

## ARTICLE TEMPLATE

# External Validation of Berten's Model for Predicting COPD Exacerbations

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## ARTICLE HISTORY

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## ABSTRACT

We are reporting an independent validation of the COPD exacerbation prediction model developed by Bertens and colleagues in the

## KEYWORDS

COPD; prediction; validation

## 1. Introduction

The Berten's model (Bertens et al. 2013).

## 2. Methods

We have followed recommendations of the Transparent Reporting of a Multivariable Prediction Model for Individual Prognosis or Diagnosis (the TRIPOD Statement) (Collins et al. 2015) in reporting our independent validation of the Bertens model. External validation was done using three years of data from COPD patients enrolled in the Evaluation of COPD Longitudinally to Identify Predictive Surrogate End-points (the ECLIPSE Study), an independent non-interventional observational longitudinal COPD cohort study that was aimed at characterizing progression of the disease (Agusti et al. 2010).

The first year of the ECLIPSE study was used to establish exacerbation history, year two was used to assess validity of one-year and two-year predictions were assessed using data from year two, and years 2-3, respectively.

We report external validation of the model in terms of calibration (the degree to which predicted and observed risk of exacerbations are in agreement), discrimination (the extent to which the model is able to separate higher and lower risk individuals), and clinical utility (net benefit across different risk thresholds for treatment decision).

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Calibration was assessed through visual examination of the calibration curve. Differentiation was assessed by plotting the Receiver Operating Characteristic (ROC) curve and its area-under-the-curve (AUC), also known as the c-statistic. Clinical utility was assessed through have reported Decision Curve Analysis (Vickers, van Calster, and Steyerberg 2019).

The study was approved by the University of British Columbia and Providence Health Research Ethics Board (H11–00786).

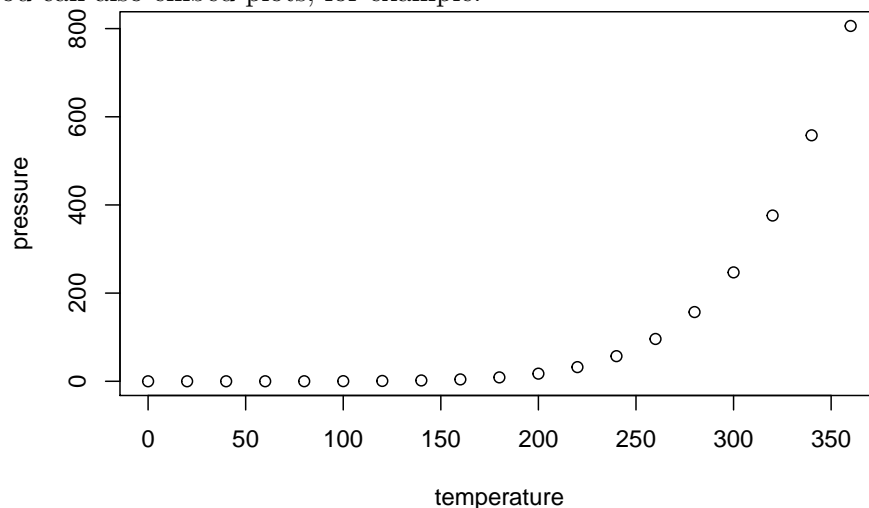
### 3. Results

### 4. Discussions

#### 4.1. *Code chunks*

#### 4.2. *Including Plots*

You can also embed plots, for example:



Note that the `echo = FALSE` parameter was added to the code chunk to prevent printing of the R code that generated the plot.

### 5. Some guidelines for using the standard features of $\text{\LaTeX}$

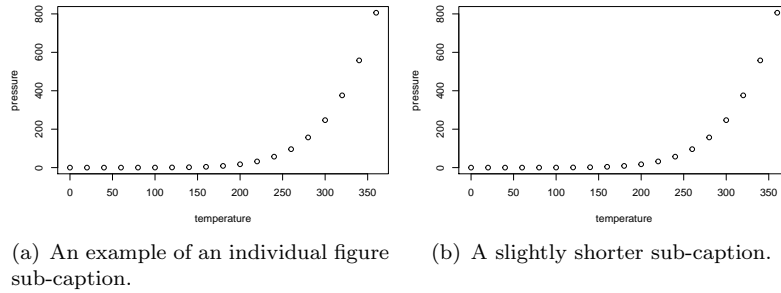
#### 5.1. *Sections*

The Interact layout style allows for five levels of section heading, all of which are provided in the `interact` class file using the standard  $\text{\LaTeX}$  commands `\section`, `\subsection`, `\subsubsection`, `\paragraph` and `\subparagraph`. Numbering will be automatically generated for all these headings by default.

