

SUPPLEMENTARY FILE

Risk of all-cause mortality by various cigarette smoking indices: a longitudinal study using the a longitudinal study using the Korea National Health Examination Baseline Cohort in South Korea

Table S1 Advantages and disadvantages of the various indices used in studies comparing two or more smoking indices

	Index							
	Ever-smoking	Smoking status	Smoking intensity	Smoking duration	Pack-year	Time since quitting	Age at initiation	CSI
Advantages	<ul style="list-style-type: none"> Easily quantified and recalled 	<ul style="list-style-type: none"> Easily quantified and recalled Comparable to other studies, as this index is most commonly used¹ 	<ul style="list-style-type: none"> Simple and easily interpreted² 	<ul style="list-style-type: none"> Easily quantified and recalled³ Considers cumulative exposure 	<ul style="list-style-type: none"> The simplest of the composite indices Considers cumulative exposure in terms of both intensity and duration 	<ul style="list-style-type: none"> Easily quantified and recalled Can assess the benefits of quitting early 	<ul style="list-style-type: none"> Easily quantified and recalled Implicitly considers cumulative exposure 	<ul style="list-style-type: none"> Integrates intensity, duration, and time since cessation into a single variable⁴ Avoids multicollinearity between measures⁴
Disadvantages	<ul style="list-style-type: none"> Does not distinguish former from current smokers^{2,4} 	<ul style="list-style-type: none"> Does not measure cumulative exposure Prone to “healthy smoker” biases⁴ 	<ul style="list-style-type: none"> Hard to quantify (e.g., decreases with age and morbidity)^{5,6} Correlates poorly with biochemical assessments⁵ 	<ul style="list-style-type: none"> Does not fully characterize the consumption behaviors of smokers⁷ 	<ul style="list-style-type: none"> Equal weights for amount/duration³ Does not explicitly consider time since quitting^{8,9} 	<ul style="list-style-type: none"> Does not consider consumption behaviors (e.g., duration, intensity)¹⁰ Collinear with age at the time of smoking initiation and duration¹ 	<ul style="list-style-type: none"> Does not consider consumption behaviors (e.g., duration, intensity)¹⁰ Collinear with time since quitting and smoking duration¹ 	<ul style="list-style-type: none"> Requires additional calculations¹¹ Hard to interpret^{10,11}

Note: The information presented is a summary of the findings of articles that we initially identified as relevant,^{2,7,12,13} and then from backward and forward citation-searching of the Web of Science using these articles. The inclusion criteria were publication in 2000 or later in a peer-reviewed journal, the inclusion of empirical evidence on how at least two smoking indices predicted health outcomes, and explicit comparisons of indices in terms of their advantages, disadvantages, and/or biological mechanisms. The full list of reviewed articles is given in Table S1.

CSI: Cumulative smoking index

Table S2 A summary of previous studies comparing two or more indices when modeling health outcomes associated with cigarette-smoking.

#	First author (published year)	Health outcome examined	Country, setting	Number of participants	Indices included	Authors' conclusions
1	Bhatt 2018 ³	Chronic obstructive pulmonary disease	USA	10,187	<ul style="list-style-type: none"> • Cigarettes smoked per day (intensity) • Smoking duration • Pack-years 	<ul style="list-style-type: none"> • Smoking duration provided stronger risk estimates than did the smoking intensity or pack-years
2	Flanders 2003 ¹⁴	Lung cancer	USA, prospective cohort	116,474	<ul style="list-style-type: none"> • Cigarettes smoked per day (intensity) • Smoking duration 	<ul style="list-style-type: none"> • Lung cancer death was more strongly associated with smoking duration than cigarettes per day • The association between smoking intensity and mortality decreased with age
3	Hudson 2010 ⁴	Systemic sclerosis	Canada	606	<ul style="list-style-type: none"> • Ever-smoking • Smoking status (current/never/former) • Cigarettes smoked per day (intensity) • Smoking duration • Time since quitting • Comprehensive Smoking Index* 	<ul style="list-style-type: none"> • Comprehensive smoking index showed a stronger association and a better model fit compared to other indices • Ever-smoking and smoking status was prone to “healthy smoker” biases
4	Leffondré 2002 ¹	Lung cancer	Canada	1,555	<ul style="list-style-type: none"> • Smoking status (current/never/former) • Cigarettes smoked per day (intensity) • Smoking duration • Cigarette-years • Age at starting • Time since quitting 	<ul style="list-style-type: none"> • Consideration of smoking intensity and duration separately may provide a better fit than cigarette-years • Including cigarette-years when estimating the impact of time since quitting or age at initiation reduced multicollinearity
5	Leffondré 2006 ¹⁰	Lung cancer	Canada, case-control study	2,668	<ul style="list-style-type: none"> • Ever-smoking • Cigarette-years • Time since quitting • Comprehensive Smoking Index* 	<ul style="list-style-type: none"> • No evidence that model fit differed significantly by the index • The Comprehensive Smoking Index may be a useful parsimonious representation of the lifetime smoking history
6	Lubin 2006 ¹⁵	Lung cancer	Europe, hospital-based case control study	23,011	<ul style="list-style-type: none"> • Cigarettes smoked per day (intensity) • Smoking duration • Pack-years 	<ul style="list-style-type: none"> • Intensity showed homogeneous patterns by different histologic types of lung cancer, but showed difference by total exposure and smoking duration

