## Survival Analysis of Mortality of Adjuvant Chemotherapy for Colon Cancer

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## 1. Data Tidy

Recall that there are two records for each patient indicated by the event type (etype) variable, where etype == 1 refers to the event of a recurrence and etype == 2 indicates death. In order to answer our first research question, which is to study the time until death, we must create a marginal model by subsetting the colon data to only include the event of mortality.

```
# import the dataset from survival package
colon <- survival::colon</pre>
# tidy mortality dataset
colon.death <- colon %>%
  dplyr::select(-id, -study, -nodes) %>%
  drop_na() %>%
  mutate(rx = as.factor(as.numeric(rx)),
         sex = as.factor(sex),
         obstruct = as.factor(obstruct),
         perfor = as.factor(perfor),
         adhere = as.factor(adhere),
         differ = as.factor(differ),
         extent = as.factor(extent),
         surg = as.factor(surg),
         node4 =as.factor(node4)) %>%
  subset(etype == 2)
```

## 2. Kaplan-Meier Survival Estimate

```
death.fit <- survfit(Surv(time, status) ~ rx, data = colon.death)
options(max.print = 10000)
print(summary(death.fit))

## Call: survfit(formula = Surv(time, status) ~ rx, data = colon.death)
##</pre>
```

##			rx=1						
##	time	n.risk		survival	std.err	lower	95% CI	upper	95% CI
##	113	308	1		0.00324		0.990		1.000
##	125	307	1	0.994	0.00458		0.985		1.000
##	145	306	1	0.990	0.00560		0.979		1.000
##	164	305	1	0.987	0.00645		0.974		1.000
##	166	304	1	0.984	0.00720		0.970		0.998
##	187	303	1	0.981	0.00788		0.965		0.996
##	201	302	1	0.977	0.00849		0.961		0.994
##	208	301	1	0.974	0.00906		0.956		0.992
##	215	300	1	0.971	0.00960		0.952		0.990
##	218	299	1		0.01010		0.948		0.988
##	238	298	1		0.01057		0.944		0.985
##	241	297	1		0.01103		0.940		0.983
##	242	296	1		0.01146		0.936		0.981
##	253	295	1		0.01187		0.932		0.978
##	259	294	2		0.01265		0.924		0.973
##	264	292	1		0.01301		0.920		0.971
##	275	291	1		0.01337		0.916		0.968
##	289	290	1		0.01371		0.912		0.966
##	311	289	1		0.01404		0.908		0.963
##	313	288	1		0.01436		0.904		0.960
##	322 331	287	1 1		0.01467 0.01498		0.900		0.958
## ##	365	286 285	1		0.01498		0.896 0.893		0.955 0.953
##	372	284	1		0.01527		0.889		0.950
##	381	283	1		0.01584		0.885		0.947
##	384	282	2		0.01638		0.878		0.942
##	390	280	1		0.01664		0.874		0.939
##	409	279	1		0.01689		0.870		0.936
##	411	278	1		0.01714		0.866		0.934
##	413	277	2		0.01762		0.859		0.928
##	417	275	1		0.01786		0.855		0.925
##	421	274	1	0.886	0.01808		0.852		0.923
##	433	273	1	0.883	0.01831		0.848		0.920
##	437	272	1	0.880	0.01853		0.844		0.917
##	438	271	1	0.877	0.01874		0.841		0.914
##	459	269	1		0.01895		0.837		0.911
##	462	268	1		0.01916		0.833		0.908
##	464	267	1		0.01936		0.830		0.906
##	465	266	2		0.01976		0.822		0.900
##	474	264	1		0.01995		0.819		0.897
##	485	263	1		0.02014		0.815		0.894
##	499	262	1		0.02032		0.812		0.891
##	506	261	1		0.02050		0.808		0.888
##	510	260	1		0.02068		0.804		0.886
##	537	259	1		0.02086		0.801		0.883
##	563 570	258	2		0.02120		0.794		0.877
##	570 576	256	1		0.02137		0.790		0.874
##	576	255	1		0.02153		0.787		0.871
## ##	587 591	254 253	1 1		0.02169 0.02185		0.783 0.780		0.868 0.865
##	591	252	1		0.02100		0.76		0.862
##	595	252	1		0.02200		0.770		0.859
π#	090	201	1	0.015	0.02210		0.112		0.003

##	599	250	1	0.811 0.02230	0.769	0.856
##	612	249	1	0.808 0.02245	0.765	0.853
##	622	248	1	0.805 0.02260	0.762	0.850
##	659	247	1	0.802 0.02274	0.758	0.847
##	663	246	1	0.798 0.02288	0.755	0.845
##	665	245	1	0.795 0.02302	0.751	0.842
##	670	244	1	0.792 0.02315	0.748	0.839
##	673	243	1	0.789 0.02328	0.744	0.836
##	685	242	1	0.785 0.02341	0.741	0.833
##	687	241	1	0.782 0.02354	0.737	0.830
##	692	240	1	0.779 0.02367	0.734	0.827
##	709	239	1	0.776 0.02379	0.730	0.824
##	716	238	1	0.772 0.02392	0.727	0.821
##	717	237	1	0.769 0.02404	0.723	0.818
##	718	236	1	0.766 0.02415	0.720	0.815
##	721	235	1	0.763 0.02427	0.716	0.812
##	743	234	1	0.759 0.02438	0.713	0.809
##	753	233	1	0.756 0.02450	0.710	0.806
##	758	232	1	0.753 0.02461	0.706	0.803
##	760	231	1	0.750 0.02472	0.703	0.800
##	761	230	1	0.746 0.02482	0.699	0.797
##	770	229	1	0.743 0.02493	0.696	0.794
##	774	228	1	0.740 0.02503	0.692	0.790
##	775	227	1	0.736 0.02513	0.689	0.787
##	832	226	1	0.733 0.02523	0.685	0.784
##	833	225	1	0.730 0.02533	0.682	0.781
##	840	224	1	0.727 0.02542	0.679	0.778
##	845	223	1	0.723 0.02552	0.675	0.775
##	854	222	1	0.720 0.02561	0.672	0.772
##	863	221	1	0.717 0.02570	0.668	0.769
##	874	220	1	0.714 0.02579	0.665	0.766
##	883	219	1	0.710 0.02588	0.661	0.763
##	887	218	1	0.707 0.02596	0.658	0.760
##	901	217 216	1 1	0.704 0.02605	0.655	0.757 0.754
## ##	924 928	215	1	0.701 0.02613 0.697 0.02621	0.651 0.648	0.754
##	929	214	1	0.694 0.02629	0.644	0.731
##	936	213	1	0.691 0.02637	0.641	0.745
##	949	212	1	0.688 0.02644	0.638	0.741
##	957	211	1	0.684 0.02652	0.634	0.738
##	961	210	1	0.681 0.02659	0.631	0.735
##	963	209	1	0.678 0.02666	0.628	0.732
##	966	208	1	0.675 0.02673	0.624	0.729
##	976	207	1	0.671 0.02680	0.621	0.726
##	1021	206	1	0.668 0.02687	0.617	0.723
##	1031	205	1	0.665 0.02693	0.614	0.720
##	1048	204	1	0.662 0.02700	0.611	0.717
##	1070	203	1	0.658 0.02706	0.607	0.714
##	1079	202	1	0.655 0.02712	0.604	0.710
##	1083	201	1	0.652 0.02718	0.601	0.707
##	1101	200	1	0.649 0.02724	0.597	0.704
##	1133	199	1	0.645 0.02730	0.594	0.701
##	1134	198	1	0.642 0.02736	0.591	0.698
##	1136	197	1	0.639 0.02741	0.587	0.695

