

Supplementary Materials 2: *Sleep-Stage Dynamics Predicts Current Sleep Disordered Breathing and Future Cardiovascular Risk*

Bechny Michal et al. (2025)

bechnymichal@gmail.com *Sensitivity Analysis and Comparison with Framingham
Risk Score*

1 Bern Sleep-Wake Registry (BSWR)

Descriptive statistics

Table 1. Characteristics of Berner Sleep-Wake Registry (BSWR) cohort stratified no-to-mild SDB ($AHI \leq 15$) versus moderate-to-high SDB ($AHI > 15$). Continuous variables are reported as mean (SD) and compared using Welch's two-sample t -test. Categorical variables, denoted by superscript*, are reported as counts (percentages) and compared using the chi-squared test. When expected cell counts were less than 5, Fisher's exact test was used instead.

Variable	Overall	$AHI \leq 15$	$AHI > 15$	p-value
N	3702	2100	1602	
Age	48.28 (19.37)	42.64 (19.53)	55.66 (16.46)	<0.001
Gender (Male)*	2325 (62.8)	1151 (54.8)	1174 (73.3)	<0.001
Smoking*				0.017
Current	179 (4.8)	99 (4.7)	80 (5.0)	
Ex	67 (1.8)	27 (1.3)	40 (2.5)	
Never	221 (6.0)	115 (5.5)	106 (6.6)	
NA	3235 (87.4)	1859 (88.5)	1376 (85.9)	
BMI	26.94 (6.46)	25.52 (6.23)	28.81 (6.29)	<0.001
AHI	19.02 (20.19)	6.31 (4.23)	35.69 (20.71)	<0.001
SDB ($AHI > 15$)*	1602 (43.3)	0 (0.0)	1602 (100.0)	<0.001
SDB category*				<0.001
Mixed	951 (25.7)	0 (0.0)	951 (59.4)	
NREM-dominant	484 (13.1)	0 (0.0)	484 (30.2)	
REM-dominant	137 (3.7)	0 (0.0)	137 (8.6)	
$AHI \leq 15$	2100 (56.7)	2100 (100.0)	0 (0.0)	
NA	30 (0.8)	0 (0.0)	30 (1.9)	
TST [mins]	339.13 (89.41)	354.88 (91.52)	318.49 (82.16)	<0.001
WASO [mins]	64.83 (54.42)	56.47 (49.68)	75.78 (58.30)	<0.001
SE [%]	80.03 (14.69)	82.42 (13.58)	76.89 (15.47)	<0.001
SL [mins]	18.64 (25.84)	18.20 (24.83)	19.22 (27.11)	0.235
REML [mins]	172.40 (186.46)	161.62 (169.84)	186.52 (205.42)	<0.001
DL [mins]	74.92 (185.01)	50.74 (137.39)	106.61 (229.36)	<0.001
W [%]	16.45 (13.74)	14.04 (12.54)	19.60 (14.58)	<0.001
N1 [%]	16.87 (10.92)	13.05 (7.77)	21.89 (12.34)	<0.001
N2 [%]	36.40 (12.46)	39.00 (11.46)	33.00 (12.89)	<0.001
N3 [%]	16.93 (10.68)	19.36 (10.70)	13.73 (9.78)	<0.001
REM [%]	13.35 (7.05)	14.55 (6.93)	11.79 (6.90)	<0.001

Occurrence of clinical conditions

Table 2 shows the number and percentage, N (%), of PSG recordings in the BSWR, stratified by conclusive sleep diagnoses and non-sleep comorbidities and by the presence of sleep-disordered breathing (SDB): no-to-mild ($AHI \leq 15$) versus moderate-to-severe ($AHI > 15$). Out of 3702 recordings from 3417 unique subjects, 2100 had $AHI \leq 15$ and 1602 had $AHI > 15$. A total of 88 recordings corresponded to healthy individuals without any sleep diagnosis or on-sleep comorbidity, or undergoing PSG as healthy controls in some of the Inselspital's conducted clinical studies, without any clinical condition identified. The classification of major sleep disorder categories in the table is consistent with ICSD-3 (International Classification of Sleep Disorders, Third Edition), which defines seven major groups, such as SDB, Insomnias, and Central Disorders of Hypersomnolence (Hypersomnias). Within the most prevalent classes, we also considered the most relevant/common diagnoses subcategories (e.g., OSA and CSA within SDB, NT1 and NT2 within Hypersomnias) versus the less frequent "Other" conditions (e.g., hypoventilation and hypoxia syndrome in SDB). Rare categories (e.g., circadian rhythm disorders) and those with non-specific clinical profiles (e.g., isolated symptoms and normal variants) were grouped into a single main class.

We further grouped the available comorbidities into broader condition categories. The *Brain* category comprises individuals with a history of major neurological events, including stroke, intracerebral hemorrhage, and traumatic brain injury (TBI), as well as cases with suspected TBI-related diagnoses. This grouping captures subjects with structural brain injuries that may influence sleep physiology or contribute to comorbid conditions. The *Neurodegenerative* category comprises individuals with a confirmed or probable diagnosis of a neurodegenerative disorder. This includes Parkinson's disease, atypical Parkinsonian syndromes, amyotrophic lateral sclerosis (ALS), dementia, and other specified neurodegenerative conditions. The *Headache* category includes individuals with a confirmed or probable diagnosis of migraine, tension-type headache, post-traumatic headache, cluster headache, trigeminal neuralgia, and other specified headache syndromes. The *Psychiatric* category includes individuals with a confirmed or probable psychiatric disorder. This encompasses depression, bipolar disorder, anxiety and panic disorders, conversion disorder, post-traumatic stress disorder (PTSD), attention-deficit/hyperactivity disorder (ADHD), and substance-related disorders (alcohol and drug abuse), as well as other specified psychiatric conditions. The *Diabetes* category includes individuals with a confirmed or probable diagnosis of diabetes mellitus. The *Cardial* category includes probable or confirmed hypertension, coronary heart disease, atrial fibrillation, and other cardiac comorbidities. The *Pulmonary* category includes individuals with a confirmed or probable diagnosis of chronic respiratory disease, including chronic obstructive pulmonary disease (COPD), asthma, and other specified pulmonary conditions.

Table 2. Number and percentage (N, %) of different health conditions in Berner Sleep-Wake Registry (BSWR), stratified by the presence of no-to-mild sleep-disordered breathing (SDB; AHI ≤ 15) versus moderate-to-severe SDB (AHI > 15). Equality of proportions between SDB groups was assessed using the chi-squared test or Fisher's exact test when expected cell counts were less than 5. Results are reported as p-values, with significant differences highlighted as follows: for $p < 0.05$, for $p < 0.01$, and for $p < 0.001$.

Diagnosis	N (%)	AHI ≤ 15	AHI > 15	p-value
Total	3702	2100	1602	
Healthy	88 (2.4)	88 (4.2)	0 (0.0)	<0.001
Sleep Disorders:				
Sleep-disordered breathing (SDB)	2695 (72.8)	1120 (53.3)	1575 (98.3)	<0.001
Obstructive Sleep Apnea (OSA)	687 (18.6)	323 (15.4)	364 (22.7)	<0.001
Central Sleep Apnea (CSA)	111 (3.0)	33 (1.6)	78 (4.9)	<0.001
Other	1957 (52.9)	786 (37.4)	1171 (73.1)	<0.001
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Insomnias	487 (13.2)	337 (16.0)	150 (9.4)	<0.001
Chronic	105 (2.8)	81 (3.9)	24 (1.5)	<0.001
Short-term	2 (0.1)	2 (0.1)	0 (0.0)	0.602
Other	385 (10.4)	257 (12.2)	128 (8.0)	<0.001
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Hypersomnias	715 (19.3)	584 (27.8)	131 (8.2)	<0.001
Narcolepsy Type 1 (NT1)	58 (1.6)	36 (1.7)	22 (1.4)	0.488
Narcolepsy Type 2 (NT2)	8 (0.2)	7 (0.3)	1 (0.1)	0.161
Idiopathic Hypersomnia (IH)	24 (0.6)	24 (1.1)	0 (0.0)	<0.001
Excessive Daytime Sleepiness (EDS)	388 (10.5)	332 (15.8)	56 (3.5)	<0.001
Other	310 (8.4)	251 (12.0)	59 (3.7)	<0.001
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Movement-related	265 (7.2)	166 (7.9)	99 (6.2)	0.051
Restless Leg Syndrome (RLS)	182 (4.9)	101 (4.8)	81 (5.1)	0.789
Periodic Limb Movement Disorder (PLMD)	34 (0.9)	27 (1.3)	7 (0.4)	0.012
Other	50 (1.4)	38 (1.8)	12 (0.7)	0.009
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Parasomnias	193 (5.2)	124 (5.9)	69 (4.3)	0.036
REM	55 (1.5)	49 (2.3)	6 (0.4)	<0.001
NREM	128 (3.5)	68 (3.2)	60 (3.7)	0.456
Other	17 (0.5)	10 (0.5)	7 (0.4)	1.000
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Circadian-rhythm-related	47 (1.3)	32 (1.5)	15 (0.9)	0.152
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Isolated symptoms and norm variants	1771 (47.8)	994 (47.3)	777 (48.5)	0.502
Non-sleep Comorbidities:				
Brain	64 (1.7)	34 (1.6)	30 (1.9)	0.646
Neurodegenerative	81 (2.2)	47 (2.2)	34 (2.1)	0.900
Epilepsy	49 (1.3)	35 (1.7)	14 (0.9)	0.052
Headache	73 (2.0)	51 (2.4)	22 (1.4)	0.030
Psychiatric	204 (5.5)	145 (6.9)	59 (3.7)	<0.001
Diabetes	41 (1.1)	22 (1.0)	19 (1.2)	0.810
Cardial	134 (3.6)	54 (2.6)	80 (5.0)	<0.001
Pulmonary	50 (1.4)	35 (1.7)	15 (0.9)	0.078

Characteristics of clinical conditions, predicted risk, and their comparison to healthy.

Table 3. Summary statistics for Gender (N (%) of males) and mean (standard deviation) for Age, Body Mass Index (BMI), Apnea-Hypopnea Index (AHI), and predicted cardiovascular risk (mortality) in Bern Sleep-Wake Registry (BSWR). The adjusted risk, reported as an estimate (95% CI), quantifies the systematic percentual difference in predicted risk for specific diagnoses (conclusive sleep disorders and non-sleep comorbidities) using logistic regression adjusting for gender, age, BMI, and AHI. Significant differences in comparison to healthy controls are highlighted as: * if p-val<0.05, ** if p-val<0.01, and *** if p-val<0.001.

Diagnosis	Gender-Male	Age	BMI	AHI	Predicted Risk	Adjusted Risk [%]
Healthy	37 (42.0%)	32.86 (18.81)	22.63 (5.31)	2.68 (1.85)	17.14 (4.10)	NA
Sleep Disorders:						
Sleep-disordered breathing (SDB)	1868 (69.3%)*	51.1 (19.0)*	27.6 (6.5)*	24.6 (20.8)*	27.9 (9.9)*	17.8 (9.5, 26.8)*
Obstructive Sleep Apnea (OSA)	476 (69.3%)*	51.9 (17.1)*	27.8 (6.5)*	22.7 (19.8)*	27.1 (8.4)*	18.5 (9.4, 28.3)*
Central Sleep Apnea (CSA)	74 (66.7%)*	45.6 (24.7)*	25.0 (6.0)*	29.6 (22.9)*	28.0 (9.5)*	39.2 (23.5, 56.9)*
Other	1359 (69.4%)*	51.1 (19.3)*	27.7 (6.6)*	24.9 (20.8)*	28.2 (10.3)*	17.4 (8.8, 26.7)*
Insomnias	262 (53.8%)*	53.6 (15.4)*	26.6 (5.3)*	13.8 (15.7)*	26.7 (9.5)*	12.4 (2.9, 22.7)*
Chronic	61 (58.1%)*	50.4 (15.8)*	26.2 (4.4)*	9.5 (9.4)*	24.4 (9.3)*	20.4 (5.6, 37.3)*
Short-term	2 (100.0%)*	61.0 (5.7)*	25.5 (3.5)	5.4 (1.1)	27.2 (3.7)	41.4 (-10.5, 123.3)
Other	202 (52.5%)*	54.5 (15.3)*	26.6 (5.5)*	15.0 (16.8)*	27.4 (9.8)*	14.7 (4.5, 25.9)*
Hypersomnias	346 (48.4%)*	39.5 (15.5)*	26.6 (6.4)*	9.3 (13.1)*	21.1 (6.9)*	11.0 (3.7, 18.9)*
Narcolepsy Type 1 (NT1)	27 (46.6%)*	37.3 (16.7)	27.6 (5.0)*	14.4 (16.1)*	23.1 (7.5)*	22.9 (8.8, 38.9)*
Narcolepsy Type 2 (NT2)	6 (75.0%)*	29.8 (20.6)	23.9 (5.0)	7.4 (8.8)	23.3 (8.9)	12.7 (-11.8, 44.0)
Idiopathic Hypersomnia (IH)	2 (8.3%)*	26.3 (7.0)*	24.3 (3.8)	2.7 (2.0)	17.2 (3.2)	13.7 (-1.7, 31.4)
Excessive Daytime Sleepiness (EDS)	162 (52.3%)*	39.3 (15.0)*	26.8 (6.8)*	9.5 (13.0)*	20.7 (6.3)*	9.7 (1.4, 18.8)*
Other	179 (46.1%)*	40.1 (15.4)*	26.6 (6.7)*	8.2 (12.0)*	20.9 (7.1)*	10.8 (2.9, 19.2)*
Movement-related	164 (61.9%)*	53.2 (17.5)*	27.3 (6.4)*	16.5 (18.5)*	28.2 (11.1)*	20.3 (8.6, 33.2)*
Restless Leg Syndrome	103 (56.6%)*	58.2 (15.1)*	27.7 (6.5)*	19.3 (20.3)*	30.0 (11.8)*	23.4 (8.5, 40.4)*
Periodic Limb Movement Disorder	23 (67.6%)*	51.1 (17.7)*	26.2 (4.7)*	9.7 (9.8)*	27.2 (9.2)*	32.6 (13.2, 55.3)*
Other	38 (76.0%)*	37.2 (15.6)	26.8 (6.7)*	11.3 (13.3)*	22.6 (7.4)*	12.9 (-0.5, 28.2)
Parasomnias	128 (66.3%)*	53.9 (19.1)*	25.8 (5.1)*	14.3 (14.5)*	27.3 (8.5)*	24.5 (13.3, 36.9)*
REM	36 (65.5%)*	34.8 (16.1)	24.3 (4.0)*	6.9 (8.1)*	21.1 (5.3)*	16.1 (3.6, 30.2)*
NREM	83 (64.8%)*	62.9 (12.4)*	26.2 (5.2)*	17.8 (15.7)*	30.2 (7.8)*	44.4 (27.0, 64.1)*
Other	14 (82.4%)*	50.6 (20.8)*	26.3 (5.4)*	11.4 (8.3)*	28.2 (11.7)*	17.3 (-9.2, 51.5)
Circadian-rhythm-related	33 (70.2%)*	44.5 (17.1)*	27.6 (5.6)*	14.5 (15.2)*	26.8 (9.5)*	27.5 (10.3, 47.3)*
Isolated symptoms and norm variants	1162 (65.6%)*	52.0 (17.7)*	27.4 (6.0)*	18.6 (18.9)*	27.4 (10.4)*	10.9 (2.9, 19.5)*
Non-sleep Comorbidities:						
Brain	47 (73.4%)*	53.6 (14.2)*	27.4 (4.6)*	21.5 (21.8)*	25.6 (9.1)*	10.2 (-5.5, 28.5)
Neurodegenerative	45 (55.6%)*	63.9 (9.7)*	26.2 (4.8)*	18.0 (17.8)*	29.9 (9.3)*	45.8 (21.4, 75.1)*
Epilepsy	35 (71.4%)*	44.7 (14.3)*	26.5 (5.7)*	11.4 (12.3)*	23.0 (6.3)*	14.5 (0.9, 30.0)*
Headache	36 (49.3%)*	42.2 (15.5)*	27.7 (7.1)*	16.4 (21.8)*	22.7 (8.4)*	13.0 (0.6, 27.0)*
Psychiatric	105 (51.5%)*	45.8 (16.2)*	28.1 (6.2)*	12.9 (15.4)*	23.6 (7.5)*	21.2 (10.1, 33.3)*
Diabetes	29 (70.7%)*	55.9 (14.3)*	30.0 (8.7)*	25.7 (25.5)*	28.6 (9.3)*	39.4 (13.9, 70.7)*
Cardial	108 (80.6%)*	57.2 (12.4)*	30.7 (6.3)*	27.8 (24.2)*	29.5 (9.0)*	25.1 (8.7, 44.0)*
Pulmonary	33 (66.0%)*	46.5 (16.7)*	29.3 (8.0)*	15.7 (20.1)*	23.8 (9.5)*	19.0 (2.3, 38.3)*

2 Sleep Heart Health Study (SHHS)

Table 4. Subsets of SHHS database stratified based on prior cardiovascular event status (E) and medication use (M). Summary statistics include the number of subjects (N), the number who developed a cardiovascular event during follow-up (N-events), the mean (SD) of age in years, and the number (%) of males.

Dataset	N	N-events	Age	Gender
SHHS1 (E = 0, M = 0)	2579	326	59.43 (11.16)	1182 (45.8)
SHHS1 (E = 0, M = 1)	2528	567	64.97 (10.15)	1157 (45.8)
SHHS1 (E = 1, M = 0)	112	60	68.61 (11.86)	67 (59.8)
SHHS1 (E = 1, M = 1)	572	320	70.67 (9.68)	354 (61.9)
SHHS2 (E = 0, M = 0)	811	62	63.16 (10.49)	358 (44.1)
SHHS2 (E = 0, M = 1)	1484	201	68.73 (9.60)	647 (43.6)
SHHS2 (E = 1, M = 0)	37	15	70.97 (10.55)	22 (59.5)
SHHS2 (E = 1, M = 1)	319	178	73.52 (9.06)	199 (62.4)

SHHS1

Table 5. Descriptive characteristics of SHHS1 (E = 0, M = 1) cohort stratified by cardiovascular event status. Continuous variables are reported as mean (SD) and compared using Welch's two-sample *t*-test. Categorical variables, denoted by superscript*, are reported as counts (percentages) and compared using the chi-squared test. When expected cell counts were less than 5, Fisher's exact test was used instead.

Variable	Overall	Event-free	Event developed	p-value
N	2528	1961	567	
Age	64.97 (10.15)	63.32 (9.97)	70.68 (8.57)	<0.001
Gender (Male)*	1157 (45.8)	859 (43.8)	298 (52.6)	<0.001
Smoking*				<0.001
Current	221 (8.7)	166 (8.5)	55 (9.7)	
Ex	1121 (44.3)	831 (42.4)	290 (51.1)	
Never	1174 (46.4)	954 (48.6)	220 (38.8)	
NA	12 (0.5)	10 (0.5)	2 (0.4)	
BMI	28.64 (5.22)	28.60 (5.24)	28.77 (5.14)	0.507
AHI	18.89 (16.90)	18.27 (16.85)	21.05 (16.90)	0.001
SDB (AHI>15)*	1179 (46.6)	863 (44.0)	316 (55.7)	<0.001
SDB category*				<0.001
Mixed	574 (22.7)	425 (21.7)	149 (26.3)	
NREM-dominant	108 (4.3)	78 (4.0)	30 (5.3)	
REM-dominant	379 (15.0)	271 (13.8)	108 (19.0)	
AHI≤15	1349 (53.4)	1098 (56.0)	251 (44.3)	
NA	118 (4.7)	89 (4.5)	29 (5.1)	
TST [mins]	358.28 (63.24)	359.36 (63.05)	354.54 (63.82)	0.110
WASO [mins]	95.97 (55.62)	93.97 (54.94)	102.90 (57.42)	0.001
SE [%]	70.89 (12.11)	71.06 (12.11)	70.28 (12.11)	0.175
SL [mins]	52.19 (42.78)	53.47 (43.32)	47.75 (40.56)	0.005
REML [mins]	122.90 (169.81)	122.04 (167.02)	125.89 (179.24)	0.634
DL [mins]	83.39 (228.77)	81.04 (225.39)	91.53 (240.14)	0.336
W [%]	20.98 (11.79)	20.58 (11.67)	22.38 (12.09)	0.001
N1 [%]	4.16 (2.85)	4.13 (2.81)	4.25 (3.00)	0.383
N2 [%]	45.87 (12.38)	45.80 (12.44)	46.09 (12.19)	0.622
N3 [%]	13.95 (9.99)	14.22 (9.98)	13.00 (9.98)	0.010
REM [%]	15.04 (6.27)	15.26 (6.23)	14.28 (6.35)	0.001

Table 6. Descriptive characteristics of SHHS1 (E = 1, M = 0) cohort stratified by cardiovascular event status. Continuous variables are reported as mean (SD) and compared using Welch's two-sample *t*-test. Categorical variables, denoted by superscript *, are reported as counts (percentages) and compared using the chi-squared test. When expected cell counts were less than 5, Fisher's exact test was used instead.

Variable	Overall	Event-free	Event developed	p-value
N	112	52	60	
Age	68.61 (11.86)	64.25 (13.48)	72.38 (8.74)	<0.001
Gender (Male)*	67 (59.8)	26 (50.0)	41 (68.3)	0.075
Smoking*				0.401
Current	10 (8.9)	5 (9.6)	5 (8.3)	
Ex	55 (49.1)	22 (42.3)	33 (55.0)	
Never	47 (42.0)	25 (48.1)	22 (36.7)	
BMI	27.80 (4.96)	27.73 (6.13)	27.86 (3.72)	0.896
AHI	20.99 (15.27)	18.97 (12.37)	22.74 (17.31)	0.194
SDB (AHI>15)*	67 (59.8)	30 (57.7)	37 (61.7)	0.814
SDB category*				0.524
Mixed	26 (23.2)	9 (17.3)	17 (28.3)	
NREM-dominant	9 (8.0)	4 (7.7)	5 (8.3)	
REM-dominant	24 (21.4)	14 (26.9)	10 (16.7)	
AHI≤15	45 (40.2)	22 (42.3)	23 (38.3)	
NA	8 (7.1)	3 (5.8)	5 (8.3)	
TST [mins]	349.95 (73.14)	370.17 (57.88)	332.42 (80.58)	0.006
WASO [mins]	101.90 (64.26)	81.72 (46.60)	119.39 (72.25)	0.002
SE [%]	69.66 (13.70)	73.91 (10.40)	65.98 (15.16)	0.002
SL [mins]	50.80 (41.73)	49.58 (35.41)	51.86 (46.79)	0.774
REML [mins]	124.81 (196.57)	126.16 (185.06)	123.63 (207.58)	0.946
DL [mins]	81.23 (222.33)	44.66 (139.63)	112.92 (271.93)	0.105
W [%]	22.47 (13.87)	18.03 (10.05)	26.32 (15.55)	0.001
N1 [%]	4.72 (3.27)	4.22 (2.96)	5.15 (3.49)	0.134
N2 [%]	45.44 (13.11)	47.31 (12.40)	43.82 (13.58)	0.160
N3 [%]	12.33 (9.73)	14.30 (11.16)	10.63 (8.01)	0.046
REM [%]	15.04 (6.39)	16.14 (5.68)	14.08 (6.84)	0.089

Table 7. Descriptive characteristics of SHHS1 (E = 1, M = 1) cohort stratified by cardiovascular event status. Continuous variables are reported as mean (SD) and compared using Welch's two-sample *t*-test. Categorical variables, denoted by superscript *, are reported as counts (percentages) and compared using the chi-squared test. When expected cell counts were less than 5, Fisher's exact test was used instead.

Variable	Overall	Event-free	Event developed	p-value
N	572	252	320	
Age	70.67 (9.68)	68.50 (10.28)	72.38 (8.83)	<0.001
Gender (Male)*	354 (61.9)	153 (60.7)	201 (62.8)	0.670
Smoking*				0.557
Current	46 (8.0)	21 (8.3)	25 (7.8)	
Ex	305 (53.3)	128 (50.8)	177 (55.3)	
Never	221 (38.6)	103 (40.9)	118 (36.9)	
BMI	28.08 (5.14)	27.81 (5.01)	28.29 (5.23)	0.271
AHI	22.06 (17.36)	20.23 (16.35)	23.50 (18.02)	0.025
SDB (AHI>15)*	323 (56.5)	131 (52.0)	192 (60.0)	0.067
SDB category*				0.296
Mixed	164 (28.7)	62 (24.6)	102 (31.9)	
NREM-dominant	34 (5.9)	14 (5.6)	20 (6.2)	
REM-dominant	82 (14.3)	37 (14.7)	45 (14.1)	
AHI≤15	249 (43.5)	121 (48.0)	128 (40.0)	
NA	43 (7.5)	18 (7.1)	25 (7.8)	
TST [mins]	347.37 (69.96)	354.70 (66.21)	341.59 (72.37)	0.026
WASO [mins]	101.47 (58.91)	96.46 (56.00)	105.42 (60.91)	0.071
SE [%]	68.79 (13.51)	70.26 (13.25)	67.63 (13.61)	0.021
SL [mins]	57.04 (49.31)	55.19 (47.87)	58.49 (50.44)	0.427
REML [mins]	130.81 (202.14)	114.44 (170.03)	143.70 (223.64)	0.086
DL [mins]	117.64 (274.90)	90.64 (232.66)	138.89 (302.73)	0.037
W [%]	22.58 (12.94)	21.30 (12.07)	23.59 (13.51)	0.035
N1 [%]	4.38 (3.22)	4.38 (2.90)	4.38 (3.46)	0.995
N2 [%]	46.09 (13.68)	46.30 (12.71)	45.92 (14.42)	0.745
N3 [%]	12.58 (10.50)	12.94 (9.68)	12.30 (11.10)	0.463
REM [%]	14.37 (6.43)	15.08 (6.31)	13.81 (6.47)	0.019

SHHS2

Table 8. Descriptive characteristics of SHHS2 (E = 0, M = 0) cohort stratified by cardiovascular event status. Continuous variables are reported as mean (SD) and compared using Welch's two-sample *t*-test. Categorical variables, denoted by superscript*, are reported as counts (percentages) and compared using the chi-squared test. When expected cell counts were less than 5, Fisher's exact test was used instead.

