BMJ Open

Methods, Applications, Interpretations and Challenges of Interrupted Time Series (ITS) Data: Protocol for a Scoping Review

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2017-016018
Article Type:	Protocol
Date Submitted by the Author:	18-Jan-2017
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Primary Subject Heading:	Research methods
Secondary Subject Heading:	Geriatric medicine, Epidemiology
Keywords:	Interrupted time series, segmented regression, scoping review

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Methods, Applications, Interpretations and Challenges of Interrupted Time Series (ITS) Data: Protocol for a Scoping Review

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ABSTRACT

Objectives: Interrupted time series (ITS) design involves collecting data across multiple time points before and after the implementation of an intervention to assess the effect of the intervention on an outcome. ITS designs have become increasingly common in recent times with frequent use in assessing impact of evidence implementation interventions. Several statistical methods are currently available for analyzing data from ITS designs, however, there is a lack of guidance on which methods are optimal for different data types and on their implications in interpreting results. Our objective is to conduct a scoping review of existing methods for analyzing ITS data, to summarize their characteristics and properties, as well as to examine how the results are reported. We also aim to identify gaps and methodological deficiencies.

Methods and analysis: We will search electronic databases from inception until August 2016 (e.g., MEDLINE, and JSTOR). Two reviewers will independently screen titles, abstracts and full-text articles and complete the data abstraction. The anticipated outcome will be a summarized description of all the methods that have been used in analyzing ITS data in health research, how those methods were applied, their strengths and limitaitons and the transparency of interpretation/reporting of the results. We will provide summary tables of the characteristics of the included studies. We will also describe the similarities and differences of the various methods.

Ethics and dissemination: Ethical approval is not required for this study since we are just considering the methods used in the analysis and there will not be identifiable patient data. Results will be disseminated through open access peer-reviewed publications.

Strengths and Limitations of this Study

- Interrupted time series (ITS) is the strongest and most commonly utilized quasi-experimental design that is used to assess the effect of an intervention when randomization is not feasible.
- This review will be the first of its kind to provide a comprehensive overview of the methods available in the analysis of data obtained from ITS designs as well as provide characteristics of these current methods as applied in health research.
- The review is limited to articles published in English language.
- This review study will not assess the quality of the papers or the methods themselves.

Keywords: Interrupted time series, segmented regression, scoping review

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INTRODUCTION

Quasi-experimental designs, such as interrupted time series and regression discontinuity designs are alternative approaches to assess the effect of interventions in healthcare settings when randomization is impossible, unethical or notfeasible due to scarce resources [1]. Interrupted time series (ITS) is a robust quasi-experimental design and is most commonly utilized in implementation science to evaluate the impact of interventions such as quality improvement programs or policy changes [2, 3]. In ITS designs, data are collected before and after the implementation or introduction of an intervention to examine whether the intervention influenced the outcome of interest versus the underlying secular trend [4].

In recent times, ITS design has been increasingly common with several applications in clinical and health services research. For instance, the ITS method has been used in assessing the impact of a variety of evidence implementation strategies in different settings, which include assessing the effect of prevention programs, policy changes and quality improvement initiatives in hospitals [3,5,6,7,8]. ITS designs are included in Cochrane reviews done by the Effective Practice and Organisation of Care Review group [9].

There are several models for analyzing ITS data such as segmented regression analysis and ARIMA. Segmented regression or change-point model islikely the most common statistical method for analyzing data from ITS design [10]. In segmented regression analysis, a piece-wise regression is fitted to the data allowing each segment of the time series to exhibit different levels and trends. The effect of the intervention is then examined by comparing the slopes and intercepts for the pre- and post-intervention phases [11]. A change in the intercept or level constitutes an immediate intervention effect while a change in slope or trend implies an effect that was experienced over time. A change in trend also allows us to measure the sustainability of

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the impact of the intervention. Furthermore, segmented regression analysis enables analysts to control for other variables, other than the intervention, that can cause a change in level or trend of the outcome of interest [11].

Despite the various statistical methods that are available for analyzing ITS data, it is not clear which methods are optimal for the different data types and how using different analyses may affect results. As such, researchers and particularly, novice users of the ITS design are unaware of the various methods available. Thus, researchers often use methods such as segmented linear regression to analyze their ITS data, which can lead to spurious results and consequently unreliable conclusions about the effect of interventions. Commonly used methods for analyzing ITS data are often inappropriate when the data are aggregated per time point or the data are from a skewed distribution, and are often susceptible to aggregation bias, imprecision and loss of power [3,7]. It is therefore imperative that the various methods available for analyzing ITS data are identified to not only inform researchers of which methods are appropriate for different data types but also to inform future research such that the limitations and gaps of the current methods can be adequately addressed.

