Coalitie
Leefstijl in de Zorg

Guide to research methods on lifestyle interventions in healthcare

Opportunities for evaluating effectiveness

Coalition for Lifestyle in Healthcare – maart 2025

Table of contents

1. Introduction

Methods | Effectiveness research | References

In line with the Integral Healthcare Agreement (IZA), the Coalition for Lifestyle in Healthcare (Coalitie Leefstijl in de Zorg) focuses on the implementation of lifestyle in curative care. The Research team of the Coalition, which identified the knowledge questions and is initiating sustainable knowledge and infrastructure, is issuing this guide to support researchers, policymakers, funders, patient organisations and healthcare professionals in choosing the optimal method for evaluating the effectiveness of a lifestyle intervention in curative healthcare. Many different evaluation methods exist, each with their own possibilities and limitations. Such a broad palette is desirable because of the diversity of lifestyle interventions and the situations in which they are deployed.
For each lifestyle intervention, it is necessary to consider which research design, analysis method and outcome measures are best suited for evaluating the effectiveness of a lifestyle intervention.

This guide, which is largely based on an exploration by the Department of Public Health & Primary Care/Health Campus The Hague of Leiden University Medical Centre in collaboration with researchers from various disciplines (epidemiology, behavioural sciences, econometrics, implementation and data sciences), is concise and pragmatic in scope. Those who want to know more, or get started with one of these methods, can find additional information via the links and footnotes. With this guide, the Coalition for Lifestyle in Healthcare aims to support researchers, patients and healthcare professionals in choosing the right research method for their research question. It also helps policymakers, funders and reviewers of research applications to set, formulate and test frameworks, all with the aim of promoting the broad implementation of carefully evaluated lifestyle interventions in curative healthcare, contributing to more effective and accessible care and the broad health of people with (chronic) diseases.

2. Design must fit (specific) lifestyle intervention

Methods | Effectiveness research | References

Effectiveness research is intended to provide practitioners and patients with a sufficient basis to make an 'evidence-informed' intervention choice. The scientific rationale should be as close as possible to practice and to real patient populations. The choice of research design is therefore determined by the question and by methodological, content-based and practical considerations.

Lifestyle interventions sometimes involve different considerations than when evaluating other interventions in curative healthcare. The complexity of lifestyle interventions can vary widely, from simple advice (generic lifestyle advice) to a combination of different interventions in a variety of areas (e.g. diet, exercise pattern, coping with stress, etc.). The comparison with 'usual care' is not always meaningful as there can be great variation in this care, with some patients already receiving generic lifestyle advice and others not.

Lifestyle interventions differ from other medical interventions such as drugs or surgical procedures because they derive efficacy from effects on a variety of biological mechanisms. Exercise, for example, affects muscle development, mood, cognition, insulin sensitivity, cardiovascular health, several biochemical reactions in the mitochondria and a and a wide range of overlapping biological processes other partially overlapping biological processes. Compared to a drug that often targets a single receptor, a lifestyle intervention is thus much broader and more complex in its effects on physical and mental health. In addition, lifestyle interventions stand out in that the patient has a much larger and more active role, and the role of the healthcare provider is often more active as well. Added to this are other unique characteristics, such as the major influence of the season in the timing and application of lifestyle interventions. For example, the season can influence effectiveness when training routines such as outdoor exercise, a healthier diet or healthy sleep behaviour and when unlearning unhealthy routines.

The mentioned differences between lifestyle interventions and other medical interventions have significant implications for effectiveness research. Choosing appropriate outcome measures is more complex because so many processes are affected. In addition, the patient's attitude, motivation and capabilities are of greater importance, and influences such as those of the season cannot be ignored.

Evaluating lifestyle interventions poses several challenges. On the one hand, there is the assessment of the effectiveness of an intervention: does it work as intended? On the other hand, there is the evaluation of implementation, which looks not only at how many healthcare providers offer the intervention and how many patients use it, but also at how healthcare providers implement the intervention and how patients integrate it into their daily lives, as well as how the broader healthcare system does or does not system does or does not secure funding for the intervention. This guide specifically focuses on evaluating the effectiveness of single lifestyle interventions, describing the pros and cons of such studies. Evaluating implementation and complex interventions (e.g. through systems analysis) is beyond the scope of this guide, although hybrid research designs, which sometimes combine effectiveness and implementation, are briefly touched upon.