##	1139	196	1	0.635 0.02746	0.584	0.692
##	1159	195	1	0.632 0.02751	0.581	0.689
##	1166	194	1	0.629 0.02757	0.577	0.685
##	1178	193	1	0.626 0.02761	0.574	0.682
##	1195	192	1	0.622 0.02766	0.571	0.679
##	1198	191	1	0.619 0.02771	0.567	0.676
##	1209	190	1	0.616 0.02775	0.564	0.673
##	1216	189	1	0.613 0.02780	0.561	0.670
##	1230	188	1	0.609 0.02784	0.557	0.666
##	1237	187	1	0.606 0.02788	0.554	0.663
##	1246	186	1	0.603 0.02792	0.551	0.660
##	1262	185	1	0.600 0.02796	0.547	0.657
##	1272	184	1	0.596 0.02800	0.544	0.654
##	1290	183	1	0.593 0.02803	0.541	0.651
##	1295	182	1	0.590 0.02807	0.537	0.648
##	1304	181	1	0.587 0.02810	0.534	0.644
##	1313	180	1	0.583 0.02813	0.531	0.641
##	1314	179	1	0.580 0.02816	0.527	0.638
##	1327	178	1	0.577 0.02819	0.524	0.635
##	1363	177	1	0.574 0.02822	0.521	0.632
##	1375	176	1	0.570 0.02825	0.518	0.628
##	1434	175	1	0.567 0.02828	0.514	0.625
##	1437	174	1	0.564 0.02830	0.511	0.622
##	1447	173	1	0.561 0.02832	0.508	0.619
##	1482	172	1	0.557 0.02835	0.504	0.616
##	1530	171	1	0.554 0.02837	0.501	0.612
##	1548	170	1	0.551 0.02839	0.498	0.609
##	1656	169	1	0.547 0.02841	0.495	0.606
##	1679	168	1	0.544 0.02842	0.491	0.603
##	1692	167	1	0.541 0.02844	0.488	0.600
##	1723	166	1	0.538 0.02845	0.485	0.596
##	1745	165	1	0.534 0.02847	0.481	0.593
##	1772	164	1	0.531 0.02848	0.478	0.590
##	1788	163	1	0.528 0.02849	0.475	0.587
##	1790	162	1	0.525 0.02850	0.472	0.584
##	1818	159	1	0.521 0.02851	0.468	0.580
##	1875	152	1	0.518 0.02853	0.465	0.577
##	1896	150	1	0.514 0.02855	0.461	0.574
##	1907	147	1	0.511 0.02857	0.458	0.570
##	1915	146	1	0.507 0.02858	0.454	0.567
##	1950	143	1	0.504 0.02860	0.451	0.563
##	2077	133	1	0.500 0.02864	0.447	0.560
##	2083	132	1	0.496 0.02867	0.443	0.556
##	2085	131	1	0.493 0.02870	0.439	0.552
##	2133	119	1	0.488 0.02876	0.435	0.548
##	2171	107	1	0.484 0.02885	0.431	0.544
##	2213	93	1	0.479 0.02900	0.425	0.539
##	2257	82	1	0.473 0.02923	0.419	0.534
##	2284	76	1	0.467 0.02950	0.412	0.528
##	2287	75	1	0.460 0.02976	0.406	0.523
##	2351	66	1	0.453 0.03011	0.398	0.516
##	2527	47	1	0.444 0.03098	0.387	0.509
##	2552	42	1	0.433 0.03199	0.375	0.501
##	2789	16	1	0.406 0.03983	0.335	0.492

##									
##			rx=2						
##	time			survival		lower		${\tt upper}$	95% CI
##	24	300	1		0.00333		0.990		1.000
##	56	299	1		0.00470		0.984		1.000
##	93	298	1		0.00574		0.979		1.000
##	122	297	1		0.00662		0.974		1.000
##	129	296	1		0.00739		0.969		0.998
##	133	295	1		0.00808		0.964		0.996
##	150	294	1		0.00872		0.960		0.994
##	165	293	1		0.00930		0.955		0.992
##	171	292	2		0.01036		0.947		0.987
##	191	290	1		0.01085		0.942		0.985
##	206	289	1		0.01131		0.938		0.982
##	219	288	2		0.01218		0.930		0.978
##	222	286	1		0.01258		0.926		0.975
##	226	285	1		0.01297		0.922		0.972
##	232	284	1 1		0.01335 0.01371		0.918		0.970
## ##	257 283	283 282	1		0.01371		0.914 0.910		0.967 0.965
##	314	281	2		0.01408		0.910		0.959
##	314	279	1		0.01473		0.898		0.959
##	323	278	1		0.01536		0.894		0.954
##	342	277	1		0.01566		0.890		0.954
##	343	276	1		0.01506		0.886		0.948
##	349	275	1		0.01624		0.882		0.946
##	355	274	1		0.01652		0.878		0.943
##	356	273	1		0.01680		0.874		0.940
##	362	272	1		0.01706		0.871		0.937
##	366	271	1		0.01732		0.867		0.935
##	376	270	1		0.01757		0.863		0.932
##	382	269	1		0.01782		0.859		0.929
##	402	268	1		0.01806		0.855		0.926
##	406	267	1		0.01830		0.852		0.923
##	420	266	1		0.01853		0.848		0.920
##	422	265	1	0.880	0.01876		0.844		0.918
##	430	264	1	0.877	0.01898		0.840		0.915
##	438	263	1	0.873	0.01920		0.836		0.912
##	439	262	1	0.870	0.01942		0.833		0.909
##	443	261	1	0.867	0.01963		0.829		0.906
##	444	260	1	0.863	0.01983		0.825		0.903
##	472	259	1	0.860	0.02003		0.822		0.900
##	475	258	1	0.857	0.02023		0.818		0.897
##	486	257	1	0.853	0.02043		0.814		0.894
##	499	256	1	0.850	0.02062		0.811		0.891
##	512	255	1	0.847	0.02080		0.807		0.888
##	522	254	1	0.843	0.02099		0.803		0.885
##	546	253	1	0.840	0.02117		0.800		0.883
##	553	252	1	0.837	0.02134		0.796		0.880
##	559	251	1		0.02152		0.792		0.877
##	569	250	1		0.02169		0.789		0.874
##	573	249	1		0.02185		0.785		0.871
##	580	248	1		0.02202		0.781		0.868
##	582	247	1	0.820	0.02218		0.778		0.865

