Dose Probabilities

Optimizing Drug Supply Outcomes with Veeva RTSM's Advanced Dose Probabilities Functionality

As the patient population in Phase 3 grows to confirm the findings from Phase 2, the complexity of trial supply management will grow in tandem. Some of this can be attributed to factors such as additional sites in expanded countries creating added regulatory compliance along with other factors; however, much of this complexity can be attributed to the increased volume of the patient population in these studies.

Drug Supply Managers often struggle using manual methods from early phase studies when moving to later phases with much larger patient populations. Determining when to send kits to sites to prevent stock outs, what kits to send to ensure they will arrive and be administered before expiration, when to replace kits at site based on expiration, all while trying to balance the cost of shipments and drug wastage, is not something that should be dependent upon inefficient and costly manual methods. These studies require real-time visibility into the supply chain to manage packaging and labeling, automated resupply, cold chain management and transportation of study products through a specialized system like Randomization and Trial Supply Management (RTSM).

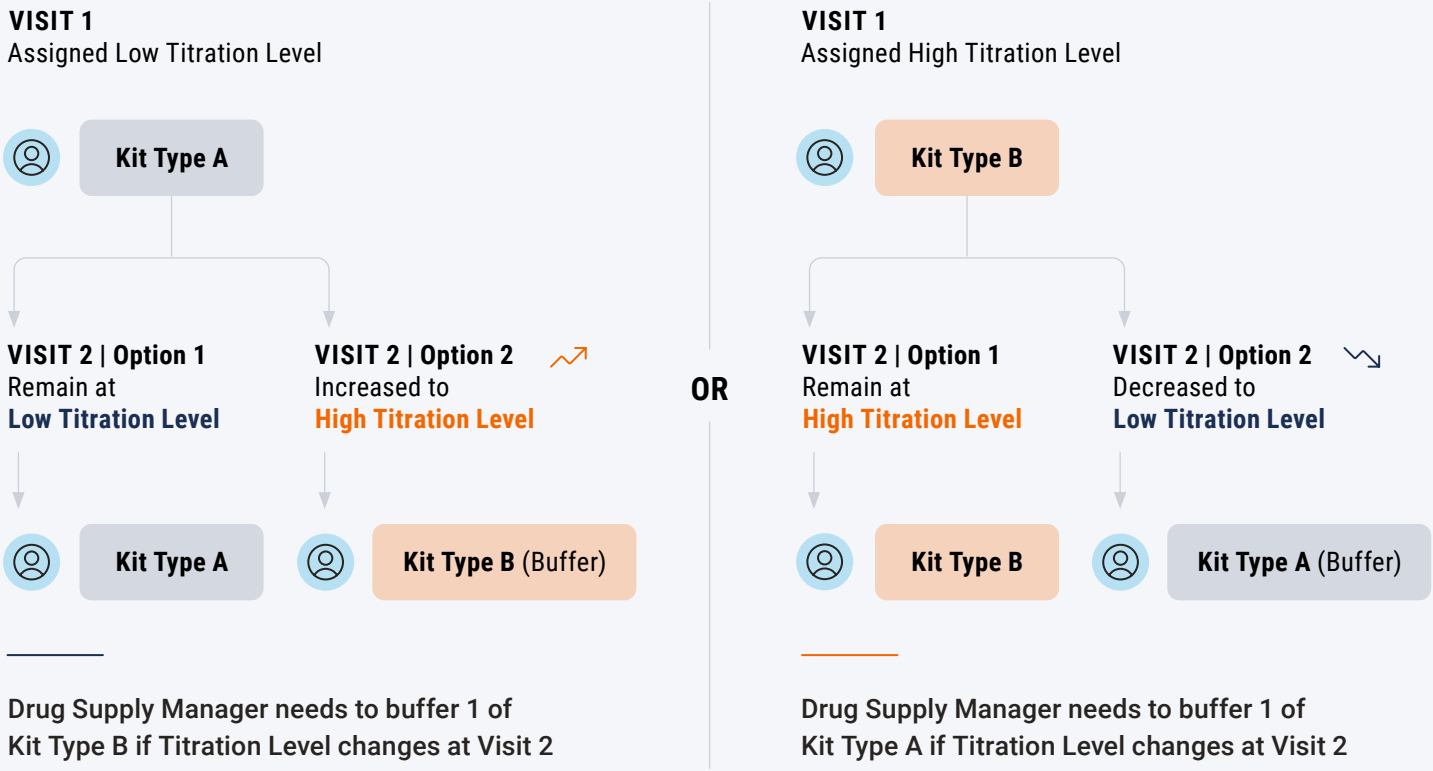
However, not all RTSMs will offer the same ease of use in their resupply management when forecasting. For patients who have multiple visits and the ability to change their dose per visit based on factors such as weight or titration level, there could be larger implications for prediction when these changes cause different quantities or kit types to be dispensed to the patient. In this case, the prediction for the patient's next visit may not be as simple as giving them the same treatment as previously dispensed. They may need to factor in the probability the patient changes dose and the drug type or quantity they will need. A standard RTSM may not account for this and any variance would need to be managed manually in the RTSM by changing buffer levels. This would require constant review and adjustment of these values to match the patient activity at site which can still create a large burden on the Drug Supply Manager to manage across all sites. A more efficient RTSM should be able to predict all the potential outcomes at the patient's next visit and cover the demand to ensure no stock outs occur, rather than to manage these alternate scenarios manually with buffers.

