Supplemental Material

An Integrated Model for Overall and Conditional Survival Analysis in Epidemiologic Studies

Reanalysis of the Colon Cancer Example with a Greater Number of Cutpoints

The largest discrepancies in the OS probabilities occurred during the first 2 years of follow-up, suggesting that additional cutpoints may be necessary to characterize the OS curves more completely. We explored this possibility in a sensitivity analysis. We adopted 3-month cutpoints during the first 24 months of follow-up, plus an additional one at month 30. Thereafter, the same cutpoints as in the original analysis were applied. This resulted in 12 cutpoints including 3, 6, 9, 12, 15, 18, 21, 24, 30, 36, 48, and 72 months, with the final interval extending through the end of follow-up. Otherwise, the PE model remained the same. Age and sex were included as covariates as before.

Table S1 reports the OS probabilities, adjusted for age and sex, from the PE model at the new set of cutpoints together with their asymptotic SEs. There was no difference in the OS probability estimates and their SEs derived from the original analysis compared to those forthcoming from this expanded set. Any discrepancies were restricted to the 3rd significant digit after the decimal and were due to rounding. Tests for between-group differences at years

2 and year 3 were also unchanged (p= 0.13 and 0.001, respectively). There was slightly more power for the overall between-group difference (p= 0.002).

Table S1 also reports OS probabilities estimates and their SEs at the expanded cutpoints from the original PH analysis. The discrepancies in the probability estimates and their standard errors between the two models followed the same patterns and were generally within ±0.01 of each other. The largest discrepancies occurred in the combination group at months 21 (+0.018), 24 (+0.017) and 30 (+0.015). This suggests that we may have been overfitting the data in these middle cutpoints.

Table S2 reports CS results from the PE model. Any discrepancies compared to the original set of cutpoints were restricted to the 3rd significant digit after the decimal point. As before, there was no significant difference at year 2 (p= 0.08) while the difference at year 3 (p= 0.0003) reached significance. The overall between-group difference was significant at p= 0.003.

Results from the conventional approach of applying a PH model restricted to those remaining event-free and uncensored at 1 year are also reported in Table S2. As with the smaller set of cutpoints in the main paper, the CS probability estimates between the two models generally fell within ±0.01 of each other. Exceptions occurred in the combination group at months 36 (- 0.012) and 48 (-0.011). Again, because the PE model takes the additional variability associated with (t_j) in the denominator into account in the calculations, the SEs were larger than their counterparts in the PH analysis.

This suggests that the number of cutpoints is not really the critical issue. Rather, identifying cutpoints that capture the dynamics of the changing survival curve is the key consideration.

Table S1: OS probabilities (SEs), adjusted for age and sex, by intervention group using a greater number of cutpoints at the beginning of follow-up from the PE model compared to the PH results

Piecewise Exponential Model			Proportional Hazards Model	
Month	**Pooled Levamisole / Observation**	**Combination Levamisole + 5-FU**	**Pooled Levamisole / Observation**	**Combination Levamisole + 5-FU**
3	0.997 (0.002)	0.984 (0.007)	0.992 (0.003)	0.994 (0.002)
6	0.976 (0.006)	0.970 (0.010)	0.971 (0.006)	0.980 (0.004)
9	0.944 (0.009)	0.957 (0.012)	0.943 (0.008)	0.960 (0.006)
12	0.915 (0.011)	0.918 (0.016)	0.907 (0.010)	0.934 (0.009)
15	0.874 (0.013)	0.895 (0.018)	0.868 (0.012)	0.906 (0.011)
18	0.841 (0.015)	0.872 (0.019)	0.836 (0.013)	0.883 (0.013)
21	0.804 (0.016)	0.835 (0.021)	0.796 (0.015)	0.853 (0.015)
24	0.760 (0.017)	0.803 (0.023)	0.752 (0.016)	0.820 (0.017)
30	0.700 (0.018)	0.760 (0.024)	0.694 (0.017)	0.775 (0.020)
36	0.641 (0.019)	0.744 (0.025)	0.645 (0.018)	0.737 (0.022)
48	0.560 (0.020)	0.681 (0.027)	0.566 (0.019)	0.672 (0.025)
72	0.489 (0.020)	0.607 (0.028)	0.489 (0.020)	0.607 (0.028)
108	0.400 (0.028)	0.540 (0.038)	0.413 (0.029)	0.540 (0.035)
Abbreviations: PE, Piecewise exponential; PH, Proportional hazards; 5-FU, fluorouracil				

Table S2: CS probabilities (SEs), adjusted for age and sex, by intervention group using a greater number of cutpoints at the beginning of follow-up from the PE Model Compared to the PH Results.

Piecewise Exponential Model			Proportional Hazards Model	
Month	**Pooled Levamisole/ Observation**	**Combination Levamisole + 5-FU**	**Pooled Levamisole/ Observation**	**Combination Levamisole + 5-FU**
15	0.954 (0.009)	0.975 (0.009)	0.956 (0.008)	0.971 (0.006)
18	0.919 (0.011)	0.950 (0.013)	0.921 (0.010)	0.948 (0.008)
21	0.879 (0.014)	0.910 (0.017)	0.876 (0.012)	0.917 (0.011)
24	0.830 (0.016)	0.874 (0.020)	0.827 (0.014)	0.883 (0.014)
30	0.765 (0.018)	0.828 (0.023)	0.762 (0.017)	0.837 (0.017)
36	0.700 (0.019)	0.810 (0.023)	0.708 (0.018)	0.798 (0.020)
48	0.611 (0.020)	0.742 (0.026)	0.619 (0.020)	0.731 (0.024)
72	0.534 (0.021)	0.661 (0.029)	0.534 (0.021)	0.664 (0.028)
108	0.437 (0.030)	0.589 (0.040)	0.450 (0.031)	0.594 (0.036)
Abbreviations: PE, Piecewise exponential; PH, Proportional hazards; 5-FU, fluorouracil				