SUPPLEMENTARY TABLE 1: OS and CSS outcomes according to diagnosis era, age group, and histologic subtype among patients with malignant mesothelioma, SEER 2004-2023.

Subgroup	Category	n	OS events, n (%)	Median OS, months	1-year OS	3-year OS	5-year OS	CSS events, n (%)	Median CSS, months	1-year CSS	3-year CSS	5-year CSS	OS log-rank p-value	CSS log-rank p-value
Diagnosis era	2004-2009	3,490	3,373 (96.6)	8 (8-9)	38.3% (36.6-39.9)	12.8% (11.8-14.0)	7.7% (6.8-8.6)	3,012 (86.3)	9 (9-10)	41.8% (40.1-43.4)	15.5% (14.2-16.8)	9.9% (8.9-11.1)	<0.001	<0.001
	2010-2015	3,417	3,245 (95.0)	9 (9-10)	39.6% (37.9-41.2)	14.9% (13.7-16.1)	9.4% (8.5-10.4)	2,965 (86.8)	10 (9-10)	42.4% (40.7-44.1)	17.2% (15.9-18.6)	11.5% (10.4-12.7)		
	2016-2023	3,966	3,004 (75.7)	11 (11-12)	47.3% (45.7-48.9)	20.5% (19.1-22.0)	11.9% (10.6-13.2)	2,709 (68.3)	13 (12-13)	50.8% (49.1-52.4)	23.8% (22.2-25.4)	15.1% (13.6-16.7)		
Age group, years	<60	1,844	1,406 (76.2)	19 (17-21)	61.1% (58.9-63.3)	34.3% (32.0-36.5)	26.5% (24.3-28.8)	1,284 (69.6)	21 (19-23)	63.5% (61.3-65.8)	37.0% (34.7-39.4)	29.6% (27.2-32.0)	<0.001	<0.001
	60-69	2,618	2,365 (90.3)	11 (10-12)	45.7% (43.8-47.6)	17.7% (16.2-19.3)	10.1% (8.9-11.4)	2,149 (82.1)	12 (12-13)	48.8% (46.9-50.7)	20.4% (18.8-22.0)	12.5% (11.1-14.0)		
	70-79	3,609	3,339 (92.5)	8 (8-9)	38.8% (37.2-40.4)	11.6% (10.5-12.7)	5.4% (4.6-6.3)	3,034 (84.1)	9 (9-10)	41.9% (40.3-43.5)	13.9% (12.7-15.2)	7.2% (6.3-8.3)		
	≥80	2,802	2,512 (89.7)	5 (5-6)	26.2% (24.5-27.8)	6.5% (5.6-7.5)	2.6% (2.0-3.3)	2,219 (79.2)	6 (6-7)	29.7% (27.9-31.4)	8.9% (7.8-10.1)	4.2% (3.3-5.2)		
Histologic subtype	Mesothelioma, NOS	4,675	4,208 (90.0)	8 (7-8)	37.6% (36.2-39.0)	14.9% (13.8-16.0)	9.0% (8.1-9.9)	3,749 (80.2)	9 (9-9)	41.1% (39.6-42.6)	18.1% (16.9-19.3)	11.9% (10.9-13.0)	<0.001	<0.001
	Epithelioid mesothelioma	4,239	3,602 (85.0)	14 (13-15)	53.7% (52.2-55.2)	21.4% (20.1-22.8)	13.0% (11.9-14.1)	3,271 (77.2)	15 (15-16)	56.8% (55.2-58.3)	24.2% (22.8-25.6)	15.5% (14.3-16.8)		
	Fibrous mesothelioma	1,139	1,064 (93.4)	4 (3-4)	17.9% (15.7-20.2)	5.4% (4.1-6.9)	4.2% (3.1-5.7)	978 (85.9)	4 (4-5)	20.3% (17.8-22.8)	6.6% (5.1-8.4)	5.3% (3.9-7.1)		
	Biphasic mesothelioma	818	748 (91.4)	8 (7-9)	36.3% (32.9-39.6)	8.4% (6.5-10.6)	4.1% (2.7-5.8)	688 (84.1)	9 (8-10)	39.3% (35.8-42.7)	10.3% (8.1-12.8)	5.1% (3.5-7.2)		

