


Interrupted time series designs in healthcare: systematic review

Protocol version: 1

Protocol Date: 9th February 2016

PhD Student

Jemma Hudson

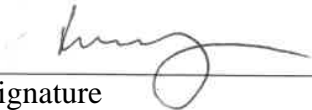

Signature

9th February 2016

Date

Supervisor

Craig Ramsay

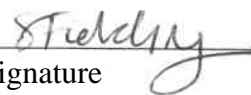

Signature

9th February 2016

Date

Supervisor

Shona Fielding


Signature

9th February 2016

Date

Version history

Amendment No.	Protocol version No.	Description of changes	Date of protocol
	Version 1	New document	

Background

Interrupted time series (ITS) are considered one of the strongest quasi-experimental designs and can be used to evaluate a variety of interventions (e.g., national guidelines, health policies, educational programs). ITS designs monitor a certain unit (e.g. population) over a period of time pre-and post-implementation of an intervention. The aim of this review is to find out how ITS studies are being reported and used in the health care setting.

Search Strategy

An electronic search will be undertaken to identify studies that have used ITS methods in MEDLINE. The search will be limited to 2015 with no language restrictions. The search strategy will mainly consist of text words and phrases using truncation symbols and adjacency operators. A detailed search strategy is documented in Appendix 1.1. Of the abstracts found, ten percent will be double assessed for inclusion and any disagreement will be resolved.

Inclusion and Exclusion Criteria

Types of studies

ITS studies will be eligible for inclusion if there is a minimum of two data points collected pre-intervention period and one post-intervention. Systematic reviews, meta-analyses, randomized trials, and studies with a separate control group will be excluded. There was no restriction on the language of study.

Types of participants

This review will have no restrictions on participants.

Types of interventions

Interventions that are associated with health and the healthcare of patients will be eligible. This could be for instance, a program to prevent infection, policies on antibiotic use, clinical or educational.

Types of outcomes

There will be no restrictions on the types of outcomes that can be included in this review.

A screening form (Appendix 1.2) will be used to identify studies that will be included in the review.

Data Extraction Strategy

Full-text copies of the titles and abstracts found eligible at the search strategy stage will be screened and assessed for inclusion by the inclusion and exclusion criteria. Ten percent of these title and abstracts will be doubled assessed and any disagreements will be resolved.

A data extraction form (Appendix 1.3) will record relevant details of the studies. For example, type of intervention; how many data points collected pre-and post-intervention; country of study; method of analysis; did they define a transition period. This form will be piloted on a randomly selected few first to check all the necessary data are being recorded.

Quality Assessment Strategy

Not required, as sections of the PhD will cover this.

Data Synthesis

If studies have multiple publications or corrections, then only the most up-to-date report will be used. Summary descriptions of the extracted data will be reported, either in tabular or graphical form (e.g., years of publications, population level and type of intervention.). The data will also be broken down by intervention type and descriptions reported to see if there are any differences (see Appendix 1.4 for dummy figures and tables).

Appendix 1.1: Search strategy

1. interrupted time series.tw,kw.
2. (pre adj1 post).tw.
3. (segmented adj3 regression).tw,kw.
4. quasi experiment\$.tw,kw.
5. (before adj1 after).tw,kw.
6. arima.tw,kw.
7. (trend adj3 analys?s).tw,kw.
8. (longitudinal adj3 chang\$).tw,kw.
9. autoregressive integrated moving average.tw,kw.
10. or/1-9
11. limit 10 to yr='2015'
12. randomi\$ control\$ trial\$.ti,tw.
13. meta analys\$.ti,kw.
14. limit 11 to "review articles"
15. 11 not (12 or 13 or 14)

Appendix 1.2: Screening form

1. Is the study a systematic review/meta-analysis?
 - Yes → Exclude
 - No

a. If yes, was the review of interrupted time series studies/methods?
 - Yes
 - No
2. Did the study collect a minimum of two data points before and one after the intervention?
 - Yes
 - No → Exclude
 - Unsure
3. Did the study use an ITS analysis?
 - Yes
 - No → Exclude
 - Unsure
4. Does the study have a separate control/comparison group?
 - Yes → Exclude
 - No
 - Unsure
5. Is the intervention in health or healthcare?
 - Yes
 - No → Exclude
 - Unsure
6. Is the study to be included in the review?
 - Yes
 - No

