

IMPERIAL COLLEGE LONDON

DOCTORAL THESIS

Counting the dead

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*A thesis submitted in fulfillment of the requirements
for the degree of Doctor of Philosophy*

in the

School of Public Health

Department of Epidemiology and Biostatistics

January 2023

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Declaration of Authorship

I, Theo Rashid, declare that this thesis titled, Counting the dead and the work presented in it are my own. I confirm that:

- This work was done wholly or mainly while in candidature for a research degree at this University.
- Where any part of this thesis has previously been submitted for a degree or any other qualification at this University or any other institution, this has been clearly stated.
- Where I have consulted the published work of others, this is always clearly attributed.
- Where I have quoted from the work of others, the source is always given. With the exception of such quotations, this thesis is entirely my own work.
- I have acknowledged all main sources of help.
- Where the thesis is based on work done by myself jointly with others, I have made clear exactly what was done by others and what I have contributed myself.

Signed:

Date:

"Nobody is going to read your thesis."

Kyle Foreman

Abstract

People died in England and we modelled the death rates. This took longer than expected.

Acknowledgements

Thanks be to James Bennett.

Majid Ezzati, Seth Flaxman. Eric Johnson Kyle Foreman, Robbie Parks. Barbara Metzler, Emily Muller. Ricky Nathvani, Honor Bixby, Sierra Clark, Victor Lhoste. Sam Acors Solange. Parents, Ros Geoff Hardern.

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List of Abbreviations

| | |
|--------------|---|
| CrI | C redible i nterval |
| CAR | C onditional a utoregressive |
| (CVD) | C ardio v ascular D isease |
| ICAR | I ntrinsic C onditional a utoregressive |
| LSOA | L ower Layer S uper O utput A rea |
| MCMC | M arkov c hain M onte C arlo |
| MSOA | M iddle Layer S uper O utput A rea |
| NUTS | N o U -turn S ampler |
| SAHSU | S mall A rea H ealth S tatistics U nit |

Chapter 1

Overview

1.1 Welcome and Thank You

Welcome to this \LaTeX Thesis Template, using the \LaTeX typesetting system and [Quarto](#) and based on the \LaTeX thesis template MastersDoctoralThesis version 2.0 downloaded from [LaTeXTemplates](#). This LaTeX document class was authored by Vel (vel@latextemplates.com) and Johannes Böttcher based on a style file by Steve R. Gunn from the University of Southampton (UK), department of Electronics and Computer Science.

1.2 A Short Math Guide for \LaTeX

If you are writing a technical or mathematical thesis, then you may want to read the document by the AMS (American Mathematical Society) called, “A Short Math Guide for \LaTeX ”. It can be found online at [AMS](#) under the “Additional Documentation” section towards the bottom of the page.

1.2.1 Common \LaTeX Math Symbols

There are a multitude of mathematical symbols available for \LaTeX and it would take a great effort to learn the commands for them all. The most common ones you are likely to use are shown on [this page](#).

You can use this page as a reference or crib sheet, the symbols are rendered as large, high quality images so you can quickly find the \LaTeX command for the symbol you need.

1.3 About this Template

This \LaTeX Thesis Template is originally based and created around a \LaTeX style file created by Steve R. Gunn from the University of Southampton (UK), department of Electronics and Computer Science. You can find his original thesis style file at his site, here: <http://www.ecs.soton.ac.uk/~srg/softwaretools/document/templates/>.

Steve's `ecsthesis.cls` was then taken by Sunil Patel who modified it by creating a skeleton framework and folder structure to place the thesis files in. The resulting template can be found on Sunil's site here: <http://www.sunilpatel.co.uk/thesis-template>.

Sunil's template was made available through [LaTeXTemplates](#) where it was modified many times based on user requests and questions. Version 2.0 and onwards of this template represents a major modification to Sunil's template and is, in fact, hardly recognisable. The work to make version 2.0 possible was carried out by Vel (vel@latextemplates.com) and Johannes Böttcher.

1.4 What this Template Includes

1.4.1 Folders

- Appendices – this is the folder where you put the appendices. Each appendix should go into its own separate qmd file. An example and template are included in the directory.
- Chapters – this is the folder where you put the thesis chapters. Each chapter should go in its own separate qmd file.
- Figures – this folder contains static figures for the thesis, i.e. figures that are not generated by code in the chapters.

