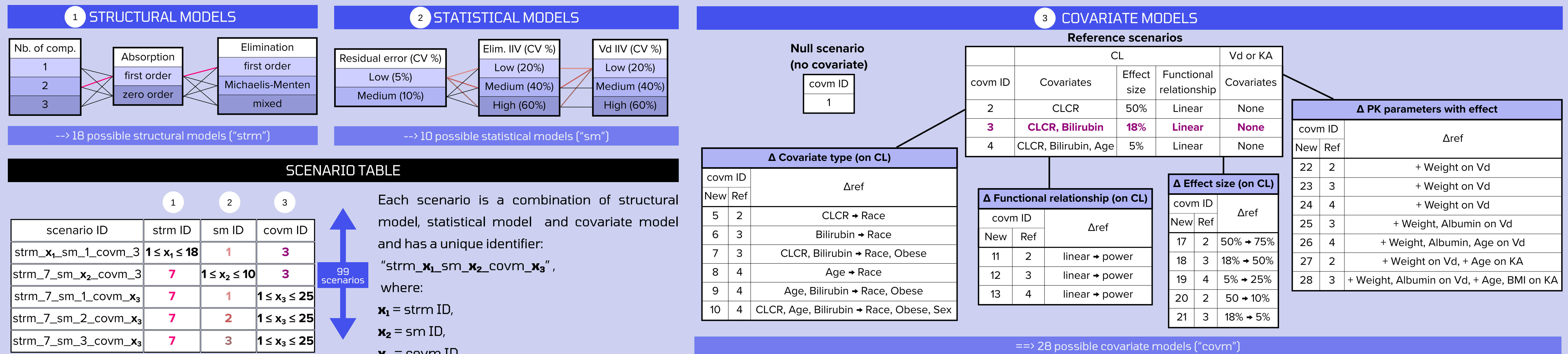


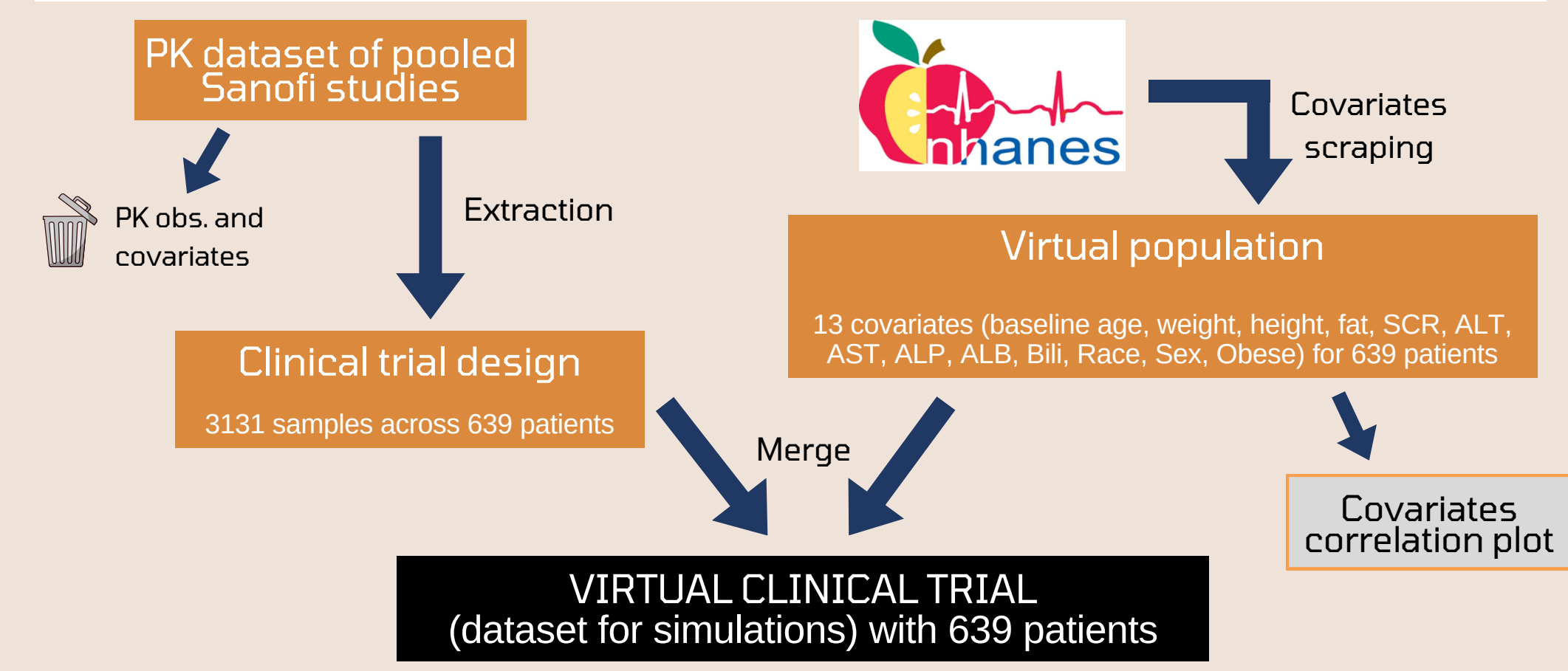
BACKGROUND AND OBJECTIVE Twenty-two methods for popPK covariate modeling have recently been referenced, however their relative performances remain uncertain due to a lack of consensus on how to evaluate these techniques [1]. **The aim is to propose PMX-CovEval, a framework enabling straightforward covariate model selection techniques evaluation and comparison.** The proposed framework consists of: (1) datasets simulated under different scenarios, (2) PSM files for all scenarios for both NONMEM and Monolix, (3) EBEs estimated under the PSMs of all scenarios, (4) a table detailing all scenarios

