Teaching Portfolio

Brice Ozenne

1 Teaching responsibilities

Current teaching activity at the University of Copenhagen (KU)

- Statistical analysis of repeated measurements: It is a 6 days, 5 ECTS, course taught in English with 40-50 students. Julie Forman is the course director.
  I am doing 3 lectures of 3 hours and 6 exercise classes of 3 hours. I have been doing the practicals since 2015 and started to lecture two years ago.

- Epidemiological methods in medical research: It is a 10 days, 7 ECTS, course taught in English with 20-30 students. I am the course director.
  I am doing 3.5 lectures of 3 hours, 7 exercise classes of 3 hours, and 3 hours of oral assessment (student presentation). I have run the course 3 times.

- Basic statistics: It is a 10 days, 9 ECTS, course taught in English with 30 students. Paul Blanche is the course director.
  I am doing 1 lectures of 3 hours and 1 exercise classe of 3 hours and 6 hours of oral assessment (student presentation). I have taught in this course twice.

All courses are for Phd students in medical sciences. This lead to a total of 22.5 hours lecture, 42 hours practicals, 9 hours oral assessment, and 1 course direction (338 hours when including preparation).

Past teaching activity:

- in 2016 I have taught a 2 hours lecture to statistics students (Master level) for the course Structural Equation Models at KU.

- between 2013 and 2015, I was a teaching assistant at the University of Lyon 1 (France) for biostatistics students (Master level). I was doing 18h of practical in a survival analysis course and 6 hours of practical in a course about Bayesian statistics.

Workshops: With Julie Forman, we have made a workshop on linear mixed models (LMMs) for the method week at Karolinska Institutet. For the Brain drug project, I have also created a workshop on time-to-event analysis for registry data.

2 Supervision

I am/have been an official supervisor or co-supervisor of:

- **Tanne Ebert Jørgensen** and **Johanne Triantafyllou Lorenzen** (Master students in epidemiology, 2023) about the childcare and symptoms of ADHD in the Danish population. The main supervisor is Anne-Marie Nybo Andersen from the section of epidemiology.
- **Simon Christoffer Ziersen** (Ph.D in biostatistics, from 2021) about causal inference in time to event analysis with competing risks. The main supervisors are Esben Budtz-Jørgensen and Thomas Alexander Gerds from the section of biostatistics.
- **Ramlah Sara Rehman** (Bachelor in data science, 2021) about clustering trajectories of the cortisol concentration, comparing several clustering algorithms. This was a co-supervision with Melanie Ganz-Benjaminsen from the department of computer science.
- **Alice Brouquet-Laglaire** (Master 2 in biostatistics, 2019) about the comparison of inference methods for generalized pairwise comparisons. The main supervisor was Julien Péron from the University Lyon 1 (France).
- **Ceren Tozlu** (Master 2 in biostatistics, 2014) about comparison of classification methods for tissue outcome after ischemic stroke. The main supervisor was Delphine Maucort-Boulch from the University Lyon 1 (France) This master project has lead to a publication (Tozlu et al., 2019)

I am also a statistical consultant at the Neurobiology research unit (NRU). I help medical doctors, psychologists, neuro-scientists, biologists, engineer of various levels (mainly Master and Ph.D. students) to plan and perform data analysis. My Tuesday afternoon is dedicated to this activity: understanding the context and research question(s), advising and explain statistic concepts and methods.
Via these consultations, I have informally supervised many Master and Ph.D. students. For instance Kristin Köhler-Forsberg (medical Ph.D., from 2016 until 2020) who I helped to use latent variable models to analyse PET data (Köhler-Forsberg et al., 2023, 2022), Camilla Borgsted (Ph.D. in neuroscience from 2018 until 2022) who I helped to use linear mixed model to analyze fMRI data (Borgsted et al., 2018), or Søren Vinther Larsen (medical Ph.D., from 2020) who I helped with multiple comparison adjustment, handling of detection limit, survival analysis and study design (Larsen et al., 2020, 2022).