#	First author (published year)	Health outcome examined	Country, setting	Number of participants	Indices included	Authors' conclusions
7	Lubin 2016 ¹⁶	CVD	USA, clinic-based prospective cohort study	14,127	<ul style="list-style-type: none"> • Cigarettes smoked per day (intensity) • Smoking duration • Pack-years 	<ul style="list-style-type: none"> • Pack-years was the primary determinant of smoking-related CVD risks • For those with equal pack-years, smoking fewer cigarettes for longer was more harmful than smoking more cigarettes for shorter durations
8	Lubin 2017 ⁷	Coronary Heart Disease	USA, prospective cohort study of licensed pesticide applicators and their spouses; Finland, trials of male smokers	89,656; 29,133	<ul style="list-style-type: none"> • Ever-smoking • Cigarettes smoked per day (intensity) • Pack-years 	<ul style="list-style-type: none"> • Pack-years was associated with coronary heart disease risks • Pack-years and smoking intensities (evaluated together) were inversely associated with intensity; smoking fewer cigarettes for longer was more harmful than smoking more cigarettes for a shorter time
9	Nance 2017 ²	CVD incidence and deaths	USA, multi-ethnic cohort	6,814	<ul style="list-style-type: none"> • Ever-smoking • Smoking status (current/never/former) • Cigarettes smoked per day (intensity) • Smoking duration • Pack-years • Age at starting smoking • Time since quitting • Comprehensive Smoking Index* 	<ul style="list-style-type: none"> • Current smoking and cigarettes smoked per day exhibited the strongest associations with incidence • Cigarettes smoked per day exhibited a better model fit than current smoking in terms of incidence • The Comprehensive Smoking Index afforded the best fit for CVD deaths
10	Ogawa 2019 ¹²	Oncogenic mutations in non-small cell lung cancer	Japan, medical institutions	876	<ul style="list-style-type: none"> • Smoking duration • Pack-years 	<ul style="list-style-type: none"> • Smoking duration and pack-year indices were not significantly different • Smoking duration alone must be considered as a simpler alternative

#	First author (published year)	Health outcome examined	Country, setting	Number of participants	Indices included	Authors' conclusions
11	Remen 2018 ⁶	Lung cancer	Canada, population based case-control	2,705	<ul style="list-style-type: none"> • Ever-smoking • Smoking status (current/never/former) • Cigarettes smoked per day (intensity) • Smoking duration • Pack-years • Age at starting • Time since quitting • Comprehensive Smoking Index* 	<ul style="list-style-type: none"> • Smoking duration and the Comprehensive Smoking Index exhibited the strongest associations and the best model fits
12	Young 2019 ¹⁷	Peripheral artery disease	North Carolina USA, hospital-based	693	<ul style="list-style-type: none"> • Packs smoked per day (intensity) • Smoking duration • Pack-years • Time since quitting 	<ul style="list-style-type: none"> • Smoking intensity best identified negative outcomes after open revascularization of patients with peripheral artery disease

* The Comprehensive Smoking Index was originally developed by Hoffman et al.,^{18,19} and incorporates smoking intensity, duration, and time since quitting. Studies have used different terms (e.g., Compound Smoking index,² Cumulative smoking index⁶) to indicate this measure. However, the formulae used to obtain the estimates were similar across all studies, with slight modifications (log transformations and addition of a lag parameter). These are all termed the “Comprehensive Smoking Index” in this Table.

