Relative Hypoglycemia in Non-Diabetics

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MIT HST.953 — Secondary Analysis of Health Records

Glycemic Control in ICU

- Why glycemic control?
  - Deviate normal physiology and lead to ↑ mortality and morbidity when the problem becomes severe
- Optimizing target for glycemic control

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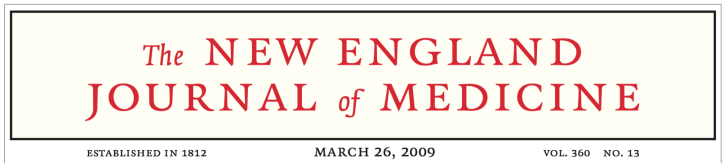
INTENSIVE INSULIN THERAPY IN CRITICALLY ILL PATIENTS

GREET VAN DEN BERGHE, M.D., PH.D., PIETER WOUTERS, M.SC., FRANK WEEKERS, M.D., CHARLES VERWAEST, M.D., FRANS BRUYNINCKX, M.D., MIET SCHETZ, M.D., PH.D., DIRK VLASSELAERS, M.D., PATRICK FERDINANDE, M.D., PH.D., PETER LAUWERS, M.D., AND ROGER BOUILLON, M.D., PH.D.



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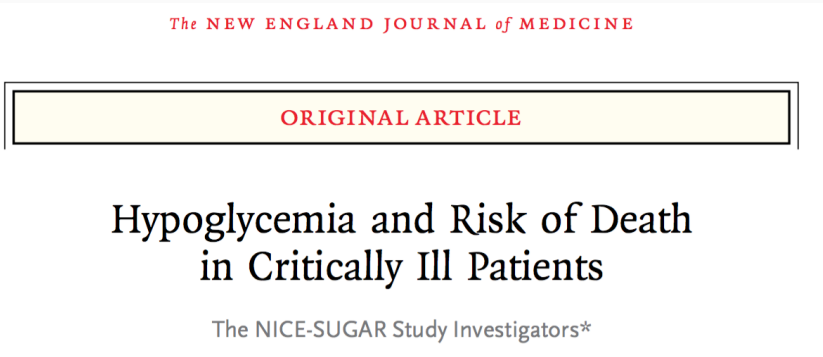
Intensive versus Conventional Glucose Control in Critically Ill Patients

The NICE-SUGAR Study Investigators*



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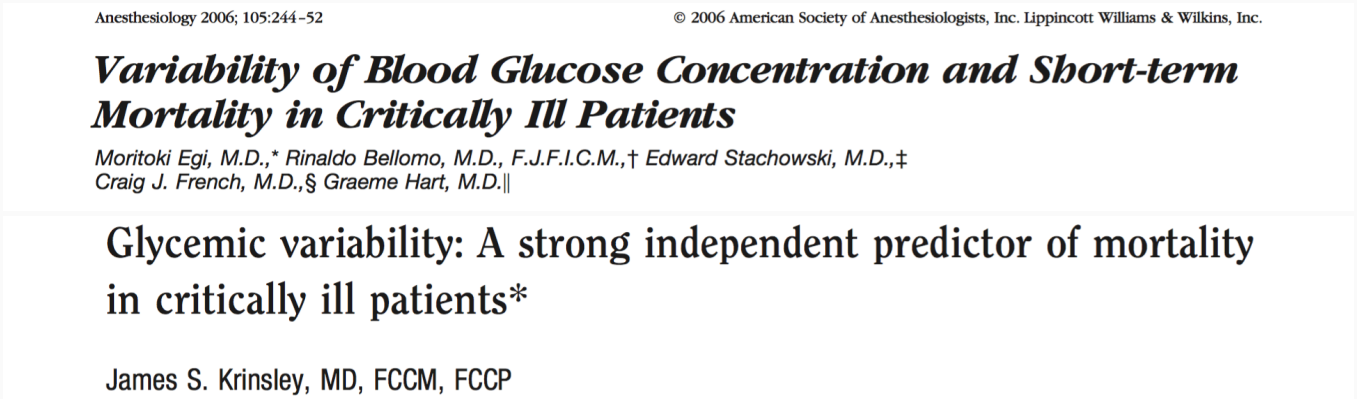
ORIGINAL ARTICLE

Hypoglycemia and Risk of Death in Critically Ill Patients

The NICE-SUGAR Study Investigators*

Current Guideline

- Guideline: 6-10 mmol/l (100-180 mg/dl) for the ICU patients
- Problem?
  - Uniform glycemic control strategy but insulin responses and body response to glucose level should be different in diabetics and non-diabetics
  - ↑ hypoglycemia or ↑ glycemic variability → mortality ↑
- Objective: Better approach to figure out the strategy for flexible glycemic control



Anesthesiology 2006; 105:244–52 © 2006 American Society of Anesthesiologists, Inc. Lippincott Williams & Wilkins, Inc.