1.4.2 Files

- `example.bib` – this is file that contains all the bibliographic information and references that you will be citing in the thesis for use with BibTeX. You can write it manually, but there are reference manager programs available that will create and manage it for you. Zotero is popular and integrates with RStudio IDE if you use that.
- `MastersDoctoralThesis.cls` – this is the class file that tells L^AT_EX how to format the thesis.
- `pdf` in docs folder – this is your typeset thesis.
- `Frontmater` folder – this has the files for the various front matter elements.

1.5 Filling in Your Information

Most of the personal information is found on in the `_quarto.yml` file.

- `author` – you; optionally add url
- `supervisor` – your supervisor; optionally add url.
- `university` – your university
- `department` – your department
- `faculty` – faculty name
- `group` – research group name (optional)
- `abstract`

1.6 The `tex\before-body.tex` File Explained

The `tex\before-body.tex` file contains the structure of the thesis and is a mix of Pandoc template and L^AT_EX code. The bits that look like `$book.university$` say are Pandoc and are referencing variables in the `_quarto.yml` file. Knowing that, you should be able to figure out what is happening.

There are plenty of written comments that explain what pages, sections and formatting the L^AT_EX code is creating. Each major document element is divided into

commented blocks with titles in all capitals to make it obvious what the following bit of code is doing. Initially there seems to be a lot of \LaTeX code, but this is all formatting, and it has all been taken care of so you don't have to do it.

Many of the sections have `$if(...)$` so that the section is only included if you included information for that in `_quarto.yml`.

In the `_quarto.yml`, `pdf: toc: false` is used so that Quarto/Pandoc doesn't add a table of contents. This template puts the table of contents before the abbreviations and symbols pages and Quarto/Pandoc doesn't let us control where it puts the table of contents. So we have to add the TOC manually for pdf and pass in `toc: false`.

The list of figures and tables are all taken care of for you and do not need to be manually created or edited. The next set of pages are more likely to be optional and can be deleted since they are for a more technical thesis: insert a list of abbreviations you have used in the thesis, then a list of the physical constants and numbers you refer to and finally, a list of mathematical symbols used in any formulae. Making the effort to fill these tables means the reader has a one-stop place to refer to instead of searching the internet and references to try and find out what you meant by certain abbreviations or symbols.

The list of symbols is split into the Roman and Greek alphabets. Whereas the abbreviations and symbols ought to be listed in alphabetical order (and this is **not** done automatically for you) the list of physical constants should be grouped into similar themes.

The next page contains a one line dedication. Who will you dedicate your thesis to?

1.7 Adding Your Chapters and Appendices

Add your chapters and appendices to `_quarto.yml`. Note that the spacing is important as is the leading `-`.

1.8 Bibliography and Citations

Citations will be added and formatted automatically for you.

Practice reference (Rashid et al. 2021) Lorem ipsum dolor sit amet (Bennett et al. 2015, 2018; Yu et al. 2021)

If you use the RStudio IDE, then you can link Zotero to RStudio and Quarto will find your citations for you when you enter @. This is in the visual editor mode. Make sure to search for videos on how to do this as using Zotero libraries will make your citation and bibliography management much much easier.

In the text use @smith2000 to produce Smith (2000) add use [@smith2000, @jones1999] to produce (Smith 2000; Jones 1999). See the natbib cheatsheet for how to do other types of formatting for your in text citations. The bibliography style (`classoption: "authoryear"`) is used for the bibliography and is a fully featured style that will even include links to where the referenced paper can be found online.

1.8.0.1 A Note on bibtex

The bibtex backend used in the template by default does not correctly handle unicode character encoding (i.e. “international” characters). You may see a warning about this in the compilation log and, if your references contain unicode characters, they may not show up correctly or at all. One solution to this is to use the biber backend instead of the outdated bibtex backend. This is done by finding this in `tex/in-header.tex`: `backend=bibtex` and changing it to `backend=biber`. Google a bit to find information on this.

1.9 Thesis Features and Conventions {sec-ThesisConventions}

To get the best out of this template, there are a few conventions that you may want to follow.