Our goal is thus to conduct a scoping review to examine the current methods used in ITS analysis, compare the methods and evaluate the appropriateness of the interpretation of findings based on the type of analyses performed. We aim to:

1. Identify and describe available methods used in ITS data analysis.
2. Describe the similarities and differences between the methods.
3. Describe the strengths and limitations of each method.
4. Provide a review of the application of the methods, that is how they are used, where they are used and the information they provide.

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5. Examine how results are reported and provide a comprehensive description of their interpretation
6. Identify gaps in methodology and provide direction for future research.

METHODS AND ANALYSIS

We will conduct a scoping review using the methods proposed by Arkley and O'Malley [12] and the Joanna Briggs Handbook for conducting systematic scoping reviews [13]. We will first perform a systematic literature search for health research studies that employed interrupted time series design and then use the methodological framework of Arkley and O'Malley to facilitate the identification of gaps and methodological deficiencies in the existing literature.

Search Strategy

For this study, an experienced information scientist helped to develop the search strategy which will be used to search electronic databases including MEDLINE, JSTOR, PUBMED, EMBASE, CINAHL, Web of Science and the CochraneLibrary from inception until August 2016 for relevant articles. Our electronic search will be supplemented by searching for published conference abstracts from relevant statistical conferences and contacting methodological experts in the field of ITS to identify difficult-to-locate or unpublished material. A draft of the literature search for MEDLINE can be found in Appendix A. The search strategy will be modified

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accordingly when necessary for other databases. Additionally, references of the included studies will be scanned for relevant articles.

Eligibility Criteria

All studies that report the development, application or comparison of methods employed in the analysis of ITS data will be included. To be included in the analysis, studies must have at least three time points before and after the intervention, have a clearly defined point in time when the intervention was implemented and the study outcomes must be measured objectively. This is in accordance with the Effective Practice and Organization of Care (EPOC) Cochrane Group definition of an ITS design [9]. There will be no restrictions on the publication status. We will exclude ITS studies that are not related to health research. We define health based on the WHO definition that is, complete mental, physical and social well-being (http://www.who.int/about/definition/en/print.html). Studies that were written in languages other than English will be excluded due to resource limitations. Review papers will be excluded but their references will be scanned for relevant articles.

Study Selection

We will import search results, screen citations and full text articles into Endnote X6 desktop version. A calibration exercise will be held prior to the commencement of screening of titles and abstracts to ensure reliability. For these pilot runs, each reviewer will screen a random sample of 50 citations for inclusion. Inter-rater agreement for study inclusion will then be calculated and a percentage agreement value >80% will imply we can commence screening. A value <80% will

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imply poor agreement and hence the eligibility criteria will be modified and clarified with the reviewers. A second pilot will be run with another random sample of 50 citations. This process will be repeated until we reach an agreement >80% and then the screening will begin. Each title and abstract will be screened independently by two reviewers (CS or EB and JEE) for inclusion using the eligibility criteria (Level 1 screening). This will be followed by full text screening of potentially relevant articles by the reviewers to determine inclusion using the same or modified eligibility criteria (Level 2 screening). If the eligibility criteria for level 2 are modified, a training session will be conducted prior to level 2 screening. Conflicts will be resolved by discussion or involvement of a third reviewer (JSH or JB). The PRISMA flow chart will be used to report study selection. A draft of the eligibility form can be found in Appendix B.

Data Abstraction

General study characteristics such as authorship and year of publication will be abstracted. Other characteristics will be abstracted based on the type of article. For instance, for methodological articles we will obtain the general description of the methods, the type of outcome (e.g. continuous, binary), and the similarities and differences of the methods either reported by the authors or based on our own perspective. For articles that report the use of an ITS design/analysis (application articles), data to be abstracted will include the characteristics of the study design (number of intervention phases, e.g. Pre-and Post-intervention for 2 phases), the rationale for using an ITS design/analysis, the statistical methods used, assumptions checked and approaches used to summarize the results. Examples used in methodological articles will be treated as separate applications and all relevant data will be extracted where necessary. A draft of the data abstraction form is found in Appendix C. The data abstraction form will be piloted on a

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random sample of 50 included studies and modified as required. The abstraction process will be completed by JEE in consultations with JSH.

