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Cost-effectiveness of risk-based low-dose computed tomography screening for lung cancer in Switzerland

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[Correction added on 12 October 2023, after first online publication: The screening age for TLHC-like category has been corrected from 50 to 55 in Table 3 and Discussion.]

Abstract

Throughout Europe, computed tomography (CT) screening for lung cancer is in a phase of clinical implementation or reimbursement evaluation. To efficiently select individuals for screening, the use of lung cancer risk models has been suggested, but their incremental (cost-)effectiveness relative to eligibility based on pack-year criteria has not been thoroughly evaluated for a European setting. We evaluate the cost-effectiveness of pack-year and risk-based screening (PLCOm2012 model-based) strategies for Switzerland, which aided in informing the recommendations of the Swiss Cancer Screening Committee (CSC). We use the MISCAN (MIcrosimulation SCreening ANalysis)-Lung model to estimate benefits and harms of screening among individuals born 1940 to 1979 in Switzerland. We evaluate 1512 strategies, differing in the age ranges employed for screening, the screening interval and the strictness of the smoking requirements. We estimate risk-based strategies to be more cost-effective than pack-year-based screening strategies. The most efficient strategy compliant with CSC recommendations is biennial screening for ever-smokers aged 55 to 80 with a 1.6% PLCOm2012 risk. Relative to no screening this strategy is estimated to reduce lung cancer mortality by 11.0%, with estimated costs per Quality-Adjusted Life-Year (QALY) gained of €19 341, and a €1.990 billion 15-year budget impact. Biennial screening ages 55 to 80 for those with 20 pack-years shows a lower mortality reduction (10.5%) and higher cost per QALY gained (€20 869). Despite model uncertainties, our estimates suggest there may be cost-effective screening policies for Switzerland. Risk-based biennial screening ages 55 to 80 for those with ≥1.6% PLCOm2012 risk conforms to CSC recommendations and is estimated to be more efficient than pack-year-based alternatives.

Abbreviations: ACER, average cost-effectiveness ratio; BMI, body mass index; CHEERS, consolidated health economic evaluation reporting standards; CI, confidence interval; COPD, chronic obstructive pulmonary disease; CPD, cigarettes per day; CSC, Swiss Cancer Screening Committee; CT, computed tomography; GDP, gross domestic product; ICER, incremental cost-effectiveness ratio; ILST, International Lung Screening Trial; LC, lung cancer; LY, life year; LYG, life years gained; MISCAN, MIcrosimulation SCreening ANalysis; NELSON, Nederlands-Leuvens Longkanker Screenings Onderzoek; NICER, Swiss National Institute of Cancer Epidemiology and Registration; NLST, National Lung cancer Screening Trial; PLCOm2012, prostate lung colorectal and ovarian cancer screening trial Model, 2012 edition; PSA, probabilistic sensitivity analysis; PY, pack-year; QALY, quality-adjusted life year; QoL, quality of life; TLHC, targeted lung health check; USPSTF, United States preventive services task force; WTP, willingness-to-pay.

Yuki Tomonaga and Koen de Nijs have contributed equally to this study.

KEYWORDS
cost-effectiveness, low-dose computed tomography, lung cancer, risk-stratified, screening

What's new?

Throughout Europe, computed tomography screening for lung cancer is in a phase of clinical implementation or reimbursement evaluation. Efficient selection of individuals for screening is however essential. This microsimulation-based cost-effectiveness analysis offers the first comparative evidence for risk-based and pack-year-based lung cancer screening with low-dose computed tomography in a European country. Risk-based screening using a 1.6% PLCOm2012 eligibility threshold achieves a higher mortality reduction (11.0% vs 10.5%) than screening individuals with 20 pack-years, at a 7.3% lower cost per quality-adjusted life year gained. Policy makers should consider the increased selection efficiency of risk prediction models when implementing population screening programmes.

1 | INTRODUCTION

Lung cancer (LC) is the leading cause of cancer-related mortality in Europe.[1] Clinical LC diagnosis typically occurs in a metastasized stage; 5-year LC survival is only 11%.[2] To facilitate diagnosis at an earlier cancer stage, individuals at high risk of LC may benefit from low-dose computed tomography (CT) screening, which has shown LC mortality reductions of 20% in the US National Lung Screening Trial (NLST) and 24% in the Dutch-Belgian lung-cancer screening trial (Nederlands-Leuvens Longkanker Screenings Onderzoek [NELSON]).[3,4]

In several European countries, policy makers are in early stages of population-based LC screening implementation.[5-8] The benefits, harms and costs, may vary by the strategy employed, urging careful selection of the screening strategy.[9,10] The United States Preventive Services Taskforce (USPSTF) recommends annual CT screening for individuals aged 50-80 with at least 20 pack-years smoked (PYs) and maximally 15 years since smoking cessation.[11] Screening with these criteria is estimated to be cost-effective, but not the most efficient strategy in terms of costs per quality-adjusted life year (QALY) gained.[9,10]

To make LC screening more effective, it may be beneficial to invite individuals based on LC risk, rather than categorical criteria such as PYs smoked. Such a strategy would invite all individuals above a certain model-based LC risk for CT screening.[12] One such model is the PLCOm2012 model of 6-year LC incidence risk, which uses smoking history and intensity, age, race, education, body mass index (BMI), presence of chronic obstructive pulmonary disease (COPD) and personal/family cancer history.[13] Screening based on the PLCOm2012 model has been shown to improve efficiency of screening in the NLST population,[14] a finding recently supported by interim results from the International Lung Screening Trial (ILST).[15]

The incremental benefits and harms of risk-based LC screening are not known for the European setting, despite individual risk prediction models being recommended for selection into LC screening.[16] The UK-based Targeted Lung Health Check (TLHC) program employs the PLCOm2012 model for selection into screening, with favourable interim results.[17,18] However, it is unknown whether the chosen 1.51% risk threshold, combined with the targeted age range of 55 to 74 years, represents the optimal strategy for other European countries. Moreover, there are no known estimates of the incremental harms and benefits of risk-based screening in the European setting, relative to PY-based criteria. Previously published estimates of the cost-effectiveness of CT screening for LC have mostly focused on the US setting or considered only PY-based eligibility.[9,10,19-24]

Recently, the Swiss Cancer Screening Committee (CSC) issued a recommendation in favour of LC screening.[25] Pending a reimbursement decision, the committee suggests biennial screening focusing on younger populations (eg, 55-80 years rather than 60-85 years) with moderate smoking histories (eg, smokers from 20 PYs and including ex-smokers), without a specific recommendation for a risk- or PY-threshold.

In this study, we present a microsimulation-based cost-effectiveness and budget impact analysis of risk-based screening, from a public payer perspective. This study builds on our analyses for the CSC-commissioned Health Technology Assessment report.[25,26] Here, we present the cost-effectiveness of CT screening, and the set of most efficient screening strategies. Compliance to CSC recommendations was considered to assess implementation feasibility.