##	589	246	1	0.817 0.02234	0.774	0.862
##	602	245	1	0.813 0.02250	0.770	0.859
##	608	244	1	0.810 0.02265	0.767	0.856
##	628	243	1	0.807 0.02280	0.763	0.853
##	629	242	1	0.803 0.02295	0.760	0.850
##	642	241	1	0.800 0.02309	0.756	0.847
##	643	240	1	0.797 0.02324	0.752	0.844
##	647	239	1	0.793 0.02338	0.749	0.841
##	664	238	1	0.790 0.02352	0.745	0.837
##	669	237	1	0.787 0.02365	0.742	0.834
##	675	236	1	0.783 0.02379	0.738	0.831
##	678	235	1	0.780 0.02392	0.735	0.828
##	684	234	1	0.777 0.02405	0.731	0.825
##	706	233	1	0.773 0.02417	0.727	0.822
##	708	232	1	0.770 0.02430	0.724	0.819
##	709	231	1	0.767 0.02442	0.720	0.816
##	720	230	1	0.763 0.02454	0.717	0.813
##	723	229	1	0.760 0.02466	0.713	0.810
##	729	228	1	0.757 0.02477	0.710	0.807
##	730	227	1	0.753 0.02489	0.706	0.804
##	739	226	1	0.750 0.02500	0.703	0.801
##	743	225	1	0.747 0.02511	0.699	0.798
##	755	224	1	0.743 0.02522	0.696	0.794
##	759	223	2	0.737 0.02543	0.688	0.788
##	764	221	1	0.733 0.02553	0.685	0.785
##	766	220	1	0.730 0.02563	0.681	0.782
##	797	219	1	0.727 0.02573	0.678	0.779
##	806	218	1	0.723 0.02583	0.674	0.776
##	833	217	1	0.720 0.02592	0.671	0.773
##	846	216	1	0.717 0.02602	0.667	0.770
##	858	215	1	0.713 0.02611	0.664	0.766
##	875	214	1	0.710 0.02620	0.660	0.763
##	885	213	1	0.707 0.02629	0.657	0.760
##	890	212	1	0.703 0.02637	0.653	0.757
##	902	211	1	0.700 0.02646	0.650	0.754
##	905	210	1	0.697 0.02654	0.647	0.751
##	909	209	1	0.693 0.02662	0.643	0.748
##	938	208	1	0.690 0.02670	0.640	0.744
##	939	207	1	0.687 0.02678	0.636	0.741
##	940	206	1	0.683 0.02686	0.633	0.738
##	942	205	1	0.680 0.02693	0.629	0.735
##	944	204	1	0.677 0.02701	0.626	0.732
##	952	203	1	0.673 0.02708	0.622	0.729
##	961	202	2	0.667 0.02722	0.615	0.722
##	968	200	1	0.663 0.02728	0.612	0.719
##	969	199	1	0.660 0.02735	0.609	0.716
##	986	198	1	0.657 0.02741	0.605	0.713
##	997	197	1	0.653 0.02748	0.602	0.709
##	1018	196	1	0.650 0.02754	0.598	0.706
##	1034	195	1	0.647 0.02760	0.595	0.703
##	1037	194	1	0.643 0.02766	0.591	0.700
##	1041	193	1	0.640 0.02771	0.588	0.697
##	1046	192	1	0.637 0.02777	0.585	0.693
##	1055	191	1	0.633 0.02782	0.581	0.690

##	1061	190	1		0.02787	0.5		0.687
##	1092	189	1		0.02793	0.5		0.684
##	1103	188	1		0.02798	0.5		0.681
##	1105	187	1		0.02802	0.5	67	0.677
##	1112	186	1	0.617	0.02807	0.5	64	0.674
##	1117	185	1	0.613	0.02812	0.5	61	0.671
##	1122	184	1		0.02816	0.5	57	0.668
##	1145	183	1	0.607	0.02820	0.5	54	0.665
##	1154	182	1	0.603	0.02824	0.5	50	0.661
##	1161	181	1	0.600	0.02828	0.5	47	0.658
##	1178	180	1	0.597	0.02832	0.5	44	0.655
##	1186	179	1	0.593	0.02836	0.5	40	0.652
##	1191	178	1	0.590	0.02840	0.5	37	0.648
##	1207	177	1	0.587	0.02843	0.5	34	0.645
##	1215	176	1	0.583	0.02846	0.5	30	0.642
##	1219	175	1	0.580	0.02850	0.5	27	0.639
##	1252	174	1	0.577	0.02853	0.5	23	0.635
##	1262	173	1	0.573	0.02856	0.5	20	0.632
##	1295	172	1	0.570	0.02858	0.5	17	0.629
##	1325	171	1	0.567	0.02861	0.5	13	0.626
##	1399	170	1	0.563	0.02863	0.5	10	0.622
##	1405	169	1	0.560	0.02866	0.5	07	0.619
##	1434	168	1	0.557	0.02868	0.5	03	0.616
##	1509	167	1	0.553	0.02870	0.5	00	0.613
##	1568	165	1	0.550	0.02872	0.4	96	0.609
##	1652	164	1	0.547	0.02874	0.4	93	0.606
##	1709	163	1	0.543	0.02876	0.4	90	0.603
##	1768	162	1	0.540	0.02878	0.4	86	0.599
##	1829	159	1	0.537	0.02880	0.4	83	0.596
##	1839	157	1	0.533	0.02882	0.4	.80	0.593
##	1850	156	1	0.530	0.02883	0.4	76	0.589
##	1851	155	1	0.526	0.02885	0.4	73	0.586
##	1885	152	1	0.523	0.02887	0.4	69	0.583
##	1932	149	1	0.519	0.02889	0.4	66	0.579
##	2023	141	1	0.516	0.02892	0.4	62	0.576
##	2079	135	1	0.512	0.02895	0.4	58	0.572
##	2128	128	1	0.508	0.02900	0.4	54	0.568
##	2152	119	1	0.504	0.02907	0.4	50	0.564
##	2171	115	1	0.499	0.02914	0.4	45	0.560
##	2458	64	1	0.491	0.02971	0.4	36	0.553
##	2593	41	1	0.479	0.03131	0.4	22	0.545
##	2683	32	1	0.464	0.03373	0.4	.03	0.535
##	2718	25	1	0.446	0.03714	0.3	79	0.525
##	2910	9	1	0.396	0.05719	0.2	99	0.526
##								
##			rx=3					
##	time	n.risk	${\tt n.event}$	survival	std.err	lower 95%	CI upper	95% CI
##	23	298	1	0.997	0.00335	0.9	90	1.000
##	34	297	1	0.993	0.00473	0.9	84	1.000
##	45	296	1	0.990	0.00578	0.9	79	1.000
##	52	295	1	0.987	0.00667	0.9	74	1.000
##	79	294	1		0.00744	0.9	69	0.998
##	127	293	1		0.00814	0.9		0.996
##	138	292	1	0.977	0.00877	0.9	59	0.994

