

# Generate ALS cohort descriptive statistics and illustrative timeline figures

Table 1. Demographics of study patients by diagnosis

```
##### Descriptive Statistics
vars <- c("age", "dx_delay", "simp_site", "C9", "censor_time", "countlong",
          "First_alsfrs_t_mnth", "first_from_dx", "First_ALSFRS_Total")
factorVars <- c("simp_site", "C9")
tab1 <- CreateTableOne(vars = vars, factorVars = factorVars, data=df_ind,
                       test = TRUE, includeNA = TRUE)
tab1.export <- print(tab1, quote = FALSE, noSpaces = TRUE,
                     printToggle = FALSE, showAllLevels = TRUE,
                     nonnormal = c("dx_delay", "censor_time", "First_alsfrs_t_mnth", "first_from_dx"))

print(tab1.export)
```

	level	Overall
n		597
age (mean (SD))		64.60 (9.77)
dx_delay (median [IQR])		10.85 [6.48, 18.02]
simp_site (%)	Spinal	408 (68.3)
	Bulbar	189 (31.7)
C9 (%)	Normal	538 (90.1)
	Expanded	59 (9.9)
censor_time (median [IQR])		31.76 [21.37, 46.36]
countlong (mean (SD))		3.69 (3.33)
First_alsfrs_t_mnth (median [IQR])		15.02 [9.96, 24.00]
first_from_dx (median [IQR])		2.93 [1.41, 5.82]
First_ALSFRS_Total (mean (SD))		36.53 (7.04)

Fit a lognormal distribution to delayed entry times for this cohort

```
tidy ( fitdistr(df_ind$dx_delay, "lognormal") )

## # A tibble: 2 x 3
##   term      estimate std.error
##   <chr>      <dbl>      <dbl>
## 1 meanlog    2.35        0.0313
## 2 sdlog      0.764       0.0221
```

Note - these values differ slightly to those used in the simulation study because we were able to include more patients after we had run the simulation study.

What is the mean value of the first ALSFRSR, mean time from onset, and mean time from diagnosis at time of first ALSFRSR

```
summary(df_ind$First_ALSFRS_Total)
```

```
##      Min. 1st Qu.  Median      Mean 3rd Qu.      Max.
##    10.00   32.00   38.00   36.53   42.00   47.00
```

```
summary(df_ind$First_alsfrs_t_mnths)
```

```
##      Min. 1st Qu.  Median      Mean 3rd Qu.      Max.
##    1.611   9.962  15.025  18.321  24.000  59.507
```

```
summary(df_ind$First_alsfrs_t_mnths - df_ind$dx_delay)
```

```
##      Min. 1st Qu.  Median      Mean 3rd Qu.      Max.
##   -8.745   1.414   2.926   4.578   5.819  49.348
```

Fit the Joint models used in the simulation study - A thru F

Note the for models E and F splines terms with 2 d.f. were used instead of polynomial terms.

Summary of Cox model hazard ratios

Variable	Model	Parameter	HazRatio	CI_2.5	CI_97.5	p.value
dx_delay	A	-0.061	0.941	0.931	0.951	0.000
dx_delay	B & E	-0.034	0.966	0.955	0.978	0.000
dx_delay	D & F	-0.007	0.993	0.983	1.003	0.184
simp_siteBulbar	A	0.267	1.306	1.086	1.570	0.004
simp_siteBulbar	B & E	0.255	1.290	1.073	1.551	0.007
simp_siteBulbar	C	0.268	1.308	1.091	1.568	0.004
simp_siteBulbar	D & F	0.247	1.280	1.064	1.539	0.009