In practice, however, lifestyle interventions are often complex and consist of combinations of components or strategies, as described in the MRC framework (1). This calls for other research approaches, such as hybrid or realist evaluation, which explicitly involve the system and practice. Although these complex approaches are of great importance, they are not further elaborated in this guide. **This guide is deliberately limited to single interventions.**

3. Choosing a research design

Methods | Effectiveness research | References

This guide describes several approaches for effectiveness research, briefly mentioning the main advantages and disadvantages. This helps researchers to determine which method is most suitable in their specific situation. The list of approaches can be supplemented in the coming years, for instance with insights from other domains such as economic or policy research. The list provides an overview and is intended as a non-prescriptive overview.

Because of the large differences between lifestyle interventions (e.g. in terms of complexity, patient efforts and the disciplines involved), it is not possible to name one single best method that is the best way to evaluate the effectiveness of an intervention in all cases. The usual hierarchy for evidence, where the randomised clinical trial (RCT) is always at the top, cannot generally be applied for lifestyle interventions. However, we can describe trade-offs that researchers can use to determine which method is best in a given situation. These trade-offs are summarised in the decision tree in Figure 1. In all cases, the approach that has the highest degree of (external) validity and that best reflects the reality of (most) patients is preferable. After all, it makes little sense if an intervention is tested methodologically flawlessly in a population that differs greatly from the reality in the consultation room.

Considerations when choosing a design

A first consideration concerns whether an **experimental** design is feasible and fits the objective of the study. If the intervention is a single clearly crystallised intervention that needs little personalisation, an experimental design is possible. In an experimental design, two or more groups are compared prospectively, with the conditions (interventions, usual care, placebo, if any) in both groups predetermined, as well as the selected outcome measures and the method of analysis. In some experimental designs, such as the trial of intervention principles (see description below), there is then some scope for adjusting the conditions, but an experiment is mainly characterised by controlling relevant variables.

If an experimental design in the form of a randomised trial is not possible, e.g. because the intervention is still under development and needs to be modified regularly or because randomisation is not considered ethical, a **quasi-experimental** design can be chosen in some cases. This is often characterised by a comparison between time periods when an intervention is or is not given and/or between an intervention group and a control group. The control group is then often composed of similar individuals (matched) rather than randomly assigned. A quasi-experimental approach can provide reliable outcomes if there are no confounding factors, such as seasonal influences.

Where a (quasi-)experimental design is not possible, feasible or appropriate, an **observational** study can still provide very valuable information about the effectiveness of an intervention. Observational research uses available data (care data, cohort studies and any data collected by participants, e.g. from e-health apps and wearables). Observational research using routine care data or wearables is also more closely aligned with everyday (healthcare) practice because it can use data from all patients ('real life data'), not just a selection that meets the inclusion criteria.

An observational design can also choose an approach that compares two or more groups. This approach offers fewer opportunities to check for unknown or unmeasured confounding factors, but can give an impression of effectiveness. When analysing, it is recommended to pay extra