##	141	291	1	0 973	0.00936	0.955	0.992
##	144	290	1		0.00991	0.951	0.989
##	186	289	1		0.01043	0.946	0.987
##	251	288	1		0.01092	0.942	0.985
##	269	287	1		0.01139	0.938	0.982
##	271	286	1		0.01183	0.933	0.980
##	274	285	1		0.01226	0.929	0.977
##	276	284	1		0.01267	0.925	0.975
##	279	283	1		0.01306	0.921	0.973
##	283	282	1		0.01344	0.917	0.970
##	293	281	1		0.01344	0.913	0.967
##	302	280	1		0.01330	0.913	0.964
##	304	279	1		0.01413	0.905	0.962
##	324	27 <i>9</i> 278	1		0.01449	0.903	0.959
##		277	1				
##	326		1		0.01515	0.897	0.956
	340	276			0.01546	0.893	0.954
##	355	275	1		0.01576	0.889	0.951
##	363	274	1		0.01606	0.885	0.948
##	389	273	1		0.01635	0.881	0.945
##	400	272	1		0.01663	0.877	0.943
##	428	271	1		0.01690	0.874	0.940
##	430	270	1		0.01717	0.870	0.937
##	441	269	1		0.01743	0.866	0.934
##	448	268	1		0.01769	0.862	0.931
##	454	267	1		0.01793	0.858	0.928
##	460	266	1		0.01818	0.854	0.926
##	484	265	1		0.01842	0.851	0.923
##	490	264	1		0.01865	0.847	0.920
##	498	263	1		0.01888	0.843	0.917
##	503	262	1		0.01910	0.839	0.914
##	529	261	1		0.01932	0.835	0.911
##	550	260	1		0.01954	0.832	0.908
##	576	259	1		0.01975	0.828	0.905
##	578	258	1		0.01995	0.824	0.902
##	580	257	1		0.02016	0.820	0.899
##	583	256	1		0.02036	0.817	0.897
##	592	255	1	0.852	0.02055	0.813	0.894
##	601	254	1		0.02074	0.809	0.891
##	603	253	1		0.02093	0.806	0.888
##	609	252	1		0.02111	0.802	0.885
##	614	251	1		0.02129	0.798	0.882
##	616	250	1	0.836	0.02147	0.795	0.879
##	641	249	1		0.02165	0.791	0.876
##	642	248	1	0.829	0.02182	0.787	0.873
##	643	247	1	0.826	0.02199	0.784	0.870
##	666	246	1	0.822	0.02215	0.780	0.867
##	674	245	1	0.819	0.02231	0.776	0.864
##	692	244	2	0.812	0.02263	0.769	0.858
##	693	242	1	0.809	0.02278	0.765	0.855
##	696	241	1	0.805	0.02293	0.762	0.852
##	712	240	1	0.802	0.02308	0.758	0.849
##	736	239	1	0.799	0.02323	0.754	0.846
##	765	238	1	0.795	0.02337	0.751	0.842
##	802	237	2	0.789	0.02365	0.744	0.836

##	806	235	1	0.785 0.02379	0.740	0.833
##	811	234	1	0.782 0.02392	0.736	0.830
##	844	233	1	0.779 0.02405	0.733	0.827
##	862	232	1	0.775 0.02408	0.729	0.824
##	884	231	1	0.772 0.02431	0.726	0.821
##	887	230	2	0.765 0.02456	0.718	0.815
##	905	228	1	0.762 0.02468	0.715	0.813
##	911	227	1	0.758 0.02480	0.713	0.809
##	916	226	1	0.755 0.02491	0.711	0.805
##	961	225	1	0.752 0.02503	0.708	0.803
##	977	224	1	0.748 0.02514	0.704	0.799
			1			
##	993	223 222	1	0.745 0.02525	0.697	0.796
##	1022			0.742 0.02536	0.694	0.793
##	1138	221	1	0.738 0.02546	0.690	0.790
##	1145	220	1	0.735 0.02557	0.686	0.787
##	1151	219	1	0.732 0.02567	0.683	0.784
##	1193	218	1	0.728 0.02577	0.679	0.780
##	1201	217	1	0.725 0.02587	0.676	0.777
##	1212	216	1	0.721 0.02597	0.672	0.774
##	1246	215	1	0.718 0.02606	0.669	0.771
##	1273	214	1	0.715 0.02616	0.665	0.768
##	1276	213	2	0.708 0.02634	0.658	0.762
##	1279	211	1	0.705 0.02643	0.655	0.758
##	1302	209	1	0.701 0.02651	0.651	0.755
##	1306	208	1	0.698 0.02660	0.648	0.752
##	1365	207	1	0.695 0.02668	0.644	0.749
##	1387	206	1	0.691 0.02677	0.641	0.746
##	1388	205	1	0.688 0.02685	0.637	0.743
##	1424	203	1	0.684 0.02693	0.634	0.739
##	1439	202	1	0.681 0.02701	0.630	0.736
##	1446	201	1	0.678 0.02708	0.627	0.733
##	1495	199	1	0.674 0.02716	0.623	0.730
##	1511	198	1	0.671 0.02724	0.620	0.726
##	1521	197	1	0.667 0.02731	0.616	0.723
##	1550	196	1	0.664 0.02738	0.612	0.720
##	1607	195	1	0.661 0.02745	0.609	0.717
##	1620	194	1	0.657 0.02752	0.605	0.713
##	1637	193	1	0.654 0.02759	0.602	0.710
##	1668	192	1	0.650 0.02766	0.598	0.707
##	1671	191	1	0.647 0.02772	0.595	0.704
##	1752	190	1	0.644 0.02778	0.591	0.700
##	1767	189	1	0.640 0.02784	0.588	0.697
##	1783	188	1	0.637 0.02790	0.584	0.694
##	1798	187	1	0.633 0.02796	0.581	0.691
##	1812	185	1	0.630 0.02802	0.577	0.687
##	1831	180	1	0.626 0.02808	0.574	0.684
##	1856	178	1	0.623 0.02814	0.570	0.681
##	1995	167	1	0.619 0.02822	0.566	0.677
##	2021	162	1	0.615 0.02830	0.562	0.673
##	2052	156	1	0.611 0.02840	0.558	0.670
##	2127	143	1	0.607 0.02852	0.554	0.666
##	2174	133	1	0.603 0.02867	0.549	0.662
##	2197	124	1	0.598 0.02884	0.544	0.657
##	2318	100	1	0.592 0.02917	0.537	0.652

0.528

0.514

0.645

0.637

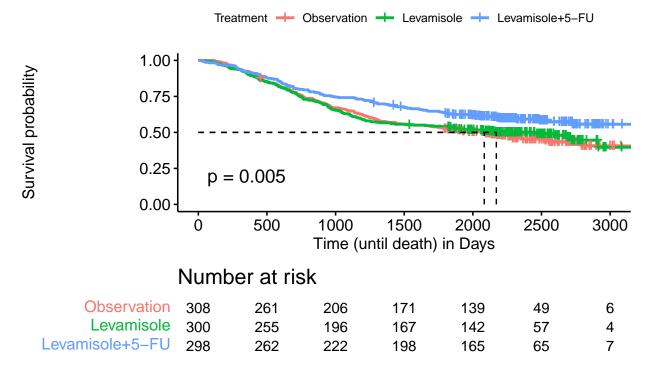
0.584 0.02990

0.573 0.03130

1

1

## Kaplan–Meier Curve for Colon Cancer Mortality by Treatment



From the plot above, there is some indication that patients who received the adjuvant treatment with levamisole plus fluorouracil (Lev+5FU) have a higher survival probability than patients with no further treatment and patients who received the treatment with levamisole alone. The median survival time for observation group and levamisole group are approximately 2100 days and 2200 days. However, until the end of the trial, the survival probability of Levamisole+5-FU treatment group is greater than 50% as we fail to observe the curve doesn't cross 50%, which means the median survival is simply undefined.

