ICU-acquired complications

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Attributable mortality of an ICU-acquired complication?

Are there specific (immune system) pathways leading to an ICU-acquired complication?

ICU-acquired complications in MARS

- **Infections – HAP / VAP**
- ARDS
- **Acute Kidney Injury**
- Thromboses/clots
- Bedsores
- Myocardial infarction
- Delirium

Appropriate quantification of the impact and burden of these complications are imperative to understanding its severity and the importance of additional preventive measures and timely treatment.

All these complications are all associated with increased ICU mortality, but…..the well-known mantra "**correlation does not imply causation**" dictates that a considerable number of patients die with, but not necessarily from, the complication.

Causal inference – counterfactual interpretation

Counterfactual:

If I could theoretically prevent a ICU-acquired complication, how many lives are saved?

Solution: create a pseudo-ICU-population that has exactly the same trajectory (severity of disease, sepsis, treatments etc) towards ICU-acquired complication, but then it was prevented (in theory).

Full definition of our counterfactual model ICU-acquired complications (1)

Estimation of ICU mortality due to ICU-acquired complication, which expresses the proportion of preventable death cases in the ICU in the absence of a ICU-acquired complication.

This (inherently causal) effect measure involves:
the nonobservable counterfactual incidence of ICU death that would have been observed if, *counter to the fact*, a ICU-acquired complication had been avoided in all considered patients.

	Definition	Formula
Attributable mortality (AM)	Increase or decrease in death (D) if a patient presents an exposure (E) at the time (t).	$AM(t) = P[D(t) = 1 \mid E(t) = 1] - P[D(t) = 1 \mid E(t) = 0]$
Attributable fraction (AF)	Proportion of deaths (D) that are attributable to an exposure (E) at the time (t). Proportion of deaths (D) that would not have occurred if no patient presented the exposure (E) at the time (t).	$AF(t) = \{(P[D(t) = 1] - P[D(t) = 1 \mid E(t) = 0]\}/P[D(t) = 1]$

Original Investigation | Caring for the Critically Ill Patient

FREE

April 12, 2016

Incidence, Risk Factors, and Attributable Mortality of Secondary Infections in the Intensive Care Unit After Admission for Sepsis

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» Author Affiliations | Article Information

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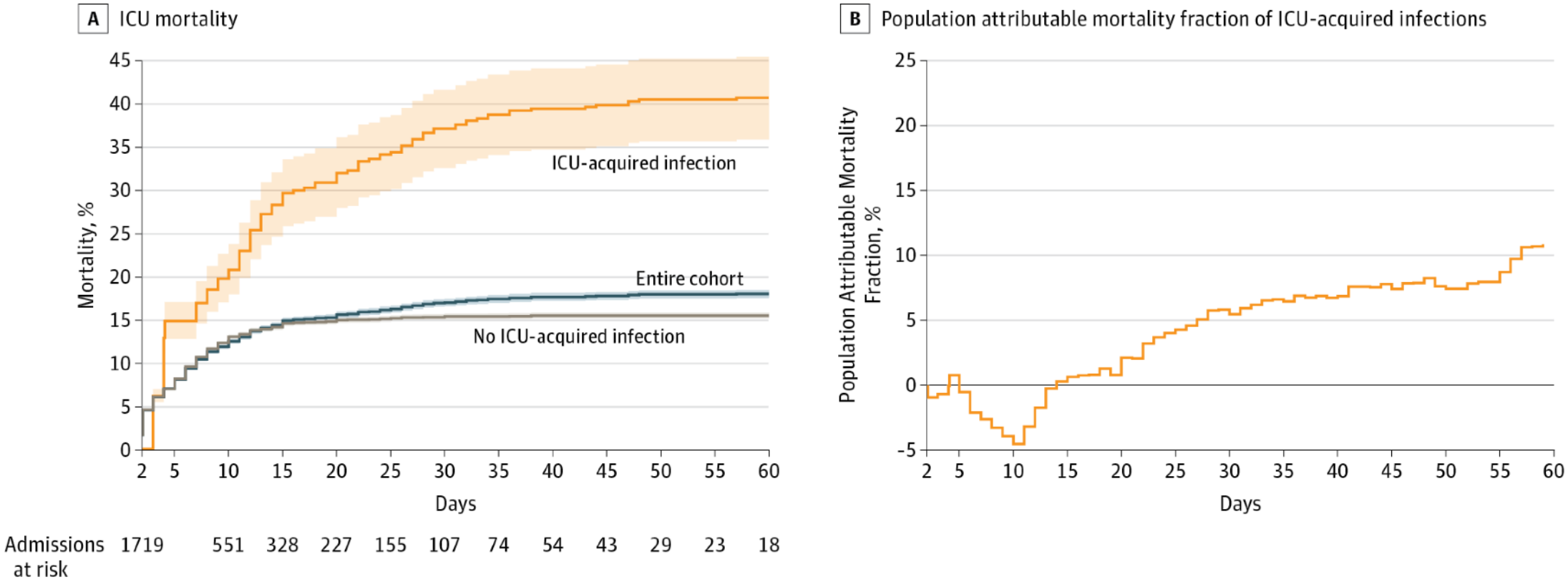
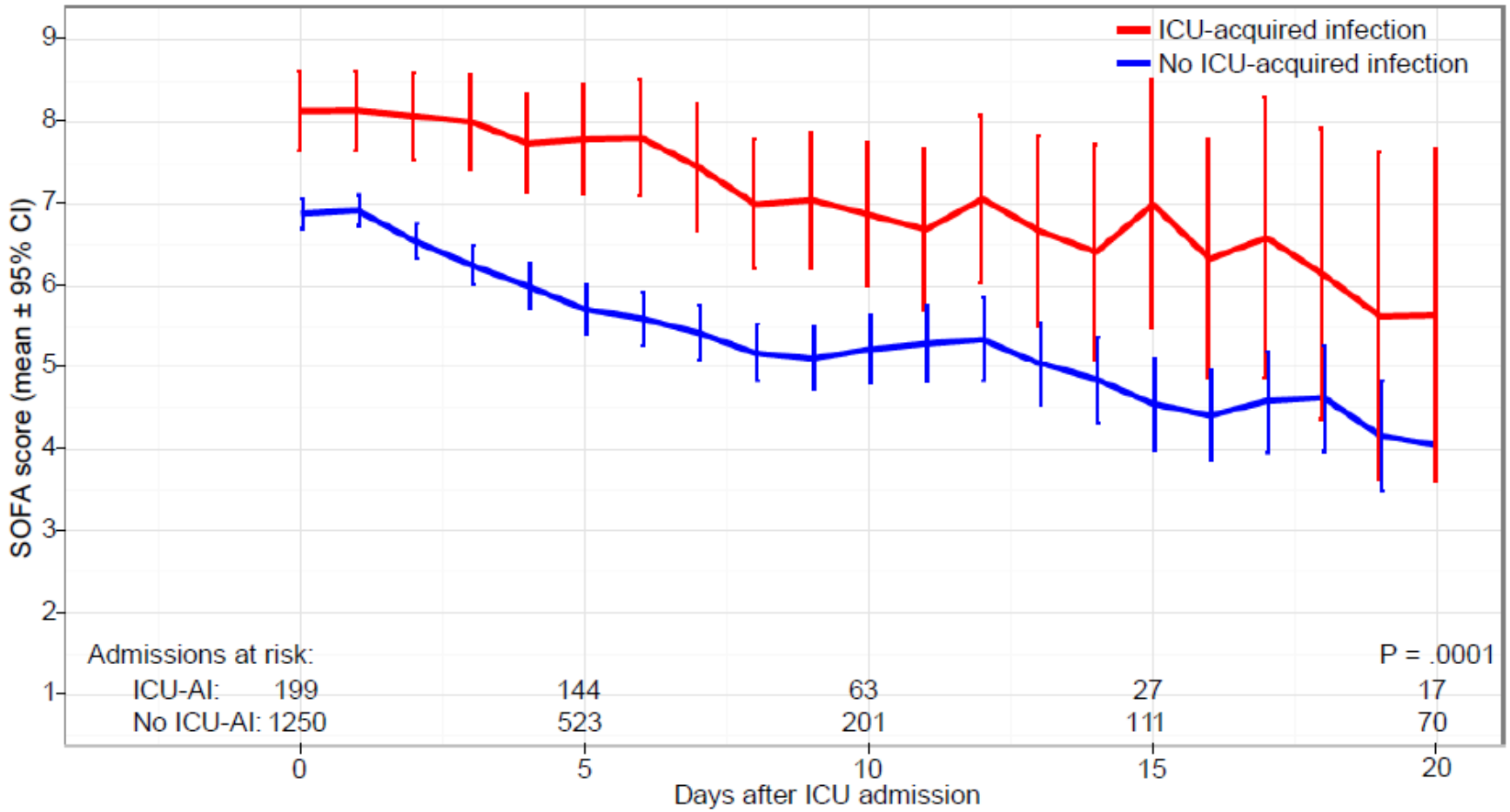
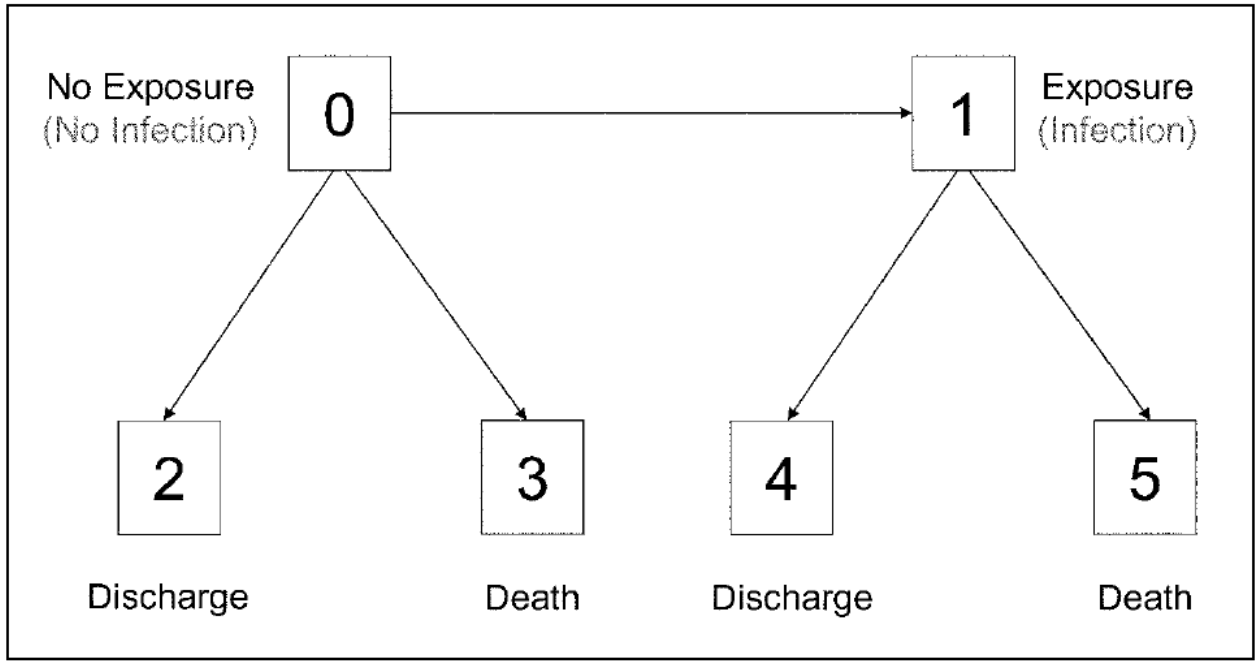