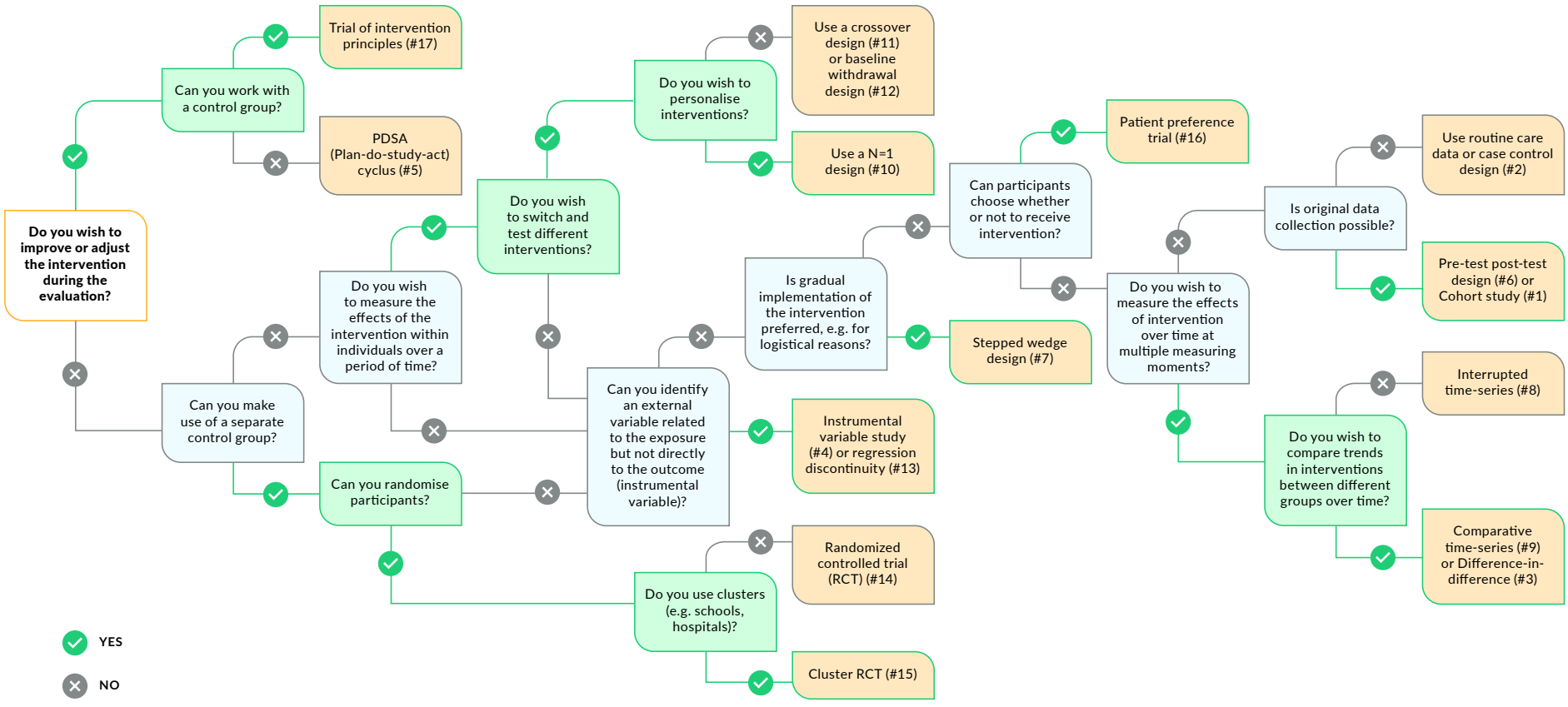

Figure 1: Decision Tree

attention to individuals with extremely high or low measured values at baseline, as these values often spontaneously exhibit regression to the mean.

The choice of a design with a control group depends on several factors. For example, an intervention that requires a lot of personalisation is less suitable to be investigated in a comparative study. Also, if it is unethical to deprive patients of the intervention, a control group is not possible. The previously mentioned problem that normal healthcare shows too much variation may also be a reason to abandon controlled study design. If a design with a control group is chosen, the next consideration is whether randomisation is possible and desirable. Since a double-blind design is often not possible in lifestyle interventions, patient preference may make randomisation difficult. Other factors such as available budget may result in randomisation not being a feasible option.

Using the descriptions of different approaches below, the choice of a specific research design can then be fleshed out. In addition to methodological considerations, practical aspects such as the local situation, the healthcare providers involved, the available time and the budget also play a role.

Many of the methods listed here are suitable for both evaluating the effectiveness of an intervention and evaluating its implementation. Some methods, such as cyclical evaluation (e.g. the classic Plan-Do-Study-Act cycle), are particularly suitable for research where interim adjustments to the intervention are desired or where implementation is being examined. The hybrid approach below combines effectiveness evaluation with implementation research.

Hybrid designs

To achieve an optimal fit between impact evaluation and implementation evaluation, a so-called hybrid design can be used, which has elements of both. There are three types of hybrid designs: type 1, type 2 and type 3. These hybrid designs are not discussed in detail in this guide.

In **type 1 hybrid designs**, the evaluation of effectiveness is paramount. Effectiveness research can use any of the above research designs. At the same time, data relevant to subsequent implementation and implementation research are also collected. In addition to measurements that evaluate the effect of the intervention on the participant's functioning (effectiveness research), the feasibility and acceptability of implementation are also identified through qualitative, process-oriented or mixed methods.

Type 2 hybrid designs also focus on effectiveness, but additionally examine the appropriateness and possible impact of an implementation strategy. To enable the latter, it is often advisable to choose the same or similar populations and settings as in the original effectiveness study.