METHODS Three steps to build the four-component framework.

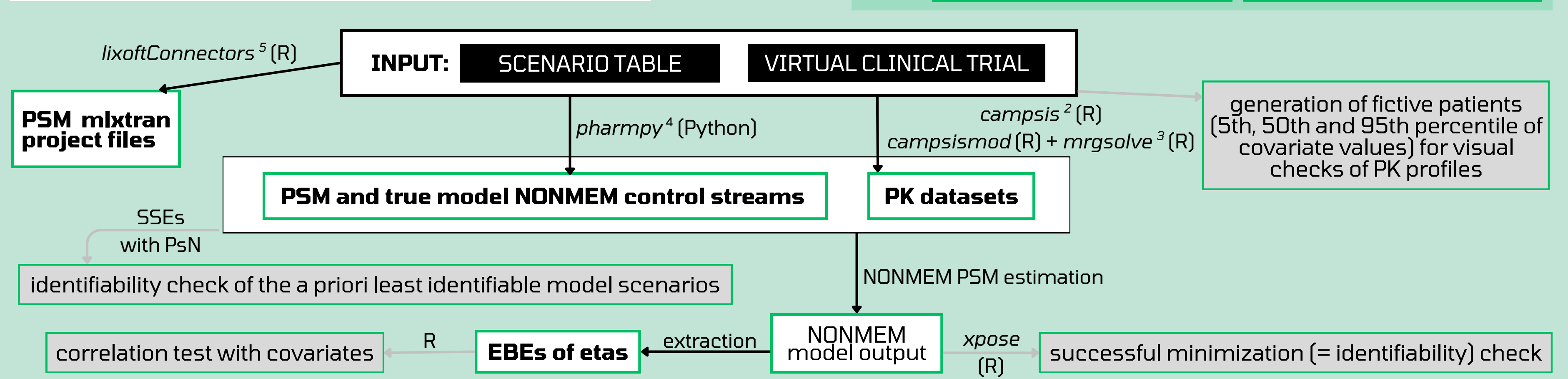
STEP 1: SCENARIO TABLE GENERATION



STEP 2: VIRTUAL CLINICAL TRIAL GENERATION



STEP 3: FRAMEWORK GENERATION



RESULTS An open-source GitHub repository

EBEs

datasets

PSM_Monolix

PSM_NONMEM

appendix

scenario_table.csv

enable direct execution of EBEs-based regression methods (e.g. machine and deep learning)

enable direct execution of Perl speaks NONMEM (PsN) or Monolix internal covariate model selection techniques