## 3. Log-Rank Test

2482

2542

53

##

##

Noticing the difference of survival probability between the three treatment groups, we do a Log-rank hypothesis test to test the null hypothesis of no difference among the three treatments in the mortality model.

```
survdiff(Surv(time, status) ~ rx, data = colon.death)
## Call:
## survdiff(formula = Surv(time, status) ~ rx, data = colon.death)
##
##
          N Observed Expected (O-E)^2/E (O-E)^2/V
## rx=1 308
                 165
                           145
                                    2.67
## rx=2 300
                 154
                           141
                                    1.13
                                              1.66
## rx=3 298
                 122
                           154
                                    6.77
                                             10.44
##
##
   Chisq= 10.6 on 2 degrees of freedom, p= 0.005
```

From this log-rank test, we get a p-value that is closed to 0.005, which is significant at a 0.05 level. We want to conclude that there is a significant difference among the three treatments in the mortality model.

### 4. Cox PH Model

### 4.1 Model Selection

##

We now use automatic stepwise selection with Akaike information criterion (AIC) to determine the covariates that best represent an appropriate cox proportional hazards model for the event of death.

```
# fit all the variables in the model
d.model.full <- coxph(Surv(time, status) ~ . -etype, data = colon.death)</pre>
# stepwise selection with AIC criterion
d.model.aic <- step(d.model.full, direction = "both", k = 2)</pre>
## Start: AIC=5583.24
## Surv(time, status) ~ (rx + sex + age + obstruct + perfor + adhere +
##
       differ + extent + surg + node4 + etype) - etype
##
##
                    AIC
              Df
## - perfor
               1 5581.2
## - sex
               1 5581.3
## - adhere
               1 5582.6
## <none>
                 5583.2
## - age
               1 5584.9
## - surg
               1 5586.3
## - obstruct 1 5586.8
## - differ
               2 5587.5
## - rx
               2 5590.7
## - extent
               3 5591.9
## - node4
               1 5662.1
##
## Step: AIC=5581.24
## Surv(time, status) ~ rx + sex + age + obstruct + adhere + differ +
##
       extent + surg + node4
```

```
##
              Df
                    AIC
## - sex
               1 5579.4
## - adhere
               1 5580.6
## <none>
                 5581.2
## - age
               1 5582.9
## + perfor
               1 5583.2
## - surg
               1 5584.3
## - obstruct 1 5584.9
## - differ
               2 5585.5
## - rx
               2 5588.7
## - extent
               3 5590.0
## - node4
               1 5660.2
##
## Step: AIC=5579.35
## Surv(time, status) ~ rx + age + obstruct + adhere + differ +
##
       extent + surg + node4
##
##
              Df
                    AIC
## - adhere
               1 5578.7
## <none>
                 5579.4
## - age
               1 5581.0
## + sex
               1 5581.2
## + perfor
               1 5581.3
               1 5582.5
## - surg
## - obstruct 1 5582.9
## - differ
               2 5583.6
## - rx
               2 5586.9
               3 5588.0
## - extent
## - node4
               1 5658.2
##
## Step: AIC=5578.74
## Surv(time, status) ~ rx + age + obstruct + differ + extent +
##
       surg + node4
##
##
              Df
                    AIC
## <none>
                 5578.7
## + adhere
               1 5579.4
## + sex
               1 5580.6
## + perfor
               1 5580.7
## - age
               1 5580.7
## - surg
               1 5582.1
## - obstruct 1 5582.3
## - differ
               2 5583.7
## - rx
               2 5586.4
## - extent
               3 5588.4
## - node4
               1 5657.3
```

The resulting model with the lowest AIC is: Surv(time, status)  $\sim$  obstruct + differ + extent + surg + node4 + age + rx

Next, we used the Analysis of Deviance procedure to get the proper Likelihood Ratio Test to confirm if each of the covariates selected by the stepwise selection method is significant to include in the Cox Proportional Model.

#### anova(d.model.aic)

```
## Analysis of Deviance Table
## Cox model: response is Surv(time, status)
## Terms added sequentially (first to last)
##
##
                     Chisq Df Pr(>|Chi|)
            loglik
## NULL
           -2847.5
           -2842.0 10.9755
## rx
                            2 0.0041372 **
## age
           -2841.8 0.5855 1 0.4441715
## obstruct -2839.4 4.7384 1 0.0294972 *
## differ
           -2831.3 16.1461 2 0.0003118 ***
           -2820.6 21.4045 3 8.675e-05 ***
## extent
## surg
           -2818.6 3.9238 1 0.0476071 *
## node4
           -2778.4 80.5441 1 < 2.2e-16 ***
## ---
## Signif. codes: 0 '*** 0.001 '** 0.01 '* 0.05 '.' 0.1 ' 1
```

We can see that p-values for covariates "obstruct, differ, extent, surg, node4 and rx" are much smaller than 0.05, except for "age", indicating that they have a significant effect on time until death. Therefore, we will include these 6 covariates in our Cox PH model.

Therefore, we obtain the resulting model, which is  $Surv(time, status) \sim obstruct + differ + extent + surg + node4 + rx$ .

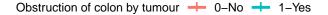
### 4.2 Model Diagnostics

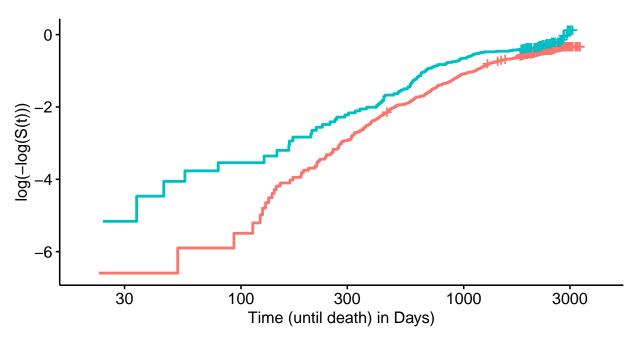
### 4.2.1 Check proportionality of hazard ratios

#### Log of Negative Log of Estimated Survival Function

To check the proportional hazards assumption for this model, we make diagnostic plots using log of negative log of estimated survival function. First comes to covariate obstruct.

