# Common Random Numbers in Discrete Event Simulation for Disease Modeling: A Statin Treatment Case Study

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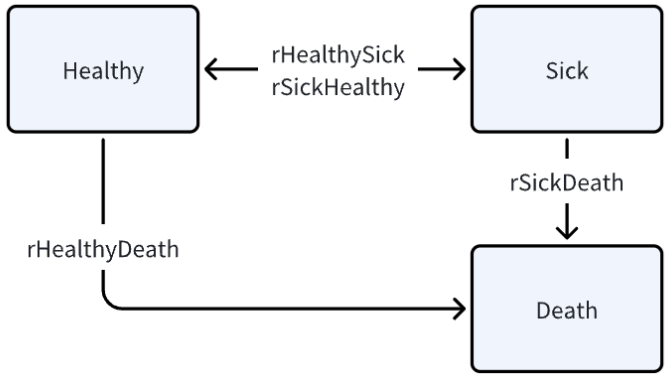
- No conflicts of interest

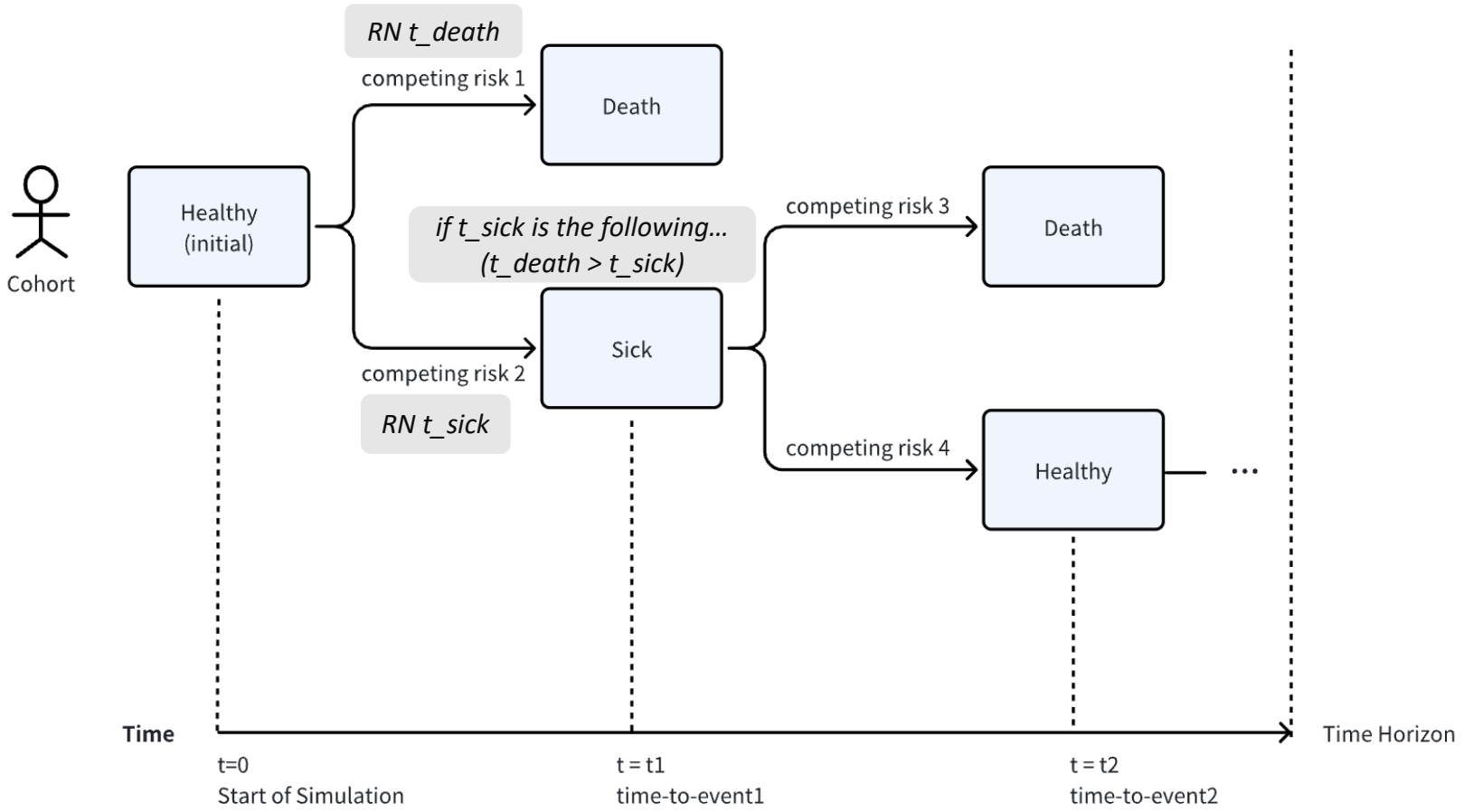
# Common Random Numbers(CRNs)