Variable	Overall	Event-free	Event developed	p-value
N	811	749	62	
Age	63.16 (10.49)	62.52 (10.16)	70.89 (11.39)	<0.001
Gender (Male)*	358 (44.1)	321 (42.9)	37 (59.7)	0.015
Smoking*				0.010
Current	62 (7.6)	51 (6.8)	11 (17.7)	
Ex	296 (36.5)	272 (36.3)	24 (38.7)	
Never	445 (54.9)	418 (55.8)	27 (43.5)	
NA	8 (1.0)	8 (1.1)	0 (0.0)	
BMI	27.72 (4.69)	27.70 (4.69)	27.90 (4.73)	0.749
AHI	15.84 (15.38)	15.46 (15.16)	20.35 (17.33)	0.016
SDB (AHI>15)*	300 (37.0)	268 (35.8)	32 (51.6)	0.019
SDB category*				0.003
Mixed	158 (19.5)	143 (19.1)	15 (24.2)	
NREM-dominant	20 (2.5)	18 (2.4)	2 (3.2)	
REM-dominant	106 (13.1)	96 (12.8)	10 (16.1)	
AHI≤15	511 (63.0)	481 (64.2)	30 (48.4)	
NA	16 (2.0)	11 (1.5)	5 (8.1)	
TST [mins]	384.11 (60.69)	385.78 (59.02)	363.86 (75.76)	0.006
WASO [mins]	155.78 (65.97)	154.41 (65.70)	172.35 (67.59)	0.040
SE [%]	64.53 (10.36)	64.74 (10.28)	62.03 (11.10)	0.047
SL [mins]	59.44 (39.19)	60.15 (39.28)	50.88 (37.36)	0.073
REML [mins]	99.65 (107.53)	97.15 (100.56)	129.87 (168.91)	0.021
DL [mins]	48.33 (132.58)	47.30 (132.59)	60.79 (132.83)	0.442
W [%]	28.45 (10.67)	28.16 (10.53)	32.03 (11.75)	0.006
N1 [%]	3.79 (3.76)	3.72 (3.80)	4.58 (3.09)	0.084
N2 [%]	40.38 (9.28)	40.35 (9.30)	40.79 (9.05)	0.715
N3 [%]	11.95 (7.86)	12.18 (7.88)	9.19 (7.19)	0.004
REM [%]	15.43 (5.40)	15.60 (5.39)	13.41 (5.18)	0.002

Table 9. Descriptive characteristics of SHHS2 (E = 0, M = 1) cohort stratified by cardiovascular event status. Continuous variables are reported as mean (SD) and compared using Welch's two-sample *t*-test. Categorical variables, denoted by superscript*, are reported as counts (percentages) and compared using the chi-squared test. When expected cell counts were less than 5, Fisher's exact test was used instead.

Variable	Overall	Event-free	Event developed	p-value
N	1484	1283	201	
Age	68.73 (9.60)	67.95 (9.51)	73.72 (8.68)	<0.001
Gender (Male)*	647 (43.6)	537 (41.9)	110 (54.7)	0.001
Smoking*				0.082
Current	101 (6.8)	80 (6.2)	21 (10.4)	
Ex	644 (43.4)	552 (43.0)	92 (45.8)	
Never	719 (48.5)	634 (49.4)	85 (42.3)	
NA	20 (1.3)	17 (1.3)	3 (1.5)	
BMI	28.72 (5.30)	28.79 (5.32)	28.26 (5.19)	0.190
AHI	18.60 (16.29)	18.18 (16.17)	21.31 (16.85)	0.011
SDB (AHI>15)*	680 (45.8)	569 (44.3)	111 (55.2)	0.005
SDB category*				0.036
Mixed	376 (25.3)	310 (24.2)	66 (32.8)	
NREM-dominant	52 (3.5)	43 (3.4)	9 (4.5)	
REM-dominant	226 (15.2)	195 (15.2)	31 (15.4)	
AHI≤15	804 (54.2)	714 (55.7)	90 (44.8)	
NA	26 (1.8)	21 (1.6)	5 (2.5)	
TST [mins]	373.67 (71.17)	376.93 (70.01)	352.85 (75.07)	<0.001
WASO [mins]	166.48 (74.83)	163.83 (73.64)	183.40 (80.18)	0.001
SE [%]	62.26 (11.95)	62.72 (11.78)	59.34 (12.59)	<0.001
SL [mins]	64.18 (46.50)	64.55 (46.24)	61.85 (48.15)	0.445
REML [mins]	118.48 (131.83)	114.62 (119.67)	143.11 (190.70)	0.004
DL [mins]	67.58 (182.98)	62.35 (173.68)	100.95 (231.55)	0.005
W [%]	30.44 (12.33)	29.91 (12.04)	33.81 (13.60)	<0.001
N1 [%]	3.88 (3.05)	3.79 (2.41)	4.43 (5.61)	0.006
N2 [%]	40.32 (10.44)	40.51 (10.36)	39.10 (10.89)	0.077
N3 [%]	11.03 (8.09)	11.20 (8.09)	9.90 (8.02)	0.033
REM [%]	14.34 (5.69)	14.58 (5.60)	12.75 (6.04)	<0.001

Table 10. Descriptive characteristics of SHHS2 (E = 1, M = 0) cohort stratified by cardiovascular event status. Continuous variables are reported as mean (SD) and compared using Welch's two-sample *t*-test. Categorical variables, denoted by superscript *, are reported as counts (percentages) and compared using the chi-squared test. When expected cell counts were less than 5, Fisher's exact test was used instead.

Variable	Overall	Event-free	Event developed	p-value
N	37	22	15	
Age	70.97 (10.55)	69.45 (12.55)	73.20 (6.43)	0.296
Gender (Male)*	22 (59.5)	11 (50.0)	11 (73.3)	0.281
Smoking*				0.242
Current	2 (5.4)	2 (9.1)	0 (0.0)	
Ex	17 (45.9)	8 (36.4)	9 (60.0)	
Never	18 (48.6)	12 (54.5)	6 (40.0)	
BMI	27.74 (5.06)	27.34 (5.73)	28.34 (3.98)	0.562
AHI	24.87 (16.70)	24.80 (19.32)	24.96 (12.56)	0.979
SDB (AHI>15)*	27 (73.0)	15 (68.2)	12 (80.0)	0.676
SDB category*				0.689
Mixed	15 (40.5)	7 (31.8)	8 (53.3)	
NREM-dominant	3 (8.1)	2 (9.1)	1 (6.7)	
REM-dominant	8 (21.6)	5 (22.7)	3 (20.0)	
AHI≤15	10 (27.0)	7 (31.8)	3 (20.0)	
NA	1 (2.7)	1 (4.5)	0 (0.0)	
TST [mins]	362.89 (65.95)	358.98 (75.93)	368.63 (49.76)	0.668
WASO [mins]	182.27 (74.72)	188.80 (89.27)	172.70 (47.33)	0.528
SE [%]	59.95 (10.58)	59.23 (12.05)	61.00 (8.24)	0.623
SL [mins]	65.80 (41.20)	65.36 (42.79)	66.43 (40.20)	0.939
REML [mins]	78.95 (50.29)	75.27 (50.41)	84.33 (51.38)	0.598
DL [mins]	45.00 (62.72)	37.82 (37.15)	55.53 (88.58)	0.407
W [%]	32.88 (11.30)	33.72 (13.45)	31.66 (7.39)	0.594
N1 [%]	3.76 (2.34)	3.87 (2.67)	3.60 (1.84)	0.739
N2 [%]	39.74 (9.57)	39.09 (10.67)	40.70 (7.96)	0.623
N3 [%]	10.38 (7.23)	9.20 (6.12)	12.12 (8.52)	0.232
REM [%]	13.23 (5.87)	14.13 (6.92)	11.92 (3.69)	0.266

Table 11. Descriptive characteristics of SHHS2 (E = 1, M = 1) cohort stratified by cardiovascular event status. Continuous variables are reported as mean (SD) and compared using Welch's two-sample *t*-test. Categorical variables, denoted by superscript*, are reported as counts (percentages) and compared using the chi-squared test. When expected cell counts were less than 5, Fisher's exact test was used instead.

Variable	Overall	Event-free	Event developed	p-value
N	319	141	178	
Age	73.52 (9.06)	71.02 (9.87)	75.50 (7.84)	<0.001
Gender (Male)*	199 (62.4)	92 (65.2)	107 (60.1)	0.410
Smoking*				0.471
Current	24 (7.5)	13 (9.2)	11 (6.2)	
Ex	161 (50.5)	73 (51.8)	88 (49.4)	
Never	129 (40.4)	54 (38.3)	75 (42.1)	
NA	5 (1.6)	1 (0.7)	4 (2.2)	
BMI	28.03 (4.54)	28.00 (4.38)	28.05 (4.67)	0.922
AHI	23.56 (17.73)	23.25 (17.40)	23.80 (18.03)	0.784
SDB (AHI>15)*	194 (60.8)	90 (63.8)	104 (58.4)	0.386
SDB category*				0.822
Mixed	122 (38.2)	55 (39.0)	67 (37.6)	
NREM-dominant	14 (4.4)	6 (4.3)	8 (4.5)	
REM-dominant	45 (14.1)	23 (16.3)	22 (12.4)	
AHI≤15	125 (39.2)	51 (36.2)	74 (41.6)	
NA	13 (4.1)	6 (4.3)	7 (3.9)	
TST [mins]	353.08 (76.90)	354.40 (77.68)	352.03 (76.48)	0.785
WASO [mins]	182.43 (79.74)	187.70 (86.63)	178.26 (73.81)	0.295
SE [%]	59.34 (12.32)	59.10 (13.26)	59.54 (11.56)	0.752
SL [mins]	62.49 (42.57)	62.05 (42.98)	62.84 (42.35)	0.869
REML [mins]	124.07 (164.14)	113.00 (144.40)	132.83 (178.15)	0.285
DL [mins]	105.08 (248.30)	102.35 (251.51)	107.23 (246.42)	0.862
W [%]	33.69 (13.32)	34.11 (14.35)	33.36 (12.47)	0.618
N1 [%]	4.41 (3.13)	4.17 (2.74)	4.61 (3.40)	0.215
N2 [%]	40.18 (11.10)	39.96 (10.95)	40.36 (11.25)	0.750
N3 [%]	9.09 (7.72)	8.90 (7.91)	9.24 (7.58)	0.696
REM [%]	12.62 (5.59)	12.86 (5.70)	12.43 (5.51)	0.497

3 Performance of Random Survival Forest model

Table 12. Performance of the Random Survival Forest (RSF) model omitting AHI predictor, evaluated across various datasets of subjects with no previous cardiovascular events ($E = 0$). The ^{CV} superscript denotes performance obtained via 5-fold cross-validation (CV) on the in-domain event- and medication-free ($E = M = 0$) baseline cohort SHHS1($E = 0, M = 0$). All other columns evaluate the performance of the final RSF model fitted to the entire baseline cohort, applied to potentially out-of-domain subjects ([†]) from either the baseline (SHHS1) or follow-up (SHHS2) studies, including subgroups taking medication ($M = 1$). For each scenario, the number of subjects with events and without events (event-free) is reported. Model performance is assessed using Harrell's Concordance Index (C-index), Integrated Brier Score (IBS), and the time-dependent Area Under the Receiver Operating Characteristic curve (tdAUROC) at 1, 5, and 10 years. Discriminatory ability is evaluated via two-sided t-tests comparing predicted mortality between event and non-event subjects, including 95% confidence intervals (CI) for the difference (Diff.). Additionally, log-rank tests with Chi-squared (χ^2) statistics compare event rates between high- and low-risk groups stratified by median predicted mortality. For the in-domain CV, mean (SD) of all metrics is reported.

Metric	SHHS1 ^{CV} ($E = 0, M = 0$)	SHHS1 [†] ($E = 0, M = 1$)	SHHS2 ($E = 0, M = 0$)	SHHS2 [†] ($E = 0, M = 0$)	SHHS2 ($E = 0, M = 1$)	SHHS2 [†] ($E = 0, M = 1$)
Events (N)	65.2 (2.4)	567	43	19	64	137
Event-free (N)	450.6 (2.7)	1961	591	158	489	794
C-index	73.3 (2.5)	69.7	74.1	78.3	70.1	66.6
IBS	6.7 (0.4)	11.9	4.1	6.2	7.1	8.8
1-year tdAUROC	77.1 (12.2)	69.8	85.2	77.1	72	64.1
5-year tdAUROC	74.9 (6.2)	72.7	73.6	83.4	71.4	69.2
10-year tdAUROC	75.3 (2.3)	74.2	-	100	-	69
Mortality ($E = 1$)	21.1 (1.8)	23.5	24.9	34.5	29.2	31.7
Mortality ($E = 0$)	11.3 (0.5)	14.5	14.1	16	17.9	21.6
Mortality Diff.	9.8 (1.8)	8.9	10.7	18.5	11.3	10.1
Mortality Diff. CI-low	5.8 (1.3)	7.6	4.7	9.1	6.4	6.6
Mortality Diff. CI-high	13.7 (2.4)	10.3	16.8	28	16.2	13.6
p-value (t-test)	0.000013 (0.000014)	$< 10^{-6}$	0.000856	0.000587	0.000019	$< 10^{-6}$
Events (N), high-risk	50.8 (1.9)	405	36	16	48	95
Events (N), low-risk	14.4 (1.9)	162	7	3	16	42
χ^2	26 (4.7)	162.5	22.1	10.4	20	28.4
p-value (log-rank test)	0.000005 (0.00001)	$< 10^{-6}$	0.000003	0.001237	0.000008	$< 10^{-6}$

Table 13. Performance of the Random Survival Forest (RSF) model including AHI predictor, evaluated across various datasets of subjects with previous cardiovascular events ($E = 1$). The columns evaluate the performance of the final RSF model fitted to the entire event- and medication-free ($E = M = 0$) baseline cohort SHHS1 ($E = 0, M = 0$), applied to potentially out-of-domain subjects (†) from either the baseline (SHHS1) or follow-up (SHHS2) studies, including subgroups taking medication ($M = 1$). For each scenario, the number of subjects with events and without events (event-free) is reported. Model performance is assessed using Harrell's Concordance Index (C-index), Integrated Brier Score (IBS), and the time-dependent Area Under the Receiver Operating Characteristic curve (tdAUROC) at 1, 5, and 10 years. Discriminatory ability is evaluated via two-sided t-tests comparing predicted mortality between event and non-event subjects, including 95% confidence intervals (CI) for the difference (Diff.). Additionally, log-rank tests with Chi-squared (χ^2) statistics compare event rates between high- and low-risk groups stratified by median predicted mortality.

Metric	SHHS1 [†] ($E = 1, M = 0$)	SHHS1 [†] ($E = 1, M = 1$)	SHHS2 ($E = 1, M = 0$)	SHHS2 [†] ($E = 1, M = 0$)	SHHS2 ($E = 1, M = 1$)	SHHS2 [†] ($E = 1, M = 1$)
Events (N)	60	320	2	13	15	163
Event-free (N)	52	252	0	22	0	141
C-index	60.8	62.6	0.0	56.6	62.9	60.8
IBS	27.4	28.5	22	22.6	32.8	28.9
1-year tdAUROC	29.2	64.9	-	78.1	100.0	62.5
5-year tdAUROC	66.6	67.4	-	57.2	91.7	65.5
10-year tdAUROC	73.2	69.3	-	-	-	-
Mortality ($\bar{E} = 1$)	25.1	27.3	25.2	25	29.8	34.6
Mortality ($E = 0$)	18.1	21.0	-	25.4	-	27.1
Mortality Diff.	7.0	6.3	-	-0.4	-	7.5
Mortality Diff. CI-low	1.2	3.6	-	-11.5	-	3.1
Mortality Diff. CI-high	12.7	9.0	-	10.7	-	11.9
p-value (t-test)	0.017856	0.000005	-	0.94043	-	0.000846
Events (N), high-risk	36	184	1	7	7	95
Events (N), low-risk	24	136	1	6	8	68
χ^2	9.2	33.1	1.0	0.6	2.6	16.3
p-value (log-rank test)	0.002405	$< 10^{-6}$	0.317311	0.442614	0.106251	0.000053

Table 14. Performance of the Random Survival Forest (RSF) model omitting AHI predictor, evaluated across various datasets of subjects with previous cardiovascular events ($E = 1$). The columns evaluate the performance of the final RSF model fitted to the entire event- and medication-free ($E = M = 0$) baseline cohort SHHS1 ($E = 0, M = 0$), applied to potentially out-of-domain subjects (†) from either the baseline (SHHS1) or follow-up (SHHS2) studies, including subgroups taking medication ($M = 1$). For each scenario, the number of subjects with events and without events (event-free) is reported. Model performance is assessed using Harrell's Concordance Index (C-index), Integrated Brier Score (IBS), and the time-dependent Area Under the Receiver Operating Characteristic curve (tdAUROC) at 1, 5, and 10 years. Discriminatory ability is evaluated via two-sided t-tests comparing predicted mortality between event and non-event subjects, including 95% confidence intervals (CI) for the difference (Diff.). Additionally, log-rank tests with Chi-squared (χ^2) statistics compare event rates between high- and low-risk groups stratified by median predicted mortality.

Metric	SHHS1 [†] ($E = 1, M = 0$)	SHHS1 [†] ($E = 1, M = 1$)	SHHS2 ($E = 1, M = 0$)	SHHS2 [†] ($E = 1, M = 0$)	SHHS2 ($E = 1, M = 1$)	SHHS2 [†] ($E = 1, M = 1$)
Events (N)	60	320	2	13	15	163
Event-free (N)	52	252	0	22	0	141
C-index	61.7	62.2	0	56.6	61.9	61.1
IBS	27.4	28.5	21.8	22.4	32.8	28.8
1-year tdAUROC	30.1	64.4	-	79.2	100	63
5-year tdAUROC	67.8	67	-	57.4	91.7	66
10-year tdAUROC	73.7	69.1	-	-	-	-
Mortality ($E = 1$)	25.0	27.3	25.1	25.5	30.1	34.6
Mortality ($E = 0$)	18.0	21.0	-	25.5	-	26.9
Mortality Diff.	7.0	6.3	-	0	-	7.7
Mortality Diff. CI-low	1.1	3.6	-	-11.3	-	3.3
Mortality Diff. CI-high	12.8	9.0	-	11.3	-	12.1
p-value (t-test)	0.019666	0.000006	-	0.997352	-	0.000583
Events (N), high-risk	36	181	1	7	7	95
Events (N), low-risk	24	139	1	6	8	68
χ^2	9.2	30.4	1.0	0.6	1.1	16.1
p-value (log-rank test)	0.002405	$< 10^{-6}$	0.317311	0.442614	0.286982	0.000061

4 Survival Plots for RSF with AHI predictor

4.1 Primary study cohort

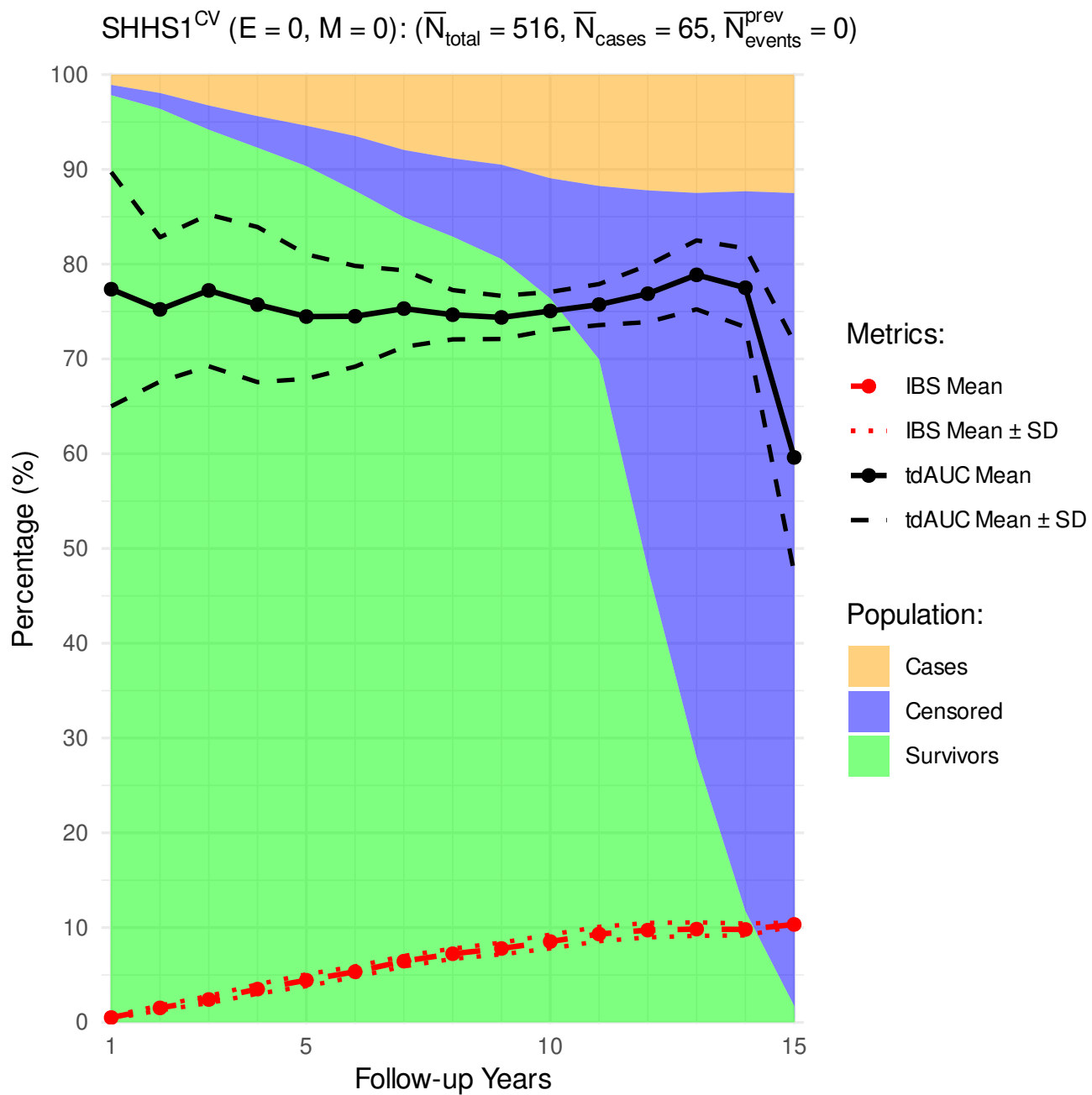


Figure 1. Distribution of cardiovascular cases, survivors, and censoring, as well as the performance metrics (time-dependent Area Under Receiver Operating Characteristic [tdAUROC] curve, Integrated Brier Score [IBS].)

4.2 SHHS1 test subjects

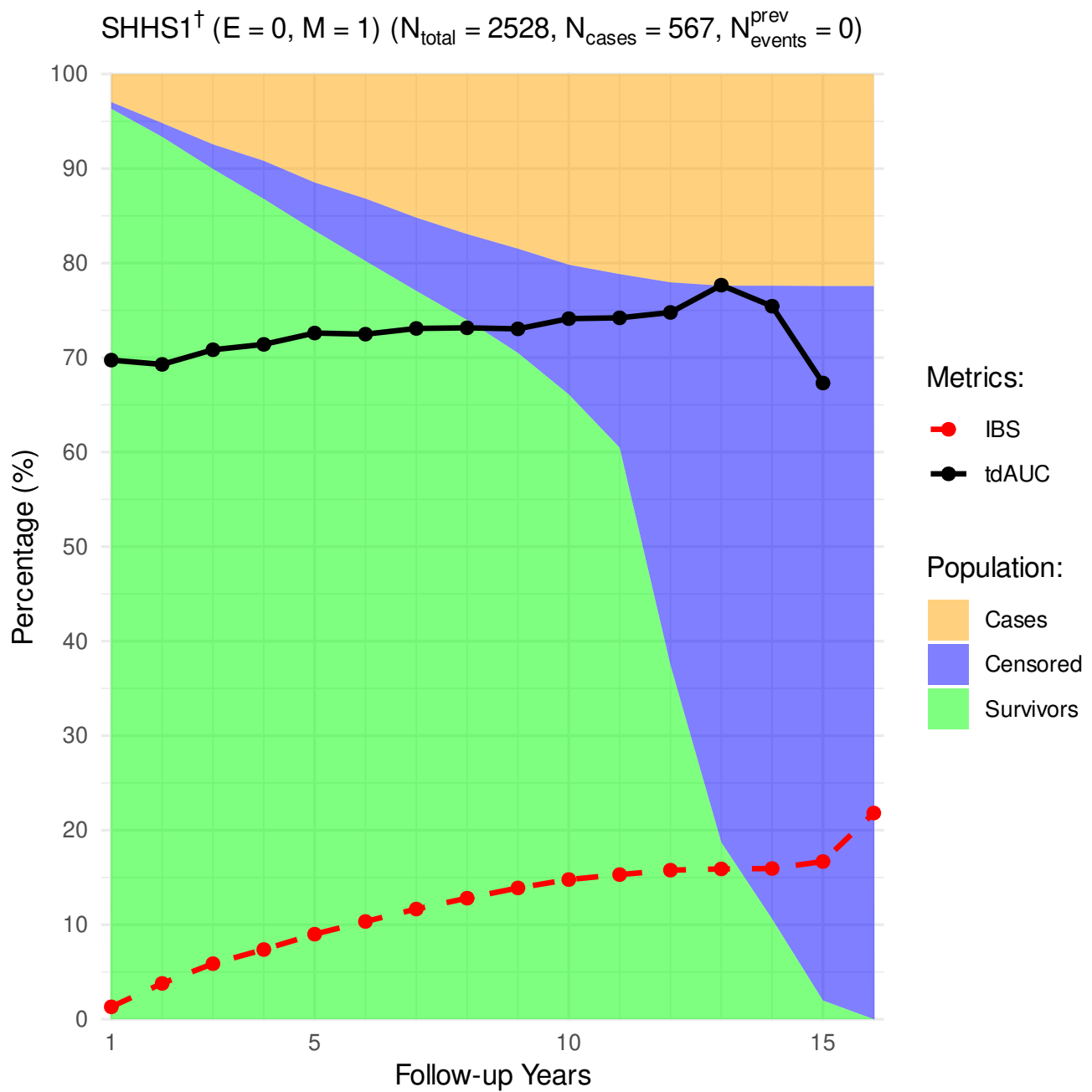


Figure 2. Distribution of cardiovascular cases, survivors, and censoring, as well as the performance metrics (time-dependent Area Under Receiver Operating Characteristic [tdAUROC] curve, Integrated Brier Score [IBS].)

