**Updating and extending the MRC guidance on using natural experiments to evaluate population health interventions: workshop briefing**

**Introduction**

The MRC guidance on natural experiments published in 2012 has been widely cited and incorporated into other, more specialised guidance, e.g., for grant applicants. Since 2012, much useful experience has accumulated in applying previously described methods to population health interventions, and new methods have been developed. Important developments have also occurred in related fields with implications for how natural experimental evaluations (NEEs) are designed and conducted.

A number of useful overviews, commentaries and position papers have been published in recent years, but there is no up-to-date comprehensive overview of all the significant developments in methods, infrastructure or governance, and some key concepts and definitions are still debated. To realise the full potential of NEEs to inform population health decision-making, it is important that publishers, funders and users – as well as producers - of evidence from natural experiments are aware of recent advances and of the strengths, weaknesses, applicability and limitations of the full range of methods now available.

The aim of updating the guidance is to provide a single, integrated, up-to-date guide to the conduct and use of NEEs, incorporating a broader range of approaches to natural experimental evaluations than in the previous guidance. It will serve to raise awareness among researchers of the range of methods available for evaluating interventions as natural experiments and provide signposts to the more detailed methodological literature. It will provide clear messages for intervention stakeholders (e.g., decision makers in local or central government) to help them decide whether a NEE would be useful, understand the trade-offs involved in choosing between a natural and a planned experiment, and to identify which of the available methods are likely to yield the most robust and relevant evidence. The guidance will also provide a framework to help journal editors, funders and peer-reviewers to assess the strengths and weaknesses of NEE research proposals and papers in a systematic and balanced way.

We are holding three workshops with producers and users of NEEs to inform the development of the guidance. This paper summarises the proposed structure of the guidance, introduces the issues we plan to cover in each section and sets out questions for discussion. There will be opportunities for participants to raise additional questions and to identify issues that we may have overlooked. Following the workshops we shall compile a draft guidance document that we plan to issue for consultation in August and September.

**Workshop Session A: Coverage, concepts and definitions**

**Coverage**

Much of the existing methodological literature on natural experiments focuses on quantitative methods of effect estimation. We believe the guidance should also cover qualitative methods and mixed methods, and should consider issues such as planning, conduct, governance and infrastructure needed to support NEE studies. That suggests the following overall structure.

* Concepts and definitions
* Design and planning
* Pre-registration
* Infrastructure and information governance
* Engaging policy-makers and other stakeholders
* Quantitative methods
* Qualitative methods
* Integrated and mixed methods
* Economic evaluation
* Reporting standards
* Critical appraisal and evidence synthesis

**Workshop questions**

1. Does the proposed list of sections provide a comprehensive and coherent structure for the guidance?
2. Are there any key issues that do not fit within the proposed structure?

# **Concepts and definitions**

For the updated guidance, we propose to retain the broad definition of natural experiments used in the previous MRC guidance. That is, natural experiments are defined as events or processes outside the control of a researcher that divide a population into exposed or unexposed subpopulations. A natural experimental evaluation uses an event or process associated with the introduction, delivery or (more rarely) withdrawal of an intervention to evaluate the impact of the intervention on some outcome or range of outcomes. Evidence from such studies can also be accumulated to evaluate questions about more general exposures (such as the effect of income or income inequality on health), but what distinguishes a natural experimental study from the broader range of observational studies is its focus on a specific event or process that determines exposure.

Methods used in the evaluation of natural experiments originated in a range of disciplines, leading to the use of different terms for similar concepts. Table S.1 defines key terms as they will be used in this guidance.

**Workshop questions**

1. Is this broad definition of natural experimental evaluations appropriate? If not, how can it usefully be made more specific?
2. Would it be useful to include in the guidance a glossary along the lines of Table S.1? If so, are there any key terms missing? Are brief summaries of the kind illustrated likely to be useful. Would links to references for more formal definitions be helpful?

**Workshop Session B: Process**

# **Design and planning**

The recently published [MRC/NIHR framework for the development and evaluation of complex interventions](https://www.bmj.com/content/374/bmj.n2061) sets out a model for planning and conducting evaluations that is meant to be applicable to natural experimental evaluations, as well as to planned experiments such as randomised controlled trials (Fig 1). The framework identified a set of ‘core elements’ that should be revisited at each stage in the planning and conduct of an evaluation.

