Appendix 1

Detailed simulation results

Table 1. Parameter estimates and simulation measures for classical mediation approach with AFT model (continuous exposure, continuous mediator)

N	Hazard	Censoring (%)	ab	c-c'	ab-(c-c')	ab	c-c'	ab	c-c'	ab	c-c'
			Estimates			Absolute bias		% bias		MSE	
250	Increasing	NC	0.363	0.363	0.001	0.003	0.003	0.705	0.928	0.006	0.010
		40	0.372	0.329	0.043	0.012	0.031	3.429	-8.539	0.020	0.028
		90	0.684	0.713	0.029	0.324	0.353	89.923	98.041	46.124	184.684
	Constant	NC	0.362	0.363	0.001	0.002	0.003	0.654	0.845	0.007	0.012
		40	0.371	0.343	0.028	0.011	0.017	3.016	-4.835	0.022	0.025
		90	0.512	0.536	0.024	0.152	0.176	42.202	48.964	5.017	422.169
	Decreasing	NC	0.362	0.363	0.001	0.002	0.003	0.577	0.790	0.009	0.015
		40	0.369	0.345	0.024	0.009	0.015	2.588	-4.136	0.018	0.020
		90	0.367	0.360	0.007	0.007	0.000	2.038	-0.035	0.053	0.056
500	Increasing	NC	0.354	0.356	0.001	0.006	0.004	-1.534	-1.196	0.003	0.006
		40	0.369	0.322	0.047	0.009	0.038	2.573	-10.482	0.014	0.023
		90	0.373	0.077	0.297	0.013	0.283	3.747	-78.656	0.234	20.264
	Constant	NC	0.354	0.355	0.001	0.006	0.005	-1.546	-1.288	0.003	0.006
		40	0.367	0.335	0.032	0.007	0.025	1.957	-6.937	0.012	0.015
		90	0.329	0.171	0.158	0.031	0.189	-8.677	-52.564	2.804	25.445
	Decreasing	NC	0.354	0.355	0.001	0.006	0.005	-1.564	-1.335	0.004	0.007
		40	0.360	0.339	0.021	0.000	0.021	0.038	-5.820	0.013	0.012
		90	0.364	0.357	0.008	0.004	0.003	1.163	-0.923	0.023	0.022

1000	Increasing	NC	0.360	0.356	0.004	0.000	0.004	-0.107	-1.172	0.001	0.003
		40	0.368	0.320	0.048	0.008	0.040	2.206	-11.194	0.014	0.021
		90	0.353	0.339	0.014	0.007	0.021	-1.818	-5.763	0.004	0.005
	Constant	NC	0.359	0.355	0.004	0.001	0.005	-0.161	-1.322	0.002	0.003
		40	0.365	0.331	0.034	0.005	0.029	1.326	-8.058	0.007	0.010
		90	0.369	0.443	0.074	0.009	0.083	2.619	23.165	0.071	46.941
	Decreasing	NC	0.359	0.355	0.004	0.001	0.005	-0.241	-1.459	0.002	0.003
		40	0.360	0.340	0.020	0.000	0.020	0.010	-5.629	0.005	0.006
		90	0.369	0.366	0.003	0.009	0.006	2.377	1.539	0.015	0.016

Table 2. Parameter estimates and simulation measures for classical mediation approach with Cox model (continuous exposure, continuous mediator)

	Conditions		Estimates			Simulation measures					
						Absolute bias		% bias		MSE	
N	Hazard	Censoring (%)	ab	c-c'	ab-(c-c')	ab	c-c'	ab	c-c'	ab	c-c'
250	Increasing	NC	0.919	0.549	0.082	0.467	0.189	0.278	52.562	-77.187	0.052
		40	0.932	0.567	0.177	0.391	0.207	0.183	57.639	-50.860	0.100
		90	0.899	0.547	0.454	0.093	0.187	0.094	52.001	26.244	0.064
	Constant	NC	0.615	0.366	0.170	0.197	0.006	0.190	1.766	-52.866	0.008
		40	0.611	0.373	0.233	0.140	0.013	0.127	3.631	-35.335	0.023
		90	0.610	0.368	0.334	0.033	0.008	0.026	2.103	-7.154	0.024
	Decreasing	NC	0.414	0.244	0.169	0.075	0.116	0.191	-32.124	-53.091	0.018
		40	0.396	0.248	0.200	0.047	0.112	0.160	-31.200	-44.317	0.021
		90	0.403	0.246	0.235	0.011	0.114	0.125	-31.538	-34.642	0.033
500	Increasing	NC	0.899	0.534	0.078	0.457	0.174	0.282	48.414	-78.415	0.038
		40	0.943	0.561	0.163	0.399	0.201	0.197	55.962	-54.817	0.077
		90	0.873	0.540	0.453	0.087	0.180	0.093	50.083	25.929	0.048
	Constant	NC	0.597	0.356	0.166	0.190	0.004	0.194	-1.008	-53.858	0.004
		40	0.609	0.367	0.229	0.138	0.007	0.131	2.025	-36.295	0.011
		90	0.622	0.362	0.335	0.027	0.002	0.025	0.586	-7.037	0.010
	Decreasing	NC	0.396	0.237	0.166	0.072	0.123	0.194	-34.029	-53.894	0.017
		40	0.403	0.240	0.197	0.044	0.120	0.163	-33.224	-45.328	0.019
		90	0.419	0.245	0.235	0.010	0.115	0.125	-32.037	-34.831	0.022
1000	Increasing	NC	0.906	0.541	0.074	0.467	0.181	0.286	50.352	-79.469	0.036
		40	0.958	0.562	0.144	0.418	0.202	0.216	56.219	-59.952	0.076
		90	0.850	0.540	0.459	0.081	0.180	0.099	49.870	27.428	0.039
	Constant	NC	0.605	0.361	0.164	0.197	0.001	0.196	0.223	-54.517	0.002