Variability of Blood Glucose Concentration and Short-term Mortality in Critically Ill Patients

Moritoki Egi, M.D., Rinaldo Bellomo, M.D., F.J.F.I.C.M.,† Edward Stachowski, M.D.,‡ Craig J. French, M.D.,§ Graeme Hart, M.D.‖*

Glycemic variability: A strong independent predictor of mortality in critically ill patients*

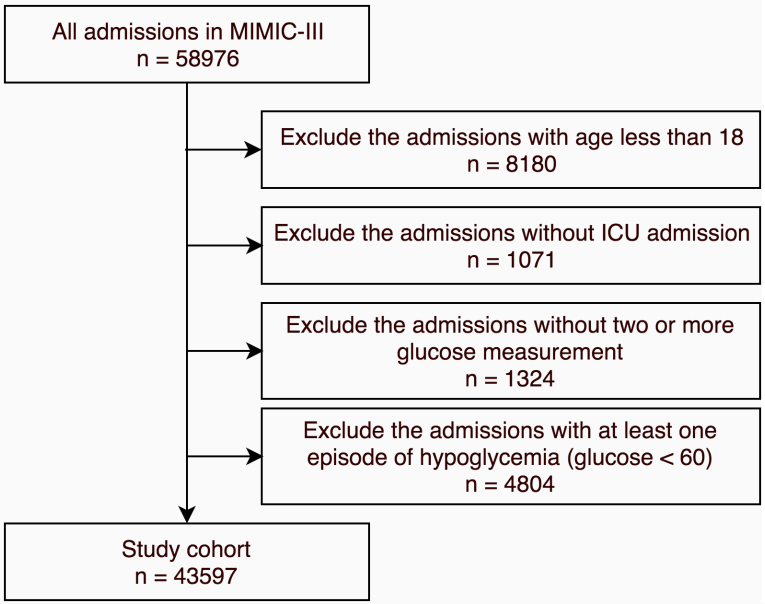
James S. Krinsley, MD, FCCM, FCCP

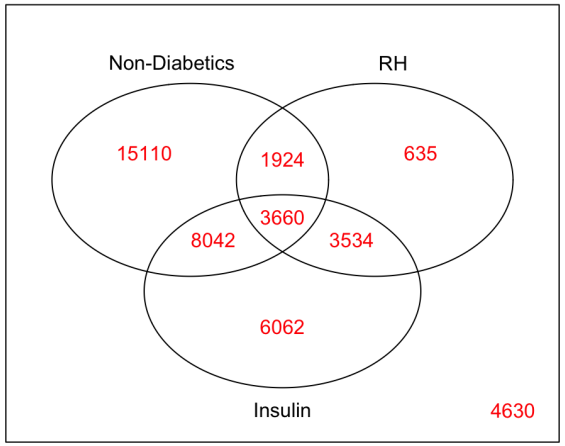
Relative Hypoglycemia

- Definition
  - Glucose level has greater variability but not dropped to the threshold of true hypoglycemia (Martensson 2016)
  - Glucose levels $\downarrow 30\%$ but ≥ 60 mg/dL, in two consecutive glucose measurements within the six-hour interval
  - Related to autonomic instability and also cause the cardiovascular impairment, and increase mortality
- Hypothesis: RH is associated with higher mortality in critically ill diabetics and non-diabetics

Study Design

- Longitudinal retrospective cohort study (43597 admissions)
- MIMIC-III, BIDMC, 2001-2012, more than 60K admissions
- ICU admission, age $\geq$ 18, no hypoglycemia (glucose $\leq$ 60)
- Exposure
  - Diabetes: ICD-9 / pre-admission HbA1c / pre-admission OHA and insulin / past medical history (diabetes)
  - RH: as defined



