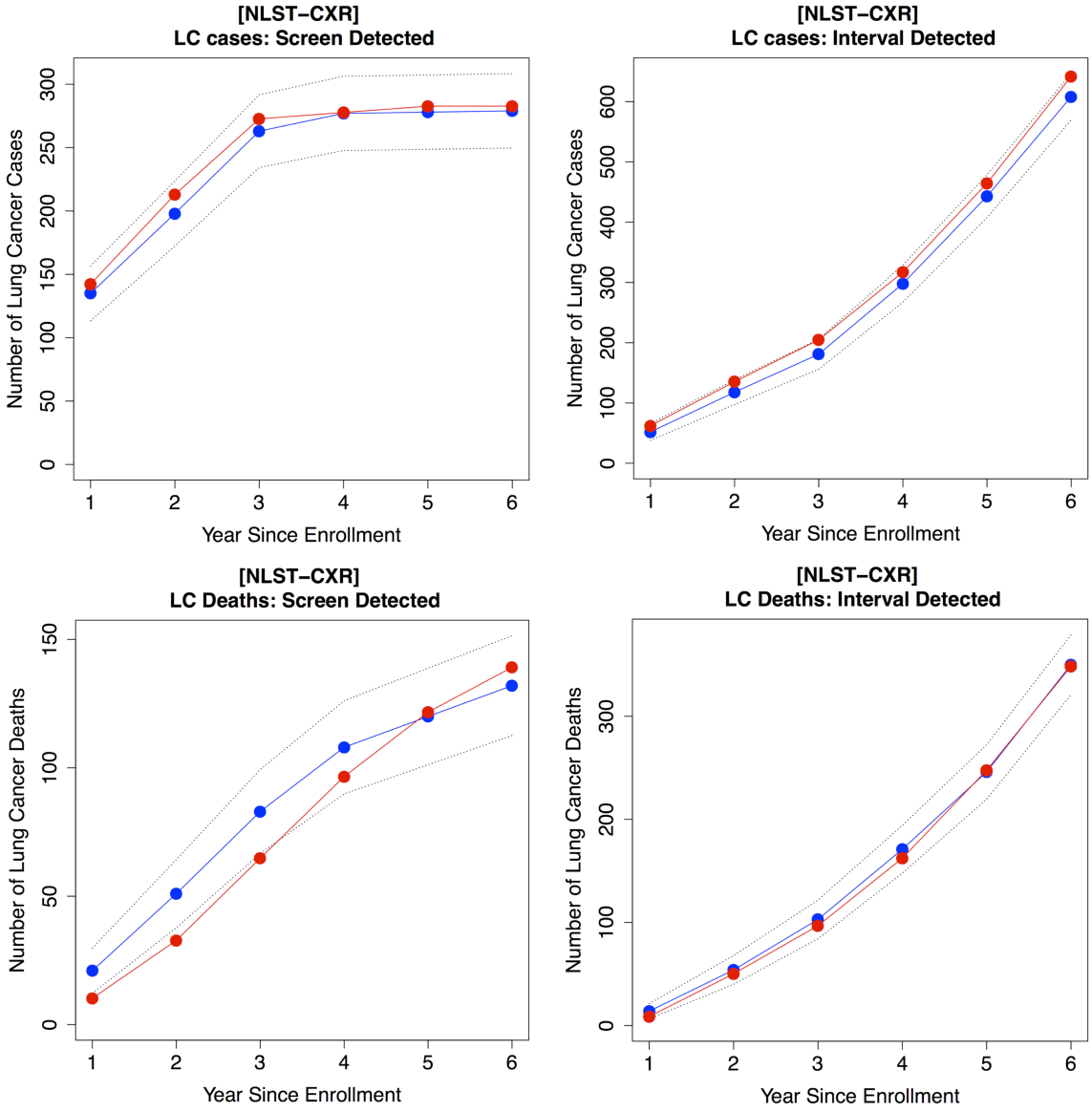


Figure S4. Model validation results using the PLCO data for the usual-care arm (control arm). Cumulative lung cancer incidence and mortality over study time. Observed data is in blue and predicted data is in red. Dotted lines are 95% confidence interval. First row is for lung cancer incidence and second row is for lung cancer death.