Example and Solution

In an example where a study is designed to have two titration levels (low and high) and different kit types dispensed per titration level (A and B respectively), we can start to see how an advanced RTSM solution can provide value by minimizing manual intervention in the system.

If we look at a standard RTSM, it only accounts for the patient's last treatment and does not include any variance: When one patient is at site, the Drug Supply Manager will always need visibility into the patient's treatment to know what kit type to use as a buffer to help prevent stock outs. If the patient was on the Low Titration Level and dispensed A the last visit, the Drug Supply Manager would need to buffer 1 of kit type B for any changes to the titration level at the next visit. If the patient was on the High Titration Level and dispensed B the last visit, the Drug Supply Manager would need to buffer 1 of kit type A for any changes to the titration level at the next visit.

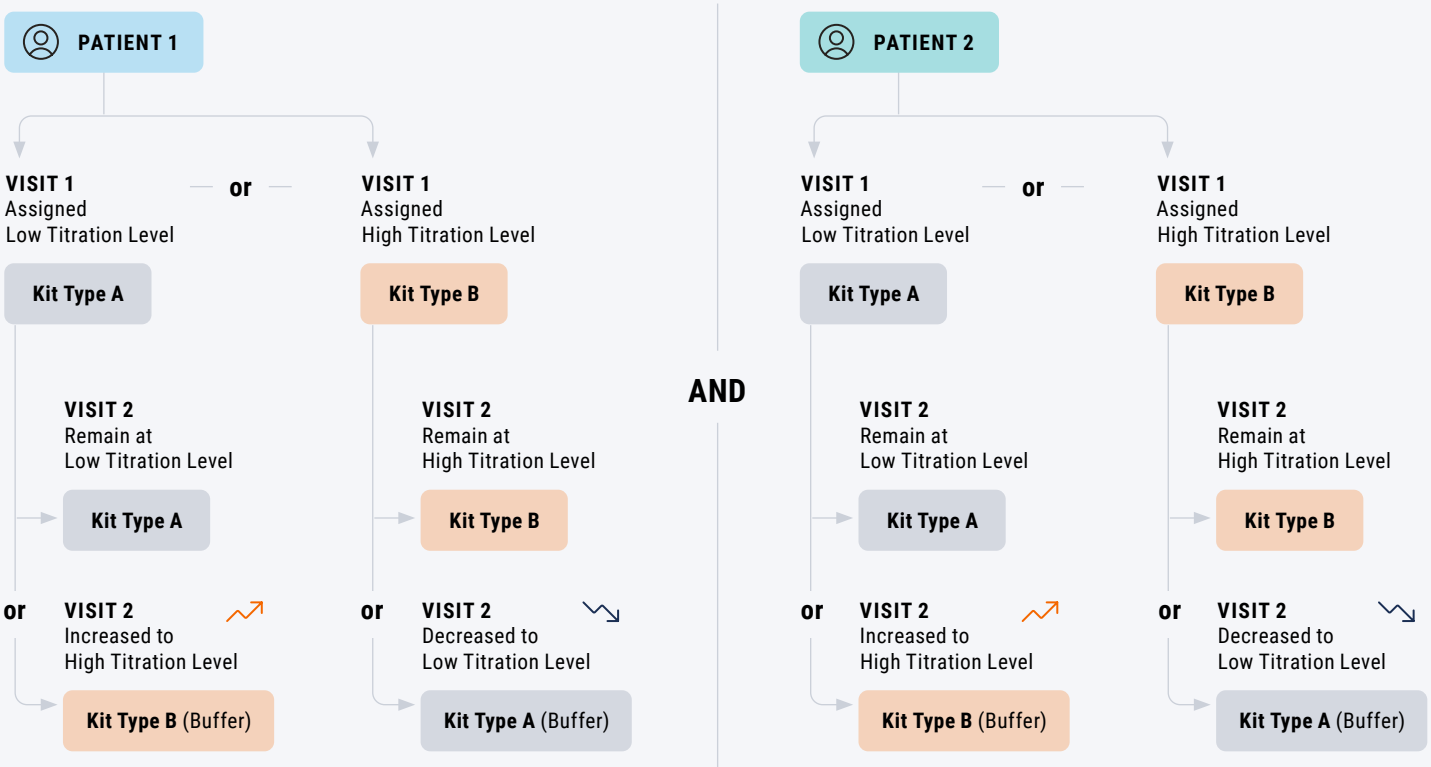
One Patient at Site Scenario



When two patients are at site, the Drug Supply Manager might need to buffer 2 of kit type A, 2 of kit type B or 1 of kit type A and 1 of kit type B based on the patient's titration levels. When three patients are at site, it increases to 4 potential buffer scenarios. Four patients will have 5 potential buffer scenarios and the complexity of scenarios and volume of patients will continue to grow in this manner.

With a much larger patient population in Phase 3 trials, it becomes increasingly important to predict multiple scenarios of dispensation at a patient's next visit aand not rely solely on buffers which risks wasting product.

