Towards the Best Practices to Create Virtual Healthy Control Populations for Organ Impairment Studies

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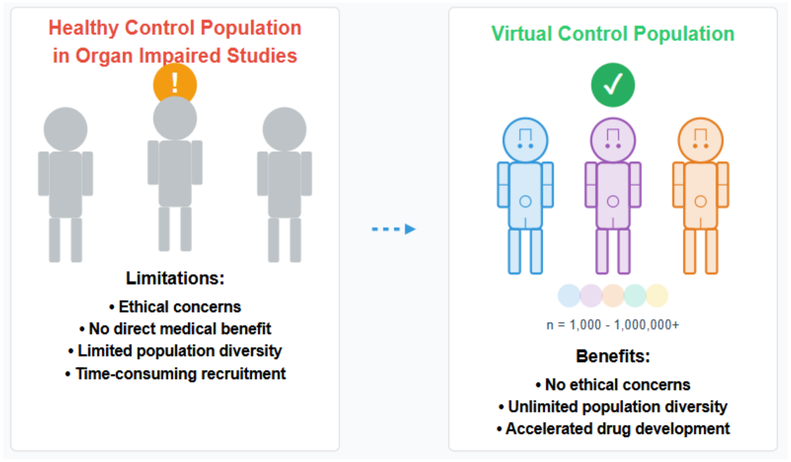
Introduction



Research aim

➢ *To establish best practices for developing virtual control population in organ impaired studies*

- This study utilized five carefully selected drugs with varied data availability and model complexity to explore optimal methodological design for generating virtual control populations.
- For each drug, data were systematically categorized into five distinct scenarios representing different stages in the drug development process, as illustrated in figure 1.

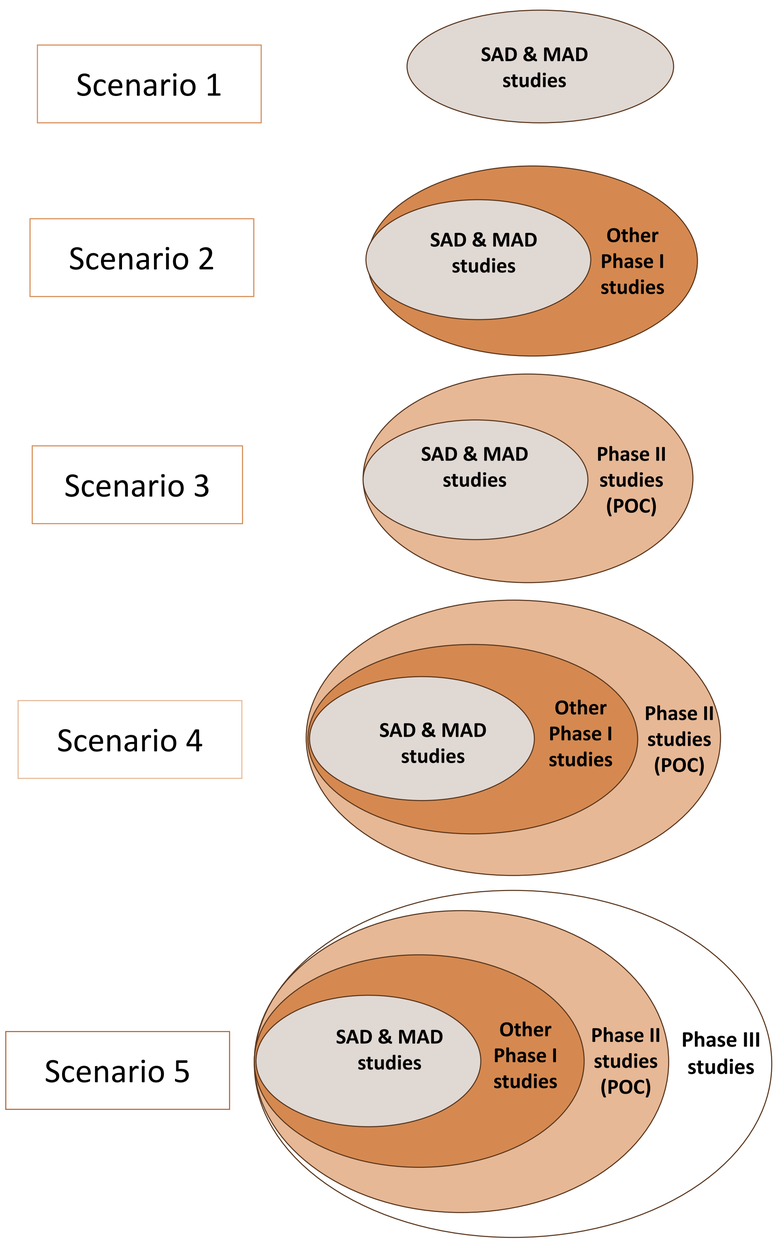
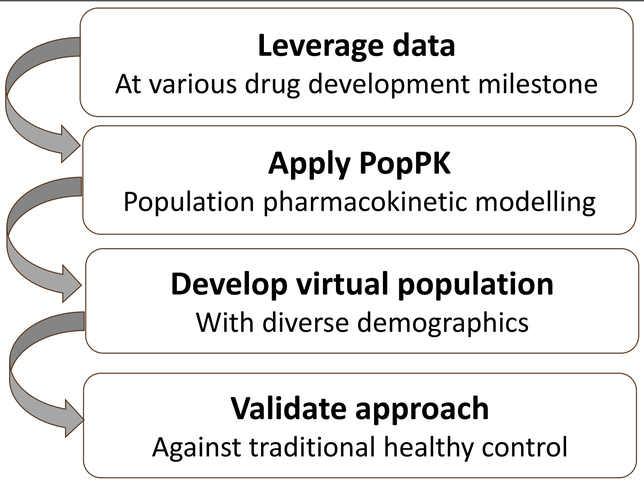