	40	0.600	0.364	0.229	0.135	0.004	0.131	0.990	-36.477	0.008
	90	0.586	0.355	0.335	0.021	0.005	0.025	-1.342	-7.041	0.005
Decreasing	NC	0.404	0.240	0.165	0.076	0.120	0.195	-33.216	-54.254	0.015
	40	0.395	0.240	0.198	0.042	0.120	0.162	-33.338	-45.062	0.017
	90	0.385	0.246	0.240	0.006	0.114	0.120	-31.627	-33.399	0.019

Table 3. Parameter estimates and simulation measures for classical mediation approach with AFT model (continuous exposure, binary mediator)

| | Conditions | | Estimates | | | Simulation measures | | | | | |
| | | | | | | Absolute bias | | % bias | | MSE | |
N	Hazard	Censoring (%)	ab	c-c'	ab-(c-c')	ab	c-c'	ab	c-c'	ab	c-c'
250	Increasing	NC	0.365	0.083	0.283	0.005	0.277	1.476	-77.074	0.026	0.080
		40	0.299	0.058	0.241	0.061	0.302	-16.815	-83.775	0.032	0.094
		90	0.379	-0.182	0.560	0.019	0.542	5.180	-150.500	3.067	42.743
	Constant	NC	0.365	0.084	0.280	0.005	0.276	1.303	-76.600	0.029	0.079
		40	0.292	0.065	0.227	0.068	0.295	-18.840	-81.996	0.039	0.090
		90	0.479	-0.302	0.781	0.119	0.662	33.134	-183.904	4.769	279.622
	Decreasing	NC	0.364	0.085	0.279	0.004	0.275	1.043	-76.348	0.037	0.079
		40	0.303	0.074	0.230	0.057	0.286	-15.779	-79.531	0.048	0.085
		90	0.294	0.069	0.224	0.066	0.291	-18.463	-80.809	0.253	0.098
500	Increasing	NC	0.366	0.085	0.281	0.006	0.275	1.578	-76.377	0.014	0.077
		40	0.297	0.058	0.239	0.063	0.302	-17.518	-83.993	0.017	0.093
		90	0.230	0.020	0.210	0.130	0.340	-36.129	-94.419	0.618	0.491
	Constant	NC	0.367	0.087	0.280	0.007	0.273	2.001	-75.705	0.017	0.076
		40	0.287	0.063	0.224	0.073	0.297	-20.158	-82.482	0.020	0.089
		90	0.544	0.210	0.334	0.184	0.150	50.996	-41.719	18.594	33.298
	Decreasing	NC	0.369	0.089	0.280	0.009	0.271	2.635	-75.255	0.021	0.075
		40	0.286	0.069	0.217	0.074	0.291	-20.550	-80.749	0.025	0.086
		90	0.299	0.070	0.229	0.061	0.290	-16.957	-80.649	0.109	0.090
1000	Increasing	NC	0.358	0.083	0.275	0.002	0.277	-0.510	-76.929	0.008	0.077
		40	0.295	0.059	0.236	0.065	0.301	-18.108	-83.741	0.011	0.092
		90	0.243	0.053	0.190	0.117	0.307	-32.403	-85.191	0.040	0.095
	Constant	NC	0.359	0.085	0.274	0.001	0.275	-0.349	-76.324	0.009	0.076

	40	0.273	0.061	0.211	0.087	0.299	-24.254	-82.980	0.015	0.090
	90	0.373	-0.471	0.845	0.013	0.831	3.734	-230.961	1.583	89.889
Decreasing	NC	0.360	0.087	0.273	0.000	0.273	-0.109	-75.956	0.011	0.076
	40	0.286	0.070	0.217	0.074	0.290	-20.433	-80.637	0.015	0.085
	90	0.323	0.077	0.246	0.037	0.283	-10.293	-78.592	0.054	0.083

Table 4. Parameter estimates and simulation measures for classical mediation approach with Cox model (continuous exposure, binary mediator)

| | Conditions | | Estimates | | | Simulation measures | | | | | |
| | | | | | | Absolute bias | | % bias | | MSE | |
N	Hazard	Censoring (%)	ab	c-c'	ab-(c-c')	ab	c-c'	ab	c-c'	ab	c-c'
250	Increasing	NC	0.553	0.001	0.553	0.193	0.359	53.730	-99.771	0.098	0.134
		40	0.457	0.024	0.433	0.097	0.336	26.855	-93.446	0.075	0.119
		90	0.398	0.075	0.323	0.038	0.285	10.581	-79.077	0.198	0.090
	Constant	NC	0.368	0.039	0.328	0.008	0.321	2.143	-89.096	0.030	0.105
		40	0.301	0.050	0.251	0.059	0.310	-16.374	-85.998	0.041	0.099
		90	0.297	0.061	0.236	0.063	0.299	-17.465	-83.030	0.135	0.095
	Decreasing	NC	0.245	0.041	0.203	0.115	0.319	-32.021	-88.506	0.030	0.103
		40	0.208	0.045	0.163	0.152	0.315	-42.114	-87.397	0.044	0.100
		90	0.194	0.044	0.149	0.166	0.316	-46.237	-87.661	0.132	0.105
500	Increasing	NC	0.552	0.003	0.549	0.192	0.357	53.247	-99.185	0.070	0.130
		40	0.452	0.024	0.428	0.092	0.336	25.440	-93.445	0.039	0.116
		90	0.378	0.078	0.300	0.018	0.282	4.944	-78.277	0.087	0.083
	Constant	NC	0.369	0.042	0.328	0.009	0.318	2.616	-88.443	0.017	0.103
		40	0.294	0.048	0.245	0.066	0.312	-18.381	-86.545	0.020	0.098
		90	0.293	0.065	0.227	0.067	0.295	-18.688	-81.853	0.061	0.090
	Decreasing	NC	0.248	0.044	0.204	0.112	0.316	-31.115	-87.868	0.022	0.101
		40	0.196	0.043	0.153	0.164	0.317	-45.604	-88.010	0.036	0.101
		90	0.200	0.046	0.154	0.160	0.314	-44.362	-87.243	0.070	0.101
1000	Increasing	NC	0.539	0.002	0.538	0.179	0.358	49.811	-99.526	0.050	0.130
		40	0.447	0.026	0.422	0.087	0.334	24.249	-92.896	0.024	0.113
		90	0.370	0.078	0.291	0.010	0.282	2.766	-78.199	0.061	0.082
	Constant	NC	0.360	0.040	0.320	0.000	0.320	0.069	-88.814	0.009	0.103

