

1 Scoping Review Protocol: Statistical Models for Longitudinal Data  
2 in Health and Biomedical Research: Current State, Challenges,  
3 and Opportunities

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## 1 Notes

As of Sept 7, 2022 this document follows the structure recommended by PRISMA-P  
<https://prisma-statement.org/documents/PRISMA-P-checklist.pdf>

## 38 **2 Registration**

39 This section will be populated with the registration number and registry name once the protocol is submitted  
40 for peer review.

## 41 **3 Author Contributions**

- 42 • AM: Writing, query design, data extraction and analysis . . .

43 Other authors to add later

## 44 **4 Amendments**

45 Protocol amendments resulting from peer review will be indicated in this section indicating the date of each  
46 amendment.

## 47 **5 Support**

48 This section will indicate the sources of financial or other support for the review

### 49 **5.1 Sources**

## 50 **6 Introduction**

### 51 **6.1 Rationale**

52 Longitudinal studies are frequently used in the health sciences (biomedical research, epidemiology, public  
53 health, among others) to examine the temporal effect of a treatment or intervention<sup>1,2</sup>. However, the  
54 statistical analysis of longitudinal data requires to take into consideration factors such as data missingness,  
55 correlation, and non-linear trends<sup>3,4</sup>, which represent an “analytic cost” associated with the complexity of  
56 longitudinal data<sup>2</sup>.

57 One of the problems derived from the “analytic cost” of longitudinal data pertains the misspecification of  
58 the statistical models used to analyze such data (i.e., the use of models that are not coherent with the  
59 data), a problem that has been shown to occur frequently in the health sciences<sup>5</sup>. This problem with  
60 model misspecification can be linked to a historical preference by researchers to use the repeated measures  
61 analysis of variance (rm-ANOVA) as the default method to analyze longitudinal data, despite the fact  
62 that the multiple assumptions required by this model are frequently not satisfied by the data collected in  
63 longitudinal studies<sup>4</sup>.

64 On the other hand, multiple modern statistical models were developed during the last 30 years to address  
65 the limitations of rm-ANOVA. Linear mixed models, generalized additive mixed models, and generalized  
66 estimating equations are among these modern statistical models developed for longitudinal data<sup>6–10</sup>. How-  
67 ever, the use of such modern statistical methods has been the exception rather than the norm in the health  
68 sciences<sup>11</sup>, even on this day and age where these modern methods have been brought to a wider audience  
69 with the development of computational tools such as Python or R.

70 Unfortunately, the misuse and lack of reproducibility of statistical analyses continue to be major problems in  
71 the health sciences<sup>12–15</sup>. In the case of longitudinal data, where modern methods exist beyond rm-ANOVA  
72 that can help researchers obtain better inference from their data, there is a need to understand what are  
73 the trends in the adoption of these statistical methods in the health sciences to measure the adoption of  
74 reproducibility practices by the field at large, while also identifying the reasons that may cause researchers  
75 use avoid the use of modern statistical methods for longitudinal data.

## 76 **7 Objectives**

77 This study aims to:

- 78 • Identify the different statistical models for longitudinal data that are used in the health sciences in  
79 order to measure the current extent in the adoption of modern statistical methods by the field (Aim  
80 1a)
- 81 • Summarize the computational tools used by researchers in the health sciences to statistically analyze  
82 longitudinal data to understand the current status of the field with regards to reproducibility. (Aim  
83 1b)

- List statistical methods for longitudinal data developed within the last decade in order to showcase newer methods that may be applicable for longitudinal data in a biomedical/health context. (Aim 2)

## 8 Review Question

- What are the statistical methods used in biomedical/health sciences research?
- Has the use of modern statistical methods increased in the field during the last 20 years?
- What computational tools are most commonly used by researchers to analyze longitudinal data, and how in turn this affects reproducibility?
- What are most recent statistical methods developed for longitudinal data, and how can they be applied in the health sciences?

## 9 Methods

### 9.1 Types of Studies

For all the study aims, studies included in the analysis correspond to peer-reviewed publications in English.

### 9.2 Eligibility Criteria

#### 9.2.1 For the Application of Modern Statistical Models on Longitudinal Biomedical/Health Data (Aims 1a and 1b)

##### 9.2.1.1 Inclusion Criteria

Articles that are written in English, belong to the biomedical/health sciences fields, describe the collection and analysis of continuous or discrete longitudinal data, indicate the statistical model used to analyze the data, and report the results of their statistical analyses.

##### 9.2.1.2 Exclusion Criteria

104 Cross-sectional studies, tutorials that present the application of existing statistical methods to biomed-  
105 ical/health data, reviews, meta-analyses, or systematic reviews on existing statistical methods for longitu-  
106 dinal data, studies that use only descriptive statistics to summarize/analyze the data, studies that collect  
107 and analyze categorical data.