A, Estimated intensive care unit (ICU)–mortality calculated using the multistate model (see the Methods section in the Supplement). Shaded areas represent 95% CIs. B, Population attributable ICU mortality fraction over time adjusted for quartiles of Acute Physiology and Chronic Health Evaluation IV score and quartiles of age. The population attributable mortality fraction was expressed as the percentage of ICU mortality caused by the ICU-acquired infections. The negative values of attributable mortality fraction in the first 14 days after ICU admission are most likely driven by the most severely ill patients encountering the competing event (death without ICU-acquired infection) before being able to develop an ICU-acquired infection[24]; additionally, the discharge hazard for patients with an ICU-acquired infection is smaller than the discharge hazard for patients without an ICU-acquired infection, resulting in a higher chance of dying (longer ICU stay) and a delay in deaths in the former group, leading to a negative attributable mortality fraction in the earlier days.

eFigure 3. SOFA scores up to 2 days before event (ICU-acquired infection or discharge/mortality) in patients admitted with sepsis stratified by development (or not) of an ICU-acquired infection



Multi-state model: progressive disability model



Progressive disability model

Exposure treated as a time-dependent variable

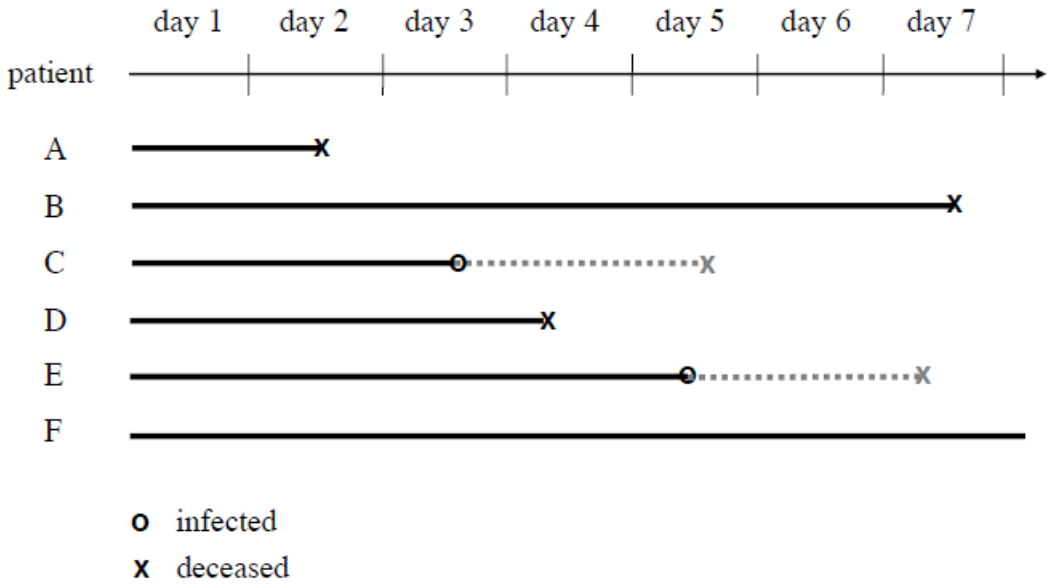
Discharge competing event for Death

Transition probabilities are estimated with the Aalen-Johansen estimator

As soon as patients acquire infection, they are excluded from the risk set and transfer their weight to patients who have until that time remained uninfected.

Schumacher M, et al. (2007) Attributable mortality due to nosocomial infections. A simple and useful application of multistate models. *Methods Inf Med*; **46**(5): 595-600.

Why multi-state-survival cannot give a causal interpretation (1)



patient	day 1	day 2	day 3	day 4	day 5	day 6	day 7
A	1	1	1.2	1.2	1.5	1.5	1.5
B	1	1	1.2	1.2	1.5	1.5	1.5
C	1	1	0	0	0	0	0
D	1	1	1.2	1.2	1.5	1.5	1.5
E	1	1	1.2	1.2	0	0	0
F	1	1	1.2	1.2	1.5	1.5	1.5
marginal odds	0/6	0/6	1/5	1/5	2/4	2/4	2/4
$\widehat{\Pr}(T^{\overline{a}=0} \leq t_K, \epsilon^{\overline{a}=0} = 1)$	0	1/6	1.2/6	2.4/6	3/6	3/6	4.5/6

counterfactual event times Ta=0
tK = interval time
Ea=0 = event type indicator

This implies that an event that has already occurred gets reweighed based on information (on future infections) that is not available at the time of that event.

Johan Steen PM, Wim Van Biesen, Johan Decruyenaere, Stijn Vansteelandt. (2023) Handling time-dependent exposures and confounders when estimating attributable fractions — bridging the gap between multistate and counterfactual modeling. *arXiv preprint arXiv*; **:04833**.

Ideal causal model ICU-acquired complications

In a hypothetical RCT: Relative mortality reduction that would be found in eligible patients that are randomly assigned to receive either a fully effective bundle of preventive measures or standard of care

Control arm: correspond to the observed cumulative incidence in an observational study where all patients received standard of care

Treatment arm: corresponds to the ‘counterfactual’ ICU-complication-free cumulative incidence

- Weight of newly ICU-A-complication should only be distributed among ICU-complication-free that are still hospitalized at the ICU at that time
- Weight of newly ICU-A-complication should only be distributed among ICU-complication-free with the same patient profile in terms of admission characteristics and evolution of disease severity up to that time wave.
- Treating ICU-A-complication as an informative censoring event

3 steps in Marginal Structural Models

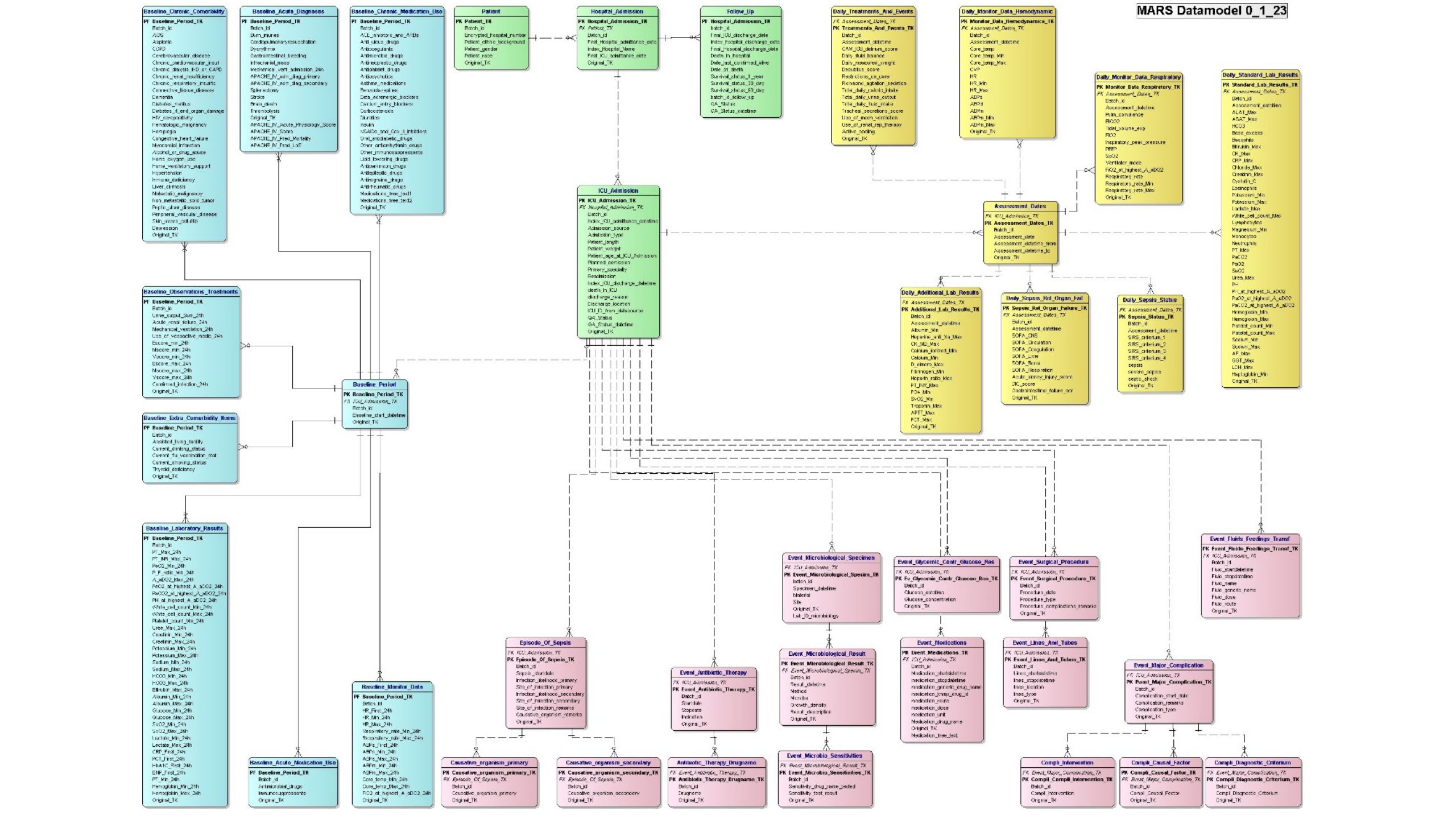
1: Make a time-dependent Survival model with ICU-acquired infections (yes) vs No ICU-acquired infections, given all covariates:

- Baseline covariates
- Time-varying covariates
- Cumulative number of treatment history

2: Extract stabilized IPWs

3: Include everyday IPW weights based in final time-dependent Survival model for ICU-death (vs ICU discharge)

$$\text{Binary stabilized IPW}_{it} = \prod_{t=1}^{t} \frac{P[X_{it}|\bar{X}_{i,t-1}, V_i]}{P[X_{it}|\bar{X}_{i,t-1}, Y_{i,t-1}, C_{it}, V_i]}$$


MARS Datamodel 0_1_23
Baseline_Chronic_Comorbidity
PF Baseline_Period_TK
Batch_Id
AIDS
Asplenic
COPD
Cerebrovascular_disease
Chronic_cardiovascular_insuf
Chronic_dialysis_IHD_or_CAPD
Chronic_renal_insufficiency
Chronic_respiratory_insuffic
Connective_tissue_disease
Dementia
Diabetes_mellitus
Diabetes_t_end_organ_damage
HIV_comorbidity
Hematologic_malignancy
Hemiplegia
Congestive_heart_failure
Myocardial_infarction
Alcohol_or_drug_abuse
Home_oxygen_use
Home_ventilatory_support
Hypertension
Immune_deficiency
Liver_cirrhosis
Metastatic_malignancy
Non_metastatic_solid_tumor
Peptic_ulcer_disease
Peripheral_vascular_disease
Skin_ulcers_cellulitis
Depression
Original_TK
Baseline_Acute_Diagnoses
PF Baseline_Period_TK
Batch_Id
Burn_injuries
Cardiopulmonary_resuscitation
Dysrhythmia
Gastrointestinal_bleeding
Intracranial_injury
Mechanical_vent_admission_24h
APACHE_IV_adm_diag_primary
APACHE_IV_adm_diag_secondary
Splenectomy
Stroke
Brain_death
Thrombolysis
Original_TK
APACHE_IV_Acute_Physiology_Score
APACHE_IV_Score
APACHE_IV_Pred_Mortality
APACHE_IV_Pred_LoS
Baseline_Chronic_Medication_Use
PF Baseline_Period_TK
Batch_Id
ACE_inhibitors_and_ARBs
Anti_tetus_drugs
Anticoagulants
Antiemetic_drugs
Antiepileptic_drugs
Antiplatelet_drugs
Antipsychotics
Asthma_medications
Benzodiazepines
Beta_adrenergic_blockers
Calcium_entry_blockers
Corticosteroids
Diuretics
Insulin
NSAIDs_and_Cox_II_inhibitors
Oral_antidiabetic_drugs
Other_antiarrhythmic_drugs
Other_immunosuppressants
Lipid_lowering_drugs
Antiparkinson_drugs
Antispasmodic_drugs
Antimigraine_drugs
Anthelmentic_drugs
Medications_free_text1
Medications_free_text2
Original_TK
Patient
PK Patient_TK
Batch_Id
Encrypted_hospital_number
Patient_ethnic_background
Patient_gender
Patient_race
Original_TK
Hospital_Admission
PK Hospital_Admission_TK
FK Patient_TK
Batch_Id
First_Hospital_admissions_date
Index_Hospital_Name
First_ICU_admittance_date
Original_TK
Follow_Up
PF Hospital_Admission_TK
batch_id
Final_ICU_discharge_date
Index_hospital_discharge_date
Final_hospital_discharge_date
Death_in_hospital
Date_last_confirmed_alive
Date_of_death
Survival_status_1_year
Survival_status_30_day
Survival_status_90_day
batch_id_follow_up
QA_Status
QA_status_datetime
Daily_Treatments_And_Events
FK Assessment_Dates_TK
PK Treatments_And_Events_TK
Batch_Id
Assessment_datetime
CAM_ICU_delirium_score
Daily_fluid_balance
Daily_measured_weight
Decubitus_score
Restrictions_on_care
Richmond_agitation_sedation
Total_daily_caloric_intake
Total_daily_urine_output
Total_daily_fluid_intake
Trachea_secretions_score
Used_of_mech_ventilation
Use_of_renal_rep_therapy
Active_cooling
Original_TK
Daily_Monitor_Data_Hemodynamic
PK Monitor_Data_Hemodynamics_TK
FK Assessment_Dates_TK
Batch_Id
Assessment_datetime
Core_temp
Core_temp_Min
Core_temp_Max
CVP
HR
HR_Min
HR_Max
ABPs
ABPd
ABPm
ABPm_Min
ABPm_Max
Original_TK
Daily_Monitor_Data_Respiratory
PK Monitor_Data_Respiratory_TK
FK Assessment_Dates_TK
Batch_Id
Assessment_datetime
Pulm_compliance
PEEP
Tidal_volume_exp
PEEP
Inspiratory_peak_pressure
PEEP
SaO2
Ventilator_mode
FiO2_at_highest_A_aDO2
Respiratory_rate
Respiratory_rate_Min
Respiratory_rate_Max
Original_TK
Daily_Standard_Lab_Results
PK Standard_Lab_Results_TK
FK Assessment_Dates_TK
Batch_Id
Assessment_datetime
ALAT_Max
ASAT_Max
HCO3
Base_excess
Basophils
Bilirubin_Max
CK_Max
CRP_Max
Chloride_Max
Creatinin_Max
Cystatin_C
Eosinophils
Potassium_Min
Potassium_Max
Lactate_Max
White_cell_count_Max
Lymphocytes
Magnesium_Min
Monocytes
Neutrophils
PT_Max
PaCO2
PaO2
SaO2
Urea_Max
Pc
P_f_at_highest_A_aDO2
PaO2_at_highest_A_aDO2
PaCO2_at_highest_A_aDO2
Hemoglobin_Min
Hemoglobin_Max
Platelet_count_Min
Platelet_count_Max
Sodium_Min
Sodium_Max
AF_Max
GGT_Max
LCH_Max
Haptoglobin_Min
Original_TK
ICU_Admission
PK ICU_Admission_TK
FK Hospital_Admission_TK
Batch_Id
Index_ICU_admittance_datetime
Admission_source
Admission_type
Patient_length
Patient_weight
Patient_age_at_ICU_Admission
Planned_admission
Primary_specialty
Readmission
Index_ICU_discharge_datetime
death_in_ICU
discharge_reason
Discharge_location
ICU_ID_from_data_source
QA_Status
QA_Status_datetime
Original_TK
Assessment_Dates
FK ICU_Admission_TK
PK Assessment_Dates_TK
Batch_Id
Assessment_date
Assessment_datetime_from
Assessment_datetime_to
Original_TK
Daily_Additional_Lab_Results
FK Assessment_Dates_TK
PK Additional_Lab_Results_TK
Batch_Id
Assessment_datetime
Albumin_Min
Heparin_anti_Xa_Max
CK_MB_Max
Calcium_ionized_Min
Calcium_Min
D_dimers_Max
Fibrinogen_Min
Heparin_ratio_Max
PT_INR_Max
PO4_Min
SvO2_Min
Troponin_Max
