

Ve401 Probabilistic Methods in Engineering

Spring 2021 Term Project 2

Date Due: 11:59 PM, Friday, the 23rd of April 2020



The goal of this term project is to apply your new-found knowledge of probability theory and statistics in extended tasks that are beyond the scope of ordinary assignments. **It is strongly recommended that you do not leave the entire project to the last minute** but rather commence work on individual parts as soon as you are able to do so.

Group Work

You will be divided into groups of 4–5 *students* each.

Each group member must be familiar with and have contributed to each part of the project report. **You may not divide up the work in such a way that only certain members are involved with certain parts.** In the event of an Honor Code violation (plagiarism or other), all members of the group will be held equally responsible for the violation. Exceptions may only be made, at my discretion, in exceptional situations.

It is therefore all group members' duty to ensure that all collaborators' contributions are plausibly their own and to check on all collaborators' work progress and verify their contributions within reason.

Project Report

The term project will be submitted **electronically only** as a typed report of **normally no more than 10 pages** in length. Handwritten submission will not be accepted! It is recommended that you use a professional type-setting program (such as \LaTeX) for your report. Unless you are able to ensure a unified font size and style for formulas and text in Microsoft Word, use of Word is *not recommended*.

Your report should have the appearance, style and contents of a professional report. It should be comprehensible without reference to this document and should be comprehensible by any other student in this course. It is strongly suggested that all members of the project team proof-read the report before submission. **The report should not look like the solution to an assignment.** Do not structure the section titles as “Answer to Question i)” or similarly.

Grading Policy

This term project accounts for 15% of the course grade; it will be scored based on

- **Form (3 points):** Does the report contain essential elements, such as a cover page (with title, date, list of authors), a synopsis (abstract giving the main conclusions of the project), table of contents, clear section headings, introduction, clear division into sections and appendices with informative titles and bibliography (if applicable)? Are the pages numbered? Are the text and formulas composed in a unified font? Are all figures (graphs and images) clearly labeled with identifiable source?
- **Language (3 points):** Is the style of english appropriate for a technical report? Do not treat the project as an assignment and simply number your results like part-exercises. Your text should be a single, coherent whole. The text should be a pleasant read for anyone wanting to find out about the subject matter. Errors in grammar and orthography (use a spell-checker!) will be penalized. Make sure that the report is interesting to read. Avoid simply repeating sentences by cut-and-paste.
- **Content (9 points):** Are the mathematical and statistical methods and deductions clearly exhibited and easy to follow? Are the conclusions well-supported by the mathematical analysis? It is important to not just copy calculations from elsewhere, but to fully make them your own, adding details and comments where necessary.

All group members will generally receive the same basic grade for the term project. Exceptions are possible in certain circumstances, such as a group member not contributing to the project. If circumstances permit, peer evaluations of the contribution of each group member will be implemented. These may have a further effect on the project grade.

On Plagiarism

Study JI's Honor Code carefully. **Any** information from third parties (books, web sites, even conversations) that you use in your project must be accounted for in the bibliography, with a reference in the text. Follow the rules regarding the correct attribution of sources that you have learned in your English course (e.g., Vy100, Vy200). All members of a group are jointly responsible for the correct attribution of all sources in all parts of the project essay, i.e., any plagiarism will be considered a violation of the Honor Code by all group members. Every group member has a duty to confirm the origin of any part of the text.

The following list includes some specific examples of plagiarism:

- Use of any passage of three words or longer from another source without proper attribution. Use of any phrase of three words or more must be enclosed in quotation marks (“example, example, example”). This excludes set phrases (e.g., “and so on”, “it follows that”) and very precise technical terminology (e.g., “without loss of generality”, “reject the null hypothesis”) that cannot be paraphrased,
- Use of material from an uncredited source, making very minor changes (like word order or verb tense) to avoid the three-word rule.
- Inclusion of facts, data, ideas or theories originally thought of by someone else, without giving that person (organization, etc.) credit.
- Paraphrasing of ideas or theories without crediting the original thinker.
- Use of images, computer code and other tools and media without appropriate credit to their creator and in accordance with relevant copyright laws.

Covid-19 Vaccine Studies

Starting from early 2020, the Covid-19 pandemic spurred a world-wide effort to develop vaccines. Both traditional approaches (e.g., adenovirus vectors [1]) and novel, state-of-the-art techniques (e.g., mRNA-based vaccines [2]) were tried. Some high-profile and promising projects were aborted or delayed [3], [4], while several others successfully produced vaccines within an unprecedentedly short timeframe.

By late 2020/early 2021 several vaccines based on different methodologies were available, mostly by licensed through emergency procedures by relevant health organizations. The main questions were

- i) Is a given vaccine safe?
- ii) Is a given vaccine effective?

The first question is very hard to measure in clinical trials (since certain side effects may be very rare; see [5] for a recent example) and poses complex ethical questions for medical professionals, since a vaccine is injected into people that are (at the time) healthy.