3 Pedagogical development projects

LMMstar: a common student feedback about practicals of the course "Statistical analysis of repeated measurements" was the difficulty to work with repeated measurements in R. Student felts it required substantial programming expertise and data management was very time consuming and were sometimes discouraged. It is true that the code was sometimes complex, relying on different software packages. Software limitations also meant that ideas developed during the lecture could not be examplified in the practicals.
During the last three years I have developed, in collaboration with Julie Forman, a software facilitating student interactions with repeated measurements, and in particular the use of linear mixed models. Having a dedicated software solution to compute relevant summary statistics (mean, correlation, number of missing data) and fit statistical models with default option suited to the course has greatly facilitated the programming aspect (see appendix A for two examples), freeing some time to discuss modeling and interpretation. Removing the feasibility issue also leads to a better alignment between what is being taught during the lectures and what is being done during the exercises.
This is still an on-going project since models for binary and count data are not yet included in the software. We would also like to write pedagogical material about the analysis of repeated measurements targeted to our students and applied researchers.

Mini Epi seminar: when I took over the epidemiology course there was no student assessment (other than attendance). I believe that having some formative assessment is useful to the student to get feedback on knowledge, skills, or competences that has been acquired. Instead of an exam I favor a form authentic assessment where students are asked to present one of their research project in relation to concepts seen during the course. The audience (other students and the teacher) then engage in a conversation with the student about working assumptions, limitations, and perspectives. Students usually really like this activity as it links the content of the course to their research.
To engage ealry the students and ensure that the activity is well understood, I recently introduced a *peer-feedback session* mid-way through the course. Students send me the output of this peer-feedback session on which I give feedback. See appendix B for details and discussion about this activity.
The quality and learning achieved during session depends on the students. A very large majority of them take it seriously, delivering interesting presentations and asking questions. This year was especially successful, maybe partly thanks to the introduction of the peer-feedback session.

4 Formal pedagogical training

I have taken two courses about pedagogy: the Introduction to University Pedagogy in April 2022 and recently finished [1] the theoretical part of the University Pedagogy (Universitetspædagogikum). My pedagogical project was about implementing a peer feedback session that is described and evaluated in appendix B.

5 Pedagogical approach

Teaching is for me sharing my entousiasm and my knowledge about a subject, hoping to facilitate the appropriation of statistical concepts and stimulate the curiosity of the students.

While I try to examplify and illustrate statistical concepts (e.g see appendix C.1), I strongly believe that proper understanding of biostatistics concepts require some mathematical representation. The level of formalism used when teaching will dependent on the audience (medical vs. mathematic students) and on the targeted level of understanding. This being said, mathematics are here to explicit an idea, not to obscure it. So I also believe that learning biostatistics involve developing one's intuition, for instance to understand the practical implications of a statistical hypothesis (e.g. see appendix C.2). Being lucid and explicit about hypotheses withstanding a scientific investigation is suprisingly difficult to master but a key part of biostatistics.

After several years of teaching, I have come to realize that a clear, rigorous but intuitive explanation of statistical concepts requires quite a substantial expertise on the topic. Examples or experience from research project are generally appreciated by students. I therefore try, when possible and relevant, to relate my teaching activity to my research activity. The LMMstar package is an example of interconnexion between the two, initially motivated by the teaching but made possible by knowledge acquired during research projects.

Finally I try to develop a learning environment open to discussion and where the students feel comfortable. Having interactions with students during lectures and practicals to assess their understanding is critical to adjust my teaching and also motivating. Using humor, being supportive, taking the time to discuss with the students, and showing vulnerability (e.g. mentioning mistakes I have made in the past) seems to help having this safe learning environment.

[1] for the practical part I am missing the observations with the educational supervisor. They are planned May 15th.