APTT_Max
PCT_Max
Original_TK
Daily_Sepsis_Rel_Organ_Fail
PK Sepsis_Rel_Organ_Failure_TK
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Batch_Id
Assessment_datetime
SOFA_CNS
SOFA_Circulation
SOFA_Coagulation
SOFA_Liver
SOFA_Renal
SOFA_Respiration
Acute_kidney_injury_score
CK_score
Gastrointestinal_failure_scr
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Daily_Sepsis_Status
FK Assessment_Dates_TK
PK Sepsis_Status_TK
Batch_Id
Assessment_datetime
SIRS_criterium_1
SIRS_criterium_2
SIRS_criterium_3
SIRS_criterium_4
sepsis
severe_sepsis
sepsis_shock
Original_TK
Baseline_Observations_Treatments
PF Baseline_Period_TK
Batch_Id
Urine_output_Sum_24h
Acute_renal_failure_24h
Mechanical_ventilation_24h
Use_of_vasoactive_medic_24h
Escore_min_24h
Mscore_min_24h
Vscore_min_24h
Escore_max_24h
Mscore_max_24h
Vscore_max_24h
Confirmed_infection_24h
Original_TK
Baseline_Period
PK Baseline_Period_TK
FK ICU_Admission_TK
Batch_Id
Baseline_start_datetime
Original_TK
Baseline_Extra_Comorbidity_Items
PF Baseline_Period_TK
Batch_Id
Assisted_living_facility
Current_drinking_status
Current_flu_vaccination_stat
Current_smoking_status
Thyroid_deficiency
Original_TK
Baseline_Laboratory_Results
PF Baseline_Period_TK
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PT_Max_24h
PT_INR_Max_24h
PaO2_Min_24h
P_F_ratio_Min_24h
A_aDO2_Max_24h
PaO2_at_highest_A_aDO2_24h
PaO2_at_highest_A_aDO2_24h
PH_at_highest_A_aDO2_24h
White_cell_count_Min_24h
White_cell_count_Max_24h
Platelet_count_Min_24h
Urea_Max_24h
Creatinin_Min_24h
Creatinin_Max_24h
Potassium_Min_24h
Potassium_Max_24h
Sodium_Min_24h
Sodium_Max_24h
HCO3_Min_24h
HCO3_Max_24h
Bilirubin_Max_24h
Albumin_Min_24h
Albumin_Max_24h
Glucose_Min_24h
Glucose_Max_24h
SvO2_Min_24h
SvO2_Max_24h
Lactate_Min_24h
Lactate_Max_24h
CRP_First_24h
PCT_First_24h
HbA1C_First_24h
BNP_First_24h
PT_Min_24h
Hemoglobin_Min_24h
Hemoglobin_Max_24h
Original_TK
Baseline_Acute_Medication_Use
PF Baseline_Period_TK
Batch_Id
Antimicrobial_drugs
Immunosuppressants
Original_TK
Baseline_Monitor_Data
PF Baseline_Period_TK
Batch_Id
HR_First_24h
HR_Min_24h
HR_Max_24h
Respiratory_rate_Min_24h
Respiratory_rate_Max_24h
ABPs_First_24h
ABPs_Min_24h
ABPs_Max_24h
ABPm_Min_24h
ABPm_Max_24h
Core_temp_Min_24h
Core_temp_Max_24h
FiO2_at_highest_A_aDO2_24h
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Episode_Of_Sepsis
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PK Episode_Of_Sepsis_TK
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Site_of_infection_primary
Infection_likelihood_secondary
Site_of_infection_secondary
Site_of_infection_remarks
Causative_organism_remarks
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Stopdate
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medication_stopdatetime
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medication_brand_drug_id
medication_route
medication_dose
medication_unit
Medication_drug_name
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Medication_free_text
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Procedure_date
Procedure_type
Procedure_complications_remarks
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PK Event_Lines_And_Tubes_TK
Batch_Id
Lines_startdatetime
Lines_stopdatetime
Lines_location
Lines_type
Original_TK
Event_Fluids_Feedings_Transf
PK Event_Fluids_Feedings_Transf_TK
FK ICU_Admission_TK
Batch_Id
Fluid_startdatetime
Fluid_stopdatetime
Fluid_name
Fluid_generic_name
Fluid_dose
Fluid_route
Original_TK
Event_Major_Complication
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PK Event_Major_Complication_TK
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Complication_remarks
Complication_type
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Original_TK
Causative_organism_secondary
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Batch_Id
Causative_organism_secondary
Original_TK
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Batch_Id
Drugname
Original_TK
Event_Microbio_Sensitivities
FK Event_Microbiological_Result_TK
PK Event_Microbio_Sensitivities_TK
Batch_Id
Sensitivity_drug_name_tested
Sensitivity_test_result
Original_TK
Compli_Intervention
FK Event_Major_Complication_TK
PK Compli_Compli_Intervention_TK
Batch_Id
Compli_Intervention
Original_TK
Compli_Causal_Factor
PK Compli_Causal_Factor_TK
FK Event_Major_Complication_TK
Batch_Id
Compli_Causal_Factor
Original_TK
Compli_Diagnostic_Criterium
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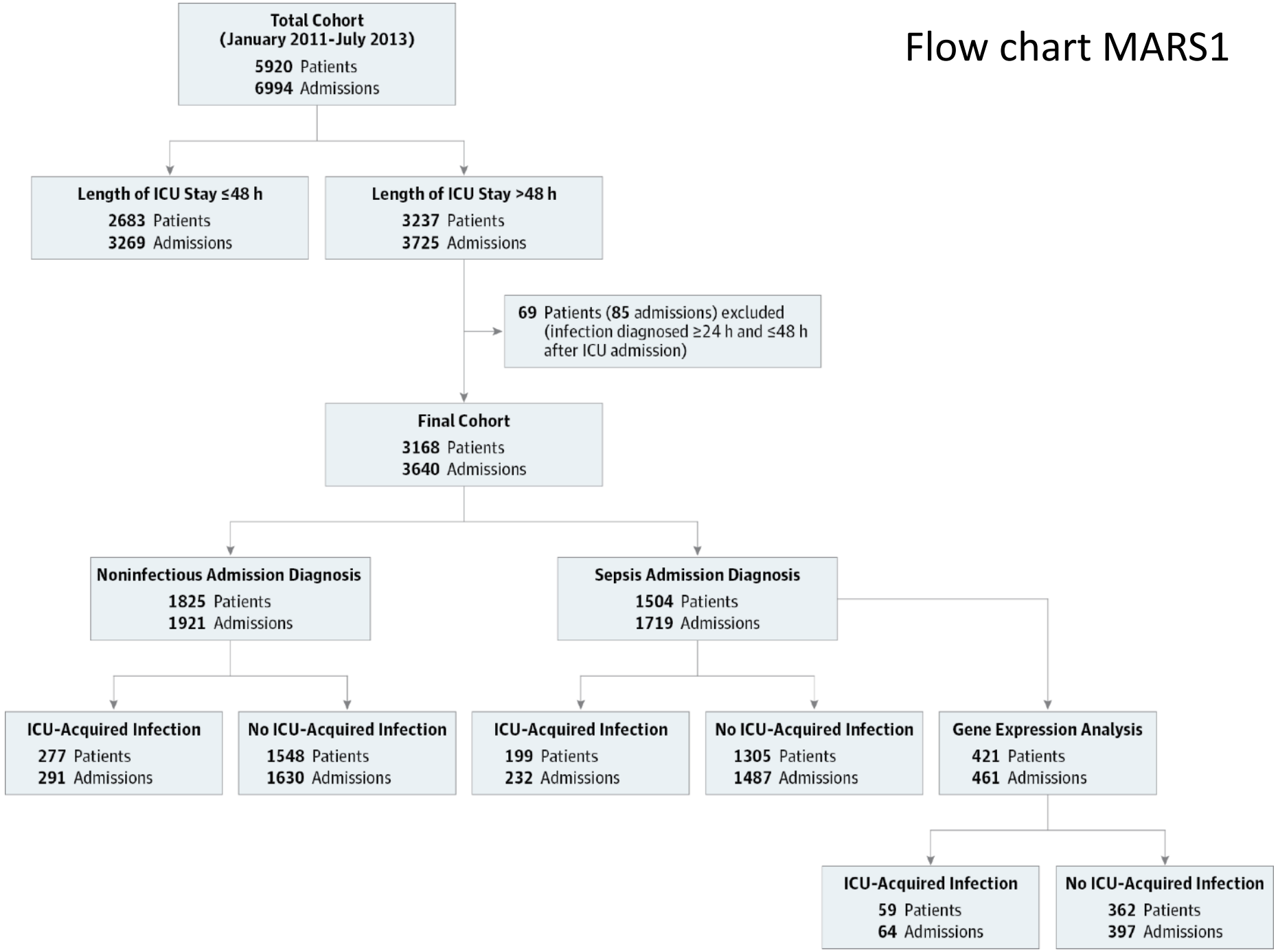
Batch_Id
Compli_Diagnostic_Criterium
Original_TK

Flow chart MARS1



Step 1: MARS dataframe

- Make within a patient for every day a row, based on ICU length of stay
- Merge daily MARS data (SOFA score, lab values, RRT, MV)
- Merge Lines/tubes
- Merge surgery events
- Merge other complications (ARDS, AKI, etc)
- Count cumulative events (MV, RRT, Lines etc)
- Include one-day LAG of all variables (SOFA score, cumulative events)