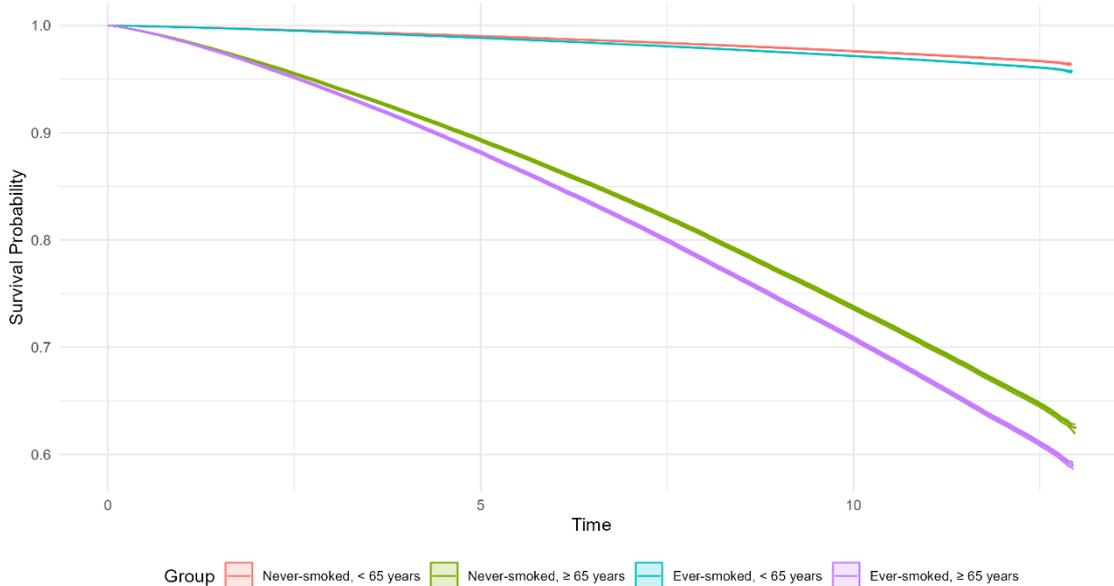


Figure S1.1 Kaplan-Meier curve by age and ever smoking status among men

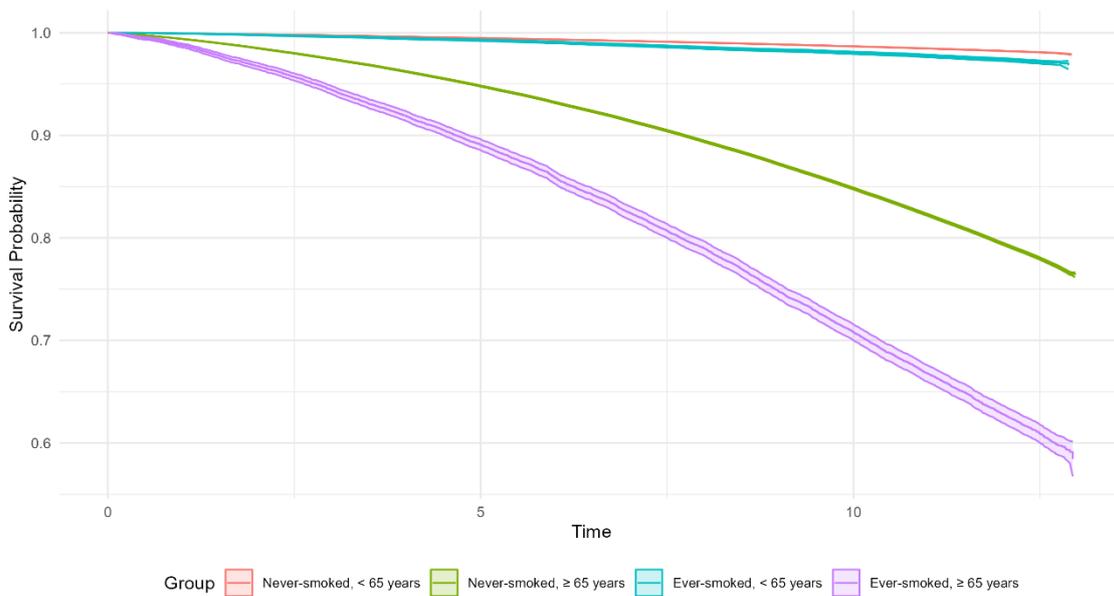


Figure S2.2 Kaplan-Meier curve by age and ever smoking status among women

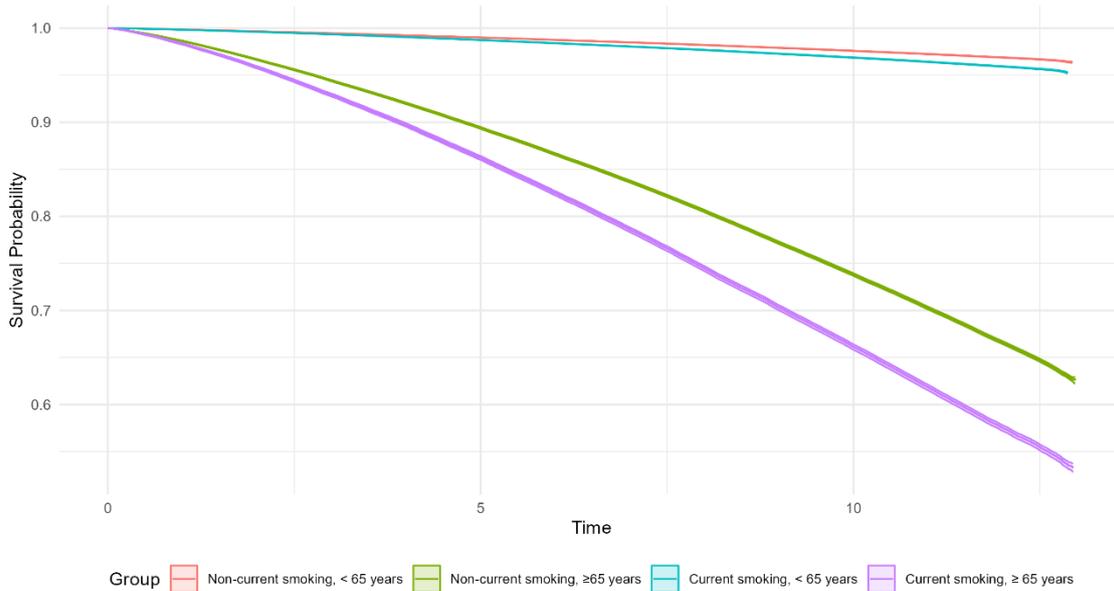


Figure S2.1 Kaplan-Meier curve by age and current smoking status among men