6 Personal development as a teacher

The formal training I received during the University Pedagogy course made me question my pedagogical approach and experience different teaching technics, often based on group work and use of online-tools (polls & quizzes):

- it helped me better structure my teaching around intended learning objectives (ILOs). I have realized that **each ILOs should be tested during the lecture with short exercises** (see appendix C.3 for an example). These short exercises provide feedback to the students and the teacher about whether the knowledge or skill has been acquired. It also creates variations during the lecture which is beneficial to the student attention.

- it made me reflect about the role of the teacher and the student in the learning process. The student has the central role whereas the teacher is here to facilitate the interaction between the student and a subject. Indeed most students learn by doing and by appropriation. I am in a process to **reduce the curriculum seen during lecture or practicals** and **rely more on self study for technical skills**. This leave more time during the class for experimentation and discussion. The self study is supported by the lecture notes, exercise solutions, or scientific articles.
  As an example, I have greatly reduced the attention given to programming in the Epidemiology course (e.g. the code and software output are given in most of the exercises). Learning programming is left to self study even though I happily answer any question and have a dedicated section in each of my lecture notes.

- it provided me tools to **create a safe learning environment**. For instance when a student answer a question, I would (try to) not immediately qualify it (correct or incorrect answer). Instead ask the opinion of other students or ask a follow-up question to make the student reflect/orient them in the right direction.

- it stressed the importance of **engaging the student** using an inductive approach, e.g. based on a motivating example where there is a need for statistical tools. Finding a simple but realistic example for a specific ILO is a suprisingly challending task - often realistic examples are complex and would cover several ILOs. I generally use classical statistical paradoxes (see appendix C.4 for an example).

Discussions and teaching material from colleagues have been a great source of inspiration. They have also contributed to my evolution as a teacher but in a more subtle and continuous way that I do not explicit here.

7 References

Borgsted, C., Ozenne, B., Mc Mahon, B., Madsen, M. K., Hjordt, L. V., Hageman, I., Baaré, W. F., Knudsen, G. M., and Fisher, P. M. (2018). Amygdala response to emotional faces in seasonal affective disorder. *Journal of affective disorders*, 229:288–295.

Köhler-Forsberg, K., Ozenne, B., Larsen, S. V., Poulsen, A. S., Landman, E. B., Dam, V. H., Ip, C.-T., Jørgensen, A., Svarer, C., Knudsen, G. M., et al. (2022). Concurrent anxiety in patients with major depression and cerebral serotonin 4 receptor binding. a neuropharm-1 study. *Translational psychiatry*, 12(1):1–8.

Köhler-Forsberg, K., Dam, V. H., Ozenne, B., Sankar, A., Beliveau, V., Landman, E. B., Larsen, S. V., Poulsen, A. S., Ip, C.-T., Jørgensen, A., et al. (2023). Serotonin 4 receptor brain binding in major depressive disorder and association with memory dysfunction. *JAMA psychiatry*.

Larsen, S. V., Ozenne, B., Köhler-Forsberg, K., Poulsen, A. S., Dam, V. H., Svarer, C., Knudsen, G. M., Jørgensen, M. B., and Frokjaer, V. G. (2022). The impact of hormonal contraceptive use on serotonergic neurotransmission and antidepressant treatment response: Results from the neuropharm 1 study. *Frontiers in endocrinology*, 13.

Larsen, S. V., Köhler-Forsberg, K., Dam, V. H., Poulsen, A. S., Svarer, C., Jensen, P. S., Knudsen, G. M., Fisher, P. M., Ozenne, B., and Frokjaer, V. G. (2020). Oral contraceptives and the serotonin 4 receptor: a molecular brain imaging study in healthy women. *Acta Psychiatrica Scandinavica*, 142(4):294–306.

Tozlu, C., Ozenne, B., Cho, T.-H., Nighoghossian, N., Mikkelsen, I. K., Derex, L., Hermier, M., Pedraza, S., Fiehler, J., Østergaard, L., et al. (2019). Comparison of classification methods for tissue outcome after ischaemic stroke. *European Journal of Neuroscience*, 50(10):3590–3598.