2 | METHODS

We performed a microsimulation-based cost-effectiveness analysis of LC screening. We include the CHEERS 2022 checklist in Data S1A.[27]

2.1 | MISCAN model

We used the MISCAN-Lung natural history model, as calibrated to individual-level data from the Prostate, Lung, Colorectal and Ovarian Cancer Screening Trial (PLCO) and the NLST.[28] The model has informed USPSTF 2013 and 2021 screening recommendations.[29,30] The model has further been used for cost-effectiveness studies for the US, Ontario and Switzerland.[9-11,24,31]

For each simulated individual, a smoking history was established, with probabilities of smoking initiation and cessation specific to birth cohort and sex. Methods and data underlying the smoking histories are reported in Data S1B. The age of death from other causes than LC

is established, accounting for individual smoking behaviour.[32] Mortality rates by smoking exposure are adapted from the literature and validated against published estimates for Switzerland, as reported in Data S1B.[33,34] If the individual develops LC, the onset age is generated based on the smoking history. At onset a cancer histology is drawn from a distribution consistent with Swiss LC incidence. Over time, the cancer may progress while remaining preclinical, or be detected clinically. When detected, a stage- and histology-specific time until death from LC is drawn from the country-specific survival distribution. Model parameters have been described previously[28] and are included in Data S1B.

CT screening rounds were simulated at the strategy-specific interval, with individual eligibility by age determined by the smoking history. LC may be detected with a sensitivity specific to the LC histology and stage at the time of screening. Relative to our previous study,[9] CT sensitivity is incremented by 5 percentage points for stage 1A to 2 to reflect advances in screening since the NLST.[3,35] A simulation of the NELSON protocol, as shown in the methodological supplement, finds a 5-percentage point increase to best replicate published NELSON lung cancer mortality rate ratios. This increment is subject to sensitivity analysis to account for uncertainty surrounding the sensitivity improvement. A screen-detected LC has a stage-specific probability of the lung cancer death being prevented. If unsuccessful, the age of death is applied from the life history without screening.

2.2 | Population

We studied birth cohorts 1940 to 1979, extending our previous study of cohorts 1935 to 1965. Cohort sizes by year and sex reflect the population composition of December 31, 2020.[36] Swiss smoking data by 5-year cohort and 5-year age group determined rates of smoking initiation and cessation and cigarettes per day, as described in Data S1B.[37] Cohort mortality tables are adjusted for LC mortality and smoking-related mortality. The use of cohort life tables represents a change relative to our previous study, for which only period lifetables were available.[9] The LC histology distribution and LC survival were adjusted to incidence data from the Swiss National Institute of Cancer Epidemiology and Registration (NICER).[38] For 10 million simulated individuals, LC outcomes were generated and recorded up to age 100.

2.3 | Evaluated outcomes

For each simulated individual, we recorded life years (LYs), QALYs lived and LC outcomes. To determine cost-effectiveness of a screening strategy, we evaluated the population gain in LYs and QALYs, relative to the scenario without screening. Strategies that gained the most QALYs for their level of cost constitute the cost-effective frontier. Secondary outcomes, such as follow-up procedures, secondary CT scans and lung biopsies were recorded per rates from the NELSON trial (Table S1). Costs, LYs, and QALYs were discounted at 3% relative to 2023, the presumed start of screening. Cost-effectiveness of a strategy on the efficiency frontier is given by the incremental cost-effectiveness ratio (ICER): the incremental cost per QALY gained relative to the next-cheapest strategy on the frontier. To set a cost-effectiveness threshold, we maintained a Willingness-to-Pay (WTP) of €38 000, equal to the most recent EU gross domestic product (GDP) per capita.[39] Additionally, we considered whether strategies meet CSC suggestions of screening moderate smokers aged 55 to 80.

TABLE 1 Characteristics of the evaluated screening scenarios.

Scenario characteristic	Considered values
Starting age[a] (years)	50, 55 60
Stopping age[a] (years)	75, 80, 85
Screening interval[a]	Annual, Biennial, Triennial
Maximum years since smoking cessation[b]	10, 15, 20, 25
Smoking criteria	
(1) NLST-like	10, 20, 30, 40 pack-years
(2) NELSON-like	(25y 10 CPD or 30y 5 CPD), (20y 15 CPD or 25y 10 CPD) (25y 15 CPD or 30y 10 CPD), (30y 15 CPD or 35y 10 CPD)
(3) PLCOm2012 risk threshold	1.00%, 1.10%, 1.20%, 1.30%, 1.40%, 1.50%, 1.51%, 1.60%, 1.70%, 1.80%, 1.90%, 2.00%, 2.10%, 2.20%, 2.30%, 2.40%, 2.50%, 2.60%, 2.70%, 2.80%, 2.90%, 3.00%, 3.10%, 3.20%

Note: Characteristics of simulated lung cancer screening strategies. Each strategy is constituted of a starting age of screening, a maximum age of screening, the interval between subsequent screens, and a smoking eligibility criterion. Smoking eligibility may be based on either (1): Minimum of pack-years smoked and maximum of years since smoking cessation, (2): Minimum smoking duration in years (y) of a given minimum average number of cigarettes per day (CPD) and maximum of years since smoking cessation, (3): Minimum PLCOm2012 (Prostate Lung Colorectal Ovarian screening trial model[13]) risk score.

[a]Characteristics varied for NLST (National Lung Screening Trial[4])-like, NELSON (Dutch Belgian Lung Screening Trial[3])-like and Risk-based screening strategies.

[b]Characteristics varied for NLST-like and NELSON-like screening strategies.

2.4 | Screening strategies

We simulated 1512 strategies, varying by starting age, stopping age, screening interval and eligibility requirement (Table 1). The CSC recommends biennial screening for Switzerland, citing capacity concerns with respect to annual screening.[25] We therefore took biennial screening as the base-case of feasible strategies, considering triennial and annual screening as sensitivity analyses. As eligibility requirements, we considered PY-based strategies, employed in the NLST[4] and advised by the USPSTF,[11] and smoking duration-based strategies, employed in the NELSON trial.[3] Additionally, we simulated screening eligibility based on PLCOm2012 risk levels,[13] as used in the ILST.[15]

TABLE 2 Cost and QALY input.

Type of cost/utility	Base value	Occurrence/maximum duration	Probabilistic sensitivity analysis distribution, mean and SD[a]
Costs in EUR			
Risk-assessment	81.60	25% of the population reaching the initial age for screening eligibility.	N(81.6, 20.4)
Invitation costs	25.50	Every screening round for eligible individuals.	N(25.5, 6.375)
Initial LC care phase	16 884.06	Monthly costs for first 3 months.	N(16 884.06, 4221.015)
Continuing LC care phase	578.34	Monthly costs between initial and terminal phase up to 5 years.	N(578.34, 144.585)
Terminal LC care phase	18 242.70	Monthly costs for final 6 months.	N(18 242.7, 4560.675)
LDCT screening or follow-up examination	420.24	Applied to every LC screening, indeterminate finding and false positive.	N(420.24, 105.06)
Biopsy	1111.80	3.9% of first screens, 0.76% of subsequent screens, as observed in the NELSON study.	N(1111.8, 277.95)
Utility weights from 0 to 1			
Terminal LC	0.59	Final 6 months of LC.	N(0.59, 0.10)
Stage 1A-2 LC	0.78	Any life-year before terminal LC when diagnosed at stage 1A to 2.	N(0.78, 0.04)
Stage 3A-4 LC	0.69	Any life-year before terminal LC when diagnosed at age 3A to 4.	N(0.69, 0.02)
Male 0-30	0.90	Applied to every life-year lived without LC in this age category.	N(0.90, 0.015)[b]
Male 30-40	0.87		N(0.87, 0.010)[b]
Male 40-50	0.85		N(0.85, 0.015)[b]
Male 50-60	0.83		N(0.83, 0.014)[b]
Male 60-70	0.83		N(0.83, 0.011)[b]
Male 70-80	0.80		N(0.80, 0.017)[b]
Male 80+	0.76		N(0.76, 0.028)[b]
Female 0-30	0.86		N(0.86, 0.016)[b]
Female 30-40	0.86		N(0.86, 0.009)[b]
Female 40-50	0.84		N(0.84, 0.010)[b]
Female 50-60	0.81		N(0.81, 0.010)[b]
Female 60-70	0.80		N(0.80, 0.012)[b]
Female 70-80	0.76		N(0.76, 0.019)[b]
Female 80+	0.74		N(0.74, 0.029)[b]

Note: Cost values for the treatment and detection of lung cancer (LC) and Probabilistic Sensitivity Analysis (PSA) distributions used to test robustness of the results to these values. In the univariate PSA, values are taken from the given distribution for each input separately, ceteris paribus. In the multivariate case, all values are taken from their given distribution, assuming zero covariance between the cost inputs.