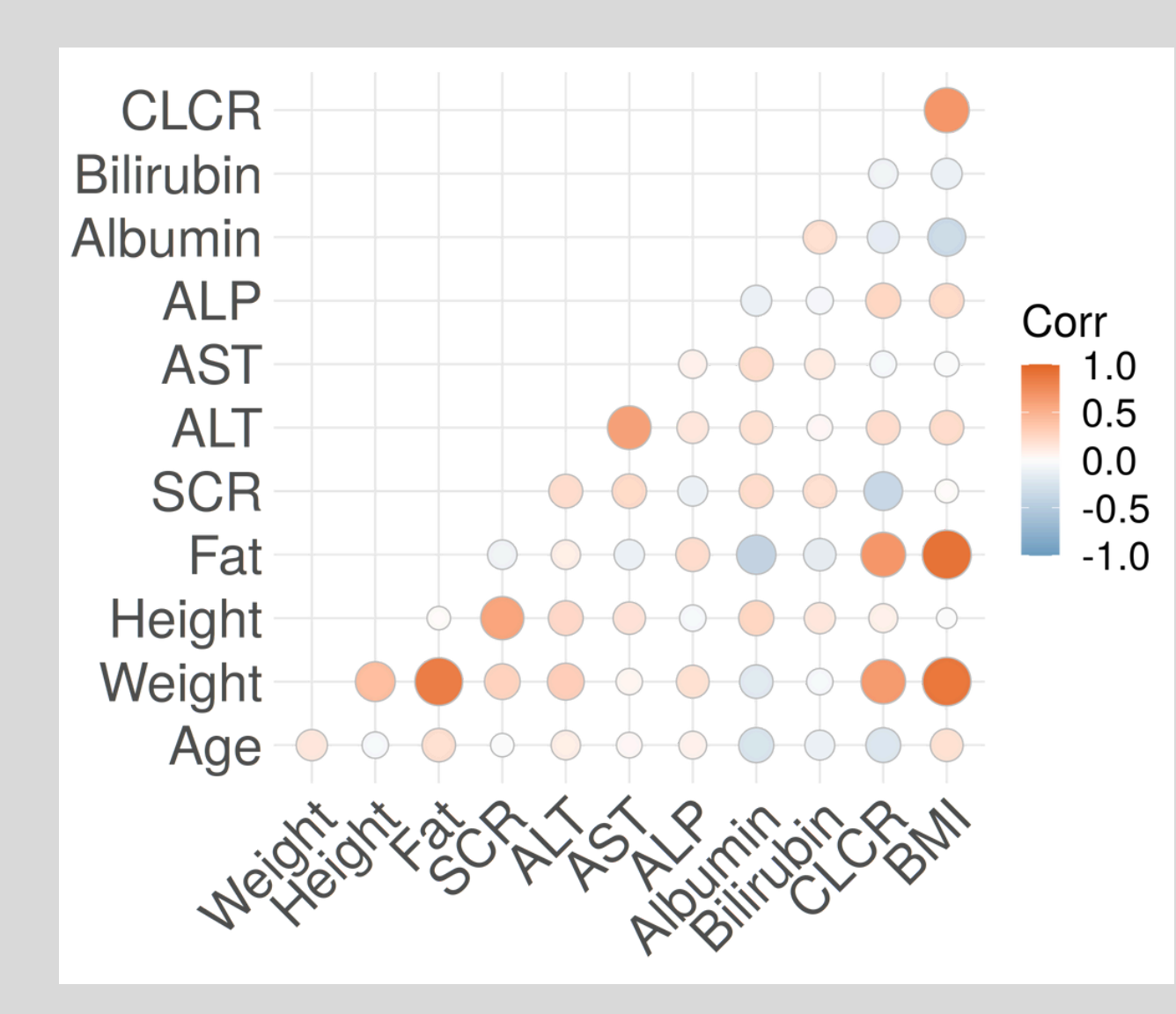
→ (Soon available) covariates correlation plot + framework **quality check*** for all scenarios.

allows to identify scenarios and thus to evaluate methods performances across varying model components