- To reduce the **stochastic noises** between simulation iterations
- Already been used in micro-simulation, but not in **discrete event simulation**

# Discrete Event Simulation(DES)

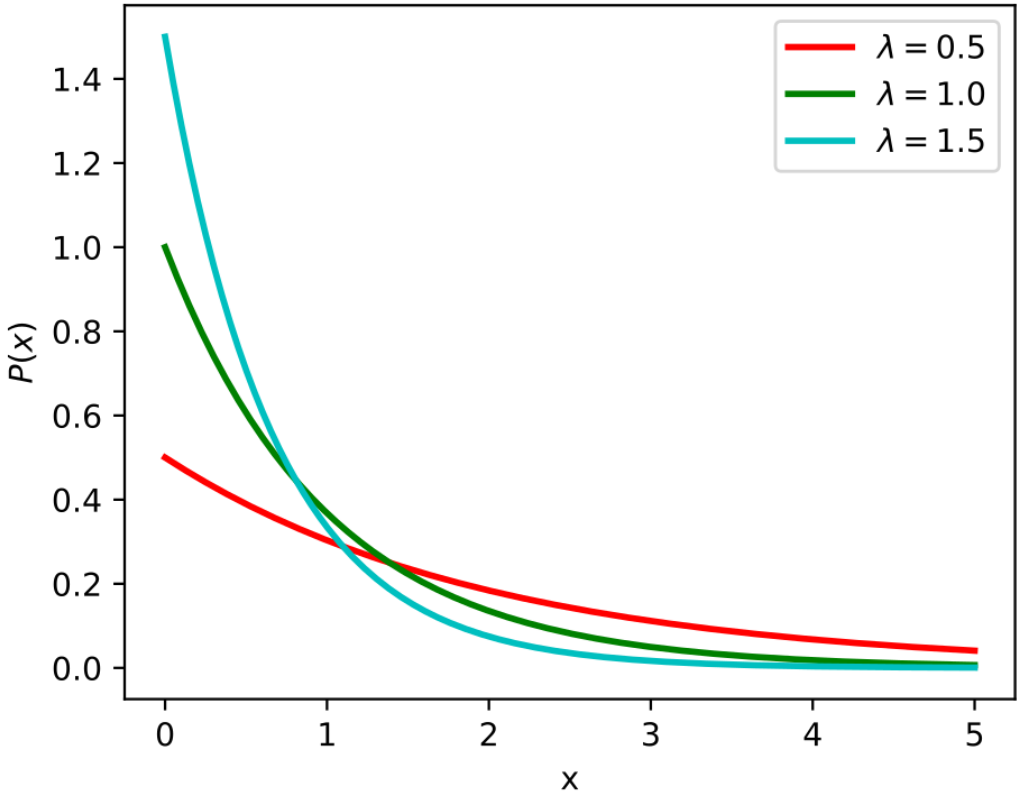



A simple structure of the DES model



# Distribution for time-to-event analysis

- How to generate random numbers in an exponential distribution
- **Inversion sampling**
  - Generate a uniform random number u in (0,1);
  - t = ln(1-u)/(-λ), λ is the rate;
  - u is the quantile.