[a]N(*a*, *b*) refers to a normal distribution with mean *a* and SD *b*.

[b]Norm utility values are taken from Perneger et al.[42] SE values are calculated from the SD reported in the publication, with n-values for each age category supplied through correspondence with the authors. Costs are converted to € from CHF values per the September 1, 2022 exchange rate of 1.020 €/CHF.[54]

We used the reduced-form PLCOm2012 model, which considers sex, smoking duration, cigarettes per day (CPD) and years since smoking cessation, with performance very close to the complete model.[40] The reduced-form model assumes reference values for covariates included in the complete model, which means that real-world screening may include more individuals, or include them at an earlier age. Our base-case assumed perfect screening attendance, with lower attendance simulations included as a sensitivity analysis.

2.5 | Costs and health utilities

Cost and utility values are given in Table 2. A public payer perspective was employed to align the cost-effectiveness analysis with a policy maker perspective. We included risk-assessment and invitation costs. Costs of LC care from the University Hospital Zurich were used from our previous study, adjusted for inflation and increased use of novel LC therapies.[9] LC-attributable costs for 1112 patients were included,

TABLE 3 Outcomes per 100 000 individuals alive in 2023 for strategies on the efficiency frontier.

Strategy[a]	Age range	Smoking requirement	Interv.	Eligible	CT Scans	False Pos.[b]	Excess biopsies[c]	LC Inc.	Of Which SD	Over-diagnosis[d]	LC Deaths	NNS/ Death prev.	LC Mortality Red.	LYG/death prev.	LY gain	QALY gain
No screening				-	-	-	-	7011	-	-	4757	-	-	-	-	-
PY1	[60, 75]	40py, 10 cess	2	6.8%	31 709	362	146	7028	519	3.3%	4548	33	4.4%	14.8	3095	2383
RISK1	[60, 75]	3.1% PLCO	2	9.3%	34 360	399	165	7031	596	3.4%	4521	39	5.0%	14.2	3338	2567
RISK2	[60, 75]	2.7% PLCO	2	10.1%	40 415	467	192	7032	642	3.3%	4501	39	5.4%	14.5	3700	2847
RISK3	[60, 75]	2.4% PLCO	2	10.9%	45 812	527	216	7033	677	3.2%	4485	40	5.7%	14.7	3992	3071
RISK4	[55, 75]	2.4% PLCO	2	11.5%	51 002	584	238	7038	766	3.5%	4453	38	6.4%	14.2	4310	3314
RISK5	[55, 80]	2.5% PLCO	2	13.7%	70 389	798	320	7072	1174	5.2%	4309	31	9.4%	12.3	5491	4235
RISK6	[55, 80]	2.4% PLCO	2	14.0%	72 971	827	331	7072	1191	5.1%	4301	31	9.6%	12.3	5607	4324
RISK7	[55, 80]	2.3% PLCO	2	14.4%	75 856	859	343	7072	1209	5.1%	4294	31	9.7%	12.4	5724	4414
RISK8	[60, 80]	2.4% PLCO	2	14.6%	78 565	888	354	7084	1307	5.6%	4262	30	10.4%	12.0	5909	4566
RISK9	[60, 80]	2.3% PLCO	2	14.9%	81 329	919	366	7085	1326	5.6%	4254	30	10.6%	12.0	6023	4654
RISK10	[55, 80]	1.7% PLCO	2	17.0%	96 944	1092	435	7077	1330	4.9%	4244	33	10.8%	12.7	6533	5039
RISK11	[55, 80]	1.6% PLCO	2	17.5%	101 323	1140	454	7077	1349	4.9%	4235	33	11.0%	12.8	6678	5151
RISK12	[50, 80]	1.7% PLCO	2	17.6%	103 875	1168	464	7089	1454	5.4%	4203	32	11.7%	12.3	6842	5288
RISK13	[50, 80]	1.51% PLCO	2	18.7%	113 184	1271	504	7090	1496	5.3%	4184	33	12.0%	12.5	7136	5516
RISK14	[50, 80]	1.4% PLCO	2	19.4%	119 292	1338	530	7091	1523	5.3%	4173	33	12.3%	12.5	7315	5655
RISK15	[50, 80]	1.3% PLCO	2	20.0%	125 616	1408	557	7092	1548	5.3%	4162	34	12.5%	12.6	7499	5797
RISK16	[50, 85]	1.3% PLCO	2	22.3%	157 003	1749	686	7169	2077	7.6%	3998	29	16.0%	11.2	8502	6611
RISK17	[50, 85]	1.1% PLCO	2	24.0%	173 882	1934	757	7173	2144	7.6%	3971	31	16.5%	11.3	8890	6912
RISK18	[50, 85]	1.0% PLCO	2	24.9%	183 613	2041	799	7175	2178	7.5%	3956	31	16.8%	11.4	9110	7083
RISK19	[55, 85]	1.0% PLCO	2	25.3%	190 605	2116	827	7201	2312	8.2%	3922	30	17.6%	11.0	9209	7166
PY2	[55, 85]	10py, 25 cess	2	26.6%	223 353	2469	960	7181	2193	7.7%	3952	33	16.9%	11.8	9527	7397
PY3	[50, 85]	10py, 25 cess	2	26.8%	234 803	2591	1006	7160	2107	7.1%	3973	34	16.5%	12.2	9596	7450
USPSTF	[50, 80]	20py, 15 cess	1	17.1%	244 536	2657	1009	7104	1738	5.3%	4027	23	15.4%	13.5	9887	7655
TLHC	[55, 75]	1.51% PLCO	1	15.1%	147 232	1618	625	7050	1125	3.4%	4268	31	10.3%	15.0	7348	5666
CSC1	[55, 80]	20py, 10 cess	2	15.1%	101 165	1130	445	7068	1219	4.7%	4282	32	10.0%	13.6	6441	4970
CSC2	[55, 80]	20py, 15 cess	2	16.5%	113 576	1267	498	7071	1286	4.7%	4255	33	10.5%	13.6	6810	5254

(Continues)

TABLE 3 (Continued)

Strategy[a]	Age range	Smoking requirement	Interv.	Eligible	CT Scans	False Pos.[b]	Excess biopsies[c]	LC Inc.	Of Which SD	Over-diagnosis[d]	LC Deaths	NNS/ Death prev.	LC Mortality Red.	LYG/death prev.	LY gain	QALY gain
CSC3	[55, 80]	20py, 20 cess	2	17.7%	125 339	1396	548	7073	1344	4.6%	4231	34	11.1%	13.6	7133	5503
CSC4	[55, 80]	20py, 25 cess	2	18.6%	135 914	1511	593	7075	1394	4.6%	4211	34	11.5%	13.5	7394	5704

Note: Simulated undiscounted outcomes of the most efficient biennial screening strategies, as well as a few inefficient strategies of interest. Outcomes are given per 100 000 individuals alive at the assumed start of screening of 2023. Strategies are sorted by their position on the efficiency frontier, equivalent to a sorting by the number of Quality Adjusted Life Years (QALYs) gained. NS refers to the non-screening scenario. PY1 to PY3 report scenarios in which a screening strategy is employed with eligibility based on a minimum of pack-years (PY) smoked and a maximum of years since smoking cessation (cess). RISK1 to RISK19 report strategies which base CT (Computed Tomography) screening eligibility on the reduced-form PLCOm2012 risk model.