Diagram, timeline

Description automatically generated  
Figure 1 The MRC/NIHR framework for developing and evaluating complex interventions

In relation to the identification of candidate interventions, we have identified five sets of circumstances which may give rise to opportunities for NEEs:

* Differences over time or between places in presence or level of exposure between otherwise similar subpopulations
* Eligibility criteria within a policy that identify some units within a population but not others as exposed
* Phased implementation of a policy across a population in which outcome data is continuously accumulating
* Randomisation used as an assignment mechanism within a policy
* Flaws or shortcomings in policy implementation

**Workshop questions**

1. Does the framework provide a useful structure for planning and conducting a natural experimental evaluation? Are there other aspects of design and planning NEEs that should be addressed in this guidance?
2. Have we identified the most important sets of circumstances that provide opportunities for NEEs? Are there others we should add to the list?

**Pre-registration of NEEs**

Registration of study protocols is now standard for clinical trials. It may be mandated by research funders and is a condition of publication of trial findings in many leading journals. Registration of protocols for natural experimental studies is possible through a range of channels, such as open access journals and open science platforms, but lacks common standards and practice varies. A well-designed and conducted NEE may use multiple analysis methods applied to datasets of which researchers have some prior knowledge. Analysis plans may be modified for good reason, as limitations in the data become apparent. It is important for users of evidence from NEEs to be able to distinguish well-motivated changes to an analysis plan from retro-fitting of hypotheses or selective publication of study findings.

**Workshop questions**

1. How can trial registration systems, designed for prospective studies, be adapted to the requirements of retrospective studies?
2. How can the benefits of registration be aligned with need for flexibility in study protocols?
3. What additional safeguards, if any, are needed to ensure transparency in the conduct and reporting of NEEs?
4. What can funders and journal editors do to support transparency in the conduct and reporting of NEEs?

**Infrastructure and information governance for the use of administrative data**

Natural experimental evaluations are often conducted as retrospective studies, using data originally collected for another purpose, such as vital events registration, population surveys, administrative datasets, sales and purchasing data and, increasingly, information gathered via mobile phones, fitness apps, etc. Such evaluations can be conducted when a prospective trial would no longer be practical, and can be highly efficient, where large data datasets are available at a tiny fraction of the cost of primary data gathering. There has been extensive investment in the infrastructure for making such data available to researchers, but the acquisition of data can be complicated and time consuming and access may only be possible in very restricted settings.

**Workshop questions**

1. What are the most important barriers to the efficient use of routinely collected data for NEEs?
2. How can these barriers be removed or minimised, while still preserving data security?
3. Are there examples of good practice (e.g., effective infrastructures for making data available, or streamlined approaches to information governance) that we should highlight in the guidance?

**Engaging policymakers and other stakeholders**

Engaging stakeholders can help to ensure that evidence from NEEs is relevant for population health decision-making and gets taken up and used in practice. The retrospective nature of many NEEs means there will often be stakeholders relevant to the evaluation of the natural experiment who were not involved in its delivery. There have been a number of recent initiatives to improve stakeholders’ understanding and use of natural experimental evidence. The UK Government’s guidance on evaluation (the ‘[Magenta Book](https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/879438/HMT_Magenta_Book.pdf)’) covers the use of ‘quasi-experiments’ in some detail, but there may be value in additional guidance for local decision-makers or others with an interest in using natural experimental evidence but lack the resources available to those in central government.

**Workshop questions**

1. Are there good examples of guidance on the use of NEES to inform policy making from countries other than the UK?
2. What other approaches might help to improve the understanding and use of NEE evidence by decision-makers, especially those outside central government?

**Workshop Session C Methods**

**Quantitative methods**

The choice of quantitative analytic method for the analysis of NEEs is dependent on factors such as availability of data, its level of aggregation, and the nature of the assignment process.

The quantitative analytic methods we propose to include in the guidance are:

* Cross-sectional
* Repeated cross-sectional
* Before-and-after
* Difference-in-differences
* Regression discontinuity
* Instrumental variable
* Interrupted time series
* Controlled interrupted time series
* Synthetic control

The methods are summarised in Table S.2, with an indication of data requirements, statistical methods, strength and weaknesses and an illustrative example of how they may be applied.