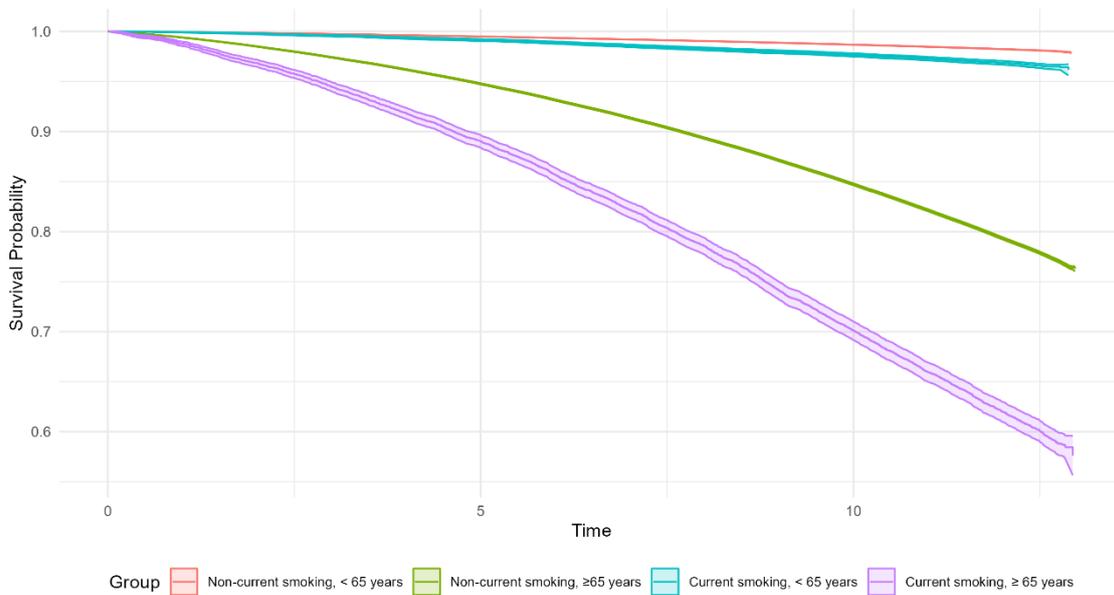


Figure S2.2 Kaplan-Meier curve by age and current smoking status among women

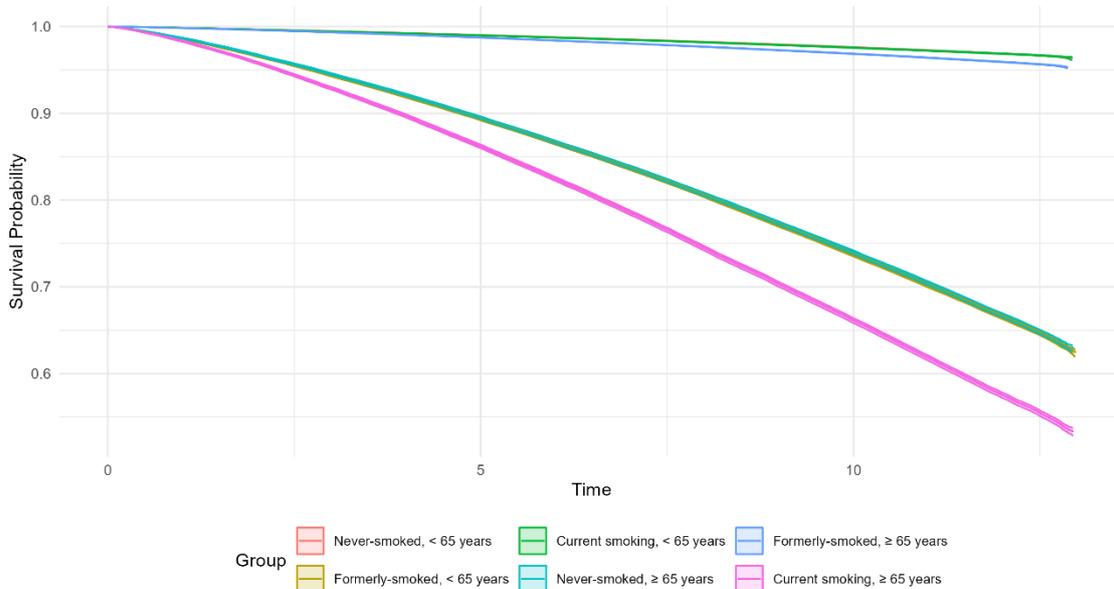


Figure S3.1 Kaplan-Meier curve by age and smoking status (never/former/current) among men

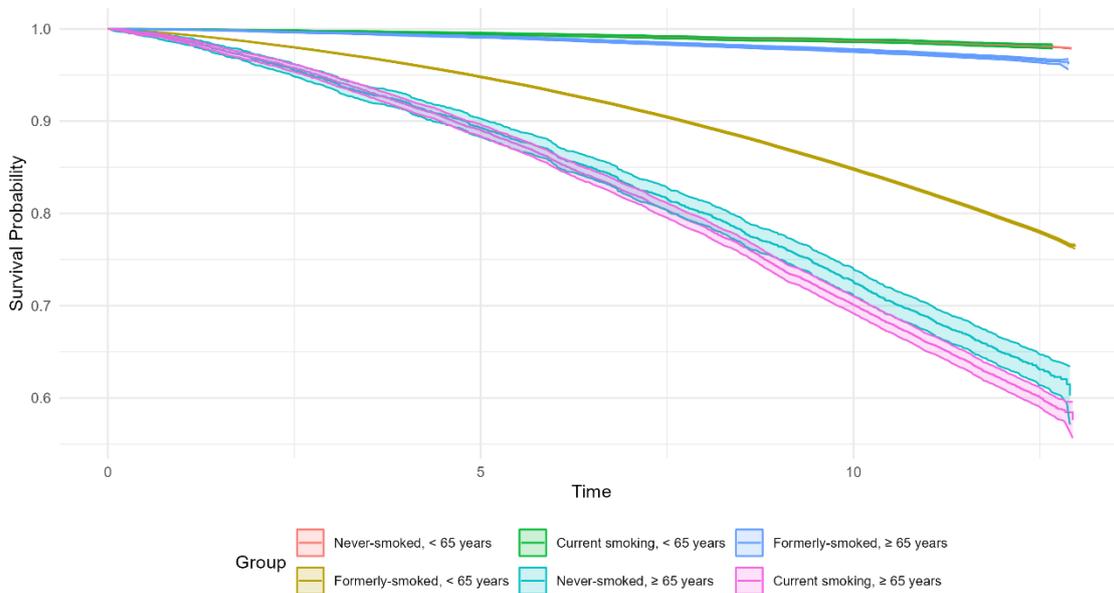


Figure S3.2 Kaplan-Meier curve by age and smoking status (never/former/current) among women

