Emulating clinical trials with digital twins on electronic health records

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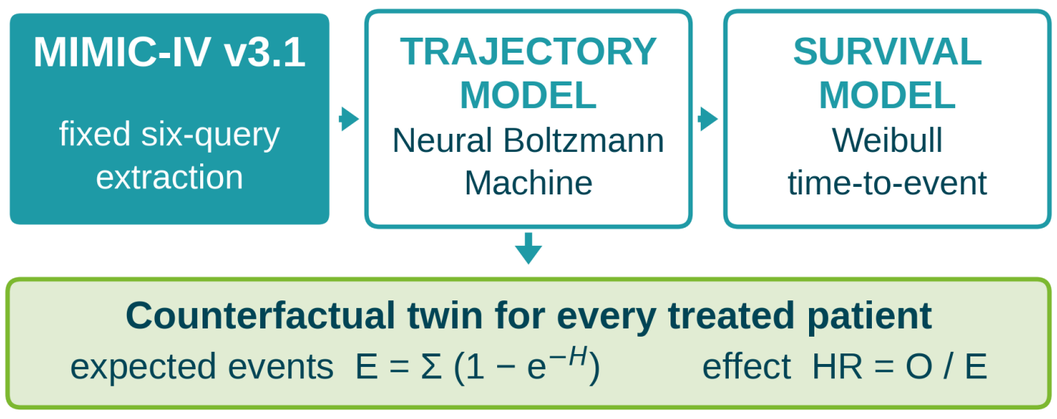
FACTS & FIGURES

Start date:	1 January 2026
End date:	31 December 2030
IHI funding:	7 110 000 €
Industry contribution:	7 110 000 €
Total Cost:	14 220 000 €
Project website:	https://genz-trials.eu/
Social media:	linkedin.com/company/genz-trials/

CHALLENGE

Randomized clinical trials (RCT) are the gold standard for generating reliable evidence, but they are costly, time-consuming, and demanding. GENz-trials aims to make clinical research faster, more efficient, ethical, and inclusive by combining AI, real-world data, and Digital Twins (DTs) with Synthetic Control Arms. Key challenge of this study: can DT–based virtual control cohorts reproduce the causal treatment effects observed in historical RCTs?

APPROACH & METHODOLOGY



- 10 trials been emulated in MIMIC-IV[1], ≥300 patients/arm.
- Digital Twin Generator[2]: a Neural Boltzmann Machine trajectory model plus a Weibull survival model.
- HR = observed treated ÷ control twin-expected events; 95% bootstrap.
- Evaluation of the results: 1) **Estimate agreement:** the RCT HR falls within the emulation's 95% CI. 2) **Regulatory agreement:** the emulation HR has the same direction (before or after 1) as the RCT HR 3) Laboratory tests' trajectories of DTs are used as negative and positive controls.

Trial	Treated	Comparison	Outcomes
CURRENT-OASIS 7[3]	477	528	3
EARLY-ACS[4]	262	2,303	3
ACCOAST[5]	713	1,031	3
PLATO[6]	665	3,679	3
ARISTOTLE[7]	3,939	8,412	3
AUGUSTUS[8]	279	758	4
RE-LY[9]	276	7,111	3
AMPLIFY[10]	806	892	3
RACE II[11]	3,550	3,736	2
ADRENAL[12]	236	2,285	2