Values are presented as number (%) or Kaplan-Meier estimates with 95% CIs unless otherwise indicated. Diagnosis era was categorized as 2004-2009, 2010-2015, and 2016-2023. Age group was categorized as <60, 60-69, 70-79, and ≥80 years. Histologic subtypes were grouped using ICD-O-3 morphology codes. OS was defined from diagnosis to death from any cause. CSS was defined from diagnosis to death attributable to mesothelioma, with deaths from other causes censored. Survival probabilities are Kaplan-Meier estimates at 12, 36, and 60 months. CIs were calculated using Greenwood standard errors with log-log transformation. Survival estimates are presented with 95% CIs. p-values for survival comparisons were calculated using the log-rank test. Zero-month survival was recoded as 0.5 months for time-to-event analyses. The multicystic or other mesothelioma category included only two patients with no recorded events and was therefore omitted from this table; it is shown in Table 1 for completeness.
CI: Confidence interval; CSS: Cancer-specific survival; NOS: Not otherwise specified; OS: Overall survival; SEER: Surveillance, Epidemiology, and End Results.

SUPPLEMENTARY TABLE 2: Sensitivity multivariable Cox regression analysis excluding unknown or unstaged disease, SEER 2004-2023.

Variable	Category	OS aHR (95% CI)	p-value	CSS aHR (95% CI)	p-value
Primary site	Pleural	1 [Reference]		1 [Reference]	
	Peritoneal	0.84 (0.78-0.91)	<0.001	0.85 (0.79-0.92)	<0.001
	Other or unknown	0.89 (0.80-0.99)	0.037	0.87 (0.77-0.97)	0.015
Age group, years	<60	1 [Reference]		1 [Reference]	
	60-69	1.33 (1.23-1.42)	<0.001	1.27 (1.18-1.37)	<0.001
	70-79	1.52 (1.42-1.63)	<0.001	1.46 (1.35-1.57)	<0.001
	≥80	1.90 (1.76-2.05)	<0.001	1.82 (1.68-1.97)	<0.001
Diagnosis era	2004-2009	1 [Reference]		1 [Reference]	
	2010-2015	0.99 (0.94-1.04)	0.570	1.00 (0.95-1.06)	0.907
	2016-2023	0.85 (0.80-0.89)	<0.001	0.84 (0.80-0.89)	<0.001
Sex	Female	1 [Reference]		1 [Reference]	
	Male	1.25 (1.19-1.32)	<0.001	1.25 (1.18-1.32)	<0.001
Race and ethnicity	Non-Hispanic White	1 [Reference]		1 [Reference]	
	Non-Hispanic Black	1.07 (0.97-1.18)	0.166	1.01 (0.91-1.12)	0.844
	Non-Hispanic American Indian or Alaska Native	0.85 (0.63-1.15)	0.282	0.85 (0.62-1.17)	0.313
