Use of interrupted time series methods in the evaluation of health system quality improvement interventions: a methodological systematic review

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SUPPLEMENTAL MATERIALS

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Appendix Table 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	4
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	5
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	9
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	10
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	10
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	10
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	10
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	10

Section/topic	#	Checklist item	Reported on page #
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	10 &11
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	10 & 11
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	11 & 12
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	N/A
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	N/A
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	N/A
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	N/A
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	13
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	13
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	N/A
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	N/A
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	N/A

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	15
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	N/A
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	16 & 17
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	17 & 18
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	18
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	N/A

Appendix Table 2. Sample of the search strategy used in the MEDLINE database

Database: Ovid MEDLINE(R) Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) <1946 to Present> Search Strategy: ----------	
1	Interrupted Time Series Analysis/ (443)
2	Interrupted Time Series Analysis.mp. (985)
3	ITS Studies.mp. (107)
4	Interrupted Time Series.mp. (2288)
5	Trend analys*.mp. (3531)
6	Time trend*.mp. (7620)
7	Time series analys*.mp. (5413)
8	Time series.mp. (25183)
9	Segmented regression.mp. (448)
10	Piecewise regression.mp. (169)
11	Broken-stick regression.mp. (10)
12	OR/1-11 (35661)
13	Quality Improvement/ (17089)
14	Quality Improvement.mp. (39797)
15	Quality Assurance, Health Care/ (53974)
16	exp Clinical Audit/ (21203)
17	(quality* adj3 (care or healthcare)).mp. (176290)
18	Quality Indicators, Health Care/ (13870)
19	"Outcome and Process Assessment (Health Care)"/ (25060)
20	(Quality adj1 (assurance or control)).ti,ab. (59520)
21	OR/13-20 (284722)
22	12 and 21 (1149)
23	Limit 22 to humans (929)

Appendix Table 3. Data elements included in the standardized data extraction form

ITS review standardized data extraction form
1. Bibliometrics
a. Publication title
b. Authors
c. Publication year
d. Journal
e. Country of affiliation for corresponding author
2. ITS design reported in the title or abstract
3. Background / Rationale
4. Study objective(s)
5. Intervention (s) of interest (Type of QI strategy)
a. Provider reminder systems
b. Facilitated relay of clinical data to providers
c. Audit and feedback
d. Provider education
e. Patient education
f. Patient reminder systems
g. Promotion of self-management
h. Organizational change
i. Financial incentives, regulation, and policy
6. Description of the intervention
7. Methodological details
a. Study setting
i. Country
ii. Multisite/scale
b. Study period
c. Study population
i. Cohort definition
ii. Inclusion criteria
iii. Sample size
d. Data sources
i. Source
ii. Time intervals
iii. Data collected regularly
iv. Outcome measure (s)
v. Format of outcome (s)
e. Individual vs aggregate
f. Specified ITS impact model
g. Type of ITS models used (e.g., segmented regression, ARIMA)
h. Methodological considerations reported:

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i. Autocorrelation
ii. Nonstationarity
iii. Seasonality
iv. Use of comparison group
v. Time points (cleared defined)
vi. Number of pre-intervention data points
vii. Number of post intervention data points
viii. Outliers
ix. Forecasting
x. Absolute/relative changes with CI or standard errors
xi. Other considerations:
1. Use of lag periods
2. Sensitivity analyses
3. Statistical software reported
8. Results
a. Participants
i. Number and characteristics in each group analyzed?
ii. Indicated missing data?
b. Outcomes
i. Report all outcomes examined over the study period?
ii. Level/trend changes or comparison of observed vs expected?
iii. Report CI or SE?
c. Graphical figures to display results?
d. Results of sensitivity analyses if done?
e. Report outliers, ceiling or floor effects where relevant
9. Discussion
a. Reported key results
b. Discussed context (related to possible confounding)
c. Discussed relevant co-interventions during the study period
d. Commented on the stability of participant characteristics over time
e. Commented on the stability of outcome coding over time
f. Discussed limitations of the study
g. Commented on data variability and appropriateness of the number of data points
h. Commented on ceiling or floor effects or outliers if relevant
i. Discussed direction and magnitude of any potential bias

Appendix Table 4. Assessing risk of bias in ITS studies.[1-3]