Type 3 hybrid designs primarily test the impact of an implementation strategy. A secondary objective is to map clinical outcomes after implementation. This provides relevant information on the effects of the lifestyle intervention in daily practice. These designs are particularly useful to check whether effects are still found after adjustments in the context.

	Name	Type	Reference example
1	Cohort study	Observational	[2]
2	Case-control	Observational	[3]
3	Difference-in-difference	Observational	[4]
4	Instrumental variable	Observational	[5]
5	Cyclische evaluatie (PDSA)	Observational	[6]
6	Pre-test Post-test study	Quasi-experimental	[7]
7	Stepped wedge design	Quasi-experimental	[8]
8	Interrupted time-series	Quasi-experimental	[9]
9	Comparative time-series	Quasi-experimental	
10	N=1	Quasi-experimental	[10]
11	Crossover design (AB/BA)	(Quasi-) experimental	[11]
12	Baseline withdrawal (ABA)	Quasi-experimental	
13	Regression discontinuity	Quasi-experimental	[12]
14	Randomised controlled trial (RCT)	Experimental	[13]
15	Cluster RCT	Experimental	[14]
16	Patient Preference trial	Experimental	[15]
17	Trial of intervention principles (TIPs)	Experimental	[16]

Table 1: Methods for evaluating the effectiveness of single lifestyle interventions (with the reference of an example in which the design was used).

1. Cohort study

This is an observational design in which the studied groups (cohort) are followed for an extended period of time and measurements are taken at different time points (e.g. annually). In some cohort studies, the design is undetermined (non-specific (i.e. not focused on a particular health condition), while others look prospectively at specific outcomes. A cohort can be either closed or open. In the case of an open cohort, participants can enter and leave the cohort, for instance if the cohort consists of one or more GP practices or residents of a particular region. Often, all participants are healthy at baseline (population cohorts), unless otherwise specified, as in the case of patient cohorts.

Advantages

Data are collected over longer periods of time, giving researchers insight into the long-term effects of risk factors, protective factors and possible interventions. Existing long-term cohort studies are therefore an important source of information. In addition, new research questions can be added in subsequent rounds of measurement, increasing the flexibility of this design: when the effects of an intervention are evaluated by analysing changes in outcome variables before and after the intervention, this is called an interrupted time-series. If desired, it can also be decided that a comparative group from the same cohort should not be offered the intervention, in which case a comparative time-series may be conducted. Another option is to conduct a nested case-control study within the cohort comparing individuals who are sick with people who are not sick and looking back at their lifestyle behaviour over time.

Disadvantages

Establishing and maintaining a cohort requires a long-term investment in both people and resources. Within the current funding structure of scientific research, it is often a major challenge to acquire sufficient resources over a long period of time to maintain a cohort and make the necessary measurements. In addition, there is a risk of confounding, making true causality difficult to determine.

2. Case-control

This is an observational study design, comparing a group of participants with a given disease/outcome with a group of participants without this disease/outcome that is as similar as possible to the first group on other variables. In this comparison, an impression of the consequences of exposure to risk factors or of protective factors can be obtained retrospectively. This design is especially suitable for retrospectively examining (lifestyle) factors that were influential in the case of a relatively rare outcome.

Advantages

By starting from a clearly measurable characteristic, this approach provides insight into factors that may contribute to that outcome. This design is thus well suited to exploring which factors contribute to a particular outcome. This could be an unwanted outcome (illness, death) or a desired outcome, such as resilience or cure for a chronic condition. Case-control studies are of great value in identifying risk factors such as smoking or asbestos exposure. A prospective experimental study in humans is obviously not possible in such cases.

Disadvantages

It is difficult to determine whether the two groups differ only in terms of the relevant characteristic or whether there are other differences that affect outcomes. The evidential strength of a case-control study is therefore lower than that of a prospective experimental study. Demonstrating causality usually requires additional evidence, such as from experimental studies.

3. Difference-in-difference analyse

This form of observational research is possible if, within a certain group of patients, there is a subgroup that undergoes the intervention and a subgroup that does not (e.g. because a healthcare institution implements an intervention in a region while others do not). Such a situation arises, for example, when a (lifestyle) intervention is already implemented in one region and not (yet) in another. Thus, no formal randomisation takes place, but there is also no active allocation by the researchers to the intervention group or the control group. The difference-in-difference analysis relies on longitudinal panel data (a series of measurements on the same individual over time) or repeated cross-sectional measurements at the group or organisation level. Statistical analysis requires a minimum of two pre-intervention measurements and one post-intervention measurement.

