



# Recruitment rate stochasticity at the design stage of a clinical trial

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## Why recruitment rates?

- Timely recruitment vital to the success of a clinical trial
- Inadequate number of subjects → lack of power
- Recruitment period too long → competing treatments
- Recruitment of patients varies at each stage
- Accrual = Cumulative Recruitment
- [Carter \(2004\)](#)



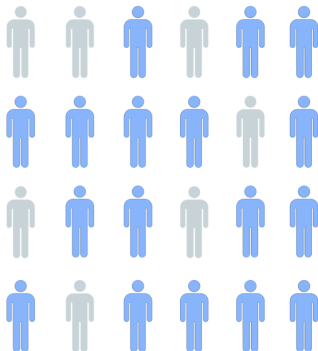
## Target Population



Target Population

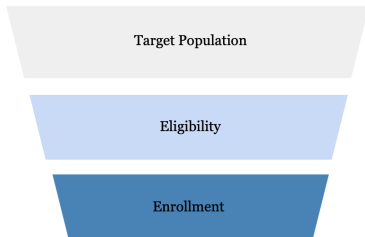
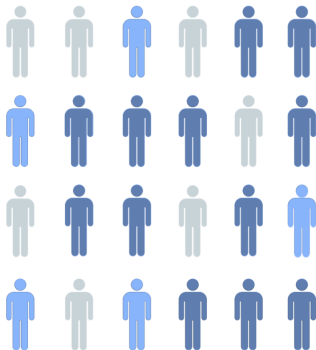


## Eligibility

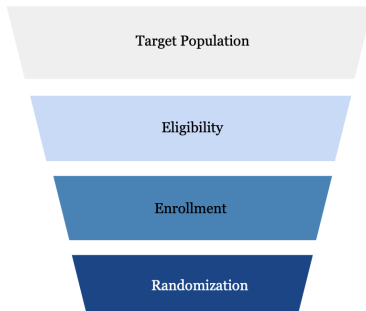
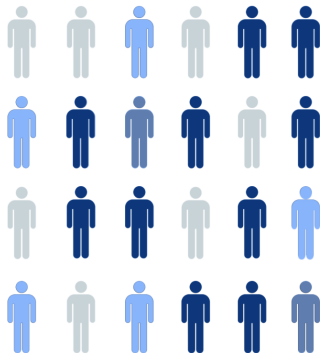




## Enrollment

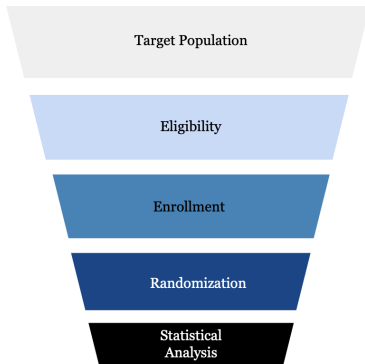
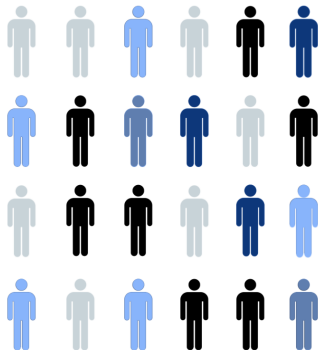


## Randomization

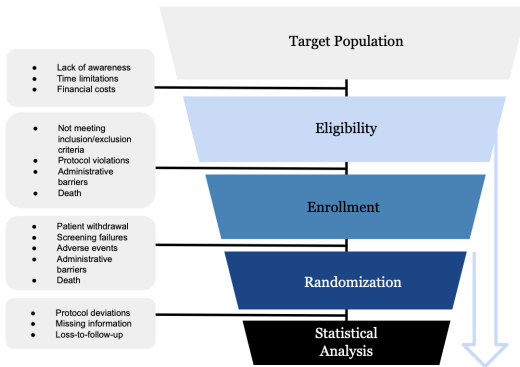




## Statistical Analysis



## Patient Attrition





## Uncertainty

- **Aleatory**: randomness inherent and unpredictable
- **Epistemic**: arises from limited knowledge about parameters

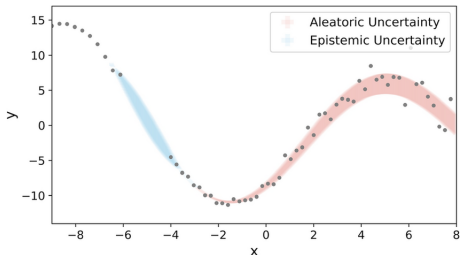


Figure: Visualization of two types of uncertainty (Yang and Li, 2023)



## Models for Counts

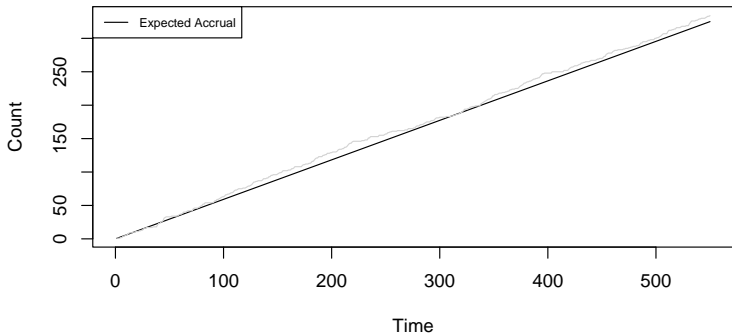
Methods	Counts	Expectation	Variance	Aleatory	Epistemic
Expectation	$C(t) = \lambda t$	$\lambda t$	0	No	No
Poisson	$C(t) \sim \text{Po}(\lambda t)$	$\lambda t$	$\lambda t$	Yes	No
Negative Binomial	$C(t) \sim \text{Po}(\cdot   t); \Lambda \sim G(\alpha, \beta)$	$\frac{\alpha}{\beta}$	$\frac{\alpha(\beta+1)}{\beta^2}$	Yes	Yes

