R hands-on session: Acute Kidney Disease progression in South-East Asia

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Preamble

- Today we will consider modeling longitudinal data in the R environemnt
- We will do this by considering a real dataset from a study of Acute Kidney Injury in south-east asia ICU patients as a case study
- Specifically, we will consider GLMMs and GEEs to study AKI progression in ICU patients in Thailand
- We will also consider a method that extends the GLMM to model AKI stage (a four-point ordinal outcome)

Preamble

The AKI-SEA study is led by Professor Nattachai Srisawat from the Faculty of Medicine, Chulalongkorn University but also includes investigators from many Thai (and other SEA) universities anf hospitals

The epidemiology and characteristics of acute kidney injury in the Southeast Asia intensive care unit: a prospective multicentre study

Nattachai Srisawat ✉, Win Kulvichit, Noppathorn Mahamitra, Cameron Hurst, Kearkiat Praditpornsilpa, Nuttha Lumlertgul, Anan Chuasuwan, Konlawij Trongtrakul, Adis Tasnarong, Ratapum Champunot ... Show more

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What we will cover....

1. Background
2. Methods
   - Sample and study design
   - Measurements
   - Statistical analysis
3. Some perliminary results
4. Modeling longitudinal outcomes in R

Background

- Acute Kidney Injury (AKI) is a serious disease causing considerable morbidity and mortality as well having a major burden on the health system.
- Importantly, etiologies of AKI vary considerably across regions.
- For example, in western countries AKI largely occurs as a complication of chronic non-communicable diseases, particularly in the advanced stages of these diseases.
- In contrast, in countries like Thailand, their is a much higher incidence of AKI with an infectious disease etiology
- One implication of this is a much higher prevalence of community-acquired AKI in Thailand (relative to western countries where AKI is largely hospital-acquired)

OUR rsearch objectives

- While the objectives of the AKI study are quite broad, today we will specifically consider **whether there is a difference in disease progression between community-acquired and hospital-acquired AKI patients**.
- We will consider more standard longitudinal approaches, but I am also going to take the oppurtunity to showcase methods that can be used to analyze 'staged' diseases like AKI (and CKD and many of the cancers)
- This is a very fruitful area of research as most studies of staged diseases (e.g. CKD and AKI) are rather unimaginative, and use simplistic approaches.

Study design and sample

- A prospective cohort study involving patients from 17 ICUs accross Thailand were included in the present study.
- Most clinical measurements were taking for the first seven days after ICU admission and then again at the 14-day and 21-day mark.
- Although the full sample also included ICU patients that did not develop AKI, for the present analysis we will only consider those that had, or developed, AKI during their observation.
- After exluding patients with end-stage renal disease, we had 1953 patients remaining in our cohort (collectively yielding 10682 observations).

Clinical endpoints

We will consider two outcomes:

1. The **ordinal outcome** AKI stage (No AKI, AKI stage-1, AKI stage-2 and AKI stage-3) as defined by the KDIGO criteria
2. A **binary outcome** that collapses AKI stage into None/Mild (AKI-0 or AKI-1) and Severe (AKI-2 or AKI-3)

Study effect and covariates

In terms of potential predictors we will consider:

1. **The Study effect**: Acqisition (Community-acquired or Hospital-acquired)
2. Covariates representing **other prognostic factors and/or confounders**, which can be divided into:
   - Demographics: Age, Gender, BMI class, Type of hospital coverage
   - Comorbidities (Hypertension, Diabetes, Coronary artery disease, Cerbro-vascular disease, Malignancy, Chronic kidney disease)
   - Clinical parameters (APACHE II, Sodium, Potassium, Hematocrit, WBC)

Statistical approach

As I have already mentioned, we will consider three different types of models:

1. Binary logistic mixed effect regression (a GLMM)
2. Binary logistic marginal model (as represnted by a GEE)
3. Ordinal logistic mixed effect regression (based on a proportional-odds model)

IF WE GET TIME, we may also do a little bit of model building

A 'Table 1' (full sample)

