Smoking, Cessation, and Lung Cancer: Results of the Framingham Heart Study

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Investigators (authors)

Tindle, Hilary A.

Duncan, Meredith S.

Greevy, Robert A.

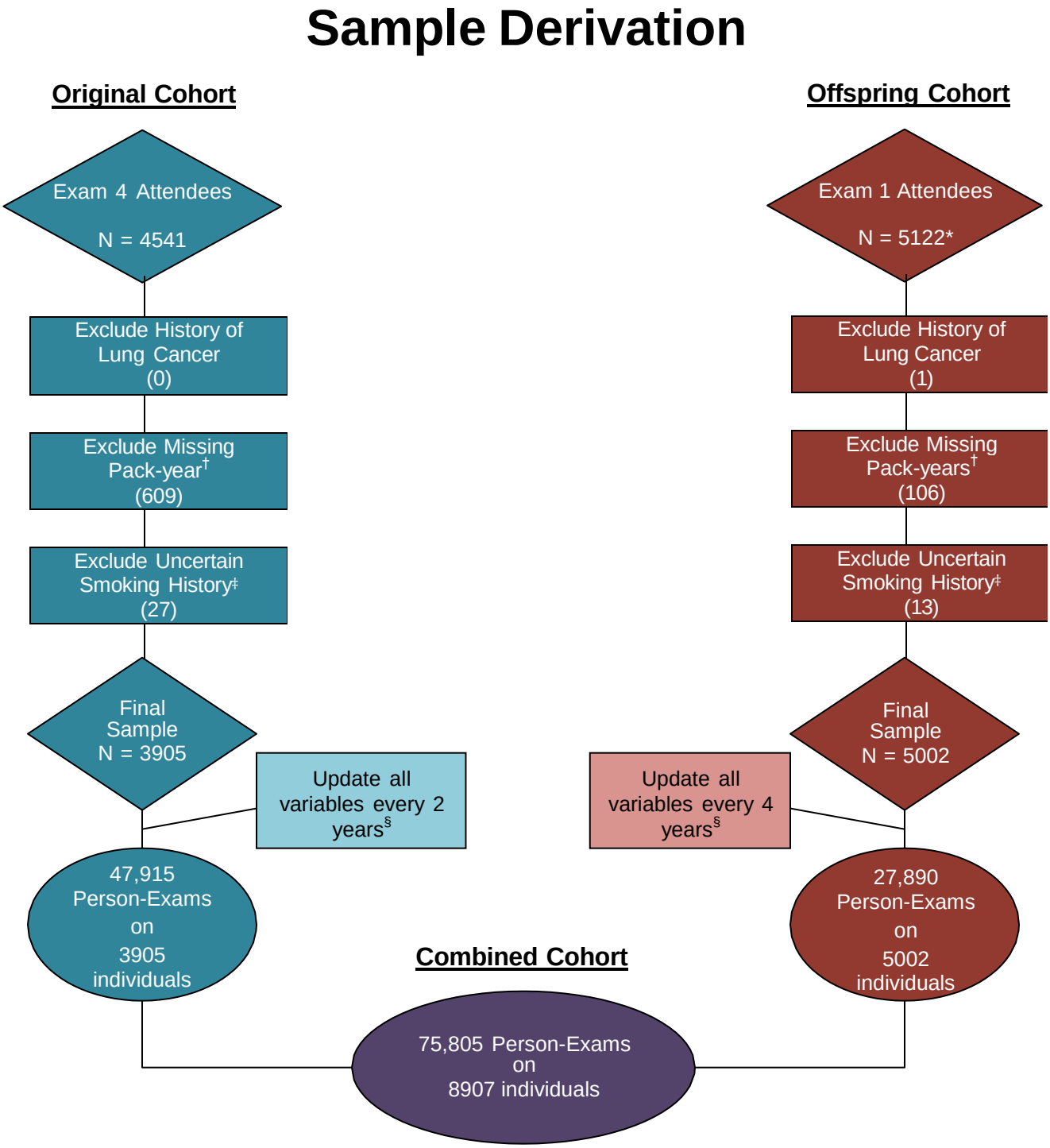
Ramachandran, Vasan S.

Kundu, Suman

Massion, Pierre P.

Freiberg, Matthew S.

Supplementary Figure 1. Derivation of Study Sample from Framingham Heart Study Data



*2 participants in the FHS Offspring cohort were considered ineligible for sample inclusion since their last follow-up date was equal to their Exam 1 date.