**Table:** Aleatory and epistemic uncertainty in accrual shown by different models for counts.



## Accrual of 1 study

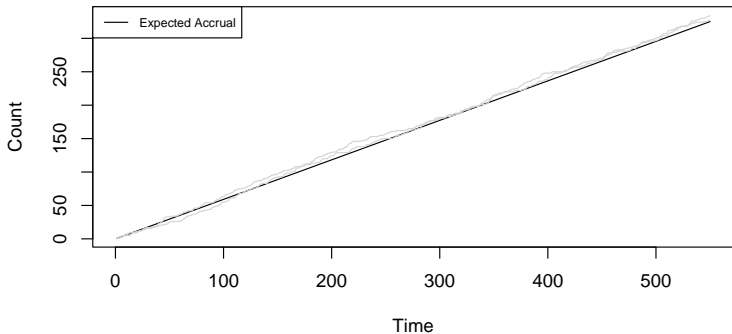
Accrual of 1 study



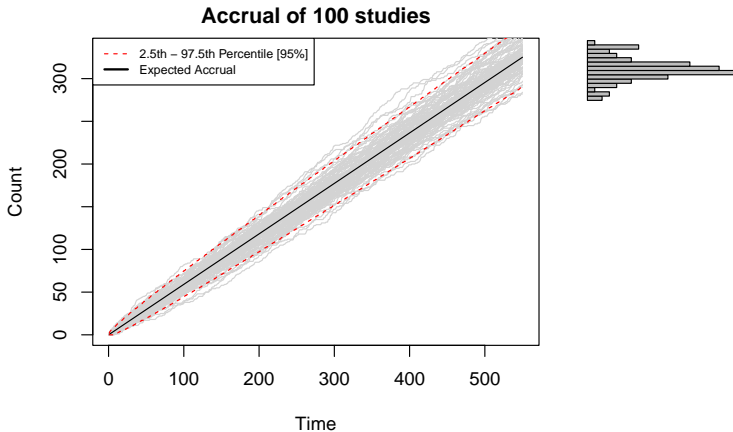


## Accrual of 2 studies

Accrual of 2 studies

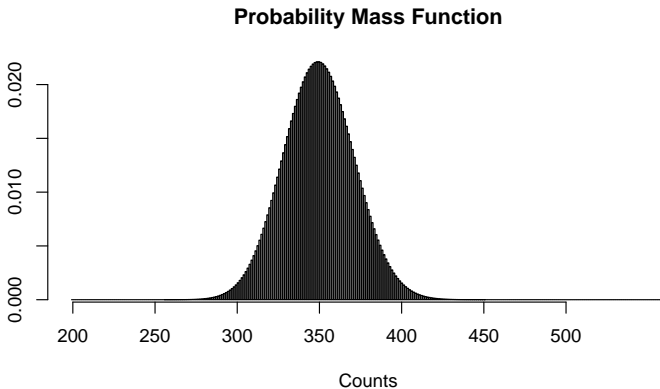


## Accrual of 100 studies



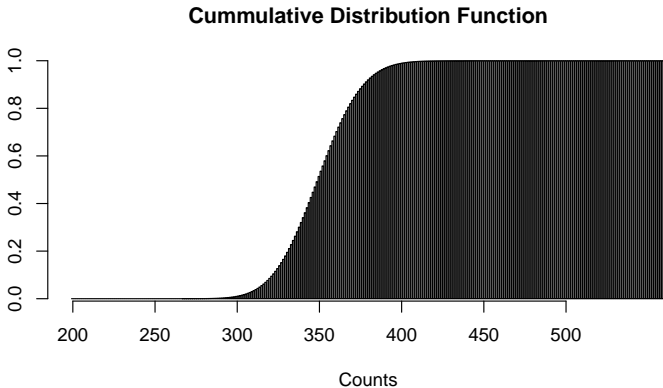


## Theoretical PMF





## Theoretical CDF





## Shrunk Slide 1





## Shrunk slide 2



## Results



## Conclusion



## Next steps



## References

- Carter, R. E. (2004). Application of stochastic processes to participant recruitment in clinical trials. *Controlled clinical trials*, 25(5):429–436.
- Liu, J., Jiang, Y., Wu, C., Simon, S., Mayo, M. S., Raghavan, R., and Gajewski, B. J. (2023). *accrual: Bayesian Accrual Prediction*. R package version 1.4.
- Spiegelhalter, D., Pearson, M., and Short, I. (2011). Visualizing uncertainty about the future. *Science*, 333(6048):1393–1400.
- Yang, C.-I. and Li, Y.-P. (2023). Explainable uncertainty quantifications for deep learning-based molecular property prediction. *Journal of Cheminformatics*, 15(1):13.