Risk of bias appraisal

Since this is a scoping review, we will not appraise methodological quality or risk of bias of included studies [12].

Data Synthesis

For the descriptive analysis, information will be summarized based on the type of articles the data was extracted from. For the methods papers, we will narratively describe the method used for analysis, the assumptions made or tested, outcome data type such as continuous or binary, and applicability of the method to different outcomes of interest based on information provided by the authors, the data summarization process for appropriate ITS analysis as well as the similarities and differences between different methods.

For the application papers, we will summarise; the frequency of use of the method; the kind of data the method is applied to such as audit, and survey data; the setting in which the ITS design was implemented, such as hospitals or communities; and number of interruption times or phases of intervention.

In addition, we will evaluate results interpretation as well as the transparency of reporting of findings by assessing the information provided by the authors. This will include information on the different ways estimates obtained are reported and interpreted. The characteristics of the included studies will be provided using summary tables and matrix tables will also be created to

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compare the various ITS methods and the different ways of reporting and interpretation of findings based on how the data was summarized for analysis. Quantitative data such as the number of time points and number of patients per timepoint will be summarized by medians and IQRs and categorical data such as outcome data type will be summarized by frequencies and percentages. Finally, we will provide a summary of the methodological gaps that will be identified and highlight some potential areas for future research.

ETHICS AND DISSEMINATION

This is a scoping review of completed studies and hence no ethical approval is required. Quasi-experimental designs, such as ITS have been identified as the best alternative to investigate the impact of an intervention when randomization is not feasible and has been utilized several times in implementation science [1]. There have been several limitations that have been identified with the frequently used methods of analyzing data from ITS design making them suboptimal [3, 4, 7, 8]. For example, when segmented regression is applied to aggregated data where data at each time point is no longer observed but estimated and hence associated with imprecision. Additionally, although several methods exist, it is not clear which of the methods are optimal for different data types. Finding out the various methods available and when each method will be appropriate is necessary to ensure quality analysis of data since using different analyses may lead to different results.

This study will provide guidance on the appropriate methods to be used under different scenarios and thus strengthen the validity of research that utilizes ITS methods. Subsequently, we will identify methodological gaps for future research into various ways of improving ITS data

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analysis through both simulation and empirical studies. This review will be the first of its kind to provide a comprehensive overview of the methods available in the analysis of data obtained from quasi-experimental designs as well as provide characteristics of these current methods as applied in health research. Informed consent and ethical assessment was not required for this study since secondary data with non-identifiable individual patient data will be used.

This scoping review will be relevant not just to statisticians and methodologists but also to other stakeholders such as health professionals and policy makers, and most importantly those interested in implementation science.

Acknowledgement

The authors thank Mr. Andrew Colgoni for helping to develop the search strategy for the literature search.

Contributors

JEE, SES and JSH conceived and designed the study and helped write the draft protocol. JB and LT helped design the study and reviewed the protocol critically for intellectual content. EB and CS participated in data collection and edited the protocol. All authors have read and approved the final protocol.

Funding

This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests

None declared.

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APPENDIX A:

Database: Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) <1946 to Present>

Search Strategy:

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1 Interrupted Time Series Analysis.mp.

2 "change point model$".mp.

3 Interrupted Time Series Analysis/

4 (interrupt$ adj3 (time$ series$ or time-series)).mp.

5 (Interven$ adj3 (time$ series$ or time-series)).mp.

6 (segment$ adj2 regression$).mp.

7 ((time$ series$ or time-series) adj2 regression$).mp.

8 1 or 2 or 3 or 4 or 5 or 6 or 7

9 limit 8 to english language

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APPENDIX B:

ELIGIBILITY CRITERIA

Level 1 screening

1. Does this paper report on a method or application/review of ITS design or analysis?

YES____

NO____

UNCLEAR____

2. Is the study related to health as defined by the WHO (i.e., philosophy, health, education)?

YES____

NO____

UNCLEAR____

If you answer NO to any of these questions, the citation/study will be excluded. All other citations will be included.

Level 2 screening

1. Does this paper report on a method or application of ITS design or analysis?

Yes____

No____

Unclear____

2. Is the study related to health (i.e., philosophy, health, education)?

Yes____

No____

Unclear____

3. Is there a clearly defined time point when intervention was started or implemented?

Yes____

No____

Unclear____

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4. Are there at least three time points before and after implementation of intervention?