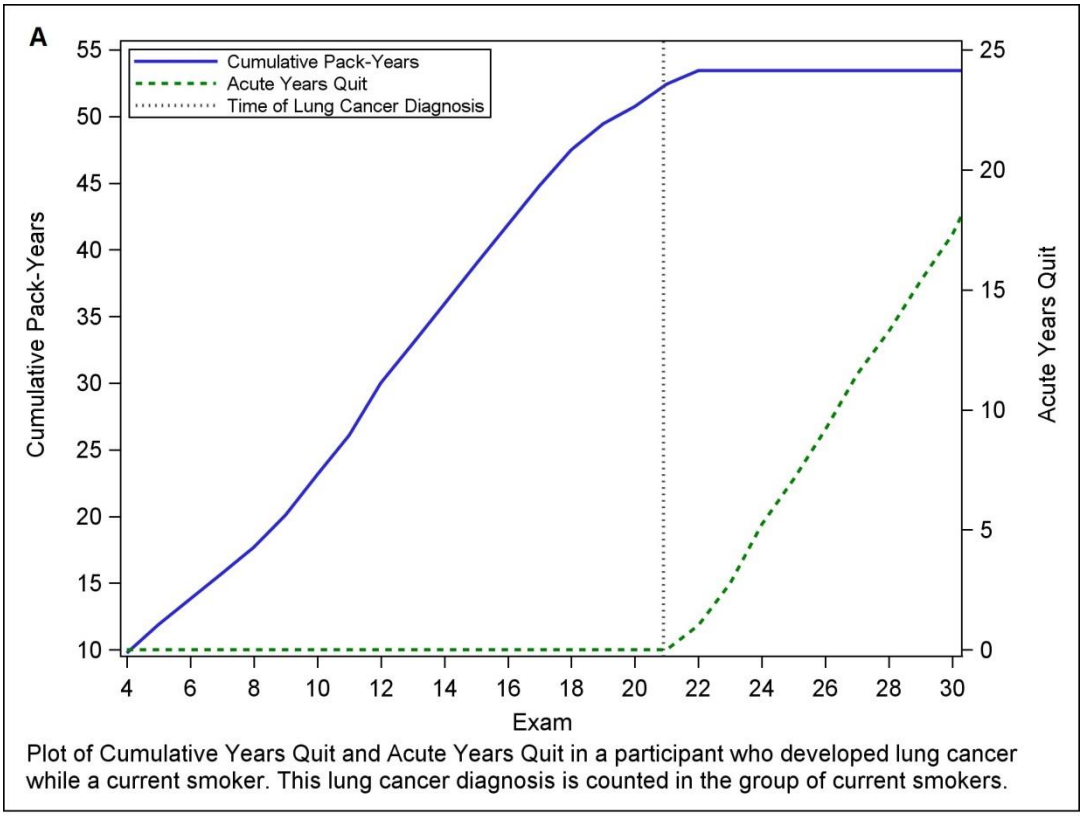
†In order to accurately calculate cumulative pack-years during the follow-up period, a reliable measure of prior smoking history at baseline was essential. Individuals excluded here were missing pack-years at baseline due to inability to

report age at starting/stopping smoking and/or intensity of smoking (cigarettes per day) prior to baseline.