## Log of Negative Log of Estimated Survival Function for Colon Cancer Mortality by obstruct

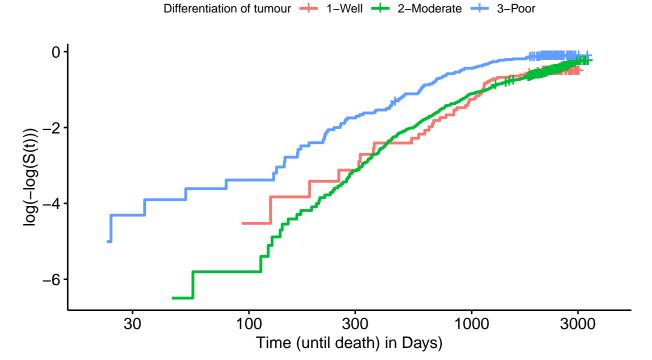




According to the plot, the distance between two obstruct curves begin to narrow after 2000 days which causes some concern that the assumption might be violated. However, it is also reasonable to assume that the curves are wider apparent earlier in the study since there are less occurrences of death before 2000 days. Hence we believe it is best to ignore the noisiness of the plot since the curves are roughly parallel after 2000 days. Thus, the cox proportional hazards assumption is valid to use for "obstruct".

We continue to plot the C-log-log plot for the covariate differ.

## Log of Negative Log of Estimated Survival Function for Colon Cancer Mortality by differ

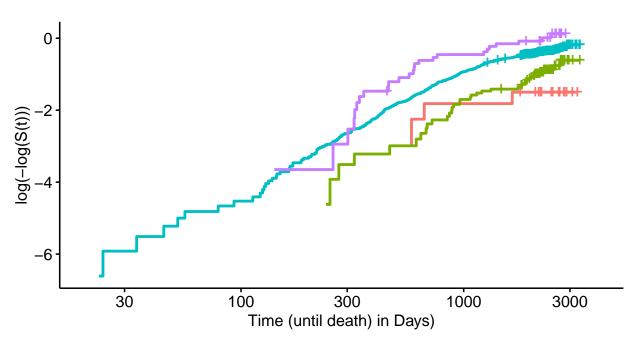


According to the plot, the curves in the C-log-log plot are crossing over after 300 days. The assumption of proportional hazard ratio between the three differ groups is violated as we fail to see three parallel lines against log time.

We continue to plot the C-log-log plot for the covariate extent.

# Log of Negative Log of Estimated Survival Function for Colon Cancer Mortality by extent

Extent of local spread + 1-Submucosa + 2-Muscle + 3-Serosa + 4-Contiguous structures

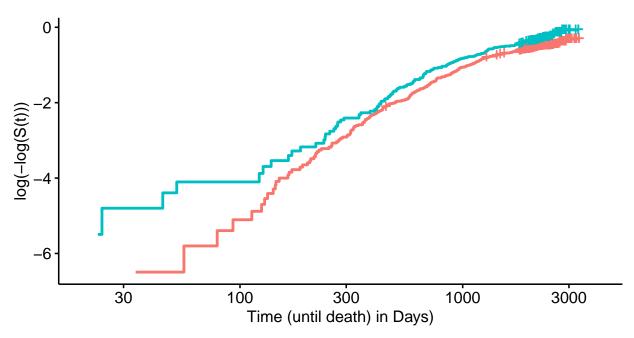


According to the plot, the curves in the C-log-log plot are crossing over after 100 days. The assumption of proportional hazard ratio of extent is violated as we fail to see four parallel lines against log time.

We continue to plot the C-log-log plot for the covariate surg.

# Log of Negative Log of Estimated Survival Function for Colon Cancer Mortality by surg

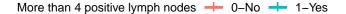


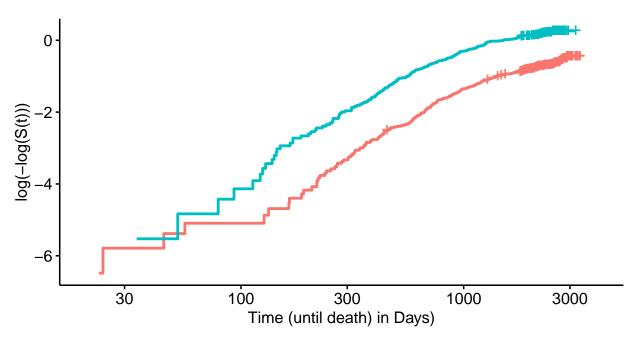


According to the plot, the distance between two surg curves begin to narrow after 100 days and becomes parallel to each other. We can assume that the cox proportional hazards assumption is valid to use for surg.

We continue to plot the C-log-log plot for the covariate node4.

## Log of Negative Log of Estimated Survival Function for Colon Cancer Mortality by node4

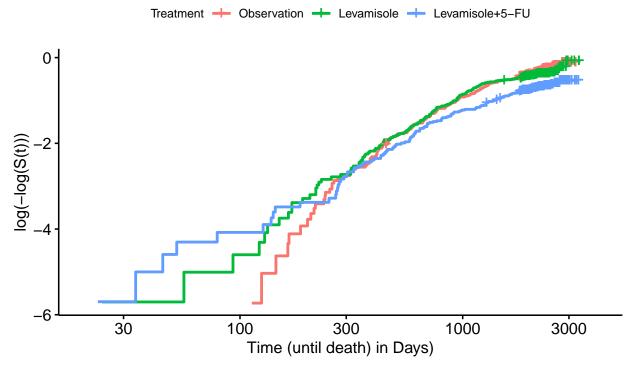




According to the plot, the two curves in this C-log-log plot cross over at the beginning of the study but appear to be parallel to each other after 100 days. Since the data is oftentimes noisy at the beginning of the study, the cross over does not cause too much concern. Overall, we believe that the cox proportional assumption is appropriate for the covariate node4 since the curves are consistently parallel throughout most of the study.

We continue to plot the C-log-log plot for the covariate rx.

## Log of Negative Log of Estimated Survival Function for Colon Cancer Mortality by rx



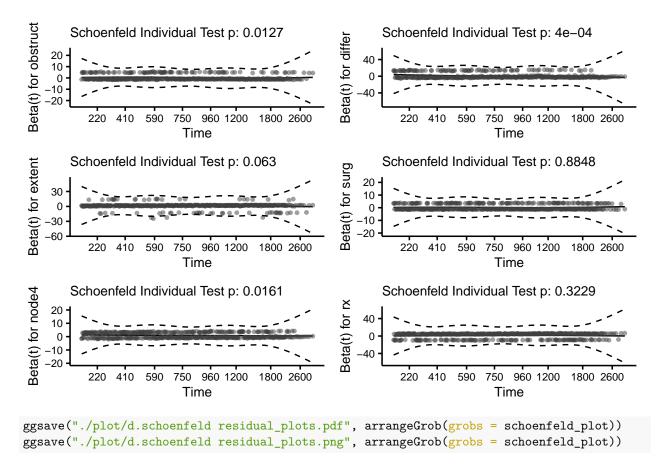
According to the plot, the distance between three treatment curves begin to narrow after 2000 days which causes some concern that the assumption might be violated. However, it is also reasonable to assume that the curves are wider apparent earlier in the study since there are less occurrences of death before 2000 days. Hence we believe it is best to ignore the noisiness of the plot since the curves are roughly parallel after 2000 days. Thus, the cox proportional hazards assumption is valid to use for this covariate.

```
# combine all the cloglog plots and save them to a pdf file
splots <- list()
splots[[1]] <- cloglog_obstruct
splots[[2]] <- cloglog_differ
splots[[3]] <- cloglog_extent
splots[[4]] <- cloglog_surg
splots[[5]] <- cloglog_node4
splots[[6]] <- cloglog_rx
cloglog_plot = arrange_ggsurvplots(splots, print = FALSE, ncol = 2, nrow = 3)

ggsave(cloglog_plot,file = "./plot/d.C-log-log-plots.pdf",width = 12,height = 15)
ggsave(cloglog_plot,file = "./plot/d.C-log-log-plots.png",width = 12,height = 15)</pre>
```