Yes____

No____

Unclear____

5. Was the study outcome objectively measured?

Yes____

No____

Unclear____

If you answer NO to any of these questions, the citation will be excluded. All other full-text articles will be included

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APPENDIX C:

DATA ABSTRACTION

General Study Characteristics

1. First author
2. Year of publication
3. Journal and type of journal (i.e., general or specialty)
4. Type of article (i.e. methodological or application)
5. Discipline
6. Title of Article
7. Key article or article complementary to a previously suggested method
8. Country
9. Sponsorship or funding source

Methodological papers:

1. Name of Method
2. General description of methods
3. Type of outcome.
4. Study type that the methodology is applicable to (only if this is clearly mentioned in the text)
5. Software used to implement method.
6. Were any assumptions made or tested?
7. Was the model validated? If so, how? How good was the performance of the model?
8. Was there a comparison of methods? What statistical methods were used to do the comparison?
9. Was the data management process reported?
10. Description of the data management process for the analysis

Application papers:

1. Discipline or field of application (pharmacy, guideline development, etc)
2. Description of study (e.g. number of interruptions)
3. Setting of study (e.g. single site, multi-site)
4. Analysis Method used
5. Number of time points in each phase
6. Type of primary outcome (Continuous, binary, count)
7. Number of outcomes

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8. Kind of data (audit, retrospective, survey)
9. Number of patients at each time point/period (if reported)
10. Assumptions tested or checked
11. Justification for performing ITS analysis
12. Methods and models used to estimate the effect of intervention
13. Approaches used reporting of summary estimates (e.g. figures, tables, text)

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ABSTRACT

Objectives: Interrupted time series (ITS) design involves collecting data across multiple time points before and after the implementation of an intervention to assess the effect of the intervention on an outcome. ITS designs have become increasingly common in recent times with frequent use in assessing impact of evidence implementation interventions. Several statistical methods are currently available for analyzing data from ITS designs, however, there is a lack of guidance on which methods are optimal for different data types and on their implications in interpreting results. Our objective is to conduct a scoping review of existing methods for analyzing ITS data, to summarize their characteristics and properties, as well as to examine how the results are reported. We also aim to identify gaps and methodological deficiencies.

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Ethics and dissemination: Ethical approval is not required for this study since we are just considering the methods used in the analysis and there will not be identifiable patient data. Results will be disseminated through open access peer-reviewed publications.

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- This review will be the first of its kind to provide a comprehensive overview of the methods available in the analysis of data obtained from ITS designs as well as provide characteristics of these current methods as applied in health research.
- The review is limited to articles published in English language.
- This review study will not assess the quality of the papers or the methods themselves.

Keywords: Interrupted time series, segmented regression, scoping review

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INTRODUCTION

Quasi-experimental designs are alternative approaches to assess the effect of interventions in healthcare settings when randomization is impossible, unethical or not feasible due to scarce resources [1]. Quasi experimental designs are divided into four study design groups namely: a) Quasi Experimental designs without control group b) Quasi experimental design with control groups but no pretest, c) Quasi experimental design with control groups and pretest and d) Interrupted time series designs. [2]

Interrupted time series (ITS) is a robust quasi-experimental design and is most commonly utilized in implementation science to evaluate the effect of interventions such as quality improvement programs or policy changes [2,3,4]. In ITS designs, data are collected before and after the implementation or introduction of an intervention to examine whether the intervention influenced the outcome of interest relative to the underlying secular trend [5] as well as competing non-contemporaneous interventions.

In recent times, ITS design has been increasingly common with several applications in clinical and health services research. For instance, the ITS method has been used in assessing the impact of a variety of evidence implementation strategies in different settings, which include assessing the effect of prevention programs, policy changes and quality improvement initiatives in hospitals [4,6,7,8,9]. ITS designs are included in Cochrane reviews done by the Effective Practice and Organisation of Care Review group [10].