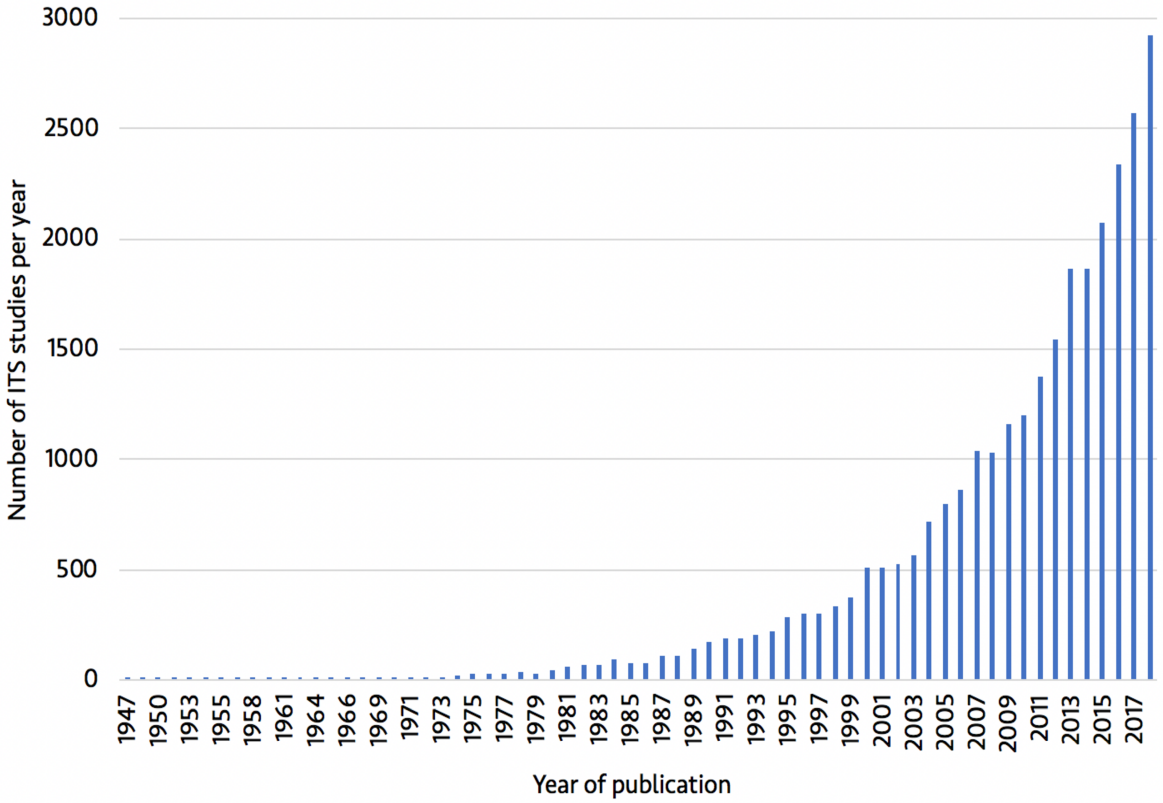
Criteria	Risk of Bias Scoring Criteria
1. Was the intervention independent of other changes?	Score "Low risk" if there are compelling arguments that the intervention occurred independently of other changes over time and the outcome was not influenced by other confounding variables/historic events during study period. If Events/variables identified, note what they are. Score "High risk" if reported that intervention was not independent of other changes in time.
2. Was the shape of the intervention effect pre-specified?	Score "Low risk" if point of analysis is the point of intervention OR a rational explanation for the shape of intervention effect was given by the author(s). Where appropriate, this should include an explanation if the point of analysis is NOT the point of intervention. Score "High risk" if it is clear that the condition above is not met.
3. Was the intervention unlikely to affect data collection?	Score "Low risk" if reported that intervention itself was unlikely to affect data collection (for example, sources and methods of data collection were the same before and after the intervention); Score "High risk" if the intervention itself was likely to affect data collection (for example, any change in source or method of data collection reported).
4. Was the primary outcome measured objectively?	Score "Low risk" if the authors state explicitly that the primary outcome variables were assessed blindly, or the outcomes are objective, e.g. length of hospital stay. Primary outcomes are those variables that correspond to the primary hypothesis or question as defined by the authors. Score "High risk" if the outcomes were not assessed blindly. Score "Unclear risk" if not specified in the paper.
5. Were incomplete outcome data adequately addressed if applicable?	Score "Low risk" if missing outcome measures were unlikely to bias the results (e.g. the proportion of missing data was similar in the pre- and post-intervention periods or the proportion of missing data was less than the effect size i.e. unlikely to overturn the study result). Score "High risk" if missing outcome data was likely to bias the results. Score "Unclear risk" if not specified in the paper (Do not assume 100% follow up unless stated explicitly).
6. Was the study free of selective outcome reporting?	Score "Low risk" if there is no evidence that outcomes were selectively reported (e.g. all relevant outcomes in the methods section are reported in the results section). Score "High risk" if some important outcomes are subsequently omitted from the results. Score "Unclear risk" if not specified in the paper.
7. Was the study analyzed appropriately using interrupted time series techniques?	Score "Low risk" if models such as segmented regression and ARIMA were used to analyse data. Authors should have considered autocorrelation, seasonality (and non-stationarity) as appropriate. Score "High risk" if ITS models were not used and key methodological recommendations such as autocorrelation and seasonality were not considered.