	Non-Hispanic Asian or Pacific Islander	1.17 (1.05-1.30)	0.004	1.17 (1.05-1.31)	0.004
	Hispanic, all races	1.03 (0.97-1.10)	0.371	0.99 (0.93-1.06)	0.827
	Non-Hispanic unknown race	0.37 (0.15-0.88)	0.025	0.33 (0.12-0.88)	0.027
Marital status	Married	1 [Reference]		1 [Reference]	
	Single or never married	1.18 (1.10-1.27)	<0.001	1.16 (1.07-1.25)	<0.001
	Divorced, separated, or widowed	1.13 (1.08-1.20)	<0.001	1.11 (1.05-1.17)	<0.001
	Unmarried or domestic partner	1.45 (1.00-2.09)	0.047	1.37 (0.92-2.03)	0.121
	Unknown	1.00 (0.89-1.13)	0.967	0.97 (0.85-1.10)	0.609
County-level median household income	≥$100,000	1 [Reference]		1 [Reference]	
	$75,000-$99,999	1.05 (0.99-1.10)	0.096	1.02 (0.97-1.08)	0.416
	<$75,000	1.05 (0.98-1.12)	0.178	1.03 (0.96-1.10)	0.483
	Unknown or missing	4.23 (0.46-38.92)	0.202	6.21 (0.63-61.47)	0.118
Rural-urban continuum	Metropolitan ≥1 million	1 [Reference]		1 [Reference]	
	Metropolitan <1 million	1.05 (0.99-1.10)	0.080	1.06 (1.01-1.12)	0.027
	Non-metropolitan	1.12 (1.03-1.21)	0.007	1.17 (1.08-1.27)	<0.001
	Unknown or missing	1.16 (0.42-3.24)	0.778	0.96 (0.30-3.11)	0.945
Histologic subtype	Epithelioid mesothelioma	1 [Reference]		1 [Reference]	
	Mesothelioma, NOS	1.22 (1.16-1.28)	<0.001	1.20 (1.14-1.26)	<0.001
	Fibrous mesothelioma	2.00 (1.86-2.15)	<0.001	2.03 (1.88-2.19)	<0.001
	Biphasic mesothelioma	1.58 (1.46-1.71)	<0.001	1.60 (1.47-1.75)	<0.001
Summary stage	Localized	1 [Reference]		1 [Reference]	
	Regional	1.26 (1.16-1.36)	<0.001	1.27 (1.16-1.38)	<0.001
	Distant	1.55 (1.44-1.66)	<0.001	1.58 (1.47-1.70)	<0.001
Cancer-directed surgery status	Surgery performed	1 [Reference]		1 [Reference]	
	Not recommended or contraindicated	1.60 (1.52-1.69)	<0.001	1.65 (1.56-1.74)	<0.001
	Recommended but not performed or unknown	1.24 (1.10-1.40)	<0.001	1.26 (1.11-1.43)	<0.001
	Unknown, DCO, or autopsy only	2.71 (2.07-3.55)	<0.001	2.07 (1.50-2.86)	<0.001
Radiation therapy	No or unknown radiation	1 [Reference]		1 [Reference]	
	Radiation given	1.01 (0.94-1.08)	0.842	1.02 (0.95-1.10)	0.511
Chemotherapy	No or unknown chemotherapy	1 [Reference]		1 [Reference]	
	Chemotherapy yes	0.70 (0.67-0.74)	<0.001	0.73 (0.69-0.76)	<0.001

