Our Treatment Stop Review tool helps maintain adherence in a large long-term trial.

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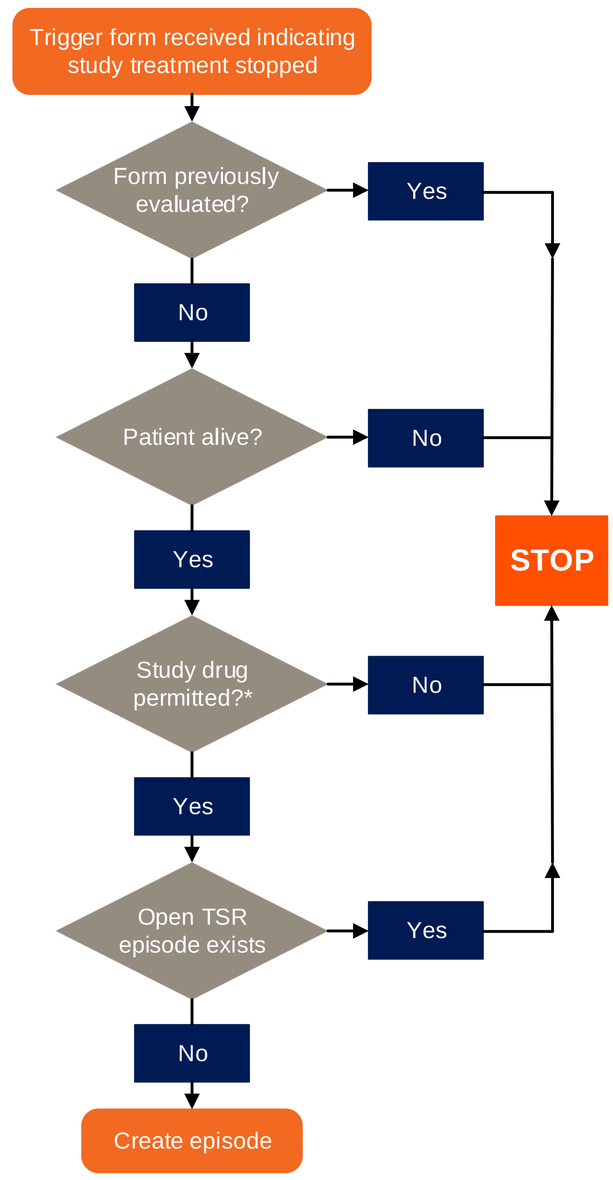
E-Module Logic

TSR Episode creation: automated logic in web-based trial management system.



*i.e. no previous safety concern logged to indicate treatment no longer permitted.