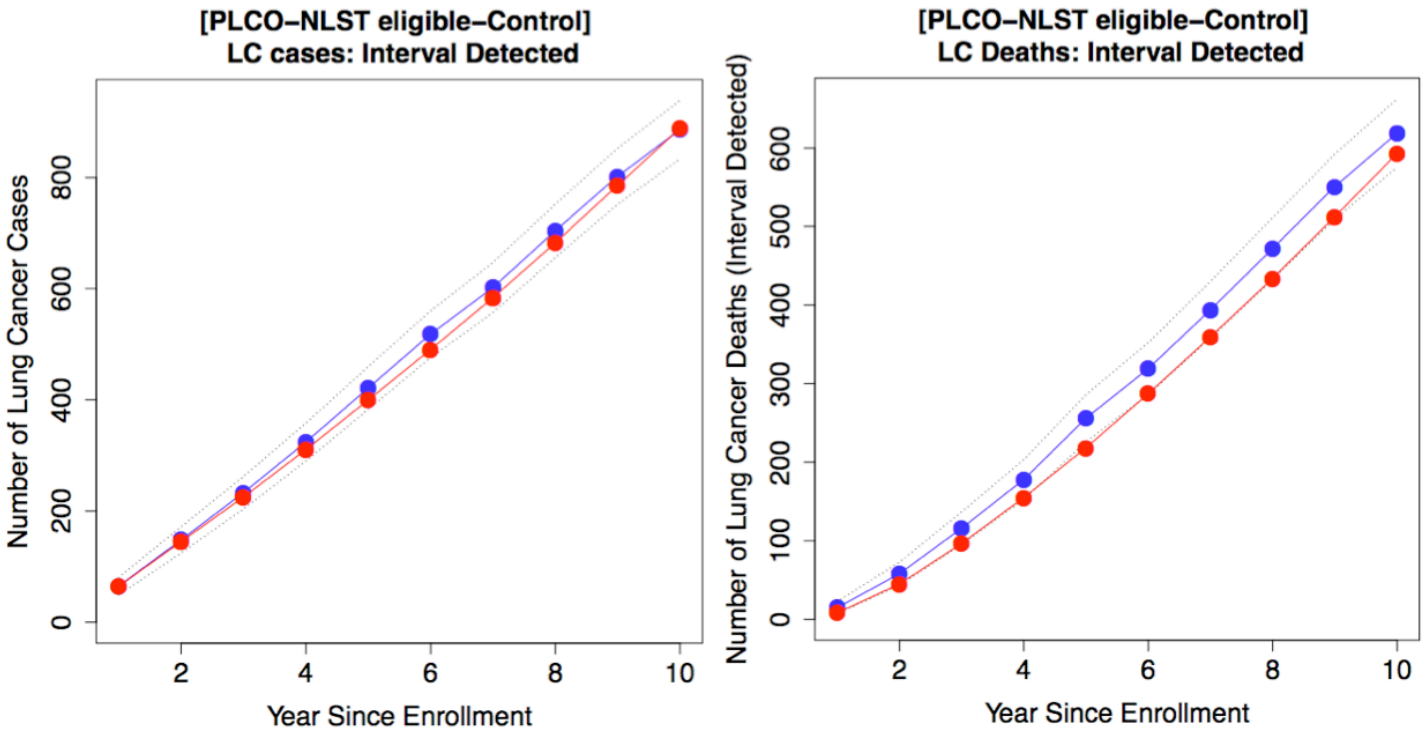
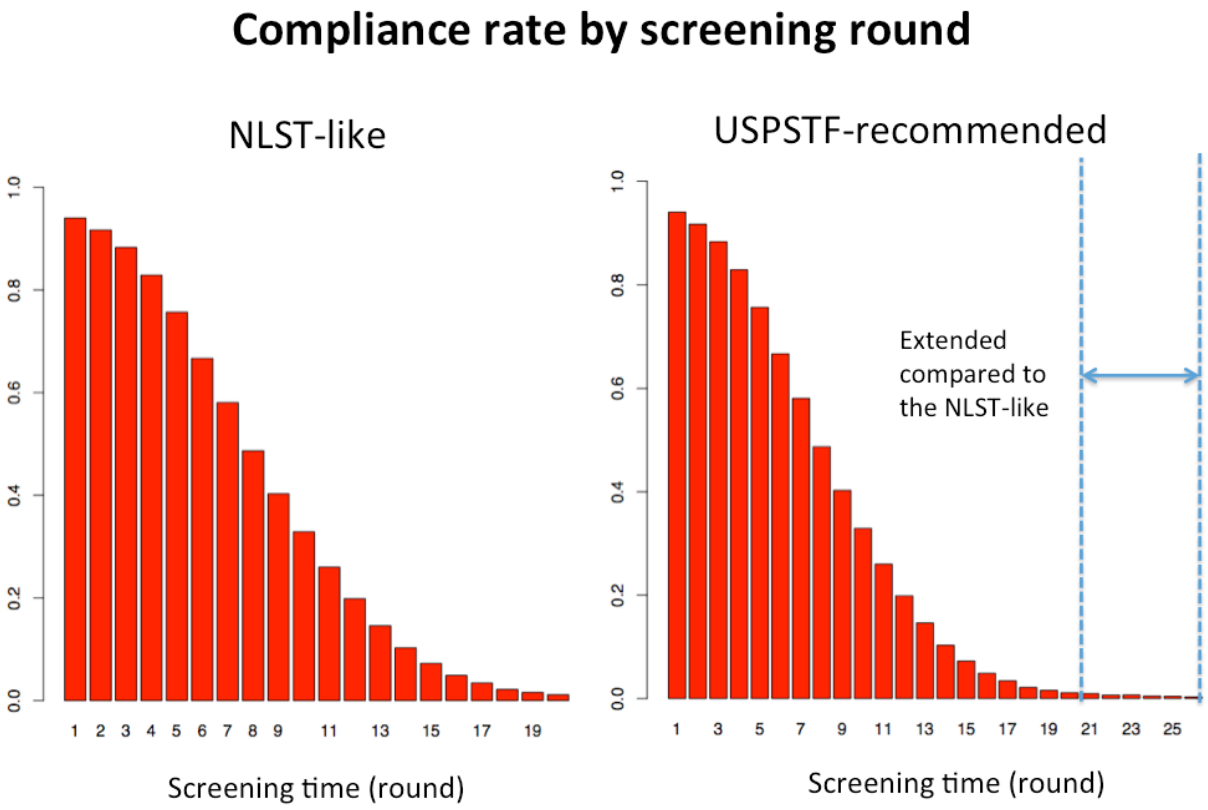


Figure S5 Compliance rate (attendance rate) of screening of the NLST-like and USPSTF recommended scenarios under imperfect compliance using transition probabilities estimated and projected using PLCO. The attendance rate was estimated using microsimulations, by calculating the fraction of individuals who attended screening for each screening round (screening time) among those who are eligible based on each criterion of the NLST-like and the USPSTF recommended programs.



References for Supplemental Materials

1. Lin RS, Plevritis SK. Comparing the benefits of screening for breast cancer and lung cancer using a novel natural history model. Cancer Causes & Control. 2012;23(1):175-85.
2. Koning HJd, Meza R, Plevritis SK, Haaf Kt, Munshi VN, Jeon J, et al. Benefits and harms of computed tomography lung cancer screening programs for high risk populations using evidence from the two largest randomized controlled trials on lung cancer screening; analyses initiated to inform the U.S. Preventive Services Task Force. (Submitted).
3. Meza R, Haaf Kt, Kong CY, Erdogan A, Black W, Tammemagi M, et al. Comparative Analysis of Five Lung Cancer Natural History and Screening Models that Reproduce Outcomes of the NLST and PLCO Trials. (Submitted).