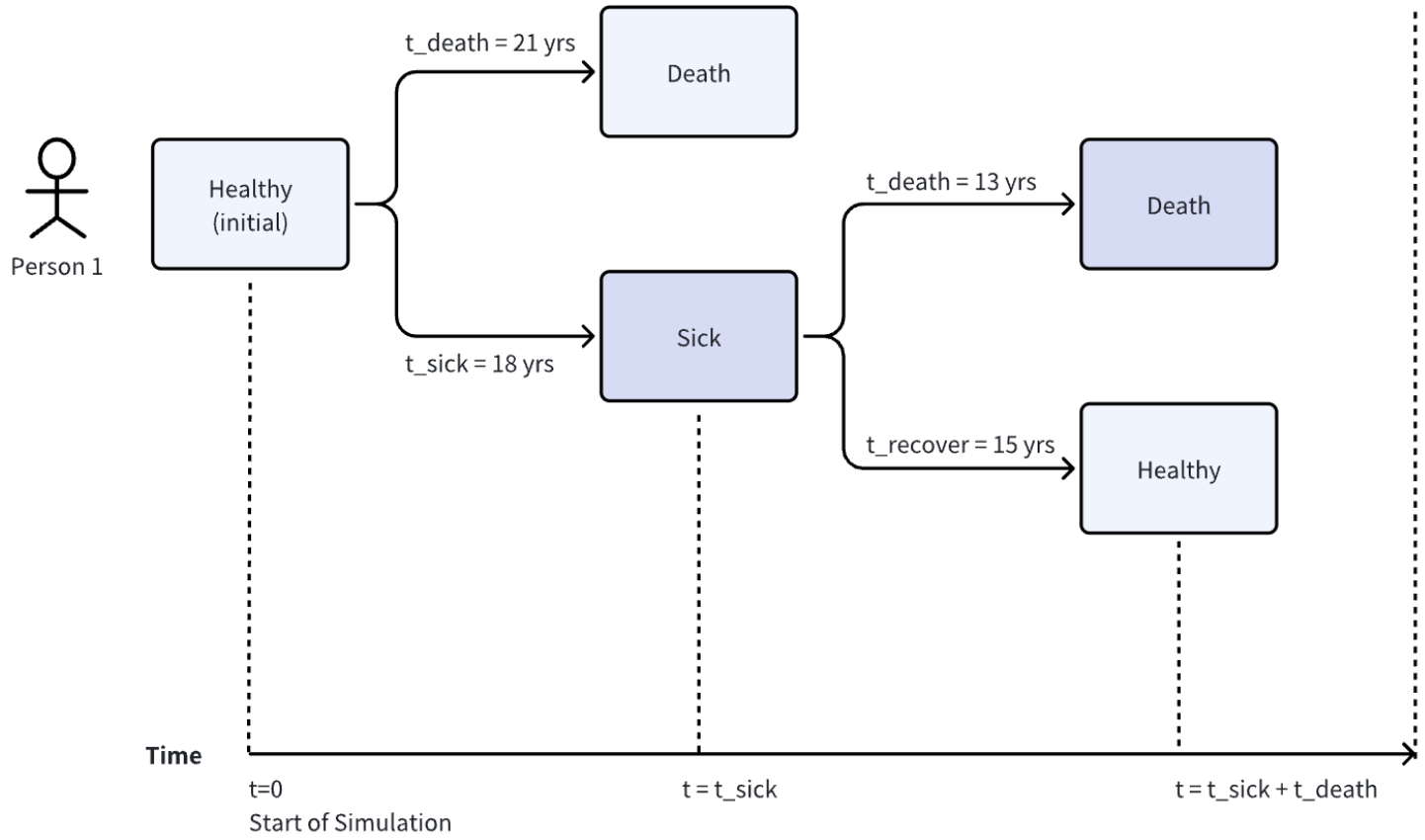



Source from wiki/Exponential_distribution

# Healthy-Sick-Death Example

- Set seed, No CRN;
- In status quo, rHealthySick = 0.1.