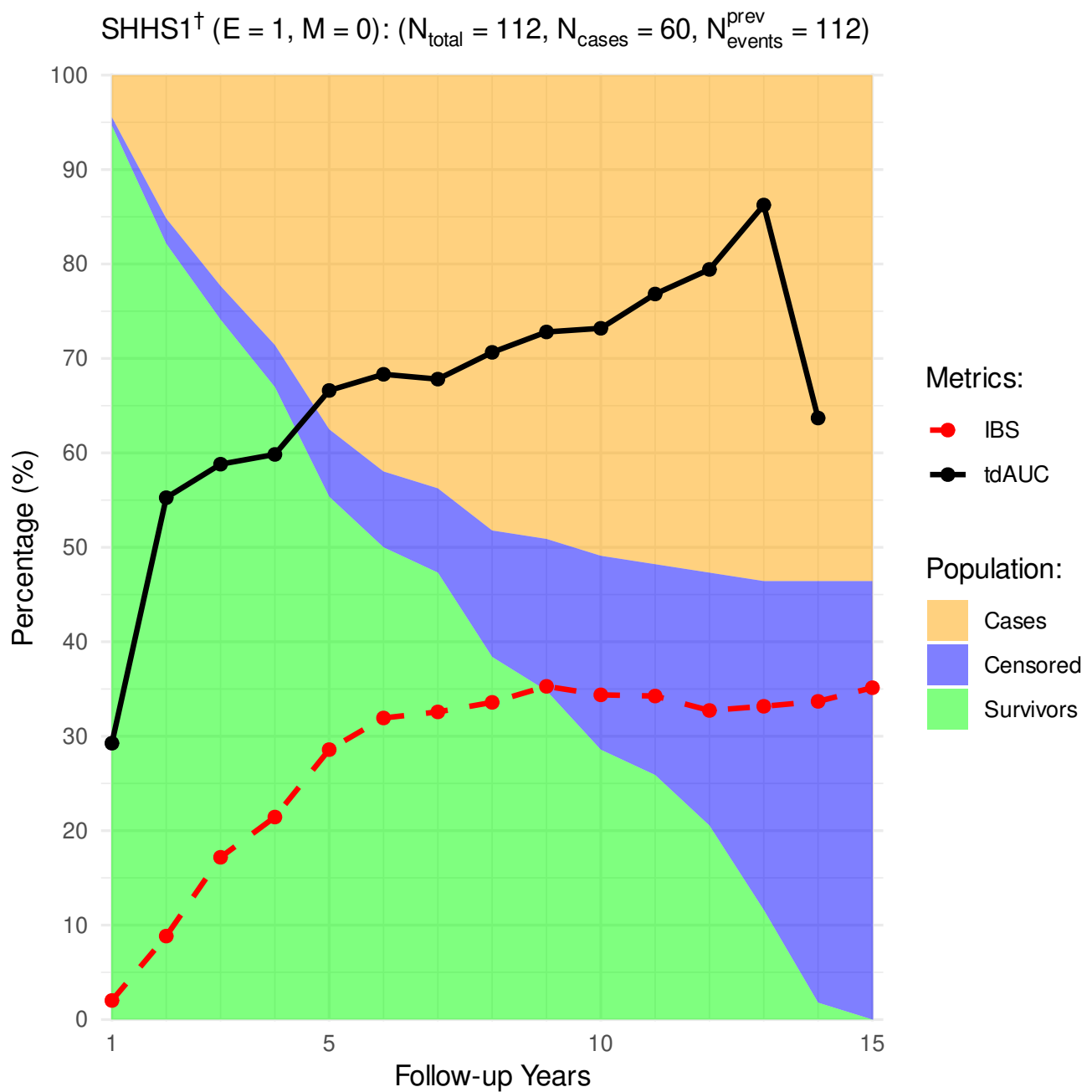


Figure 3. Distribution of cardiovascular cases, survivors, and censoring, as well as the performance metrics (time-dependent Area Under Receiver Operating Characteristic [tdAUROC] curve, Integrated Brier Score [IBS].)

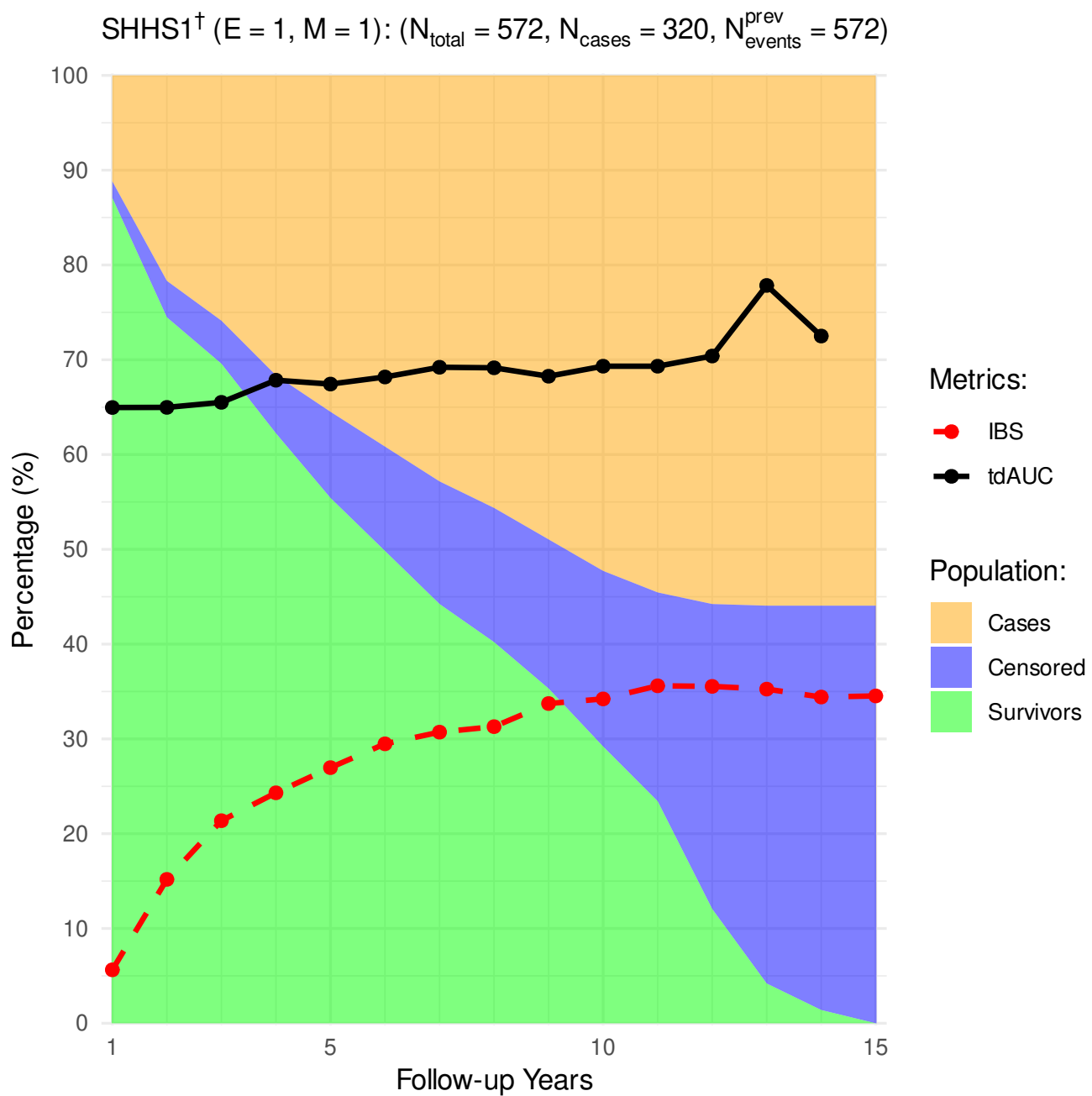


Figure 4. Distribution of cardiovascular cases, survivors, and censoring, as well as the performance metrics (time-dependent Area Under Receiver Operating Characteristic [tdAUROC] curve, Integrated Brier Score [IBS].)

4.3 SHHS2 train subjects

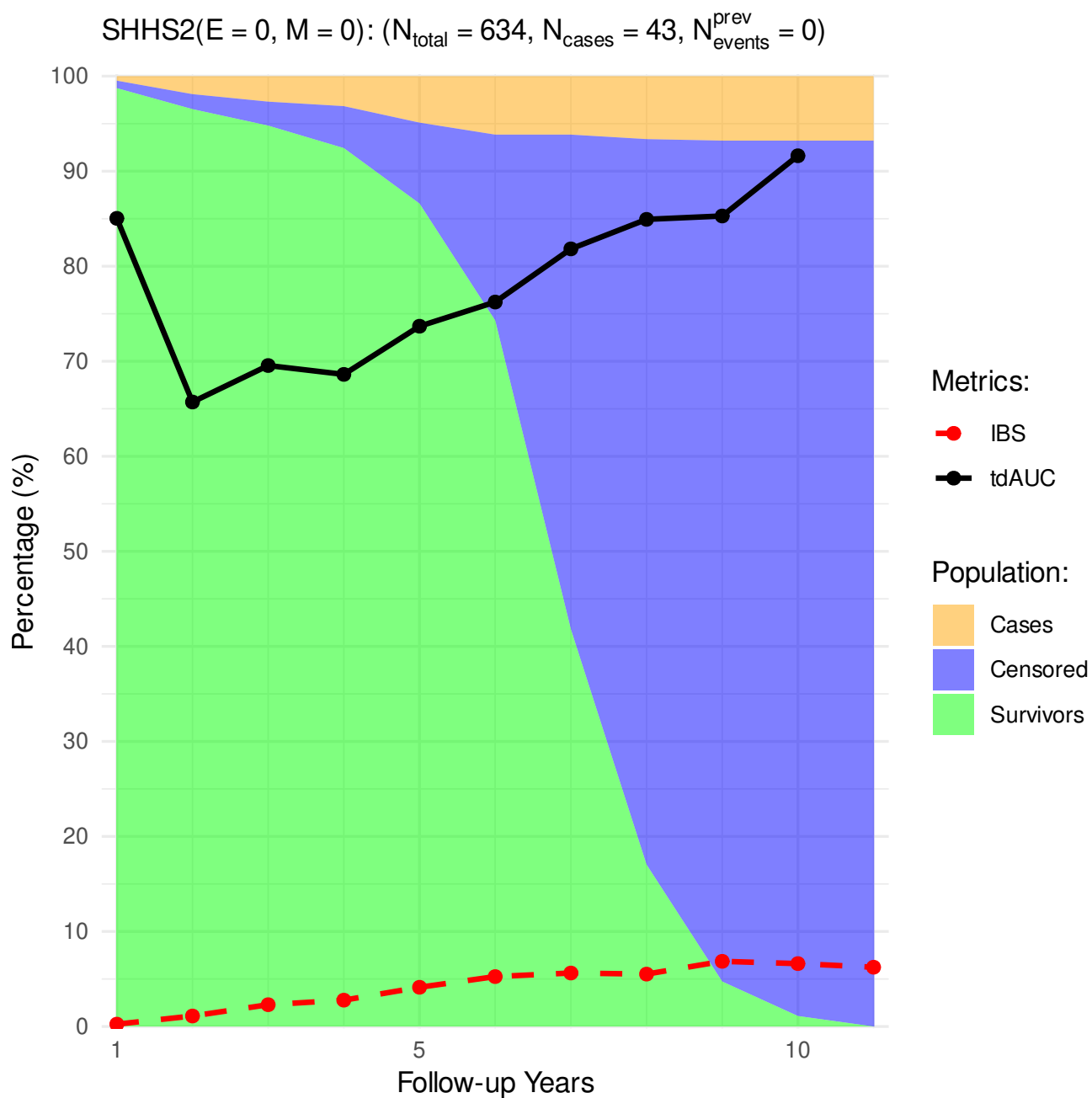


Figure 5. Distribution of cardiovascular cases, survivors, and censoring, as well as the performance metrics (time-dependent Area Under Receiver Operating Characteristic [tdAUROC] curve, Integrated Brier Score [IBS].)

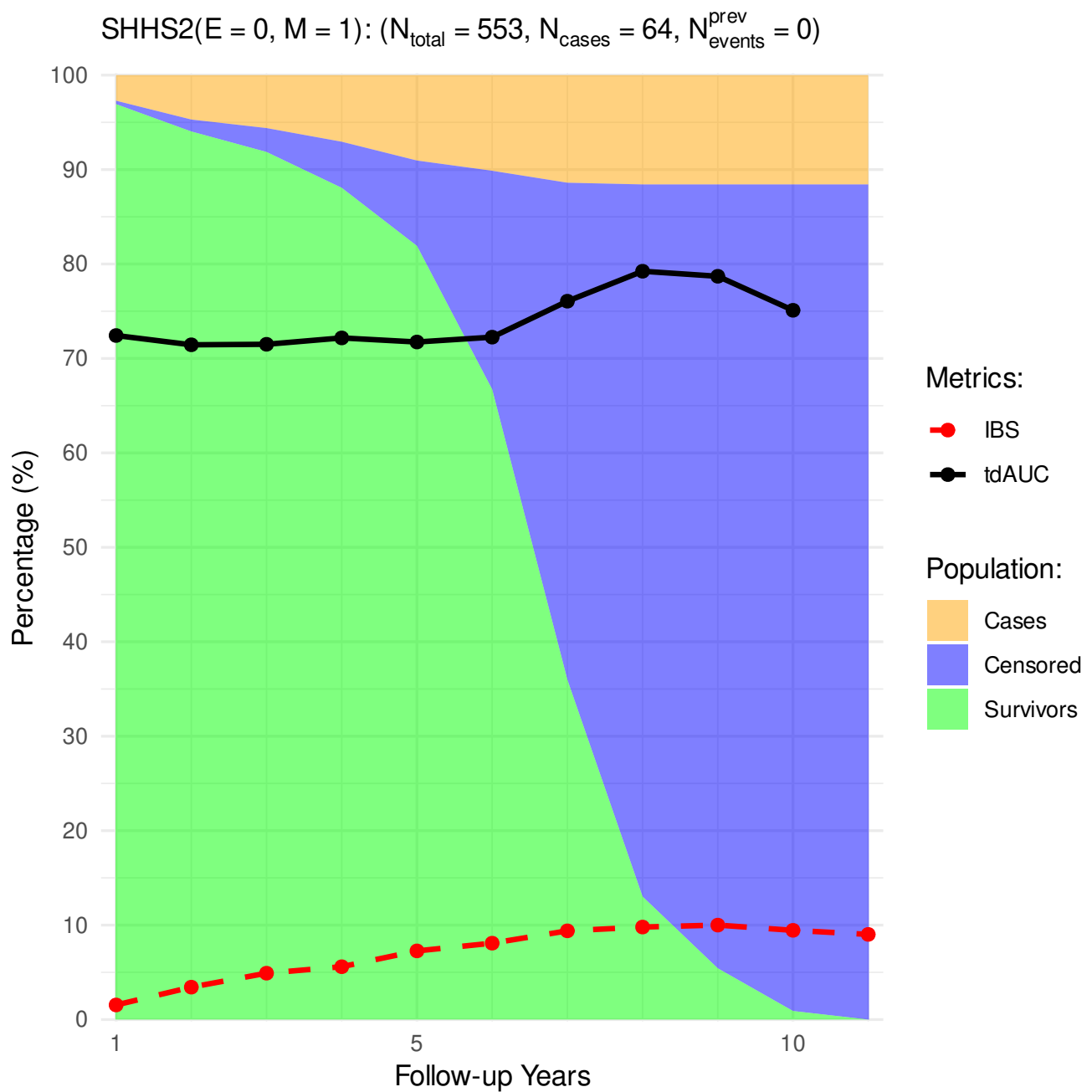


Figure 6. Distribution of cardiovascular cases, survivors, and censoring, as well as the performance metrics (time-dependent Area Under Receiver Operating Characteristic [tdAUROC] curve, Integrated Brier Score [IBS].)

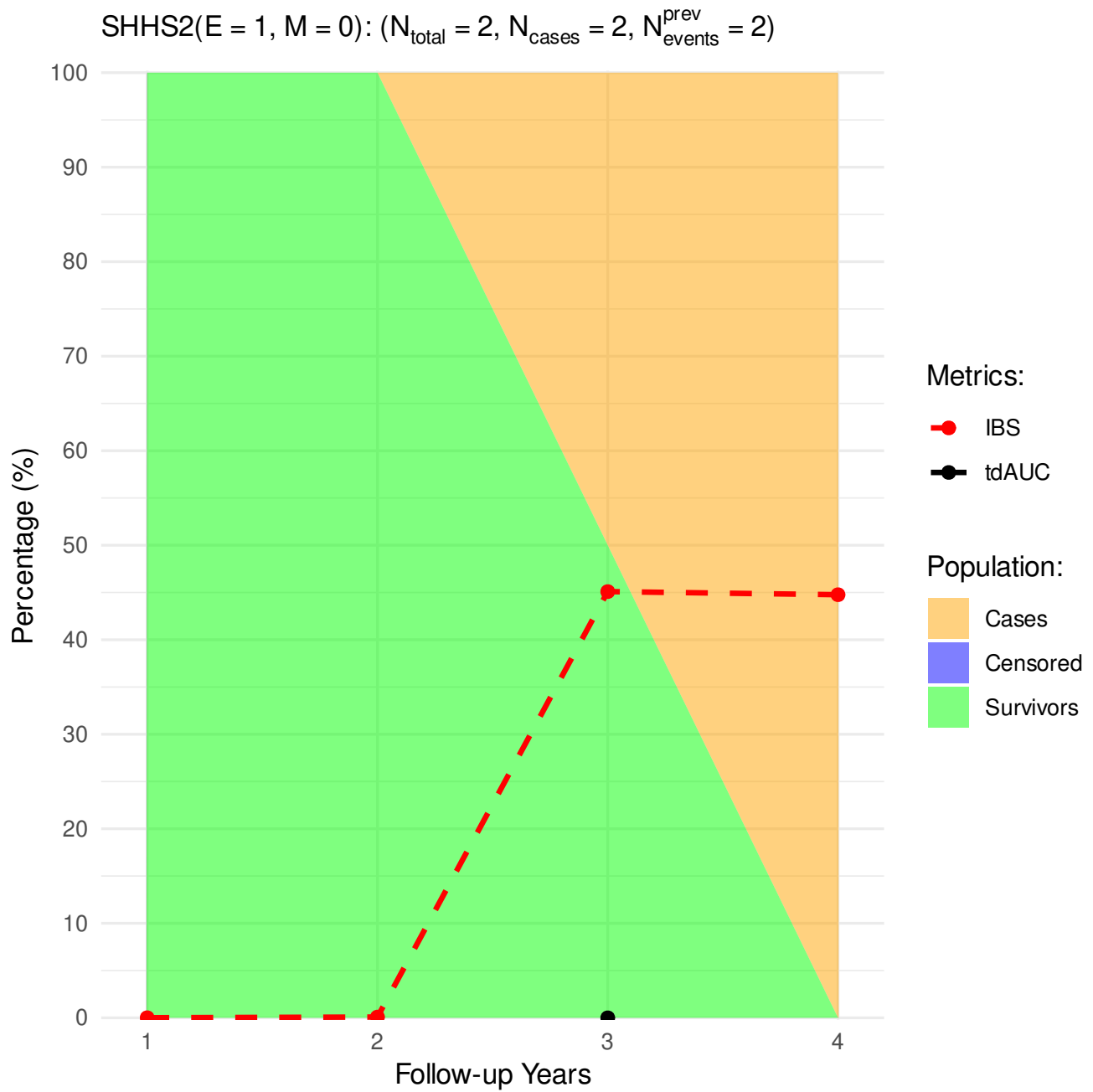


Figure 7. Distribution of cardiovascular cases, survivors, and censoring, as well as the performance metrics (time-dependent Area Under Receiver Operating Characteristic [tdAUROC] curve, Integrated Brier Score [IBS].)

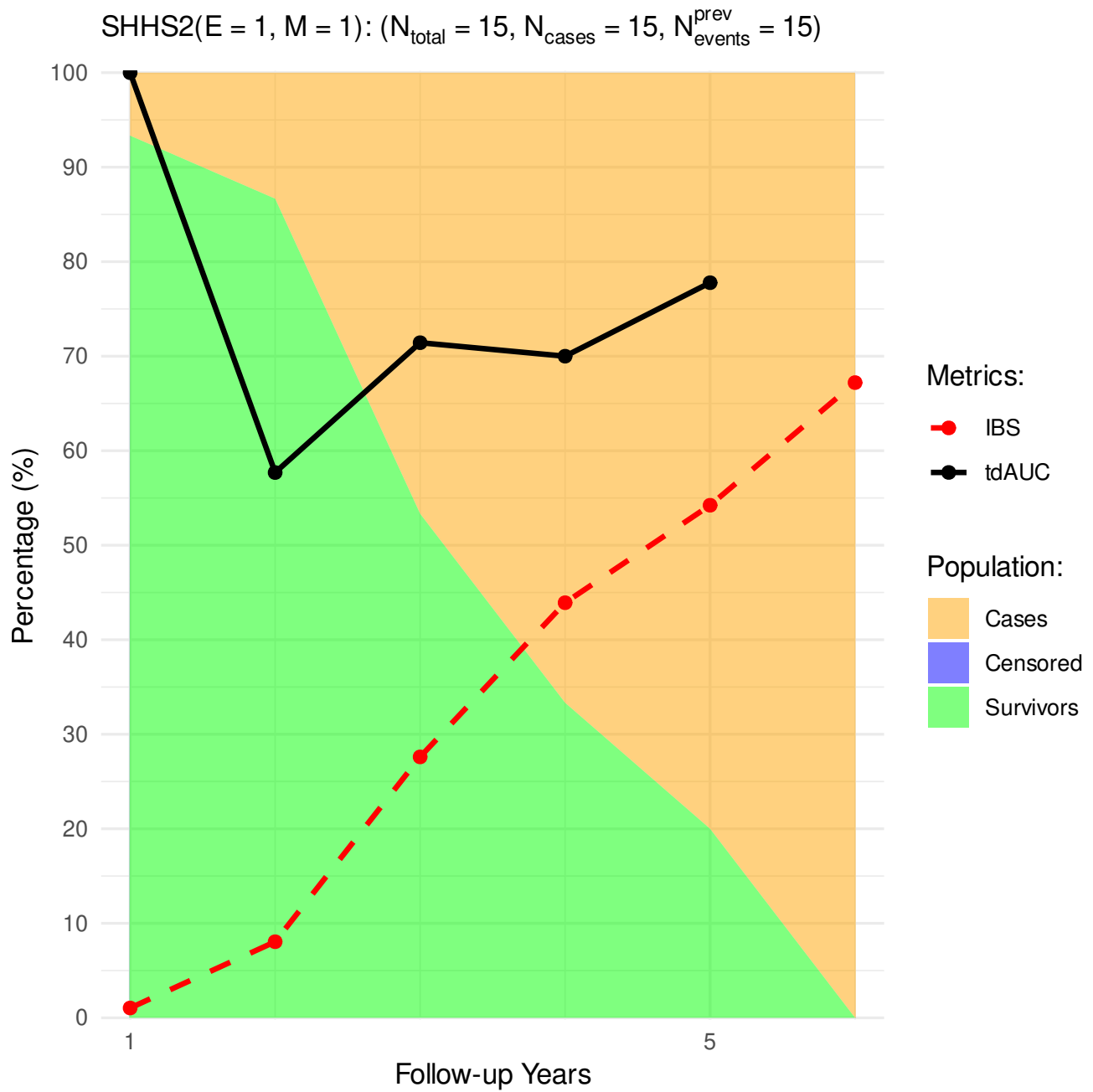


Figure 8. Distribution of cardiovascular cases, survivors, and censoring, as well as the performance metrics (time-dependent Area Under Receiver Operating Characteristic [tdAUROC] curve, Integrated Brier Score [IBS].)