The analysis looks at the trend in the data (e.g. a gradual decline in physical fitness in patients with a chronic condition or a steady blood sugar level in a group of diabetic patients). If the trends in both groups are parallel prior to the introduction of the intervention, the two groups are considered sufficiently comparable and a difference-in-difference analysis can be performed.
It is recommended to also verify that the two groups do not differ significantly in respect of other variables (e.g. socioeconomic factors or age). The control group is then used to see how the trend in the intervention group would have continued if the intervention had not been introduced.
The groups are thus not directly compared with each other.

Advantages

With this method, a good impression of the effect of an intervention can be obtained prospectively or in an existing dataset. By looking at parallel trends in the intervention group and research group, there is a check on the comparability of both groups. The method is also very suitable for testing interventions at a policy, district or organisational level.

Disadvantages

A relatively large number of measurements are needed, especially to establish a parallel trend between the two groups before the start of the intervention and to establish a difference after the start. Preferably, measurements are used that are routinely determined at regular intervals, such as blood pressure in hypertensive patients. It is important that the control group is as similar as possible to the intervention group.

4. Instrumental variable

In this type of observational study, patients who receive the intervention are compared with patients who do not receive the intervention. In doing so, the choice of who is offered the intervention is determined by a so-called instrumental variable: a factor unrelated to prognosis or other patient characteristics. Examples of such variables are differences between healthcare providers and practices or the second letter of the surname. The group classification is therefore largely arbitrary. Analysis takes place at the instrumental variable level, such as treatment centres or districts. A specific genetic variant can also be used as an instrumental variable (Mendelian randomisation). This is the case, for example, when this variant influences a particular nutritional state or an aspect of lifestyle behaviour.

Advantages

Like true randomisation, this pseudo randomisation can help reduce the problem of unmeasured confounding variables (confounders).

Disadvantages

It remains possible that there are unmeasured confounding variables, for example differences in socio-economic position or age structure between groups. Only a few genetic variants are reliably associated with lifestyle behaviour.

5. Cyclische evaluatie (Plan-Do-Study-Act, PDSA)

Implementing a lifestyle intervention often requires a cyclical approach, with implementation continuously refined and tailored to local needs and circumstances. A formalised way of doing this is the Plan-Do-Study-Act (PDSA) cycle. The ‘plan’ phase identifies a possible improvement, the ‘do’ phase tests this change, the ‘study’ phase examines the success of the change, and the ‘act’ phase identifies which possible improvements can be addressed in the next cycle.

6. Pre-test post-test

This is a quasi-experimental research design in which participants are assigned to an intervention group or a control group without random allocation. A baseline measurement is carried out prior to the intervention and one or more post-measurements take place. This design is also called non-randomised trial or non-randomised before and after study.

Advantages

This is a simple design without lots being drawn or blinding, which can easily give an impression of the effectiveness of an intervention. In its simplest form, it is even possible to conduct a pre-test post-test study without a control group. This is often done in a cohort. It is then often referred to as an interrupted time-series.

Disadvantages

The non-randomised allocation to intervention group or control group may create systematic differences between the two groups that affect the outcome. For example, if patients with a more severe disease or less motivation are more likely to end up in the control group, the results may be biased in favour of the intervention.

Variants of pre-test post-test studies

The three research designs discussed below (stepped wedge design, interrupted time-series and comparative time-series) are examples of pre-test post-test studies. The interrupted time-series is the simplest variant, in which no control group is formed. In the stepped wedge design and the comparative time-series, there is a control group. In the stepped wedge design, the control group gradually merges into the intervention group; in the comparative time-series, both groups remain the same throughout the study.

7. Stepped wedge design

In this quasi-experimental research design, the intervention is introduced incrementally to different groups (clusters), e.g. different locations of a hospital or different GP practices. Measurements begin when all clusters are still in the baseline condition (control condition). Gradually, clusters start the intervention condition one by one. At each step, participants in all clusters are measured. Eventually, all clusters receive the intervention, but 'early' clusters have more intervention measurements and 'late' clusters have more control measurements. Thus, at the start, all participants are still in the 'control group'; at the end of the study, all participants are included in the 'intervention group'.