A [target trial framework](https://bmcmedresmethodol.biomedcentral.com/articles/10.1186/s12874-021-01224-x) has recently been proposed as a guide to appraising natural experimental study designs. In this approach, elements of the study (eligibility criteria, treatments, assignment procedures, follow-up period, outcomes, causal contrasts of interest, and analysis plan) are compared with the corresponding elements of a well-designed (but not necessarily feasible) randomised trial.

**Workshop questions**

1. Are any important methods missing from the list above? Have we included any that do not belong (e.g., because they could not be used to identify a causal effect in any circumstances)?
2. Is there a hierarchy among the methods, or should they be seen as a toolkit?
3. Is a target trial framework as useful way of evaluating NEE study designs? Are there more straightforward alternatives?

**Economic evaluation of NEEs**

Few examples exist of full economic evaluations of population health interventions alongside NEEs. Designing, conducting, and reporting economic evaluations without specifically considering the NE framework can lead to sub-optimal design, data collection and analysis for NEEs, leading to bias in the estimates of costs and outcomes. Depending on the outcome of interest, economic evaluations can take the form of: cost-effectiveness analysis, where outcomes are expressed as a single natural unit; cost-utility analysis, measuring outcomes in terms of quality-adjusted life years (QALY); cost-benefit analysis, where health benefits are measured in monetary terms; and cost-consequence analysis, where multiple outcomes are reported in a summary table rather than aggregated into an overall estimate.

Challenges posed by NEE for the design of an economic evaluation include:

* comprehensive identification and measurement of costs and outcomes
* where outcomes emerge slowly, there may be a requirement for routinely collected data over a long observational period to enable analysis of costs and outcomes over an appropriate time horizon
* the need for quantitative methods to deal with the additional complexity generated by correlated costs and outcomes, skewed and non-normal distributions of costs and outcomes, potentially correlated multiple outcomes, and clustering, alongside the identification of effects
* methods for exploring equity as well as efficiency impose additional data requirements which may not be satisfied by routinely collected data

**Workshop questions**

1. The MRC/NIHR framework for developing and evaluating complex interventions recommends CCA and CBA as the most appropriate forms of economic evaluation, and the adoption of a broad (e.g. societal) rather than a narrow (e.g. provider) perspective for identifying costs and outcomes. Do these recommendations also apply to NEEs?
2. Does the incorporation of economic evaluation into a natural experimental evaluation pose specific challenges over and above those associated with any evaluation of a complex Intervention. Are there good examples of how these have been addressed??

**Qualitative methods**

Qualitative evidence in evaluations of natural experiments can help to ensure that the system, context, and intervention are well characterised; the assignment process is well understood, and exposed/non-exposed groups appropriately defined; causal mechanisms are understood; indicators of effect selected are meaningful; and stakeholder perspectives on the intervention and its effects are understood. Well-analysed qualitative data can enhance the ability to make credible claims about causality within the case, understand how the intervention affected the system, and generalise beyond the case. NEEs will therefore benefit from including a substantial qualitative component, which is integrated throughout the evaluation and in the report.

**Workshop questions**

1. The guidance currently focuses on practical issues and not on methodological theory around qualitative natural experimental evaluation design. Do you agree with this emphasis?
2. The section is aiming to be ‘theory neutral’ and does not compare different theoretical frameworks or designs, e.g., realist designs, normalization process theory, etc. Do you agree?
3. Can an NEE rely entirely on qualitative methods, for example to understand change, mechanisms and mediators, or the perspectives and practices of intervention stakeholders, or should such methods always be used in conjunction with quantitative methods of effect estimation?

**Integrated, mixed- and multi-method evaluations**

Natural experiments typically occur within complex systems that influence health. A complex systems perspective can help researchers understand why interventions may fail or succeed. While invaluable, a complex systems perspective has major implications for research design, usually requiring multiple methodological approaches. The availability of resources and time will influence how much of a comprehensive approach can be taken. The terms ‘multi-methods’, ‘mixed-methods’ and ‘integrated methods’ are often used to describe evaluations which bring together different methods. This may be the inclusion of qualitative and quantitative data, or multiple methods within each of these traditions, i.e., only drawing on qualitative data or only drawing on quantitative data.