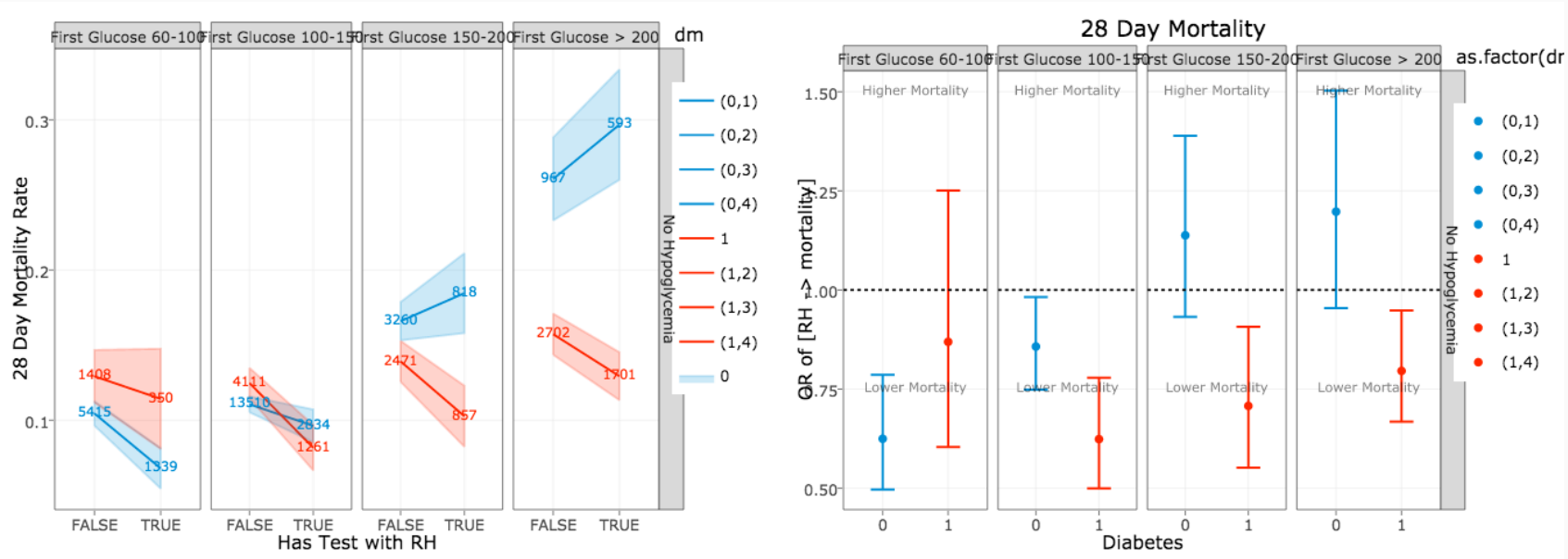


Study Design

- Primary outcome: 28-day mortality (short-term mortality)
- Covariates/Confounders
    - age, gender, Sequential Organ Failure Assessment (SOFA) score and Elixhauser comorbidity index on admission, insulin usage
- Odds ratio with 95% confidence interval

