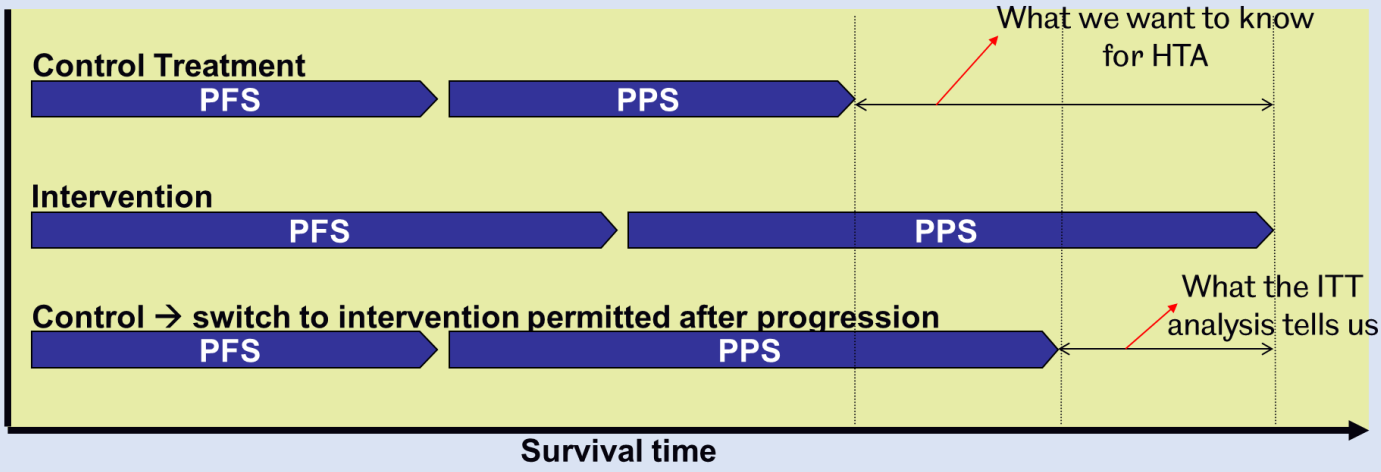
TSD 24: Adjusting survival time estimates in the presence of treatment switching

Treatment switches often occur in clinical trials. If these affect outcomes and do not represent switches that would occur in standard clinical practice, it may be appropriate to use adjustment methods to estimate outcomes that would have been observed if the switches had not occurred.



PFS: Progression-free survival; PPS: Post-progression survival; OS: Overall survival

Switches can occur in either randomised group, onto:

- the treatment received in the other arm of the trial
- other treatments

Whether it is relevant to adjust depends on whether the switches represent treatment pathways that would occur in standard clinical practice

If it is relevant to adjust, it is acceptable to present adjustment analyses alongside standard intention-to-treat analyses.
Several adjustment methods are available. Those used most often are:

- Rank preserving structural failure time models (RPSFTM)
- Inverse probability of censoring weights (IPCW)
- Two-stage estimation (TSE)

It is usually inappropriate to simply exclude or censor switchers

All methods make important assumptions

Adjustment analyses are often poorly planned and poorly reported.

Recommendations

- External assessment groups, appraisal committees, and companies should routinely consider whether switching is an issue
- Describe the treatment switching. Justify which switches require adjustment
- Consider switching when planning trials. Switching could affect the required sample size and analysis plans – adjustment analyses should be pre-specified and data on prognostic characteristics should be collected throughout trial follow-up
- Follow the detailed reporting guidelines included in TSD 24, including:

Description of the data	Adjustment method selection	Method-specific reporting requirements

- Follow guidance in both TSD 16 and TSD 24 to assist with addressing treatment switching