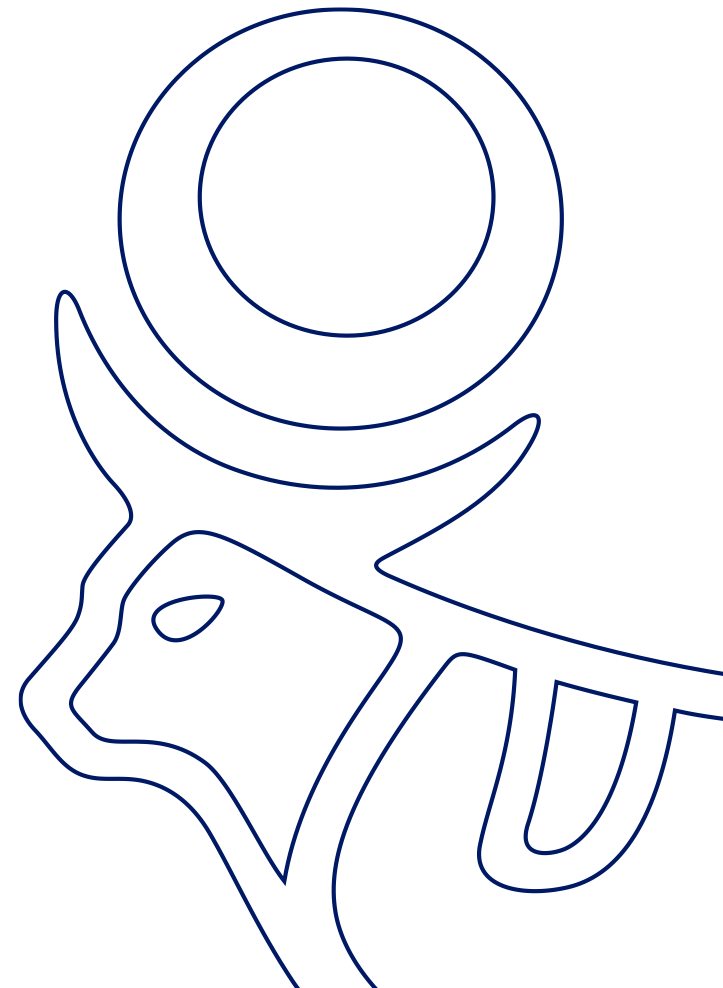


Faster Patient Recruitment in Clinical Trials through Simulations

Keerthana Udupa
Sr Statistician
Novo Nordisk Service Centre India Private Ltd.

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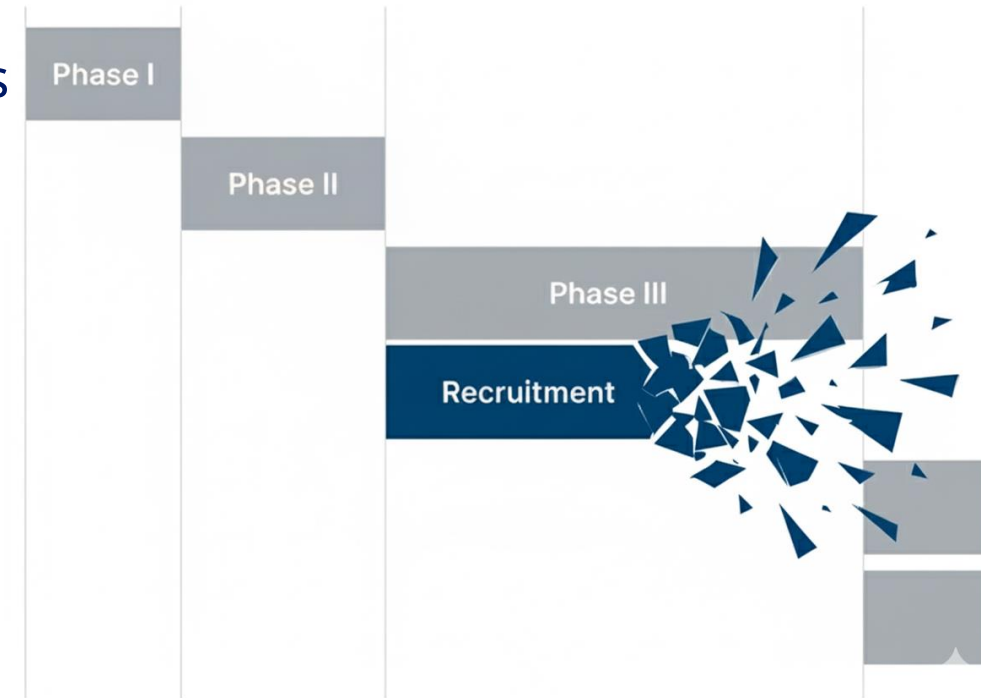
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Recruitment is where Clinical Trial Timelines Break