Appendix 1.3: Data extraction form

Study ID (<i>surname of first author and year first full report of study was published</i>)
Report IDs of other reports of this study (<i>e.g. duplicate publications, follow-up studies</i>)

Eligibility – review inclusion criteria	
Did the study collect a minimum of two data points before and one after the intervention?	<input type="checkbox"/> Yes <input type="checkbox"/> No
Did the study use ITS analysis?	<input type="checkbox"/> Yes <input type="checkbox"/> No
Does the study have a separate control/comparison group?	<input type="checkbox"/> Yes <input type="checkbox"/> No
Is the intervention in the health or healthcare?	<input type="checkbox"/> Yes <input type="checkbox"/> No
Is it a full text paper?	<input type="checkbox"/> Yes <input type="checkbox"/> No
Decision	<input type="checkbox"/> Include <input type="checkbox"/> Exclude

<i>Publication characteristics</i>		<i>Page/Table/ Figure</i>
What did the authors define the design as in the title?	<input type="checkbox"/> Interrupted time series <input type="checkbox"/> Time series <input type="checkbox"/> Before and after <input type="checkbox"/> Controlled before and after <input type="checkbox"/> Change analysis <input type="checkbox"/> Regression analysis <input type="checkbox"/> Change point <input type="checkbox"/> Time series regression analysis <input type="checkbox"/> Other, please specify: <input type="checkbox"/> None	
Is the paper published in one of the top four journals?	<input type="checkbox"/> Yes <input type="checkbox"/> No	
Language of study		
Reference to protocol	<input type="checkbox"/> Yes <input type="checkbox"/> No	
Funding source statement	<input type="checkbox"/> Yes <input type="checkbox"/> No	
Country of study		

<i>Study design</i>		<i>Page/Table/ Figure</i>
Were the study objectives defined?	<input type="checkbox"/> Yes <input type="checkbox"/> No	
Was a background/rationale given for doing a ITS study?	<input type="checkbox"/> Yes <input type="checkbox"/> No <ul style="list-style-type: none"> • If yes, what was the reason? <ul style="list-style-type: none"> <input type="checkbox"/> Practical <input type="checkbox"/> Ethical <input type="checkbox"/> Natural experiment (no control over the intervention) <input type="checkbox"/> No adequate control group <input type="checkbox"/> Other, please specify: 	
How many interruptions (interventions) are there across multiple time points?		

Outcome	<input type="checkbox"/> Primary only <input type="checkbox"/> Primary and secondary <input type="checkbox"/> Not specified	
Questions below correspond to the primary outcome or the first reported		
Type of intervention	<input type="checkbox"/> Policy/programs <input type="checkbox"/> Guidelines <input type="checkbox"/> Financial <input type="checkbox"/> Health systems <input type="checkbox"/> Behavioural <input type="checkbox"/> Sales and dispensing <input type="checkbox"/> Other, please specify:	
Level of intervention	<input type="checkbox"/> Individual <input type="checkbox"/> Organisational <input type="checkbox"/> Groups, please specify: <input type="checkbox"/> Large scale/population <input type="checkbox"/> Multiple countries <input type="checkbox"/> Other, please specify:	
Participants: who was the target group/recipient?	Population based on: <input type="checkbox"/> Disease (patients) <input type="checkbox"/> Demographic <input type="checkbox"/> Occupational <input type="checkbox"/> Health professionals <input type="checkbox"/> Population <input type="checkbox"/> Other, please specify:	
Study design description	<input type="checkbox"/> Interrupted time series <input type="checkbox"/> Time series <input type="checkbox"/> Before and after <input type="checkbox"/> Controlled before and after <input type="checkbox"/> Change analysis <input type="checkbox"/> Regression analysis <input type="checkbox"/> Change point <input type="checkbox"/> Time series regression analysis <input type="checkbox"/> Other, please specify: <input type="checkbox"/> None	

All further questions relate to the primary outcome or the first outcome reported.