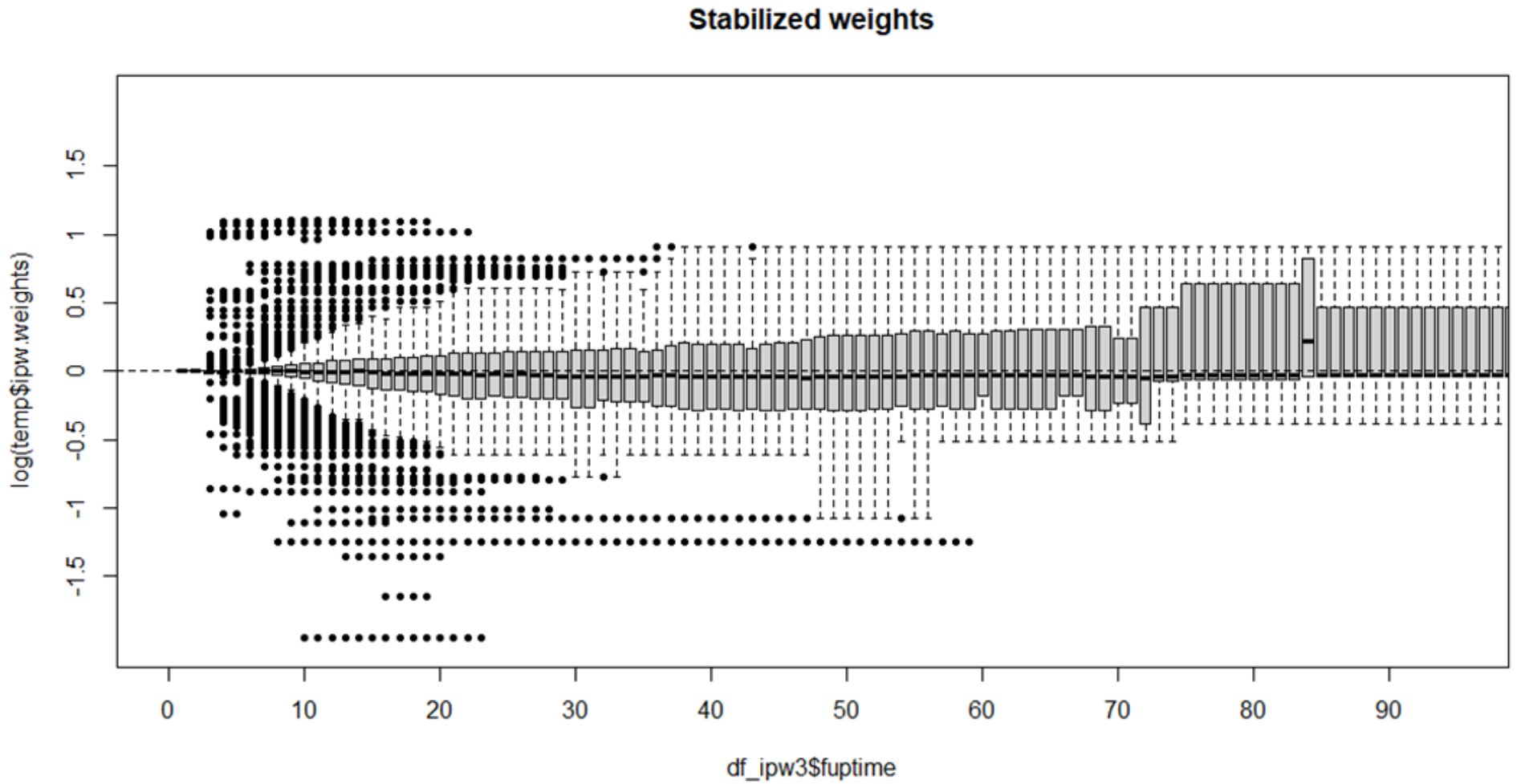
Step 1: impute some missing data

- Impute missing daily values with Mixed models
  - Applied for SOFA score (~1.5% missing)

```
> anova(sofa.lme)
                                numDF denDF   F-value p-value
(Intercept)                         1 18227 14642.701  <.0001
ns(fuptime, 3)                      3 18227   633.226  <.0001
Charlson_without_age                1  1884    42.903  <.0001
Patient_age_at_ICU_Admission        1  1884    12.513   4e-04
icu_sepsis2                         1 18227   103.985  <.0001
Acute_kidney_injury_score_imputed   3 18227  1008.673  <.0001
ALI_ARDS2                           1 18227   171.716  <.0001
Use_of_mech_ventilation_imputed     1 18227   506.275  <.0001
vasopressor                         1 18227  3539.187  <.0001
```

	ICU_ID_from_datasource	Patient_TK	Patient_race	Patient_gender	urinary_catheter	central_venous_catheter	arterial_catheter	peripheral_catheter	surgical_drain	diff_daily	tstart	fuptime	icu_sepsis	event2
1	157	18339	non-caucasian	male	0	0	0	0	0	0	-1	0	0	No-death
2	157	18339	non-caucasian	male	1	1	1	1	0	1	0	1	0	No-death
3	157	18339	non-caucasian	male	1	1	1	1	0	1	1	2	0	No-death
4	157	18339	non-caucasian	male	1	1	1	1	0	1	2	3	0	No-death
5	157	18339	non-caucasian	male	1	1	1	1	0	1	3	4	0	No-death
6	157	18339	non-caucasian	male	1	1	1	1	0	1	4	5	0	No-death
7	157	18339	non-caucasian	male	1	1	1	1	0	1	5	6	0	No-death
8	157	18339	non-caucasian	male	1	1	1	1	0	1	6	7	0	No-death
9	157	18339	non-caucasian	male	1	1	1	1	0	1	7	8	0	No-death
10	157	18339	non-caucasian	male	1	1	1	1	0	1	8	9	0	No-death
11	157	18339	non-caucasian	male	1	1	1	1	0	1	9	10	0	ICU-discharge
12	160	18472	caucasian	female	1	0	0	1	0	0	-1	0	0	No-death
13	160	18472	caucasian	female	1	1	1	1	0	1	0	1	0	No-death
14	160	18472	caucasian	female	1	0	1	1	0	1	1	2	0	No-death
15	160	18472	caucasian	female	1	0	1	1	0	1	2	3	0	No-death
16	160	18472	caucasian	female	1	0	1	1	0	1	3	4	0	No-death
17	160	18472	caucasian	female	1	0	1	1	0	1	4	5	0	No-death
18	160	18472	caucasian	female	1	0	1	1	0	1	5	6	0	No-death
19	160	18472	caucasian	female	1	1	1	1	0	1	6	7	0	ICU-discharge
20	165	19052	caucasian	female	0	0	0	0	0	0	-1	0	0	No-death
21	165	19052	caucasian	female	1	1	1	1	0	1	0	1	0	No-death
22	165	19052	caucasian	female	1	1	1	1	0	1	1	2	0	No-death

Step 2: extract weights

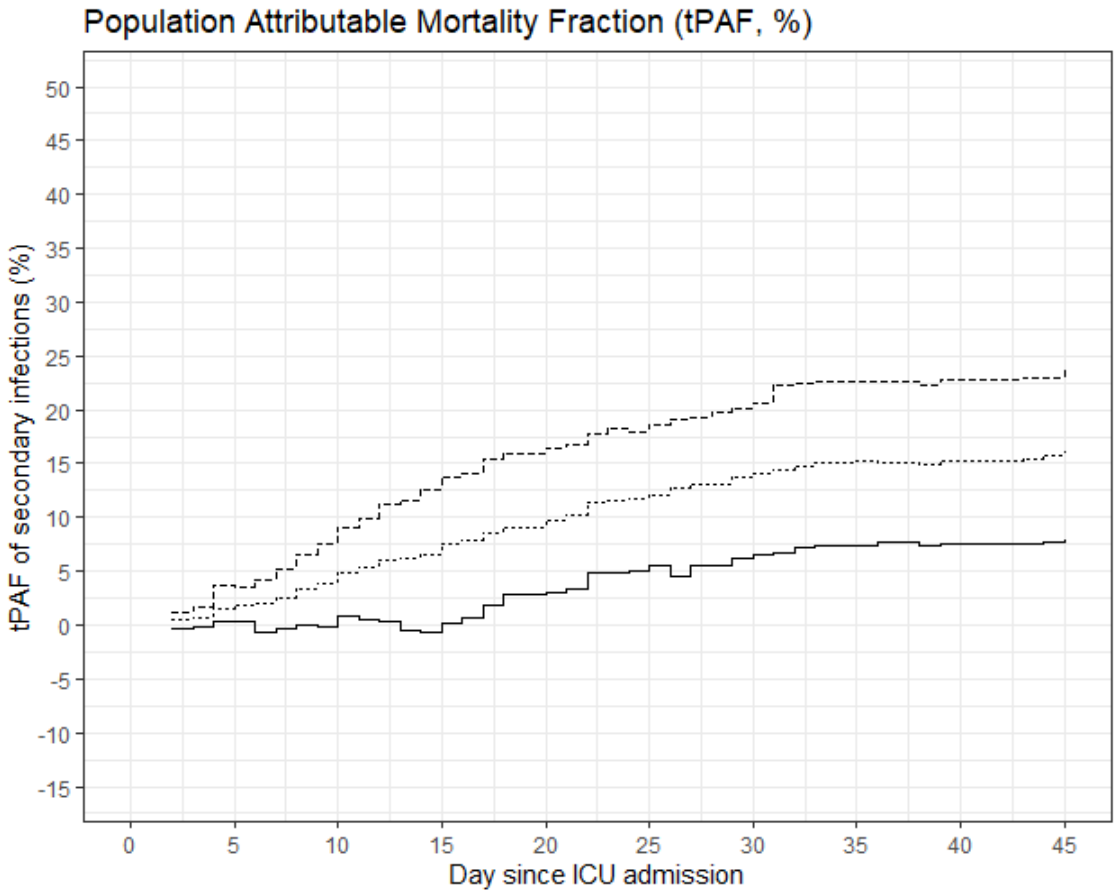


numerator = ~ Patient_age_at_ICU_Admission + ns(APACHE_IV_Acute_Physiology_Score,3),
denominator = ~ Patient_age_at_ICU_Admission + ns(APACHE_IV_Acute_Physiology_Score,3) + ns(SOFAtot_imputed.lag2,3) + ns(SOFAtot_imputed.evo,3)+
Use_of_mech_ventilation_imputed+Acute_kidney_injury_score_imputed,