Figure 1: Scenarios evaluated

Approach



Result

- We report the results of the first two drugs.
- Overall, the best predictions were observed with Scenario 4 for both drugs.
- There was higher variability in all simulated data than the observed data (figure 2).
- However, greater variability was observed in Scenarios 3, 4, and 5 compared to scenarios 1, and 2, but captures the mean value better.
- The exposure ratios between renal impairment patients and healthy participants were similar between observed and virtual healthy population as shown in figure 3.

Table 1: Summary of the GMR simulated vs observed (reference) data

Drug 1			Drug 2		
Scenarios	AUC	Cmax	Scenarios	AUC	Cmax
1	0.871 (0.697–1.12)	1.11 (0.77–1.55)	1	1.14 (0.961–1.42)	1.45 (1.28–1.84)
2	0.997 (0.787–1.30)	1.02 (0.702–1.42)	2	1.13 (0.927–1.44)	1.42 (1.24–1.79)
3	1.07 (0.476–2.45)	0.99 (0.420–1.960)	3	1.01 (0.43-2.37)	0.934 (0.34-2.0)
4	1.04 (0.484–2.26)	1.00 (0.443–1.89)	4	1.02 (0.450–2.30)	0.959 (0.367–1.99)
5	1.10 (0.448–2.74)	1.01 (0.439–2.73)	5	1.06 (0.434–2.55)	0.963 (0.352–2.08)
RI study*	1.01 (0.819–1.23)	0.973 (0.769–1.36)	RI study	0.987 (0.788–1.23)	0.973 (0.803–1.38)