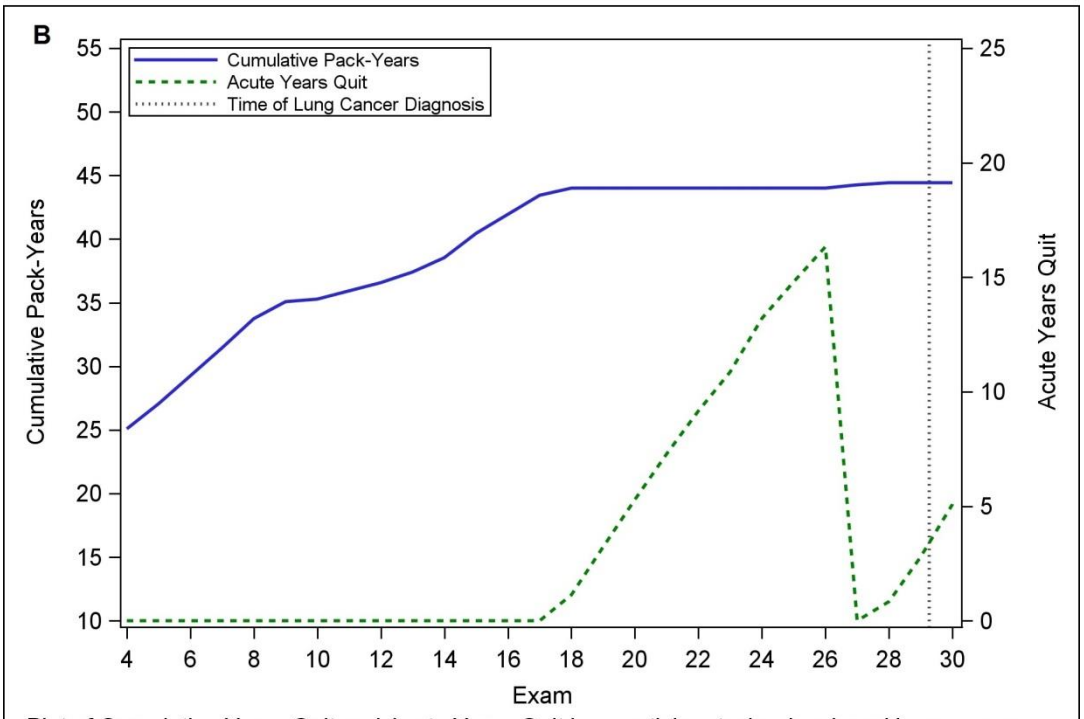
‡This includes individuals who, at baseline, reported: being a former/current smoker but with no pack-year history; being a never smoker with >0 pack-year history; or age at quitting smoking that was older than baseline age.

§Original cohort participants were seen roughly every 2 years. After 5 years without an update (effectively one missed exam plus an additional year), individuals were censored in order to avoid carrying values forward for an extended period without reassessment. Similarly, Offspring participants were seen roughly every 4 years and were thus censored after 9 years without an update (also corresponding to a single missed exam plus an additional year).

Supplementary Figure 2. Plot of Cumulative Pack-years and Years Since Quitting in a Current and Former Smoker who Developed Lung Cancer in the Original Cohort