Step 3: make final model

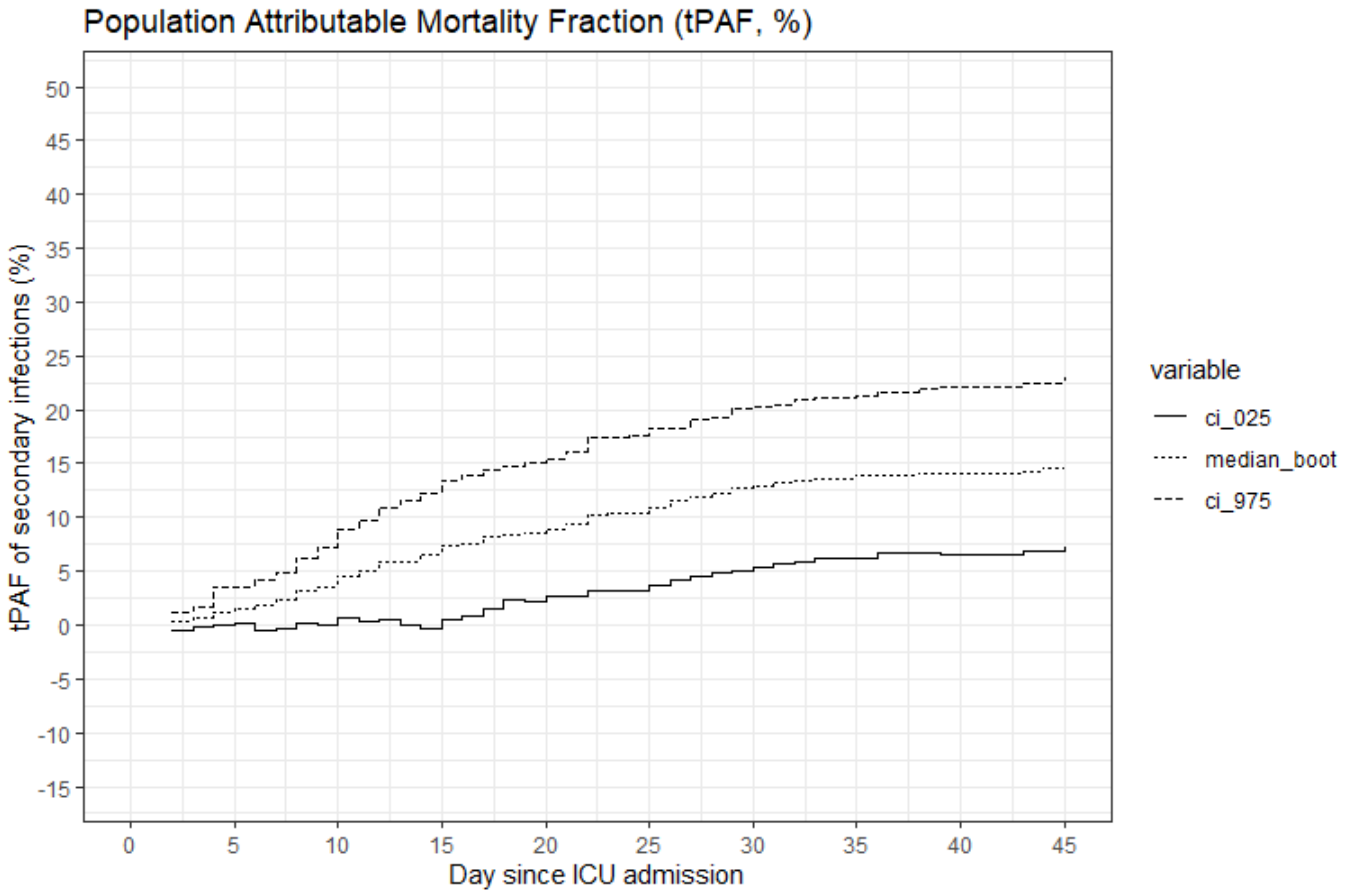
Model	HR (95%CI)	P-value
Unadjusted		
ICU-acquired infections	1.59 (1.23-2.07)	0.000422
Adjusted (only baseline)		
ICU-acquired infections	1.52 (1.17-1.98)	0.00181
Adjusted (baseline + (t-2)SOFA)		
ICU-acquired infections	1.34 (1.02-1.75)	0.0348
Adjusted (baseline + (t-2)SOFA + evoSOFA + MV + AKI)		
ICU-acquired infections	1.31 (0.99-1.74)	0.0565

Inverse probability treatment weighting (IPTW)



Day ICU	tPAF
10	4.4 % (0.5 – 8.8)
20	8.3 % (2.1 – 14.9)
30	13.1% (5.3 – 20.2)

Inverse probability treatment censoring weighting (IPTCW)



Day ICU	tPAF
10	3.5 % (-0.1 – 7.2)
20	8.5 % (2.3 – 15.0)
30	12.7% (5.1 – 20.0)

Conclusions I

IPCW (with MSM) ideal method for estimating causal effects in ICU data

Easy quantifiable interpretation of how much mortality is reduced by theoretically preventing ICU-acquired infection

Assumptions of MSM

- exchangeability
- positivity
- consistency
- no measurement error
- no model misspecification

ICU-acquired Acute Kidney Failure (AKI)

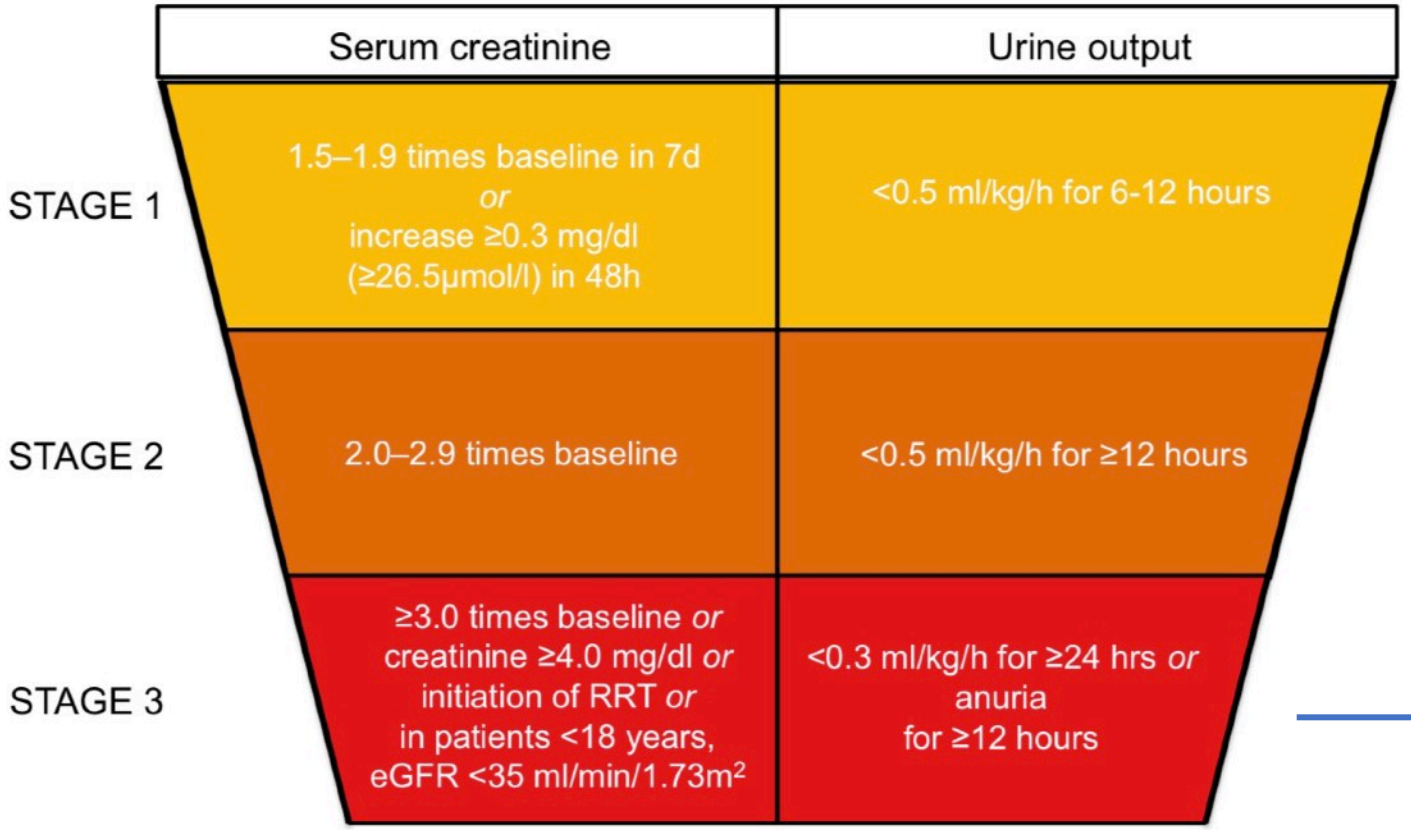
NIERSTICHTING
Je nieren zijn je leven.

Objectives:

Attributable mortality of an ICU-acquired AKI?

Are there specific (immune system) pathways leading to development of AKI?