Abbreviations: LYG, life-years gained; LY, life-years; NNS, number of unique individuals needed to screen to achieve the given outcome; SD, screen-detected.

[a]USPTF-2021, and TLHC strategies, not part of the efficiency frontier. CSC1 (Cancer Screening Committee) to CSC4 report pack year-based strategies that follow suggestions in the recent CSC recommendations.[25]

[b]Total false positive results from all CT screening events, per rates from the NELSON trial.

[c]Biopsies pertaining to false positive screening outcomes.

[d]Overdiagnosis is reported as the percentage of simulated screen-detected cancers that were not associated with a lung-cancer death in the non-screening scenario over a lifetime horizon.

and distributed by phase of care: Initial care (first 3 months after diagnosis), terminal care (final 6 months of life) and continuing care (up to a maximum of 5 years). For individuals with LC, we use quality of life values from a meta-analysis of LC health utilities.[41] Terminal-phase utilities are applied for the final 6 months, otherwise stage-specific utilities are applied in tandem with the costing phase (initial or continuing care). Population-level utilities were taken from a study of Swiss individuals.[42] The lower value of the age-specific and lung cancer health state utility is applied. LDCT screening cost was estimated at €420.

2.6 | Sensitivity analyses

We repeated our analysis with discount rates of 0.0%, 1.5%, 3.0% (the base-case), 4.5% and 6.0%. The cost and utility values were subject to a univariate sensitivity analysis, as well as a multivariate probabilistic sensitivity analysis (PSA), for which statistical distributions are reported in Table 2.

We studied the effect of the assumed CT sensitivity for early-stage LC. The CT sensitivity by stage and histology per estimates from the NLST and the PLCO was considered,[28] as well as a 5 (the base-case), 10 and 15 percentage point increase in CT sensitivity for stages 1A to 2.

Additionally, we considered a scenario where screening was limited to those with a minimum 5-year remaining life expectancy. This scenario reflects the potential impact of shared decision-making preceding entrance into a screening programme. This strategy has been shown to reduce overdiagnosis projections in population-level screening.[10]

We also repeat our analysis with varying attendance rates. We consider 100%, 75% and 50% attendance rates. We assumed non-attendance to be caused partly by never-attendance and partly by incidental non-attendance. For an attendance level p, it is assumed $1-\sqrt{p}$ of eligibles never attend, while $\sqrt{p}$ of eligibles attend $\sqrt{p}$ of their scans for an overall attendance rate of p.

Finally, we test our adjustment of cessation rates to fit Swiss LC incidence, relative to the alternative of adjusting background risk. The methodological Data S1B specifies this analysis, which finds screening to be 4.5% less cost effective (per the RISK16 ACER) when decreasing baseline risk relative to our assumption of increased cessation.

3 | RESULTS

We report primary results in the main text, with additional Tables and Figures reported in Data S1C. Table 3 summarizes the most efficient biennial screening strategies. Without screening, we project 7011 lifetime LC cases per 100 000 individuals alive in 2023, associated with 4757 LC deaths. Screening strategies on the efficient frontier reduce LC mortality by 4.4% for strategy PY1 (biennial screening ages 60-75 those with >40 pack-years), to 17.6% for RISK19 (annual screening ages 55-85 those with >1.0% PLCOm2012 risk).

TABLE 4 Stratified costs in millions of EUR and Incremental Cost Effectiveness Ratios (ICERs) for strategies on the efficiency frontier.

Strategy	Age range	Smoking requirement[a]	Interv.	Eligible	Costs	LY gain	QALY gain	CT scans	Screening and invitation costs	Risk assessment costs	Initial and continued care costs	Terminal care costs	ICER (€/QALY)
NS	-	-	-	-							€176.29	€233.44	-
PY1	[60, 75]	40py, 10cess	2	6.8%	€18.27	1592	1228	31 709	€11.83	€1.72	€190.33	€224.13	14 883
RISK1	[60, 75]	3.1% PLCO	2	9.3%	€19.58	1693	1305	34 360	€12.43	€1.72	€191.90	€223.26	16 987
RISK2	[60, 75]	2.7% PLCO	2	10.1%	€22.09	1873	1444	40 415	€14.63	€1.72	€193.16	€222.31	17 996
RISK3	[60, 75]	2.4% PLCO	2	10.9%	€24.34	2013	1551	45 812	€16.56	€1.72	€194.19	€221.60	21 037
RISK4	[55, 75]	2.4% PLCO	2	11.5%	€27.12	2171	1672	51 002	€18.28	€1.84	€196.36	€220.38	22 988
RISK5	[55, 80]	2.5% PLCO	2	13.7%	€37.55	2745	2122	70 389	€24.19	€1.92	€206.14	€215.03	23 192
RISK6	[55, 80]	2.4% PLCO	2	14.0%	€38.60	2802	2166	72 971	€25.10	€1.92	€206.60	€214.70	23 861
RISK7	[55, 80]	2.3% PLCO	2	14.4%	€39.70	2859	2210	75 856	€26.11	€1.92	€207.03	€214.37	24 978
RISK8	[60, 80]	2.4% PLCO	2	14.6%	€41.56	2944	2281	78 565	€26.73	€1.81	€209.37	€213.39	25 930
RISK9	[60, 80]	2.3% PLCO	2	14.9%	€42.68	2996	2322	81 329	€27.68	€1.81	€209.84	€213.08	27 636
RISK10	[55, 80]	1.7% PLCO	2	17.0%	€48.07	3253	2515	96 944	€33.52	€1.92	€210.18	€212.18	27 906
RISK11	[55, 80]	1.6% PLCO	2	17.5%	€49.71	3323	2570	101 323	€35.07	€1.92	€210.68	€211.77	29 852
RISK12	[50, 80]	1.7% PLCO	2	17.6%	€51.73	3398	2634	103 875	€35.57	€2.00	€213.11	€210.78	31 705
RISK13	[50, 80]	1.51% PLCO	2	18.7%	€55.26	3537	2743	113 184	€38.81	€2.00	€214.20	€209.99	32 406
RISK14	[50, 80]	1.4% PLCO	2	19.4%	€57.63	3626	2812	119 292	€40.96	€2.00	€214.90	€209.51	34 367
RISK15	[50, 80]	1.3% PLCO	2	20.0%	€60.01	3714	2880	125 616	€43.17	€2.00	€215.54	€209.03	35 028
RISK16	[50, 85]	1.3% PLCO	2	22.3%	€75.10	4169	3254	157 003	€51.91	€2.00	€227.31	€203.62	40 324
RISK17	[50, 85]	1.1% PLCO	2	24.0%	€81.35	4352	3397	173 882	€57.62	€2.00	€228.96	€202.51	43 838
RISK18	[50, 85]	1.0% PLCO	2	24.9%	€84.87	4450	3473	183 613	€60.88	€2.00	€229.81	€201.92	45 874
RISK19	[55, 85]	1.0% PLCO	2	25.3%	€88.09	4487	3504	190 605	€62.47	€1.92	€232.46	€200.97	104 886
PY2	[55, 85]	10py, 25cess	2	26.6%	€100.66	4639	3614	223 353	€76.61	€1.92	€230.33	€201.53	113 911
PY3	[50, 85]	10py, 25cess	2	26.8%	€105.35	4683	3650	234 803	€82.34	€2.00	€228.69	€202.05	132 671