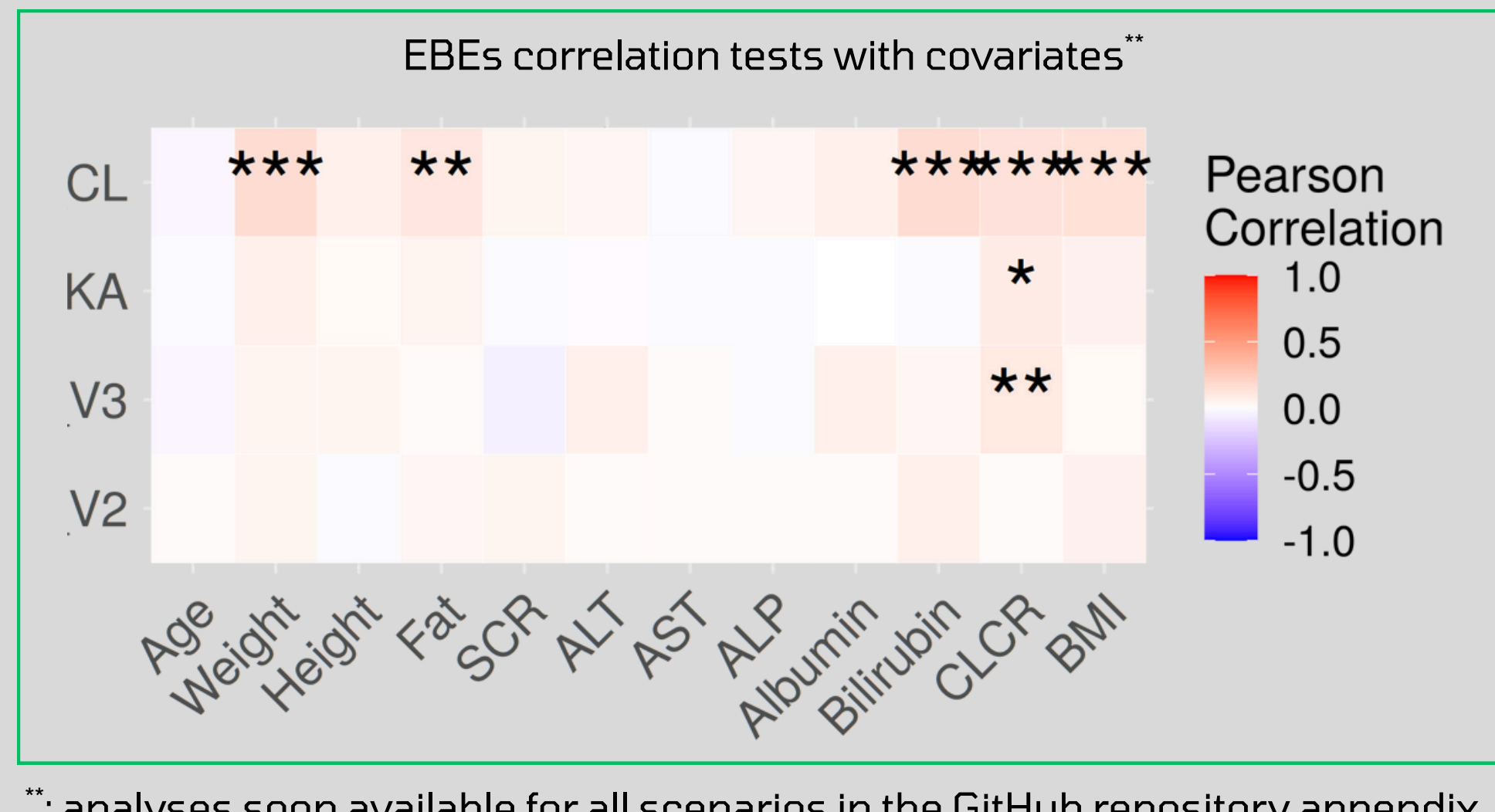
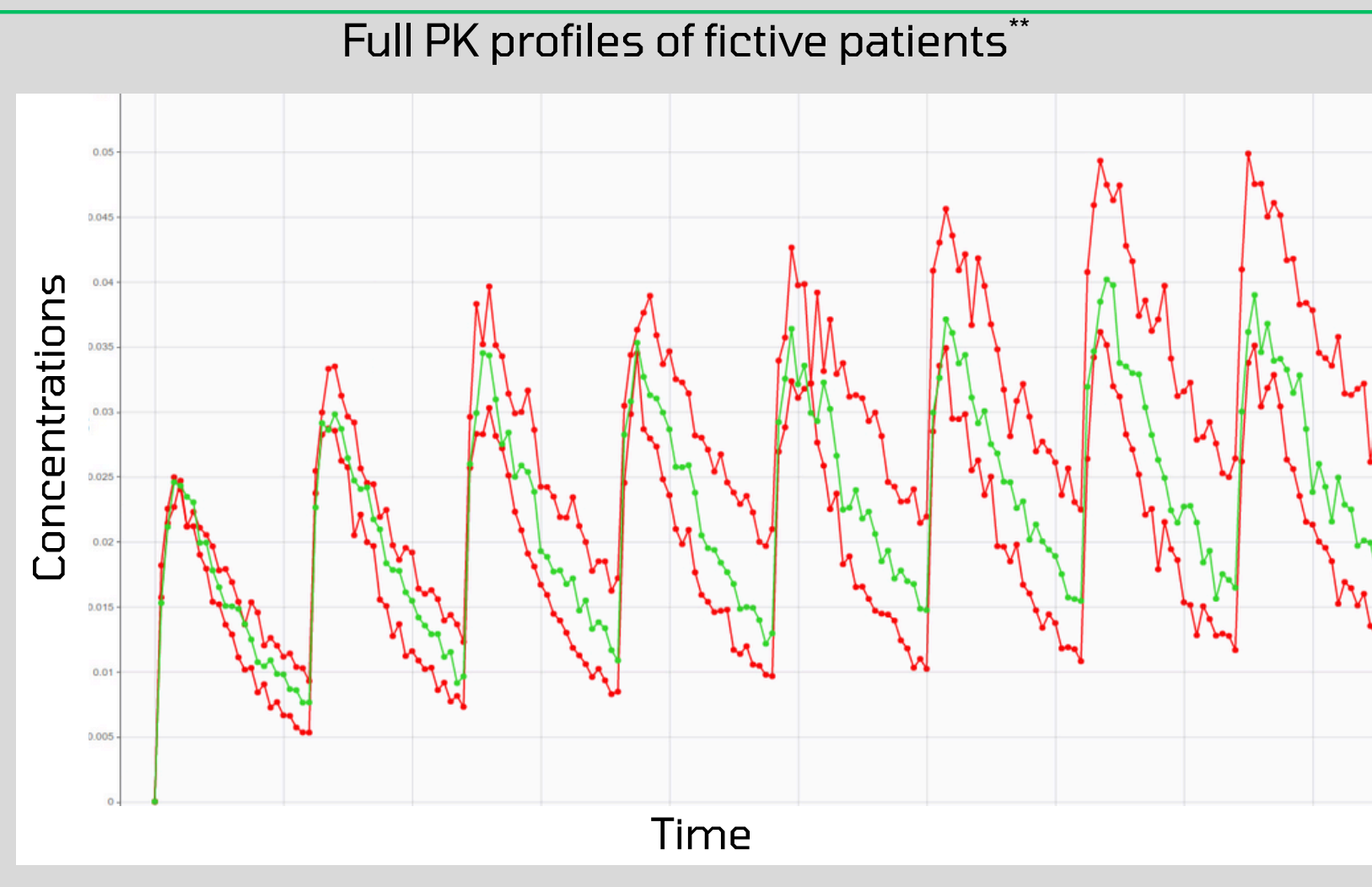