There are several models for analyzing ITS data such as segmented regression analysis and ARIMA. Segmented regression or change-point model is likely the most common statistical method for analyzing data from ITS design [11]. In segmented regression analysis, a piece-wise regression is fitted to the data allowing each segment of the time series to exhibit different levels

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Despite the various statistical methods that are available for analyzing ITS data, it is not clear which methods are optimal for the different data types and how using different analyses may affect results. As such, researchers and particularly, novice users of the ITS design are unaware of the various methods available. Thus, researchers often use methods such as segmented linear regression to analyze their ITS data, which can lead to spurious results and consequently unreliable conclusions about the effect of interventions. Commonly used methods for analyzing ITS data are often inappropriate when the data are aggregated per time point or the data are from a skewed distribution, and are often susceptible to aggregation bias, imprecision and loss of power [4,8]. It is therefore imperative that the various methods available for analyzing ITS data are identified to not only inform researchers of which methods are available for different data types but also to inform future research such that the limitations and gaps of the current methods can be adequately addressed.

Our goal is thus to conduct a scoping review to identify the available methods used in ITS analysis, compare the methods in terms of their strengths and limitations and evaluate the application of the methods as well as identify the methodological gaps with the purpose of addressing the gaps. We aim to:

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1. Identify and describe available methods used in ITS data analysis.
2. Describe the similarities and differences between the methods.
3. Describe the strengths and limitations of each method.
4. Provide a review of the application of the methods, that is how they are used, where they are used and the information they provide.
5. Examine how results are reported and provide a comprehensive description of their interpretation
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METHODS AND ANALYSIS

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Eligibility Criteria

All studies that report the development, application or comparison of methods employed in the analysis of ITS data will be included. To be included in the analysis, studies must have at least three time points before and after the intervention, have a clearly defined point in time when the intervention was implemented or a definition of the time within which the intervention was rolled out since most interventions are rolled out over a period. Also, the study outcomes must be measured objectively. This criteria is in accordance with the Effective Practice and Organization of Care (EPOC) Cochrane Group definition of an ITS design [10]. There will be no restrictions on the publication status. We will exclude ITS studies that are not related to health research. We define health based on the WHO definition that is, complete mental, physical and social well-being (http://www.who.int/about/definition/en/print.html). Studies that were written in languages other than English will be excluded due to resource limitations. Review papers will be excluded but their references will be scanned for relevant articles.

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Data Abstraction

General study characteristics such as authorship and year of publication will be abstracted. Other characteristics will be abstracted based on the type of article. For instance, for methodological articles we will obtain the general description of the methods, the type of outcome (e.g. continuous, binary), and the similarities and differences of the methods either reported by the authors or based on our own perspective. For articles that report the use of an ITS

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design/analysis (application articles), data to be abstracted will include the characteristics of the study design (number of intervention phases, e.g. Pre-and Post-intervention for 2 phases), the rationale for using an ITS design/analysis, the statistical methods used, assumptions checked and approaches used to summarize the results. Examples used in methodological articles will be treated as separate applications and all relevant data will be extracted where necessary. A draft of the data abstraction form is found in Appendix C. The data abstraction form will be piloted on a random sample of 50 included studies and modified as required. The abstraction process will be completed by JEE in consultations with JSH.

Risk of bias appraisal

Since this is a scoping review, we will not appraise methodological quality or risk of bias of included studies [13].

Data Summary

For the descriptive analysis, information will be summarized based on the type of articles the data was extracted from. For the methods papers, we will narratively describe each of the methods used for analyses such as segmented linear regression and ARIMA, the assumptions made or tested, outcome data type such as continuous or binary, and applicability of the method to different outcomes of interest based on information provided by the authors, the data summarization process for appropriate ITS analysis as well as the similarities and differences between different methods.

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For the application papers, we will summarise; the frequency of use of the method; the kind of data the method is applied to such as audit, and survey data; the setting in which the ITS design was implemented, such as hospitals or communities; and number of interruption times or phases of intervention.

In addition, we will evaluate results interpretation as well as the transparency of reporting of findings by assessing the information provided by the authors. This will include information on the different ways estimates obtained are reported and interpreted. The characteristics of the included studies will be provided using summary tables and matrix tables will also be created to compare the various ITS methods and the different ways of reporting and interpretation of findings based on how the data was summarized for analysis. Quantitative data such as the number of time points and number of patients per timepoint will be summarized by medians and IQRs and categorical data such as outcome data type will be summarized by frequencies and percentages. Finally, we will provide a summary of the methodological gaps that will be identified and highlight some potential areas for future research.