Appendix A Old vs. new software solution

A.1 Computing summary statistics

Initially, we were teaching the students to use the `aggregate` function to evaluate the mean and other statistics per timepoint:

```
w.summaries <- aggregate(glucagonAUC~time, data=gastricbypassL,
                         FUN = function(iAUC){
  c("observed" = sum(!is.na(iAUC)),
    "missing" = sum(is.na(iAUC)),
    "mean" = mean(iAUC, na.rm = TRUE),
    "sd" = sd(iAUC, na.rm = TRUE),
    "min" = min(iAUC, na.rm = TRUE),
    "median" = median(iAUC, na.rm = TRUE),
    "max" = max(iAUC, na.rm = TRUE))},
  na.action=na.pass)

w.summaries <- data.frame(w.summaries[1],w.summaries[[2]])
print(w.summaries, digits=4)
```

```
           time observed missing  mean   sd  min median   max
1 3monthsBefore       20       0  7860 3781 2500   6786 16798
2   1weekBefore       19       1  7149 3289 2376   6202 16300
3    1weekAfter       19       1 16954 6153 7906  16269 29980
4  3monthsAfter       20       0 11063 4479 4551  10911 23246
```

While this is a very flexible approach, it was difficult for medical students to understand. Instead we now use the `summarize` function from LMMstar which has well suited default output for the applications we have in mind in the course:

```
summarize(glucagonAUC ~ time|id, data = gastricbypassL, na.rm = TRUE)
```

```
           time observed missing      mean       sd    min       q1  median       q3
1 3monthsBefore       20       0  7860.443 3781.459 2500.5  5185.875  6786.0 10337.51
2   1weekBefore       19       1  7148.589 3288.933 2376.0  5113.500  6202.5  8082.75
3    1weekAfter       19       1 16953.671 6152.867 7906.5 12466.500 16269.0 20271.00
4  3monthsAfter       20       0 11063.025 4479.478 4551.0  7914.225 10911.0 12340.50
```

```
 Pearson's correlation:
```

```
              3monthsBefore 1weekBefore  1weekAfter 3monthsAfter
3monthsBefore     1.0000000  0.83158346  0.13902263   -0.2496747
1weekBefore       0.8315835  1.00000000 -0.09418889   -0.2232003
1weekAfter        0.1390226 -0.09418889  1.00000000    0.5988570
3monthsAfter     -0.2496747 -0.22320033  0.59885696    1.0000000
```

Note that key arguments, such as how to handle missing data are kept to stress their importance to the students. One functionality has been added to obtain the correlation matrix by explaining in the formula interface how the data are grouped. This enable to have a single statement outputing all the standard descriptive statistics. The student can now focus on the interpretation of these statistics and their implication in term of statistical modeling.

A.2 Fitting linear mixed models

Another difficulty was to estimate linear mixed models with unstructured covariance patterns. We advocate their use during the course but, at the time, the R syntax was complicated:

```
fit.main <- gls(glucagonAUC ~ time,
                data = gastricbypassL,
                correlation = corSymm(form=~as.numeric(time)|id),
                weights = varIdent(form=~1|time),
                na.action=  na.exclude,
                control = glsControl(opt="optim"))
logLik(fit.main)
```

```
'log Lik.' -712.161 (df=14)
```

We developed our own mixed model implementation, with a simpler syntax that stresses the choice of the covariance structure (one of the learning point of the course):

```
fit.main2 <- lmm(glucagonAUC ~ time,
                data = gastricbypassL,
                repetition = ~time|id,
                structure = "UN")
logLik(fit.main2)
```

```
[1] -712.161
```

Appendix B Pedagogy project (without appendix)

Preparing students for their half day seminar

Brice Ozenne[1,2]

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[2] Neurobiology Research Unit, University Hospital of Copenhagen, Rigshospitalet