Two Patients at Site Scenario

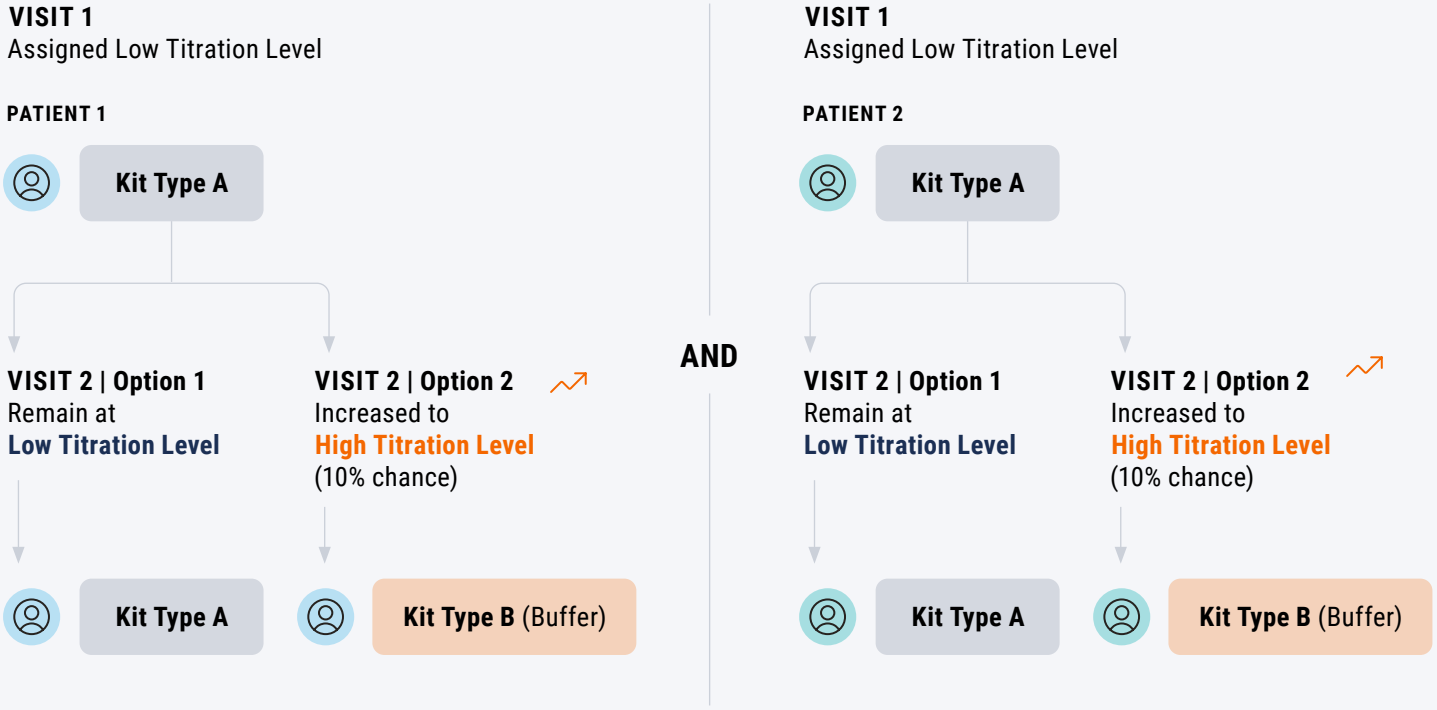


Drug Supply Manager might need to buffer 2 of Kit Type A or 2 of Kit Type B or 1 of Kit Type A and 1 of Kit Type B based on the patient's Titration Levels.
Potential buffer scenarios increased based on complexity of scenarios and volume of patients.

Veeva RTSM has the ability to use its Dose Probabilities functionality to predict all potential demand scenarios for a patient at future visits, to ensure no settings need to be altered as new patients enter treatment or existing patients switch treatment. The amount of drug needed to prevent stock out will dynamically be calculated and changed to match the number of patients and their respective treatments. The above example was illustrated by treatment changes due to titration level but can be applied to any variable factors such as weight, BMI, BSA, etc.

Dose Probabilities can be taken a step further to help save trial supply by predicting partial demand for alternate scenarios, if they are not likely to occur. For example, if there is only a 10% chance a patient may need to titrate at their next visit, there would be a 1% chance two patients at that same level would need to titrate at their next visit. If both patients at site were on a Low Titration Level and dispensed A the last visit, it may make sense to only buffer and predict for 1 of kit type B to save drug and take the 1% risk of stockout if both patients did need to titrate. If this is too aggressive per the supply strategy, the probabilities can be scaled to the appropriate ratio for your study and risk level (2 