Note: Costs per 100 000 individuals alive in 2023 for each strategy on the efficiency frontier, stratified by primary cost category. The Incremental Cost Effectiveness Ratio (ICER) of each strategy is also given, which reports the incremental cost per QALY (Quality Adjusted Life Year) gained of implementing a strategy, relative to the strategy preceding it on the efficiency frontier. Cost values are given as millions of EUR per 100 000 individuals, except for the ICERs which are given nominally. Costs, LYs and QALYs are discounted by 3% annually starting from 2023. The number of computed tomography (CT) scans per 100 000 individuals are not discounted.

Abbreviation: LY, life-years.

[a]Eligibility requirement, based on PLCOm2012[13] risk or pack-year (PY) based with a maximum number of years of smoking cessation (cess).

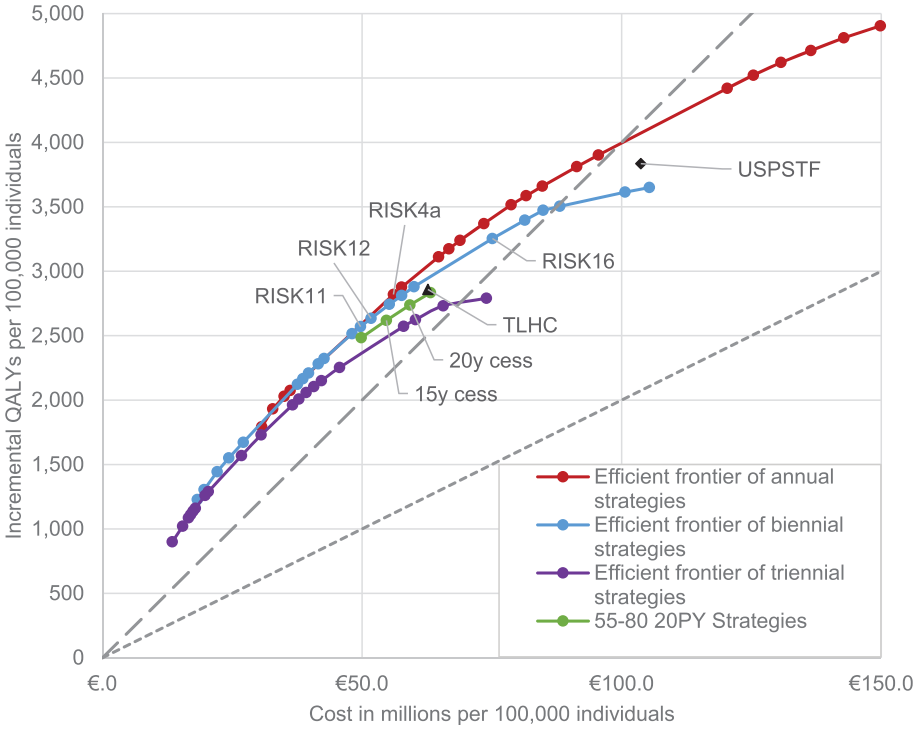

FIGURE 1 QALYs gained vs Incremental Costs (per 100 000 individuals alive in 2023) vs No Screening by strategy. Incremental costs and QALYs (Quality-Adjusted Life Years) relative to no screening for the efficiency frontiers of biennial and annual screening strategies (ie, the selection of strategies that realize the highest number of QALYs at a given level of cost), as well as selected strategies of interest. Strategies include screening those with 20 pack-years (PYs) between ages 55 and 80, the Targeted Lung Health Check (TLHC) strategy and the United States Preventive Services Task Force (USPSTF) 2021 recommended strategy. Outcomes are scaled to 100 000 individuals alive at the presumed start of screening of 2023. Both QALYs and costs are discounted at a rate of 3%. The strategies constituting the efficiency frontier are reported in Table 3. RISK11 represents a strategy of biennially screening of smoking individuals with 1.6% PLCOm2012 risk between the ages of 55 and 80. RISK12 represents a strategy of biennial screening of individuals with 1.7% PLCOm2012 risk between the ages of 50 and 80. Diagonal lines report the QALYs at each cost level required to meet a given willingness-to-pay (WTP) threshold.

3.1 | Effective screening strategies

Nineteen risk-based and three pack-year-based strategies constitute the efficient frontier, dominating all duration-based (NELSON-like) strategies. The CSC recommends biennial screening for those with moderate smoking histories (eg, 20 PY). We found strategies employing a 20 PY threshold (CSC1 to CSC4 in Table 4) to be dominated by risk-based screening strategies, yielding more QALYs for similar costs.

Strategy CSC2, which matches USPSTF-2021 eligibility criteria (20 PYs and maximum 15 years since smoking cessation), is estimated to yield 2859 discounted QALYs per 100 000 individuals, at a cost of €49.8 million. The average cost-effectiveness ratio (ACER, the costs per QALY gained relative to no screening) is €20 884. Strategy RISK11, which screens ages 55 to 80 those with 1.6% PLCOm2012 risk, maintains the CSC-suggested age range, and has a similar population coverage as the 20PY eligibility criterion (17.5% for RISK11, 15.1-18.6% for CSC1-CSC4). However, RISK11 is estimated to cost 9.1% less and require 11% fewer CT scans, yielding only 2% fewer QALYs. Furthermore, RISK11 is on the efficiency frontier, with an ACER of €19 341 (7.9% less than CSC2) and a €29 852 ICER (relative to strategy RISK10). With a €38 000 WTP, screening may be expanded up to strategy RISK15, screening ages 50-80 those with 1.3% risk. Although cost-effective per the estimated ICER, RISK15 would depart from the CSC-suggested age range and screening coverage. RISK11 may therefore be the most feasible. If we maximize life-years gained (LYG), RISK11 remains on the frontier, with a €23 138 ICER relative to RISK10 (Table S2).