A course typically ends with an assessment of what has been learned. Students get some feedback on knowledge, skills, or competences they have acquired and have not yet fully acquired. Teachers can identify part of the curriculum where students need more support to reach the intended learning objectives (ILOs). Traditionally, this assessment is performed via an exam (written or oral) or a written assignment. At a Ph.D. level these assessment formats may not be the most relevant since the main ILOs are competence-based. Asking the students to use the knowledge, skills, and competences that have developed during the course in a situation of their choice (typically one of their Ph.D. project) and discuss their experience with the class is an alternative format. The hope is that the students will be exposed to a variety of realistic situations, with opportunities to get and provide feedback, in a safe environment. It is a formative assessment favoring reflexion upon the practical application of the content of the course instead of providing a grade.

I have introduced this assessment format when I became the course director of a Ph.D. course called 'Epidemiological method in medical research', two years ago. I asked students to prepare a 10 minutes presentation for the last afternoon of the course, which will be followed by a 10 minutes discussion with the class. Even though students were generally satisfied, I do not think this assessment format completely fulfilled its promises:

- the aim was sometimes **misunderstood** leading to presentations and discussion outside of topic of the course. Students, which are mainly medical students, would typically mostly elaborate on the medical aspect of a study while the course is about methodology (study design and data analysis). This methodological type of presentation seemed abstract to the students. I think too little was done during the course to ensure that students understood this format (mainly an oral explanation by the teacher).
- the **quality** of the student presentations was variable, often good but sometimes poor. I felt this was sometimes due to a lack of involvement from the students but also because young Ph.D. students may not already have collected

their own data, and they felt they had no material for their presentation. This is unfortunate as, ideally, this course should be taken early in the Ph.D., before the student has had to make decision about study design and data analysis.

- the **quantity** of presentations make it difficult for the students and the teacher to focus during the whole session. Students where divided into two groups of 12 students, leading to 4 hour of presentations/discussions. Toward the end of the day, there was much less interactions.

This project aims at mitigating these issues, by involving the students earlier during the course in the preparation of their presentation, allowing group presentation, and providing them a source of inspiration and feedback.

The course

The course where I have implemented this project is a Ph.D. course called **Epidemiological methods in medical research** (7 ECTS). It is 10 full day course (once day a week) alternating between lectures and practicals (except the last day). The audience is students in health science, e.g. medicine or epidemiology. The class used to be for 24 students but, due to the high demand, I included 30 students this year. The pedagogical team is composed of biostatisticians and epidemiologists. The learning objectives include competences in biostatistics and epidemiology (e.g. choice of a study design, notion in causal inference and statistical modeling) as well as some practical skills like programming. At the end of the course, participants should be able to read and understand scientific articles in epidemiology, design and analyze standard studies. Students pass the course by achieving 80% attendance and attending and actively participating during the half day seminar.

The project

The main element of the project was to organize a **peer-feedback** session mid-way through the course. To prepare this session, the students were reminded on day 5 about their contribution to the half day seminar. Three possible formats were suggested:

(i) presenting results from your own research project with focus on the methodology

(ii) discussing the planning of a study

(iii) discussing a methodological point based on a scientific article. Examples of article were uploaded on the course webpage.

Presentation could be done alone or in pairs. Students were asked, as homework, to reflect on the general content of their presentation and use a template to structure

their reflexions (see appendix A). To help them a document describing important dates, expectations for the presentations, and some advices was provided (appendix B).

The peer-feedback session took place on day 6 and was structured as follow:

- in pairs, each student presents his plan to another student. The other student provides some feedback (10 minutes per student).
- each student updates (individually) his project description and write down feedback to the teacher (10 minutes). He sends an email with the project description to the course director.

I then read each project description and provided individual feedback to the students by email.