buffer kits for every 3 patients, or 3 buffer kits for every 4 patients and so on). By not fully buffering for each highly unlikely scenario, Drug Supply Managers are able to save drug wastage on high enrolling studies using dose probabilities. **Veeva biostatisticians can help consult on how to properly utilize dose probabilities in each study design.**

Both Patients on Low Titration Level at last visit Scenario



Drug Supply Manager can account for the 1% chance of both patients requiring Kit Type B as appropriate. Probabilities can be scaled to appropriate ratio for study and risk level.

Conclusion

For Phase 3 studies with dynamic dosing criteria like titration levels or factor-based dosing across multiple visits, a standard RTSM resupply strategy is no longer tenable due to the increased burden on the Drug Supply Manager in overseeing all potential factors across an expanded volume of patients and sites.

By utilizing an advanced RTSM that includes dynamic Dose Probability functionality, as found in Veeva RTSM, Sponsors can automatically predict potential outcomes at the next visit for all patients and cover the demand to ensure no stockouts are caused by these scenarios. The management of buffers will no longer need to include these scenarios, creating a buffer value that is much more likely to be stable and not need manual adjustment. Dose Probability can be taken a step further to partially predict quantities for alternative scenarios and allow for the study to save kits at predefined inflection points in the site's patient volume.

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