3.2 | Screening Interval

Current programmes of LC screening advise annual screening.[4,6] However, the CSC recommend biennial screening in light of capacity concerns.[25] Figure 1 shows the efficiency frontiers of annual, biennial and triennial strategies (the complete set of strategies are shown in Figure S1). We find that for strategies with expenses similar to strategy RISK11, the incremental benefit of annual screening is marginal. The closest annual strategy to RISK11 in projected screening volume is RISK4a (Data S3), screening ages 60 to 80 from 3.0% risk. We estimate it would yield 9.7% more QALYs for 12.7% additional costs and 20.5% more screens. Both TLHC-like (annual screening ages 55-75

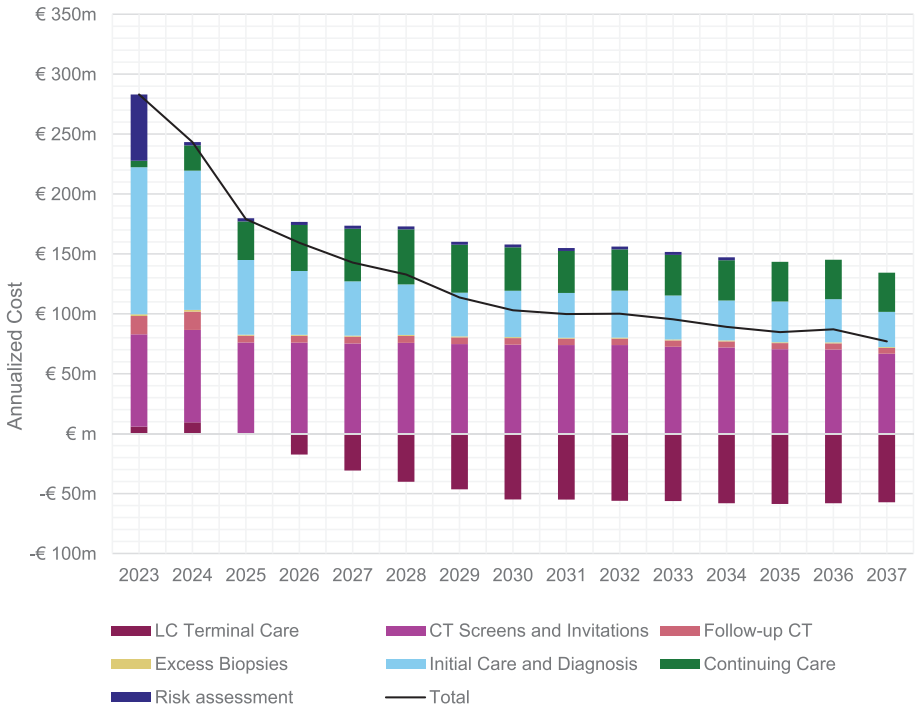

FIGURE 2 Budget Impact of Risk-based (1.6% PLCOm2012) biennial computed tomography (CT) Screening for Swiss 1940 to 1979 cohorts. Budget impact of biennially screening the 1940 to 1979 Swiss birth cohorts with a minimum risk score for screening eligibility of 1.6%, a minimum age of 55 and a maximum age of 80. Primary cost categories are reported, as well as the gross annual costs reported by the black line. The costs from 10 million simulated individuals are scaled to the estimated cohort size of January 1, 2023 of 4 079 544, obtained by applying the 2022 population size per the Swiss bureau of statistics to the expected MISCAN-Lung estimate for the number of individuals from these cohorts alive in the respective calendar year.

with >1.51% PLCOm2012) and USPSTF 2021 (annual screening ages 50-80 from 20 PYs and maximally 15 cessation years) strategies were not on the estimated efficiency frontier, dominated by risk-based annual screening strategies. The frontier of efficient triennial strategies (reported in Table S4) is found to be dominated by the most efficient biennial strategies.

3.3 | Budget Impact

We calculated the budget impact of screening cohorts 1940 to 1979 with the RISK11 strategy, which is CSC-compliant and estimated to be cost-effective. Figure 2 shows projected annual costs for 2023 to 2037. CT scans constitute 55% of costs. Increased initial care costs are a major cost contributor, but the annual costs decrease from €122 million (43% of costs) in 2023 to €29 million (38%) in 2037. Terminal-phase care costs are reduced from 2025 onwards, by up to €58 million. The total burden is €1990 million for 2023 to 2037, with costs per individual alive in 2023 decreasing from €69 (2023) to €19 (2037). Table S7 reports the predicted first-year CT capacity requirement by strategy. RISK11 may require 172 620 screens, equal to 15% of 2019 Swiss CT volume.[43]

3.4 | Sensitivity analyses

Table S6 and Figure S6 show the changes in costs and QALYs for the efficient biennial strategies for 50% and 75% screening attendance. RISK11 has a 3.7% higher ACER (€20 056) at 50% attendance, suggesting screening with imperfect attendance is less efficient, but still cost-effective.

Table S5 shows the change in outcomes when screening is limited to those with a minimum 5-year life expectancy, per their individually generated other-cause mortality age. For RISK11, this reduces projected overdiagnosis from 4.9% to 0.9%, with 7.3% fewer screens and 0.3% fewer QALYs gained.

We evaluate the sensitivity of our results to cost and utility inputs. The ACER of RISK11 is evaluated at the bounds of the 95% confidence interval (95% CI) of input-specific distributions per Table 2. Figures S2 and S3 report the results. We find the cost-effectiveness of LC screening to be sensitive to CT costs (ACER ranging from €12 816-€25 106 per QALY) and LC care costs (€16 181-€21 741 for initial care, €23 012-€14 910 for terminal care). Of the utility inputs, only early-stage LC utility has a sizeable effect on the cost-effectiveness estimate. Both the screening-induced stage shift and the earlier detection of lung cancer increase the projected years spent in initial and continuing-phase early-stage lung cancer. Figures S4 and S5 show the results of the PSA, showing the 95% CI of the ACER to be €10 545 to €28 609 for RISK11. Only 0.01% of draws yields an ACER above the €38 000 WTP. Finally, Table S8 reports the sensitivity of the ACER to the discount rate. For RISK11, the ACER ranges €11 929 to €29 298 for a 0.0% to 6.0% discount rate.

4 | DISCUSSION

We present the cost-effectiveness of LC screening in Switzerland. Our estimates from the MISCAN-Lung model find screening to be a cost-effective measure, consistent with previous European and US estimates.[9,10,19-23] For biennial screening ages 55 to 80, risk-based screening with a 1.6% PLCOm2012 risk is estimated to cost €19 341

per QALY gained relative to no screening, 7.9% less than the equivalent pack-year-based strategy (minimum 20PY and maximally 15 years of cessation).

Relative to annual screening, biennial and triennial screening are expected to reduce the total QALY benefit. However, less frequent screening reduces the required CT capacity, and is still estimated to be cost-effective. In 2019, 1.18 million CT scans were conducted in Switzerland.[43] Biennial screening ages 55 to 80 from 1.6% PLCOm2012 risk would require an estimated 172 000 additional scans in the first year, a 15% increase. A TLHC-like strategy of annual screening ages 55 to 75 from 1.51% risk would require 290 000 scans (+25%). The USPSTF2021 strategy of annually screening ages 50 to 80 from 20 PYs is estimated to require 530 000 scans (+45%). Even with imperfect attendance, the CT volume for annual screening may be difficult to achieve, warranting deference to biennial screening.

We find screening to be more cost-effective than our previous analysis of older cohorts.[9] We attribute the difference to the increased life expectancy of the newer cohorts, yielding more QALYs per life saved. Our analysis also includes higher CT sensitivity estimates, which favour screening effectiveness.

We find the cost per QALY gained of screening those with 1.6% PLCOm2012 risk to be robust to changes in input parameters. Our PSA showed a 95% CI of the ACER of €10 545 to €28 609. This suggests that screening with this strategy is cost-effective at our assumed cost-effectiveness threshold of €38 000, even for unfavourable parameter combinations. However, the assumed independence of cost input distributions means that unfavourable cost scenarios across inputs may have a larger effect than estimated here.

The cost-effectiveness of screening is sensitive to the CT cost, and terminal LC care costs. The optimal strategy will therefore depend on CT affordability. Terminal care costs for LC are also of interest for the cost-effectiveness of screening. The onset of targeted therapies has inflated costs for late-stage cancers.[44-48] This may improve the cost-effectiveness of screening, since these costs are partly supplanted by surgical costs for the early-detected cancers. However, if targeted therapies are implemented for earlier-stage cancers, this stage-shift effect may diminish.[49] Of the quality of life inputs, screening cost-effectiveness was most sensitive to early stage LC utility.