1.9.1 Printing Format

This thesis template is designed for double sided printing (i.e. content on the front and back of pages) as most theses are printed and bound this way. Switching to one sided printing is as simple as adding "oneside" to `classoptions:` in the `_quarto.yml` file. The headers for the pages contain the page number on the outer side (so it is easy to flick through to the page you want) and the chapter name on the inner side.

The text is set to 11 point by default with single line spacing, again, you can tune the text size and spacing should you want or need to using the class options. The spacing can be changed similarly by replacing the "singlespacing" with "onehalfspacing" or "doublespacing" in the class options.

1.9.2 Using US Letter Paper

The paper size used in the template is A4, which is the standard size in Europe. If you are using this thesis template elsewhere and particularly in the United States, then you may have to change the A4 paper size to the US Letter size. This can be by editing `geometry:` in `_quarto.yml` in the pdf format section.

1.10 Tables

When you render your Quarto thesis to PDF, it will process \LaTeX table code just fine. However, if you are doing that, I am guessing you would be writing your thesis in \LaTeX not Quarto. So I will not discuss \LaTeX tables. Instead here is how you create tables using R. Python and Julia users, you'll have your own table packages but the idea will be similar.

See the Quarto manual for full examples and instructions.

1.11 Figures

Again we write in Quarto (markdown) not \LaTeX for our figures. You can write in \LaTeX if you really want but it would only be interpreted for the PDF output.

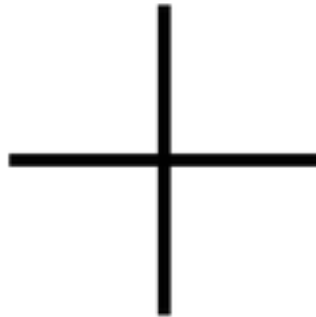


FIGURE 1.1: icon

The `#|` is what sets up our cross-references and you can then reference the table as `@fig-icon`.

This is Figure [1.1](#).

See the Quarto manual for full examples and instructions.

1.11.1 Typesetting mathematics

If your thesis is going to contain heavy mathematical content, \LaTeX will make it look beautiful, for HTML or PDF output.

The [Not So Short Introduction to LaTeX](#) should tell you everything you need to know for most cases of typesetting mathematics. If you need more information, a much more thorough mathematical guide is available from the AMS called, [A Short Math Guide to LaTeX](#).

1.12 In Closing

Good luck and have lots of fun!

This guide was written originally by

Sunil Patel: [{www.sunilpatel.co.uk}](http://www.sunilpatel.co.uk)

and Vel: <http://www.LaTeXTemplates.com>

and heavily shortened and adapted for [Quarto](#) by [Eli Holmes](#).

Chapter 2

Background

2.1 Small area health statistics (unit)

In 1983, a documentary on the fallout produced from a fire at the Sellafield nuclear site in Cumbria claimed that there was a ten-fold increase in cases of childhood leukaemia in the surrounding community. This anomaly had gone undetected by public health authorities, raising concern that routinely collected data were not able to identify local clusters of disease. The subsequent enquiry confirmed the excess, and recommended that a research unit was set up to monitor small area statistics and respond quickly to *ad hoc* queries on local health hazards. The Small Area Health Statistics Unit (SAHSU) was established in 1987 (Elliott et al. 1992).

Beyond producing substantive research studies on environment and health, a core aim of SAHSU is to develop small area statistical methodology (Wakefield and Elliott 1999) for:

- *Point source type studies.* Is there an increased risk close to an environmental hazard?
- *Geographic correlation studies.* Is there a correlation between disease risk and environmental variables?
- *Clustering.* Does a disease to produce non-random spatial patterns of incidence?
If the aetiology is unknown, this could suggest the disease is infectious.
- *Disease mapping.* Summarising the spatial variation in risk.

In a pilot study for SAHSU, Elliott et al. (1992) investigated the mortality from mesothelioma and asbestosis near the Plymouth docks. Death registrations with postcode information were held by SAHSU. Both diseases are related to industrial exposure and asbestos, so concentric circular bands were drawn around the Plymouth dockyards as a way to approximate the exposure from a point source of environmental pollution. There was a clear increase in risk within 3km of the docks. A similar distance-based approach was adopted to look at excess respiratory disease mortality near two factories in Barking and Havering (Aylin et al. 1999), kidney disease mortality near chemical plants in Runcorn (Hodgson et al. 2004). In response to public concern over exposure to toxic chemicals in landfill, SAHSU conducted the most extensive study ever into health effects of landfill sites. Postcodes within a 2km buffer of a landfill site were classified as exposed. Compared to those living beyond 2km , SAHSU found a small unexplained excess of congenital anomalies (Elliott, Briggs, et al. 2001), no increase in rates of cancer (Jarup, Briggs, et al. 2002), and no excess risk of Down syndrome (Jarup et al. 2007).