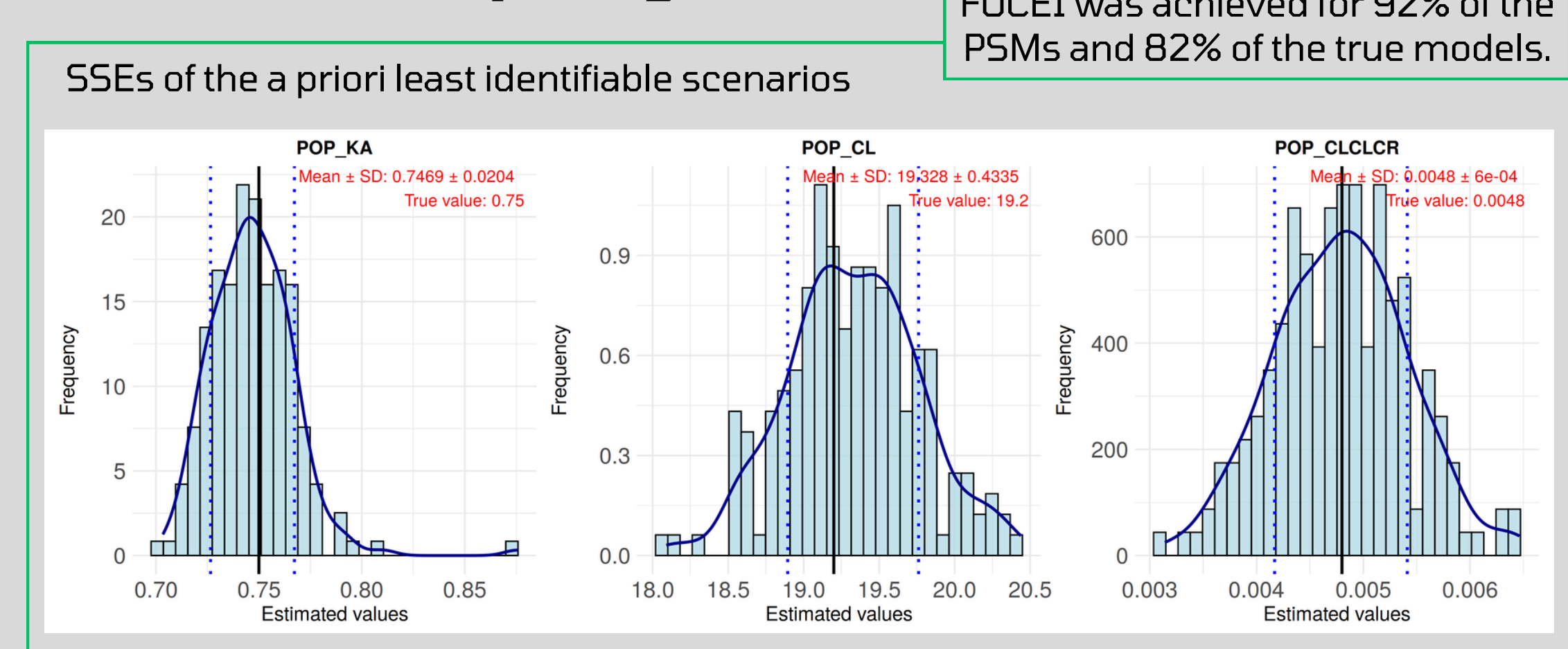
<https://github.com/Sanofi-Public/PMX-CovEval>