- Large-scale clinical trials are the strong base for medical approvals, but their success strongly depends on recruiting the right number of patients in the shortest possible time.
- Failure to meet recruitment targets can invalidate a trial's hypothesis, delay of life-saving treatments, and bear massive costs.
- The core challenge is not just finding patients, but accurately forecasting the time it will take.
- Traditional, linear planning often fails because recruitment is not a simple, predictable process.



Source: Generated by "Google, Gemini Chat [Internet]. 2026 Jan 13 [cited 2026 Jan 13]."

Acute vs. Chronic Disease Dynamics

The pattern of patient arrivals varies dramatically based on the nature of the disease.

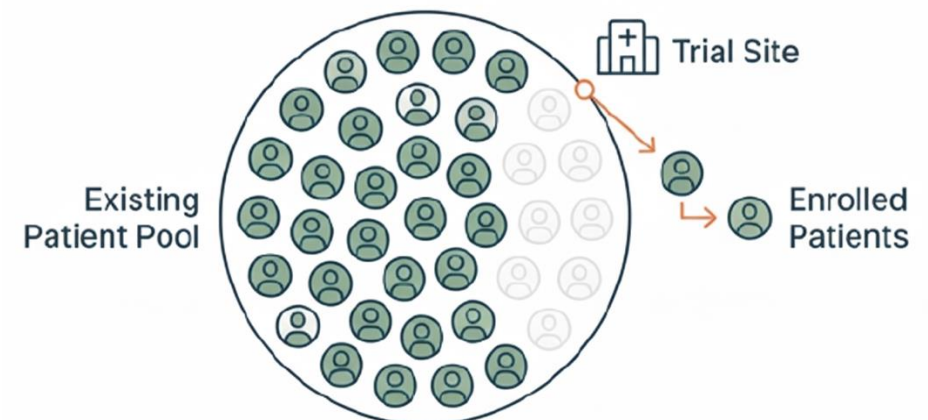
Driven by Incidence

- Characterised by short disease episodes.
- Recruitment is constrained by the rate of new cases appearing on the population.
- The pool of potential patients is constantly being refreshed.



Driven by Prevalence

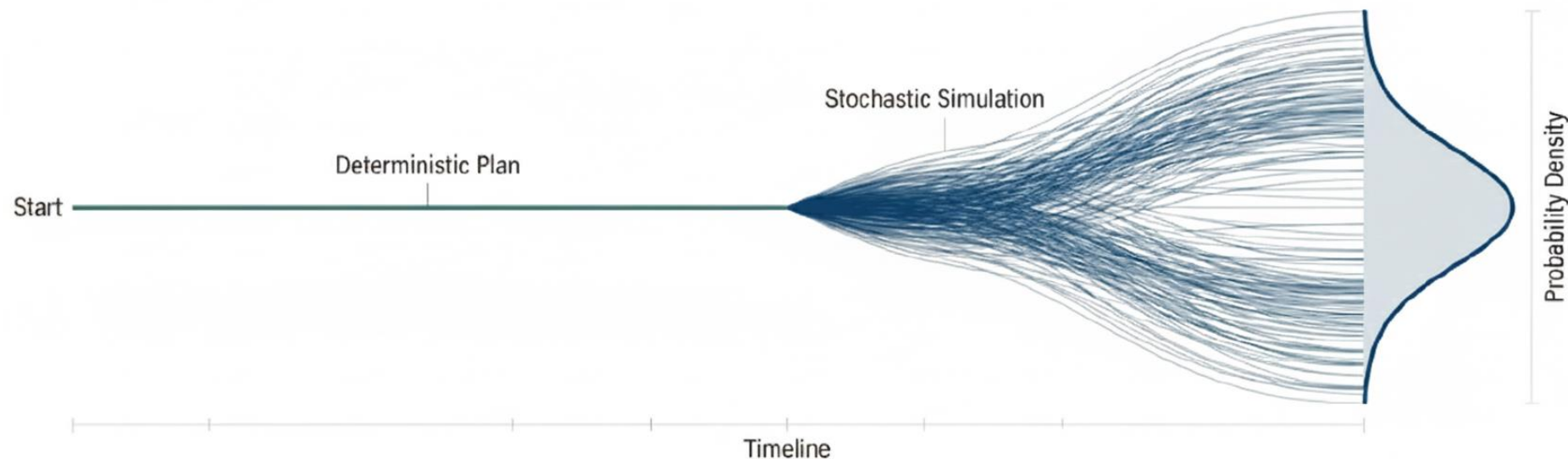
- Characterised by long durations, often lifelong.
- Recruitment is constrained by the existing pool of diagnosed patients.
- This pool is finite and depletes as patients are enrolled.