Distance from source is, however, only a basic model for the exposure, which can often exhibit more complex, directional spatial patterns. A number of SAHSU studies have employed physics-informed models to create an exposure surface, and assess the geographic correlations between this surface and the health outcome, notably for a plume of mercury pollution (Hodgson et al. 2007), exposure to mobile phone base station during pregnancy (Elliott et al. 2010), noise from aircrafts near Heathrow (Hansell et al. 2013), road traffic noise in London (Halonen et al. 2015), and PM10 from incinerators during pregnancy (Parkes et al. 2020). SAHSU published an environment and health atlas for England and Wales, showing the geographic patterns of 14 health conditions at census ward level over an aggregated 25 year period alongside five environmental exposure surfaces (Hansell, Anna L. et al. 2014).

2.1.1 Disease mapping at SAHSU

Many of the studies at SAHSU focus on rare diseases at small areas. The data for the number of cases, or number of deaths, in a region are likely to be small numbers. This sparseness issue is even more pertinent when the population is also stratified by

age group. Rates calculated from observed data present apparent variability between spatial units, which is larger than the true differences in the risk. There is a need for statistical smoothing techniques to obtain robust estimates of rates by sharing information between strata. Aylin et al. (1999) mapped diseases for wards in Kensington, Chelsea and Westminster using a simple model that smoothed rates towards the mean of the risks across the region. SAHSU thereafter published a plethora of studies for disease mapping models with explicit spatial dependence, which are designed to give more weight to nearby areas than those further away.

There are three main categories for modelling spatial effects. First, we can treat space a continuous surface, such as Gaussian processes or splines. Second, we can use areal models, which make use of spatial neighbourhood structure of the units. Thirdly, we can explicitly build effects based on a nested hierarchy of geographical units, for example between state, county and census tract in the US.

In the context of disease mapping, events are usually aggregated to areas rather than assigned specific geographical coordinates. Wakefield and Elliott (1999) model aggregated counts as realisations of a Poisson process, in which the expected number of cases is calculated by integrating a continuous surface that generates the cases integrated over the area. The surface was some function of spatially-referenced covariates. Kelsall and Wakefield (2002) describe an alternative model, where the log-transformed risk surface is modelled by a Gaussian process, whose correlation function depends on distance.

Best, Richardson, and Thomson (2005) provide a review of the use of hierarchical models with spatial dependence for disease mapping. In particular, the authors focus on Bayesian estimation, and different classes of spatial prior distributions.

The first prior proposed for spatial effects $\mathbf{S} = S_1, \dots, S_n$ is the multivariate normal

$$\mathbf{S} \sim \mathcal{N}(\boldsymbol{\mu}, \boldsymbol{\Sigma}), \quad (2.1)$$

where $\boldsymbol{\mu}$ is the mean effect vector, $\boldsymbol{\Sigma} = \sigma^2 \boldsymbol{\Omega}$ and $\boldsymbol{\Omega}$ is a symmetric, positive semi-definite matrix defining the correlation between spatial units. A common choice

when specifying the structure of the correlation matrix is to assume a function that decays with the distance between the centroids of the areas, so that places nearby in space share similar disease profiles. Note, this is mathematically equivalent to the practical implementation of a Gaussian process, which uses a finite set of points. An example in Elliott, Wakefield, et al. (2001) chooses the exponential decay function to map cancer risk in northwest England.