#### Schoenfeld residuals

## Global Schoenfeld Test p: 0.0001202



From the output above, the tests for covariates "obstruct", "node4", "differ" are statistically significant, and the global test is also statistically significant. Therefore, we can assume the violation of proportional hazards on these covariates, which requires corrections of non-proportional hazard ratio.

#### 4.2.2 Test influential observations

It's also possible to check outliers by visualizing the influence of each point, in terms of DFBETA - the impact on the coefficient of covariates in the model were that specific point to be removed from the data set. In general, we can identify the observations with positive and negative DFBETAs. Comparing the magnitudes of the largest dfbeta values to the regression coefficients suggests that none of the observations is terribly influential individually, even though some of the dfbeta values for extent are large compared with the others.

### 4.3 Corrections for violation of the PH Assumption

```
colon.death.inter <- colon.death %>%
 mutate(rxt = as.numeric(rx)*log(time),
 differt = as.numeric(differ)*log(time),
 extentt = as.numeric(extent)*log(time),
 surgt = as.numeric(surg)*log(time),
 node4t = as.numeric(node4)*log(time),
 obstructt = as.numeric(obstruct)*log(time))
d.model.inter <- coxph(Surv(time, status) ~ obstruct + differ + extent + surg + node4 + rx + obstructt
summary(d.model.inter)
## Call:
## coxph(formula = Surv(time, status) ~ obstruct + differ + extent +
      surg + node4 + rx + obstructt + differt + extentt + rxt +
##
      node4t + surgt, data = colon.death.inter)
##
##
##
    n= 906, number of events= 441
##
##
                  coef exp(coef)
                                    se(coef)
                                                   z Pr(>|z|)
## obstruct1 4.306e+00 7.411e+01
                                   1.314e+00
                                               3.276 0.00105 **
## differ2
             1.027e+01 2.882e+04 1.473e+00
                                               6.973 3.10e-12 ***
## differ3
             1.957e+01 3.167e+08 2.743e+00
                                              7.137 9.57e-13 ***
## extent2
             4.587e+01 8.324e+19
                                   2.827e+00 16.225 < 2e-16 ***
## extent3
             8.849e+01
                        2.697e+38
                                   5.455e+00
                                              16.221
                                                     < 2e-16 ***
## extent4
             1.237e+02 5.296e+53 7.492e+00 16.511 < 2e-16 ***
## surg1
             7.629e+00 2.057e+03 1.302e+00
                                              5.857 4.70e-09 ***
## node41
             5.247e+00 1.900e+02 1.244e+00
                                               4.218 2.47e-05 ***
                                   6.925e-01
## rx2
             1.913e+00 6.776e+00
                                               2.763 0.00573 **
             3.773e+00 4.350e+01 1.367e+00
                                               2.760 0.00579 **
## rx3
## obstructt -6.361e-01 5.293e-01 2.030e-01
                                              -3.133 0.00173 **
                                   2.033e-01 -7.149 8.77e-13 ***
           -1.453e+00 2.338e-01
## differt
## extentt
            -5.784e+00 3.076e-03 3.535e-01 -16.361
                                                     < 2e-16 ***
## rxt
            -2.967e-01 7.433e-01 1.001e-01 -2.965 0.00303 **
## node4t
            -7.774e-01 4.596e-01 1.882e-01 -4.131 3.61e-05 ***
            -1.123e+00 3.252e-01 1.952e-01 -5.756 8.61e-09 ***
## surgt
## ---
## Signif. codes: 0 '*** 0.001 '** 0.01 '* 0.05 '.' 0.1 ' 1
##
##
            exp(coef) exp(-coef) lower .95 upper .95
## obstruct1 7.411e+01 1.349e-02 5.637e+00 9.744e+02
## differ2
           2.882e+04 3.470e-05 1.608e+03 5.167e+05
            3.167e+08 3.158e-09 1.466e+06 6.843e+10
## differ3
## extent2
            8.324e+19
                      1.201e-20 3.265e+17 2.122e+22
            2.697e+38 3.708e-39 6.128e+33 1.187e+43
## extent3
            5.296e+53 1.888e-54 2.221e+47 1.263e+60
## extent4
            2.057e+03 4.862e-04 1.602e+02 2.641e+04
## surg1
## node41
            1.900e+02 5.263e-03 1.659e+01 2.176e+03
## rx2
            6.776e+00 1.476e-01 1.744e+00 2.633e+01
            4.350e+01 2.299e-02 2.984e+00 6.342e+02
## rx3
## obstructt 5.293e-01 1.889e+00 3.556e-01 7.881e-01
```

```
## differt
            2.338e-01 4.276e+00 1.570e-01 3.483e-01
            3.076e-03 3.251e+02 1.538e-03 6.150e-03
## extentt
## rxt
            7.433e-01 1.345e+00 6.109e-01 9.043e-01
            4.596e-01 2.176e+00 3.179e-01 6.646e-01
## node4t
## surgt
            3.252e-01 3.075e+00 2.218e-01 4.767e-01
##
## Concordance= 0.986 (se = 0.002)
## Likelihood ratio test= 3120 on 16 df,
                                           p=<2e-16
                                          p=<2e-16
## Wald test
                       = 584.1 on 16 df,
## Score (logrank) test = 2559 on 16 df,
                                           p = < 2e - 16
```

anova(d.model.inter)

```
## Analysis of Deviance Table
  Cox model: response is Surv(time, status)
## Terms added sequentially (first to last)
##
##
             loglik
                       Chisq Df Pr(>|Chi|)
## NULL
            -2847.5
## obstruct -2845.2
                      4.7665 1 0.0290194 *
## differ
            -2837.4
                     15.4677
                              2 0.0004378 ***
            -2826.6
                    21.5515 3 8.086e-05 ***
## extent
## surg
            -2824.6
                      3.9913 1 0.0457345 *
## node4
            -2786.1
                      77.0443 1 < 2.2e-16 ***
            -2780.3 11.5302 2 0.0031351 **
## rx
## obstructt -1904.1 1752.5175 1 < 2.2e-16 ***
## differt -1641.7 524.8644 1 < 2.2e-16 ***
## extentt
            -1315.8 651.7571 1
                                < 2.2e-16 ***
## rxt
            -1311.2
                      9.0697 1 0.0025988 **
## node4t
            -1304.8
                     12.8056 1 0.0003456 ***
            -1287.5
                     34.7200 1 3.807e-09 ***
## surgt
## Signif. codes: 0 '***' 0.001 '**' 0.05 '.' 0.1 ' ' 1
```

Based on the test interaction for proportionality, the result shows that all the interactions of covaraites with 'log(time)' are significant (i.e., less than 0.05). Therefore, we can include these interactions with function of time as the method of PH assumption verification and solution to its violation.