	40	0.279	0.048	0.231	0.081	0.312	-22.633	-86.796	0.014	0.098
	90	0.261	0.060	0.201	0.099	0.300	-27.530	-83.266	0.044	0.092
Decreasing	NC	0.241	0.042	0.198	0.119	0.318	-33.131	-88.211	0.019	0.101
	40	0.196	0.044	0.152	0.164	0.316	-45.552	-87.872	0.032	0.100
	90	0.215	0.051	0.164	0.145	0.309	-40.248	-85.906	0.044	0.097

Table 5. Parameter estimates and simulation measures for classical mediation approach with AFT model (binary exposure, continuous mediator)

N	Hazard	Censoring (%)	ab	c-c'	ab-(c-c')	ab	c-c'	ab	c-c'	ab	c-c'
	Conditions		Estimates			Simulation measures					
						Absolute bias		% bias		MSE	
250	Increasing	NC	0.358	0.358	0.000	0.002	0.002	-0.463	-0.601	0.007	0.012
		40	0.320	0.261	0.059	0.040	0.099	-11.024	-27.490	0.008	0.019
		90	0.389	0.194	0.195	0.029	0.166	8.057	-46.234	0.286	24.536
	Constant	NC	0.358	0.357	0.001	0.002	0.003	-0.449	-0.741	0.007	0.013
		40	0.308	0.277	0.031	0.052	0.083	-14.559	-23.109	0.009	0.015
		90	0.567	-1.145	1.712	0.207	1.505	57.556	-417.935	46.046	1091.328
	Decreasing	NC	0.358	0.357	0.001	0.002	0.003	-0.428	-0.842	0.009	0.015
		40	0.318	0.300	0.018	0.042	0.060	-11.575	-16.677	0.012	0.015
		90	0.367	0.366	0.000	0.007	0.006	1.816	1.703	0.048	0.053
500	Increasing	NC	0.362	0.360	0.002	0.002	0.000	0.424	-0.042	0.003	0.006
		40	0.316	0.257	0.059	0.044	0.103	-12.245	-28.670	0.005	0.015
		90	0.370	2.057	1.687	0.010	1.697	2.800	471.465	0.200	1417.884
	Constant	NC	0.361	0.359	0.002	0.001	0.001	0.405	-0.140	0.004	0.007
		40	0.307	0.275	0.032	0.053	0.085	-14.828	-23.675	0.007	0.012
		90	0.513	-0.109	0.623	0.153	0.469	42.593	-130.384	11.135	236.982
	Decreasing	NC	0.361	0.359	0.002	0.001	0.001	0.376	-0.225	0.005	0.008
		40	0.312	0.297	0.015	0.048	0.063	-13.432	-17.592	0.007	0.009
		90	0.347	0.344	0.003	0.013	0.016	-3.568	-4.409	0.022	0.022
1000	Increasing	NC	0.361	0.362	0.000	0.001	0.002	0.318	0.439	0.002	0.003
		40	0.316	0.259	0.057	0.044	0.101	-12.353	-28.068	0.004	0.012
		90	0.344	0.351	0.007	0.016	0.009	-4.402	-2.521	0.004	0.005
	Constant	NC	0.361	0.361	0.000	0.001	0.001	0.282	0.295	0.002	0.004

	40	0.312	0.278	0.034	0.048	0.082	-13.377	-22.719	0.004	0.009
	90	0.361	0.451	0.091	0.001	0.091	0.151	25.317	0.543	49.483
Decreasing	NC	0.361	0.361	0.000	0.001	0.001	0.229	0.151	0.003	0.004
	40	0.314	0.298	0.016	0.046	0.062	-12.832	-17.175	0.005	0.007
	90	0.357	0.356	0.001	0.003	0.004	-0.794	-1.104	0.011	0.011