Summary of JM event coefficients

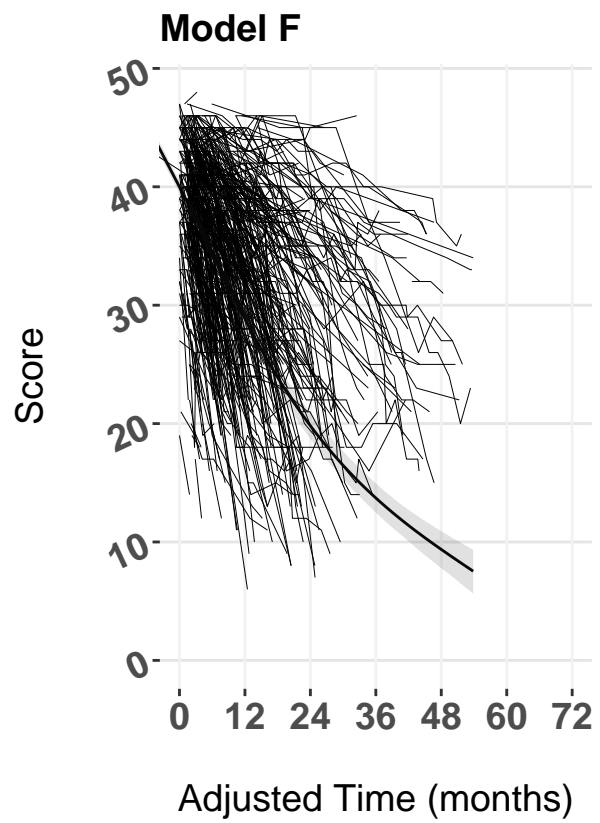
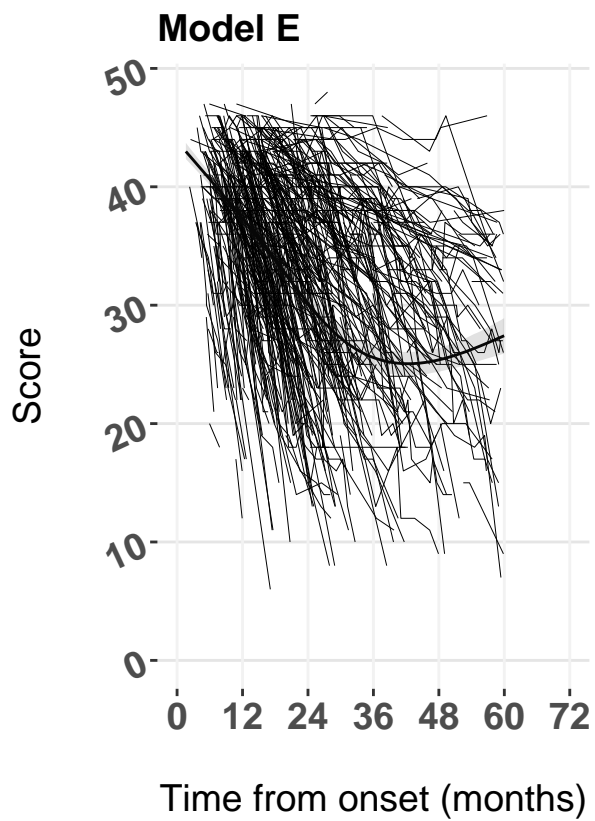
Variable	Model	Parameter	HazRatio	CI_2.5	CI_97.5	P
Assoct	A	-0.064	0.938	0.928	0.948	0.000
Assoct	B	-0.062	0.940	0.931	0.949	0.000
Assoct	C	-0.063	0.939	0.929	0.948	0.000
Assoct	D	-0.065	0.937	0.928	0.946	0.000
Assoct	E	-0.071	0.931	0.923	0.940	0.000
Assoct	F	-0.071	0.932	0.923	0.941	0.000
dx_delay	A	-0.039	0.962	0.950	0.974	0.000
dx_delay	B	-0.011	0.989	0.976	1.002	0.091
dx_delay	D	-0.012	0.988	0.978	0.998	0.011
dx_delay	E	-0.016	0.984	0.972	0.995	0.004
dx_delay	F	-0.009	0.991	0.980	1.001	0.082
simp_siteBulbar	A	0.212	1.237	1.000	1.517	0.051
simp_siteBulbar	B	0.204	1.226	0.998	1.487	0.053
simp_siteBulbar	C	0.213	1.237	1.021	1.485	0.032
simp_siteBulbar	D	0.180	1.197	0.978	1.447	0.078

Variable	Model	Parameter	HazRatio	CI_2.5	CI_97.5	P
simp_siteBulbar	E	0.149	1.160	0.968	1.395	0.102
simp_siteBulbar	F	0.166	1.180	0.974	1.428	0.095

### Summary of JM longitudinal coefficients

Variable	Model	Parameter	CI_2.5	CI_97.5	P
(Intercept)	A	48.374	47.496	49.293	0
(Intercept)	B	48.374	47.373	49.306	0
(Intercept)	C	40.245	39.659	40.808	0
(Intercept)	D	40.263	39.667	40.851	0
(Intercept)	E	42.984	42.338	43.712	0
(Intercept)	F	47.680	46.932	48.433	0
alsfrs_t_mnths	A	-0.798	-0.855	-0.744	0
alsfrs_t_mnths	B	-0.799	-0.853	-0.742	0
adj_time	C	-0.974	-1.037	-0.914	0
adj_time	D	-0.974	-1.032	-0.915	0
ns(alsfrs_t_mnths, 3)1	E	-17.784	-19.569	-16.067	0
ns(alsfrs_t_mnths, 3)2	E	-24.193	-25.772	-22.598	0
ns(alsfrs_t_mnths, 3)3	E	-11.766	-13.499	-10.109	0
ns(adj_time, 3)1	F	-26.779	-28.718	-24.892	0
ns(adj_time, 3)2	F	-45.208	-47.086	-43.403	0
ns(adj_time, 3)3	F	-35.106	-36.867	-33.386	0

Marginal effect plots of longitudinal submodels for models E and F



## pdf  
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