From a Flawed Guess to a Powerful Forecast

To master recruitment uncertainty, we need to move beyond simple, deterministic calculations. We need a method that embraces randomness and complexity.

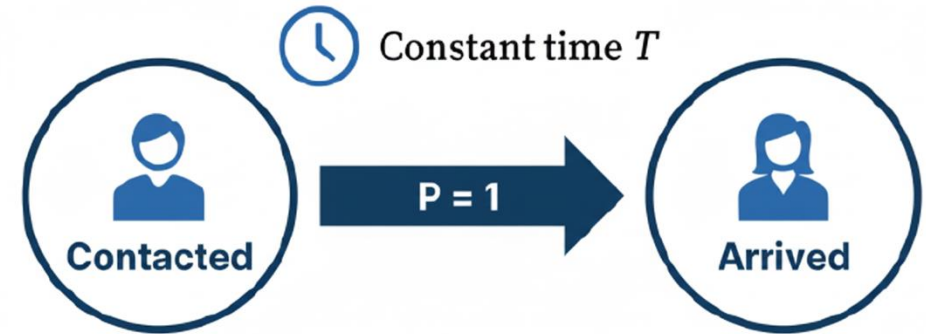
- Monte Carlo Simulation Markov Models provide a framework to design and test recruitment strategies before a trial begins.
- Instead of predicting a single outcome, these models run thousands of simulations to generate a distribution of possible outcomes
- This allows us to quantify risk, estimate variability, and understand the probability of success



A Simple, Deterministic Model

How it works?

- Assumes patient arrivals are perfectly regular and predictable.
- Time is treated as a continuous variable.
- Uses a constant time T between each patient arrival.
- If expected number of patients per month is np , then $T = \frac{1}{np}$
- Total Recruitment Time = $\frac{N}{np}$, where N is the required sample size.



Source: Generated by "Google, Gemini Chat [Internet]. 2026 Jan 13 [cited 2026 Jan 13]."

The Fatal Flaw

This model ignores the fundamental reality of recruitment: randomness. Not every contacted patient enrolls, and arrivals are never perfectly spaced.

Adding Reality with Constant Probability (S1)

- **The core idea**

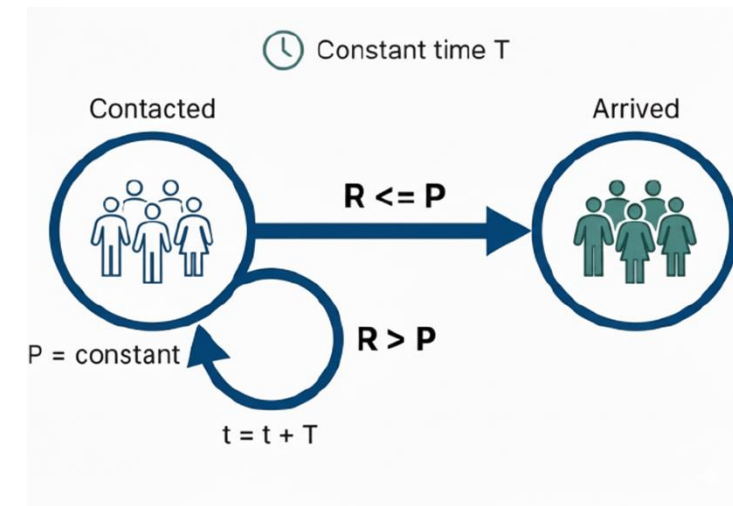
- Not all contacted patients are recruited. We can model this by introducing probability of success, P .

- **How it works?**

- For each contacted patient, a random number R (from 0 to 1) is generated.
- If $R \leq P$, the patient is recruited.
- If $R > P$, the contact fails, and time advances to next attempt.
- This introduces stochasticity. The time between arrivals is no longer fixed; it's a random variable.

- **The Impact**

- The recruitment time becomes longer and, crucially, variable
- Lowering the probability P increases both the average recruitment time and its variability.