5 SHHS2 test subjects

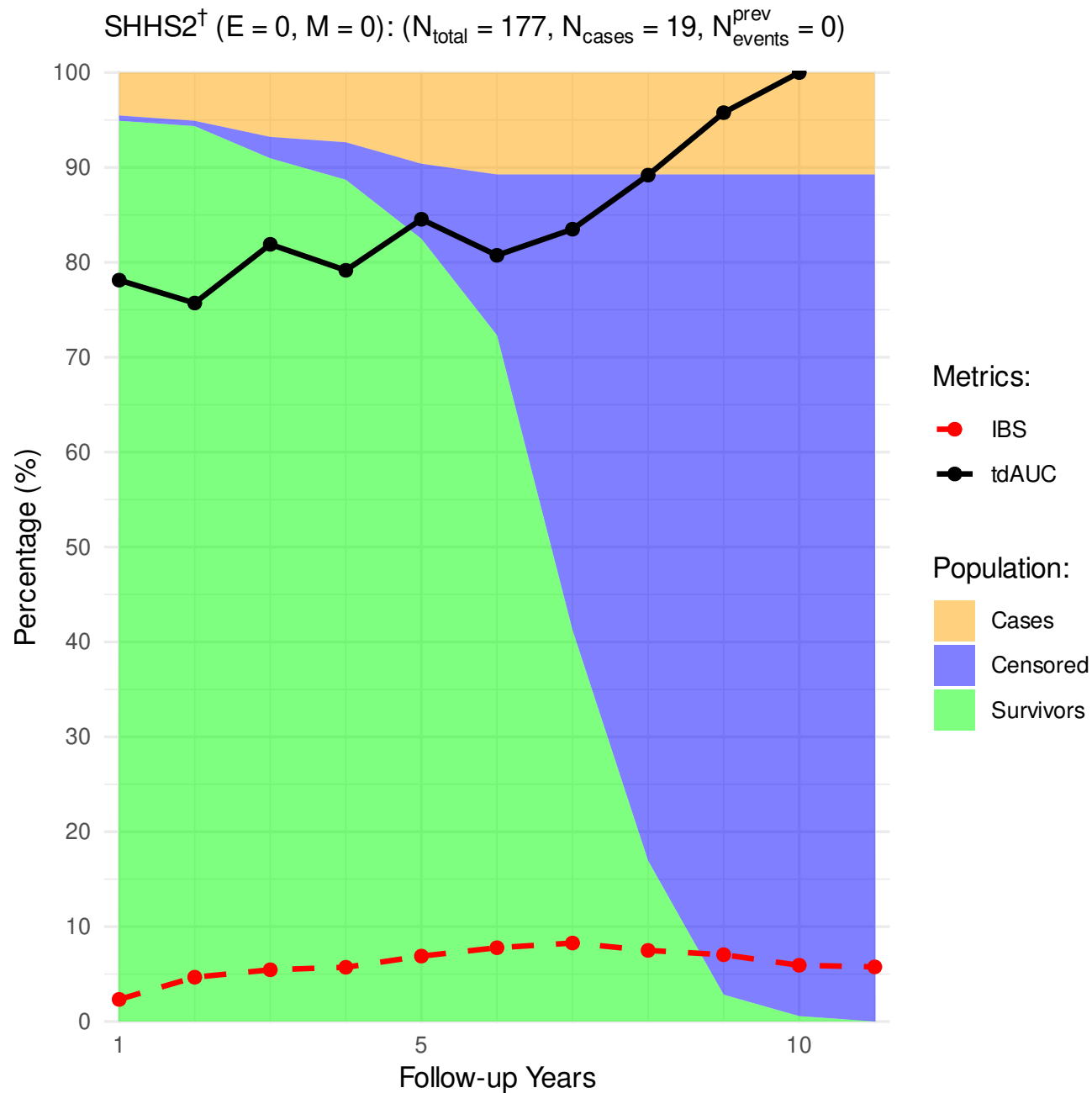


Figure 9. Distribution of cardiovascular cases, survivors, and censoring, as well as the performance metrics (time-dependent Area Under Receiver Operating Characteristic [tdAUROC] curve, Integrated Brier Score [IBS].)

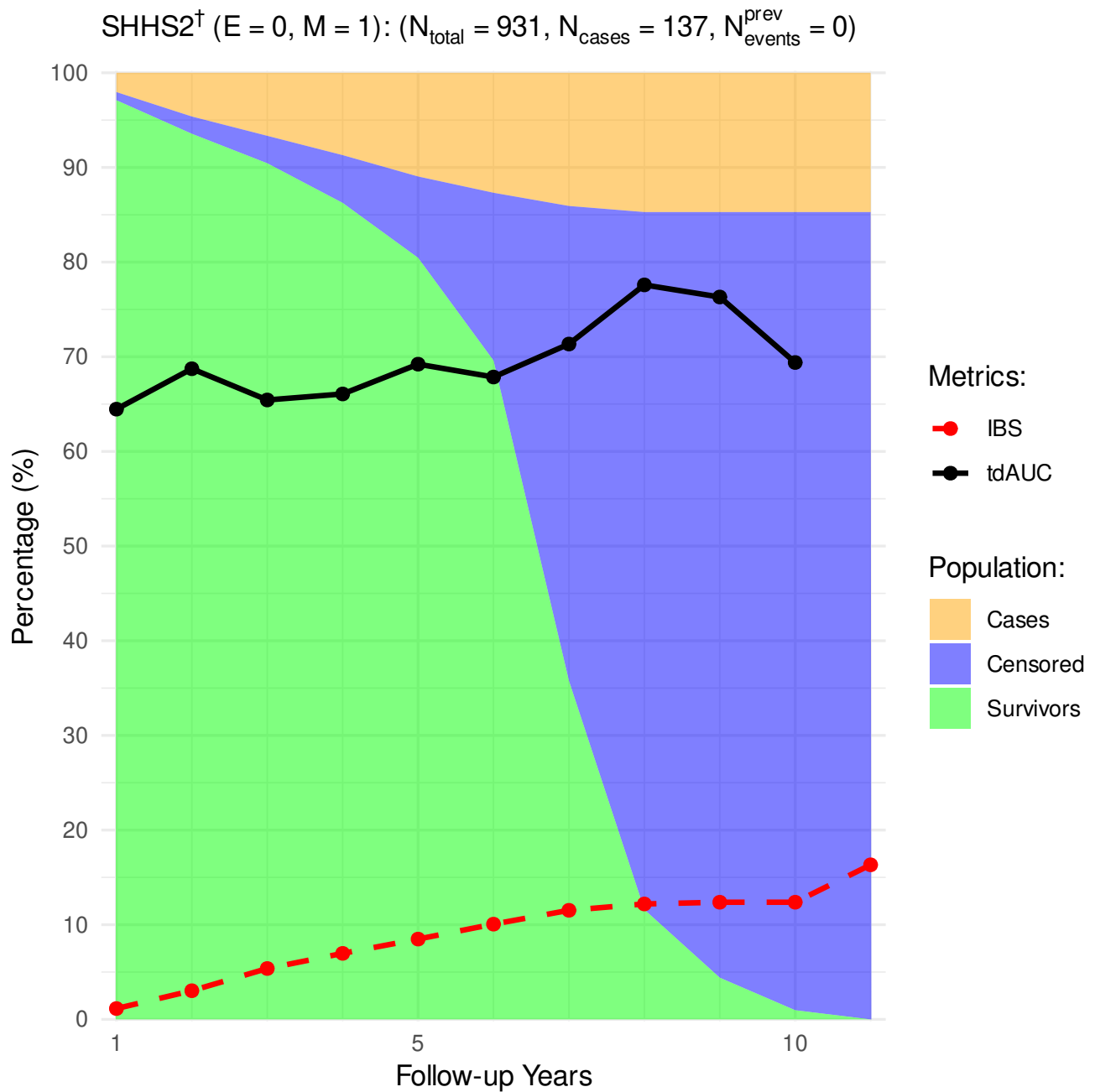


Figure 10. Distribution of cardiovascular cases, survivors, and censoring, as well as the performance metrics (time-dependent Area Under Receiver Operating Characteristic [tdAUROC] curve, Integrated Brier Score [IBS].)

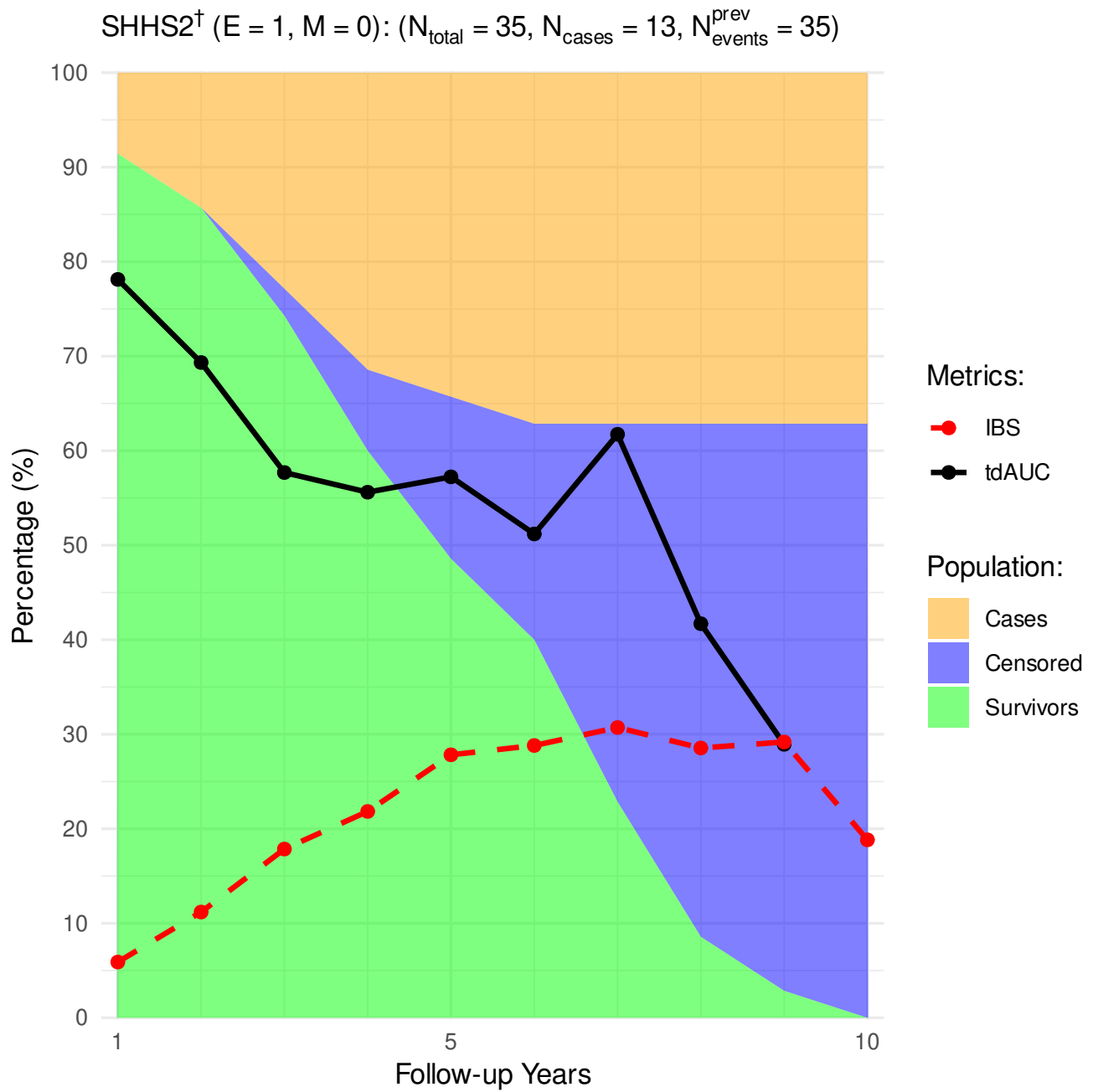


Figure 11. Distribution of cardiovascular cases, survivors, and censoring, as well as the performance metrics (time-dependent Area Under Receiver Operating Characteristic [tdAUROC] curve, Integrated Brier Score [IBS].)

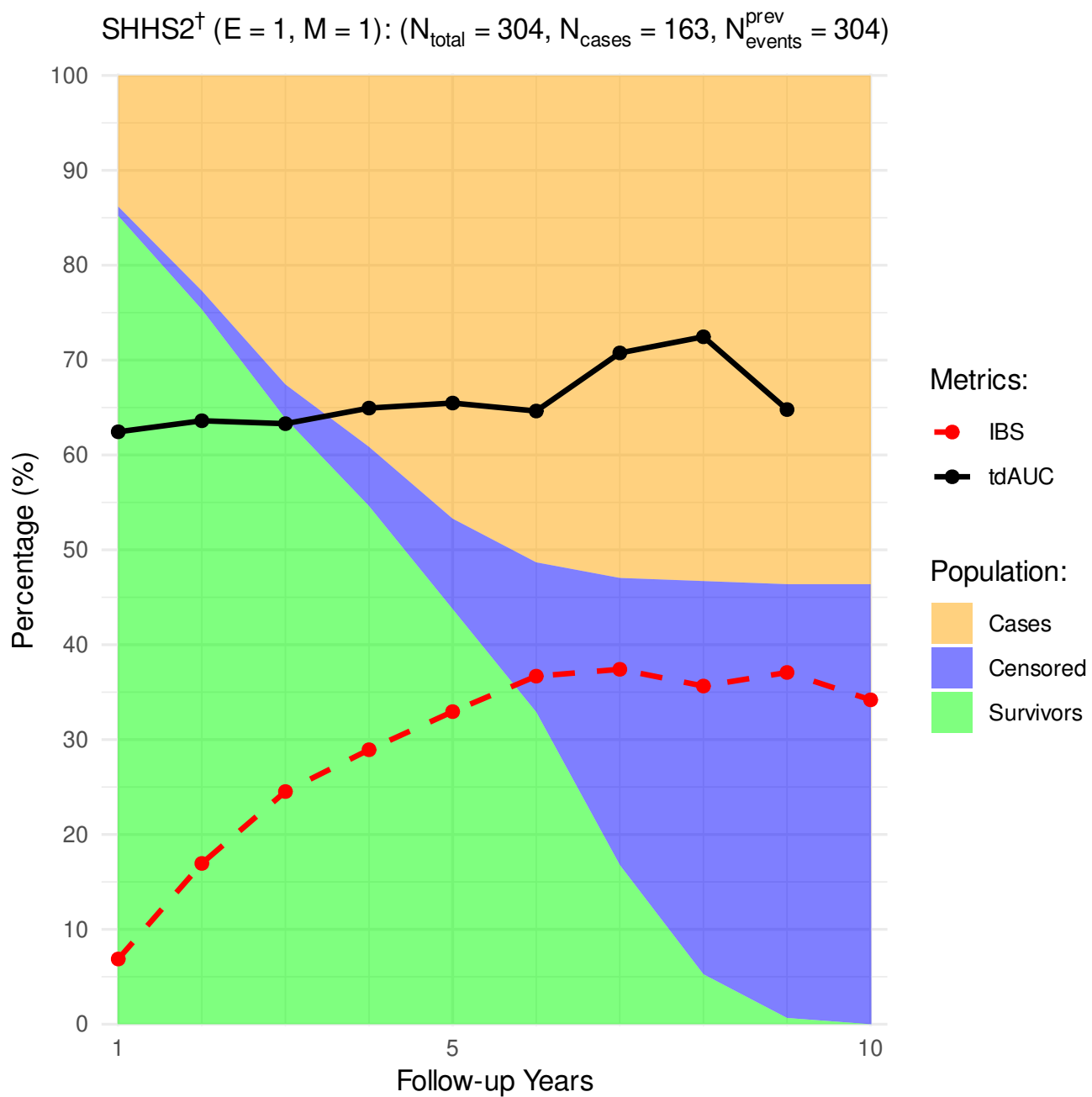


Figure 12. Distribution of cardiovascular cases, survivors, and censoring, as well as the performance metrics (time-dependent Area Under Receiver Operating Characteristic [tdAUROC] curve, Integrated Brier Score [IBS].)

6 Survival Plots without AHI predictor

6.1 Primary study cohort

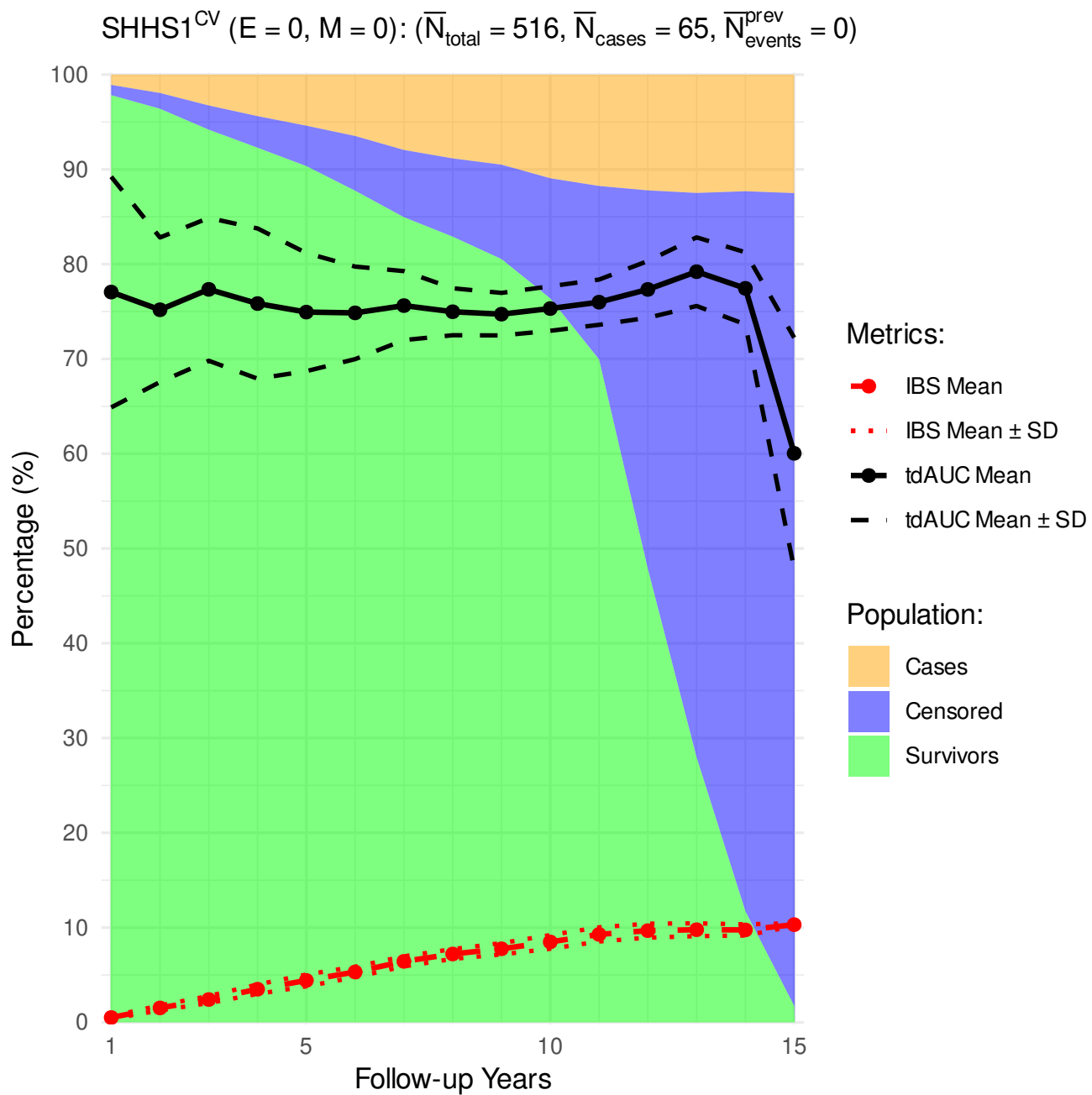


Figure 13. Distribution of cardiovascular cases, survivors, and censoring, as well as the performance metrics (time-dependent Area Under Receiver Operating Characteristic [tdAUROC] curve, Integrated Brier Score [IBS].)

6.2 SHHS1 test subjects

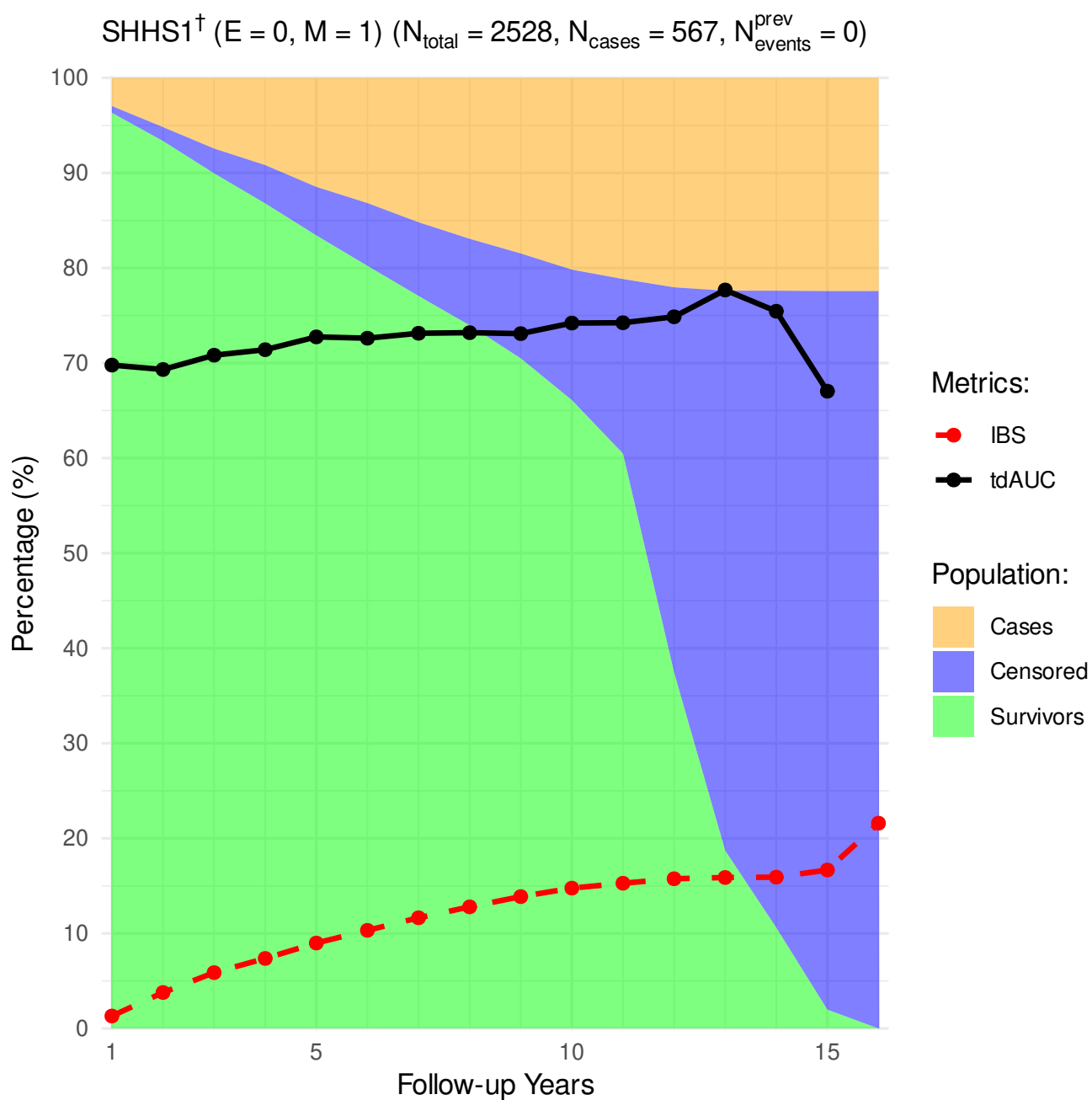


Figure 14. Distribution of cardiovascular cases, survivors, and censoring, as well as the performance metrics (time-dependent Area Under Receiver Operating Characteristic [tdAUROC] curve, Integrated Brier Score [IBS].)