A more popular prior is the conditional autoregressive (CAR) prior, also known as a Gaussian Markov random field. These form a joint distribution as in Equation 2.1, but the covariance is usually defined instead in terms of the precision matrix

$$\mathbf{P} = \mathbf{\Sigma}^{-1} = \tau(\mathbf{D} - \rho\mathbf{A}),$$

where τ controls the overall precision of the effects, \mathbf{A} is the spatial adjacency matrix formed by the small areas, \mathbf{D} is a diagonal matrix with entries equal to the number of neighbours for each spatial unit, and the autocorrelation parameter ρ describes the amount of correlation. This can be seen as a tuning the degree of spatial dependence, where $\rho = 0$ implies independence between areas, and $\rho = 1$ full dependence. The case with $\rho = 1$ is called the intrinsic conditional autoregressive (ICAR) model. Besag, York, and Mollié (1991) proposed the model (hereafter called BYM)

$$S_i = U_i + V_i, \tag{2.2}$$

where U_i follow an ICAR distribution, and V_i are independent and identically distributed random effects. The BYM distribution was employed to model spatial variation in the relative risk of testicular (Toledano et al. 2001) and prostate (Jarup, Best, et al. 2002) cancers for small areas in regions of England.

Further disease mapping studies at SAHSU have also looked at age patterns and trends over time of disease. Asaria et al. (2012) analysed cardiovascular disease death rates by fitting a spatial model for all wards in England separately for each age group and time period. Bennett et al. (2015) considered a model to estimate spatial, age group and temporal effects jointly for all-cause mortality in England at

the district level.

In building models which consider the hierarchy of geographical units, these relationships are often incorporated into the model as a nested hierarchy of random effects. These models account for which spatial units lie within common administrative boundaries, but, by design, there is no knowledge of spatial distance included. This is often a desirable property of the model for certain geographies, like states in the US, which are administrative. Policy is decided at these geographies, so there is reason to believe these boundaries may have a greater effect on health outcomes than spatial structure. Although not used in previous SAHSU studies, Finucane et al. (2014) demonstrate how country-level blood pressure can be modelled as such, in this case exploiting the hierarchy global, subregion, region and country. Note, although these models group by geographical region, these models are not spatial as they do not contain any information on the position relative to other units.

2.1.2 Small area analyses of mortality (over space, but also time age)

Population issue, measuring between census, migration. Look at sahsu spatial epi book, Wakefield 1999. Births, deaths and migration for population between census years

People who have calculated SMR. **Indirect** model vs direct model (calculate age specific and use life tables) of mortality

Over space:

Rotterdam Jonker 2012

Australia, Stephens 2013 NSW

South Korea

Rasulo, D., Bajekal, M., Yar, M., 2007. Inequalities in health expectancies in England and Wales—small area analysis from the 2001 Census. *Health Stat Q* 34 (35), 35.

SALURBAL. Santiago Chile Bilal 2019

Over space and time: United States LDL King county 2015, LDL 2016

United Kingdom Bennett 2015 (Bennett et al. 2015)

Canada, Yu 2022 (Yu et al. 2021)

London wards DALY Congdon 2014

Practice reference (Rashid et al. 2021) Lorem ipsum dolor sit amet, consectetur adipiscing elit. Aliquam ultricies lacinia euismod. Nam tempus risus in dolor rhoncus in interdum enim tincidunt. Donec vel nunc neque. In condimentum ullamcorper quam non consequat. Fusce sagittis tempor feugiat. Fusce magna erat, molestie eu convallis ut, tempus sed arcu. Quisque molestie, ante a tincidunt ullamcorper, sapien enim dignissim lacus, in semper nibh erat lobortis purus. Integer dapibus ligula ac risus convallis pellentesque.

2.2 Cause-specific analyses

See Kyle's thesis

Nunc posuere quam at lectus tristique eu ultrices augue venenatis. Vestibulum ante ipsum primis in faucibus orci luctus et ultrices posuere cubilia Curae; Aliquam erat volutpat. Vivamus sodales tortor eget quam adipiscing in vulputate ante ullamcorper. Sed eros ante, lacinia et sollicitudin et, aliquam sit amet augue. In hac habitasse platea dictumst.