This sensitivity analysis excluded patients with unknown or unstaged disease in the SEER Combined Summary Stage with Expanded Regional Codes variable. The multivariable Cox proportional hazards models included 10,117 patients and were adjusted for all variables shown in the table. Variables were selected a priori based on clinical relevance, epidemiologic importance, and availability in the SEER database rather than statistical significance in univariable analyses. OS was defined as death from any cause. CSS was defined as death attributable to mesothelioma, with deaths from other causes censored. Estimates for categories with fewer than 10 patients are unstable and are not interpreted. The multicystic or other mesothelioma category included only two patients and was not included in Cox regression models because of sparse data and unstable HR estimation. Zero-month survival was recoded as 0.5 months for time-to-event modeling.
aHR: Adjusted hazard ratio; CI: Confidence interval; CSS: Cancer-specific survival; DCO: Death certificate only; NOS: Not otherwise specified; OS: Overall survival; SEER: Surveillance, Epidemiology, and End Results.

SUPPLEMENTARY TABLE 3: Fine-Gray competing-risk regression for mesothelioma-specific mortality, SEER 2004-2023.

Variable	Category	Adjusted subdistribution HR (95% CI)	p-value
Primary site	Pleural	1 [Reference]	
	Peritoneal	0.87 (0.81-0.94)	<0.001
	Other or unknown	0.89 (0.81-0.99)	0.035
Age group, years	<60	1 [Reference]	
	60-69	1.18 (1.10-1.28)	<0.001
	70-79	1.32 (1.22-1.42)	<0.001
	≥80	1.53 (1.42-1.66)	<0.001
Diagnosis era	2004-2009	1 [Reference]	
	2010-2015	1.01 (0.96-1.07)	0.588
	2016-2023	0.84 (0.80-0.89)	<0.001
Sex	Female	1 [Reference]	
	Male	1.18 (1.12-1.24)	<0.001
Race and ethnicity	Non-Hispanic White	1 [Reference]	
	Non-Hispanic Black	0.90 (0.81-1.01)	0.062
	Non-Hispanic American Indian or Alaska Native	0.97 (0.70-1.34)	0.844
	Non-Hispanic Asian or Pacific Islander	1.11 (0.99-1.24)	0.072
	Hispanic, all races	0.94 (0.88-1.00)	0.050
	Non-Hispanic unknown race	0.33 (0.14-0.77)	0.011
Marital status	Married	1 [Reference]	
	Single or never married	1.05 (0.98-1.13)	0.191
	Divorced, separated, or widowed	1.04 (0.98-1.09)	0.207
	Unmarried or domestic partner	1.06 (0.72-1.54)	0.781
	Unknown	0.88 (0.79-0.99)	0.035
County-level median household income	≥$100,000	1 [Reference]	
	$75,000-$99,999	0.98 (0.93-1.04)	0.548
	<$75,000	1.00 (0.94-1.08)	0.895
	Unknown or missing	8.16 (0.96-69.55)	0.055
Rural-urban continuum	Metropolitan ≥1 million	1 [Reference]	
	Metropolitan <1 million	1.06 (1.00-1.11)	0.042
	Non-metropolitan	1.22 (1.12-1.32)	<0.001
	Unknown or missing	0.73 (0.24-2.21)	0.577
Histologic subtype	Epithelioid mesothelioma	1 [Reference]	
	Mesothelioma, NOS	1.12 (1.06-1.17)	<0.001
	Fibrous mesothelioma	1.62 (1.50-1.74)	<0.001
	Biphasic mesothelioma	1.40 (1.29-1.53)	<0.001
Summary stage	Localized	1 [Reference]	
	Regional	1.17 (1.07-1.28)	<0.001
	Distant	1.39 (1.29-1.50)	<0.001
	Unknown or unstaged	1.06 (0.95-1.18)	0.317
Cancer-directed surgery status	Surgery performed	1 [Reference]	
	Not recommended or contraindicated	1.49 (1.41-1.58)	<0.001
	Recommended but not performed or unknown	1.17 (1.03-1.32)	0.018
	Unknown, DCO, or autopsy only	1.14 (0.91-1.43)	0.258
Radiation therapy	No or unknown radiation	1 [Reference]	
	Radiation given	1.06 (0.99-1.14)	0.116
Chemotherapy	No or unknown chemotherapy	1 [Reference]	
	Chemotherapy yes	0.85 (0.82-0.89)	<0.001

Fine-Gray competing-risk regression was performed for mesothelioma-specific mortality, treating death from other causes as a competing event. The model was adjusted for all variables shown in the table. Variables were selected a priori based on clinical relevance, epidemiologic importance, and availability in the SEER database rather than statistical significance in univariable analyses. Mesothelioma-specific death was defined according to the SEER cause-specific death classification. Estimates for categories with fewer than 10 patients are unstable and are not interpreted. This applies to the unknown or missing income category (n=1) and the unknown or missing rural-urban category (n=5). The multicystic or other mesothelioma category included only two patients and was not included in the model because of sparse data and unstable subdistribution hazard ratio estimation. Zero-month survival was recoded as 0.5 months for time-to-event modeling.
CI: Confidence interval; DCO: Death certificate only; HR: Hazard ratio; NOS: Not otherwise specified; SEER: Surveillance, Epidemiology, and End Results; sHR: Subdistribution hazard ratio.

SUPPLEMENTARY TABLE 4: Metastatic site distribution among patients with distant-stage malignant mesothelioma according to primary site, SEER 2010-2023.