#### 5.2. *Lists*

Numbered lists are produced using the `enumerate` environment, which will number each list item with arabic numerals by default. For example,

1. first item



**Figure 1.** Example of a two-part figure with individual sub-captions showing that captions are flush left and justified if greater than one line of text.

2. second item
3. third item

Alternative numbering styles can be achieved by inserting an optional argument in square brackets to each `item`, e.g. `\item[(i)] first item`, to create a list numbered with roman numerals at level one.

Bulleted lists are produced using the `itemize` environment. For example,

- First bulleted item
- Second bulleted item
- Third bulleted item

### 5.3. *Figures*

```
plot(pressure)
```

The `interact` class file will deal with positioning your figures in the same way as standard  $\text{\LaTeX}$ . It should not normally be necessary to use the optional `[htb]` location specifiers of the `figure` environment in your manuscript; you may, however, find the `[p]` placement option or the `endfloat` package useful if a journal insists on the need to separate figures from the text.

Figure captions appear below the figures themselves, therefore the `\caption` command should appear after the body of the figure. For example, Figure~1 with caption and sub-captions is produced using the following commands:

```
\begin{figure}
\centering
\subfigure[An example of an individual figure sub-caption.]{%
\resizebox*{5cm}{!}{\includegraphics{path/to/fig}}}\hspace{5pt}
\subfigure[A slightly shorter sub-caption.]{%
\resizebox*{5cm}{!}{\includegraphics{path/to/fig}}}
\caption{Example of a two-part figure with individual sub-captions
showing that captions are flush left and justified if greater
than one line of text.} \label{sample-figure}
\end{figure}
```

To ensure that figures are correctly numbered automatically, the `\label` command should be included just after the `\caption` command, or in its argument.

**Table 1.** Example of a table showing that its caption is as wide as the table itself and justified.

Class	Type					
	One	Two	Three	Four	Five	Six
Alpha <sup>a</sup>	A1	A2	A3	A4	A5	A6
Beta	B2	B2	B3	B4	B5	B6
Gamma	C2	C2	C3	C4	C5	C6

<sup>a</sup>This footnote shows how to include footnotes to a table if required.

The `\subfigure` command requires `subfigure.sty`, which is called in the preamble of the `interacttfssample.tex` file (to allow your choice of an alternative package if preferred) and included in the `Interact LATEX` bundle for convenience. Please supply any additional figure macros used with your article in the preamble of your `.tex` file.

The source files of any figures will be required when the final, revised version of a manuscript is submitted. Authors should ensure that these are suitable (in terms of lettering size, etc.) for the reductions they envisage.

The `epstopdf` package can be used to incorporate encapsulated PostScript (`.eps`) illustrations when using PDF<sup>L</sup><sub>A</sub>T<sub>E</sub>X, etc. Please provide the original `.eps` source files rather than the generated PDF images of those illustrations for production purposes.

#### 5.4. Tables

The `interact` class file will deal with positioning your tables in the same way as standard L<sup>A</sup>T<sub>E</sub>X. It should not normally be necessary to use the optional `[htb]` location specifiers of the `table` environment in your manuscript; you may, however, find the `[p]` placement option or the `endfloat` package useful if a journal insists on the need to separate tables from the text.