Each criterion scored 0 if low risk and 1 otherwise. For each study, we created an aggregate score by combining scores across the seven criteria, and subsequently categorized the aggregate score as low (risk of bias =0), moderate (risk of bias = 1 or 2), high (risk of bias = 3 or 4), and very high (risk of bias > 4).

Appendix Table 5. Reported considerations of autocorrelation, seasonality, and non-stationarity by segmented regression and ARIMA models

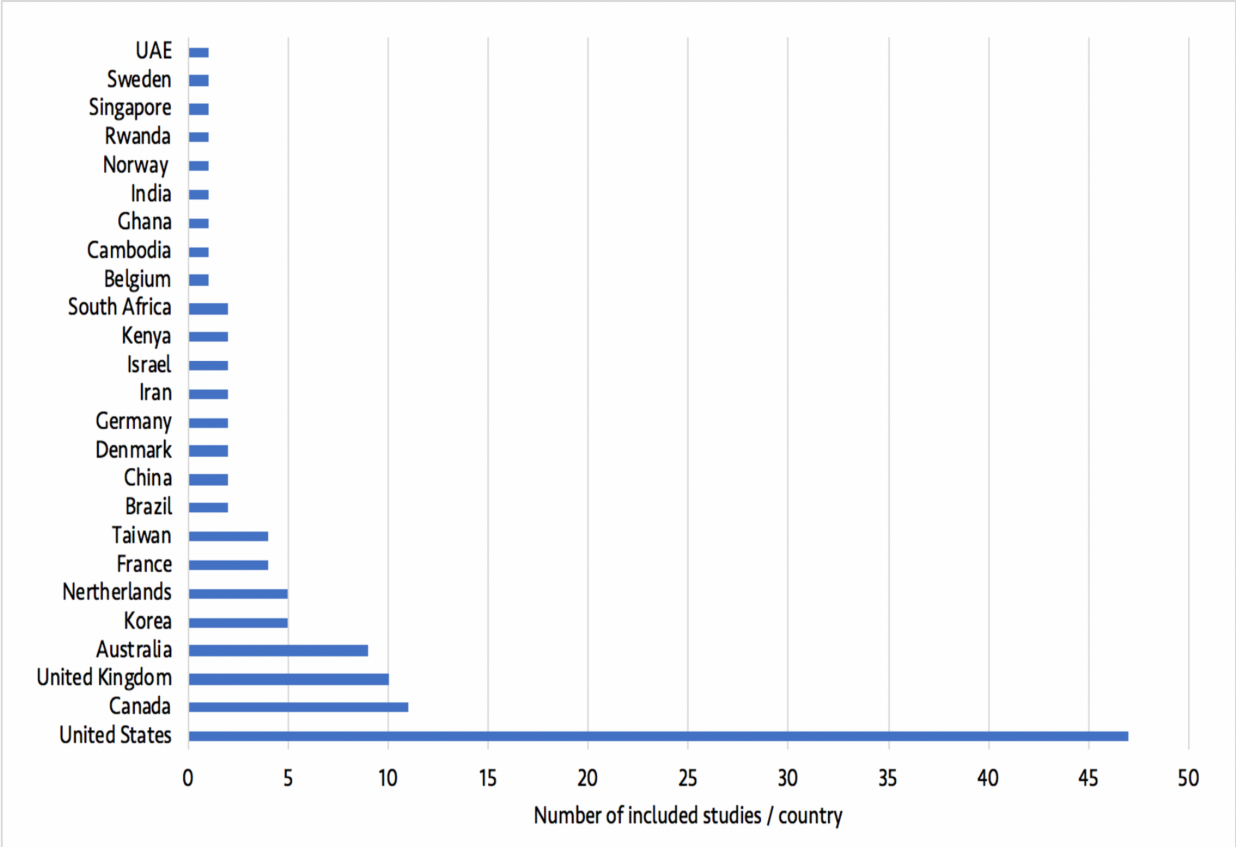
Methodological considerations	Segmented regression (n=75)	ARIMA (n=19)
Autocorrelation considered, n (%)	40 (53.3)	19 (100)
Seasonality considered, n (%)	16 (21.3)	7 (36.8)
Non-stationarity considered, n (%)	5 (6.7)	5 (26.3)