<i>Methodology characteristics</i>		<i>Page/Table/ Figure</i>
Temporal design	<input type="checkbox"/> Retrospective (i.e. identification of subjects from past records) <input type="checkbox"/> Prospective (i.e. recruitment of subjects before any intervention)	
Were the investigators in control of the interruption/intervention?	<input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Not stated	
Unit of intervention	<input type="checkbox"/> Country <input type="checkbox"/> Region <input type="checkbox"/> Individuals <input type="checkbox"/> Household <input type="checkbox"/> Community <input type="checkbox"/> Company <input type="checkbox"/> Hospital/healthcare practice <input type="checkbox"/> Department <input type="checkbox"/> Ward <input type="checkbox"/> Other, please specify:	
Number of units		
Number of sites		
Type of outcome	<input type="checkbox"/> Binary <input type="checkbox"/> Continuous <input type="checkbox"/> Rate <input type="checkbox"/> Other, please specify:	

<i>Data collection</i>		<i>Page/Table/ Figure</i>
Data Source	<input type="checkbox"/> Hospital data <input type="checkbox"/> National data <input type="checkbox"/> Health records <input type="checkbox"/> Patient self-reported <input type="checkbox"/> Other, please specify:	
What was the frequency of the data collection?	<input type="checkbox"/> Yearly <input type="checkbox"/> Quarterly <input type="checkbox"/> Monthly <input type="checkbox"/> Weekly <input type="checkbox"/> Other, please specify:	
How many data points in the pre intervention period?		
How many data points in the post intervention period?		
How many data points were included in a transition period?		
How many data points were included in other time periods apart from the transition period?		

<i>Statistical analysis</i>		<i>Page/Table/ Figure</i>
Was there a description of the analysis?	<input type="checkbox"/> Yes <input type="checkbox"/> No • If yes, what was the method? <input type="checkbox"/> Segmented regression <input type="checkbox"/> ARIMA <input type="checkbox"/> GEE <input type="checkbox"/> Other, please specify:	
Was autocorrelation considered?	<input type="checkbox"/> Yes <input type="checkbox"/> No • If yes, what was the method used to identify autocorrelation? <input type="checkbox"/> Durbin Watson test <input type="checkbox"/> ACF <input type="checkbox"/> PACF <input type="checkbox"/> Other, please specify: • If yes, was autocorrelation present? <input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Not stated • If yes, what method was used to adjust for autocorrelation?: If yes, what order was the autocorrelation?:	
Was nonstationary considered?	<input type="checkbox"/> Yes <input type="checkbox"/> No • If yes, was it present? <input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Not stated If yes, what was the method used to adjust for it?:	
Was seasonality considered?	<input type="checkbox"/> Yes <input type="checkbox"/> No • If yes, was it present? <input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Not stated If yes, what was the method used to adjust for it?:	

Were covariates adjusted for?	<input type="checkbox"/> Yes <input type="checkbox"/> No	
Was the unit of analysis the same as the unit of intervention?	<input type="checkbox"/> Yes <input type="checkbox"/> No <ul style="list-style-type: none"> • If no, what was the unit of analysis? <ul style="list-style-type: none"> <input type="checkbox"/> Country <input type="checkbox"/> Region <input type="checkbox"/> Individuals <input type="checkbox"/> Household <input type="checkbox"/> Community <input type="checkbox"/> Company <input type="checkbox"/> Hospital/healthcare practice <input type="checkbox"/> Department <input type="checkbox"/> Ward <input type="checkbox"/> Other, please specify: 	
Was there a sample size calculation undertaken?	<input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> No formal calculation <ul style="list-style-type: none"> • Was there a rationale to the sample size used? <ul style="list-style-type: none"> <input type="checkbox"/> Yes <input type="checkbox"/> No 	
Was there a description of how missing data will be handled?	<input type="checkbox"/> Yes, please specify: <input type="checkbox"/> No	
Which period was the intervention time point included?	<input type="checkbox"/> Pre <input type="checkbox"/> Post <input type="checkbox"/> Not included <input type="checkbox"/> Not clear	
Was the statistical software used reported?	<input type="checkbox"/> Yes <input type="checkbox"/> No	
Was a transition period used in the primary analysis?	<input type="checkbox"/> Yes <input type="checkbox"/> No <ul style="list-style-type: none"> • Was an explanation given to why there was or was not a transition period? <ul style="list-style-type: none"> <input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Limited • Where the points included in the model <ul style="list-style-type: none"> <input type="checkbox"/> Yes 	