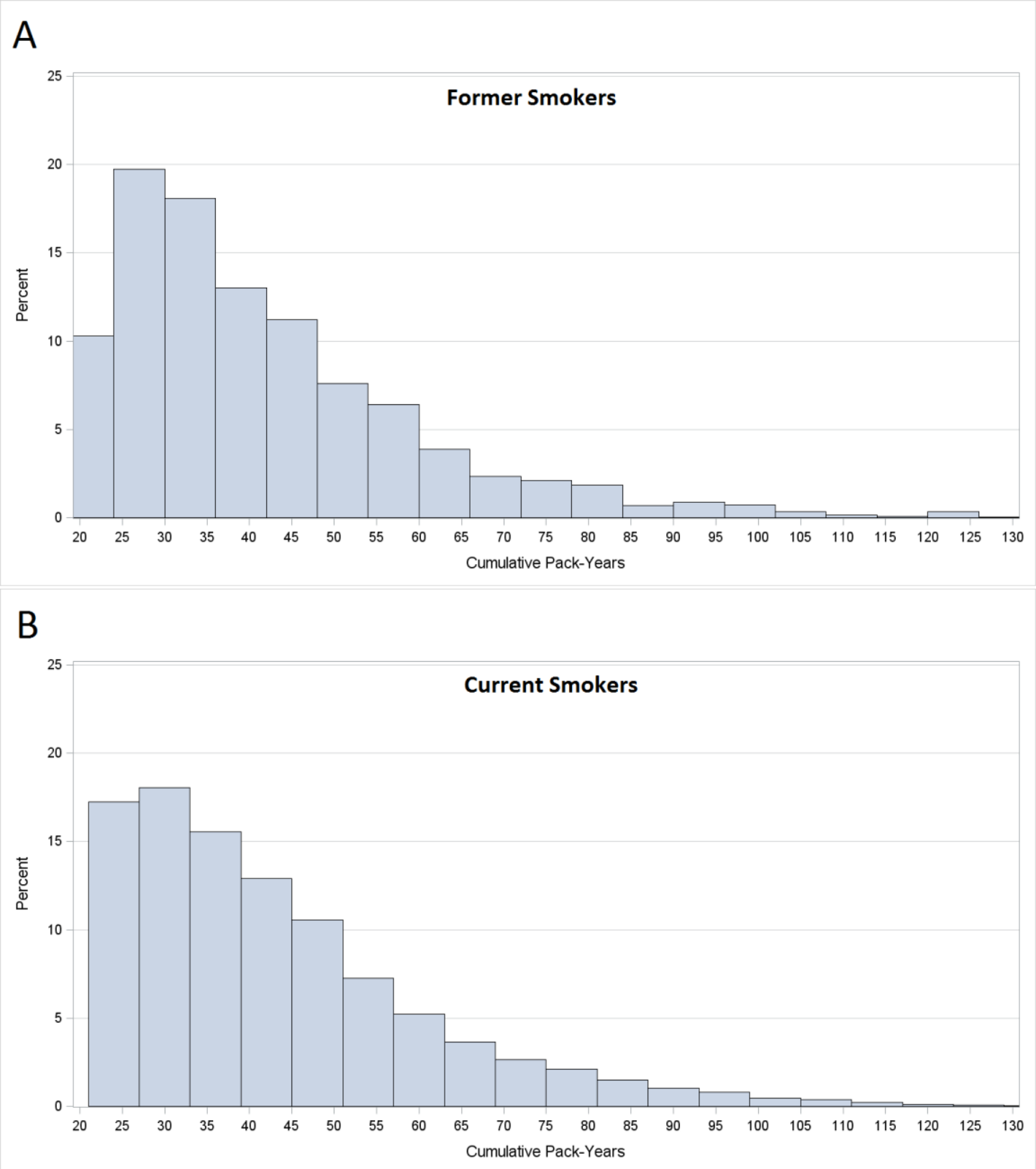


Plot of Cumulative Years Quit and Acute Years Quit in a participant who developed lung cancer while a current smoker. This lung cancer diagnosis is counted in the group of current smokers.



Plot of Cumulative Years Quit and Acute Years Quit in a participant who developed lung cancer while a former smoker. This lung cancer diagnosis is counted in the group of former smokers quit <5 years.

Supplementary Figure 3. Histogram of Cumulative Pack-Years among "Heavy" Former and Current Smokers with at least Median Pack-Year Exposure (≥21.3)



Supplementary Table 1. Adjusted Risk of Lung Cancer in Heavy Former vs. Current Smokers, Additionally Adjusted for Cumulative Pack-Years*

YSQ Category	*Person-Exams*	*Lung Cancers*	*Adjusted Hazards Ratio† [95% CI]*	*p-value‡*
Combined Cohorts				
Current Smokers (referent)	14,118	137	1.00	--
<5 YSQ	2828	27	0.67 [0.44, 1.03]	0.07
[5, 10) YSQ	2301	27	0.73 [0.48, 1.09]	0.13
[10, 15) YSQ	1564	15	0.52 [0.30, 0.90]	0.02
[15, 25) YSQ	2332	22	0.46 [0.28, 0.77]	0.003
25+ YSQ	1459	12	0.38 [0.20, 0.75]	0.005
Original Cohort				
Current Smokers (referent)	9963	85	1.00	--
<5 YSQ	1882	13	0.54 [0.30, 0.97]	0.04
[5, 10) YSQ	1409	11	0.53 [0.28, 0.98]	0.04
[10, 15) YSQ	951	9	0.56 [0.27, 1.14]	0.11
[15, 25) YSQ	1280	12	0.50 [0.25, 0.97]	0.04
25+ YSQ	770	7	0.48 [0.21, 1.10]	0.08
Offspring Cohort				
Current Smokers (referent)	4155	52	1.00	--
<5 YSQ	946	14	0.92 [0.50, 1.68]	0.78
[5, 10) YSQ	892	16	0.98 [0.56, 1.72]	0.95
[10, 15) YSQ	613	6	0.48 [0.20, 1.13]	0.09
[15, 25) YSQ	1052	10	0.43 [0.20, 0.93]	0.03
25+ YSQ	689	5	0.29 [0.10, 0.85]	0.02

*This analysis is limited to current and former smokers with at least 21.3 cumulative pack-years. CI=confidence interval; YSQ = Years since quitting.

†Hazards Ratios are adjusted for age, sex, education, examination decade, alcohol consumption, and cumulative pack-years. All variables are time-updated.

‡P-values were derived from a two-sided χ^2 test.