Source: Generated by "Google, Gemini Chat [Internet], 2026 Jan 13 [cited 2026 Jan 13]."

Modelling uncertainty in our Assumptions (S2)

- **The scenario**

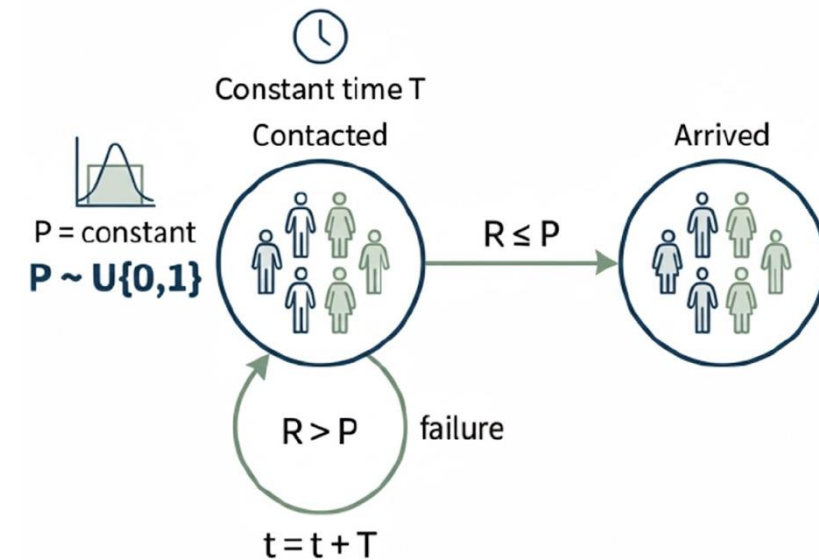
- What if we don't have reliable estimate for the recruitment probability P ? It might vary over time or between patients.

- **How it works?**

- Instead of using a fixed P , we treat P itself as a random variable drawn from a probability distribution for each contact attempt.
- For example, we can assume P is drawn from a Uniform distribution between 0 and 1 ($P = U\{0,1\}$).
- This means some contacts will be “easy” (a high P is drawn) and some will be “hard” (a low P is drawn).

- **The Impact**

- This model captures a higher degree of real-world variability.
- The average outcome might be similar to S1 with $P=0.5$, but the spread of possible recruitment times (the variance) will be significantly larger.



Source: Generated by "Google, Gemini Chat [Internet], 2026 Jan 13 [cited 2026 Jan 13]."

Modelling Recruitment in Discrete Time (S3)

- **When to Use This**

- When the data is aggregated by periods (e.g., “number of patients recruited per week”).
- When individual patient arrival times are not available or not relevant.

- **The Core Idea**

- Time advances in fixed intervals (days, weeks, months).
- The model calculates the number of patients expected to arrive in each period, not the time between them.
- Assumes the pool of potential participants is “with replacement,” meaning it’s large enough not to be depleted (suitable for acute diseases or broad recruitment campaigns).



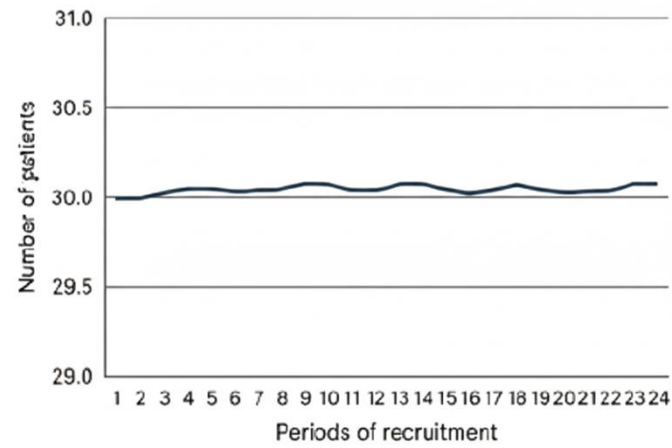
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Modelling Diverse Recruitment Patterns with S3

The discrete time model can be adapted to reflect different real-world scenarios by changing the probability of recruitment (P) across periods. Here are three examples from a hypothetical trial to recruit 720 patients.