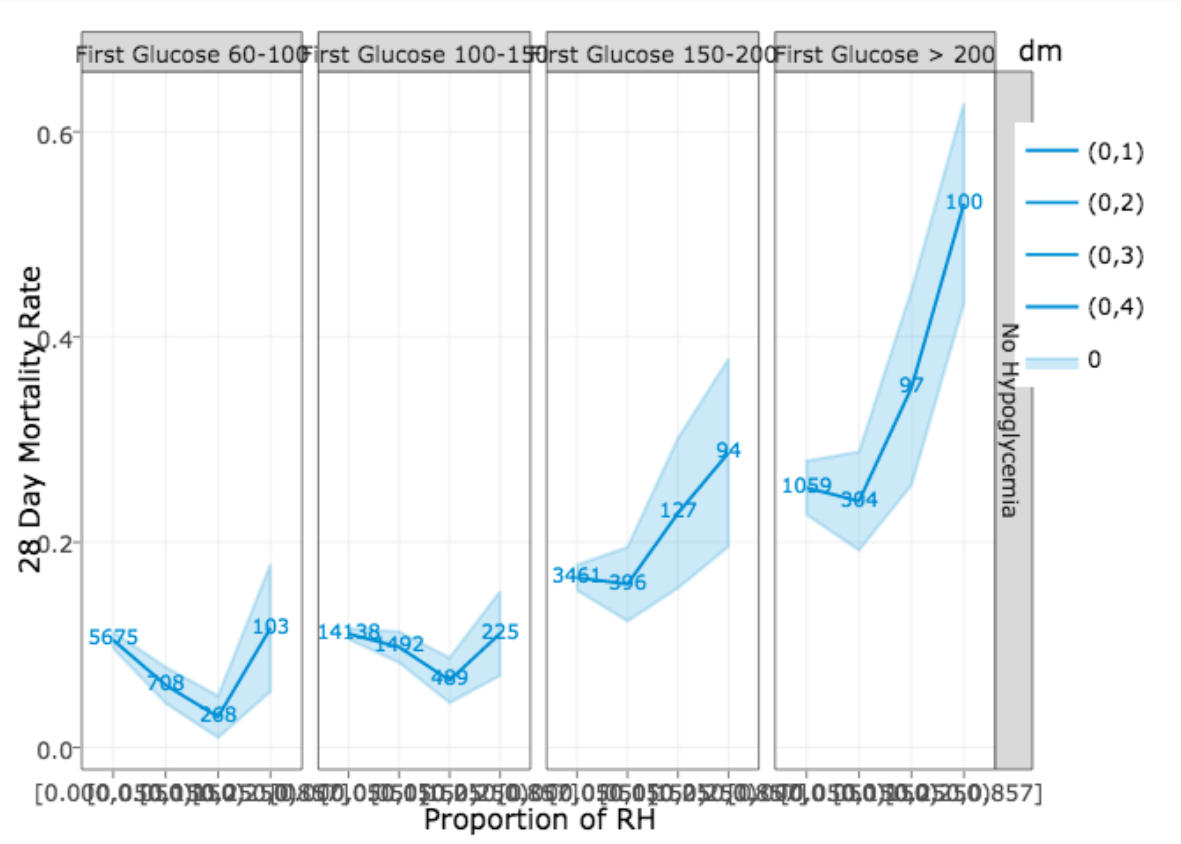
RH / Non-Diabetics

- RH has effect on short-term mortality in non diabetic patient with higher initial glucose level
- Different signals between diabetics and non-diabetics and also the first blood sugar level



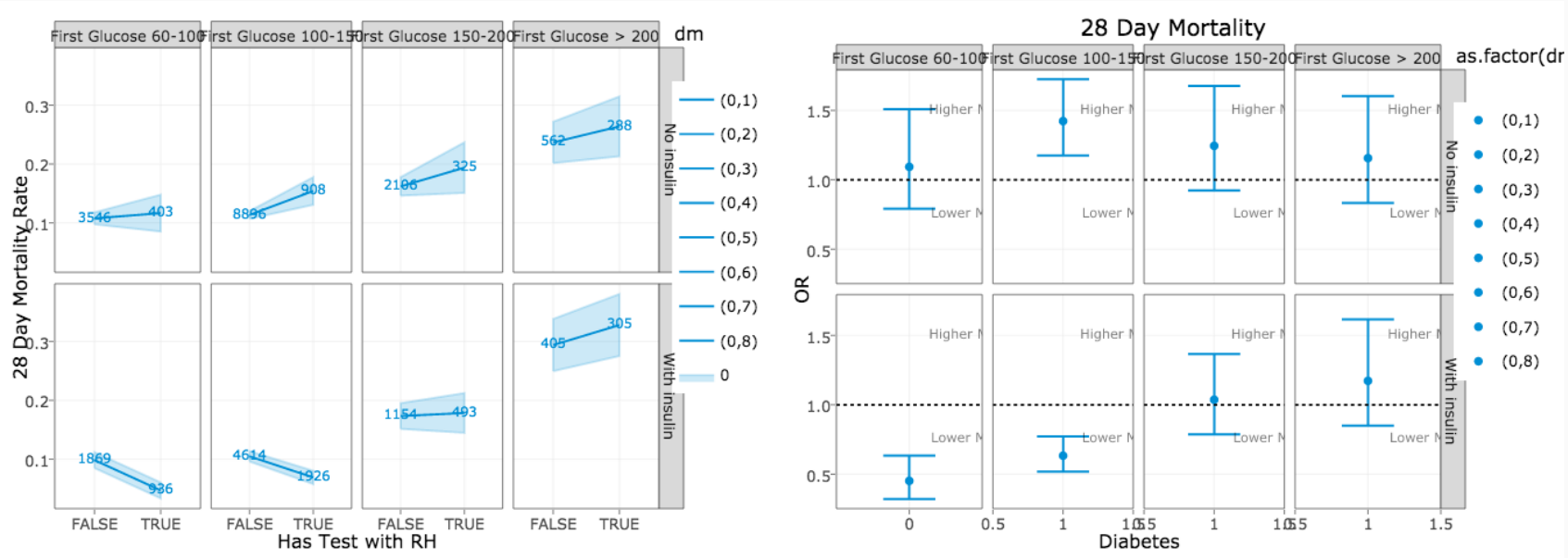
RH Dose Dependent Effect

- Focusing on non-diabetics... (28736 admissions)
- RH has dose dependent effect on the short-term mortality of non diabetic patients with higher initial glucose level
- Might suggest some causality