Supplementary Table 2. Adjusted Risk of Lung Cancer Using 6 Assessments of Smoking Status*

YSQ Category	*Person-Exams*	*Lung Cancers*	*Adjusted Hazards Ratio† [95% CI]*	*p-value‡*
Combined Cohorts – Former vs. Current				
Current Smokers (referent)	6860	212	1.00	---
<5 YSQ	1380	34	0.55 [0.38, 0.80]	0.002
[5, 10) YSQ	917	30	0.56 [0.38, 0.83]	0.004
[10, 15) YSQ	691	10	0.25 [0.13, 0.47]	<0.001
[15, 25) YSQ	1119	24	0.32 [0.21, 0.51]	<0.001
25+ YSQ	623	7	0.16 [0.07, 0.35]	<0.001
Combined Cohorts – Former vs. Never				
<5 YSQ	1380	34	11.15 [6.64, 18.72]	<0.001
[5, 10) YSQ	917	30	10.80 [6.45, 18.10]	<0.001
[10, 15) YSQ	691	10	4.78 [2.26, 10.08]	<0.001
[15, 25) YSQ	1119	24	5.96 [3.35, 10.62]	<0.001
25+ YSQ	623	7	2.85 [1.17, 6.97]	0.02
Never Smokers (referent)	14,636	31	1.00	---

*This analysis is limited to never smokers and ever smokers with at least 21.3 cumulative pack years. CI=confidence interval; YSQ = Years since quitting.

†. Hazards Ratios are adjusted for age, sex, education, examination decade, and alcohol consumption. All variables are time-updated.

‡P-values were derived from a two-sided χ^2 test.

Supplementary Table 3. Adjusted Risk of Lung Cancer Using 2 Assessments of Smoking Status*

YSQ Category	*Person-Exams*	*Lung Cancers*	*Adjusted Hazards Ratio† [95% CI]*	*p-value‡*
Combined Cohorts – Former vs. Current				
Current Smokers (referent)	3284	256	1.00	---
<5 YSQ	184	1	0.13 [0.02, 0.96]‖	0.046
[5, 10) YSQ	626	30	0.35 [0.24, 0.52]	<0.001
[10, 15) YSQ	128	3	0.18 [0.06, 0.55]‖	0.003
[15, 25) YSQ	193	9	0.30 [0.15, 0.61]	<0.001
25+ YSQ	29	0	<0.01 [<0.01, <0.01]‖	<0.001
Combined Cohorts – Former vs. Never				
Former Smokers				
5 YSQ	184	1	2.35 [0.31, 17.96]‖	0.41
[5, 10) YSQ	626	30	6.04 [3.38, 10.80]	<0.001
[10, 15) YSQ	128	3	2.97 [0.88, 10.06]‖	0.08
[15, 25) YSQ	193	9	5.29 [2.06, 13.55]	<0.001
25+ YSQ	29	0	<0.01 [<0.01, <0.01]‖	<0.001
Never Smokers (referent)	6126	32	1.00	---

*This analysis is limited to never smokers and ever smokers with at least 21.3 cumulative pack years. CI = Confidence Interval; YSQ = Years since quitting.

†Hazards Ratios are adjusted for age, sex, education, examination decade, and alcohol consumption. All variables are time-updated.

‡P-values were derived from a two-sided χ^2 test.

‖Because fewer than 5 lung cancer events contributed to the estimation of the hazard ratios in these cells, these estimates should be interpreted with caution.

Supplementary Table 4. Adjusted Risk of Lung Cancer in Full Sample

YSQ Category	*Person-Exams*	*Lung Cancers*	*Adjusted Hazards Ratio* [95% CI]*	*p-value*†
Combined Cohorts – Former vs. Current				
Current Smokers (referent)	22,085	139	1.00	---
<5 YSQ	5166	29	0.54 [0.36, 0.81]	0.003
[5, 10) YSQ	4366	27	0.45 [0.30, 0.67]	<0.001
[10, 15) YSQ	3213	15	0.27 [0.16, 0.46]	<0.001
[15, 25) YSQ	5385	28	0.23 [0.15, 0.34]	<0.001
25+ YSQ	4743	21	0.13 [0.08, 0.22]	<0.001
Combined Cohorts – Former vs. Never Former Smokers				
<5 YSQ	5166	29	8.97 [5.17, 15.57]	<0.001
[5, 10) YSQ	4366	27	7.32 [4.21, 12.73]	<0.001
[10, 15) YSQ	3213	15	4.38 [2.28, 8.42]	<0.001
[15, 25) YSQ	5385	28	3.59 [2.09, 6.15]	<0.001
25+ YSQ	4743	21	2.04 [1.13, 3.68]	0.02
Never Smokers (referent)	30,847	25	1.00	---

YSQ = Years since quitting.

*Hazards Ratios are adjusted for age, sex, education, examination decade, and alcohol consumption. All variables are time-updated.