Constant Recruitment

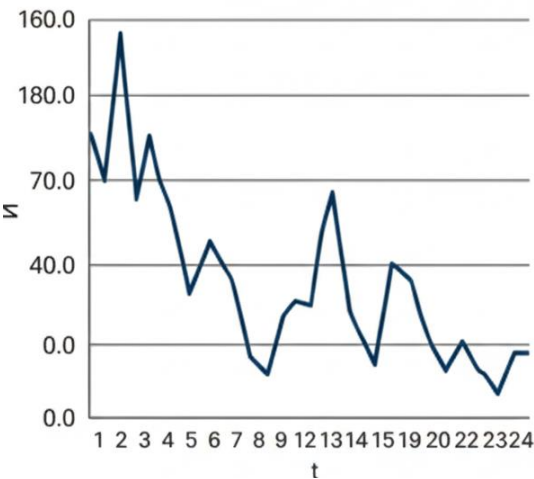
Assumes a fixed probability in every period. This results in a stable, predictable number of arrivals per month.



Source: Generated by "Google. Gemini Chat [Internet]. 2026 Jan 13 [cited 2026 Jan 13]."

Variable Recruitment

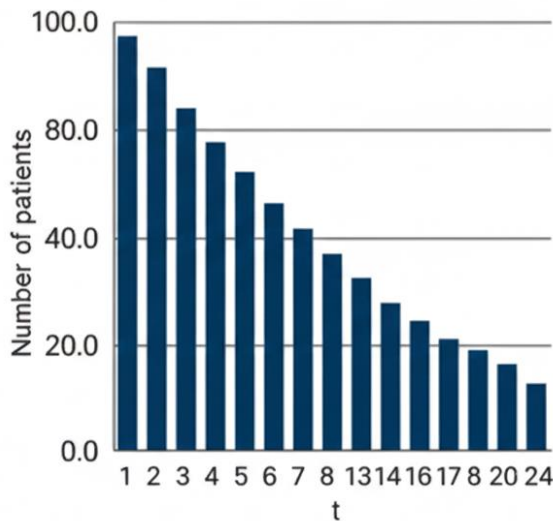
Assumes probability changes from period to period. This can model the effect of specific events, like advertising campaigns creating initial surges that trail off.



Source: Generated by "Google. Gemini Chat [Internet]. 2026 Jan 13 [cited 2026 Jan 13]."

Declining Recruitment

Assumes a consistently decreasing probability over time. This can model a natural drop-off in enthusiasm or initial patient availability.



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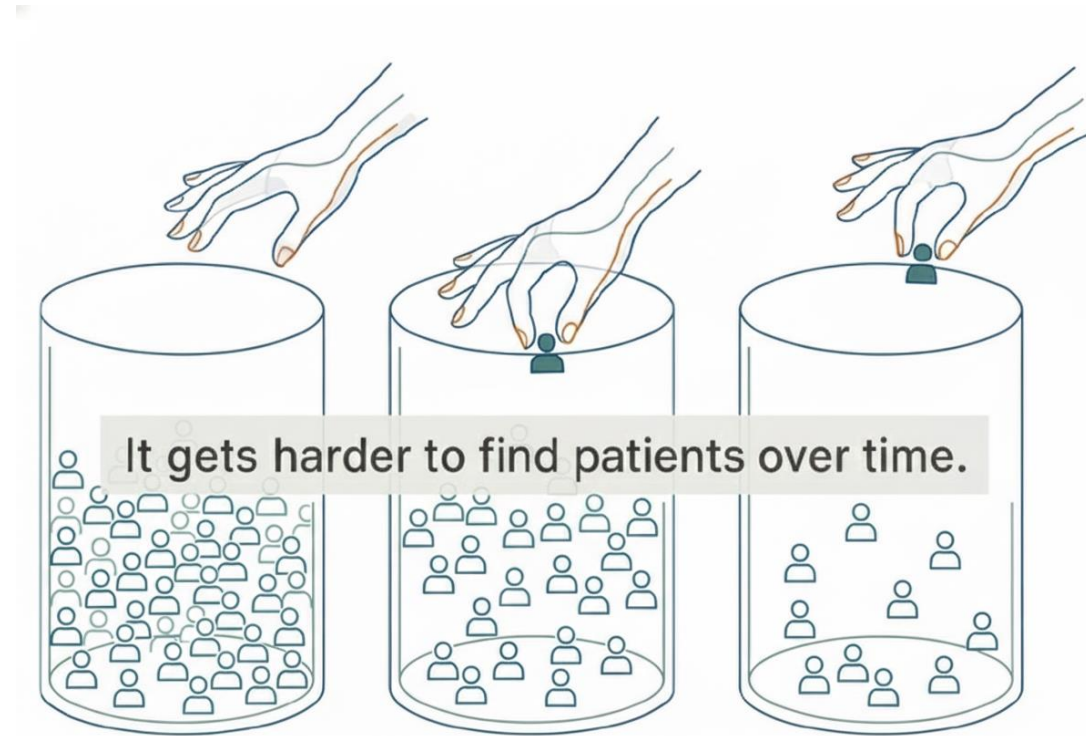
The Challenge: The Depleting Pool in Chronic Disease Trials

- **The Problem Revisited**

- In many trials (especially for chronic or rare diseases), the number of eligible and willing patients is finite.
- Every patient recruited permanently removes one person from the available pool.
- This is a “without replacement” process.