Screening efficiency may be improved when participation depends on remaining life expectancy. Although an idealized scenario, in practice screening may be reserved for those without excess morbidities prohibitive of benefiting from screening. The benefits of screening should therefore, in practice, be between the base scenario in which every eligible individual is screened, and the scenario in which only those with a minimum 5-year life expectancy are screened. Consequently, the base-case overdiagnosis projection of 4.9% of screen-detected cases, represents a pessimistic scenario.

Our study results are limited by the validity of the MISCAN-Lung model as applied to this particular context. Structural assumptions on the natural history of lung cancer (such as the preclinical sojourn time length) and the effectiveness of screening (eg, use of a stage-shift or cure model) are known to influence the estimated benefits and harms.[50] Comparative modelling studies[10,24] that aggregate various model specifications may give a more robust estimate of the effectiveness of lung cancer screening. Future research may also focus on more elaborate recalibration of the smoking dose-response model to novel epidemiological contexts, which may improve the projected lung cancer burden for a particular setting. Real-world lung cancer screening effectiveness will also depend on the success of encouraging (repeat) attendance. There is further debate about the assumptions regarding quality of life of lung cancer patients, and potential impacts on quality of life from indeterminate or false positive findings.[51]

The cost-effectiveness of LC screening may increase further with novel strategies of screening. The 4-IN-the-LUNG-RUN trial,[52] currently underway in five European countries, will investigate whether individuals with a negative baseline scan may benefit equally from a biennial screening as they would from an annual scan. Our analysis includes annual and biennial strategies, but does not consider personalized intervals. 4-IN-THE-LUNG-RUN results may inform whether baseline-dependent risk stratification may improve screening efficiency. Screening has also been shown to be associated with smoking cessation,[53] which our analysis does not assume to occur in excess of the cessation rate without screening.

5 | CONCLUSION

We present the first comparative cost-effectiveness analysis of risk-based and PY-based screening for a European country. Incorporating recommendations from the CSC, we project the optimal strategy for Switzerland would be biennial screening of smokers and ex-smokers with 1.6% PLCOm2012 risk between the ages of 55 and 80.

AUTHOR CONTRIBUTIONS

Yuki Tomonaga: Conceptualization, Methodology, Investigation, Writing—Original Draft, Project Administration, Funding Acquisition; Koen de Nijs: Conceptualization, Methodology, Software, Validation, Formal Analysis, Investigation, Data Curation, Writing—Original Draft; Heiner Bucher: Writing—Review & Editing, Supervision, Project Administration, Funding Acquisition; Kevin ten Haaf: Conceptualization, Methodology, Investigation, Writing—Original Draft, Supervision, Project Administration; Harry J de Koning: Conceptualization, Writing—Review & Editing, Supervision, Project Administration. The work reported in the paper has been performed by the authors, unless clearly specified in the text.

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CONFLICT OF INTEREST STATEMENT

Yuki Tomonaga reports no other interests. Koen de Nijs reports grants from the NIH and the European Union. Heiner C. Bucher reports speaking fees from Moderna and grants from Gilead and has served as the president of the Association Contre le HIV et autres infections transmissible, receiving support from ViiV Healthcare, Gilead, BMS and MSD. Kevin ten Haaf reports grants from the NIH, the European Union and the Dutch Research Council. Harry J. de Koning reports consulting fees from Bayer and speaking fees from Teva, Menarini and Astra Zeneca.

DATA AVAILABILITY STATEMENT

Data used as input for the MISCAN-Lung model can be requested from the primary sources, as specified in the methodological Data S1B. Model outcome data can be made available upon reasonable request.

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REFERENCES

1. Carioli G, Malvezzi M, Bertuccio P, et al. European cancer mortality predictions for the year 2021 with focus on pancreatic and female lung cancer. *Ann Oncol*. 2021;32:478-487.
2. European Cancer Information System. Union E, ed., 2022. 2022.
3. de Koning HJ, van der Aalst CM, de Jong PA, et al. Reduced lung-cancer mortality with volume CT screening in a randomized trial. *N Engl J Med*. 2020;382:503-513.
4. National Lung Screening Trial Research T, Aberle DR, Adams AM, et al. Reduced lung-cancer mortality with low-dose computed tomographic screening. *N Engl J Med*. 2011;365:395-409.
5. van Meerbeeck JP, Franck C. Lung cancer screening in Europe: where are we in 2021? *Transl Lung Cancer Res*. 2021;10:2407-2417.
6. Wait S, Alvarez-Rosete A, Osama T, et al. Implementing lung cancer screening in Europe: taking a systems approach. *JTO Clin Res Rep*. 2022;3:100329.
7. Rzyman W, Szurowska E, Adamek M. Implementation of lung cancer screening at the national level: polish example. *Transl Lung Cancer Res*. 2019;8:S95-S105.
8. Crosbie PA, Balata H, Evison M, et al. Implementing lung cancer screening: baseline results from a community-based "Lung health Check" pilot in deprived areas of Manchester. *Thorax*. 2019;74:405-409.
9. Tomonaga Y, ten Haaf K, Frauenfelder T, et al. Cost-effectiveness of low-dose CT screening for lung cancer in a European country with high prevalence of smoking-a modelling study. *Lung Cancer*. 2018;121:61-69.
10. Toumazis I, de Nijs K, Cao P, et al. Cost-effectiveness evaluation of the 2021 US preventive services task force recommendation for lung cancer screening. *JAMA Oncol*. 2021;7:1833-1842.
11. U.S. Preventive Services Task Force, Krist AH, Davidson KW, et al. Screening for lung cancer: US preventive services task force recommendation statement. *Jama*. 2021;325:962-970.
12. Toumazis I, Bastani M, Han SS, Plevritis SK. Risk-based lung cancer screening: a systematic review. *Lung Cancer*. 2020;147:154-186.
13. Tammemagi MC, Katki HA, Hocking WG, et al. Selection criteria for lung-cancer screening. *N Engl J Med*. 2013;368:728-736.
14. Tammemagi MC, Church TR, Hocking WG, et al. Evaluation of the lung cancer risks at which to screen ever- and never-smokers: screening rules applied to the PLCO and NLST cohorts. *PLoS Med*. 2014;11:e1001764.
15. Tammemagi MC, Ruparel M, Tremblay A, et al. USPSTF2013 versus PLCOm2012 lung cancer screening eligibility criteria (international lung screening trial): interim analysis of a prospective cohort study. *Lancet Oncol*. 2022;23:138-148.
16. Oudkerk M, Devaraj A, Vliegenthart R, et al. European position statement on lung cancer screening. *Lancet Oncol*. 2017;18:e754-e766.
17. Lee R, Nair A, Graham C, et al. 45: NHS England's National Targeted Lung Health Check—preliminary findings. *Lung Cancer*. 2022;165:S21-S22.
18. Crosbie PA, Balata H, Evison M, et al. Second round results from the Manchester "Lung health Check" community-based targeted lung cancer screening pilot. *Thorax*. 2019;74:700-704.
19. Criss SD, Cao P, Bastani M, et al. Cost-effectiveness analysis of lung cancer screening in the United States: a comparative modeling study. *Ann Intern Med*. 2019;171:796-804.
20. Gomez-Carballo N, Fernandez-Soberon S, Rejas-Gutierrez J. Cost-effectiveness analysis of a lung cancer screening programme in Spain. *Eur J Cancer Prev*. 2022;31:235-244.
21. Hofer F, Kauczor HU, Stargardt T. Cost-utility analysis of a potential lung cancer screening program for a high-risk population in Germany: a modelling approach. *Lung Cancer*. 2018;124:189-198.
22. Snowsill T, Yang H, Griffin E, et al. Low-dose computed tomography for lung cancer screening in high-risk populations: a systematic review and economic evaluation. *Health Technol Assess*. 2018;22:1-276.
23. Veronesi G, Navone N, Novellis P, et al. Favorable incremental cost-effectiveness ratio for lung cancer screening in Italy. *Lung Cancer*. 2020;143:73-79.
24. Toumazis I, Cao P, de Nijs K, et al. Risk model-based lung cancer screening: a cost-effectiveness analysis. *Ann Intern Med*. 2023;176:320-332.
25. Cancer Screening Committee. Cancer Screening Committee Recommendation on Low-Dose CT Screening for Lung Cancer. 2022.
26. Aghlmandi S, Bhadhuri A, Bucher HC, et al. Low-dose CT screening for lung cancer. Basel Institute for Clinical Epidemiology and Biostatistics. 2022.
27. Husereau D, Drummond M, Augustovski F, et al. Consolidated health economic evaluation reporting standards 2022 (CHEERS 2022) statement: updated reporting guidance for health economic evaluations. *BMJ*. 2022;376:e067975.
28. ten Haaf K, van Rosmalen J, de Koning HJ. Lung cancer detectability by test, histology, stage, and gender: estimates from the NLST and the PLCO trials. *Cancer Epidemiol Biomarkers Prev*. 2015;24:154-161.
29. de Koning HJ, Meza R, Plevritis SK, et al. Benefits and harms of computed tomography lung cancer screening strategies: a comparative modeling study for the US preventive services task force. *Ann Intern Med*. 2014;160:311-320.
30. Meza R, Jeon J, Toumazis I, et al. Evaluation of the benefits and harms of lung cancer screening with low-dose computed tomography: modeling study for the US preventive services task force. *Jama*. 2021;325:988-997.
31. ten Haaf K, Tammemagi MC, Bondy SJ, et al. Performance and cost-effectiveness of computed tomography lung cancer screening scenarios in a population-based setting: a microsimulation modeling analysis in Ontario, Canada. *PLoS Med*. 2017;14:e1002225.
32. Meza R, Hazelton WD, Colditz GA, Moolgavkar SH. Analysis of lung cancer incidence in the Nurses' health and the health Professionals'