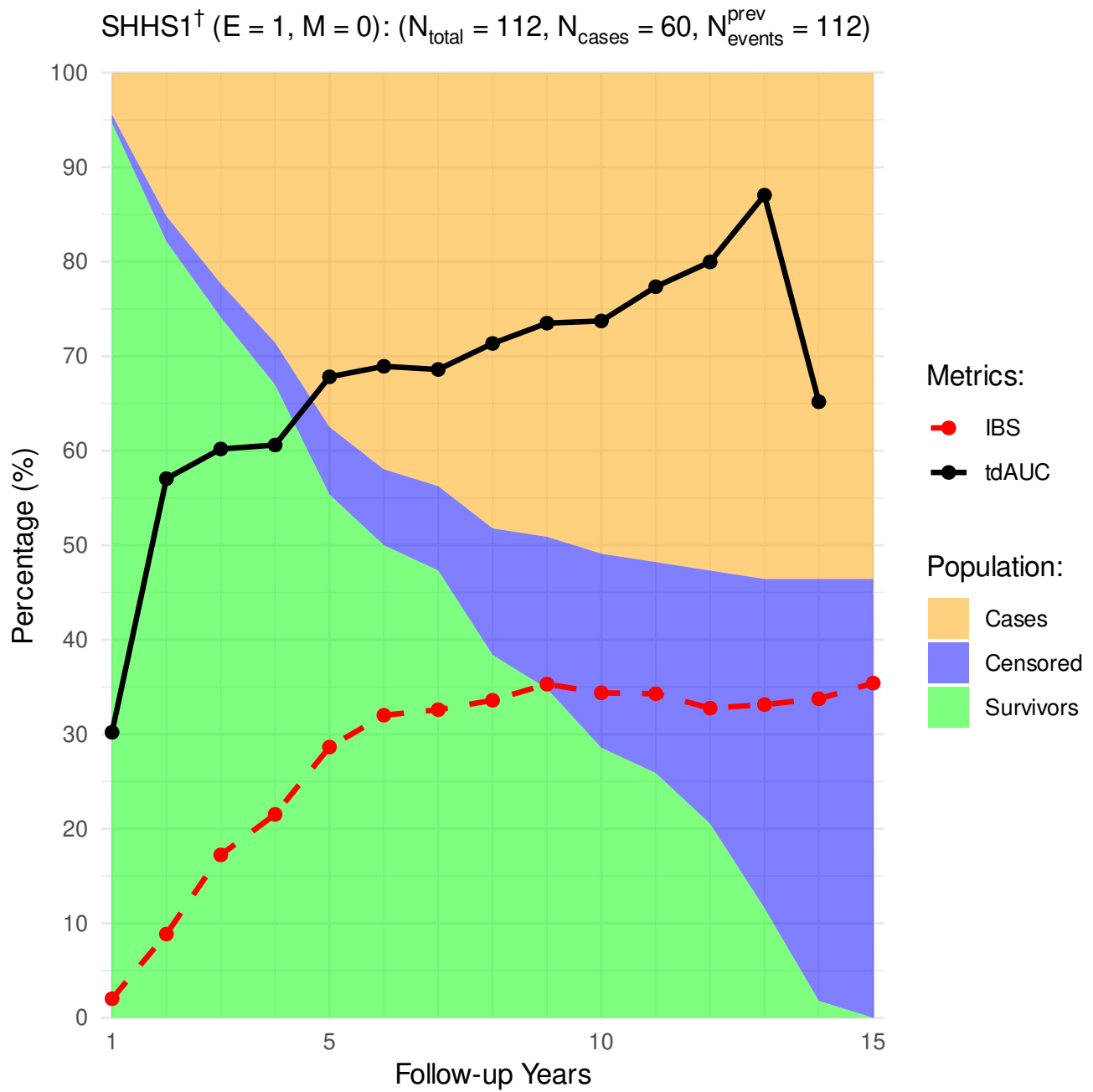


Figure 15. Distribution of cardiovascular cases, survivors, and censoring, as well as the performance metrics (time-dependent Area Under Receiver Operating Characteristic [tdAUROC] curve, Integrated Brier Score [IBS].)

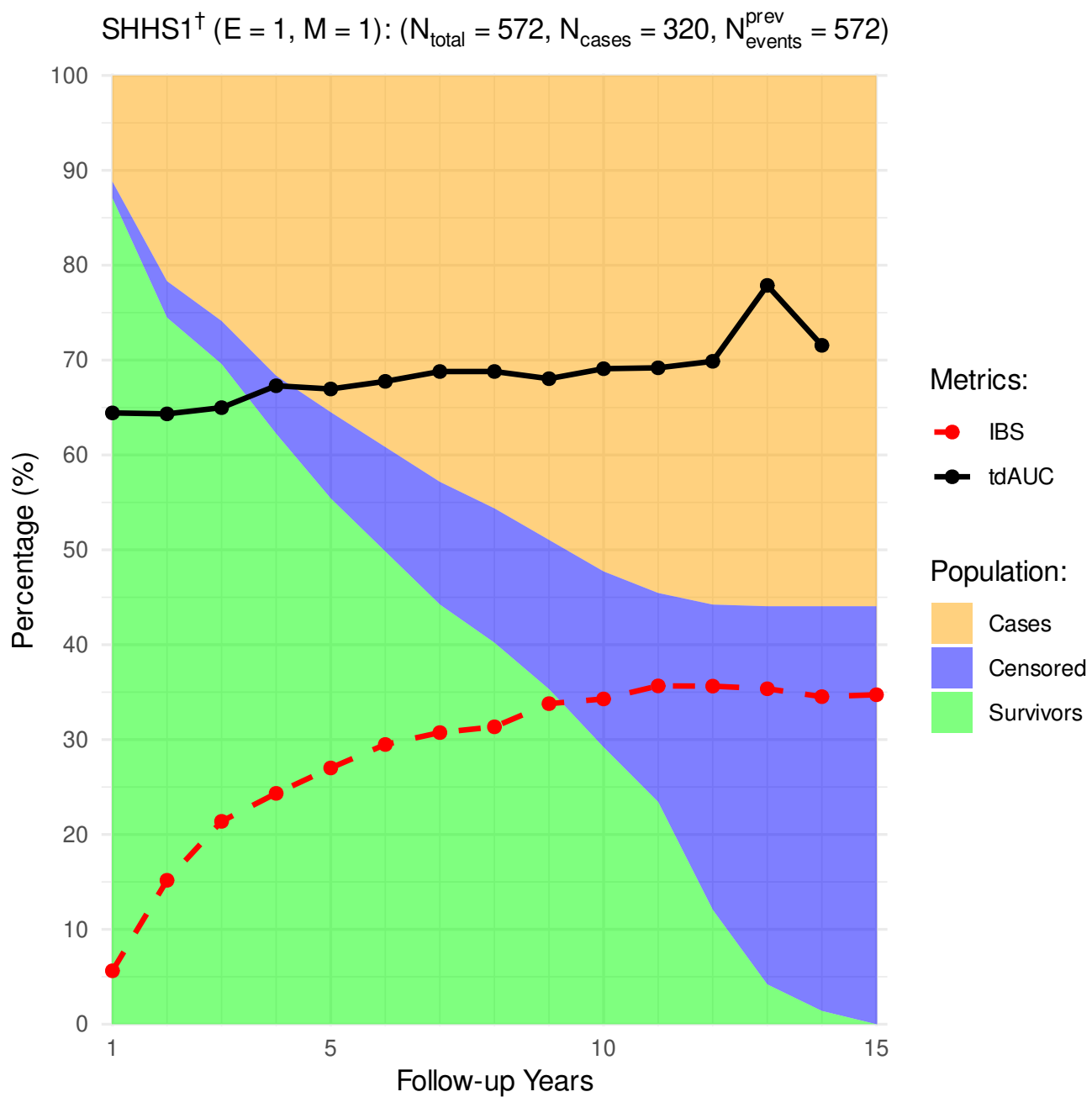


Figure 16. Distribution of cardiovascular cases, survivors, and censoring, as well as the performance metrics (time-dependent Area Under Receiver Operating Characteristic [tdAUROC] curve, Integrated Brier Score [IBS].)

6.3 SHHS2 train subjects

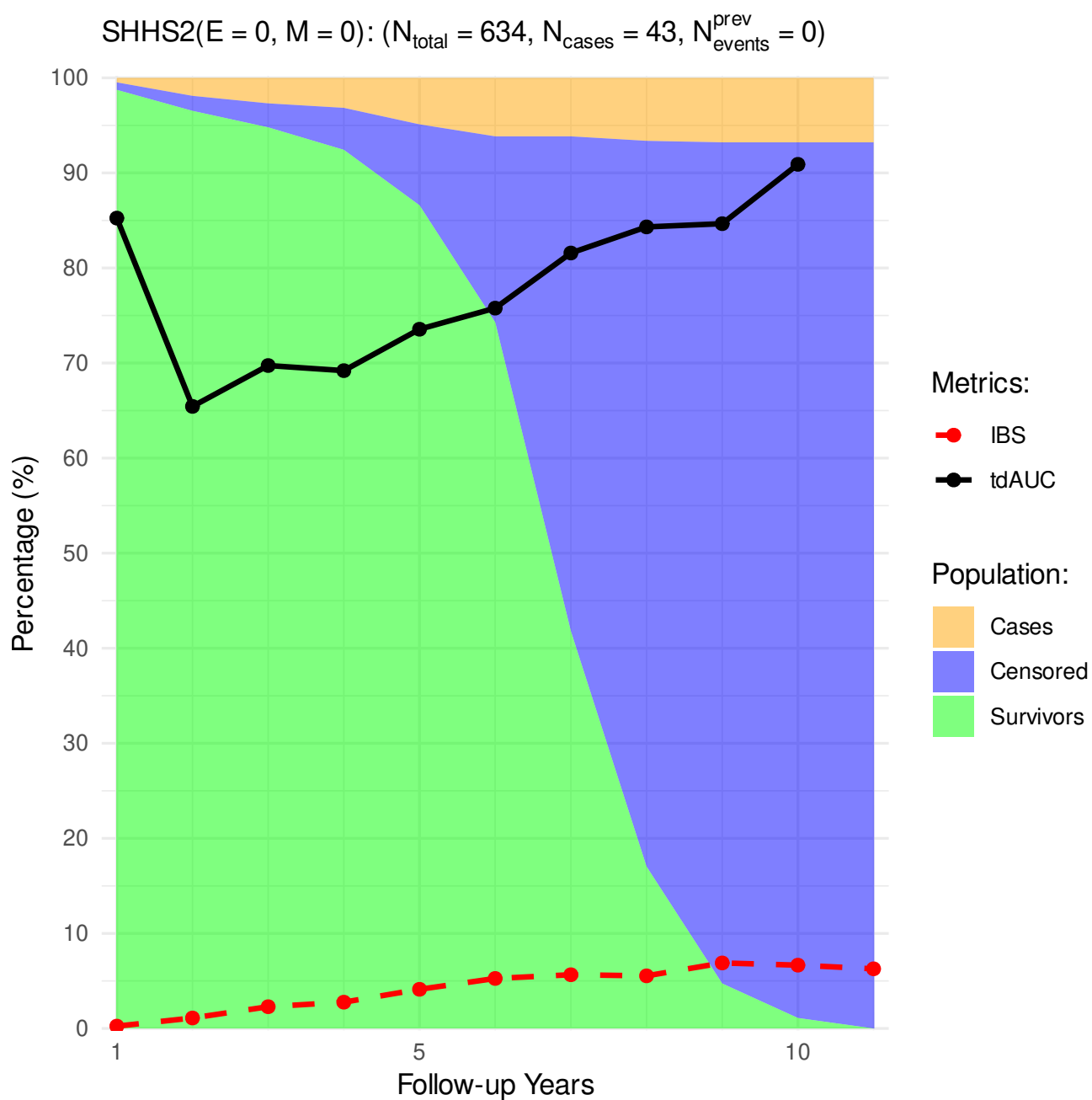


Figure 17. Distribution of cardiovascular cases, survivors, and censoring, as well as the performance metrics (time-dependent Area Under Receiver Operating Characteristic [tdAUROC] curve, Integrated Brier Score [IBS].)

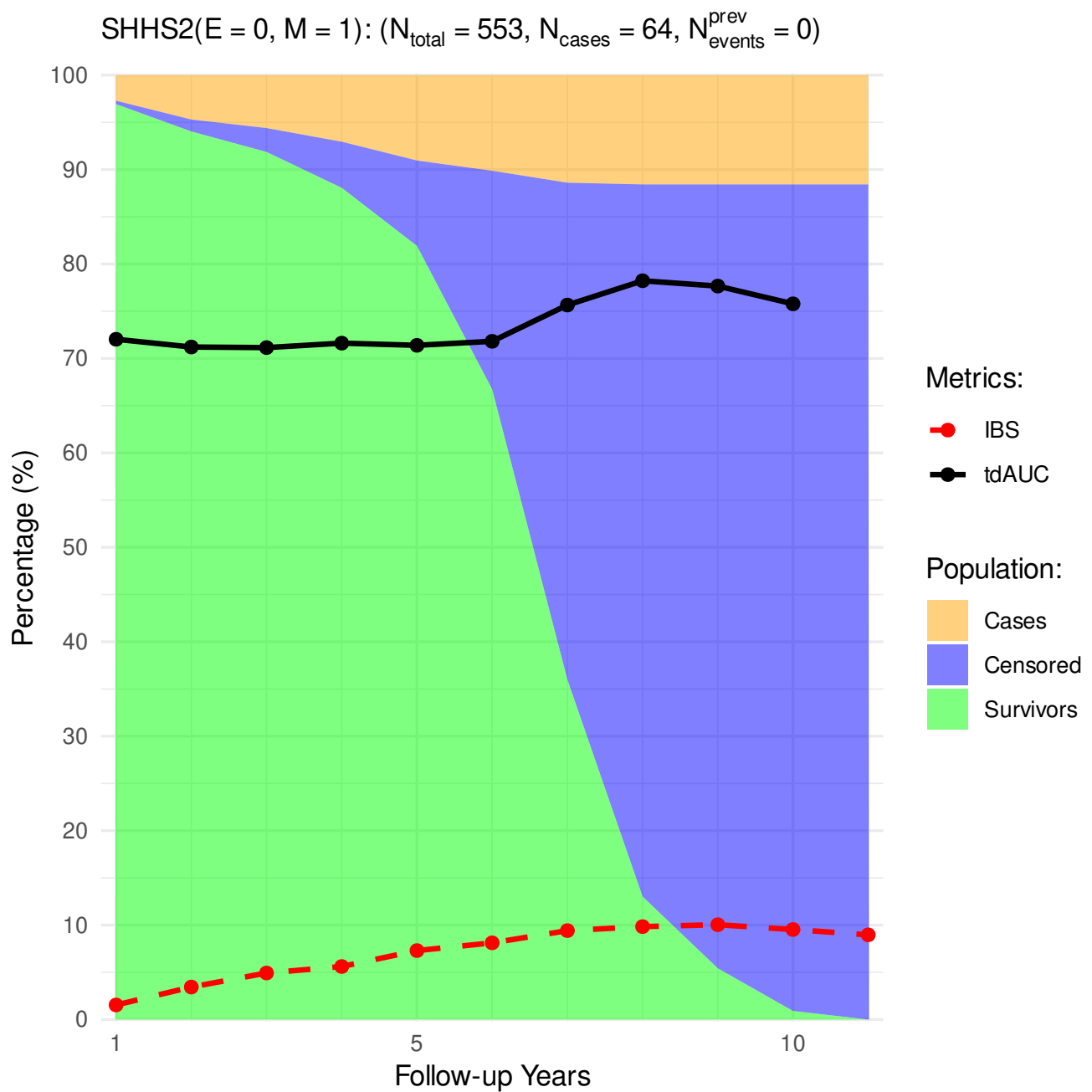


Figure 18. Distribution of cardiovascular cases, survivors, and censoring, as well as the performance metrics (time-dependent Area Under Receiver Operating Characteristic [tdAUROC] curve, Integrated Brier Score [IBS].)

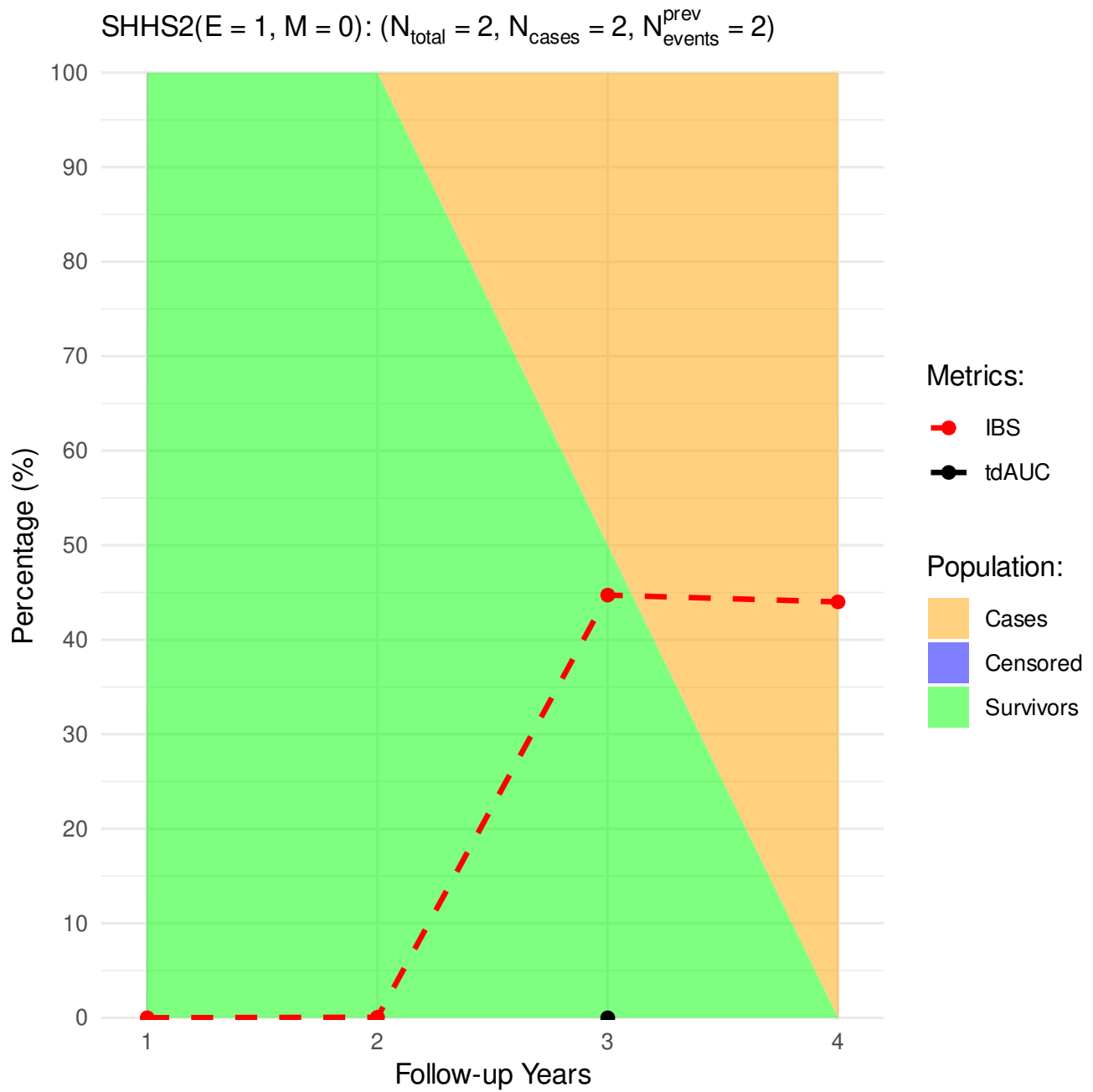


Figure 19. Distribution of cardiovascular cases, survivors, and censoring, as well as the performance metrics (time-dependent Area Under Receiver Operating Characteristic [tdAUROC] curve, Integrated Brier Score [IBS].)

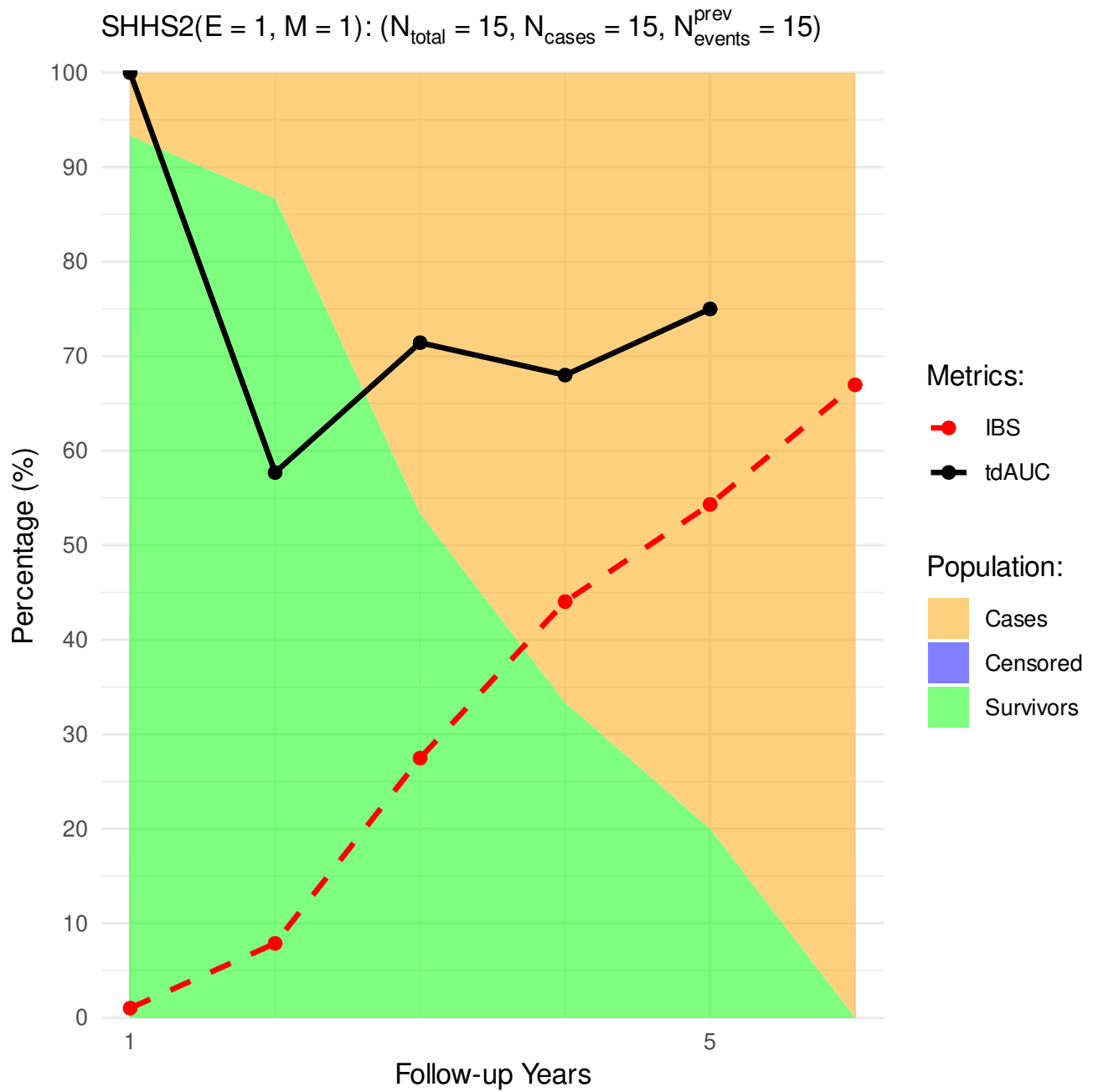


Figure 20. Distribution of cardiovascular cases, survivors, and censoring, as well as the performance metrics (time-dependent Area Under Receiver Operating Characteristic [tdAUROC] curve, Integrated Brier Score [IBS].)

7 SHHS2 test subjects

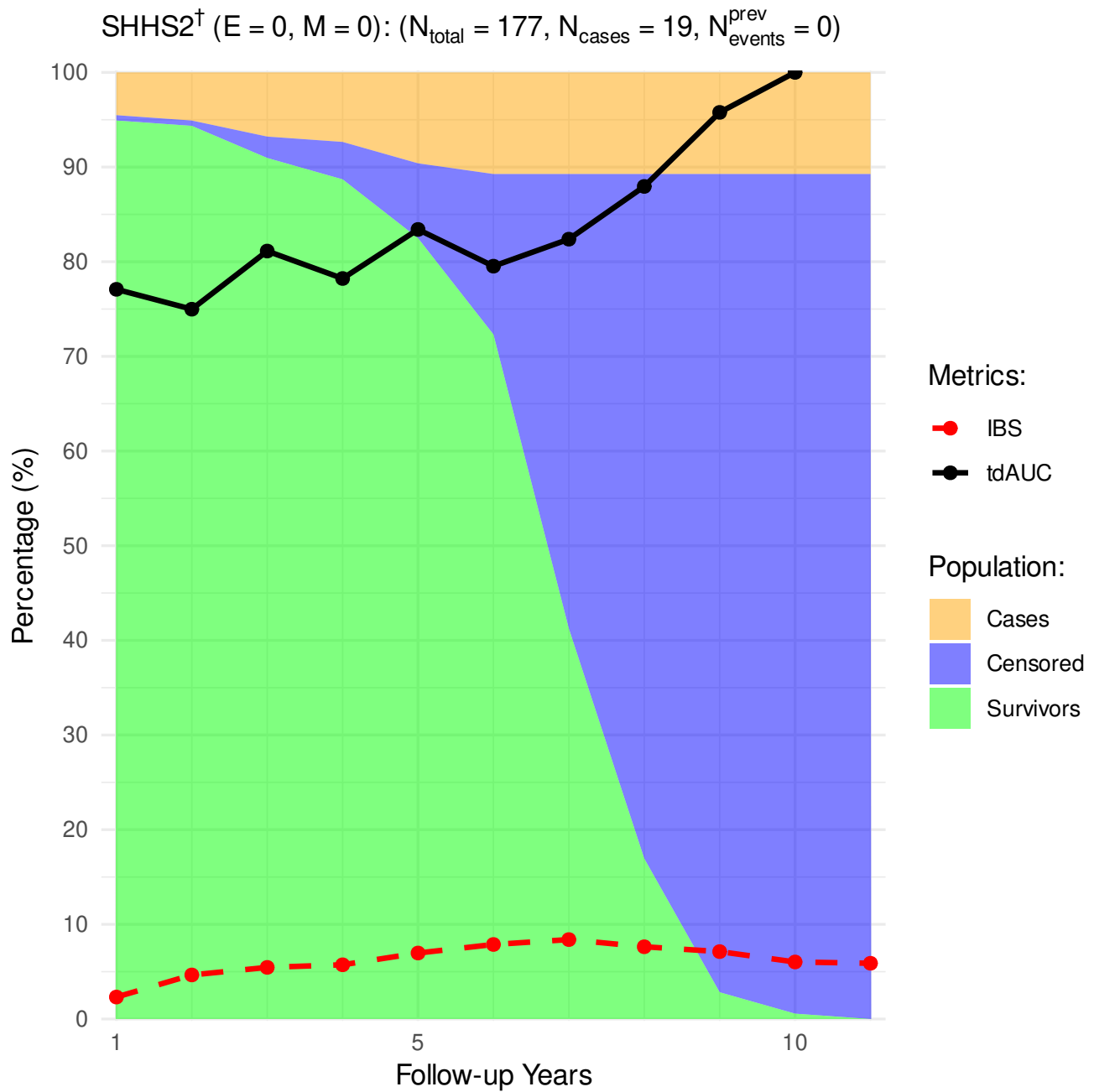


Figure 21. Distribution of cardiovascular cases, survivors, and censoring, as well as the performance metrics (time-dependent Area Under Receiver Operating Characteristic [tdAUROC] curve, Integrated Brier Score [IBS].)