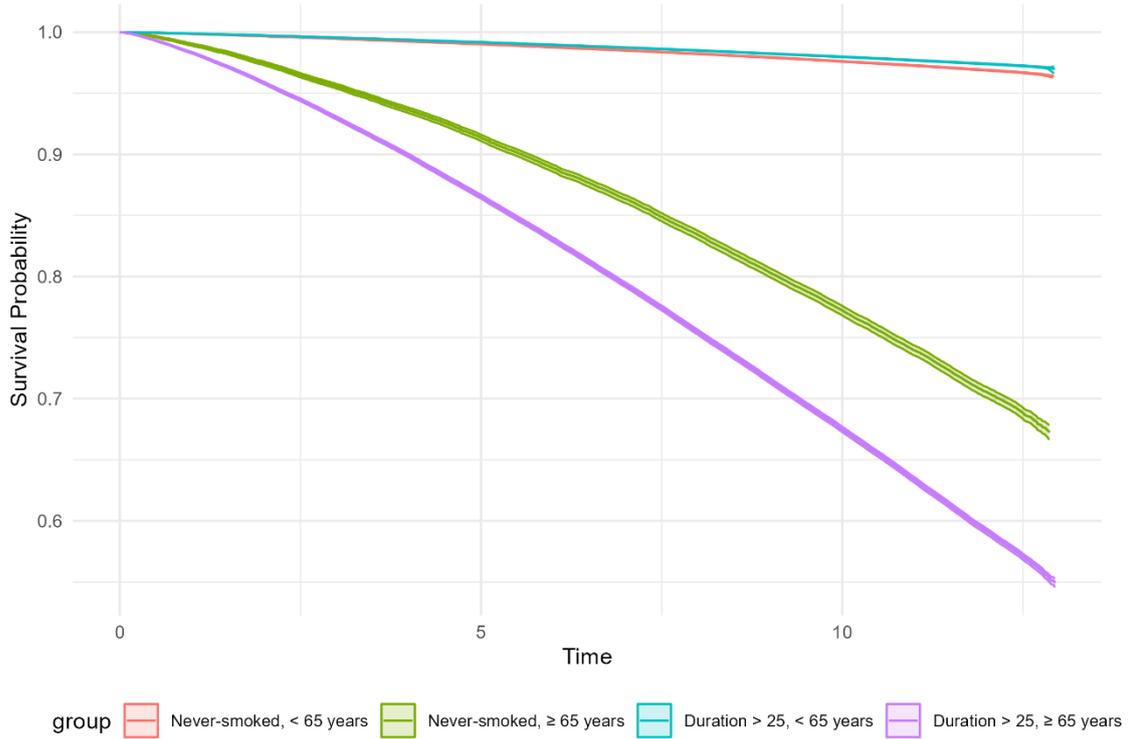


Figure S4.1 Kaplan-Meier curve by age and smoking duration among men

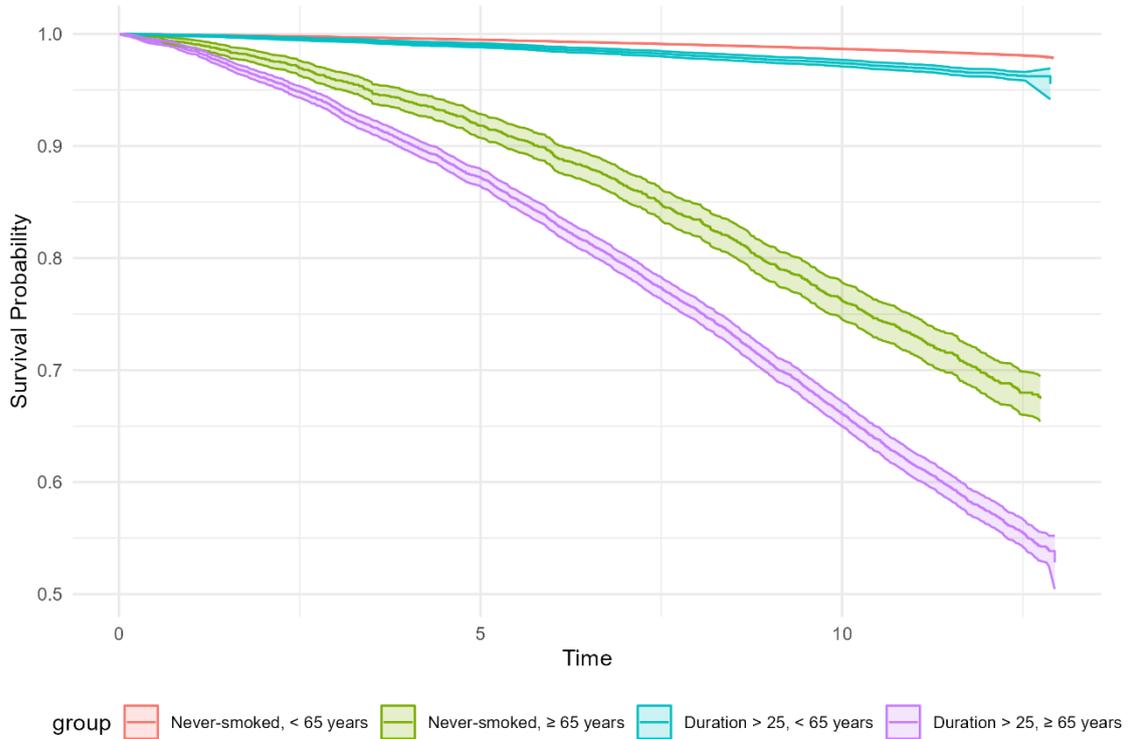


Figure S4.2 Kaplan-Meier curve by age and smoking duration among women

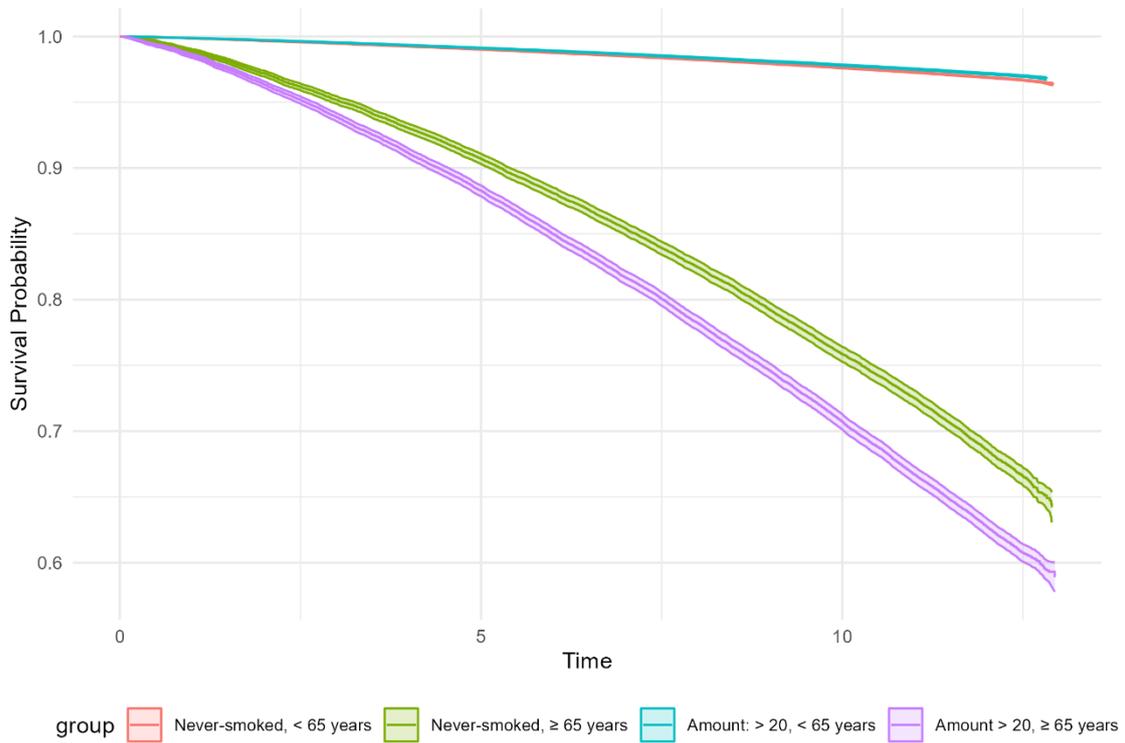


Figure S5.1 Kaplan-Meier curve by age and smoking intensity among men

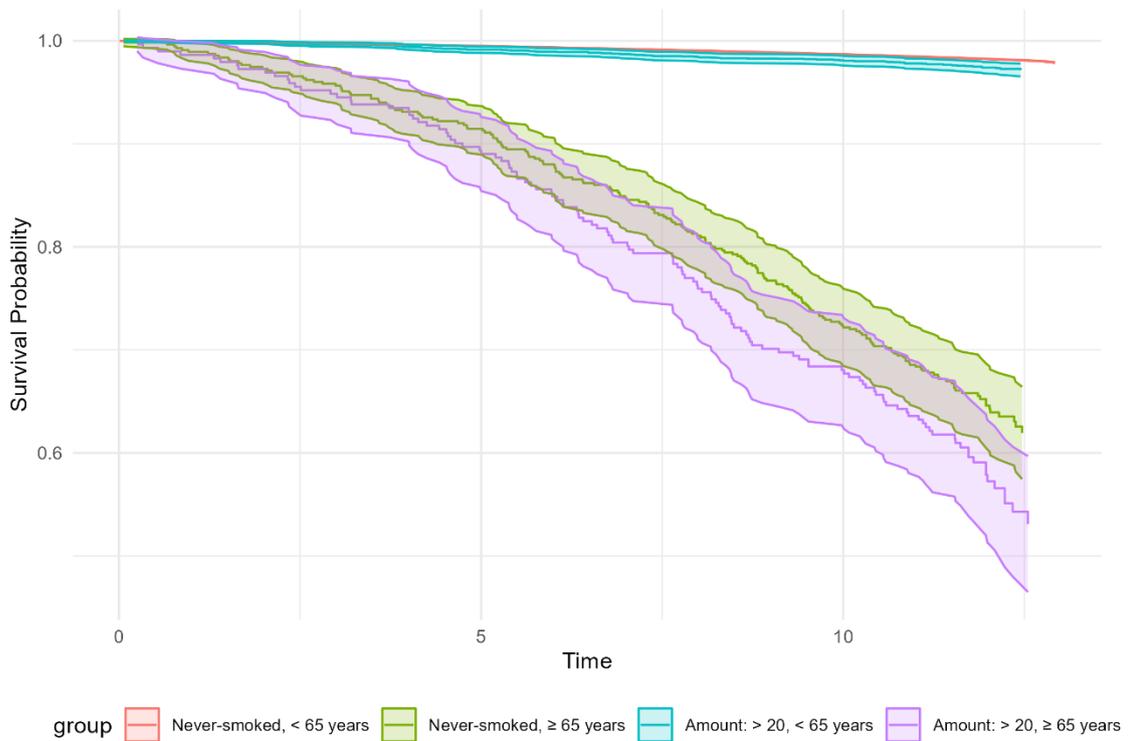


Figure S5.2 Kaplan-Meier curve by age and smoking intensity among women

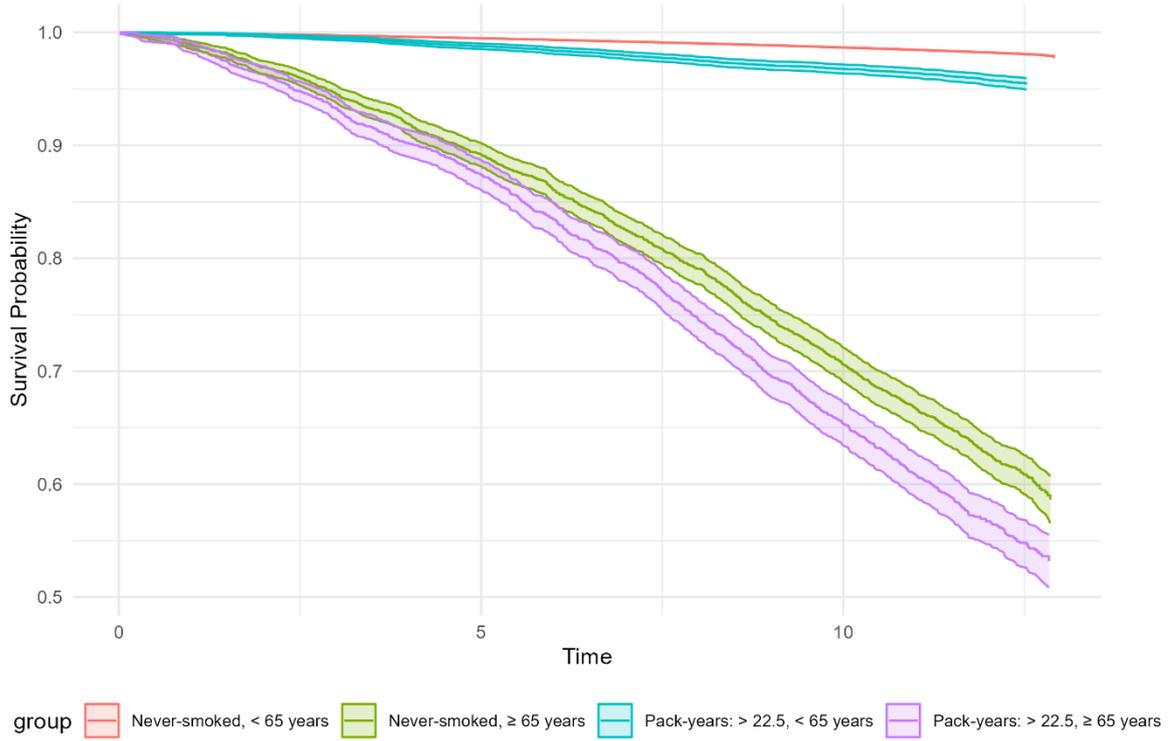


Figure S6.1 Kaplan-Meier curve by age and pack-year among men

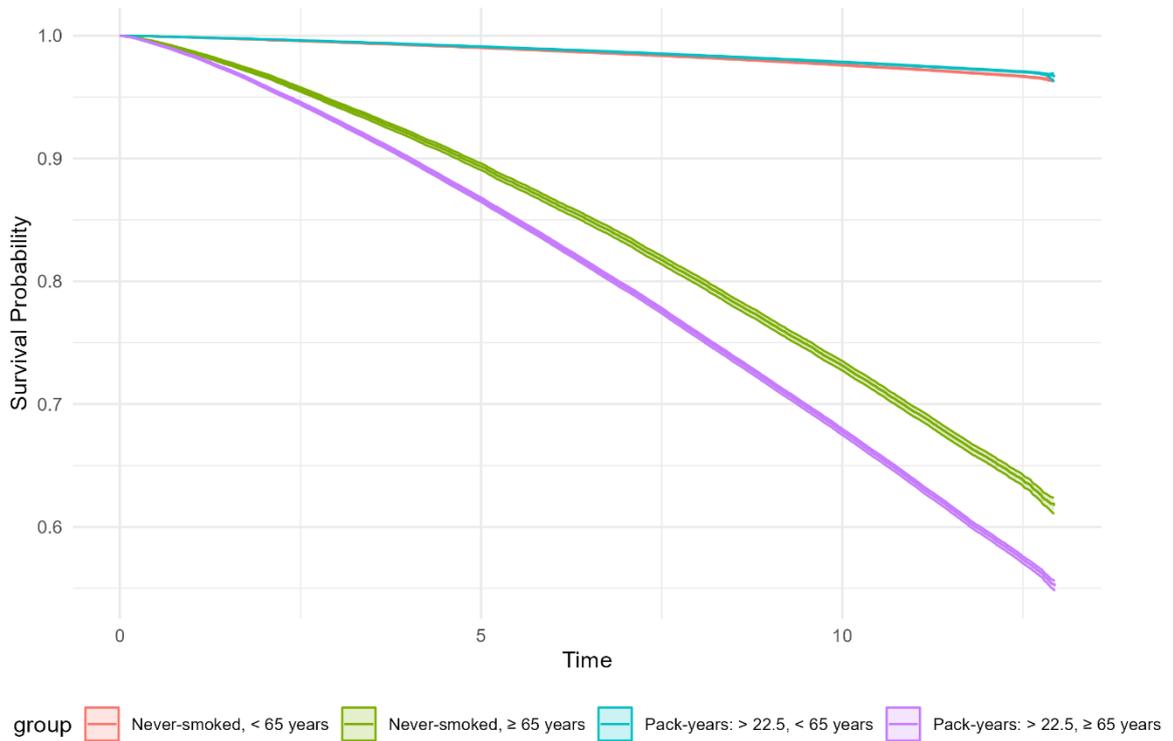


Figure S6.2 Kaplan-Meier curve by age and pack-year among women

Table S3 Hazard ratios, 95% confidence intervals, and the goodness-of-fits of models assessing the impacts of different smoking measures on all-cause deaths among all participants

Smoking index	Men					Women				