AKI epidemiology (RIFLE criteria)



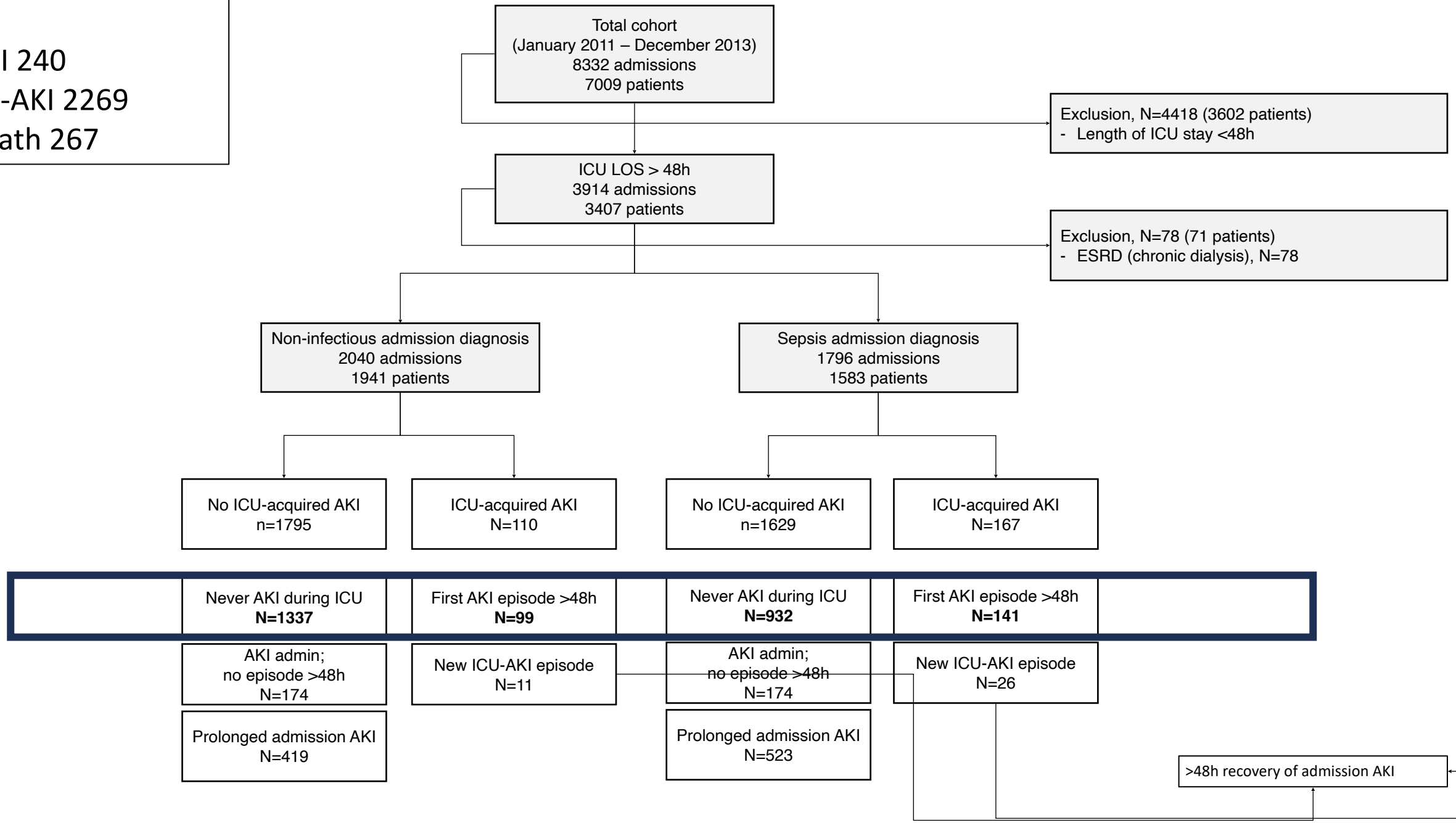
→ >50% develop stage 1 AKI in ICU

→ Dialyses ~10%

Hoste EAJ, Kellum JA, Selby NM et al. (2018). *Nat Rev Nephrol*.

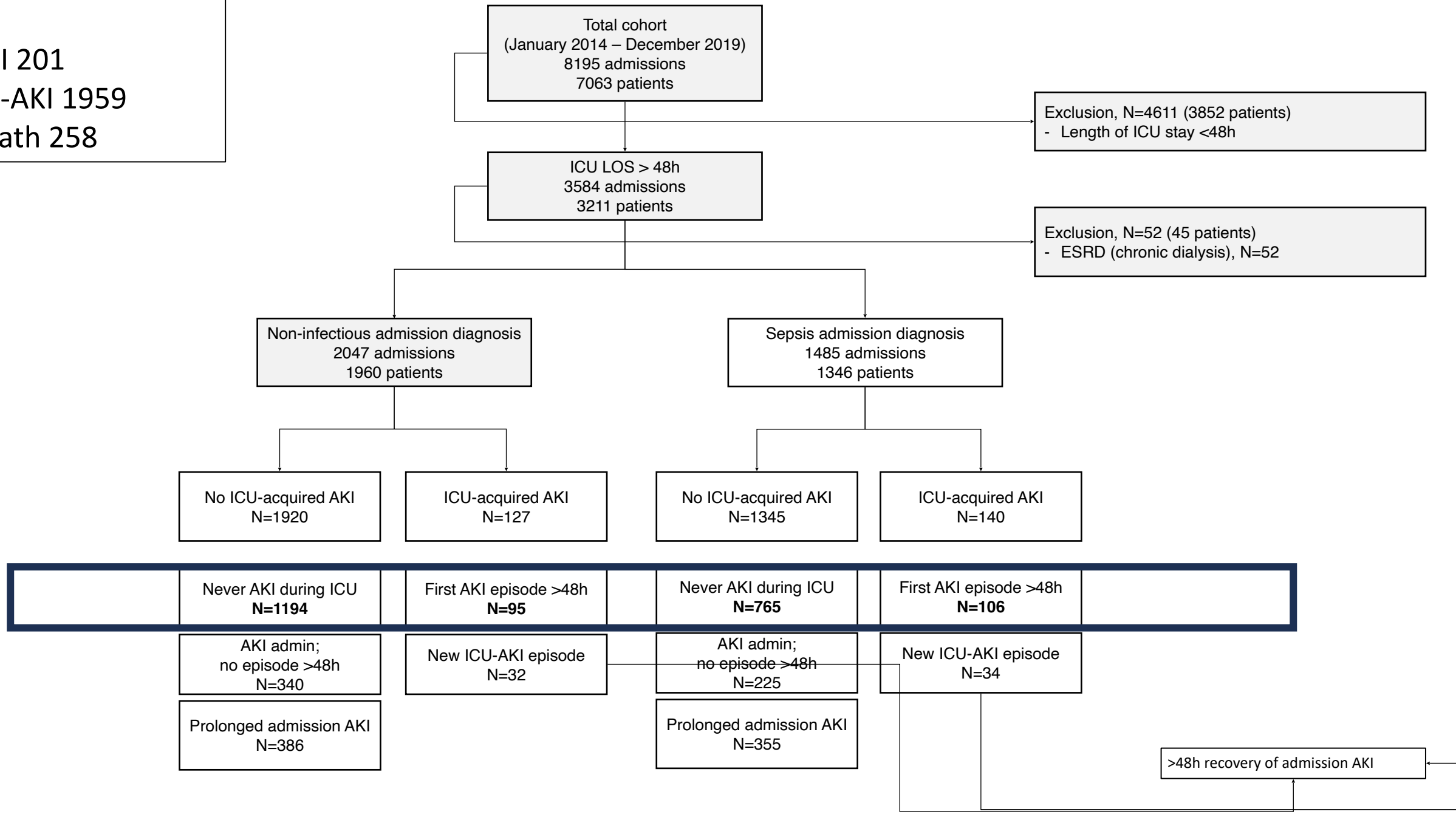
MARS1

ICU-AKI 240
No ICU-AKI 2269
ICU-death 267



MARS2

ICU-AKI 201
No ICU-AKI 1959
ICU-death 258



KNMP (Dutch library of Pharmacie)

Grouped >400 different ICU meds into KNMP categories, based on mechanistic functions

1. glycopeptide antibiotics
2. sulfanomides
3. aminoglycosides
4. antimycotic antibiotics
5. penicillins
6. phosphodiesterase inhibitors
7. antiarrhythmics
8. loop diuretics
9. sympathomimetics alpha/beta
10. phenethylamine derivatives
11. antihypertensives
12. immunosuppressants
13. neurological
14. opioids
15. polypeptides
16. calcineurin inhibitors

Drug Safety (2022) 45:389–398
https://doi.org/10.1007/s40264-022-01173-4

ORIGINAL RESEARCH ARTICLE

Consensus Obtained for the Nephrotoxic Potential of 167 Drugs in Adult Critically Ill Patients Using a Modified Delphi Method

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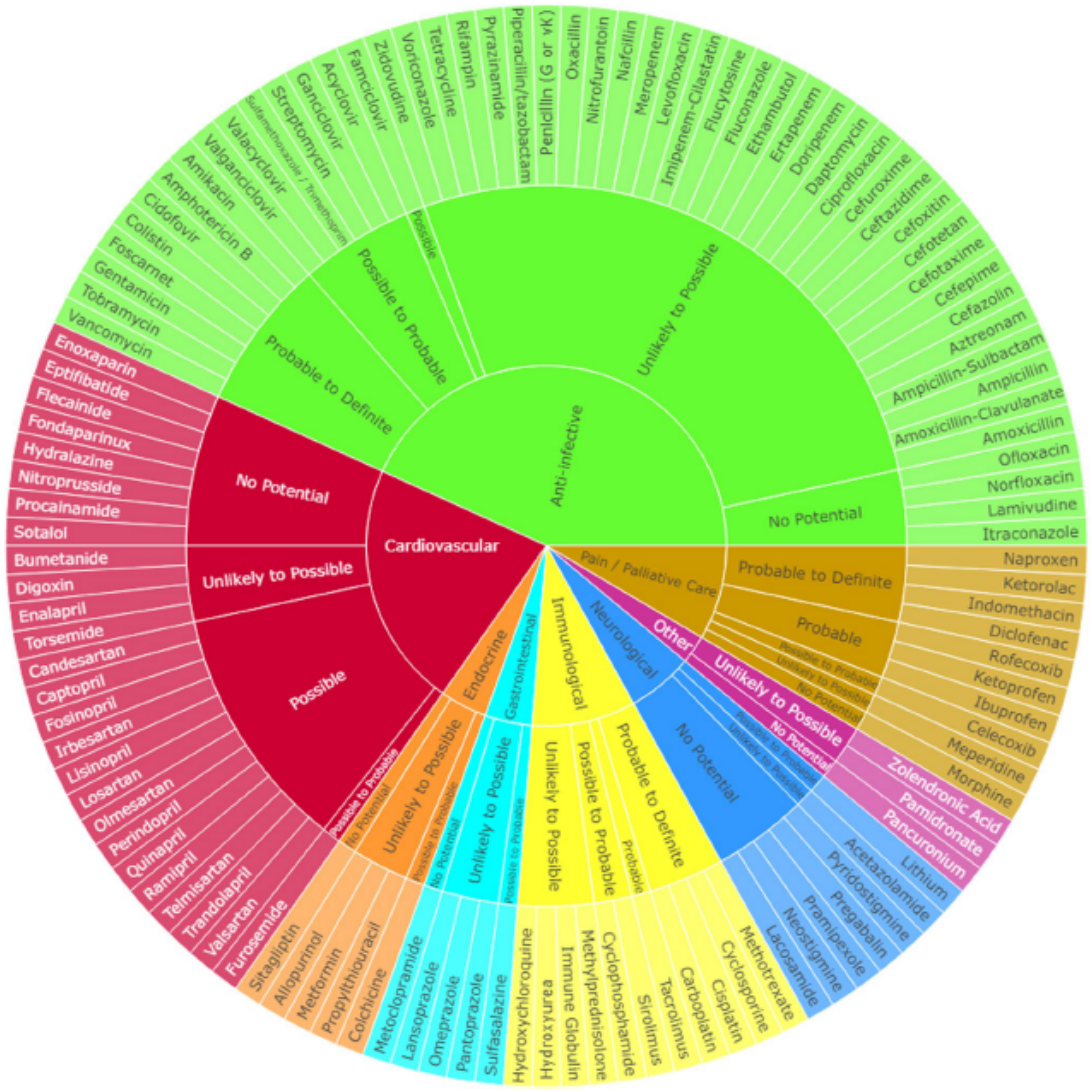