Outcome

27 out of 30 students (90%) had sent their project description. I received two more project descriptions a week later, so 29 out of 30 students (96.7%). All students who sent me a project description had title and identified a theme. Two students decided to work in pair and 27 alone. A large majority of the students planned to present results from their own data analysis (20 out of 29, 69%). A few planed to present the design of a new study (6 out of 29, 21%) and two (7%) about a methodological point based on scientific articles. For one student it was unclear which format he has chosen. None of the student referred to articles uploaded on the course webpage.

11 students (31%) filled the "feedback to the teacher" section or wrote some feedback in the email containing their project description. One was a practical question about the last day, 5 were asking for feedback on their project description. The remaining 5 provided feedback on the organization of the course. I would judge most of the feedback about the course legitimate, except one that misread the course description and was therefore disappointed about the course.

Providing individual feedback to each student required about 6 hours of work but gave me an overview of the topics and thought process of the students. I had some concerns about the scope of the study for only a minority of the students (about 5 students, see appendix C for an example) and could communicate with them. The section 'Plan' was not filled or with very minimal input for several students (about 10 students) while a few indicated a detailed timeline. 8 students (27.6%) thanks me for the feedback and indicated it was useful.

All but one (due to illness) students made their presentation the last day. Subjective assessment of the quality of the presentations by the teachers was very positive.

In the group I was responsible for about a half of the students would end their presentation asking a question to the audience about a methodogical point e.g.:

- what would be the most appropriate: include death in a composite endpoint or treat it as a competing risk?
- which one of the two study designs, self-controlled case-series or interrupted time series, is the most appropriate for my study?

Feedback from the student about the last half day was only positive (13 out 30, i.e. 43.3%, provided feedback), e.g.:

- Great – it was really nice to hear about the different project and how they used the methods.
- The presentations were much more informative and interesting than I anticipated!
- Nice, but be aware, that things like this is also taught in similar causes. Nevertheless I think you should keep it as it is.
- Really good seminar, very comfortable and good atmosphere.

Discussion

A very large majority of the students sent me the project description and some showed clear interest in getting some feedback. So the peer feedback session may help students getting involved early in their contribution to the half day seminar. I think that it also improved the communication with the students and helps clarifying what was expected from them at an early stage. I was positively surprised by the fact that most students already seemed to have a somehow clear idea about what they want to present. Compare to previous years a few more students chose to present about planning a study / presenting an article, and they seemed confident about it. So this activity may have been beneficial to the young Ph.D. students.

Surprisingly, only a minority of students provided feedback or asked for feedback. I am not sure how to interpret that: the student is satisfied and does not need help, lack of interest, or not feeling safe enough to provide feedback.
I have also mixed feelings about the usefulness of getting feedback on the content of the course. On one side it is interesting to get access to what the students think, clarify misunderstandings, and fix what can be improved. The students may also appreciate being heard. In practice, I got few answers so I do not know if the comments represent an individual or a majority of the class. I may get worried and/or

implement a change because of a one or few comments that may not be representative of the rest of the group. A follow-up feedback session, involving the whole class on selected topics, would help clarifying the representativity of the feedback. But since it would take some more time, I see it appropriate only if some serious concerns are raised.

I presented the activity and discussed the outcome with the former course director, Professor Per Kragh Anderson. One important point for the success of the last day is that the focus of the presentations should about the methodology and not the (medical) application. He pointed out that the template provided to the student was not very explicit about this point. We also discussed how to facilitate interactions between students, in particular young Ph.D. students who (I think) would benefit from working in pairs.