Table 6. Parameter estimates and simulation measures for classical mediation approach with Cox model (binary exposure, continuous mediator)

| | Conditions | | Estimates | | | Simulation measures | | | | | |
| | | | | | | Absolute bias | | % bias | | MSE | |
N	Hazard	Censoring (%)	ab	c-c'	ab-(c-c')	ab	c-c'	ab	c-c'	ab	c-c'
250	Increasing	NC	0.543	0.075	0.468	0.183	0.285	50.700	-79.243	0.049	0.096
		40	0.491	0.183	0.307	0.131	0.177	36.253	-49.037	0.031	0.046
		90	0.556	0.513	0.043	0.196	0.153	54.499	42.543	0.072	0.062
	Constant	NC	0.362	0.165	0.197	0.002	0.195	0.449	-54.156	0.008	0.046
		40	0.317	0.219	0.099	0.043	0.141	-11.848	-39.246	0.009	0.027
		90	0.365	0.349	0.016	0.005	0.011	1.466	-3.079	0.022	0.023
	Decreasing	NC	0.241	0.166	0.076	0.119	0.194	-32.929	-53.961	0.019	0.042
		40	0.221	0.186	0.035	0.139	0.174	-38.668	-48.396	0.024	0.035
		90	0.246	0.239	0.007	0.114	0.121	-31.692	-33.518	0.032	0.034
500	Increasing	NC	0.545	0.078	0.468	0.185	0.282	51.486	-78.382	0.043	0.087
		40	0.480	0.183	0.296	0.120	0.177	33.219	-49.109	0.022	0.038
		90	0.538	0.509	0.029	0.178	0.149	49.403	41.266	0.046	0.037
	Constant	NC	0.364	0.167	0.196	0.004	0.193	0.987	-53.488	0.004	0.041
		40	0.315	0.217	0.098	0.045	0.143	-12.426	-39.585	0.006	0.024
		90	0.358	0.338	0.019	0.002	0.022	-0.687	-5.998	0.011	0.012
	Decreasing	NC	0.242	0.168	0.075	0.118	0.192	-32.644	-53.437	0.016	0.039
		40	0.215	0.185	0.031	0.145	0.175	-40.194	-48.709	0.023	0.033
		90	0.235	0.230	0.006	0.125	0.130	-34.662	-36.227	0.025	0.026
1000	Increasing	NC	0.544	0.077	0.467	0.184	0.283	51.159	-78.637	0.038	0.084
		40	0.479	0.187	0.292	0.119	0.173	32.950	-48.031	0.018	0.033
		90	0.530	0.499	0.031	0.170	0.139	47.263	38.724	0.036	0.027
	Constant	NC	0.363	0.167	0.195	0.003	0.193	0.781	-53.498	0.002	0.039

	40	0.321	0.219	0.101	0.039	0.141	-10.921	-39.050	0.003	0.022
	90	0.355	0.341	0.014	0.005	0.019	-1.482	-5.309	0.005	0.006
Decreasing	NC	0.242	0.168	0.074	0.118	0.192	-32.828	-53.347	0.015	0.038
	40	0.217	0.186	0.030	0.143	0.174	-39.849	-48.308	0.022	0.031
	90	0.238	0.233	0.004	0.122	0.127	-33.935	-35.184	0.019	0.020

Table 7. Parameter estimates and simulation measures for classical mediation approach with AFT model (binary exposure, binary mediator)

	Conditions		Estimates			Simulation measures					
						Absolute bias		% bias		MSE	
N	Hazard	Censoring (%)	ab	c-c'	ab-(c-c')	ab	c-c'	ab	c-c'	ab	c-c'
250	Increasing	NC	0.354	0.076	0.278	0.006	0.284	-1.747	-78.964	0.027	0.083
		40	0.153	0.026	0.126	0.207	0.334	-57.564	-92.697	0.062	0.113
		90	0.070	0.151	0.081	0.290	0.209	-80.658	-58.182	3.719	6.265
	Constant	NC	0.353	0.079	0.274	0.007	0.281	-1.957	-78.176	0.031	0.082
		40	0.164	0.040	0.124	0.196	0.320	-54.580	-88.916	0.060	0.104
		90	0.139	-0.796	0.934	0.221	1.156	-61.483	-320.999	5.355	216.572
	Decreasing	NC	0.352	0.080	0.272	0.008	0.280	-2.272	-77.730	0.039	0.082
		40	0.189	0.048	0.141	0.171	0.312	-47.515	-86.566	0.059	0.099
		90	0.182	0.047	0.135	0.178	0.313	-49.506	-86.869	0.234	0.110
500	Increasing	NC	0.370	0.080	0.290	0.010	0.280	2.885	-77.676	0.013	0.079
		40	0.156	0.027	0.129	0.204	0.333	-56.758	-92.547	0.052	0.112
		90	0.166	0.041	0.126	0.194	0.319	-53.841	-88.748	0.090	0.105
	Constant	NC	0.371	0.084	0.287	0.011	0.276	3.049	-76.734	0.015	0.077
		40	0.167	0.040	0.127	0.193	0.320	-53.698	-88.957	0.048	0.103
		90	0.173	-0.090	0.263	0.187	0.450	-51.828	-125.010	0.216	9.381
	Decreasing	NC	0.372	0.086	0.286	0.012	0.274	3.295	-76.133	0.019	0.077
		40	0.197	0.052	0.145	0.163	0.308	-45.181	-85.549	0.046	0.096
		90	0.235	0.060	0.175	0.125	0.300	-34.830	-83.305	0.146	0.098
1000	Increasing	NC	0.355	0.077	0.279	0.005	0.283	-1.257	-78.677	0.007	0.081
		40	0.151	0.026	0.126	0.209	0.334	-57.965	-92.854	0.051	0.112
		90	0.191	0.047	0.143	0.169	0.313	-47.039	-86.880	0.068	0.100
	Constant	NC	0.356	0.080	0.276	0.004	0.280	-1.197	-77.779	0.008	0.079

	40	0.170	0.042	0.128	0.190	0.318	-52.776	-88.386	0.043	0.102
	90	0.370	0.398	0.028	0.010	0.038	2.838	10.477	31.468	196.930
Decreasing	NC	0.356	0.082	0.274	0.004	0.278	-1.106	-77.201	0.010	0.078
	40	0.186	0.049	0.137	0.174	0.311	-48.312	-86.413	0.039	0.097
	90	0.247	0.062	0.185	0.113	0.298	-31.371	-82.852	0.076	0.093