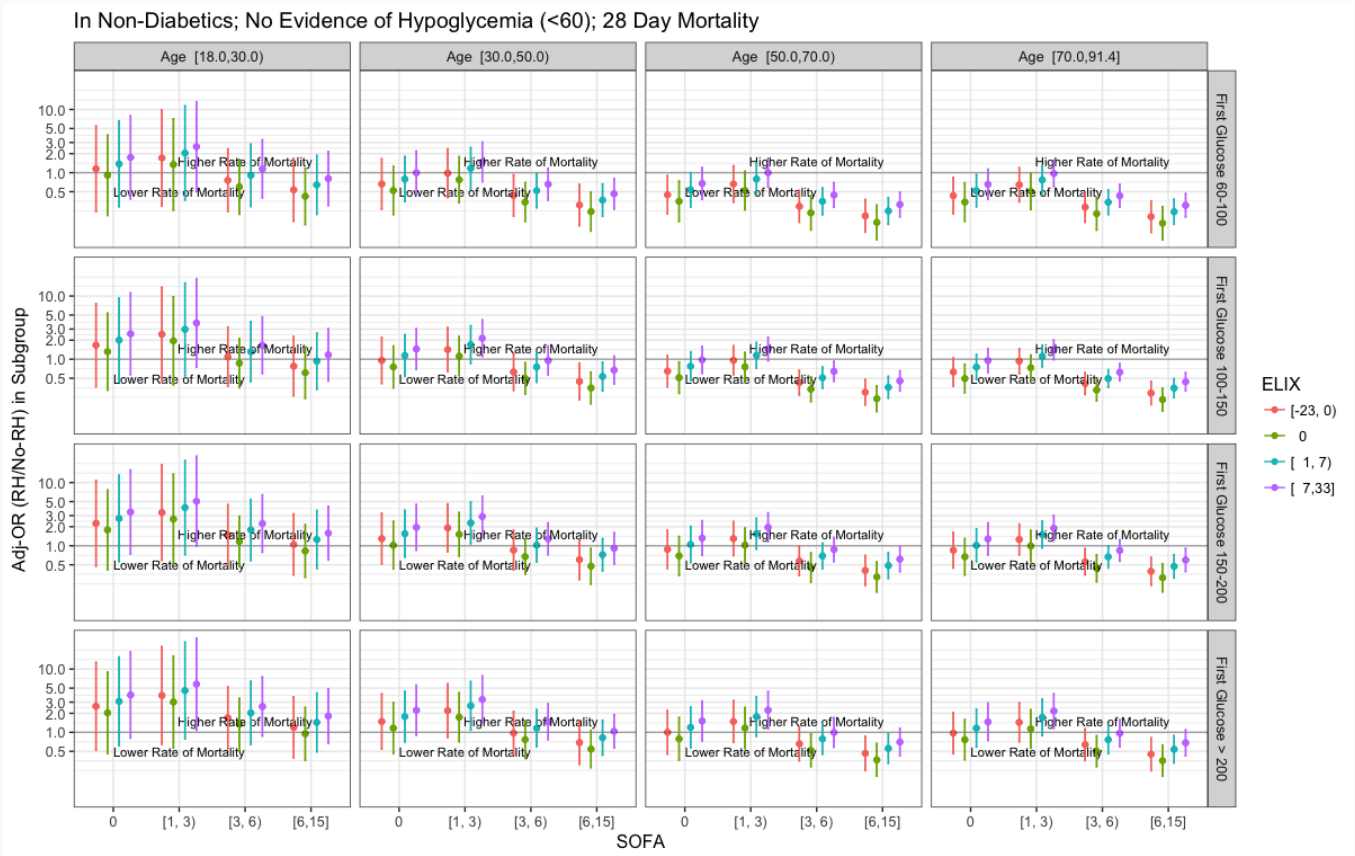
Insulin / RH / Non-Diabetics

- Driver may not be not insulin
- Might be RH only, or we may not have enough power to see the effect, or other factors?