	aHR (95% CI)*	p-value	AIC	BIC	c-index	aHR (95% CI)*	p-value	AIC	BIC	c-index
Ever-smoking	1.07 (1.06, 1.08)	<0.0001	6467020	6467147	0.837	1.12 (1.09, 1.14)	<0.0001	3069422	3069541	0.853
Smoking status										
Never	Reference		6466446	6466583	0.840	Reference		3069415	3069543	0.853
Former	1.01 (1.00, 1.02)	0.0082				1.05 (1.00, 1.10)	0.0690			
Current	1.14 (1.13, 1.15)	<0.0001				1.14 (1.11, 1.18)	<0.0001			
Current smoking	1.13 (1.12, 1.14)	<0.0001	6466451	6466577	0.840	1.14 (1.11, 1.18)	<0.0001	3069416	3069535	0.853
Smoking duration (years)										
0 (never smoker)	Reference		6466361	6466520	0.837	Reference		3069421	3069569	0.853
≤ 10	0.95 (0.93, 0.96)	<0.0001				1.12 (1.07, 1.18)	<0.0001			
(10, 20]	1.00 (0.99, 1.01)	0.9453				1.19 (1.12, 1.26)	<0.0001			
(20, 25]	1.08 (1.06, 1.10)	<0.0001				1.17 (0.99, 1.39)	0.0681			
> 25	1.12 (1.11, 1.13)	<0.0001				1.09 (1.05, 1.12)	<0.0001			