Table 8. Parameter estimates and simulation measures for classical mediation approach with Cox model (binary exposure, binary mediator)

| | Conditions | | Estimates | | | Simulation measures | | | | | |
| | | | | | | Absolute bias | | % bias | | MSE | |
N	Hazard	Censoring (%)	ab	c-c'	ab-(c-c')	ab	c-c'	ab	c-c'	ab	c-c'
250	Increasing	NC	0.553	0.001	0.553	0.193	0.359	53.730	-99.771	0.098	0.134
		40	0.238	0.002	0.236	0.122	0.358	-33.840	-99.473	0.062	0.133
		90	0.281	0.064	0.217	0.079	0.296	-21.903	-82.246	0.162	0.097
	Constant	NC	0.357	0.037	0.319	0.003	0.323	-0.911	-89.611	0.032	0.106
		40	0.172	0.031	0.140	0.188	0.329	-52.268	-91.289	0.059	0.110
		90	0.223	0.054	0.169	0.137	0.306	-37.953	-85.032	0.143	0.101
	Decreasing	NC	0.237	0.039	0.198	0.123	0.321	-34.124	-89.106	0.033	0.104
		40	0.133	0.030	0.102	0.227	0.330	-63.128	-91.557	0.066	0.110
		90	0.126	0.032	0.094	0.234	0.328	-65.090	-91.139	0.146	0.113
500	Increasing	NC	0.558	0.006	0.552	0.198	0.354	54.957	-98.346	0.070	0.127
		40	0.242	0.003	0.239	0.118	0.357	-32.796	-99.051	0.040	0.129
		90	0.253	0.059	0.194	0.107	0.301	-29.689	-83.566	0.132	0.097
	Constant	NC	0.373	0.042	0.331	0.013	0.318	3.486	-88.371	0.015	0.102
		40	0.174	0.032	0.143	0.186	0.328	-51.655	-91.240	0.047	0.109
		90	0.202	0.049	0.153	0.158	0.311	-43.810	-86.316	0.099	0.101
	Decreasing	NC	0.249	0.043	0.206	0.111	0.317	-30.810	-88.118	0.021	0.101
		40	0.138	0.033	0.105	0.222	0.327	-61.669	-90.811	0.059	0.108
		90	0.157	0.039	0.118	0.203	0.321	-56.301	-89.028	0.099	0.106
1000	Increasing	NC	0.535	0.002	0.533	0.175	0.358	48.573	-99.553	0.047	0.130
		40	0.235	0.003	0.231	0.125	0.357	-34.855	-99.128	0.033	0.129
		90	0.292	0.070	0.222	0.068	0.290	-18.857	-80.578	0.097	0.089
	Constant	NC	0.357	0.039	0.318	0.003	0.321	-0.855	-89.264	0.009	0.104

	40	0.177	0.033	0.144	0.183	0.327	-50.748	-90.753	0.041	0.107
	90	0.184	0.046	0.138	0.176	0.314	-48.770	-87.164	0.094	0.102
Decreasing	NC	0.238	0.041	0.198	0.122	0.319	-33.831	-88.713	0.020	0.102
	40	0.130	0.031	0.099	0.230	0.329	-63.859	-91.265	0.057	0.108
	90	0.166	0.041	0.125	0.194	0.319	-53.781	-88.611	0.066	0.104

Table 8. Parameter estimates and simulation measures for classical mediation approach with Cox model (binary exposure, binary mediator)

| | Conditions | | Estimates | | | Simulation measures | | | | | |
| | | | | | | Absolute bias | | % bias | | MSE | |
N	Hazard	Censoring (%)	ab	c-c'	ab-(c-c')	ab	c-c'	ab	c-c'	ab	c-c'
250	Increasing	NC	0.553	0.001	0.553	0.193	0.359	53.730	-99.771	0.098	0.134
		40	0.238	0.002	0.236	0.122	0.358	-33.840	-99.473	0.062	0.133
		90	0.281	0.064	0.217	0.079	0.296	-21.903	-82.246	0.162	0.097
	Constant	NC	0.357	0.037	0.319	0.003	0.323	-0.911	-89.611	0.032	0.106
		40	0.172	0.031	0.140	0.188	0.329	-52.268	-91.289	0.059	0.110
		90	0.223	0.054	0.169	0.137	0.306	-37.953	-85.032	0.143	0.101
	Decreasing	NC	0.237	0.039	0.198	0.123	0.321	-34.124	-89.106	0.033	0.104
		40	0.133	0.030	0.102	0.227	0.330	-63.128	-91.557	0.066	0.110
		90	0.126	0.032	0.094	0.234	0.328	-65.090	-91.139	0.146	0.113
500	Increasing	NC	0.558	0.006	0.552	0.198	0.354	54.957	-98.346	0.070	0.127
		40	0.242	0.003	0.239	0.118	0.357	-32.796	-99.051	0.040	0.129
		90	0.253	0.059	0.194	0.107	0.301	-29.689	-83.566	0.132	0.097
	Constant	NC	0.373	0.042	0.331	0.013	0.318	3.486	-88.371	0.015	0.102
		40	0.174	0.032	0.143	0.186	0.328	-51.655	-91.240	0.047	0.109
		90	0.202	0.049	0.153	0.158	0.311	-43.810	-86.316	0.099	0.101
	Decreasing	NC	0.249	0.043	0.206	0.111	0.317	-30.810	-88.118	0.021	0.101
		40	0.138	0.033	0.105	0.222	0.327	-61.669	-90.811	0.059	0.108
		90	0.157	0.039	0.118	0.203	0.321	-56.301	-89.028	0.099	0.106
1000	Increasing	NC	0.535	0.002	0.533	0.175	0.358	48.573	-99.553	0.047	0.130
		40	0.235	0.003	0.231	0.125	0.357	-34.855	-99.128	0.033	0.129
		90	0.292	0.070	0.222	0.068	0.290	-18.857	-80.578	0.097	0.089
	Constant	NC	0.357	0.039	0.318	0.003	0.321	-0.855	-89.264	0.009	0.104