Covariates correlation heatmap



*PMX-CovEval quality check



CONCLUSION By incorporating scenarios with variability across multiple model elements, PMX-CovEval enables rigorous evaluation and consistent comparison of existing and future covariate modeling methods. It is available at <https://github.com/Sanofi-Public/PMX-CovEval>

PERSPECTIVES (1) Keep adding other relevant scenarios in the framework.
(2) Run covariate modeling methods on PMX-CovEval, then analyse the results:

scenario ID	# comp	Abs model	Elim model	Abs IIV	Elim IIV	Covariates on Elim.	...	SAMBA TPR	SAMBA TNR	...	SCM TPR
strm_1_psm_5_covm_3	1	fo	fo	low	low	CLCR, Bilirubin	...	100%	100%	...	80%
strm_2_psm_5_covm_3	1	fo	mm	low	low	CLCR, Bilirubin	...	100%	100%	...	80%
.	.	.	.	.	.	.	.	.	.	.	.
.	.	.	.	.	.	.	.	.	.	.	.
.	.	.	.	.	.	.	.	.	.	.	.

→ Covariates analysis on methods performance metrics

(3) Write Pumas PSM files for all scenarios

- REFERENCES** [1] M. Karlsen, et al., "Covariate Model Selection Approaches for Population Pharmacokinetics: A Systematic Review of Existing Methods, From SCM to AI", CPT Pharmacometrics Syst Pharmacol, 2025.
[2] <https://calvagone.github.io/> or www.campsis.org
[3] <https://github.com/metrumresearchgroup/mrgsolve>
[4] <https://pharmPy.github.io/>
[5] <https://monolixsuite.slp-software.com/r-functions/2024R1/reference>

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