	<input type="checkbox"/> No	
Apart from the transition period, was there any time period within the study accounted for?	<input type="checkbox"/> Yes, please specify: <input type="checkbox"/> No <ul style="list-style-type: none"> • Where the points included in the model <input type="checkbox"/> Yes <input type="checkbox"/>No 	
Was a sensitivity analysis carried out?	<input type="checkbox"/> Yes <input type="checkbox"/> No What was the analysis? <ul style="list-style-type: none"> • Transition period <input type="checkbox"/>Yes <input type="checkbox"/>No • Where the time points included in the model? <input type="checkbox"/>Yes <input type="checkbox"/>No • Shape of the pre-intervention line investigated? <input type="checkbox"/>Yes <input type="checkbox"/>No • Was any other period apart from the transition period accounted for? <input type="checkbox"/>Yes <input type="checkbox"/>No • Where the time points included in the model? <input type="checkbox"/>Yes <input type="checkbox"/>No • Subgroup analysis? <input type="checkbox"/>Yes, please specify: <input type="checkbox"/>No 	

Results		Page/Table/ Figure
Were the characteristics of the unit of intervention reported?	<input type="checkbox"/> Yes <input type="checkbox"/> No	
Missing Data	<p>Was the number of units the same in the pre and post period?</p> <input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Not clear <p>Was there a description of how missing data was handled?</p> <input type="checkbox"/> Yes, please specify: <input type="checkbox"/> No <input type="checkbox"/> Not relevant	
Are there any outliers?	<input type="checkbox"/> Yes <input type="checkbox"/> No	
Are results presented graphically?	<input type="checkbox"/> Yes <input type="checkbox"/> No <ul style="list-style-type: none"> • Is the quality good enough for data to be extracted? <input type="checkbox"/> Yes <input type="checkbox"/> No	
How are the numeric figures reported?	<input type="checkbox"/> Absolute <input type="checkbox"/> Relative change(s) <input type="checkbox"/> Other, please specify: <ul style="list-style-type: none"> • How were they calculated? <input type="checkbox"/> Relative to last pre point <input type="checkbox"/> Relative to average baseline period <input type="checkbox"/> Baseline <input type="checkbox"/> Not stated <input type="checkbox"/> Other, please specify:	
Are effect sizes reported?	<input type="checkbox"/> AUC <input type="checkbox"/> Change in level, please specify if its immediate change or any other period of change: <input type="checkbox"/> Change in slope <input type="checkbox"/> Decay effect <input type="checkbox"/> Intercept <input type="checkbox"/> Pre intervention slope <input type="checkbox"/> Other, please specify:	

Are confidence intervals given?	<input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Some	
Are standard deviations reported?	<input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Some	
Are p-values reported?	<input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Some <ul style="list-style-type: none"> • If yes or some how are they reported? <input type="checkbox"/>Exact values <input type="checkbox"/>Only an indication if they were significant or not 	

<i>Discussion</i>		<i>Page/Table/ Figure</i>
Are key results summarized with reference to the relevant objectives?	<input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Some	
Was there a discussion/statement of any other interventions/events that could have impacted the results?	<input type="checkbox"/> Yes <input type="checkbox"/> No	
Was there a discussion of stability of unit of intervention (e.g. ward, region) characteristics over time?	<input type="checkbox"/> Yes <input type="checkbox"/> No	
Were outliers discussed and the potential implications this could have?	<input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> No indication of outliers	
Was potential bias discussed?	<input type="checkbox"/> Yes <input type="checkbox"/> No	
Were weaknesses/limitations discussed?	<input type="checkbox"/> Yes <input type="checkbox"/> No	
Were strengths discussed?	<input type="checkbox"/> Yes <input type="checkbox"/> No	
Was an overall interpretation of results given considering all of the findings?	<input type="checkbox"/> Yes <input type="checkbox"/> No	

<i>Title/ Abstract</i>	
Was the intervention clearly defined?	<input type="checkbox"/> Yes <input type="checkbox"/> No
Was the design of the study clearly defined?	<input type="checkbox"/> Yes <input type="checkbox"/> No
Was the method of analysis given?	<input type="checkbox"/> Yes <input type="checkbox"/> No
Was the number of pre-intervention time points reported?	<input type="checkbox"/> Yes <input type="checkbox"/> No
Was the number of post-intervention time points reported?	<input type="checkbox"/> Yes <input type="checkbox"/> No
Was the main results reported?	<input type="checkbox"/> Yes <input type="checkbox"/> No
Was the impact of the intervention discussed?	<input type="checkbox"/> Yes <input type="checkbox"/> No