	40	0.177	0.033	0.144	0.183	0.327	-50.748	-90.753	0.041	0.107
	90	0.184	0.046	0.138	0.176	0.314	-48.770	-87.164	0.094	0.102
Decreasing	NC	0.238	0.041	0.198	0.122	0.319	-33.831	-88.713	0.020	0.102
	40	0.130	0.031	0.099	0.230	0.329	-63.859	-91.265	0.057	0.108
	90	0.166	0.041	0.125	0.194	0.319	-53.781	-88.611	0.066	0.104

Table 9. Parameter estimates and simulation measures for potential outcomes mediation approach with AFT model (continuous exposure, continuous mediator)

	Conditions		Estimates		Simulation measures		
N	Hazard	Censoring (%)	NDE	NIE	Absolute bias	% bias	MSE
250	Increasing	NC	0.591	0.372	0.012	3.436	0.010
		40	0.590	0.376	0.016	4.412	0.019
		90	1.690	16.809	16.449	4569.038	5011.352
	Constant	NC	0.589	0.377	0.017	4.636	0.011
		40	0.605	0.366	0.006	1.551	0.012
		90	0.645	2.645	2.285	634.663	489.775
	Decreasing	NC	0.585	0.386	0.026	7.177	0.014
		40	0.580	0.378	0.018	4.989	0.014
		90	0.767	0.611	0.251	69.784	0.103
500	Increasing	NC	0.597	0.363	0.003	0.824	0.004
		40	0.594	0.363	0.003	0.914	0.015
		90	2.044	50.735	50.375	13992.995	147140.774
	Constant	NC	0.598	0.364	0.004	1.231	0.005
		40	0.588	0.360	0.000	-0.002	0.009
		90	1.824	0.999	0.639	177.511	51.659
	Decreasing	NC	0.599	0.368	0.008	2.204	0.005
		40	0.591	0.367	0.007	1.872	0.008
		90	0.662	0.503	0.143	39.851	0.038
1000	Increasing	NC	0.596	0.365	0.005	1.523	0.002
		40	0.604	0.359	0.001	-0.140	0.016
		90	3.527	49.074	48.714	13531.680	84448.291
	Constant	NC	0.595	0.366	0.006	1.688	0.002
		40	0.599	0.355	0.005	-1.367	0.007
		90	0.613	0.379	0.019	5.178	0.007

Decreasing	NC	0.594	0.368	0.008	2.152	0.003
	40	0.593	0.355	0.005	-1.307	0.005
	90	0.625	0.424	0.064	17.863	0.015

Table 10. Parameter estimates and simulation measures for potential outcomes mediation approach with Cox model (continuous exposure, continuous mediator)

	Conditions		Estimates		Simulation measures		
N	Hazard	Censoring (%)	NDE	NIE	Absolute bias	% bias	MSE
250	Increasing	NC	0.808	0.111	0.249	0.014	-69.145
		40	0.688	0.085	0.275	0.009	-76.267
		90	0.726	0.155	0.205	0.029	-56.969
	Constant	NC	0.575	0.088	0.272	0.009	-75.635
		40	0.499	0.074	0.286	0.006	-79.537
		90	0.619	0.158	0.202	0.042	-56.174
	Decreasing	NC	0.402	0.072	0.288	0.006	-80.100
		40	0.357	0.067	0.293	0.005	-81.420
		90	0.536	0.144	0.216	0.023	-60.058
500	Increasing	NC	0.800	0.106	0.254	0.013	-70.426
		40	0.695	0.069	0.291	0.006	-80.769
		90	0.679	0.120	0.240	0.019	-66.743
	Constant	NC	0.566	0.080	0.280	0.007	-77.691
		40	0.489	0.057	0.303	0.004	-84.136
		90	0.537	0.118	0.242	0.023	-67.136
	Decreasing	NC	0.392	0.061	0.299	0.004	-82.959
		40	0.348	0.051	0.309	0.003	-85.780
		90	0.425	0.104	0.256	0.011	-71.185
1000	Increasing	NC	0.796	0.106	0.254	0.012	-70.439
		40	0.692	0.064	0.296	0.005	-82.318
		90	0.651	0.099	0.261	0.012	-72.535
	Constant	NC	0.563	0.078	0.282	0.007	-78.292
		40	0.488	0.051	0.309	0.003	-85.890
		90	0.489	0.089	0.271	0.011	-75.347

Decreasing	NC	0.388	0.057	0.303	0.003	-84.290
	40	0.347	0.042	0.318	0.002	-88.300
	90	0.375	0.078	0.282	0.007	-78.321

Table 11. Parameter estimates and simulation measures for potential outcomes mediation approach with AFT model (continuous exposure, binary mediator)