The `tabular` environment can be used as shown to create tables with single horizontal rules at the head, foot and elsewhere as appropriate. The captions appear above the tables in the `Interact` style, therefore the `\tbl` command should be used before the body of the table. For example, Table~1 is produced using the following commands:

```
\begin{table}
\tbl{Example of a table showing that its caption is as wide as
the table itself and justified.}
{\begin{tabular}{lcccccc} \toprule
& \multicolumn{2}{l}{Type} \\ \cmidrule{2-7}
Class & One & Two & Three & Four & Five & Six \\ \midrule
Alpha\textsuperscript{a} & A1 & A2 & A3 & A4 & A5 & A6 \\
Beta & B2 & B2 & B3 & B4 & B5 & B6 \\
Gamma & C2 & C2 & C3 & C4 & C5 & C6 \\ \bottomrule
\end{tabular}}
\tabnote{\textsuperscript{a}This footnote shows how to include
footnotes to a table if required.}
\label{sample-table}
\end{table}
```

To ensure that tables are correctly numbered automatically, the `\label` command should be included just before `\end{table}`.

The `\toprule`, `\midrule`, `\bottomrule` and `\cmidrule` commands are those used by `booktabs.sty`, which is called by the `interact` class file and included in the `Interact LATEX` bundle for convenience. Tables produced using the standard commands of the `tabular` environment are also compatible with the `interact` class file.

### 5.5. *Landscape pages*

If a figure or table is too wide to fit the page it will need to be rotated, along with its caption, through 90° anticlockwise. Landscape figures and tables can be produced using the `rotating` package, which is called by the `interact` class file. The following commands (for example) can be used to produce such pages.

```
\setcounter{figure}{1}
\begin{sidewaysfigure}
\centerline{\epsfbox{figname.eps}}
\caption{Example landscape figure caption.}
\label{landfig}
\end{sidewaysfigure}

\setcounter{table}{1}
\begin{sidewaystable}
\tbl{Example landscape table caption.}
{\begin{tabular}{@{}llllc1l}
.
.
.
\end{tabular}}\label{landtab}
\end{sidewaystable}
```

Before any such float environment, use the `\setcounter` command as above to fix the numbering of the caption (the value of the counter being the number given to the preceding figure or table). Subsequent captions will then be automatically renumbered accordingly. The `\epsfbox` command requires `epsfig.sty`, which is called by the `interact` class file and is also included in the `Interact LATEX` bundle for convenience.

Please note that if the `endfloat` package is used, one or both of the commands

```
\DeclareDelayedFloatFlavor{sidewaysfigure}{figure}
\DeclareDelayedFloatFlavor{sidewaystable}{table}
```

will need to be included in the preamble of your `.tex` file, after the `endfloat` package is loaded, in order to process any landscape figures and/or tables correctly.

### Acknowledgement(s)

An unnumbered section, e.g. `\section*{Acknowledgements}`, may be used for thanks, etc. if required and included *in the non-anonymous version* before any Notes or References.

## Disclosure statement

An unnumbered section, e.g. `\section*{Disclosure statement}`, may be used to declare any potential conflict of interest and included *in the non-anonymous version* before any Notes or References, after any Acknowledgements and before any Funding information.

## Funding

An unnumbered section, e.g. `\section*{Funding}`, may be used for grant details, etc. if required and included *in the non-anonymous version* before any Notes or References.

## Notes on contributor(s)

An unnumbered section, e.g. `\section*{Notes on contributors}`, may be included *in the non-anonymous version* if required. A photograph may be added if requested.

## Nomenclature/Notation

An unnumbered section, e.g. `\section*{Nomenclature}` (or `\section*{Notation}`), may be included if required, before any Notes or References.

## Notes

An unnumbered **Notes** section may be included before the References (if using the **endnotes** package, use the command `\theendnotes` where the notes are to appear, instead of creating a `\section*`).

## 6. References

### 6.1. *References cited in the text*

### 6.2. *The list of references*

References should be listed at the end of the main text in alphabetical order by authors' surnames, then chronologically (earliest first). If references have the same author(s), editor(s), etc., arrange by year of publication, with undated works at the end. A single-author entry precedes a multi-author entry that begins with the same name. If the reference list contains two or more items by the same author(s) in the same year, add a, b, etc. and list them alphabetically by title. Successive entries by two or more authors when only the first author is the same are alphabetized by co-authors' surnames. If a reference has more than ten named authors, list only the first seven, followed by 'et al.'. If a reference has no author or editor, order by title; if a date of publication is impossible to find, use 'n.d.' in its place.

The following list shows some sample references prepared in the Taylor & Francis Chicago author-date style.

(??)