- **The Consequence**

- The rate of recruitment will naturally decrease over time, not because of changing effort, but because it becomes progressively harder to find the remaining eligible patients.
- Models that assume an infinite pool (“with replacement,” like S3) will overestimate recruitment rates in later stages and produce dangerously optimistic timelines.



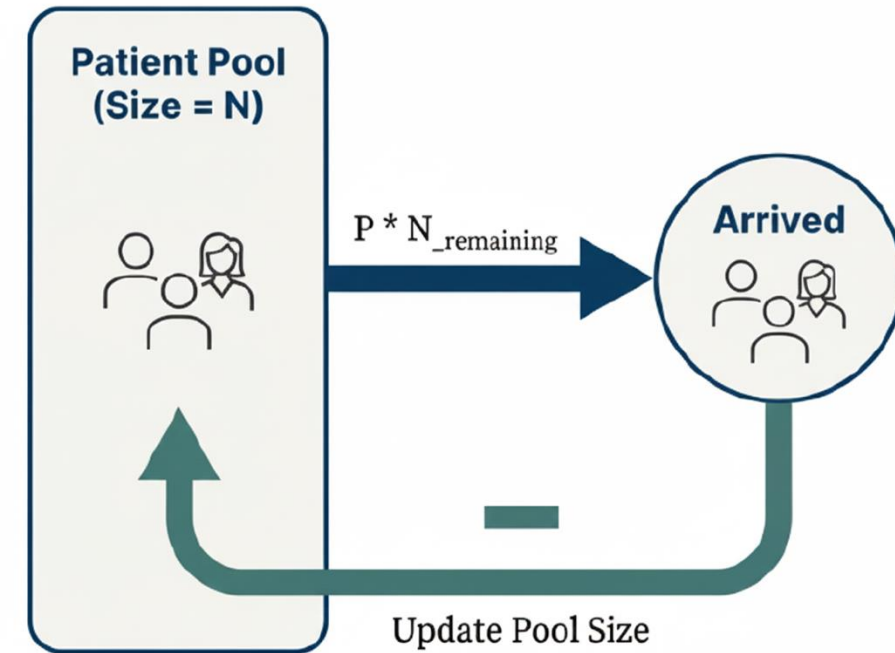
The Tool: Modelling Depletion with Discrete time, Without Replacement (S3)

- **How it works**

- This model is exclusively designed for the scenarios where the patient pool is finite.
- The probability of recruiting a patient in any given period depends on the number of patients remaining in the pool.
- For example, if $P=0.125$ and the pool is 720, we expect to recruit 90 in the first period. The pool is now 630. In the second period, the number of expected recruits is $0.125 \times 630 = 79$, and so on.

- **Key outputs**

- This model can calculate crucial metrics for planning.
- Expected Delay: The average time a trial is likely to be stalled waiting for patients.
- Effective Duration of Recruitment: The actual time spent actively recruiting, accounting for delays.



Source: Generated by "Google, Gemini Chat [Internet], 2026 Jan 13 [cited 2026 Jan 13]."

Case Study

A hypothetical trial to recruit 720 patients, with an initial plan of 24 months.