†P-values were derived from a two-sided χ^2 test.

Supplementary Table 5. Adjusted Risk of Lung Cancer in Former vs. Current Smokers with ≥ 30 Pack-Years Exposure

	Combined Cohorts			
YSQ Category	***Person -Exams***	***Lung Cancers***	***Adjusted Hazards Ratio* [95% CI]***	***p-value***[†]
Combined Cohorts				
Current Smokers (referent)	10,402	130	1.00	--
<5 YSQ	2123	26	0.64 [0.42, 0.99]	0.04
[5, 10) YSQ	1681	27	0.68 [0.45, 1.02]	0.06
[10, 15) YSQ	1113	13	0.40 [0.22, 0.72]	0.002
[15, 25) YSQ	1568	16	0.28 [0.16, 0.49]	<0.001
25+ YSQ	850	7	0.19 [0.08, 0.43]	<0.001
Original Cohort				
Current Smokers (referent)	7283	79	1.00	--
<5 YSQ	1405	13	0.53 [0.29, 0.97]	0.04
[5, 10) YSQ	1021	11	0.50 [0.27, 0.93]	0.03
[10, 15) YSQ	677	8	0.45 [0.21, 0.95]	0.04
[15, 25) YSQ	850	10	0.35 [0.17, 0.71]	0.004
25+ YSQ	439	3	0.19 [0.06, 0.61][‡]	0.006
Offspring Cohort				
Current Smokers (referent)	3119	51	1.00	--
<5 YSQ	718	13	0.80 [0.43, 1.50]	0.49
[5, 10) YSQ	660	16	0.89 [0.50, 1.57]	0.68
[10, 15) YSQ	436	5	0.34 [0.13, 0.88]	0.03
[15, 25) YSQ	718	6	0.20 [0.08, 0.50]	<0.001
25+ YSQ	411	4	0.18 [0.06, 0.54][‡]	0.002

YSQ = Years since quitting.

*Hazards Ratios are adjusted for age, sex, education, examination decade, and alcohol consumption. All variables are time-updated.

[†]P-values were derived from a two-sided χ^2 test.

[‡]Because fewer than 5 lung cancer events contributed to the estimation of the hazard ratios in these cells, these estimates should be interpreted with caution.

Supplementary Table 6. Adjusted Risk of Lung Cancer in Former Smokers with ≥ 30 Pack-Years Exposure vs. Never Smokers

YSQ Category	*Person-Exams*	*Lung Cancers*	*Adjusted Hazard Ratio* [95% CI]*	*p-value*[†]
Combined Cohorts				
<5 YSQ	2123	26	13.86 [7.85, 24.46]	<0.001
[5, 10) YSQ	1681	27	14.82 [8.45, 25.98]	<0.001
[10, 15) YSQ	1113	13	8.77 [4.25, 18.10]	<0.001
[15, 25) YSQ	1568	16	6.02 [3.07, 11.81]	<0.001
25+ YSQ	850	7	3.97 [1.60, 9.87]	0.003
Never Smokers (referent)	30,847	25	1.00	--
Original Cohort				
<5 YSQ	1405	13	14.70 [6.86, 31.49]	<0.001
[5, 10) YSQ	1021	11	14.13 [6.20, 32.23]	<0.001
[10, 15) YSQ	677	8	12.74 [4.78, 33.94]	<0.001
[15, 25) YSQ	850	10	9.91 [4.05, 24.27]	<0.001
25+ YSQ	439	3	5.25 [1.41, 19.48][‡]	0.01
Never Smokers (referent)	20,384	13	1.00	--
Offspring Cohort				
<5 YSQ	718	13	12.70 [5.42, 29.74]	<0.001
[5, 10) YSQ	660	16	14.54 [6.56, 32.21]	<0.001
[10, 15) YSQ	436	5	5.88 [1.97, 17.57]	0.002
[15, 25) YSQ	718	6	3.49 [1.23, 9.87]	0.02
25+ YSQ	411	4	3.32 [0.996, 11.08][‡]	0.05
Never Smokers (referent)	10,463	12	1.00	--

YSQ = Years since quitting.

*Hazard Ratios are adjusted for age, sex, education, examination decade, and alcohol consumption. All variables are time-updated.

[†]P-values were derived from a two-sided χ^2 test.

[‡]Because fewer than 5 lung cancer events contributed to the estimation of the hazard ratios in these cells, these estimates should be interpreted with caution.