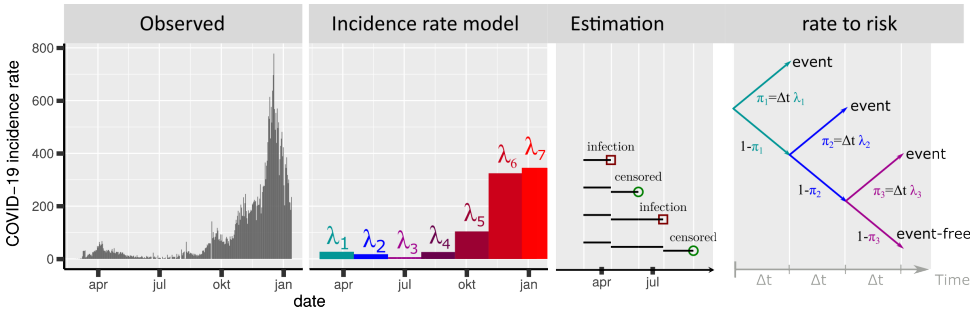
Overall, I think this peer-feedback session is an improvement. It seems to be helpful to (at least some of) the students. It gives me an idea of the class and provides me feedback from the students mid-way through the course. Having more knowledge about the students will also help me divide the students into more relevant groups the last half day (this year we will be 3 teachers so have groups of 9 to 10 students which will reduce the quantity of presentations).
For the following years, I think the template for the project description can be improved: to stimulate more feedback from the students and better reflect the expectations for the presentations. My own feedback could also have been better if I would have spread out the workload (I was sick that week which did not help). Giving feedback is a difficult task as good feedback requires time and that the student has provided a substantial description of his plan.

Appendix C Example of teaching material

C.1 Course on Epidemiology (illustration)

Slide explaining how to evaluate the risk of a disease based on the incidence rate. The intuition behind the mathematical formula is illustrated via a series of graphs.

Risk rate relationship (2/2)



With varying incidence rates (3 time intervals):

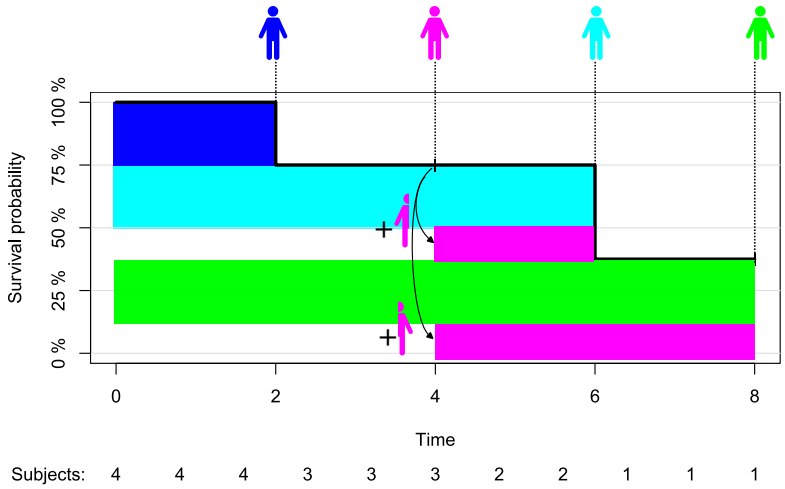
$$r(\tau) = 1 - (1 - \lambda_1 \Delta t)(1 - \lambda_2 \Delta t)(1 - \lambda_3 \Delta t)$$
$$\approx 1 - \exp(-(\lambda_1 + \lambda_2 + \lambda_3)\Delta t)$$

→ useful to deal with right-censoring!

C.2 Course on Epidemiology (intuition)

Slide illustrating the implications of the independent censoring assumption used by the Kaplan Meier estimator. This estimator can be re-formulated as a simple weighted average (Efron's redistribution to-the-right algorithm), where the weight accounts for the lost to follow-up, and help making explicit the implications of the Kaplan Meier approach.