## References

Agusti, Alvar, Peter MA Calverley, Bartolome Celli, Harvey O. Coxson, Lisa D. Edwards, David A. Lomas, William MacNee, et al. 2010. "Characterisation of COPD heterogeneity in the ECLIPSE cohort." *Respiratory Research* 11 (1): 122. Accessed 2018-09-19. <https://doi.org/10.1186/1465-9921-11-122>.

Bertens, Loes, Reitsma, Moons, van Mourik, Berna Broekhuizen, Hoes, Rutten, and Lammers. 2013. "Development and validation of a model to predict the risk of exacerbations in chronic obstructive pulmonary disease." *International Journal of Chronic Obstructive Pulmonary Disease* 493. Accessed 2018-12-06. <http://www.dovepress.com/development-and-validation-of-a-model-to-predict-the-risk-of-exacerbations-peer-reviewed-article-ijcopd>.

Collins, Gary S, Johannes B Reitsma, Douglas G Altman, and Karel Moons. 2015. "Transparent reporting of a multivariable prediction model for individual prognosis or diagnosis (TRIPOD): the TRIPOD Statement." *BMC Medicine* 13 (1): 1. Accessed 2018-11-20. <http://www.biomedcentral.com/1741-7015/13/1>.

Vickers, Andrew J., Ben van Calster, and Ewout W. Steyerberg. 2019. "A simple, step-by-step guide to interpreting decision curve analysis." *Diagnostic and Prognostic Research* 3 (1): 18. Accessed 2021-03-24. <https://doi.org/10.1186/s41512-019-0064-7>.

## 7. Appendices

Any appendices should be placed after the list of references, beginning with the command `\appendix` followed by the command `\section` for each appendix title, e.g.

```
\appendix
\section{This is the title of the first appendix}
\section{This is the title of the second appendix}
```

produces:

**Appendix A. This is the title of the first appendix**

**Appendix B. This is the title of the second appendix**

Subsections, equations, figures, tables, etc. within appendices will then be automatically numbered as appropriate. Some theorem-like environments may need to have their counters reset manually (e.g. if they are not numbered within sections in the main text). You can achieve this by using `\numberwithin{remark}{section}` (for example) just after the `\appendix` command.

Please note that if the `endfloat` package is used on a document containing appendices, the `\processdelayedfloats` command must be included immediately before the `\appendix` command in order to ensure that the floats in the main body of the text are numbered as such.

## Appendix A. Troubleshooting

Authors may occasionally encounter problems with the preparation of a manuscript using L<sup>A</sup>T<sub>E</sub>X. The appropriate action to take will depend on the nature of the problem:

- (i) If the problem is with L<sup>A</sup>T<sub>E</sub>X itself, rather than with the actual macros, please consult an appropriate L<sup>A</sup>T<sub>E</sub>X 2<sub>ε</sub> manual for initial advice. If the solution cannot be found, or if you suspect that the problem does lie with the macros, then please contact Taylor & Francis for assistance ([latex.helpdesk@tandf.co.uk](mailto:latex.helpdesk@tandf.co.uk)).
- (ii) Problems with page make-up (e.g. occasional overlong lines of text; figures or tables appearing out of order): please do not try to fix these using ‘hard’ page make-up commands – the typesetter will deal with such problems. (You may, if you wish, draw attention to particular problems when submitting the final version of your manuscript.)
- (iii) If a required font is not available on your system, allow T<sub>E</sub>X to substitute the font and specify which font is required in a covering letter accompanying your files.

## Appendix B. Obtaining the template and class file

### B.1. *Via the Taylor & Francis website*

This article template and the `interact` class file may be obtained via the ‘Instructions for Authors’ pages of selected Taylor & Francis journals.

Please note that the class file calls up the open-source L<sup>A</sup>T<sub>E</sub>X packages `booktabs.sty`, `epsfig.sty` and `rotating.sty`, which will, for convenience, unpack with the downloaded template and class file. The template calls for `natbib.sty` and `subfigure.sty`, which are also supplied for convenience.

### B.2. *Via e-mail*

This article template, the `interact` class file and the associated open-source L<sup>A</sup>T<sub>E</sub>X packages are also available via e-mail. Requests should be addressed to [latex.helpdesk@tandf.co.uk](mailto:latex.helpdesk@tandf.co.uk), clearly stating for which journal you require the template and class file.