2.3 Health inequalities in the UK

Whitehall study Marmot 1991 Class Wilkinson. Income distribution and life expectancy, 1997 Class Whitehead Marmot report 1 and 2 GBD paper People modelling over space Bennett 2015 Bennett et al. (2015) Deprivation Bennett 2018 Bennett et al. (2018)

Effect of austerity: Whitehead M. Investigating the impact of the English health inequalities strategy: time trend analysis. Austerity measures hit the sickest hardest BMJ Dorling D. Why is life expectancy in England and Wales 'stalling'? Goodman

PS. In Britain, austerity is changing everything. May 28, 2018. The New York Times
Stalling life expectancy and rising inequalities in England Local government funding
and life expectancy in England: a longitudinal ecological study Dorling opendemoc-
racy

Chapter 3

The model

3.1 Model

Lorem ipsum dolor sit amet, consectetur adipiscing elit. Aliquam ultricies lacinia euismod. Nam tempus risus in dolor rhoncus in interdum enim tincidunt. Donec vel nunc neque. In condimentum ullamcorper quam non consequat. Fusce sagittis tempor feugiat. Fusce magna erat, molestie eu convallis ut, tempus sed arcu. Quisque molestie, ante a tincidunt ullamcorper, sapien enim dignissim lacus, in semper nibh erat lobortis purus. Integer dapibus ligula ac risus convallis pellentesque.

3.1.1 Contributions to open source

Nunc posuere quam at lectus tristique eu ultrices augue venenatis. Vestibulum ante ipsum primis in faucibus orci luctus et ultrices posuere cubilia Curae; Aliquam erat volutpat. Vivamus sodales tortor eget quam adipiscing in vulputate ante ullamcorper. Sed eros ante, lacinia et sollicitudin et, aliquam sit amet augue. In hac habitasse platea dictumst.

3.1.2 NumPyro quicker than nimble

Chapter 4

Small: Life expectancy trends in England, LPH

4.1 Introduction

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4.1.1 Methods

Nunc posuere quam at lectus tristique eu ultrices augue venenatis. Vestibulum ante ipsum primis in faucibus orci luctus et ultrices posuere cubilia Curae; Aliquam erat volutpat. Vivamus sodales tortor eget quam adipiscing in vulputate ante ullamcorper. Sed eros ante, lacinia et sollicitudin et, aliquam sit amet augue. In hac habitasse platea dictumst.

4.1.2 Results

4.1.3 Discussion

4.1.4 Conclusion

Chapter 5

Smaller: Life expectancy inequality in London

5.1 Introduction

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5.1.1 Methods

Nunc posuere quam at lectus tristique eu ultrices augue venenatis. Vestibulum ante ipsum primis in faucibus orci luctus et ultrices posuere cubilia Curae; Aliquam erat volutpat. Vivamus sodales tortor eget quam adipiscing in vulputate ante ullamcorper. Sed eros ante, lacinia et sollicitudin et, aliquam sit amet augue. In hac habitasse platea dictumst.

5.1.2 Results

5.1.3 Discussion

5.1.4 Conclusion

Chapter 6

Cancers

6.1 Introduction

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6.1.1 Methods

Nunc posuere quam at lectus tristique eu ultrices augue venenatis. Vestibulum ante ipsum primis in faucibus orci luctus et ultrices posuere cubilia Curae; Aliquam erat volutpat. Vivamus sodales tortor eget quam adipiscing in vulputate ante ullamcorper. Sed eros ante, lacinia et sollicitudin et, aliquam sit amet augue. In hac habitasse platea dictumst.

6.1.2 Results

6.1.3 Discussion

6.1.4 Conclusion

Chapter 7

Cause-specific

7.1 Introduction

Lorem ipsum dolor sit amet, consectetur adipiscing elit. Aliquam ultricies lacinia euismod. Nam tempus risus in dolor rhoncus in interdum enim tincidunt. Donec vel nunc neque. In condimentum ullamcorper quam non consequat. Fusce sagittis tempor feugiat. Fusce magna erat, molestie eu convallis ut, tempus sed arcu. Quisque molestie, ante a tincidunt ullamcorper, sapien enim dignissim lacus, in semper nibh erat lobortis purus. Integer dapibus ligula ac risus convallis pellentesque.

7.1.1 Methods

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7.1.2 Results

7.1.3 Discussion

7.1.4 Conclusion

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Appendix A

Frequently Asked Questions

A.1 How do I change the colors of links?

Pass in `urlcolor:` in yaml. Or set these in the include-in-header file.

If you want to completely hide the links, you can use:

```
{\hypersetup{allcolors=.}}, or even better:
```

```
{\hypersetup{hidelinks}}.
```

If you want to have obvious links in the PDF but not the printed text, use:

```
{\hypersetup{colorlinks=false}}.
```