Smoking intensity (cigarettes/day)										
0 (never smoker)	Reference		6466633	6466792	0.838	Reference		3069413	3069561	0.853
≤ 10	1.02 (1.01, 1.03)	0.0001				1.10 (1.07, 1.13)	<0.0001			
(10, 15]	1.04 (1.02, 1.06)	<0.0001				1.13 (1.00, 1.26)	0.0471			
(15, 20]	1.11 (1.10, 1.12)	<0.0001				1.16 (1.09, 1.23)	<0.0001			
> 20	1.16 (1.14, 1.18)	<0.0001				1.49 (1.28, 1.74)	<0.0001			
Pack-years										
0 (never smoker)	Reference		6466335	6466494	0.838	Reference		3069426	3069574	0.853
≤ 7.5	0.95 (0.94, 0.97)	<0.0001				1.1 (1.06, 1.15)	<0.0001			
(7.5, 15]	1.02 (1.01, 1.03)	0.0009				1.1 (1.05, 1.16)	<0.0001			
(15, 22.5]	1.08 (1.06, 1.09)	<0.0001				1.12 (1.04, 1.2)	0.0026			
> 22.5	1.13 (1.12, 1.14)	<0.0001				1.16 (1.1, 1.23)	<0.0001			

*All models adjusted for age, type of health insurance, income quintile, residential region, weekly alcohol consumption, weekly MVPA, and the body mass index.