Appendix 1.4: Dummy figures and tables

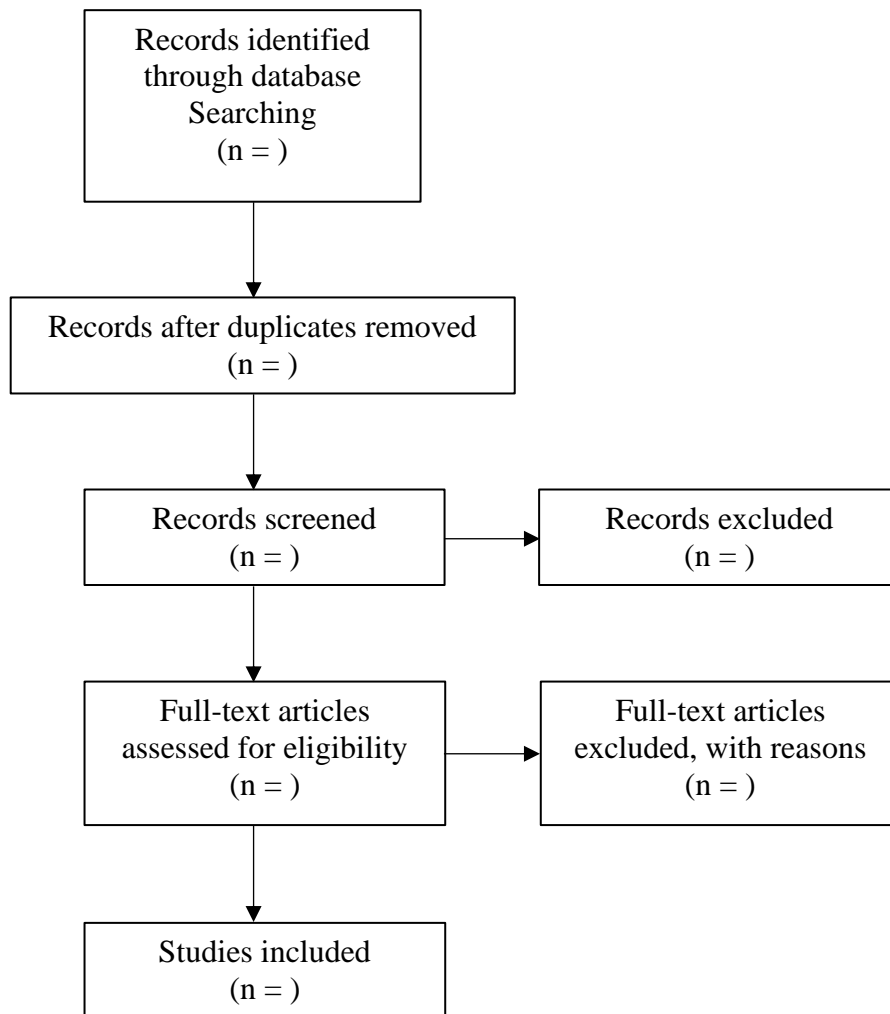


Figure 1. Flow diagram

Table 1. Publication Characteristics

	N =
Top four journal	
Language of study	
English	
French	
⋮	
Country of study	
UK	
USA	
Australia	
⋮	
Definition of study design in the title:	
Interrupted time series	
Time series	
Before and after	
Controlled before and after	
Change analysis	
Regression analysis	
Change point	
Time series regression analysis	
Other	
None	
Funding Source statement	
Protocol referenced	

Values are numbers and percentages

Table 2. Study Design

	N =
The study objectives defined	
Background/rationale given for doing a ITS study	
Outcomes	
Primary only	
Primary and secondary	
Not specified	
The number of interruptions (interventions) across multiple time points	
One	
Two	
Three	

Values are numbers and percentages

Tables below correspond to the primary outcome or the first reported outcome

Table 3. Study Design continued

	N=
Type of intervention	
Policy/programs	
Guidelines	
Financial	
Behavioural	
Screening	
Sales and dispensing	
Other	
Level of intervention	
Individual	
Organisational	
Groups	
Large scale/population	
Multiple countries	
Other	
Target population	
Disease (patients)	
Demographic	
Occupational	
Health professionals	
Population	
Other	
Study design description	
ITS	
Time series	
Time series regression	
Before and after	
Controlled before and after	
Change analysis	
Regression analysis	
Change point	
Time series regression analysis	
Other	
None	