Another view at Kaplan Meier



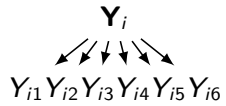
- patients who stay are **representative** of those who drop-out
- we evaluate the survival effect **had nobody been censored**! (same for the risk or treatment effect)

C.3 Course on repeated measurement (exercise)

Exercise slide where the students are asked to associate a study design (symbolized by a graph) with a correlation structure. This tests the ILO: "Describing a correlation structure via a graph"

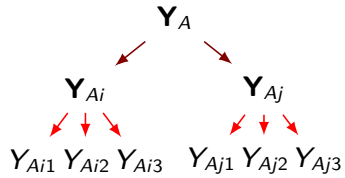
Who is what ❓

2 level



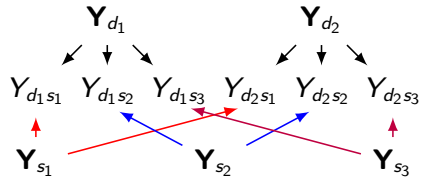
$$R_A = \begin{bmatrix} 1 & \rho_d & \rho_d & \rho_s & 0 & 0 \\ \rho_d & 1 & \rho_d & 0 & \rho_s & 0 \\ \rho_d & \rho_d & 1 & 0 & 0 & \rho_s \\ \rho_s & 0 & 0 & 1 & \rho_d & \rho_d \\ 0 & \rho_s & 0 & \rho_d & 1 & \rho_d \\ 0 & 0 & \rho_s & \rho_d & \rho_d & 1 \end{bmatrix}$$

3 level (nested)



$$R_B = \begin{bmatrix} 1 & \rho & \rho & \rho & \rho & \rho \\ \rho & 1 & \rho & \rho & \rho & \rho \\ \rho & \rho & 1 & \rho & \rho & \rho \\ \rho & \rho & \rho & 1 & \rho & \rho \\ \rho & \rho & \rho & \rho & 1 & \rho \\ \rho & \rho & \rho & \rho & \rho & 1 \end{bmatrix}$$

3 level (crossed)



$$R_C = \begin{bmatrix} 1 & \rho_p & \rho_p & \rho_h & \rho_h & \rho_h \\ \rho_p & 1 & \rho_p & \rho_h & \rho_h & \rho_h \\ \rho_p & \rho_p & 1 & \rho_h & \rho_h & \rho_h \\ \rho_h & \rho_h & \rho_h & 1 & \rho_p & \rho_p \\ \rho_h & \rho_h & \rho_h & \rho_p & 1 & \rho_p \\ \rho_h & \rho_h & \rho_h & \rho_p & \rho_p & 1 \end{bmatrix}$$

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C.4 Course on Epidemiology (paradox)

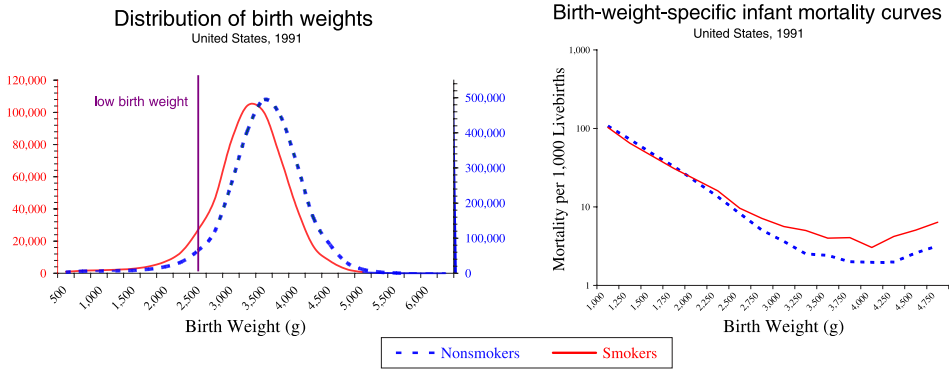
Example of statistical paradox that should make the student reflect upon:

- what do we actually mean by *beneficial* or *having an effect*?
- when one should or should not adjust an analysis for covariates?

Birth weight paradox

Birth weight (BW) is a strong predictor of infant mortality

- investigators stratify on BW when evaluating risk factors



This leads to an apparent paradox (Hernández-Díaz et al., 2006)

- is maternal smoking beneficial? Sometimes beneficial?