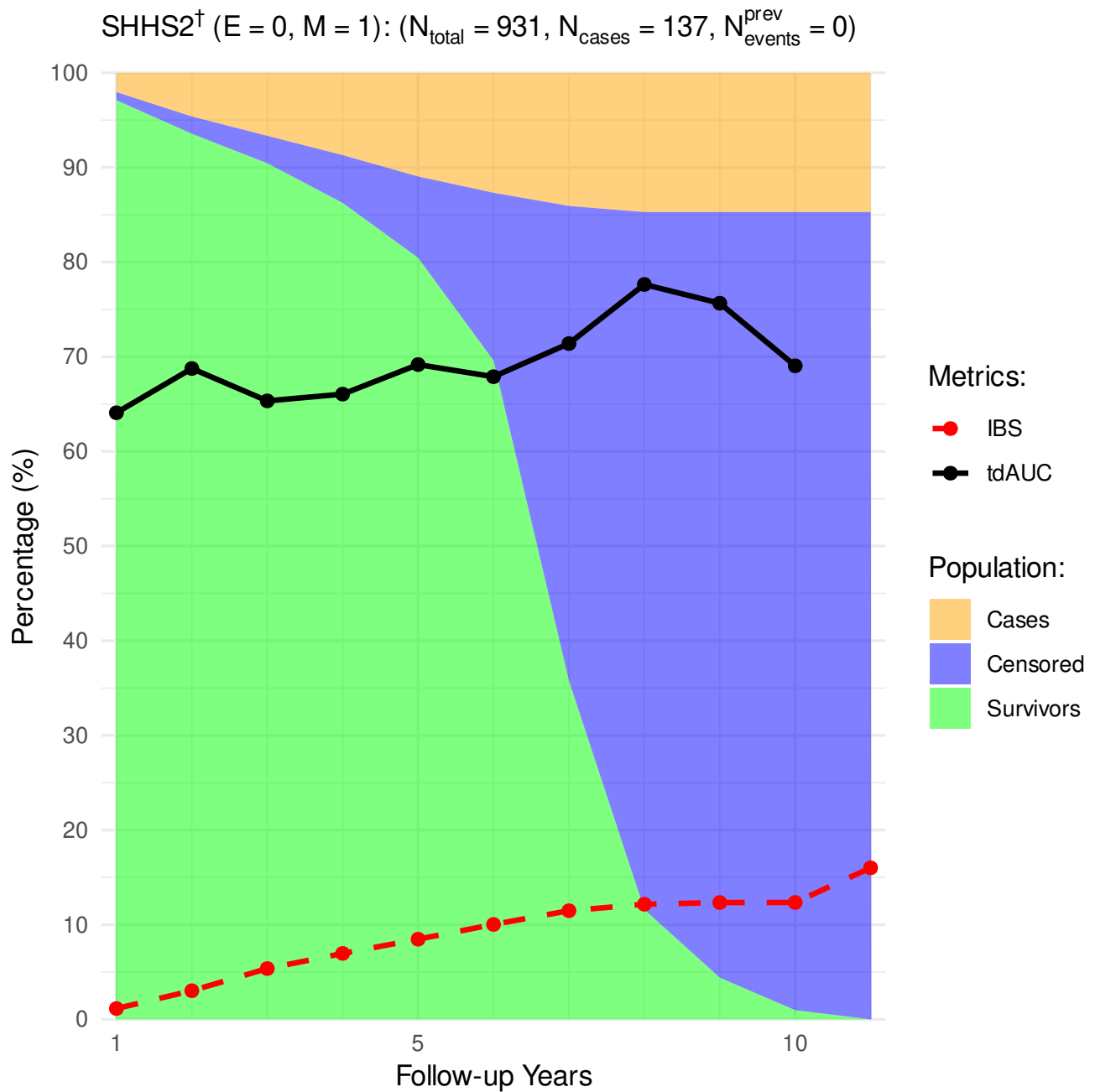


Figure 22. Distribution of cardiovascular cases, survivors, and censoring, as well as the performance metrics (time-dependent Area Under Receiver Operating Characteristic [tdAUROC] curve, Integrated Brier Score [IBS].)

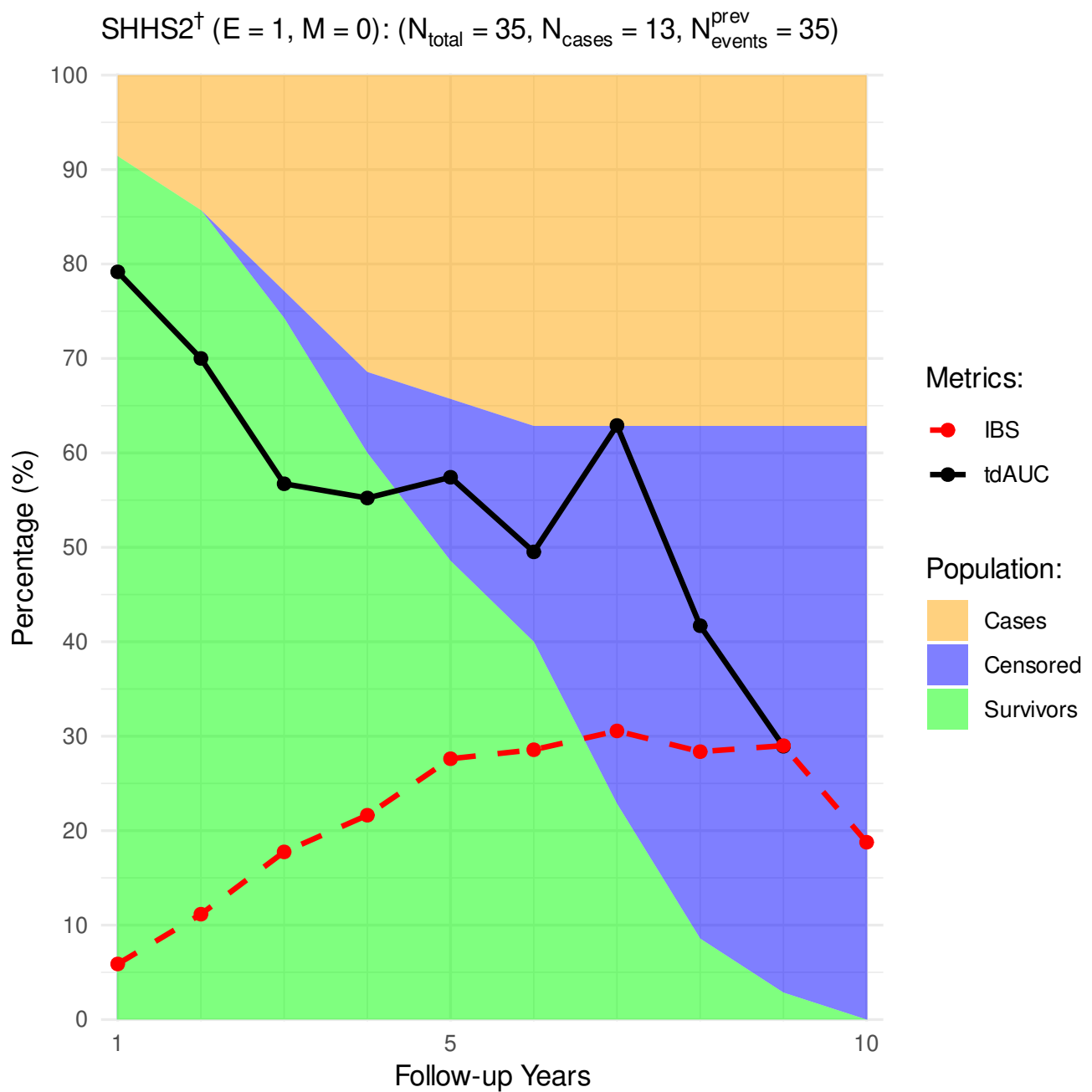


Figure 23. Distribution of cardiovascular cases, survivors, and censoring, as well as the performance metrics (time-dependent Area Under Receiver Operating Characteristic [tdAUROC] curve, Integrated Brier Score [IBS].)

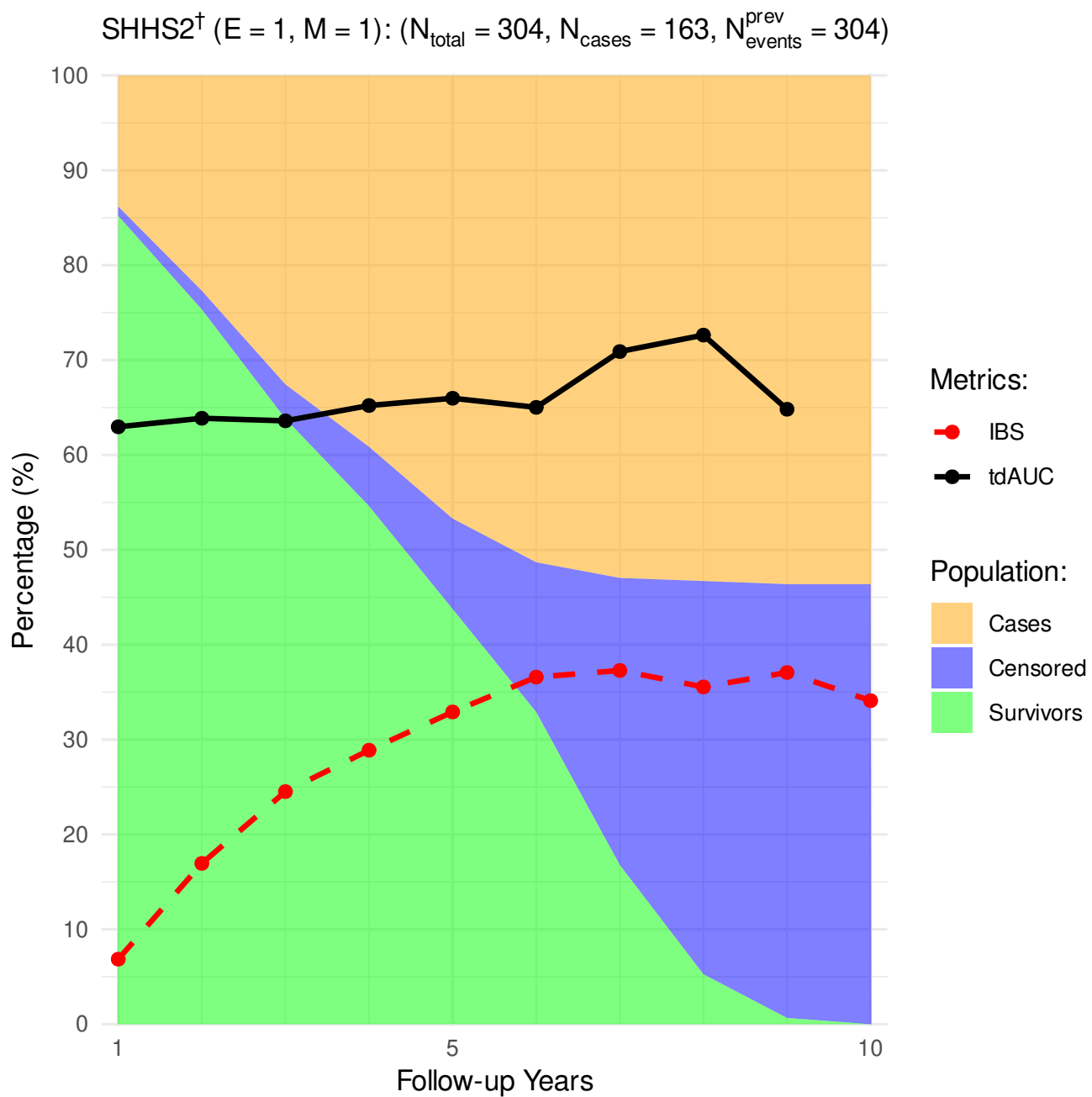


Figure 24. Distribution of cardiovascular cases, survivors, and censoring, as well as the performance metrics (time-dependent Area Under Receiver Operating Characteristic [tdAUROC] curve, Integrated Brier Score [IBS].)

8 Partial Effects for RSF without AHI predictor

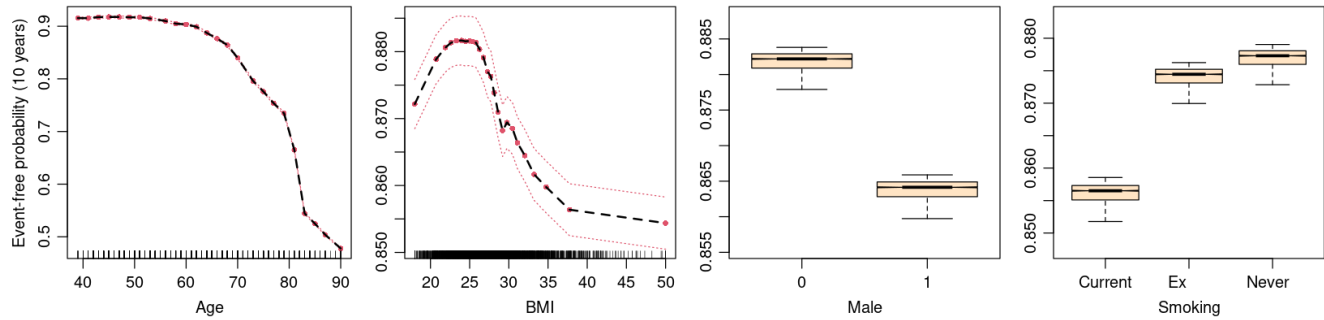


Figure 25. Partial effects and their 95% CIs for 10-year cardiovascular event-free probability for the age in years, Body Mass Index (BMI), Apnea-Hypopnea Index (AHI), gender (0 = female, 1 = male), and smoking status, for RSF without AHI predictor. Data points for continuous predictors are shown as ticks on the x-axis.

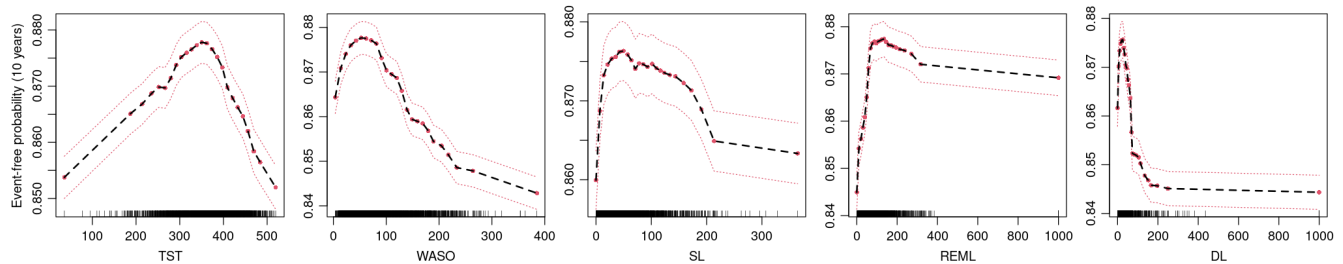


Figure 26. Partial effects and their 95% CIs for 10-year cardiovascular event-free probability for the minutes of Total Sleep Time (TST), Wake After Sleep Onset (WASO), Sleep Latency (SL), REM Latency (REM), and Deep-sleep Latency (DL), for RSF without AHI predictor. Data points are shown as ticks on the x-axis.

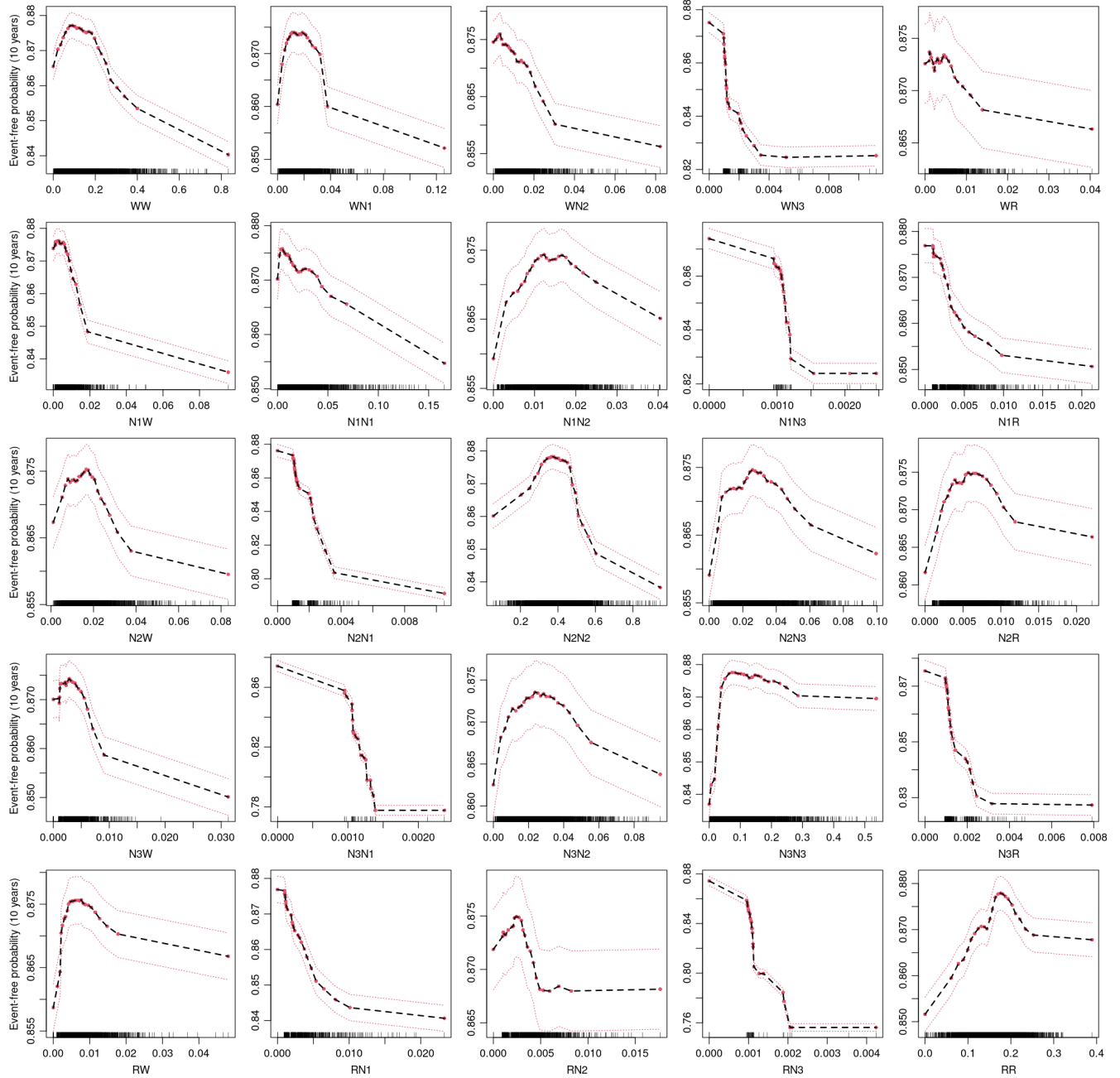


Figure 27. Partial effects and their 95% CIs for 10-year cardiovascular event-free probability for the relative frequencies of transitions between sleep-stage (W, N1, N2, N3, REM), for RSF without AHI predictor. Each subplot's x-axis label indicates the transition's direction (e.g., WN1 corresponds to transitions from W to N1). Data points are shown as ticks on the x-axis.

9 Robustness of partial effects related to cardiovascular risk

9.1 Leave-one-fold robustness validation

PDP Robustness: Baseline Variables

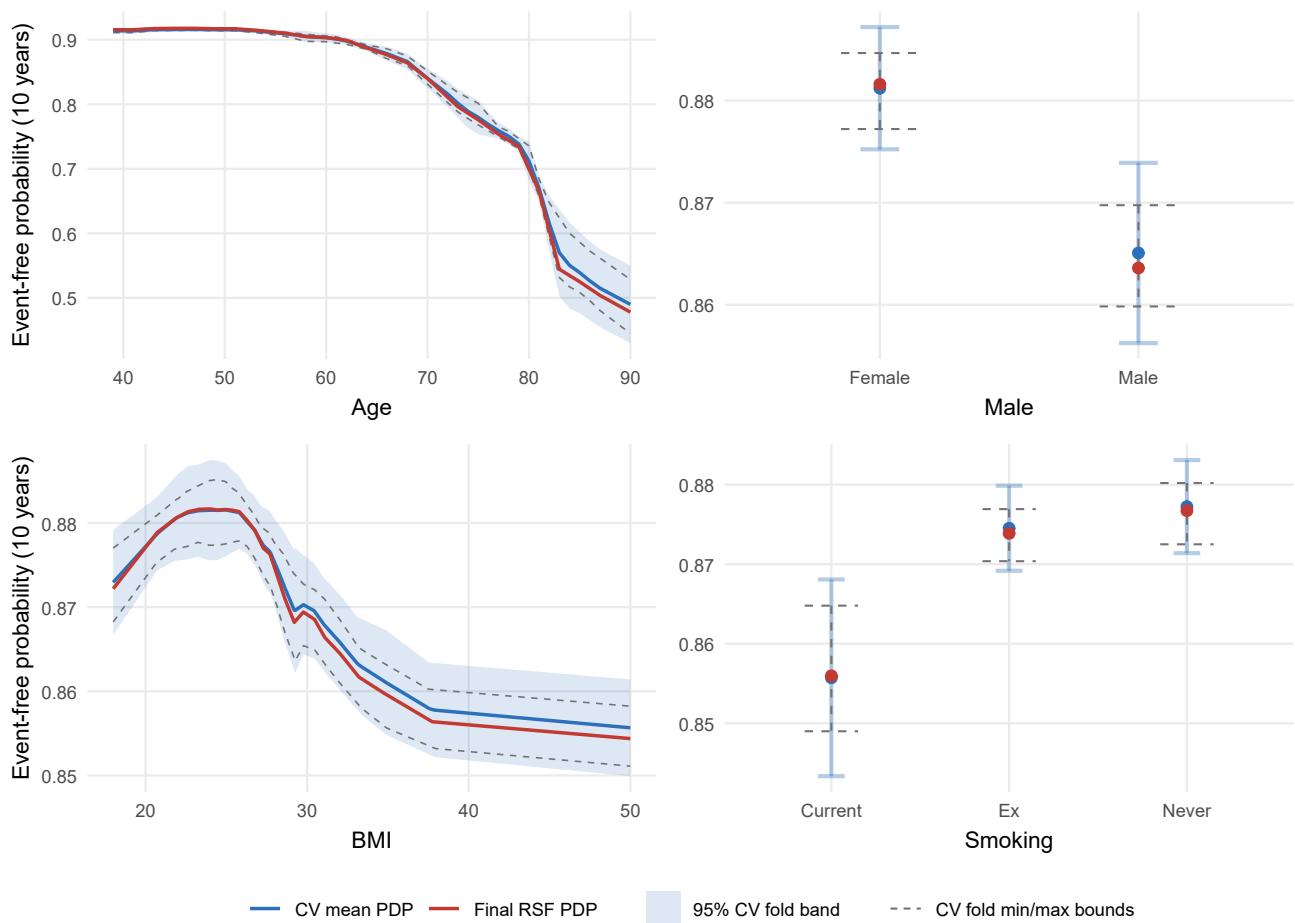


Figure 28. Leave-one-fold robustness of partial dependence effects for baseline variables.