Values are numbers and percentages

Table 4. Methodological Characteristics

	N =
Temporal design	
Retrospective	
Prospective	
Investigators were in control of the intervention?	
Unit of intervention	
Country	
Region	
Household	
Community	
Hospital/healthcare practice	
Department	
Ward	
Other	
Number of units	
Number of sites	
Type of outcome	
Binary	
Continuous	
Rate	
Other	

Values are numbers and percentages

Table 5. Data collection

	N=
Data source	
Hospital data	
National data	
Health records	
Patient self-reported	
Other	
Frequency of data points	
Yearly	
Quarterly	
Monthly	
Weekly	
Other	
Pre-intervention period data points	
Post-intervention period data points	
Data points in the transition period	
Data points in other time periods used apart from the transition period	

Values are numbers and percentages or median (interquartile range), range

Table 6. Statistical analysis

	N=
A description of the analysis	
The method used	
Segmented regression	
ARIMA	
GEE	
Other	
Autocorrelation was considered	
Method used to identify autocorrelation	
Durbin Watson test	
ACF	
PACF	
Autocorrelation present	
Yes	
No	
Not stated	
Method used to adjust for	
Autocorrelation	
The order of the autocorrelation	
One	
Two	
Nonstationary was considered	
Nonstationary was present	
Method used for nonstationary	
Seasonality was considered	
Seasonality was present	
Method used to account for seasonality	
Covariates adjusted for	
Unit of analysis the same as the unit of intervention	
The unit of analysis if not the same	
Country	
Region	
Individuals	
Department	
:	
A sample size was undertaken	
Yes	
No	
No formal calculation	
A rationale to the sample size used	
A description of how missing data was handled	
The period the intervention time point was included	
Pre	
Post	
:	
Description of the statistical software used	
The transition period was used in the primary analysis	
Explanation for a transition period	
Yes	

No Limited Other time period used that were not a transition period Sensitivity analysis carried out Transition period Shape of pre-intervention line Other periods excluded apart from the transition period Subgroup analysis	
--	--

Values are numbers and percentages

Table 7. Results

	N=
Characteristics of the unit of intervention reported Missing Data Number of units in the pre and post period the same Yes No Not clear Description of the missing data Yes No Not relevant Outliers Graph of results Quality good enough Figures reported Absolute Relative Both Other The calculation of relative Relative to last pre point Baseline : Effect sizes reported AUC Change in level Change in slope : Confidence intervals reported Standard deviations reported p-values reported Reported as Exact Only an indication of significance	

Values are numbers and percentages

Table 8. Discussion

	N=
Key results summarised with reference to objectives	
Discussion/statement of any other interventions/events that could have impacted results	
Stability of the characteristics of the unit of intervention over time	
Outliers and there potential implications	
Bias	
Weaknesses/limitations	
Strengths	
Over interpretation of results	

Values are numbers and percentages

Table 9. Title/Abstract

	N=
Intervention clearly defined	
Design of the study clearly defined	
Method of analysis	
Number of pre-intervention time points stated	
Number of post-intervention time points stated	
Main results reported	
Impact of intervention discussed	

Values are numbers and percentages

Table 10. Number of time points

	Number of time points
Method of analysis	
Segmented regression	
ARIMA	
GEE	
Temporal design	
Retrospective	
Prospective	
Investigators in control of the intervention	
Data source	
Hospital data	
National data	
Health records	
Patient self-reported	
Sample size calculation used	
Frequency of data collection	
Yearly	
Quarterly	
Monthly	

Weekly	
Other	

Values are median, interquartile range, range

Table 11. Method of analysis and what was considered

Method of analysis	Autocorrelation	Nonstationary	Seasonality
Segmented regression			
ARIMA			
GEE			
⋮			

Values are numbers and percentages

Table 12. The number of time points and the use of a transition period

Time points	Transition period
< 6	
6-10	
11-20	
21-30	
31-40	
> 41	

Values are numbers and percentages

Table 13. Frequency of data points and was seasonality adjusted for

Frequency	Seasonality
Yearly	
Quarterly	
Monthly	
Weekly	
Other	

Values are numbers and percentages

Table 14. Study design description and the method of analysis

	Segmented regression	ARIMA	GEE	Other
ITS				
Time series				
Before and after				
Control before and after				
Change analysis				
Regression analysis				
Change point				
Time series regression analysis				
Other				