ETHICS AND DISSEMINATION

This is a scoping review of completed studies and hence no ethical approval is required. Quasi-experimental designs, such as ITS have been identified as the best alternative to investigate the effect of an intervention when randomization is not feasible and has been utilized several times in implementation science [1]. There have been several limitations that have been identified with the frequently used methods of analyzing data from ITS design making them suboptimal [4,5,8,9]. For example, when segmented regression is applied to aggregated data where data at

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each time point is no longer observed but estimated and hence associated with imprecision. Additionally, although several methods exist, it is not clear which of the methods are optimal for different data types. Finding out the various methods available and when each method will be appropriate is necessary to ensure quality analysis of data since using different analyses may lead to different results.

This study will provide detailed information on the available methods used under different scenarios and thus strengthen the validity of research that utilizes ITS methods. Subsequently, we will identify methodological gaps for future research into various ways of improving ITS data analysis through both simulation and empirical studies. Thus, this review will serve as a ground work towards developing a guidance manuscript or book on methods for ITS analysis. This review will be the first of its kind to provide a comprehensive overview of the methods available in the analysis of data obtained from quasi-experimental designs as well as provide characteristics of these current methods as applied in health research. Informed consent and ethical assessment was not required for this study since secondary data with non-identifiable individual patient data will be used.

This scoping review will be relevant not just to statisticians and methodologists but also to other stakeholders such as health professionals and policy makers, and most importantly those interested in implementation science.

Acknowledgement

The authors thank Mr. Andrew Colgoni for helping to develop the search strategy for the literature search.

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Contributors

JEE, SES and JSH conceived and designed the study and helped write the draft protocol. JB and LT helped design the study and reviewed the protocol critically for intellectual content. EB and CS participated in data collection and edited the protocol. All authors have read and approved the final protocol.

Funding

This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests

None declared.

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APPENDIX A:

Database: Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) <1946 to Present>
Search Strategy:
---

1 Interrupted Time Series Analysis.mp.

2 "change point model$".mp.

3 Interrupted Time Series Analysis/

4 (interrupt$ adj3 (time$ series$ or time-series)).mp.

5 (Interven$ adj3 (time$ series$ or time-series)).mp.

6 (segment$ adj2 regression$).mp.

7 ((time$ series$ or time-series) adj2 regression$).mp.

8 1 or 2 or 3 or 4 or 5 or 6 or 7

9 limit 8 to english language

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APPENDIX B:

ELIGIBILITY CRITERIA

Level 1 screening

1. Does this paper report on a method or application/review of ITS design or analysis?

YES____

NO____

UNCLEAR____

2. Is the study related to health as defined by the WHO (i.e., philosophy, health, education)?

YES____

NO____

UNCLEAR____

If you answer NO to any of these questions, the citation/study will be excluded. All other citations will be included.

Level 2 screening

1. Does this paper report on a method or application of ITS design or analysis?

Yes____

No____

Unclear____

2. Is the study related to health (i.e., philosophy, health, education)?

Yes____

No____

Unclear____

3. Is there a clearly defined time point when intervention was started or implemented?

Yes____

No____

Unclear____

4. Are there at least three time points before and after implementation of intervention?

Yes____

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No____

Unclear____

5. Was the study outcome objectively measured?

Yes____

No____

Unclear____

If you answer NO to any of these questions, the citation will be excluded. All other full-text articles will be included

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APPENDIX C:

DATA ABSTRACTION

General Study Characteristics

1. First author
2. Year of publication
3. Journal and type of journal (i.e., general or specialty)
4. Type of article (i.e. methodological or application)
5. Discipline
6. Title of Article
7. Key article or article complementary to a previously suggested method
8. Country
9. Sponsorship or funding source

Methodological papers:

1. Name of Method
2. General description of methods
3. Type of outcome.
4. Study type that the methodology is applicable to (only if this is clearly mentioned in the text)
5. Software used to implement method.
6. Were any assumptions made or tested?
7. Was the model validated? If so, how? How good was the performance of the model?
8. Was there a comparison of methods? What statistical methods were used to do the comparison?
9. Was the data management process reported?
10. Description of the data management process for the analysis

Application papers:

1. Discipline or field of application (pharmacy, guideline development, etc)
2. Description of study (e.g. number of interruptions)
3. Setting of study (e.g. single site, multi-site)
4. Analysis Method used
5. Number of time points in each phase
6. Type of primary outcome (Continuous, binary, count)
7. Number of outcomes
8. Kind of data (audit, retrospective, survey)
9. Number of patients at each time point/period (if reported)
10. Assumptions tested or checked
11. Justification for performing ITS analysis

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12. Methods and models used to estimate the effect of intervention
13. Approaches used reporting of summary estimates (e.g. figures, tables, text)

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