Why it matters

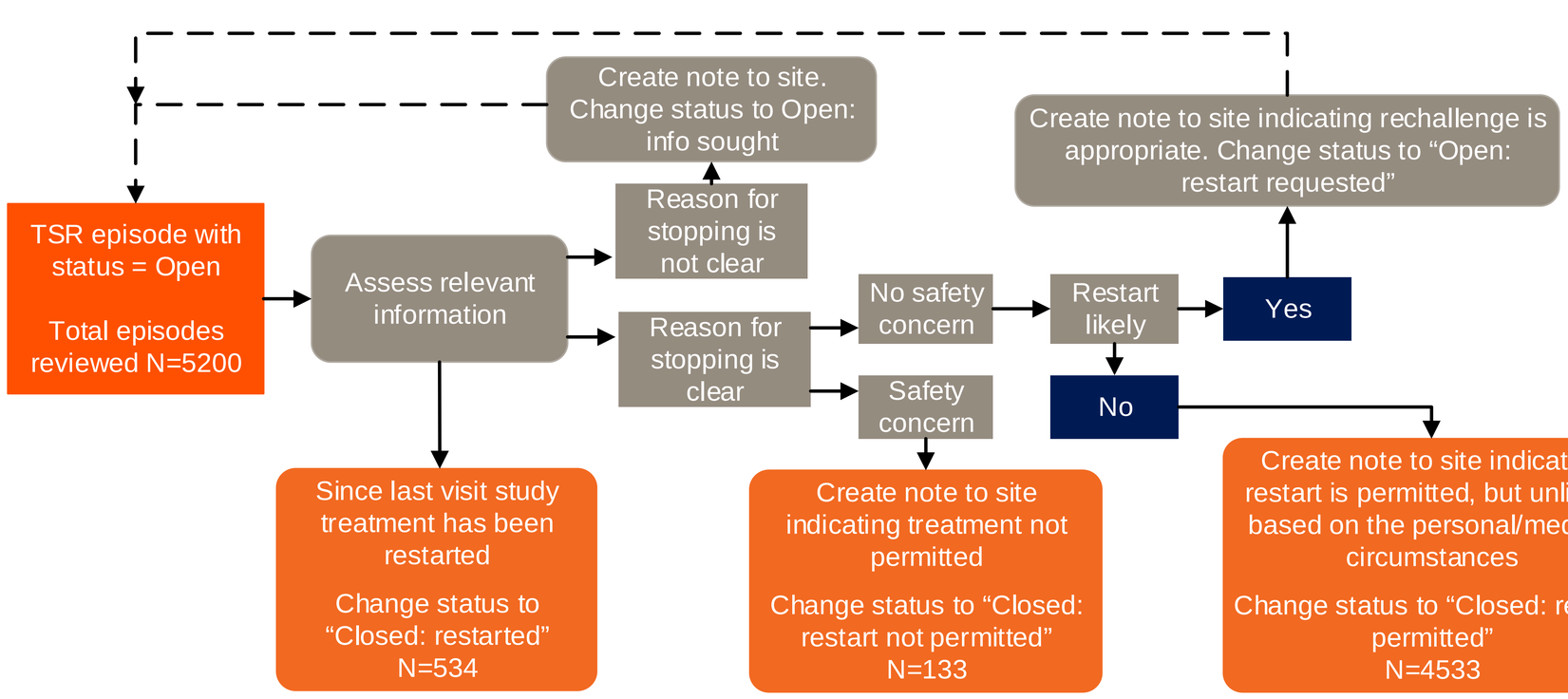
Good adherence to study treatment in clinical trials is essential to ensure the reliable detection of the effects of an intervention. However, maintaining adherence can be challenging in large-scale trials with long follow up durations.

The HPS3/TIMI-55: REVEAL Randomized EValuation of the Effects of Anacetrapib through Lipid-modification (REVEAL) trial, randomized 30,449 participants at 431 sites in Europe, North America and China and followed them up for 4.1 years[1,2]. To facilitate good adherence, an electronic reporting and review module, Treatment Stop Review (TSR), was integrated into a bespoke web-based trial management system.

Our approach

A scheduled job run every 24-hours identified participants who stopped their study treatment on a recent follow-up form. Based on the reason for stopping, "TSR episodes" were routed to clinicians and administrators from the central or regional coordinating centres for further review.

Working together, they confirmed the reason for stopping and ensured that emergent safety concerns were appropriately managed. The module was also used to monitor those who restarted treatment and the outcome of re-challenges.



Key insights

REVEAL maintained very good adherence to study treatment: 90% at the trial midpoint, 85% at the final visit.

- There were 5200 TSR episodes (4863 unique participants, 16% of those randomized).
- Final status of reviewed episodes:
  - Closed: restarted = 534
  378 participants on study drug at end of trial
  - Closed: restart not permitted at that time (for safety reasons) = 133
  6 participants on study drug at end of trial
  - Closed: restart permitted = 4533
  543 participants on study drug at end of trial
- Overall, 19% of those reviewed in the TSR module (927 participants) were on study treatment at the end of the trial.
- TSR ensured participant safety where clinical factors required treatment to be stopped.

Outcome of TSR episode review by region (closed episodes)

	Region (total randomized)				
	UK (8381)	Other Europe† (7357)	North America (6082)	China (8629)	Total (30449)
Restarted	147	93	124	170	534
Treatment not permitted	43	26	45	19	133
Restart permitted	1573	1122	1017	821	4533
Total episodes reviewed	1763	1241	1186	1010	5200

† Italy, Germany, Scandinavia

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References

1. REVEAL Collaborative Group . Effects of anacetrapib in patients with atherosclerotic vascular disease. N Engl J Med 2017;377:1217–1227.

2. REVEAL Collaborative Group . Randomized Evaluation of the Effects of Anacetrapib through Lipid-modification (REVEAL) - a large-scale, randomized, placebo-controlled trial of the clinical effects of anacetrapib among people with established vascular disease: trial design, recruitment, and baseline characteristics. Am Heart J 2017;187:182–190.