Conditions			Estimates		Simulation measures		
N	Hazard	Censoring (%)	NDE	NIE	Absolute bias	% bias	MSE
250	Increasing	NC	0.591	0.372	0.012	3.436	0.010
		40	0.590	0.376	0.016	4.412	0.019
		90	1.690	16.809	16.449	4569.038	5011.352
	Constant	NC	0.589	0.377	0.017	4.636	0.011
		40	0.605	0.366	0.006	1.551	0.012
		90	0.645	2.645	2.285	634.663	489.775
	Decreasing	NC	0.585	0.386	0.026	7.177	0.014
		40	0.580	0.378	0.018	4.989	0.014
		90	0.767	0.611	0.251	69.784	0.103
500	Increasing	NC	0.597	0.363	0.003	0.824	0.004
		40	0.594	0.363	0.003	0.914	0.015
		90	2.044	50.735	50.375	13992.995	147140.774
	Constant	NC	0.598	0.364	0.004	1.231	0.005
		40	0.588	0.360	0.000	-0.002	0.009
		90	1.824	0.999	0.639	177.511	51.659
	Decreasing	NC	0.599	0.368	0.008	2.204	0.005
		40	0.591	0.367	0.007	1.872	0.008
		90	0.662	0.503	0.143	39.851	0.038
1000	Increasing	NC	0.596	0.365	0.005	1.523	0.002
		40	0.604	0.359	0.001	-0.140	0.016
		90	3.527	49.074	48.714	13531.680	84448.291
	Constant	NC	0.595	0.366	0.006	1.688	0.002
		40	0.599	0.355	0.005	-1.367	0.007
		90	0.613	0.379	0.019	5.178	0.007

Decreasing	NC	0.594	0.368	0.008	2.152	0.003
	40	0.593	0.355	0.005	-1.307	0.005
	90	0.625	0.424	0.064	17.863	0.015

Table 12. Parameter estimates and simulation measures for potential outcomes mediation approach with Cox model (continuous exposure, binary mediator)

Conditions			Estimates		Simulation measures		
N	Hazard	Censoring (%)	NDE	NIE	Absolute bias	% bias	MSE
250	Increasing	NC	0.807	0.131	0.229	-63.717	0.055
		40	0.793	0.123	0.237	-65.775	0.058
		90	0.737	0.201	0.159	-44.225	0.029
	Constant	NC	0.573	0.096	0.264	-73.281	0.071
		40	0.548	0.097	0.263	-73.055	0.070
		90	0.633	0.196	0.164	-45.451	0.031
	Decreasing	NC	0.398	0.075	0.285	-79.060	0.082
		40	0.382	0.082	0.278	-77.266	0.078
		90	0.522	0.184	0.176	-48.909	0.034
500	Increasing	NC	0.796	0.127	0.233	-64.842	0.056
		40	0.797	0.109	0.251	-69.583	0.064
		90	0.684	0.146	0.214	-59.340	0.047
	Constant	NC	0.563	0.089	0.271	-75.360	0.074
		40	0.542	0.080	0.280	-77.734	0.079
		90	0.550	0.137	0.223	-61.853	0.051
	Decreasing	NC	0.389	0.064	0.296	-82.208	0.088
		40	0.374	0.065	0.295	-81.995	0.087
		90	0.420	0.131	0.229	-63.745	0.054
1000	Increasing	NC	0.791	0.126	0.234	-65.062	0.056
		40	0.780	0.106	0.254	-70.519	0.065
		90	0.680	0.119	0.241	-66.948	0.060
	Constant	NC	0.559	0.087	0.273	-75.941	0.075
		40	0.546	0.074	0.286	-79.483	0.082
		90	0.537	0.108	0.252	-70.122	0.066

Decreasing	NC	0.384	0.060	0.300	-83.466	0.091
	40	0.365	0.054	0.306	-84.932	0.094
	90	0.406	0.098	0.262	-72.862	0.069

Table 13. Parameter estimates and simulation measures for potential outcomes mediation approach with AFT model (binary exposure, continuous mediator)

Conditions			Estimates		Simulation measures		
N	Hazard	Censoring (%)	NDE	NIE	Absolute bias	% bias	MSE
250	Increasing	NC	0.600	0.361	0.001	0.329	0.009
		40	0.508	0.312	0.048	-13.436	0.008
		90	0.949	21.199	20.839	5788.586	23827.002
	Constant	NC	0.601	0.365	0.005	1.379	0.009
		40	0.505	0.312	0.048	-13.414	0.010
		90	16.227	16.947	16.587	4607.505	60942.858
	Decreasing	NC	0.604	0.373	0.013	3.639	0.010
		40	0.529	0.336	0.024	-6.594	0.010
		90	0.750	0.542	0.182	50.662	0.062
500	Increasing	NC	0.601	0.363	0.003	0.877	0.005
		40	0.506	0.312	0.048	-13.196	0.005
		90	1.088	13.787	13.427	3729.652	2542.897
	Constant	NC	0.602	0.365	0.005	1.349	0.005
		40	0.506	0.315	0.045	-12.593	0.006
		90	2.816	3.006	2.646	735.048	2510.863
	Decreasing	NC	0.603	0.369	0.009	2.540	0.006
		40	0.517	0.327	0.033	-9.089	0.006
		90	0.686	0.452	0.092	25.656	0.029
1000	Increasing	NC	0.598	0.362	0.002	0.457	0.002
		40	0.506	0.308	0.052	-14.451	0.004
		90	1.217	18.481	18.121	5033.746	5532.414
	Constant	NC	0.598	0.363	0.003	0.870	0.002
		40	0.508	0.311	0.049	-13.717	0.004
		90	13.646	13.477	13.117	3643.544	65059.866

Decreasing	NC	0.598	0.366	0.006	1.703	0.003
	40	0.518	0.317	0.043	-11.930	0.004
	90	0.608	0.398	0.038	10.626	0.010

Table 14. Parameter estimates and simulation measures for potential outcomes mediation approach with Cox model (binary exposure, continuous mediator)