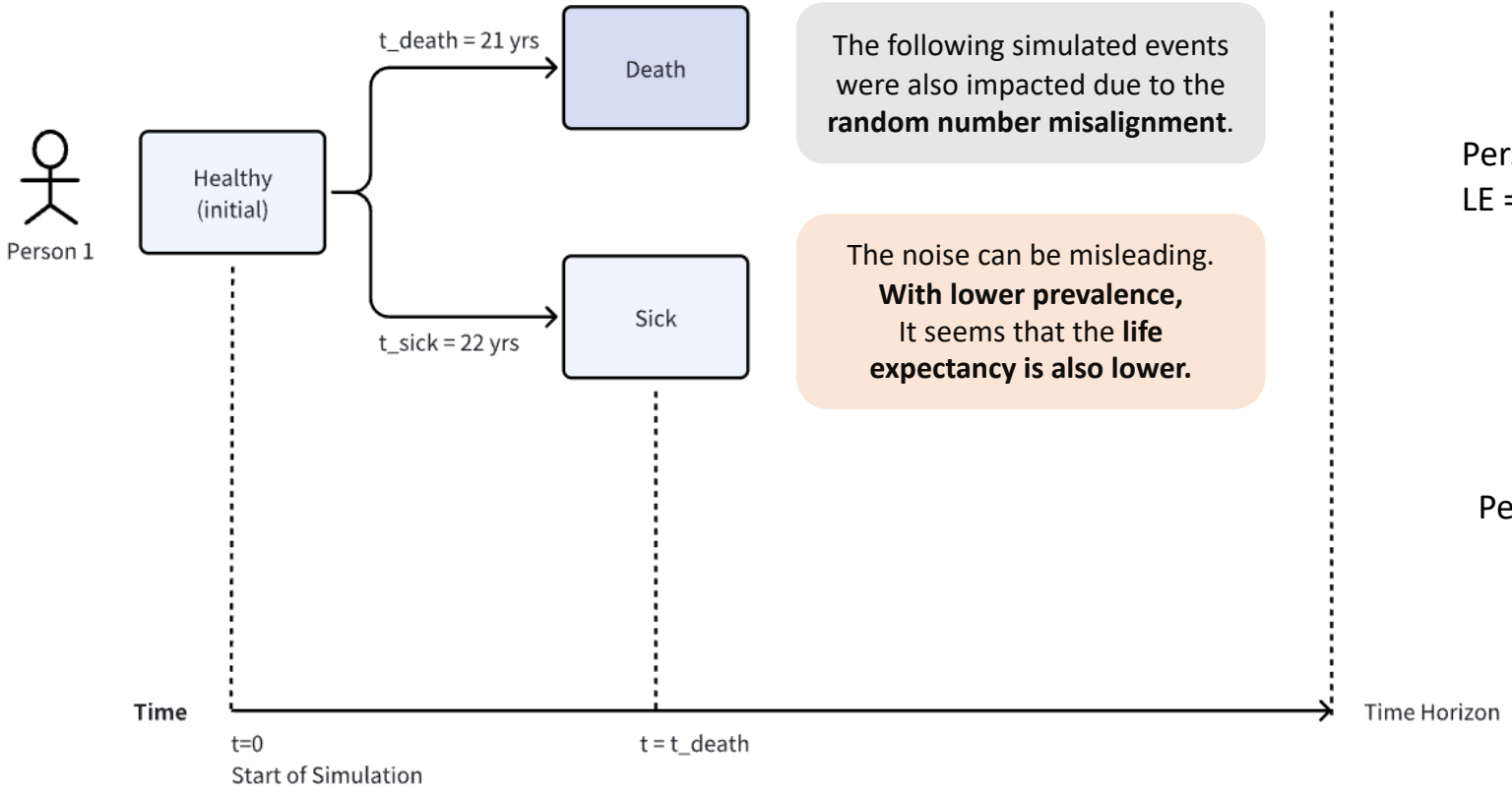
rHealthyDeath = 0.03
rHealthySick = 0.1
rSickDeath = 0.2
rSickHealthy = 0.05




| | | | |
|---|---|---|---|
| Person 1, LE = 31 yrs | 1 | 0.467 | 21 yrs |
| | 2 | 0.834 | 18 yrs |
| | 3 | 0.926 | 13 yrs |
| | 4 | 0.527 | 15 yrs |
| Person 2, LE = 30 yrs | 5 | 0.593 | 30 yrs |
| | 6 | 0.959 | 32 yrs |
| Person 3 | 7 | 0.808 | 55 yrs |
| | 8 | 0.393 | 5 yrs |
| | 9 | 0.889 | 11 yrs |
| | 10 | 0.295 | 7 yrs |
| | ... | ... | ... |

# Healthy-Sick-Death Example

- Set seed, No CRN;
- An intervention reduces rHealthySick to 0.08.




The following simulated events were also impacted due to the **random number misalignment**.