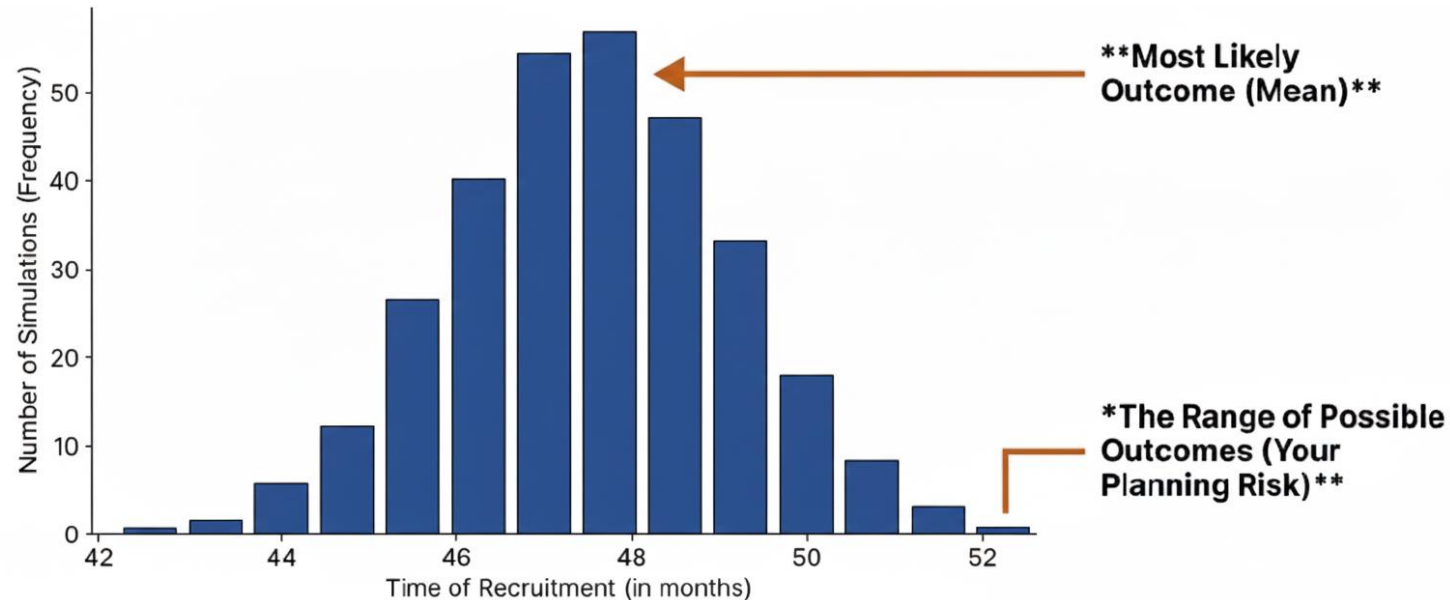
Model Used	Estimated Time (months)	Standard Deviation
Simple Model ($P = 1$)	24.00	0.00
S1 (Constant $P = 0.8$)	30.00	0.51
S1 (Constant $P = 0.5$)	48.03	1.29
S2 ($P \sim \text{Uniform}\{0,1\}$)	47.97	1.24

Ignoring probability and uncertainty (the simple model) leads to a plan that is off by 100%. The choice of model directly impacts the budget, timeline, and risk assessment.

Simulation gives the full picture!

The goal of simulation is not to predict a single, exact recruitment time. It is to understand the distribution of possible futures.

Distribution of Total Recruitment Times (1000 Simulations, S2 Model)



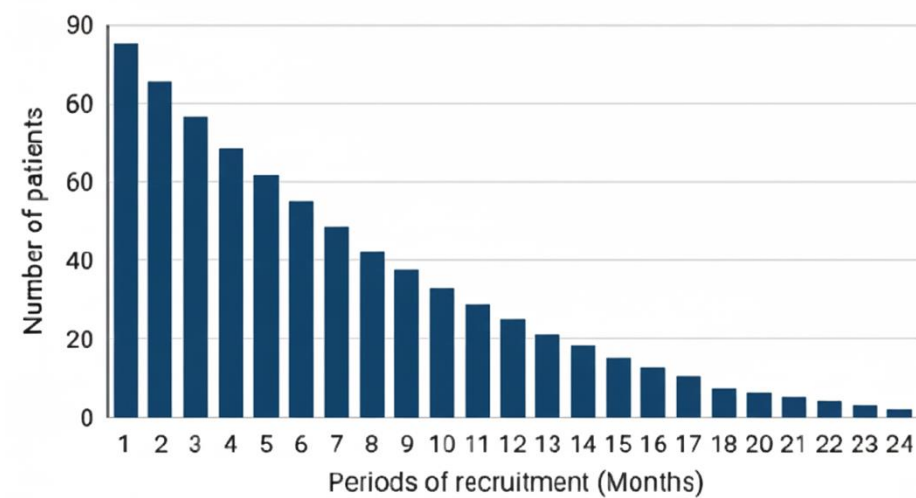
Source: Generated by "Google, Gemini Chat [Internet]. 2026 Jan 13 [cited 2026 Jan 13]."

This graph tells that while the average time is ~48 months, there's a real chance it could take over 50 months. This is critical information for setting realistic deadlines and contingency plans.