Five different approaches to bringing together different research components can be identified:

* Embedded design: one approach that is dominant within the evaluation, with another providing a supportive role and perhaps addressing a different research question.
* Exploratory design: using one study design to explore and understand the natural experiment and its context first, followed by another method to conduct a more definitive evaluation.
* Explanatory design: one method used to provide explanations to the findings observed by a different method, e.g. using qualitative methods to examine when quantitative results suggesting no effect of an intervention, or why the intervention was successful.
* Triangulation: using multiple methods or sources of data to address the same research question.
* Integration: draws on multiple analyses to answer different but highly inter-related research questions. Integration can be viewed as the creation of a jigsaw of evidence to understand a natural experiment. An integrated approach would ideally be highly interlinked and pursued synchronously.

**Workshop questions**

1. Practicalities aside, are any of the methods listed clearly preferable to the others?
2. Taking practicalities into account, which method or methods are most appropriate to NEEs?

**Reporting**

There are well-established reporting guidelines for observational studies ([STROBE](https://www.strobe-statement.org/)), non-randomised studies of interventions ([TREND](https://jamanetwork.com/journals/jamasurgery/article-abstract/2778466)), and for describing interventions ([TIDieR](https://www.equator-network.org/reporting-guidelines/tidier/) and [TIDieR-PHP](https://www.equator-network.org/reporting-guidelines/tidier-php-a-reporting-guideline-for-population-health-and-policy-interventions/)).

Workshop questions

1. Are existing reporting guidelines adequate for reporting NEEs, or is there value in extending them to cover issues specific to NEES?

**Critical appraisal and evidence synthesis:**

Issues specific to identifying, appraising, and synthesising NEE evidence occur at each stage of evidence synthesis. Particular issues to consider are conceptualising the evidence synthesis, appraising risk of bias and assessing certainty of the evidence. Defining the overarching research question for a given evidence synthesis, what is the most useful question, why a set of studies is being synthesised, e.g., establishing causality, exploring mechanisms, etc., will inform practical decisions on how best to conduct the synthesis.

When appraising risk of bias, assuming the main objective is achieving an effect size estimate, [ROBINS-I](https://sites.google.com/site/riskofbiastool/welcome/home/current-version-of-robins-i) is the most thorough critical appraisal tool. However, ROBINS-I requires expertise and is not currently designed to assess non-interventions, and, generally, ‘moderate’ is likely the most favourable assessment for NEEs, despite some NEE designs accounting for issues such as selection and confounding. In other circumstances, a critical appraisal framework like those used for qualitative research may be more appropriate.

If relevant, the principles of the Grading of Recommendations, Assessment, Development and Evaluations ([GRADE](https://doi.org/10.1136/bmj.39489.470347.AD)) framework may be applied to assess certainty of the evidence. Challenges in applying GRADE include the assessment may overlooking design features of NEEs that address risk of bias, the lack of scale available may hinder differentiating between assessments and outcomes in NEEs may be difficult to select and prioritise or interpret. When the subject of interest involves NEE evidence, ‘conditional’ rather than ‘weak’ recommendations from low certainty evidence may be necessary, and there may be implications of small effect sizes at population level.

**Workshop questions**

1. What balance would users find most useful between conceptual and practical issues in guidance for appraising and synthesising NEE evidence?
2. To what extent are the challenges for critical appraisal and evidence synthesis of NEEs particular to NEEs?
3. Is it best to use ROBINS-I and GRADE to assess risk of bias and certainty of evidence, despite the challenges involved, or are there other approaches that are sufficiently rigorous but more straightforward?