The noise can be misleading. **With lower prevalence,** It seems that the **life expectancy is also lower.**

rHealthyDeath = 0.03
rHealthySick = 0.08
rSickDeath = 0.2
rSickHealthy = 0.05

| | | | |
|---|---|---|---|
| Person 1, LE = 21 yrs | 1 | 0.467 | 21 yrs |
| | 2 | 0.834 | 22 yrs |
| Person 2, LE = 13 yrs | 3 | 0.926 | 87 yrs |
| | 4 | 0.527 | 9 yrs |
| | 5 | 0.593 | 4 yrs |
| | 6 | 0.959 | 64 yrs |
| Person 3 | 7 | 0.808 | 55 yrs |
| | 8 | 0.393 | 6 yrs |
| | 9 | 0.889 | 11 yrs |
| | 10 | 0.295 | 7 yrs |
| | ... | ... | ... |

# Common Random Numbers(CRNs)

Status quo
rHS = 0.1

| Event Order | Person 1 (LE = 9 yrs) | | | | Person 2 (LE = 17 yrs) | | | | … |
|---|---|---|---|---|---|---|---|---|---|
| | H -> S (r = 0.1) | H -> D (r = 0.03) | S -> H (r = 0.05) | S -> D (r = 0.2) | H -> S (r = 0.1) | H -> D (r = 0.03) | S -> H (r = 0.05) | S -> D (r = 0.2) | … |
| 1 | 0.467 (6 yrs) | 0.661 (36 yrs) | 0.986 | 0.805 | 0.596 (9 yrs) | 0.375 (23 yrs) | 0.538 | 0.199 | … |
| 2 | 0.834 | 0.305 | 0.965 (67 yrs) | 0.475 (3 yrs) | 0.913 | 0.085 | 0.701 (24 yrs) | 0.814 (8 yrs) | … |
| 3 | 0.926 | 0.237 | 0.156 | 0.405 | 0.975 | 0.543 | 0.020 | 0.294 | … |
| 4 | 0.527 | 0.737 | 0.960 | 0.675 | 0.770 | 0.325 | 0.757 | 0.279 | … |