MARSID 1503
ICU admission: 2011-08-29 07:57:00
ICU discharge: 2011-08-29 07:57:00

Day
1
2
3
4
5
6

Day	RIFLE score
1	0
2	0
3	0
4	1
5	1
6	1

Day	RIFLE score	Event
1	0	No-death
2	0	No-death
3	0	No-death
4	1	No-death
5	1	No-death
6	1	ICU-discharge

1. Make rows according to Admission and ICU-discharge

2. Merge baseline & daily data

- 15% of patients RIFLE score is missing
- Mostly at last day of ICU, solution:
  - Last AKI carried forward
  - If >40% of daily AKIs is missing pp, exclude (32 pts)

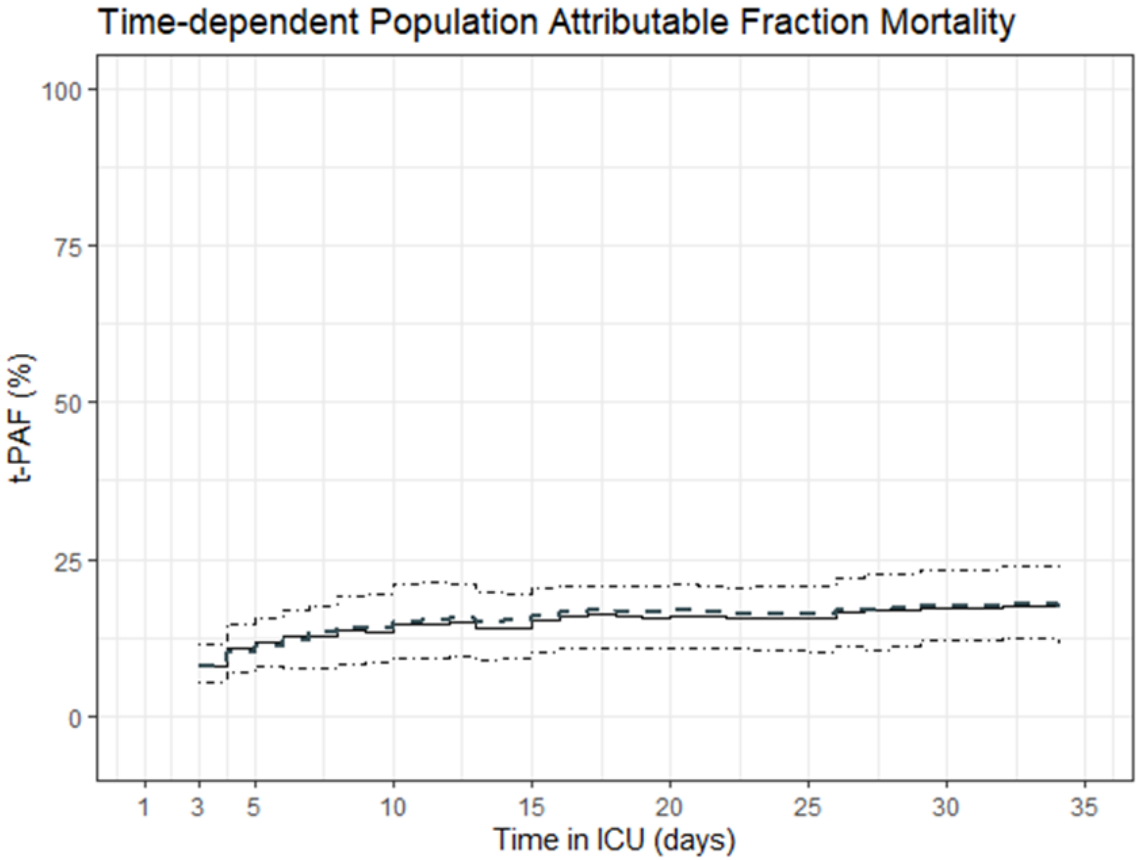
2. Merge other longitudinal data

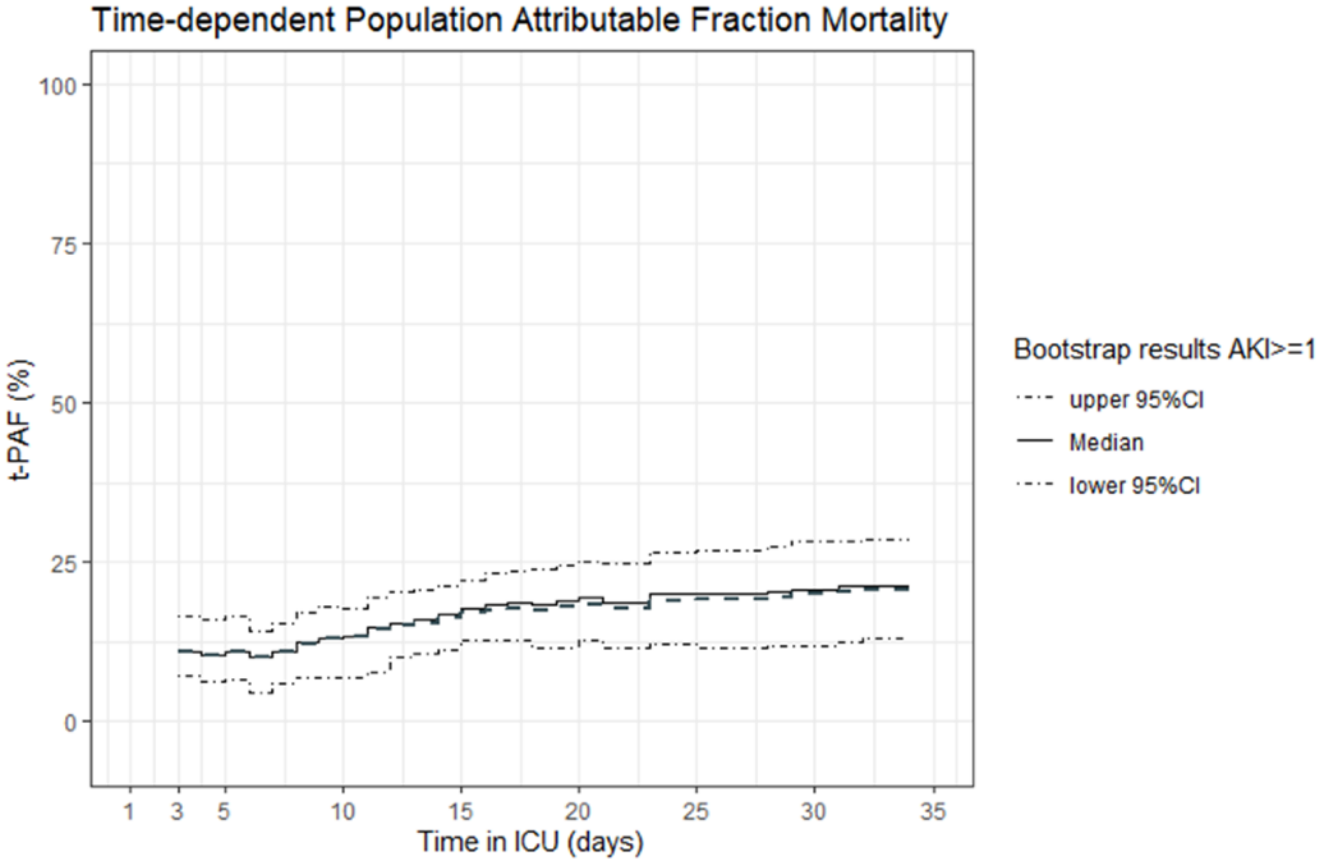
- Cumulative dosages of nephrotoxic meds
- Shock
- Complications

Note. Contrast media not retrievable

Dataset MARS1 (2011-2013):
17870 days of data

Dataset MARS2 (2014-2019):
25092 days of data





Conclusions II

- ICU-acquired AKI has an incidence of ~10%
- tPAF day 10 was 10.2% (95%CI 6.3-15.2)
- tPAF day 20 was 16.3% (95%CI 12.1-24.9)
- tPAF increased in the MARS2 cohort

Patients with ICU-acquired AKI exhibited increasingly higher levels of biomarkers over time reflecting:

- inflammatory response
- endothelial activation

AKI Team

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