**Supplementary Material**

**Table S.1 Glossary**

|  |  |
| --- | --- |
| Term | Usage |
| Assignment, allocation      Concurrent interventions | The process that determines whether units (which may be individual people, or aggregates of some kind) are exposed to the intervention that is being studied. Also referred to as the data generating process.  A common source of confounding in natural experimental evaluations is when one or more interventions other than the intervention being studied are implemented at the same time. Depending on the extent of overlap in exposure, effects can be disentangled, for example by focusing on outcomes specific to the intervention of interest, or on populations exposed to one intervention but not the other(s). |
| Confounding, confounder (observed, unobserved) | Confounding refers to the mixing up of the effects of the intervention with the effects of characteristics associated with exposure. Confounding by observed characteristics (i.e. those on which data are available) can be addressed using a statistical model. Some natural experimental study designs go a step further and use a combination of assumptions about the assignment process and statistical modelling to address confounding by unobservables. |
| Control, counterfactual | Controls are unexposed units. Outcomes among the controls constitute the counterfactual, in the sense that they represent the outcomes that would occur in the absence of exposure. |
| Exposure | A general term for receipt of an intervention; effectively synonymous with treatment in natural experimental studies. |
| Exchangeability | Also known as ignorability. Groups are exchangeable if their outcomes would be expected to be the same under identical exposure conditions. If one group is exposed to an intervention and the other unexposed, the difference in outcomes can be interpreted as the effect of exposure. The groups are conditionally exchangeable if outcomes are expected to be the same after conditioning on a set of covariates. |
| Identification, identifying assumption | Identification refers to the method used to obtain an estimate of the effect of the intervention. All such methods rely on identifying assumptions, such as the assumption that pre-intervention trends in outcomes will continue in the absence of intervention. Testing how well the assumptions are met is an important element of good natural experimental study design. |
| Instrument, instrumental variable | A variable that is associated with exposure to an intervention. An instrumental variable can be used to identify the effect of exposure on an outcome if (1) it is associated with the outcome but (2) only through its association with the exposure (the ‘exclusion restriction’) and (3) it is unrelated to any other factors associated with the outcome. |
| Intervention | A general term for any policy, programme, service or treatment that is being evaluated. Interventions may be evaluated at the point of introduction, when they are in place (using a process that determines exposure at an individual unit level within a population) or when they are withdrawn. |
| Natural experiment | An event or process that divides a population into exposed and unexposed sub-populations, or into sub-populations with differing levels of exposure. The division may be spatial, temporal or based on the characteristics of individual units, such as test scores. A natural experimental evaluation uses that event or process to identify, measure or understand the effect of the intervention. |
| Negative controls | Also referred to as non-equivalent dependent variables. Outcomes that are not expected to change can be used as a robustness check. If changes in such outcomes are observed following exposure to the intervention, that might suggest residual confounding due to selective exposure to the intervention or to the presence of co-occurring interventions. |
| Observational study | A study that does not involve any manipulation of exposure for research purposes. Natural experimental studies are a subset of observational studies that focus on a specific event or process that generates differences in exposure |
| Outcome, potential outcome | Outcome is used as a general term for the effect of treatment or exposure to the intervention being studied. Potential outcomes are the outcomes that would occur in the presence or absence of treatment, only one of which can be directly observed. Comparison of actual with potential outcomes is the basis for identifying treatment effects in a natural experimental study. The potential outcome for the exposed group is measured in a group that is not exposed to the intervention but is otherwise similar to the exposed group. |
| Placebo tests | A form of robustness check using assignments that do not actually occur, such as dates on which the intervention did not take place in an interrupted time series study, or units that were not exposed to the intervention in a synthetic control study. |
| Positivity | (Also known as common support) The assumption that any combination of covariate values is possible within any exposure stratum. |
| Quasi-experiment | Natural experimental studies are often referred to as quasi-experiments, but quasi-experiment is also sometimes used to refer to non-randomised experiments. To avoid confusion, the term natural experiment is preferred in this guidance. |
| Selection | A process that leads exposed and unexposed units to differ in ways other than exposure to the intervention that are associated with differences in outcome. Selective exposure to the intervention is the source of confounding in natural experimental studies. Selection in this sense is different from the idea of selective participation in a study, which may also cause bias if participation is associated with factors that are also associated with outcomes. |
| Stable Unit Treatment Value Assumption | The assumption that the outcome for each unit is independent of the outcomes for all other units. |
| Target trial | A trial design that mimics the conditions that occur in a natural experiment. Comparison of a natural experimental study with a target trial can be used to identify possible sources of bias. |
| Time varying confounding | In studies where exposure varies over time, confounders whose values vary over time are a common source of bias and one that is not addressed by methods that deal with differences in the fixed characteristics of exposed and unexposed groups, or in observed differences in time varying characteristics. |
| Treatment | Treatment is often used as a general term for exposure to an intervention, rather than to denote a medical treatment. |
| Treatment effect | Also referred to as the causal estimand. The average treatment effect (ATE) is the difference between the average outcome when all units are exposed and the average outcome when none are. The local average treatment effect (LATE) is the ATE among compliers, i.e., units whose exposure status is determined by their assignment. Different methods estimate different causal effects (see Section x, Table y) |
| Triangulation | Comparison of effects obtained using different methods as a sensitivity or robustness check. If the effect estimates are comparable, despite differences in the assumptions underpinning the methods used, they can be considered more robust. |