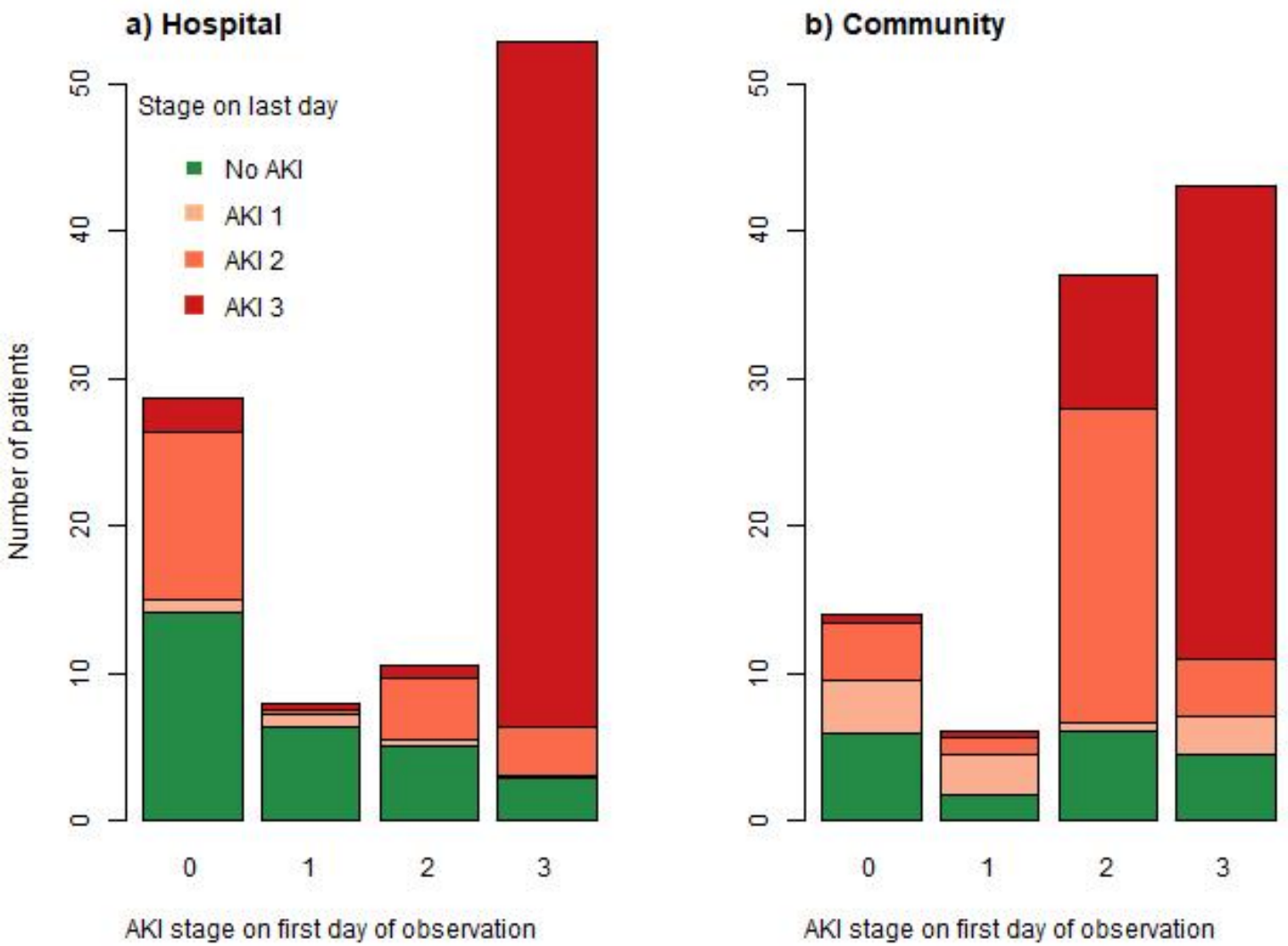
Table: Patient characteristics(last day of observation) by AKI stage

Effect	No AKI	Stage 1	Stage 2	Stage 3
N	230	366	798	1195
Female (%)	82 (35.7)	185 (50.5)	379 (47.5)	539 (45.1)
BMI (%)				
Norm	149 (65.6)	211 (58.1)	440 (55.4)	707 (59.5)
Under	33 (14.5)	63 (17.4)	101 (12.7)	123 (10.4)
Over	35 (15.4)	66 (18.2)	188 (23.7)	273 (23.0)
Obese	10 (4.4)	23 (6.3)	65 (8.2)	85 (7.2)
Community-acquired (%)	172 (74.8)	259 (70.8)	589 (73.8)	861 (72.1)
HT (%)	79 (34.3)	146 (39.9)	355 (44.5)	551 (46.1)
DM (%)	48 (21.0)	86 (23.6)	202 (25.4)	378 (31.7)
CAD (%)	28 (12.2)	38 (10.4)	96 (12.0)	106 (8.9)
Cerebro-vascular dis. (%)	14 (6.1)	21 (5.8)	62 (7.8)	74 (6.2)
Malignancy (%)	16 (7.0)	31 (8.5)	71 (8.9)	80 (6.7)
CKD (%)	7 (3.0)	13 (3.6)	38 (4.8)	213 (17.8)
Age (mean (sd))	64.65 (16.88)	66.98 (16.81)	66.70 (17.12)	64.11 (17.77)
APACHE II (mean (sd))	19.56 (5.69)	18.36 (6.63)	18.29 (6.85)	21.49 (7.50)
Serum sodium (mean (sd))	-0.11 (0.82)	-0.16 (0.67)	-0.14 (0.66)	-0.18 (0.73)
Serum potassium (mean (sd))	-0.21 (1.07)	-0.30 (0.93)	-0.19 (0.81)	0.05 (1.16)
Hematocrit (mean (sd))	-0.52 (1.28)	-0.73 (1.32)	-0.68 (1.23)	-0.96 (1.37)
WBC (mean (sd))	0.66 (1.31)	0.45 (1.36)	0.42 (1.38)	0.46 (1.37)

Some observations (Table 1)

- A majority of our patients were Stage 2 or 3 on their last day of observation (77%)
- **A large proportion of our AKI patients were community-acquired**
- Higher proportion of overweight and obese patients in Stages 2 and 3
- Prevalence of HT increases (continually) with AKI stage
- Same with DM, but not as pronounced
- CAD doesn't seem associated with severity or is negatively associated; CAD prevalence decreases somewhat with increasing AKI stage.
- Low prevlalence of CKD in lower to intermediate AKI stages, but sharp increase in CKD prevlance in AKI stage 3 group.

AKI stage at first day vs last day by acquirsition



Now, let's get to the pointy end...

- For the rest of the session, I will be working in R itself (or rather R studio)
- You can just watch, but if you really want to get a feel for R I suggest you follow along (actually type the syntax in)
- I am happy to provide the syntax file at the end of the session.
- There are two main things we need to do before we start:
  1. Read in the data (you can either use the RData file I provided (an R session), or the raw CSV file)
  2. Download and install three R libraries (`lme4`, `geepack` and `ordinal`)

Hint for modeling in R

There are a few main things to remember about modeling in R...

```
mymodel<-modeltype(formula, data, extras)
summary(mymodel)
```

For example, consider the binary ogistic regression...

```
mymodel<-glm(disease~age,
data=mystudydata, family=binomial())
summary(mymodel)
```