Characteristic	Category	Total	Pleural	Peritoneal	Other or unknown	p-value
Distant-stage cohort, 2010-2023	n	4,480	3,666	606	208	
Bone metastasis	Yes, n (%)	350 (7.8)	299 (8.2)	9 (1.5)	42 (20.2)	<0.001
Brain metastasis	Yes, n (%)	49 (1.1)	43 (1.2)	0 (0.0)	6 (2.9)	0.001
Liver metastasis	Yes, n (%)	276 (6.2)	154 (4.2)	95 (15.7)	27 (13.0)	<0.001
Lung metastasis	Yes, n (%)	512 (11.4)	416 (11.3)	43 (7.1)	53 (25.5)	<0.001
Bone, brain, liver, or lung site burden	No recorded metastatic site	3,512 (78.4)	2,924 (79.8)	469 (77.4)	119 (57.2)	<0.001
	Single recorded metastatic site	782 (17.5)	597 (16.3)	127 (21.0)	58 (27.9)	
	Multiple recorded metastatic sites	186 (4.2)	145 (4.0)	10 (1.7)	31 (14.9)	
Distant-stage cohort, 2016-2023	n with distant lymph node or other metastasis variables	2,136	1,613	409	114	
Distant lymph node metastasis	Yes, n (%)	249 (11.7)	177 (11.0)	53 (13.0)	19 (16.7)	0.124
Other metastasis	Yes, n (%)	847 (39.7)	560 (34.7)	244 (59.7)	43 (37.7)	<0.001

Values are presented as number (%) unless otherwise indicated. Percentages are column percentages within each primary-site group. The metastatic subgroup included patients with distant-stage malignant mesothelioma diagnosed from 2010 to 2023, because SEER site-specific metastasis variables for bone, brain, liver, and lung are available from 2010 onward. Distant lymph node and other metastasis variables are available from 2016 onward and were therefore summarized in the 2016-2023 subset. Site burden was calculated as the number of recorded metastatic sites among the bone, brain, liver, and lung variables. p-values were calculated using the χ^2 test or Fisher exact test, as appropriate. Percentages were calculated using the corresponding full distant-stage subgroup as the denominator, including patients with unknown or blank site-specific metastasis values. Unknown or blank site-specific entries did not add a recorded metastatic site to the burden count. Thus, no recorded metastatic site does not establish absence of metastasis and may reflect incomplete recording or involvement of other organs. All patients in this subgroup had distant-stage disease.
SEER: Surveillance, Epidemiology, and End Results.

SUPPLEMENTARY TABLE 5: Survival outcomes in the metastatic subgroup according to metastatic site, SEER 2010-2023.