This project will instead focus on the second question. The goal is to investigate and explain many of the measures for vaccine effectiveness that have been referenced in the popular press and in technical publications.

You may make your own choice as to which aspects to discuss from the suggestions given below, or choose entirely different topics.

- What do “vaccine efficacy” and “(relative) risk ratio (RR)” mean? What are the guidelines of the WHO for minimum vaccine efficacy?
- Give some examples of confidence intervals quoted for vaccine efficacy. Some of these confidence intervals are basically useless (for example, “The vaccine was also associated with a lower risk of hospitalization due to COVID-19 (RR 0.0; 95% CI 0.0 to 1.10; evidence type 3), corresponding to a vaccine efficacy of 100% ([95% confidence Interval] -9.9%, 100%).” [6]) Explain why that is. What are the most important factors for obtaining a useful confidence interval?
- Discuss the misunderstanding that led to the widely publicized claim that “the Oxford AstraZeneca vaccine is ineffective for older people”? (You may use, e.g., [7] as a starting point and investigate from there.)
- There are different approaches to finding confidence intervals for the RR (see, for example, [8]). Describe these approaches and their assumptions.
- What does it mean that a study for vaccine efficacy must be “sufficiently powered” [9]? How is the power calculated?
- Choose some other aspect related to the statistics surrounding the Covid-19 disease. For example, you could look at one or more studies concerning treatments rather than vaccines. An overview of treatments that are currently being investigated can be found in [10].

You should write somewhere between 5 and 10 pages. Your report should be written in such a way that a typical classmate would be able to follow the contents.

So feel free to write about some aspect of studies concerning Covid-19 that you find interesting!

References

- [1] Lowe, D. How you make an adenovirus vaccine. In the Pipeline, February 2nd, 2021. <https://blogs.sciencemag.org/pipeline/archives/2021/02/08/how-you-make-an-adenovirus-vaccine> [Online; accessed March 28th, 2021].
- [2] Hubert, B. Reverse engineering the source code of the BioNTech/Pfizer SARS-CoV-2 vaccine, December 25th, 2020. <https://berthub.eu/articles/posts/reverse-engineering-source-code-of-the-biontech-pfizer-vaccine/> [Online; accessed March 28th, 2021].
- [3] Kuchler, H. and Abboud, L. Merck abandons bid to develop Covid-19 vaccine. *Financial Times*, January 25th, 2021. <https://www.ft.com/content/6a0a7d49-4557-45bc-afd1-54a2ca7413fe> [Online; accessed March 28th, 2021].

- [4] Aripaka, P. and Blamont, M. GSK and Sanofi start with new COVID-19 vaccine study after setback. *Reuters*, February 22nd, 2021. <https://www.reuters.com/article/us-health-coronavirus-gsk-sanofi/gsk-and-sanofi-start-with-new-covid-19-vaccine-study-after-setback-idUSKBN2AM108> [Online; accessed March 28th, 2021].
- [5] Kupferschmidt, K. and Vogel, G. A rare clotting disorder may cloud the world’s hopes for AstraZeneca’s COVID-19 vaccine. *Science Magazine*, March 27th, 2021. DOI: <https://doi.org/10.1126/science.abi7283>.
- [6] Advisory Committee on Immunization Practices (ACIP). Grading of Recommendations, Assessment, Development, and Evaluation (GRADE): Pfizer-BioNTech COVID-19 vaccine. Technical report, CDC, December 15th, 2020. <https://www.cdc.gov/vaccines/acip/recs/grade/covid-19-pfizer-biontech-vaccine.html> [Online; accessed March 28th, 2021].
- [7] Boytchev, H. Why did a German newspaper insist the Oxford AstraZeneca vaccine was inefficacious for older people—without evidence? *BMJ*, 372(n414), February 12th, 2021. DOI <https://doi.org/10.1136/bmj.n414>.
- [8] Fu, W. and Li, J. and Sheet, P. Covid-19 vaccine efficacy: Accuracy, uncertainty and projection of cases. Preprint, MedRxiv, December 18th, 2020. DOI: <https://doi.org/10.1101/2020.12.16.20248359>.
- [9] Hodgson, S. H. and Mansatta, K. and Mallet, G. and Harris, V. and Emary, K. R. W. and Pollard, A. J. What defines an efficacious COVID-19 vaccine? A review of the challenges assessing the clinical efficacy of vaccines against SARS-CoV-2. *The Lancet*, 21(2, E26-E35), February 1st, 2021. DOI: [https://doi.org/10.1016/S1473-3099\(20\)30773-8](https://doi.org/10.1016/S1473-3099(20)30773-8).
- [10] Wu, K. J. and Zimmer, C. and Corum, J. Coronavirus drug and treatment tracker. *The New York Times*, March 22nd, 2021. <https://www.nytimes.com/interactive/2020/science/coronavirus-drugs-treatments.html> [Online; accessed March 28th, 2021].