Table S.2 Quantitative methods for the evaluation of natural experiments

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Study design | Comparison | Data | Statistical approaches | Characteristics | Illustrative example – Cardiovascular disease (CVD) ‘health check’ delivered in primary care centres (i.e., screening for CVD risk factors). Outcome measure – incident CVD events (hospitalisations / deaths) |
| 1) Cross-sectional | Individual level | post-intervention; random sample (ideally); single time point of data collection; data potentially collected in control group(s) | Descriptive statistics for effect size – with representation of uncertainty; possible matching of intervention group(s) with control group(s) | No information on pre-intervention outcome, so effect size unclear | Study conducted in all / subset of primary care centres post-intervention; rate of incident CVD events compared to control group(s) (or compared to literature); possible matching of control group(s) to intervention group(s) before comparison |
| 2) Repeated cross-sectional | Individual level | pre- and post-intervention; random samples (ideally); data collection at unequally spaced time intervals; no data from control group(s) | Difference between pre- and post-intervention in means / proportions / rates (depending on nature of outcome measure variable) – with representation of uncertainty; regression models – to adjust for confounding variables / assess effect modification | Allows for comparison with pre-intervention outcome, but because pre/post groups include different people this might bias comparisons. | Study conducted in all / subset of primary care centres pre- and post-intervention (two time points); difference in rate of incident CVD events compared pre- and post-intervention |
| 3) Before and after | Individual level | pre- and post-intervention; random sample (ideally); two time points of data collection (on same individuals – repeat measurements); no data from control group(s) | Average difference between pre- and post-intervention measurements of the outcome measure; regression models – to adjust for confounding variables / assess effect modification | Allows for comparison with pre-intervention outcome based on repeated measures of the same group, but does not have a control group. Issues of missing data might bias comparison. | Not possible given nature of outcome measure (incident CVD events); would be possible if SBP was outcome measure |
| 4) Difference in differences | Individual level | random samples (ideally); pre- and post-intervention; intervention and control group | Regression models; possible matching of intervention group with control group | Before-and-after design with a control group. Can be difficult to identify comparable control unit(s) | Difference between intervention and control groups in difference in rate of incident CVD events compared pre- and post-intervention |
| 5) Regression discontinuity | Individual level | random samples (ideally); data collected either side of a ‘cut-off’ for a variable determines if an individual is eligible for intervention (and assignment to intervention or control group) | Nonparametric methods; regression models; assess effect modification | Limited situations where a cut-off can be identified | Use one of the eligibility criteria of health check (systolic blood pressure (SBP) > 140mmHg) as ‘cut-off’ |
| 6) Instrumental variable | Individual level | Individual level; random samples (ideally); an ‘instrument’ is a variable that is associated with exposure to the intervention but not itself associated with outcome | Regression models; assess effect modification | Strong instruments are difficult to identify (in public health) | Use distance to primary care centre where health check is being offered as ‘instrument’ |
| 7) Interrupted time series | Aggregated data | pre- and post-intervention; data collection on multiple occasions at equally spaced time intervals; ‘interruption’ is at time point when intervention starts; no data from control group(s) | Time series; (s)ARIMA / (panel) regression models; adjustment for confounding variables; assess effect modification | Allows for comparison with pre-intervention outcome based on multiple repeated measures of the same group, but does not have a control group. | Study time series of rates of incident CVD events; single time series (data from primary care centres combined) or multiple time series (for each/sub-groups of primary care centres) |
| 8) Controlled interrupted time series | Aggregated data | pre- and post-intervention; multiple time points of data collection (evenly spaced intervals); ‘interruption’ is at time point when intervention starts; intervention and control group(s) | Time series; ARIMA / (panel) regression models; adjustment for confounding variables; assess effect modification | Interrupted timeseries with control group.  Pre-intervention time period differences between intervention and control groups may cast doubt on intervention effect estimates. | Study time series of rates of incident CVD events in intervention and control group(s) |
| 9) Synthetic control | Aggregated data | pre- and post-intervention; multiple time points of data collection (evenly spaced intervals); ‘interruption’ is at time point when intervention starts; intervention and control groups | Use the pre-intervention data to create the synthetic control; a weighting procedure is applied using the outcome variable and possible confounding variables from the pool of control groups | If appropriate controls cannot be identified, a synthetic control can be developed to obtain counterfactual. Quality of synthetic control not always easy to establish. Communication to practitioners difficult. | Study time series of rates of incident CVD events in intervention and synthetic control group |