Statistical significance at $p < 0.0017$

The lowest AIC value among all models for each sex is presented in **bold**.

Table S4 Effect size comparisons for models addressing all participants

Variable1	Variable2	HR1	SE1	HR2	SE2	ln(HR1)	ln(HR2)	ln(HR2- HR1)	SE diff *	Ratio of relative risks	95% CI		p value **
Men													
Ever smoking	Current smoking	1.07	0.004	1.13	0.004	0.07	0.12	0.05	0.006	1.06	1.04	1.07	<0.0001
Ever smoking	Smoking status	1.07	0.004	1.14	0.005	0.07	0.13	0.06	0.006	1.06	1.05	1.07	<0.0001
Ever smoking	Smoking duration	1.07	0.004	1.12	0.004	0.07	0.11	0.04	0.006	1.05	1.03	1.06	<0.0001
Ever smoking	Smoking intensity	1.07	0.004	1.16	0.008	0.07	0.15	0.08	0.009	1.08	1.06	1.10	<0.0001
Ever smoking	Pack-years	1.07	0.004	1.13	0.005	0.07	0.12	0.05	0.006	1.06	1.04	1.07	<0.0001
Current smoking	Smoking status	1.13	0.004	1.14	0.005	0.12	0.13	0.01	0.006	1.01	0.99	1.02	0.3666
Current smoking	Smoking duration	1.13	0.004	1.12	0.004	0.12	0.11	-0.01	0.006	0.99	0.98	1.00	0.1155
Current smoking	Smoking intensity	1.13	0.004	1.16	0.008	0.12	0.15	0.03	0.009	1.03	1.01	1.04	0.0041
Current smoking	Pack-years	1.13	0.004	1.13	0.005	0.12	0.12	0.00	0.006	1.00	0.99	1.01	0.8762
Smoking status	Smoking duration	1.14	0.005	1.12	0.004	0.13	0.11	-0.02	0.006	0.98	0.97	1.00	0.0181
Smoking status	Smoking intensity	1.14	0.005	1.16	0.008	0.13	0.15	0.02	0.009	1.02	1.00	1.04	0.0294
Smoking status	Pack-years	1.14	0.005	1.13	0.005	0.13	0.12	0.00	0.007	1.00	0.98	1.01	0.4790
Smoking duration	Smoking intensity	1.12	0.004	1.16	0.008	0.11	0.15	0.04	0.009	1.04	1.02	1.05	0.0001
Smoking duration	Pack-years	1.12	0.004	1.13	0.005	0.11	0.12	0.01	0.006	1.01	1.00	1.02	0.1015
Smoking intensity	Pack-years	1.16	0.008	1.13	0.005	0.15	0.12	-0.02	0.009	0.98	0.96	0.99	0.0072

Variable1	Variable2	HR1	SE1	HR2	SE2	ln(HR1)	ln(HR2)	ln(HR2- HR1)	SE diff *	Ratio of relative risks	95% CI		p value **
Women													
Ever smoking	Current smoking	1.12	0.013	1.14	0.015	0.11	0.13	0.02	0.020	1.02	0.98	1.06	0.2487
Ever smoking	Smoking status	1.12	0.013	1.14	0.015	0.11	0.13	0.02	0.020	1.02	0.98	1.07	0.2335
Ever smoking	Smoking duration	1.12	0.013	1.09	0.018	0.11	0.08	-0.03	0.022	0.97	0.93	1.02	0.2186
Ever smoking	Smoking intensity	1.12	0.013	1.49	0.078	0.11	0.40	0.29	0.079	1.34	1.14	1.56	<i>0.0003</i>
Ever smoking	Pack-years	1.12	0.013	1.16	0.029	0.11	0.15	0.04	0.032	1.04	0.98	1.11	0.2036
Current smoking	Smoking status	1.14	0.015	1.14	0.015	0.13	0.13	0.00	0.021	1.00	0.96	1.04	0.9715
Current smoking	Smoking duration	1.14	0.015	1.09	0.018	0.13	0.08	-0.05	0.023	0.95	0.91	1.00	<i>0.0312</i>
Current smoking	Smoking intensity	1.14	0.015	1.49	0.078	0.13	0.40	0.27	0.080	1.30	1.12	1.53	<i>0.0008</i>
Current smoking	Pack-years	1.14	0.015	1.16	0.029	0.13	0.15	0.02	0.033	1.02	0.95	1.08	0.5965
Smoking status	Smoking duration	1.14	0.015	1.09	0.018	0.13	0.08	-0.05	0.023	0.95	0.91	0.99	0.0287
Smoking status	Smoking intensity	1.14	0.015	1.49	0.078	0.13	0.40	0.27	0.080	1.30	1.12	1.52	<i>0.0009</i>
Smoking status	Pack-years	1.14	0.015	1.16	0.029	0.13	0.15	0.02	0.033	1.02	0.95	1.08	0.6129
Smoking duration	Smoking intensity	1.09	0.018	1.49	0.078	0.08	0.40	0.32	0.080	1.37	1.17	1.61	<i>0.0001</i>
Smoking duration	Pack-years	1.09	0.018	1.16	0.029	0.08	0.15	0.07	0.034	1.07	1.00	1.14	<i>0.0466</i>
Smoking intensity	Pack-years	1.49	0.078	1.16	0.029	0.40	0.15	-0.25	0.083	0.78	0.66	0.92	<i>0.0028</i>

* $\sqrt{SE1^2 + SE2^2}$

**Statistically significant p-values (p<0.05) are *italicized*

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