Conditions			Estimates		Simulation measures		
N	Hazard	Censoring (%)	NDE	NIE	Absolute bias	% bias	MSE
250	Increasing	NC	0.621	0.363	0.003	0.954	0.008
		40	0.626	0.377	0.017	4.801	0.009
		90	1.041	0.561	0.201	55.788	0.092
	Constant	NC	0.494	0.285	0.075	-20.830	0.011
		40	0.477	0.280	0.080	-22.095	0.012
		90	0.724	0.364	0.004	1.149	0.029
	Decreasing	NC	0.373	0.210	0.150	-41.553	0.026
		40	0.369	0.209	0.151	-42.079	0.027
		90	0.560	0.269	0.091	-25.259	0.021
500	Increasing	NC	0.611	0.366	0.006	1.551	0.005
		40	0.623	0.382	0.022	6.091	0.005
		90	0.885	0.544	0.184	51.125	0.049
	Constant	NC	0.482	0.287	0.073	-20.311	0.008
		40	0.480	0.289	0.071	-19.778	0.008
		90	0.626	0.365	0.005	1.364	0.018
	Decreasing	NC	0.360	0.212	0.148	-40.999	0.024
		40	0.350	0.209	0.151	-41.821	0.025
		90	0.483	0.244	0.116	-32.245	0.022
1000	Increasing	NC	0.607	0.364	0.004	1.025	0.002
		40	0.617	0.377	0.017	4.821	0.002
		90	0.850	0.542	0.182	50.433	0.040
	Constant	NC	0.478	0.287	0.073	-20.410	0.007
		40	0.472	0.287	0.073	-20.159	0.007
		90	0.579	0.368	0.008	2.240	0.015

Decreasing	NC	0.356	0.213	0.147	-40.837	0.022
	40	0.345	0.206	0.154	-42.894	0.025
	90	0.430	0.234	0.126	-34.898	0.020

Table 15. Parameter estimates and simulation measures for potential outcomes mediation approach with AFT model (binary exposure, binary mediator)

	Conditions		Estimates		Simulation measures		
N	Hazard	Censoring (%)	NDE	NIE	Absolute bias	% bias	MSE
250	Increasing	NC	0.591	0.372	0.012	3.436	0.010
		40	0.590	0.376	0.016	4.412	0.019
		90	1.690	16.809	16.449	4569.038	5011.352
	Constant	NC	0.589	0.377	0.017	4.636	0.011
		40	0.605	0.366	0.006	1.551	0.012
		90	0.645	2.645	2.285	634.663	489.775
	Decreasing	NC	0.585	0.386	0.026	7.177	0.014
		40	0.580	0.378	0.018	4.989	0.014
		90	0.767	0.611	0.251	69.784	0.103
500	Increasing	NC	0.597	0.363	0.003	0.824	0.004
		40	0.594	0.363	0.003	0.914	0.015
		90	2.044	50.735	50.375	13992.995	147140.774
	Constant	NC	0.598	0.364	0.004	1.231	0.005
		40	0.588	0.360	0.000	-0.002	0.009
		90	1.824	0.999	0.639	177.511	51.659
	Decreasing	NC	0.599	0.368	0.008	2.204	0.005
		40	0.591	0.367	0.007	1.872	0.008
		90	0.662	0.503	0.143	39.851	0.038
1000	Increasing	NC	0.596	0.365	0.005	1.523	0.002
		40	0.604	0.359	0.001	-0.140	0.016
		90	3.527	49.074	48.714	13531.680	84448.291
	Constant	NC	0.595	0.366	0.006	1.688	0.002
		40	0.599	0.355	0.005	-1.367	0.007
		90	0.613	0.379	0.019	5.178	0.007

Decreasing	NC	0.594	0.368	0.008	2.152	0.003
	40	0.593	0.355	0.005	-1.307	0.005
	90	0.625	0.424	0.064	17.863	0.015

Table 16. Parameter estimates and simulation measures for potential outcomes mediation approach with Cox model (binary exposure, binary mediator)

N	Hazard	Censoring (%)	NDE	NIE	Absolute bias	% bias	MSE
			Estimates		**Simulation measures**		
250	Increasing	NC	0.601	0.563	0.265	-73.696	0.071
		40	0.468	0.248	0.288	-80.113	0.084
		90	1.159	0.291	16.394	4553.831	13049.245
	Constant	NC	0.601	0.367	0.247	-68.710	0.062
		40	0.477	0.182	0.267	-74.184	0.072
		90	16.131	0.233	20.767	5768.545	81320.548
	Decreasing	NC	0.603	0.247	0.219	-60.766	0.049
		40	0.493	0.143	0.230	-63.988	0.054
		90	0.736	0.136	0.039	10.876	0.013
500	Increasing	NC	0.601	0.568	0.273	-75.925	0.075
		40	0.474	0.252	0.304	-84.446	0.093
		90	0.835	0.263	30.943	8595.275	39452.883
	Constant	NC	0.601	0.383	0.262	-72.738	0.069
		40	0.472	0.184	0.290	-80.439	0.084
		90	8.517	0.212	8.020	2227.757	11771.654
	Decreasing	NC	0.602	0.259	0.244	-67.778	0.060
		40	0.494	0.148	0.263	-73.048	0.070
		90	0.595	0.167	0.077	-21.316	0.010
1000	Increasing	NC	0.597	0.545	0.277	-76.941	0.077
		40	0.475	0.245	0.311	-86.393	0.097
		90	0.824	0.302	34.421	9561.440	59583.314
	Constant	NC	0.596	0.367	0.269	-74.847	0.073
		40	0.476	0.187	0.300	-83.360	0.090
		90	0.473	0.194	0.222	-61.781	0.055

Decreasing	NC	0.594	0.248	0.259	-71.846	0.067
	40	0.497	0.140	0.283	-78.557	0.080
	90	0.523	0.176	0.156	-43.366	0.026