ARIMA: Auto Regressive Integrated Moving Average



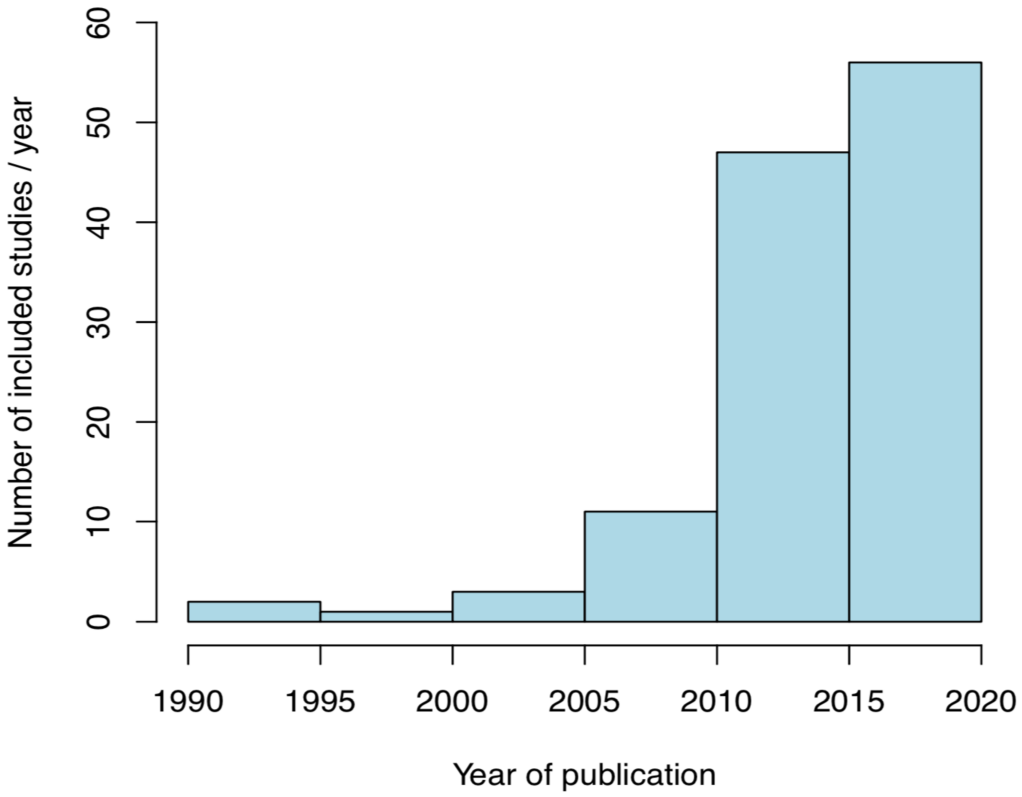
Appendix Figure 1. Use of interrupted time series in health research.

ITS studies published in peer reviewed journals indexed in PUBMED, from inception to October 2019, were retrieved using the following search strategy combining subject heading terms and / or key words of ITS: (((((((("interrupted time series analysis") OR "ITS Studies") OR "Interrupted Time Series") OR "Trend analys$") OR "Time trend$") OR "Time series analys$") OR "Time series") OR "Segmented regression") OR "Piecewise regression".



Appendix Figure 2. Study setting of included studies.

UAE, United Arab Emirates



Appendix Figure 3. Trend in use of ITS in the evaluation of health system QI interventions. Our literature search end date was June 2018 and as such, studies published after June 2018 were not captured by our search strategy.

References

1. EPOC. EPOC Methods Paper: Including Interrupted Time Series (ITS) Designs in a EPOC Review. 1998.
2. Ramsay CR, Matowe L, Grilli R, et al. Interrupted time series designs in health technology assessment: lessons from two systematic reviews of behavior change strategies. *nternational journal of technology assessment in health care* 2003; 19: 613-623.
3. Cochrane Effective Practice and Organisation of Care (EPOC). *EPOC Resources for review authors*. 2017.