Intervention
rHS = 0.08

| Event Order | Person 1 (LE = 11 yrs) | | | | Person 2 (LE = 19 yrs) | | | | … |
|---|---|---|---|---|---|---|---|---|---|
| | H -> S (r = 0.08) | H -> D (r = 0.03) | S -> H (r = 0.05) | S -> D (r = 0.2) | H -> S (r = 0.08) | H -> D (r = 0.03) | S -> H (r = 0.05) | S -> D (r = 0.2) | … |
| 1 | 0.467 (8 yrs) | 0.661 (36 yrs) | 0.986 | 0.805 | 0.596 (11 yrs) | 0.375 (23 yrs) | 0.538 | 0.199 | … |
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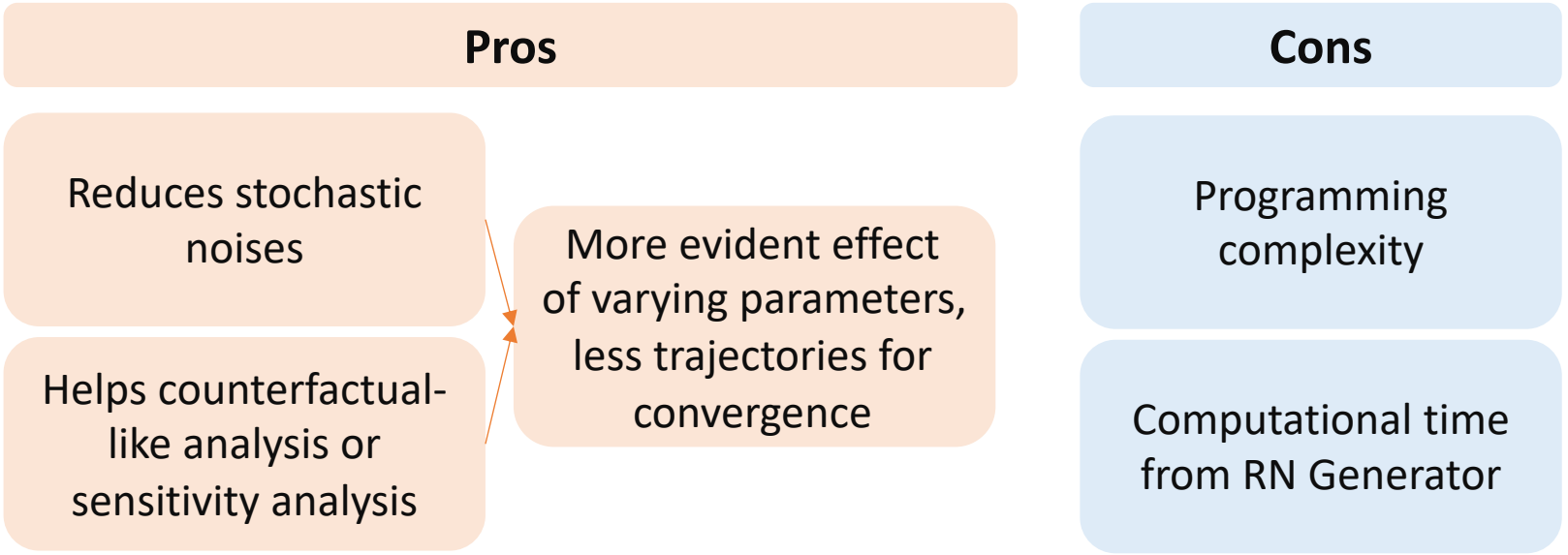
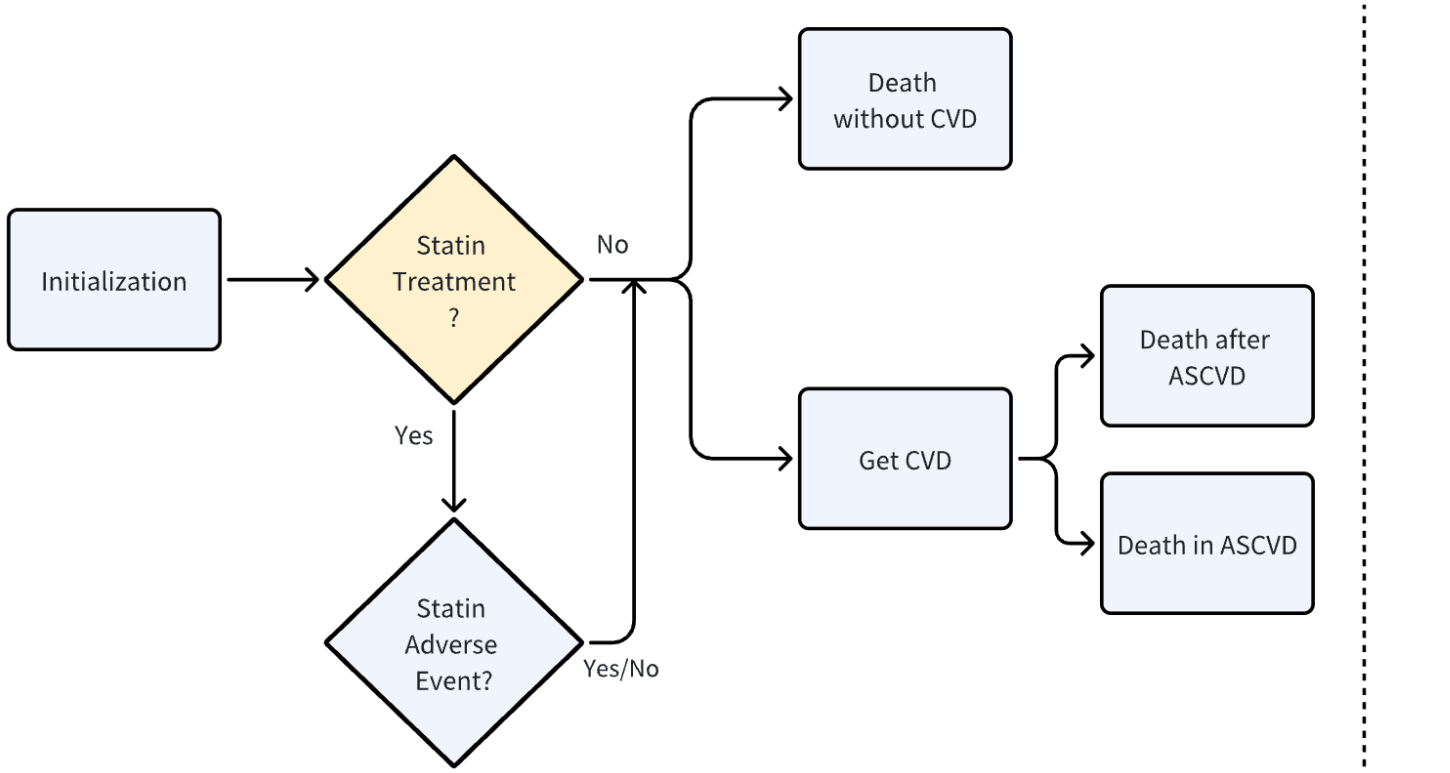
# Common Random Numbers (CRNs)