Quantifying the impact of Pool Depletion

For chronic disease trials where the patient pool shrinks, using a model that accounts for depletion is essential.

The Declining curve (S3)



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The model predicts a sharp drop-off, from ~95 patients in the first month to fewer than 10 by month 18. A linear plan would completely miss this.

The Delay Metrics (S4)

S4 Results for 10,000 Simulations

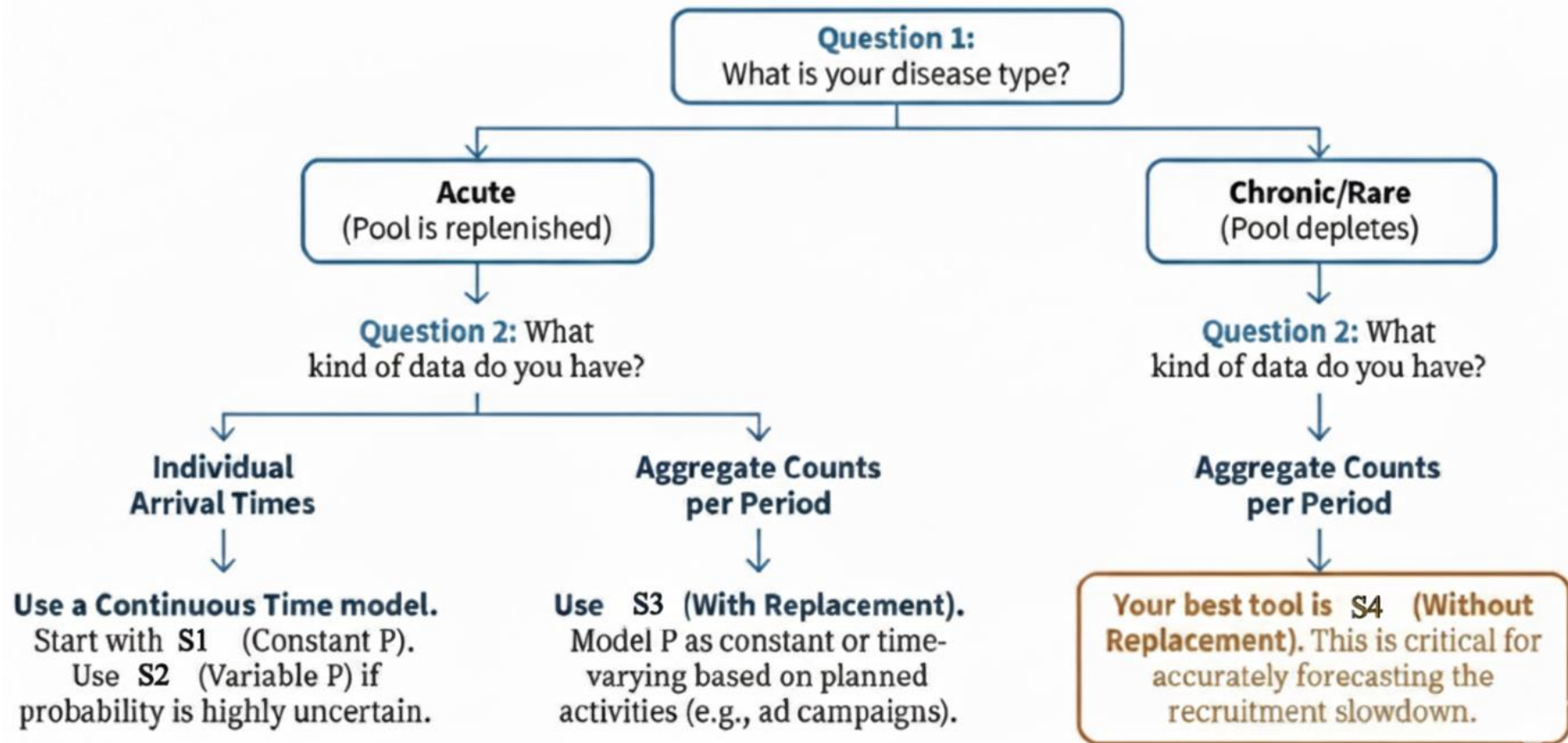
Expected Delay:	6.5 – 6.8 months
Effective duration of recruitment:	17.2 – 17.5 months

This model doesn't just give a total duration; it separates it into effective work time and expected delay, allowing for more precise operational planning.

Which Model is Right for Your Trial?

Framework to select the appropriate simulation model based on trial's characteristics and the data available.

17



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Thank You

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