PDP Robustness: Sleep Macrostructure

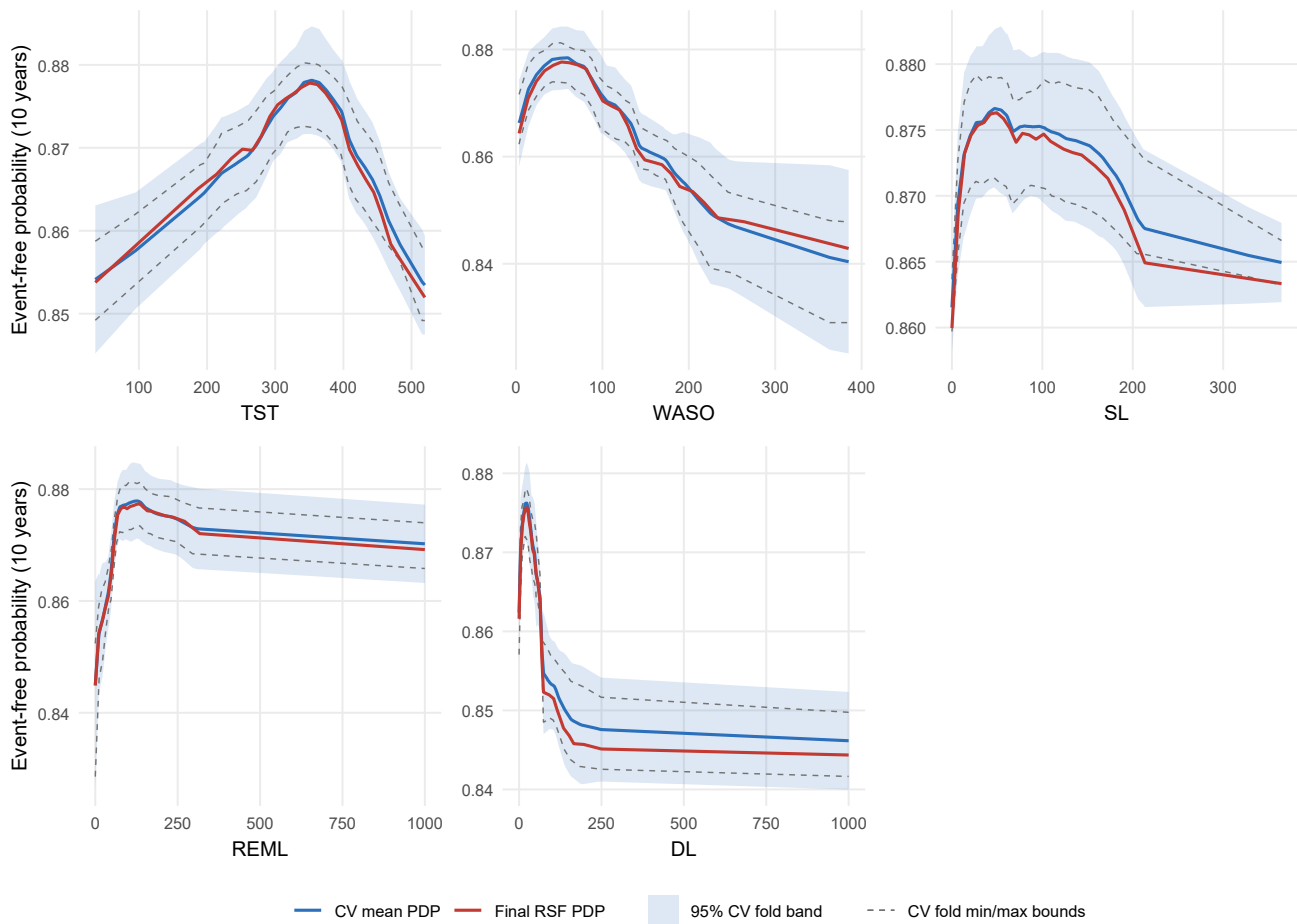


Figure 29. Leave-one-fold robustness of partial dependence effects for sleep macro-structure variables.

PDP Robustness: Sleep Dynamics

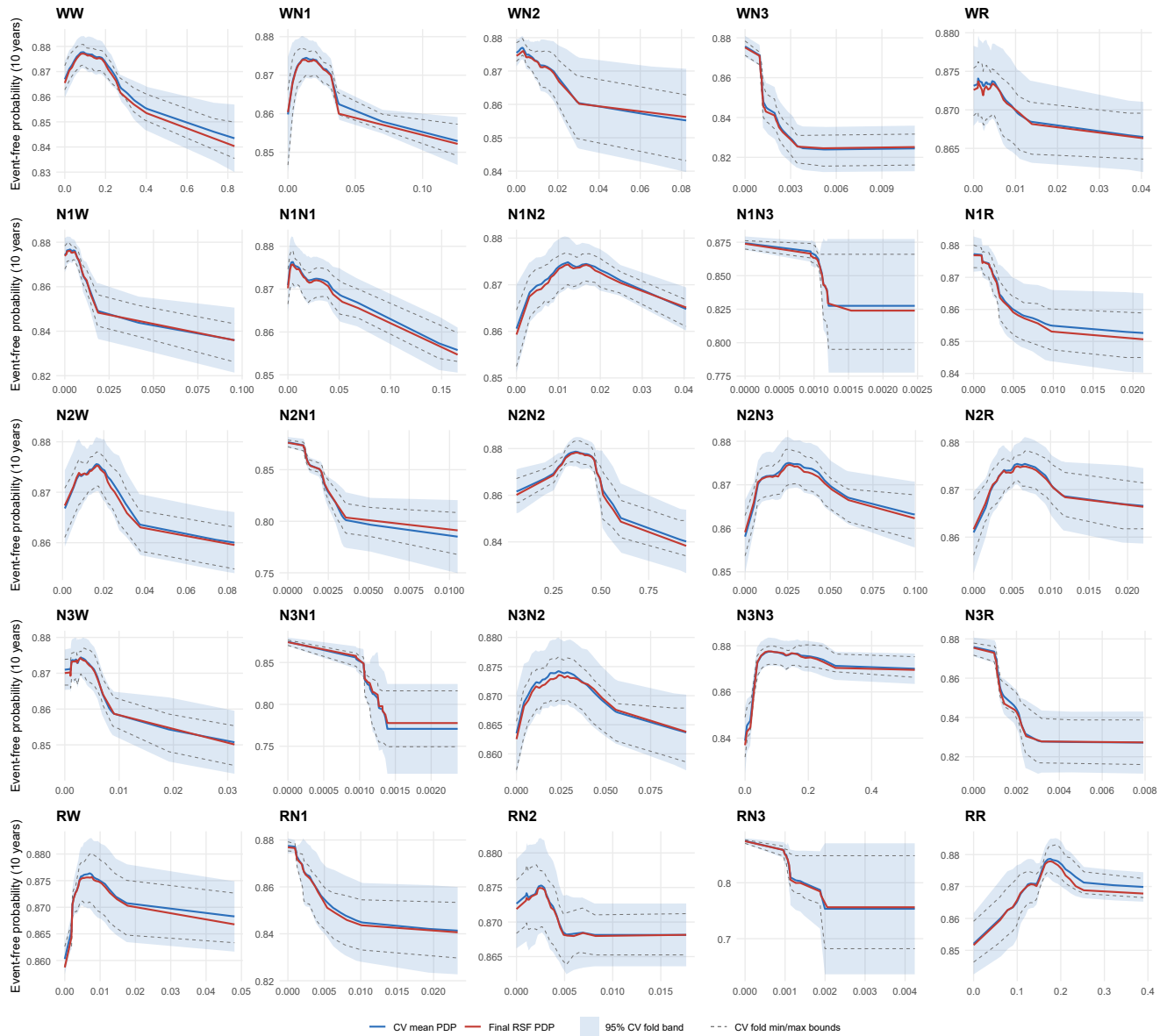


Figure 30. Leave-one-fold robustness of partial dependence effects for sleep-stage dynamics variables.

9.2 Accumulated Local Effects (ALE)

9.2.1 ALE - overall

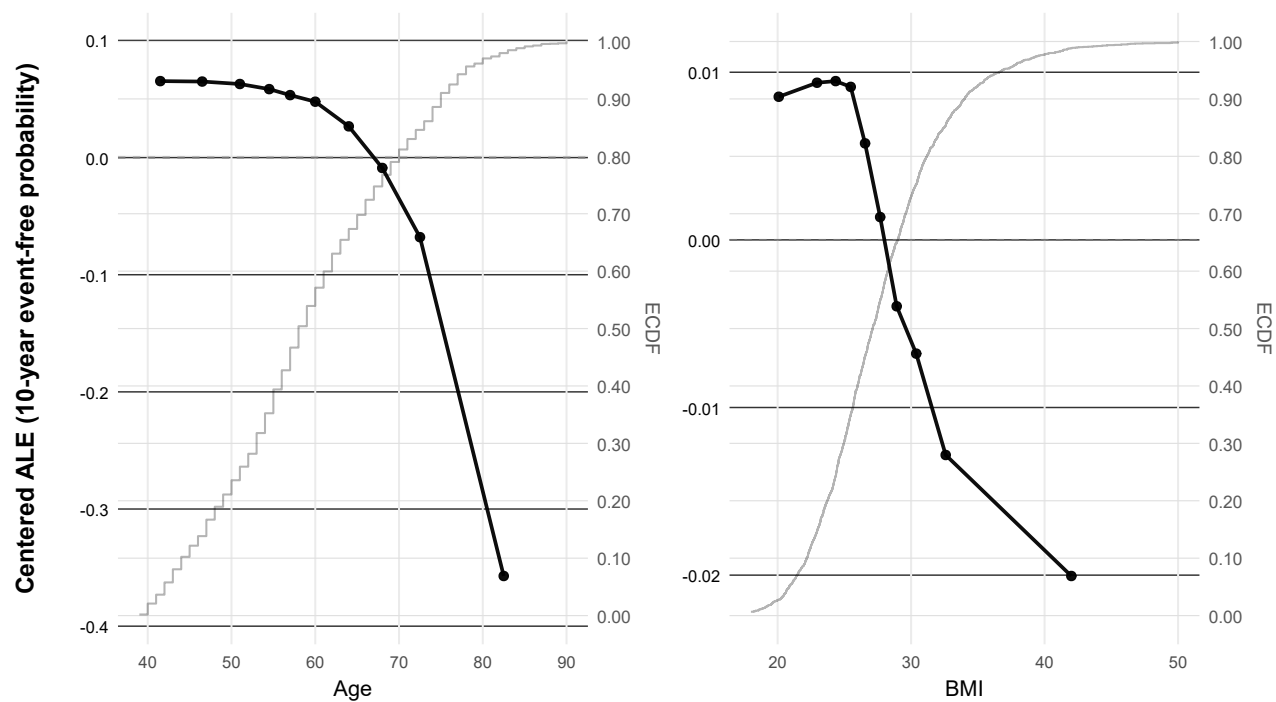


Figure 31. Overall accumulated local effects for baseline variables in the final RSF model.

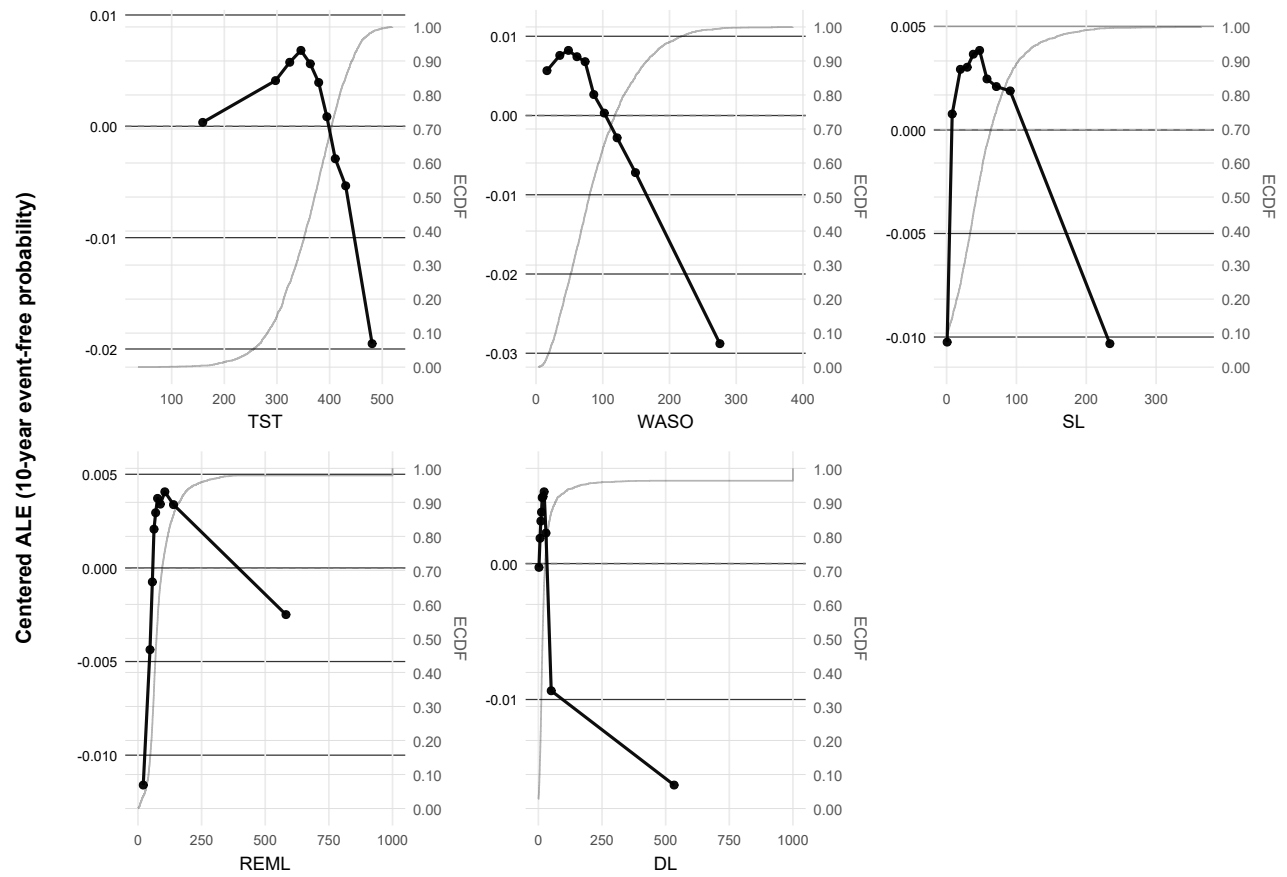


Figure 32. Overall accumulated local effects for sleep macrostructure variables in the final RSF model.

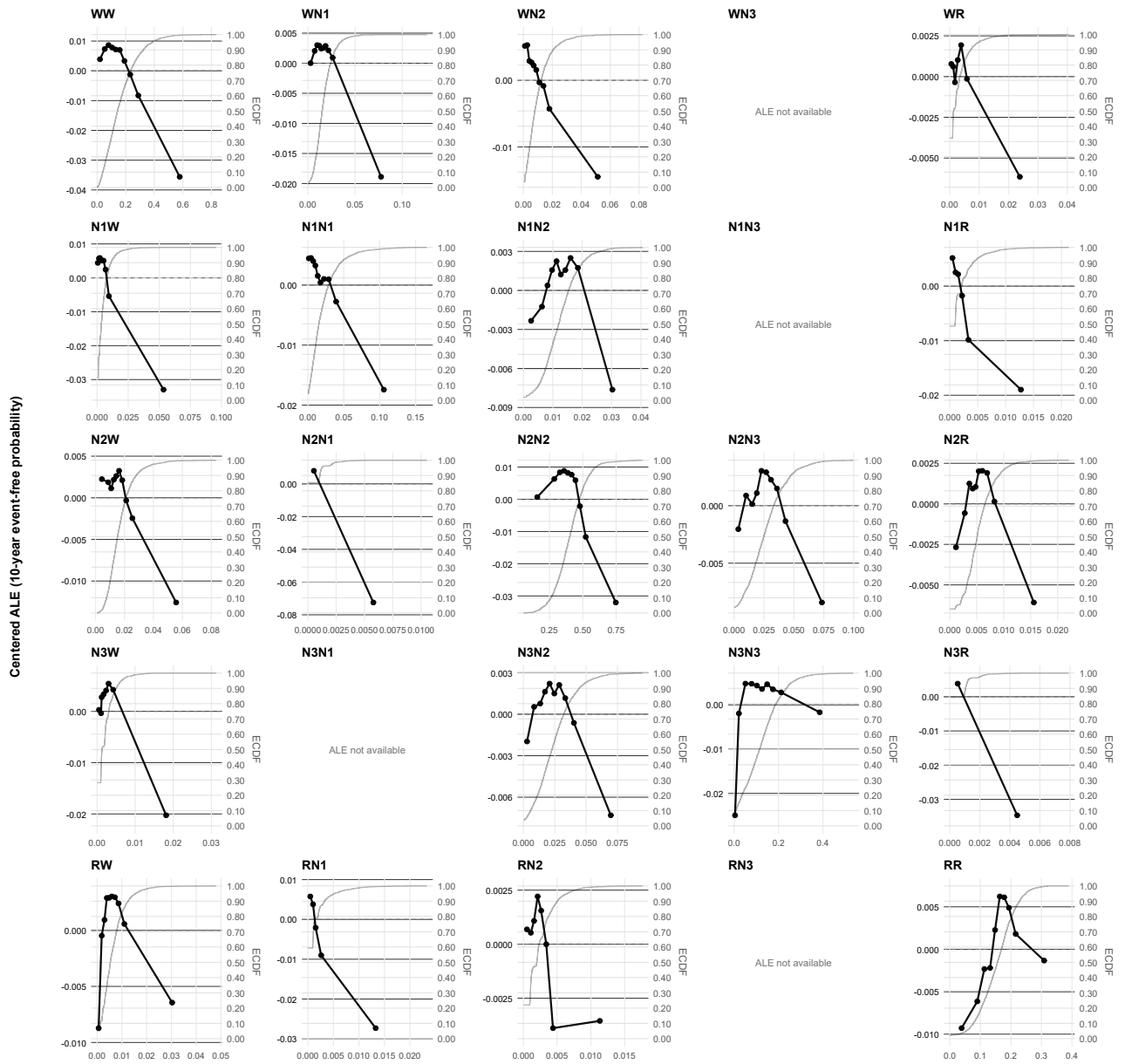


Figure 33. Overall accumulated local effects for sleep dynamics variables in the final RSF model.

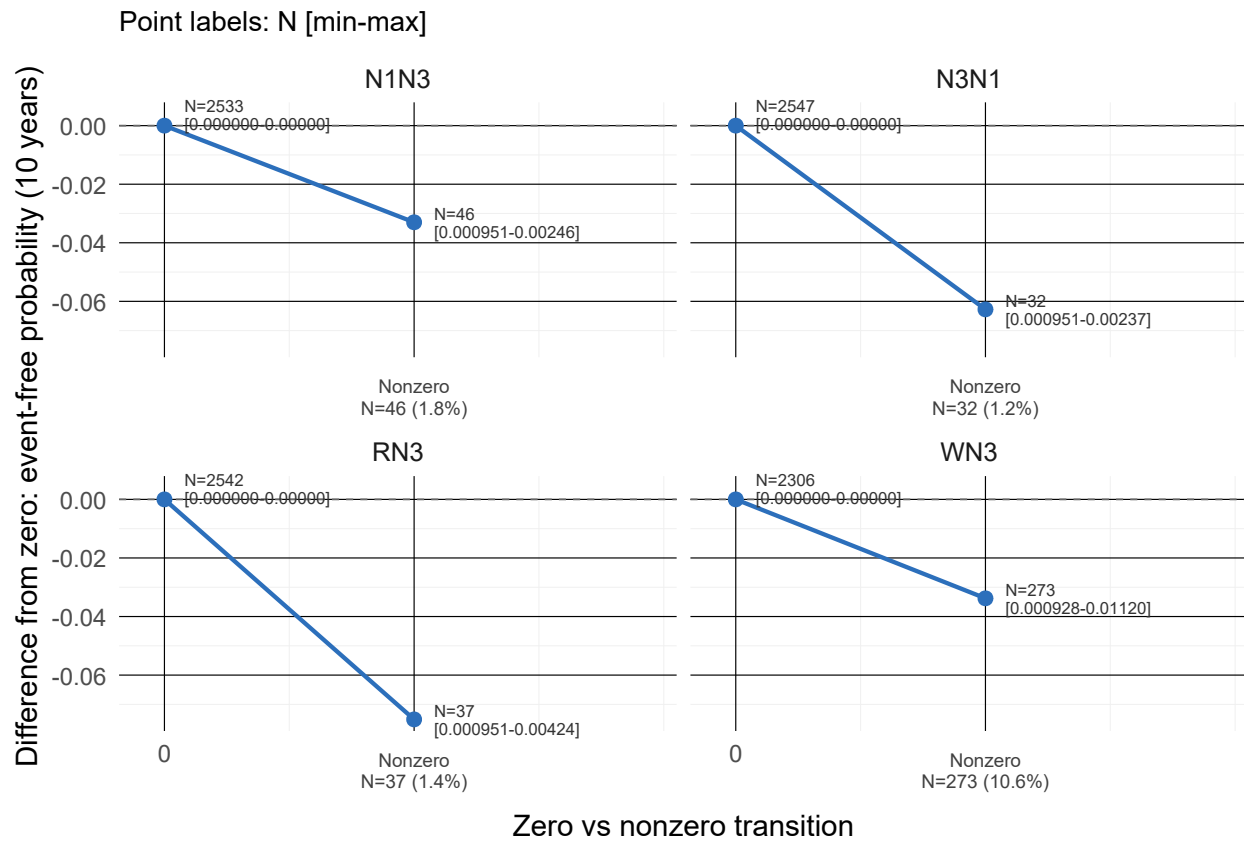


Figure 34. Overall model-based zero-versus-nonzero contrasts for sparse sleep-stage dynamics variables.

9.2.2 ALE - conditional on age

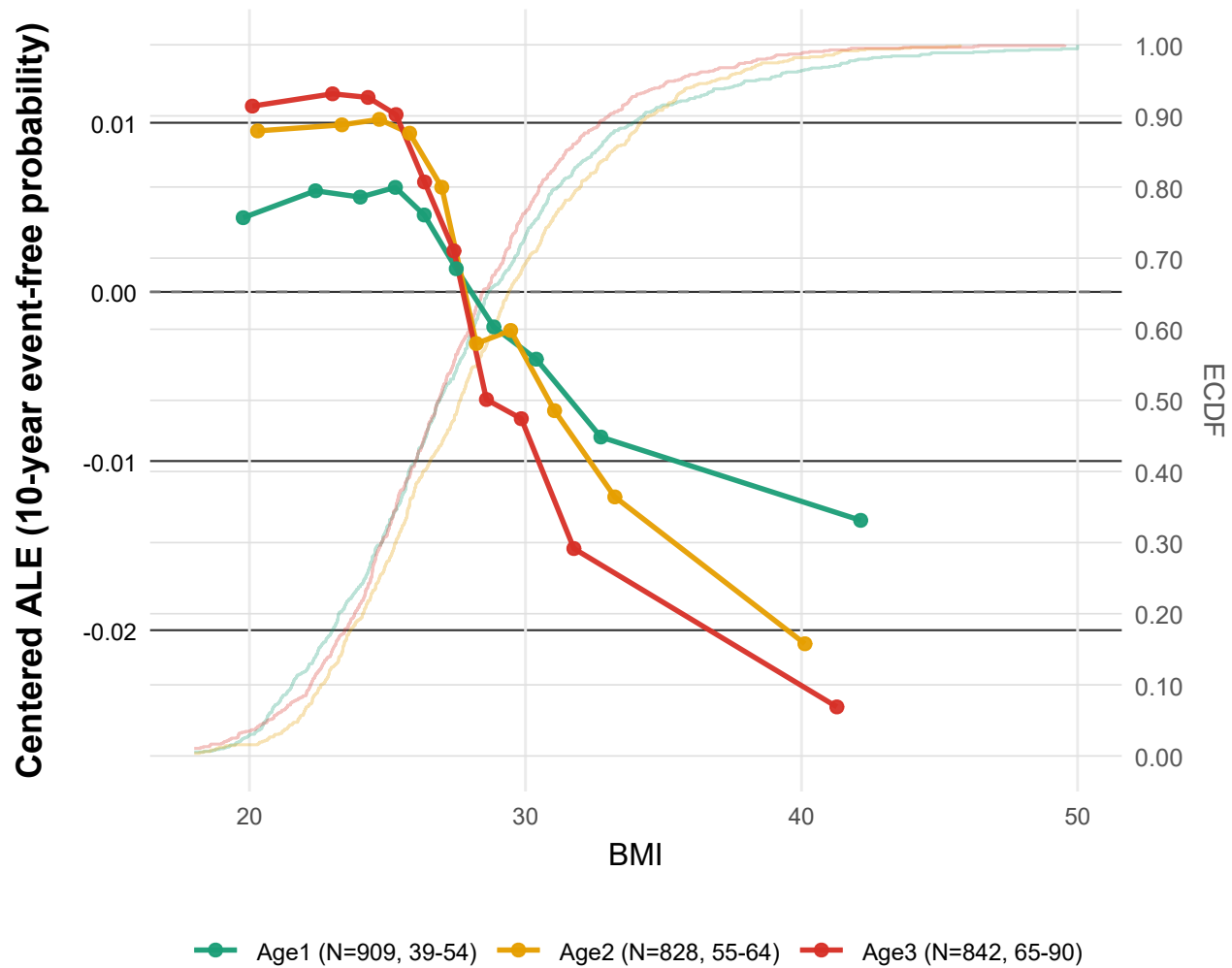


Figure 35. Accumulated local effects of BMI conditional on age in the final RSF model.