# Case Study: Statin Treatment

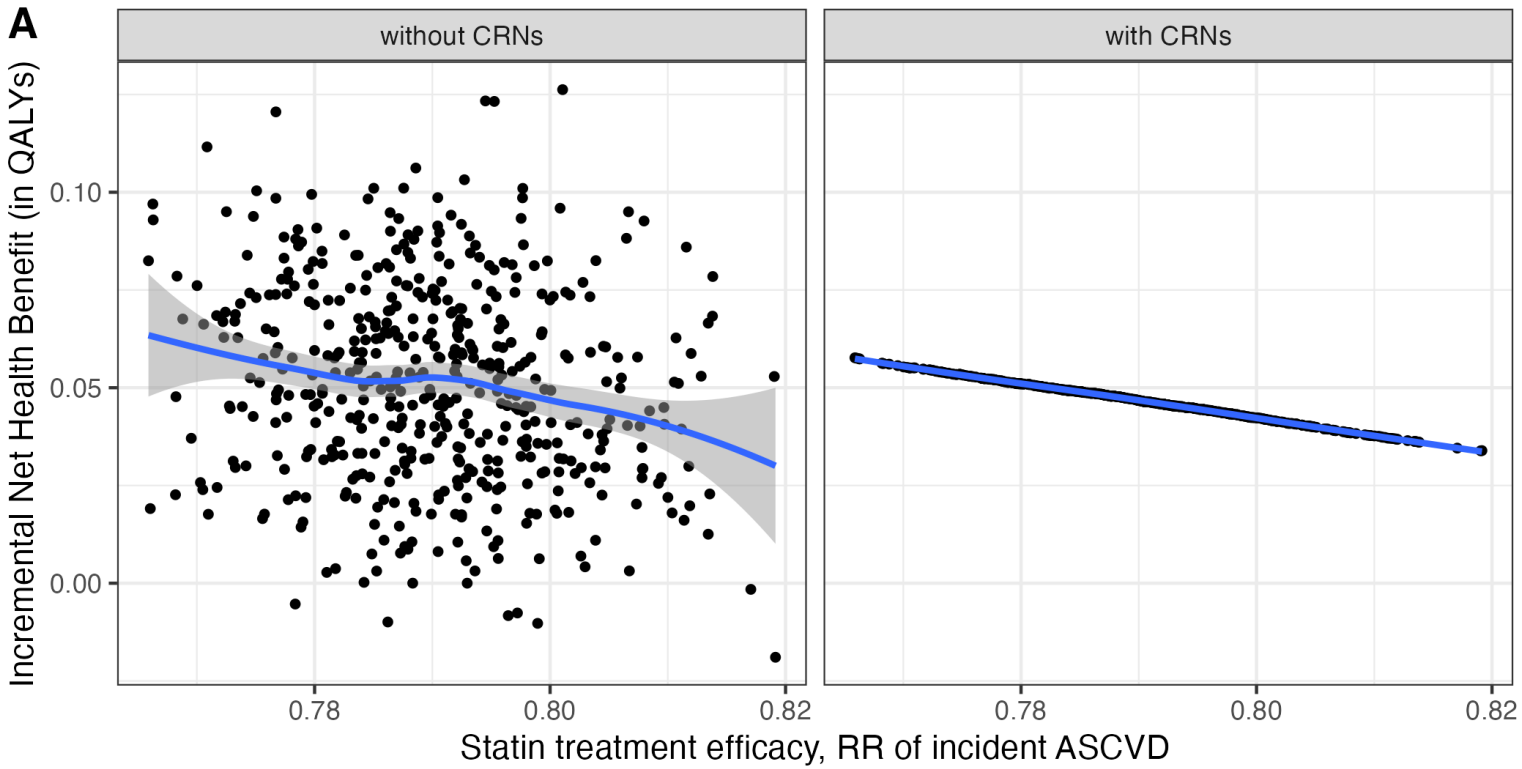
- **Cohort**: US people aged 40~80 at the risk of atherosclerotic cardiovascular disease (ASCVD), populated with the National Health and Nutrition Examination Survey.
- **Parameterization**: Spahillari A., etc. (2020)
- **Strategy**: Use Statins / Not Use
- **Outcome:** Net Health Benefit(NHB)