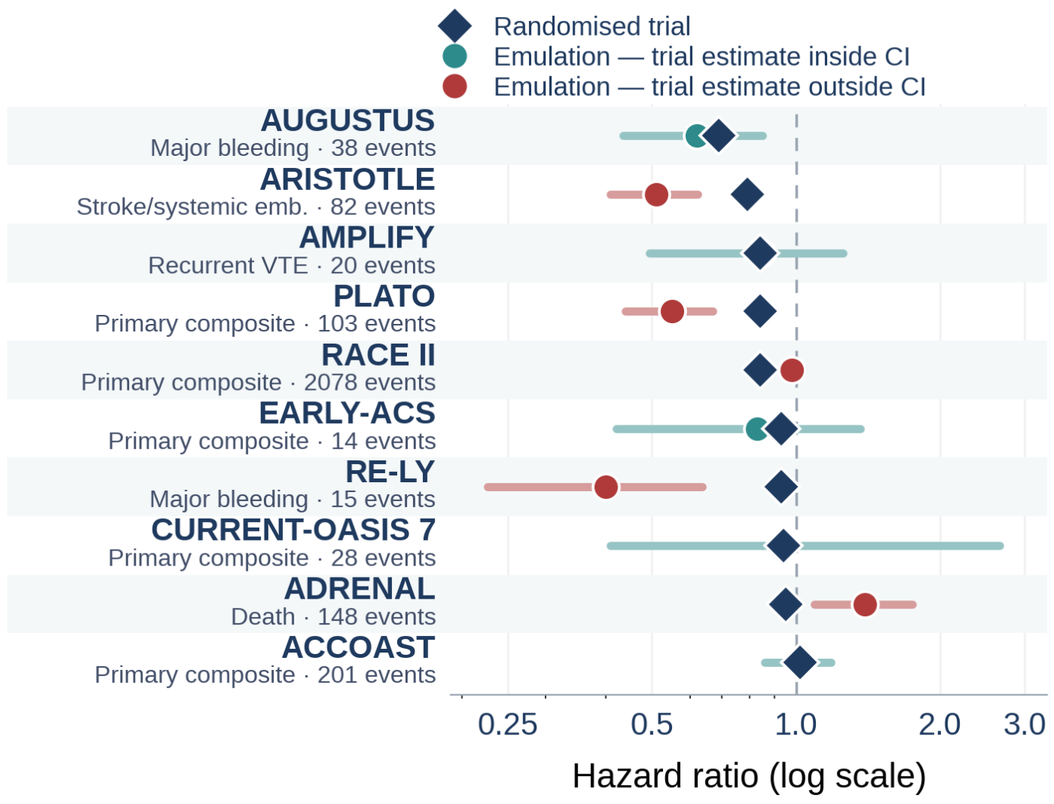
RESULTS

29 endpoints, 10 trials

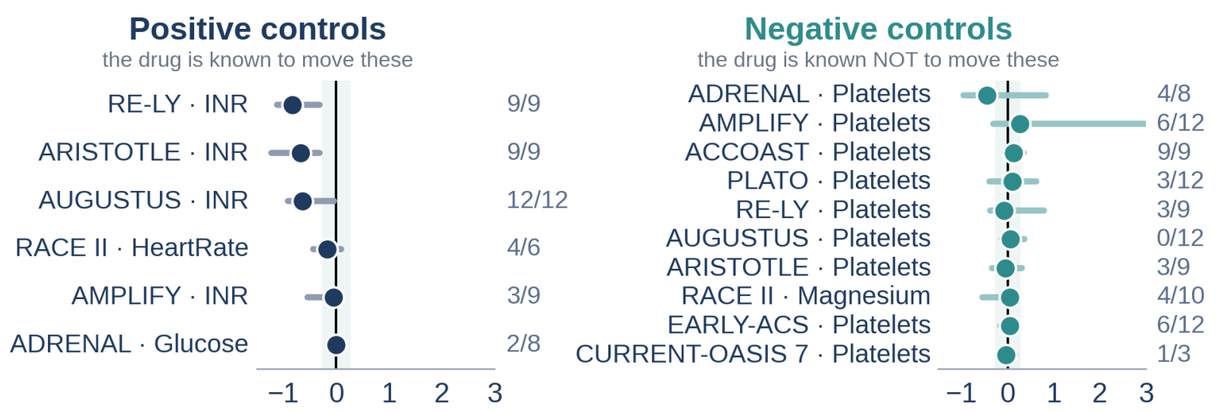
55% estimate agreement

28% regulatory agreement

28% CI width<0.45



- Considering only on primary endpoint of trials, 50% of HR predictions is aligned with the trial's HR.
- Two studies failed in positive and negative controls (AMPLIFY and ADRENAL)



VALUE OF IHI COLLABORATION

Validating a DT control arm is not a modelling problem alone: the method only matters if trial sponsors will use it and regulators will accept it. IHI's public-private structure brings clinical data access, trial expertise and regulatory dialogue into a single consortium.

CAREER IMPACT

GENz-trials showed me the value of bringing causal ML and EHR expertise together with clinical trial, industry, and regulatory perspectives. This collaboration helped me understand how Digital Twin–based synthetic controls are shaped not only by methodological choices, but also by clinical applicability, trial requirements, and regulatory expectations.

REFERENCES

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