#### 4.4 Final model

With the inclusion of treatment, our final model is given by:  $Surv(time, status) \sim obstruct + differ + extent + surg + node4 + rx + obstructt + differt + extentt + surgt + rxt + node4t.$ 

```
d.final.model <- coxph(Surv(time, status) ~ obstruct + differ + extent + surg + node4 + rx + obstructt
summary(d.final.model)</pre>
```

```
## Call:
## coxph(formula = Surv(time, status) ~ obstruct + differ + extent +
## surg + node4 + rx + obstructt + differt + extentt + rxt +
## node4t + surgt, data = colon.death.inter)
```

```
##
##
     n= 906, number of events= 441
##
##
                    coef
                          exp(coef)
                                      se(coef)
                                                      z Pr(>|z|)
##
  obstruct1
              4.306e+00
                          7.411e+01
                                     1.314e+00
                                                  3.276
                                                        0.00105 **
                          2.882e+04
  differ2
              1.027e+01
                                     1.473e+00
                                                  6.973 3.10e-12 ***
##
## differ3
              1.957e+01
                          3.167e+08
                                     2.743e+00
                                                  7.137 9.57e-13 ***
## extent2
              4.587e+01
                          8.324e+19
                                     2.827e+00
                                                 16.225
                                                         < 2e-16 ***
## extent3
              8.849e+01
                          2.697e+38
                                     5.455e+00
                                                 16.221
                                                         < 2e-16 ***
## extent4
              1.237e+02
                          5.296e+53
                                     7.492e+00
                                                 16.511
                                                         < 2e-16 ***
## surg1
              7.629e+00
                          2.057e+03
                                     1.302e+00
                                                  5.857 4.70e-09 ***
## node41
              5.247e+00
                          1.900e+02
                                     1.244e+00
                                                  4.218 2.47e-05 ***
                                                  2.763
              1.913e+00
                          6.776e+00
                                     6.925e-01
                                                         0.00573 **
## rx2
## rx3
              3.773e+00
                          4.350e+01
                                     1.367e+00
                                                  2.760
                                                         0.00579 **
## obstructt -6.361e-01
                          5.293e-01
                                     2.030e-01
                                                 -3.133
                                                         0.00173 **
## differt
             -1.453e+00
                          2.338e-01
                                     2.033e-01
                                                 -7.149 8.77e-13 ***
             -5.784e+00
                          3.076e-03
                                     3.535e-01 -16.361
                                                         < 2e-16 ***
## extentt
             -2.967e-01
                          7.433e-01
                                     1.001e-01
                                                 -2.965
                                                         0.00303 **
## rxt
             -7.774e-01
                          4.596e-01
                                     1.882e-01
                                                 -4.131 3.61e-05 ***
## node4t
##
   surgt
             -1.123e+00
                          3.252e-01
                                     1.952e-01
                                                 -5.756 8.61e-09 ***
##
                  0 '*** 0.001 '** 0.01 '* 0.05 '. ' 0.1 ' ' 1
## Signif. codes:
##
##
             exp(coef) exp(-coef) lower .95 upper .95
## obstruct1 7.411e+01
                         1.349e-02 5.637e+00 9.744e+02
## differ2
             2.882e+04
                         3.470e-05 1.608e+03 5.167e+05
## differ3
                         3.158e-09 1.466e+06 6.843e+10
             3.167e+08
## extent2
             8.324e+19
                         1.201e-20 3.265e+17 2.122e+22
## extent3
             2.697e+38
                         3.708e-39 6.128e+33 1.187e+43
## extent4
             5.296e+53
                         1.888e-54 2.221e+47 1.263e+60
## surg1
             2.057e+03
                         4.862e-04 1.602e+02 2.641e+04
## node41
             1.900e+02
                         5.263e-03 1.659e+01 2.176e+03
## rx2
             6.776e+00
                         1.476e-01 1.744e+00 2.633e+01
             4.350e+01
                         2.299e-02 2.984e+00 6.342e+02
## rx3
   obstructt 5.293e-01
                         1.889e+00 3.556e-01 7.881e-01
## differt
             2.338e-01
                         4.276e+00 1.570e-01 3.483e-01
## extentt
             3.076e-03
                         3.251e+02 1.538e-03 6.150e-03
                         1.345e+00 6.109e-01 9.043e-01
## rxt.
             7.433e-01
                         2.176e+00 3.179e-01 6.646e-01
## node4t
             4.596e-01
## surgt
             3.252e-01
                        3.075e+00 2.218e-01 4.767e-01
##
## Concordance= 0.986
                        (se = 0.002)
## Likelihood ratio test= 3120
                                 on 16 df,
                                              p=<2e-16
## Wald test
                         = 584.1
                                  on 16 df,
                                               p=<2e-16
## Score (logrank) test = 2559
                                 on 16 df,
                                              p=<2e-16
```

From the results of the summary function for the final mortality model, we see that after we control for all other covariates in the model the coefficient for covariate rxLev is -0.031, which indicates a protective effect. And the hazard rate of death for the group treated with rxlev is 3% less than observation group, with a p-value of 0.78. Furthermore, the confidence interval for the hazard ratio is (0.78, 1.21).

On the other hand, the coefficient for covariate rxLev+5Fu is -0.36, which indicates a protective effect. And the hazard rate of death for the group treated with rxLev+5Fu is 32.2% less than observation group, with a p-value of 0.003. Furthermore, the confidence interval for the hazard ratio is (0.55, 0.89).

### 5. Discussion

We can now observe whether treatments Levamisole and Levamisole+5-FU help improve the survival rate in colon cancer patients from negative coefficients of different treatment groups. Our result indicates that the hazard rate for the group treated with Levamisole is 97% of what it is for the observation group. Since the p-value for the coefficient is 0.78 which is greater than 0.05, there is no significant evidence to indicate a difference between the hazard rate of the group treated with Levamisole and the hazard rate of the observation group. Therefore, we conclude that the treatment Levamisole is not effective on improving the survival probability in colon cancer patients. On the other hand, our result indicates that the hazard rate for the group treated with Levamisole+5-FU is 67.8% of the hazard rate for the observation group. Since the p-value for the coefficient is close to 0, this indicates that there is a significant difference between the hazard rate of the group treated with Levamisole+5-FU and the hazard rate for the observation group. Therefore, we conclude that the treatment Levamisole+5-FU is effective on improving the survival rate in colon cancer patients. There is a 32.2% chance that patients who received the treatment Levamisole+5-FU survive longer than patients who do not receive any treatments and patients who received Levamisole alone.