Flow Chart of the Simulation Model

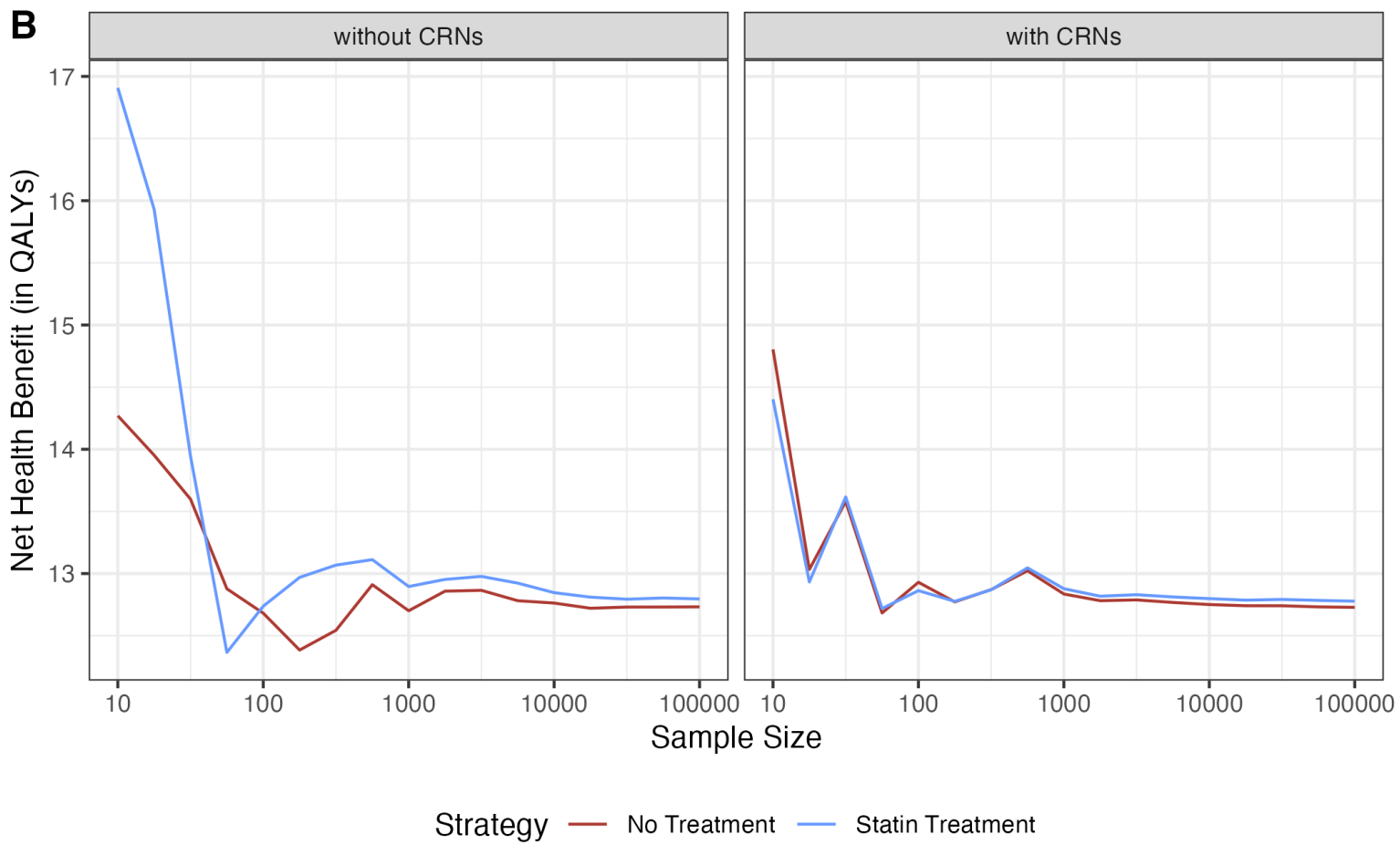
# Effect of CRNs on Model Outputs

- When running the one-way sensitivity analysis for the relative risk of ASCVD (where a lower RR leads to a higher incremental NHB), CRN reduced the stochastic noise.



# Effect of CRNs on Model Outputs

- CRNs resulted in faster stabilization of the model-estimated iNHB around the true value with smaller sample sizes.



# Conclusions

- Reduce the noise around the true value;
- Enhance efficiency in computationally intensive tasks.
    - PSA, calibrations, VOI…

# Thank You for Listening!

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