follow-up studies using a multistage carcinogenesis model. *Cancer Causes Control*. 2008;19:317-328.
33. Maag J, Braun J, Bopp M, Faeh D, Swiss NC. Direct estimation of death attributable to smoking in Switzerland based on record linkage of routine and observational data. *Nicotine Tob Res*. 2013;15:1588-1597.
34. Thun MJ, Carter BD, Feskanich D, et al. 50-year trends in smoking-related mortality in the United States. *N Engl J Med*. 2013;368:351-364.
35. Horeweg N, van Rosmalen J, Heuvelmans MA, et al. Lung cancer probability in patients with CT-detected pulmonary nodules: a pre-specified analysis of data from the NELSON trial of low-dose CT screening. *Lancet Oncol*. 2014;15:1332-1341.
36. Swiss Federal Statistical Office. *Permanent Resident Population by Age, Gender and Citizenship Category, 2010-2022*. Neuchâtel, Switzerland: Swiss Federal Statistical Office; 2022.
37. Swiss Federal Statistical Office. *Swiss Health Survey, 1992, 1997, 2002, 2007, 2012, 2017*. Bern, Switzerland; Federal Office of Public Health; 2017.
38. National Institute of Cancer Epidemiology and Registration (NICER). Cancer Incidence, 2004-2018. 2018.
39. GDP per capita (current US$): World Bank, 2022. 2022.
40. ten Haaf K, Jeon J, Tammemagi MC, et al. Risk prediction models for selection of lung cancer screening candidates: a retrospective validation study. *PLoS Med*. 2017;14:e1002277.
41. Blom EF, Haaf KT, de Koning HJ. Systematic review and meta-analysis of community- and choice-based health state utility values for lung cancer. *Pharmacoeconomics*. 2020;38:1187-1200.
42. Perneger TV, Combescure C, Courvoisier DS. General population reference values for the French version of the EuroQol EQ-5D health utility instrument. *Value Health*. 2010;13:631-635.
43. Bundesamt für Statistik (BFS). Medizintechnische Ausstattung von Spitälern und Arztpraxen imh Jahr 2019. 2021.
44. Bhadhuri A, Insinga R, Guggisberg P, Panje C, Schwenkglenks M. Cost effectiveness of pembrolizumab vs chemotherapy as first-line treatment for metastatic NSCLC that expresses high levels of PD-L1 in Switzerland. *Swiss Med Wkly*. 2019;149:w20170.
45. Hofmarcher T, Lindgren P, Wilking N, Jonsson B. The cost of cancer in Europe 2018. *Eur J Cancer*. 2020;129:41-49.
46. Panje CM, Lupatsch JE, Barbier M, et al. A cost-effectiveness analysis of consolidation immunotherapy with durvalumab in stage III NSCLC responding to definitive radiochemotherapy in Switzerland. *Ann Oncol*. 2020;31:501-506.
47. Barbier MC, Pardo E, Panje CM, Gautschi O, Lupatsch JE, Swiss Group for Clinical Cancer R. A cost-effectiveness analysis of pembrolizumab with or without chemotherapy for the treatment of patients with metastatic, non-squamous non-small cell lung cancer and high PD-L1 expression in Switzerland. *Eur J Health Econ*. 2021;22:669-677.
48. Lythgoe MP, Krell J, Mahmoud S, Mills EC, Vasudevan A, Savage P. Development and economic trends in anticancer drugs licensed in the UK from 2015 to 2019. *Drug Discov Today*. 2021;26:301-307.
49. O'Brien M, Paz-Ares L, Marreaud S, et al. Pembrolizumab versus placebo as adjuvant therapy for completely resected stage IB-IIIA non-small-cell lung cancer (PEARLS/KEYNOTE-091): an interim analysis of a randomised, triple-blind, phase 3 trial. *Lancet Oncol*. 2022;23:1274-1286.
50. Meza R, ten Haaf K, Kong CY, et al. Comparative analysis of 5 lung cancer natural history and screening models that reproduce outcomes of the NLST and PLCO trials. *Cancer*. 2014;120:1713-1724.
51. Ngo PJ, Cressman S, Behar-Harpaz S, Karikios DJ, Canfell K, Weber MF. Applying utility values in cost-effectiveness analyses of lung cancer screening: a review of methods. *Lung Cancer*. 2022;166:122-131.
52. 4-IN THE LUNG RUN: towards INdividually tailored INvitations, screening INtervals, and INtegrated co-morbidity reducing strategies in lung cancer screening. 2020.
53. Moldovanu D, de Koning HJ, van der Aalst CM. Lung cancer screening and smoking cessation efforts. *Transl Lung Cancer Res*. 2021;10:1099-1109.
54. European Central Bank. Euro Foreign Exchange Reference Rates, ed. 01/09/2022: European Central Bank.

SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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