Chapter 16 - Crossover Designs

Balanced Case - Each subject receives each treatment once (over time)

- Each treatment appears the same number of times in each period
- Each treatment directly follows every other trt an equal number of times
- All possible sequences occur equal # of times (this implies previous two statements)

Very similar to RCB, except that there is potential for carryover effects from one trt to another in consecutive periods.

Model $\left[\begin{array}{l} t \text{ trts,} \\ n \text{ sequences} \\ r_i \text{ subj/seq. } i \end{array}\right]$ ($n = t!$ when all possible sequences appear)

$$Y_{ijk} = \mu + \alpha_i + b_{ij} + \gamma_k + \tau_{d(i,k)} + \lambda_{c(i,k-1)} + e_{ijk} \qquad \begin{array}{l} i = 1, \dots, n \\ j = 1, \dots, r_i \\ k = 1, \dots, p \\ d, c = 1, \dots, t \end{array}$$

where: $Y_{ijk} \equiv$ response for j^{th} subject w/in i^{th} sequence in period k

$\mu \equiv$ overall mean

$\alpha_i \equiv$ Effect of i^{th} sequence

$b_{ij} \equiv$ Random effect of j^{th} subject w/in sequence i ~~b_{ij}~~ $b_{ij} \sim NID(0, \sigma_b^2)$

$\gamma_k \equiv$ Effect of k^{th} period

$\tau_{d(i,k)} \equiv$ Direct effect of trt d in sequence i & period k

$\lambda_{c(i,k-1)} \equiv$ Carryover effect of trt c that appeared in period $k-1$ in sequence i

$e_{ijk} \equiv$ Random error $\quad e_{ijk} \sim NID(0, \sigma^2) \quad \{e\} \perp \{b\}$

Common Simplifying Assumptions

$\tau_{d(i,k)} \equiv \tau_d \Rightarrow$ Direct effect of trt d is constant across sequences and periods.

$\lambda_{c(i,k-1)} \equiv \lambda_c \Rightarrow$ Carryover effect of TRT i is constant across sequences and period

Case of 3 TRTS IN 3 PERIODS ($\Rightarrow 3! = 6$ POSSIBLE SEQUENCES)

($\tau_1, \lambda_1 \equiv$ TRT A, $\tau_2, \lambda_2 \equiv$ TRT B $\tau_3, \lambda_3 \equiv$ TRT C)

SEQUENCE (i)	$E[\bar{Y}_{i\cdot 1}]$	$E[\bar{Y}_{i\cdot 2}]$	$E[\bar{Y}_{i\cdot 3}]$
$A \to B \to C$ (1)	$\mu + \alpha_1 + \gamma_1 + \tau_1$	$\mu + \alpha_1 + \gamma_2 + \tau_2 + \lambda_1$	$\mu + \alpha_1 + \gamma_3 + \tau_3 + \lambda_2$
$A \to C \to B$ (2)	$\mu + \alpha_2 + \gamma_1 + \tau_1$	$\mu + \alpha_2 + \gamma_2 + \tau_3 + \lambda_1$	$\mu + \alpha_2 + \gamma_3 + \tau_2 + \lambda_3$
$B \to A \to C$ (3)	$\mu + \alpha_3 + \gamma_1 + \tau_2$	$\mu + \alpha_3 + \gamma_2 + \tau_1 + \lambda_2$	$\mu + \alpha_3 + \gamma_3 + \tau_3 + \lambda_1$
$B \to C \to A$ (4)	$\mu + \alpha_4 + \gamma_1 + \tau_2$	$\mu + \alpha_4 + \gamma_2 + \tau_3 + \lambda_2$	$\mu + \alpha_4 + \gamma_3 + \tau_1 + \lambda_3$
$C \to A \to B$ (5)	$\mu + \alpha_5 + \gamma_1 + \tau_3$	$\mu + \alpha_5 + \gamma_2 + \tau_1 + \lambda_3$	$\mu + \alpha_5 + \gamma_3 + \tau_2 + \lambda_1$
$C \to B \to A$ (6)	$\mu + \alpha_6 + \gamma_1 + \tau_3$	$\mu + \alpha_6 + \gamma_2 + \tau_2 + \lambda_3$	$\mu + \alpha_6 + \gamma_3 + \tau_1 + \lambda_2$

Assume Huynh-Feldt condition holds (equal variances for all possible pairwise differences w/in experimental units)

Computational Aspects of Analysis (Variables assigned to each observation)

$y \equiv$ Response (sequence i, subject $j(i)$, period k)

SEQ $\equiv$ Sequence # $(1, \ldots, n = t!)$

SUBJ(SEQ) $\equiv$ SUBJ # nested w/in trt $(1, \ldots, r_i)$

PERIOD $(1, \ldots, p)$ (typically $p = t$)

TRT $\equiv$ TRT # $(1, \ldots, t)$

CO $\equiv$ CARRYOVER TRT (0 if Period 1, $1, \ldots, t$ ow)

① To test for carryover effects, fit model w/ CO listed last in model statement

(carryover & direct effects not orthogonal, since no carryover effects exist in period 1).

SS for CO are adjusted for TRT (Direct)

② To test for direct effects, fit model w/ TRT listed last in model statement

SS for TRT are adjusted for carryover

③ ① & ② can be obtained from Type III sums of squares (partial).

Analysis of Variance $\left(N = \sum_{i=1}^{\hat{}} r_i = rt \text{ when } r \text{ reps/sequence for all possible sequences} \right)$

	Source	df	SS
BTW subjects	SEQUENCE	$n-1$	$p\sum_i r_i(\bar{y}_{i..}-\bar{y}_{...})^2$
	SUBJ(seq)	$\sum_i (r_i-1)$	$p\sum_i\sum_j (\bar{y}_{ij.}-\bar{y}_{i..})^2$
subjects	PERIOD	$p-1$	$\left(\sum_i r_i\right)\sum_k (\bar{y}_{..k}-\bar{y}_{...})^2$
	DIRECT effects	$t-1$	Model dependent (w/w/out carryover)
	Carryover effects	$t-1$	" " (" " direct)
	Error	$(N-1)(p-1)-2(t-1)$	By subtraction
	Total	$Np-1$	$\sum_i\sum_j\sum_k (y_{ijk}-\bar{y}_{...})^2$

Intuitively (Adjusted SS)

SS(DIRECT) = SSE(R) − SSE(F) where Reduced model does not contain Direct TRT var, Full model does.

SS(CO) = SSE(R) − SSE(F) where reduced model does not contain carryover effects, Full model does.