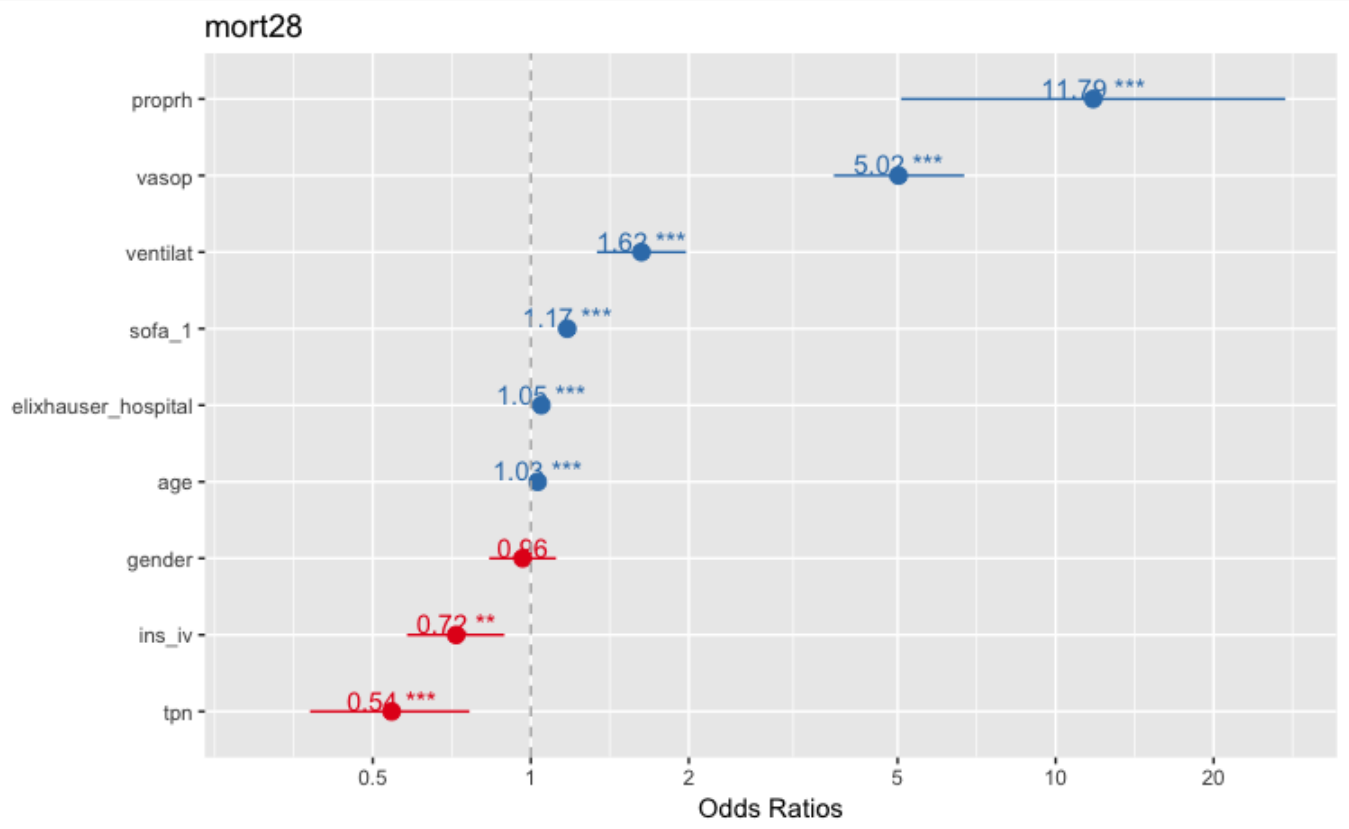
Considering Covariates

- Logistic regression with stepwise model selection (Akaike Information Criteria, AIC)
- Younger / higher initial glucose / low SOFA / abnormal Elixhauser



Considering Covariates

- Logistic regression (28-day mortality)
- Non-diabetics / Higher initial glucose ($\geq$ 150 mg/dl)



Summary

- In non-diabetics (28736 admissions)
  - RH is associated with the increasing short-term morality
  - Dose dependent effect between RH and short-term mortality
  - Young age, lower SOFA score, other morbidities and higher initial glucose level $\rightarrow$ RH-associated increasing short-term mortality $\uparrow$
- Pros: large cohort and fine data granularity
- Cons: potential confounders, single-center, causation
- Next: Philips eICU, revisiting insulin
- May change the ICU glucose control strategy in the future
- Acknowledgement
  - Dr. Francisco Salgueiro, Dr. Rinaldo Bellomo
  - HST.953 staff, MIMIC developers