## 108 **9.2.2 For Methods on Longitudinal Data (Aim 2)**

### 109 **9.2.2.1 Inclusion Criteria**

- 110 • Articles that:

111 Are written in English, present new methodologies or significant improvements to existing methods for  
112 longitudinal data.

### 113 **9.2.2.2 Exclusion Criteria**

114 Systematic reviews, meta-analyses, or reviews of statistical methods for longitudinal data, tutorials that  
115 present the application of existing statistical methods to biomedical/health longitudinal data.

## 116 **9.3 Information Sources**

117 Studies will be retrieved from PubMed and Web of Science.

## 118 **9.4 Search Strategy**

119 PubMed and Web of Science databases will be used. Below the full search strategy for PubMed is presented  
120 for all the aims of the scoping review.

### 121 **9.4.1 For the Application of Modern Models on Longitudinal Biomedical/Health Data**

#### 122 **9.4.1.1 PubMed**

##### 123 **9.4.1.1.1 Query:**

124 (biomedical OR health) AND ((repeated measures) OR (longitudinal study) OR (longitudinal data))  
125 AND ((statistical analyses) OR (statistical analysis)) NOT (Review[Publication Type] OR Meta

126 analy\*[Publication Type]) NOT ( “Statistics as Topic/methods”[Majr] OR “Statistics as Topic/statistics  
127 and numerical data”[Majr] OR “Models, Statistical”[Mesh] OR “Research Design”[Mesh])

128 Hits: 10,972

## 129 **9.4.2 For Methods on Longitudinal Data**

### 130 **9.4.2.1 PubMed**

#### 131 **9.4.2.1.1 Query 1:**

132 (“Models, Statistical” [Mesh] OR “Biostatistics/methods”[Mesh]) AND (“Longitudinal Studies”[Mesh])  
133 NOT (Review[Publication Type] OR Meta Analys\*[Publication Type] OR “editorial”[Publication Type])  
134 NOT (“survival”[Title/abstract]) NOT (“tutorial”[title/abstract] OR “orientation”[title/abstract]) NOT  
135 (Humans[Mesh] OR Adolescent [Mesh] OR Animals[Mesh])

136 Hits: 142

## 137 **9.5 Data Collection and Analysis**

### 138 **9.5.1 Selection Process and Data Management**

139 Two reviewers will independently analyze the database search results and pre-screen articles based on ti-  
140 tle and abstract content following the aforementioned inclusion/exclusion criteria. Manuscripts from the  
141 database(s) search will be stored in the Covidence platform, where duplicated entries will be removed. For  
142 articles where pre-screening inclusion (or exclusion) is unclear based on title and abstract analysis, full-text  
143 review will be used to make a decision following review by a third independent reviewer. Manuscripts  
144 included after title and abstract pre-screening will be further screening by two reviewers that will indepen-  
145 dently examine the full text of each article.

### 146 **9.5.2 Data Collection Process**

147 Pilot forms (electronic spreadsheets) will be tested using a representative sample of the studies to be  
148 reviewed (~100 studies). Information in the forms will be independently included by each reviewer. The  
149 forms will be updated (if needed), after the pilot test by consensus between the reviewers.

150 Information obtained from each study (statistical method used, software, etc.) will be tabulated indepen-  
151 dently by the reviewers in an electronic spreadsheet.

## 152 **9.6 Data Items**

153 Aims 1a and 1b:

154 Statistical method used, sub-area of application (oncology, psychology, public health, etc), computational  
155 tool used, congruence between statistical method used and the data, year of publication

156 Aim 2:

157 Statistical method reported, assumptions of the model, computational tools available for its implementation,  
158 year of publication

## 159 **9.7 Risk of Bias in Individual Studies**

160 N/A

## 161 **9.8 Data Synthesis**

162 The data from the results of each included study will be extracted into electronic spreadsheets. Summary  
163 measures for Aims 1a and 1b include plots (pie, bar, etc.) to show the relative use of each statistical  
164 method reported, computational tool, and congruence between statistical method and the data. Each plot  
165 will be segmented by year to show trends over time. Table 1 presents the headers of the pilot electronic  
166 spreadsheet.

167 The pilot electronic spreadsheet can be found in the following link: [Pilot Spreadsheet](#)

168 For Aim 2, a table will be created where statistical method, year of publication, assumptions of the model,  
169 and applicability to health data is reported.

## 170 **9.9 Meta-Biases**

171 N/A



## 10 References

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Table 1: Pilot spreadsheet for data extraction

DOI	Title	Subfield	Journal	Question	Country	Source of Result (Data)	Year	Statistical Method	Software	Model assumptions checked?	Data/Model Congruency?	Code available?	Notes
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