Key: RI = renal impaired, * = reference study

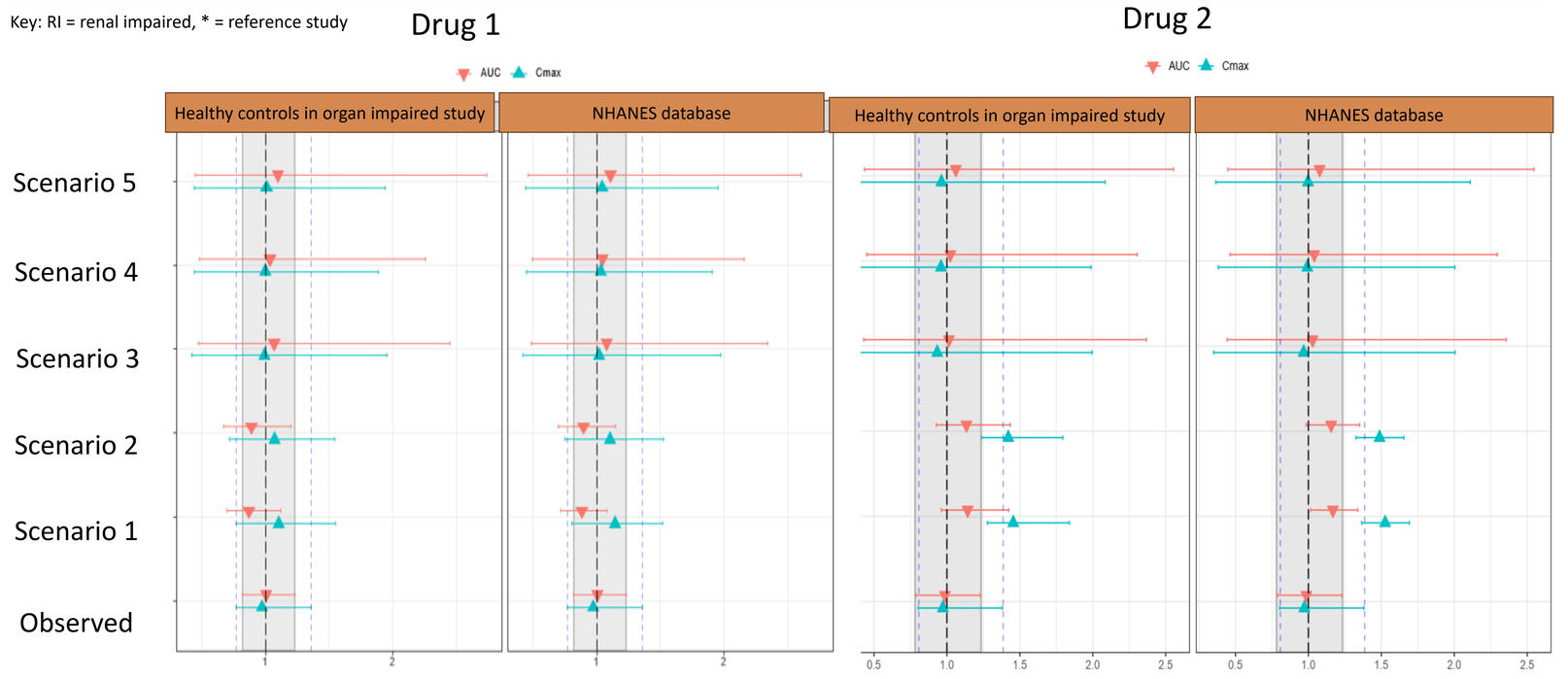


Figure 2: GMR of simulated vs observed (reference) data

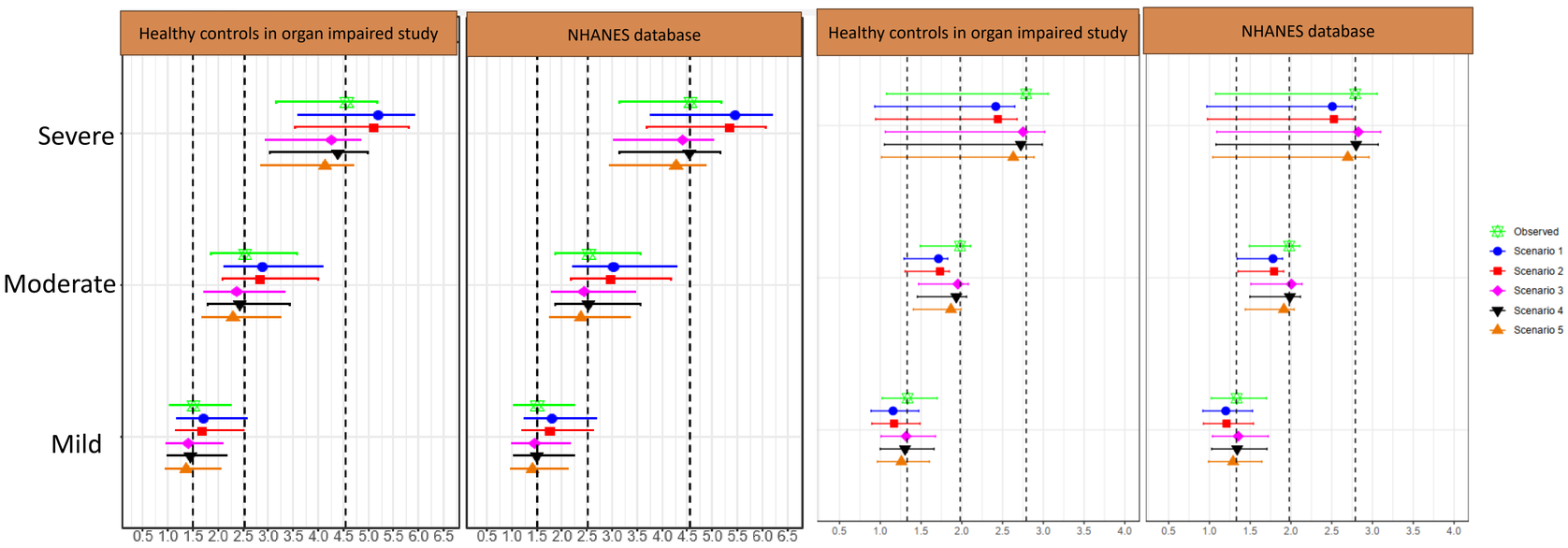


Figure 3: GMR of exposure in participants with renal impairment vs virtual or observed (reference) healthy participants

Conclusion

- The study contributes to growing body of knowledge on the potential of leveraging existing data to replace healthy control groups in organ impairment studies.
- The trends of our finding suggest that in using simulated virtual control participants, incorporating data from phase 2, and 3 trials yields more accurate and predictive outcomes.

References
[1] Moore KT et al. J Clin Pharmacol. (2022) 62(12), 1465-1467.
[2] Walker RL et al. J Med Philos. (2018) 43(1), 83-114.