Characteristic	Category	n	OS events, n (%)	Median OS, months	1-year OS	3-year OS	CSS events, n (%)	Median CSS, months	1-year CSS	3-year CSS	OS log-rank p-value	CSS log-rank p-value
Bone metastasis	No	3,928	3,443 (87.7)	9 (9-10)	40.9% (39.3-42.4)	14.9% (13.8-16.1)	3,170 (80.7)	10 (10-11)	43.8% (42.2-45.4)	17.2% (15.9-18.6)	<0.001	<0.001
	Yes	350	325 (92.9)	3 (3-4)	17.5% (13.6-21.7)	4.7% (2.6-7.6)	301 (86.0)	3 (3-5)	19.0% (14.8-23.5)	6.1% (3.5-9.6)		
Brain metastasis	No	4,224	3,715 (87.9)	9 (8-9)	39.3% (37.8-40.8)	14.2% (13.1-15.4)	3,420 (81.0)	10 (9-10)	42.2% (40.6-43.7)	16.5% (15.3-17.8)	<0.001	<0.001
	Yes	49	48 (98.0)	2 (1-3)	10.5% (3.9-21.1)	2.1% (0.2-9.7)	47 (95.9)	2 (1-3)	10.5% (3.9-21.1)	2.1% (0.2-9.7)		
Liver metastasis	No	4,004	3,530 (88.2)	9 (8-9)	39.8% (38.2-41.3)	14.2% (13.1-15.4)	3,254 (81.3)	10 (9-10)	42.6% (41.0-44.2)	16.4% (15.1-17.7)	<0.001	<0.001
	Yes	276	240 (87.0)	4 (3-5)	27.9% (22.6-33.4)	12.6% (8.7-17.2)	220 (79.7)	4 (3-6)	30.6% (25.0-36.4)	15.9% (11.3-21.1)		
Lung metastasis	No	3,757	3,285 (87.4)	9 (9-10)	41.4% (39.7-43.0)	15.1% (13.9-16.4)	3,033 (80.7)	10 (10-11)	44.0% (42.3-45.6)	17.4% (16.0-18.7)	<0.001	<0.001
	Yes	512	473 (92.4)	4 (3-5)	22.1% (18.6-25.9)	6.3% (4.3-8.8)	430 (84.0)	5 (4-6)	25.8% (21.8-29.9)	8.1% (5.6-11.1)		
Bone, brain, liver, or lung site burden	No recorded metastatic site	3,512	3,088 (87.9)	10 (9-10)	42.5% (40.9-44.2)	15.4% (14.2-16.7)	2,844 (81.0)	11 (10-11)	45.3% (43.6-47.0)	17.7% (16.3-19.1)	<0.001	<0.001
	Single recorded metastatic site	782	698 (89.3)	5 (4-6)	26.1% (23.0-29.3)	9.0% (7.0-11.3)	643 (82.2)	6 (5-7)	29.2% (25.8-32.6)	11.1% (8.7-13.8)		
	Multiple recorded metastatic sites	186	178 (95.7)	2 (2-3)	13.6% (9.1-19.1)	3.5% (1.4-7.1)	163 (87.6)	2 (2-3)	15.4% (10.3-21.3)	4.9% (2.1-9.6)		
Distant lymph node metastasis, 2016-2023 subset	No	1,831	1,441 (78.7)	9 (8-10)	41.5% (39.2-43.9)	17.2% (15.3-19.2)	1,331 (72.7)	10 (9-11)	44.4% (42.0-46.8)	19.8% (17.6-22.0)	0.333	0.389
	Yes	249	198 (79.5)	8 (6-11)	38.1% (31.8-44.4)	14.7% (10.1-20.1)	182 (73.1)	9 (6-11)	40.6% (34.1-47.0)	17.4% (12.2-23.5)		
Other metastasis, 2016-2023 subset	No	1,252	1,019 (81.4)	9 (8-10)	40.3% (37.5-43.1)	15.6% (13.4-18.0)	946 (75.6)	10 (9-11)	43.2% (40.3-46.1)	17.7% (15.3-20.2)	0.071	0.043
	Yes	847	638 (75.3)	9 (7-10)	42.0% (38.5-45.4)	18.4% (15.5-21.6)	583 (68.8)	10 (9-11)	44.6% (41.0-48.1)	21.9% (18.6-25.4)		

The metastatic subgroup included patients with distant-stage malignant mesothelioma diagnosed from 2010 to 2023. Bone, brain, liver, and lung metastasis variables were available from 2010 onward. Distant lymph node and other metastasis variables were available from 2016 onward and were analyzed in the 2016-2023 subset. OS was defined as death from any cause. CSS was defined as death attributable to mesothelioma, with deaths from other causes censored. Survival probabilities are Kaplan-Meier estimates at 12 and 36 months. Confidence intervals were calculated using Greenwood standard errors with log-log transformation. Survival estimates are presented with 95% CIs. p-values were calculated using the log-rank test. Patients with unknown or blank values for a given site-specific metastasis variable were excluded from the corresponding site-specific survival comparison. Unknown or blank site-specific entries did not add a recorded metastatic site to the burden count. Thus, no recorded metastatic site does not establish absence of metastasis and may reflect incomplete recording or involvement of other organs. All patients in this subgroup had distant-stage disease.
CI: Confidence interval; CSS: Cancer-specific survival; OS: Overall survival; SEER: Surveillance, Epidemiology, and End Results.