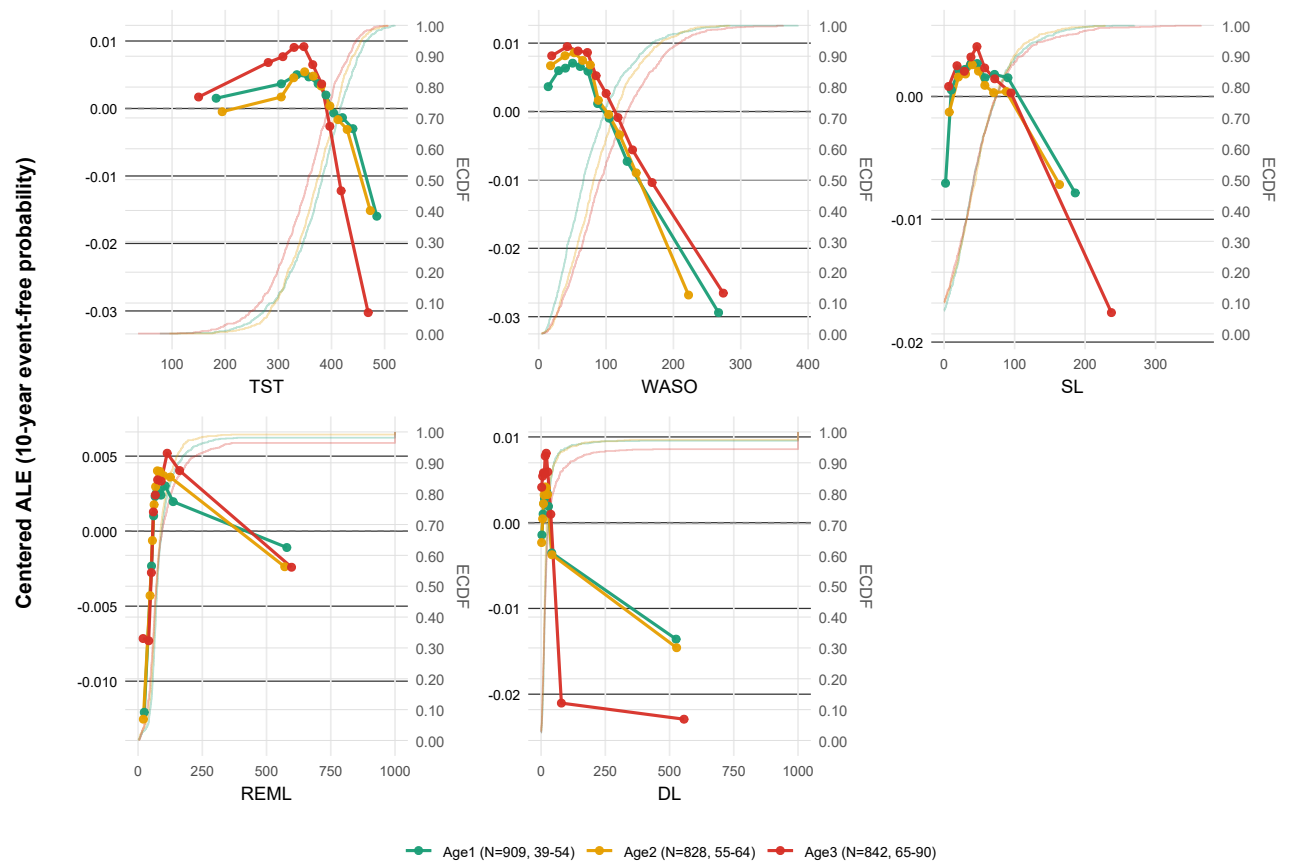


Figure 36. Accumulated local effects conditional on age for sleep macrostructure variables in the final RSF model.

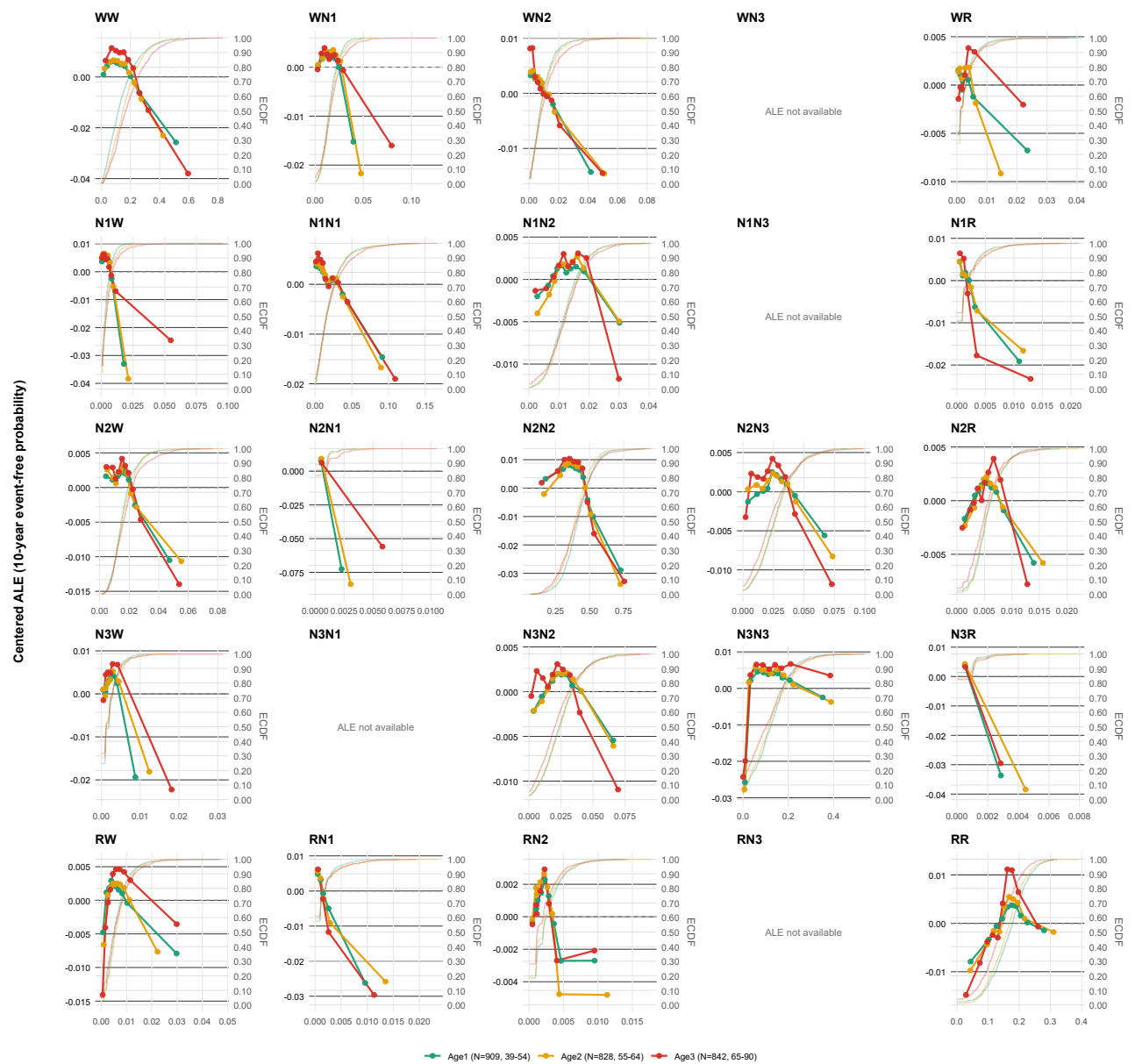


Figure 37. Accumulated local effects conditional on age for sleep-stage dynamics variables in the final RSF model.

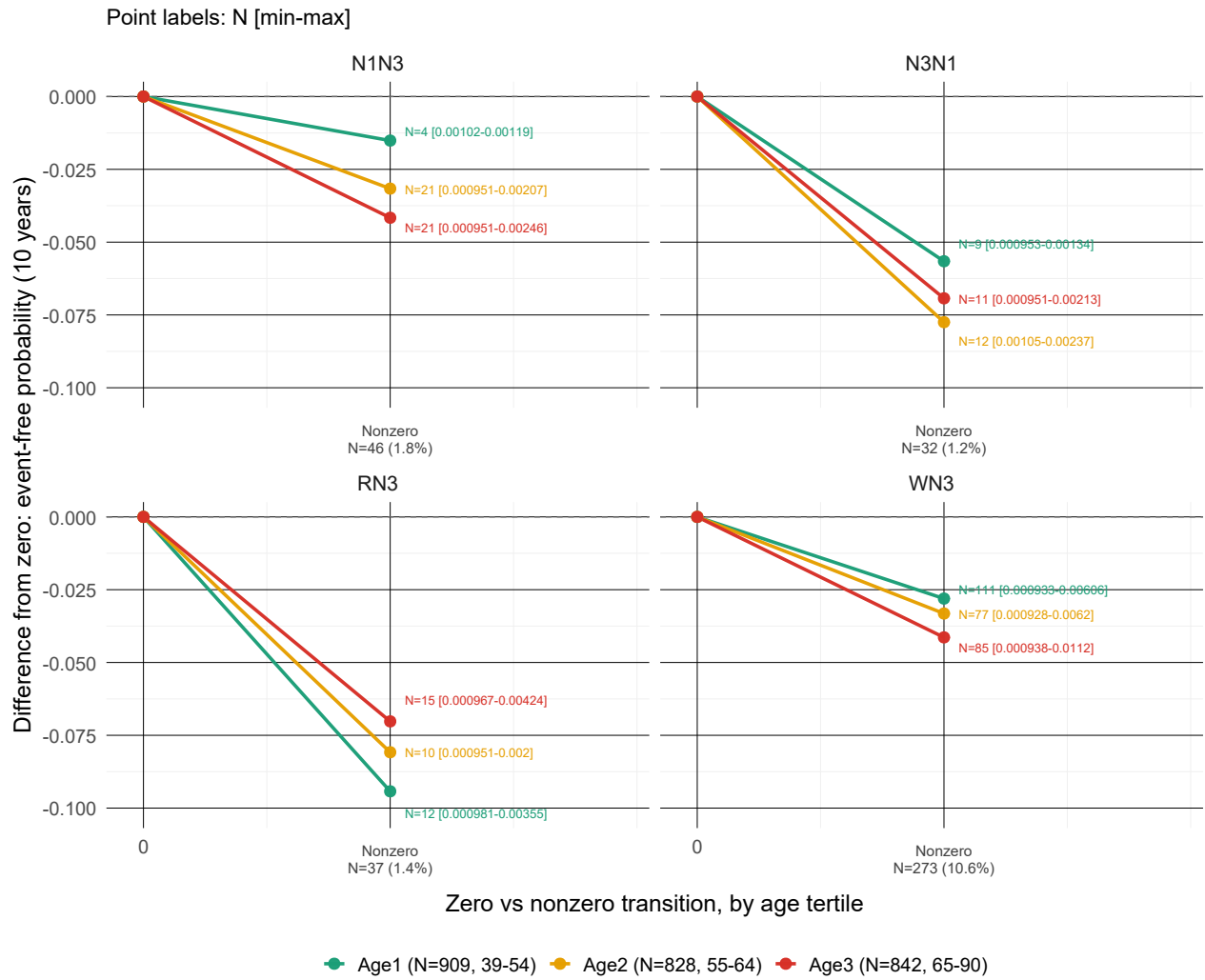


Figure 38. Model-based zero-versus-nonzero contrasts conditional on age for sparse sleep-stage dynamics variables.

9.2.3 ALE - conditional on BMI

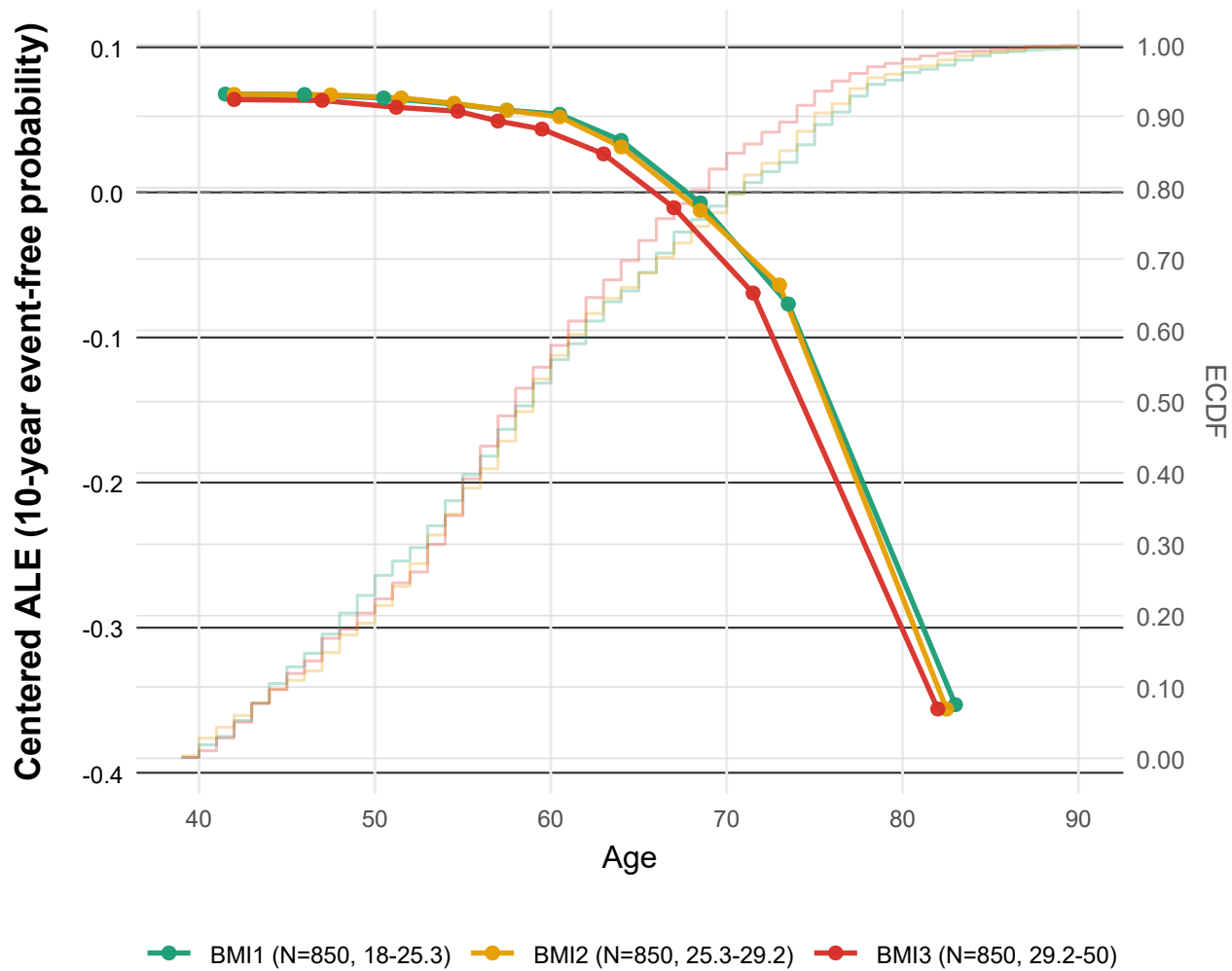


Figure 39. Accumulated local effects of age conditional on BMI in the final RSF model.

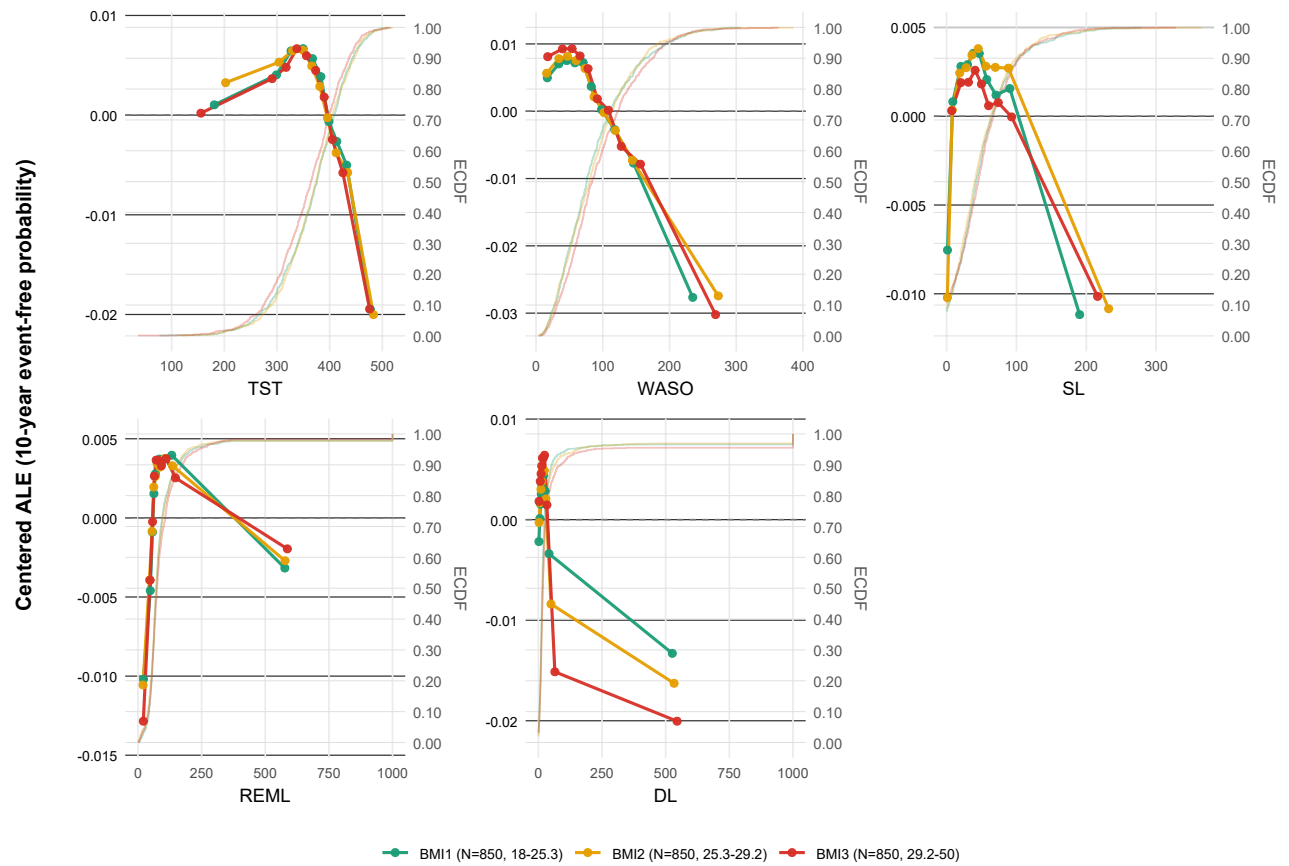


Figure 40. Accumulated local effects conditional on BMI for sleep macrostructure variables in the final RSF model.

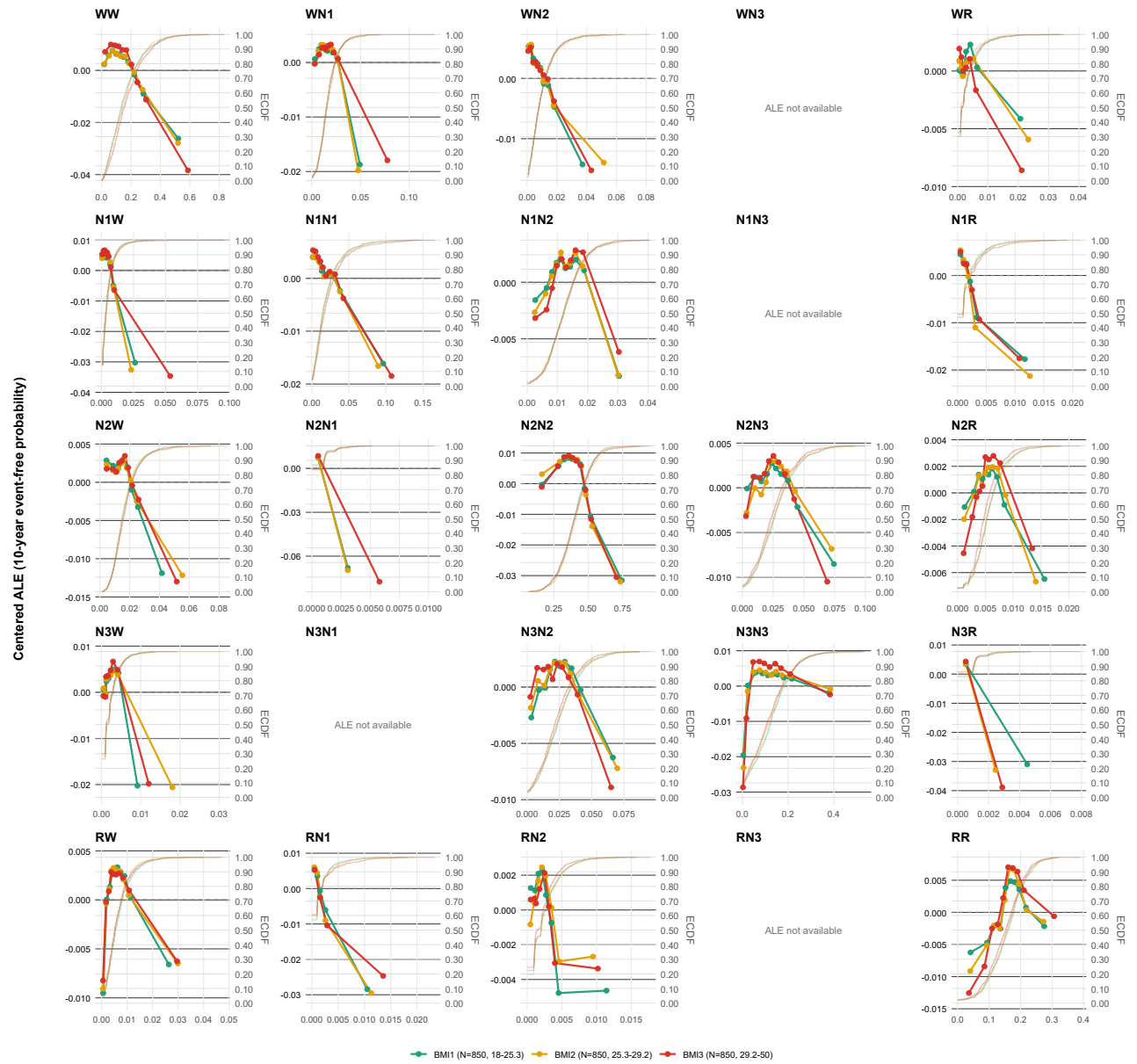


Figure 41. Accumulated local effects conditional on BMI for sleep-stage dynamics variables in the final RSF model.

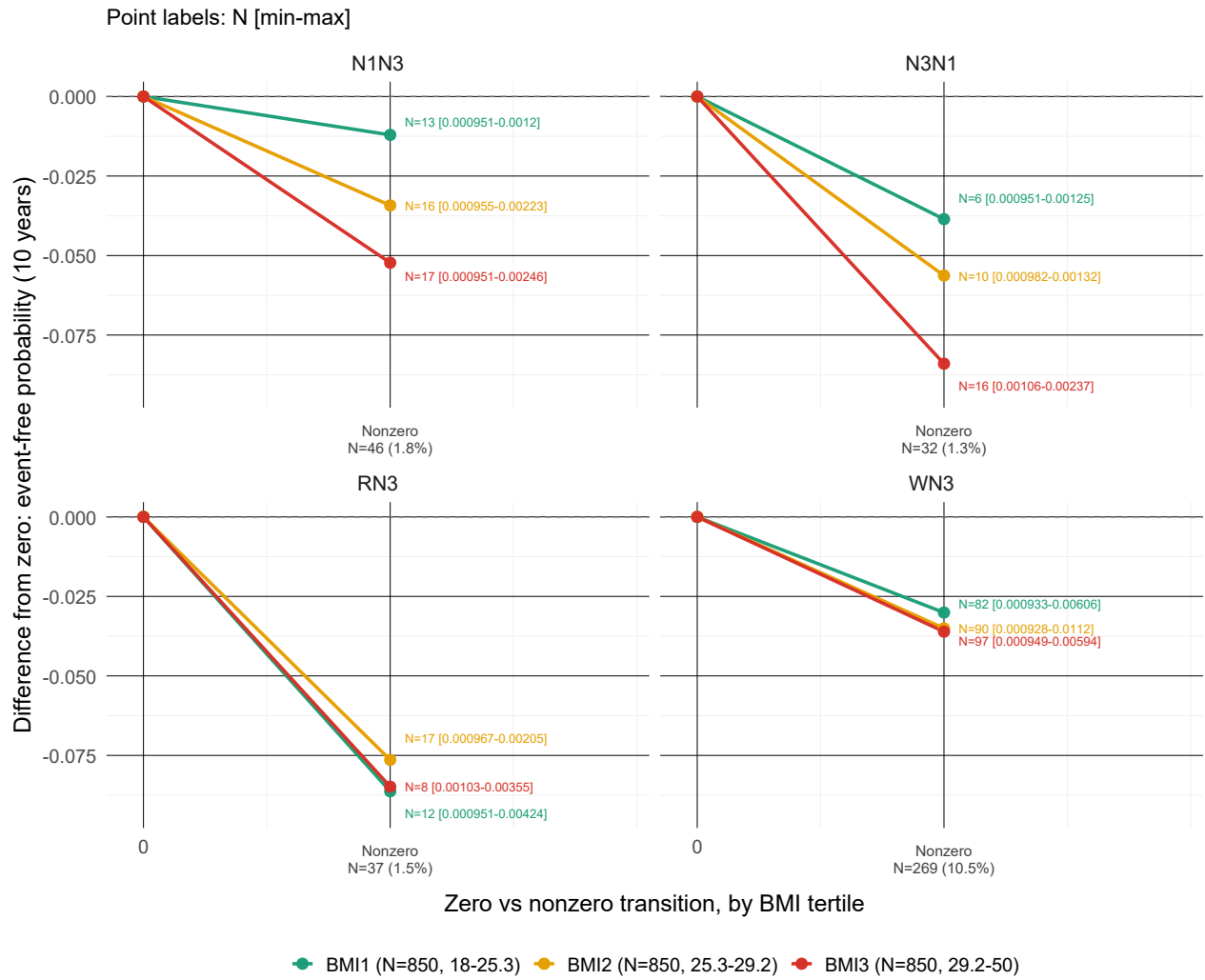


Figure 42. Model-based zero-versus-nonzero contrasts conditional on BMI for sparse sleep-stage dynamics variables.