Advantages

This set-up elegantly exploits the possibilities of an implementation process at different locations. Often, there are organisational reasons to implement incrementally, e.g. the availability of implementation experts. Data from all patients can be used, providing a realistic picture of the implementation and its effects. Any differences between locations (number of patients, socio-economic background, etc.) will also become visible in the data. Because data of all participating patients are ultimately available from before and after the implementation, each patients effectively serves as their own control. This greatly increases statistical power, allowing for smaller sample sizes.

Disadvantages

The situation does not always lend itself to the application of this research design. In a pragmatic stepwise implementation at different locations, it is conceivable that healthcare providers who are enthusiastic for the intervention will be among the leading group while healthcare providers who are more reluctant will be the last to implement the intervention. To counter this, randomisation of the clusters can also be chosen: a stepped wedge cluster RCT. In all cases, it is recommended to test to what extent the clusters are comparable, for instance in size and overall composition (age, socio-economic position, etc.).

8. Interrupted time-series

This is a quasi-experimental research design, where measurements take place at multiple points in time while an intervention is being implemented (at the group level) or deployed at the individual level. Thus, the 'interruption' refers to the point at which the intervention in introduced. In this research design, there is no control group.

Advantages

Repeated measurements provide insight into the variation in outcome measures prior to the intervention and reveal whether there is a trend change due to the intervention and whether it is in the desired direction. This approach is thus more reliable than a single pre-test post-test design, especially if there is variation in outcome measures (e.g. inflammatory activity in rheumatoid arthritis or shortness of breath in COPD).

Disadvantages

In the absence of a control group, it is not possible to account for the placebo effect, researcher/or practitioner bias and other factors affecting the outcome of the intervention.

9. Comparative time-series

This quasi-experimental research design is similar to the previous design, but includes a control group. In the intervention group and in the control group, the same measurements are taken at several moments before and after the intervention.

Advantages

In addition to the benefits mentioned under interrupted time-series, there is the additional benefit of a control group here.

Disadvantages

Because this design usually does not involve randomisation, differences between the intervention group and the control group may affect the outcome.

10. N=1

The research is conducted on a single individual. In principle, there are several possibilities: observational research, with or without a time-series (see interrupted time-series), or (quasi-) experimental. In the latter case, a randomised, controlled and sometimes even blinded study can take place. The participant undergoes multiple alternating interventions and control periods determined at random. The participant serves as his or her own control. Careful collection of data from individual N=1 studies creates a valuable data set that can be used to form a hypothesis and for the initial substantiation of a hypothesis.

Advantages

This approach can make it very clear to the individual patient which intervention provides the most health benefits. This can be a powerful motivation to subsequently sustain an effective intervention. An N=1 experiment can also be a first pilot to explore the added value of an intervention. Moreover, many different variables can be measured in a single participant, including measurements from wearable devices in the context of lifestyle interventions. N=1 studies can also be conducted for (very) rare disorders.

Disadvantages

Outcomes from a single study participant cannot be generalised to all people with the same disorder. A favourable outcome in an N=1 study is, at most, an indication that one is on the right track. Therefore, in the context of lifestyle research, a single N=1 study will rarely be relevant; at most, in an early exploratory phase. Combined data from a number of N=1 studies may be of greater value, as mentioned above.

11. Crossover design (AB/BA)

This research design is also known as 2X2 design. Here, two groups receive an intervention and a control condition or other intervention during the course of the experiment. One group receives the intervention first and then the control condition, while the order is reversed in the other group. Participants are randomly assigned to one of the two groups and the design is blinded if possible. Sometimes, a pause (washout period) is needed, for example when a drug has to exit the body first. A measurement takes place before and after each period. Although this approach is unsuitable for many lifestyle interventions (see disadvantages), it can sometimes be used, for example when evaluating dietary measures or nutritional supplements.

Advantages

Because all participants eventually undergo the intervention and the control condition, each participant is their own control subject. As a result, fewer participants are needed to achieve statistically significant results. All study participants also benefit from potential advantages of the intervention.

Disadvantages

The experiment lasts longer than the comparison between two groups. The method is unsuitable for lifestyle interventions based on behaviour change as it is practically unfeasible to learn and unlearn behaviour during the study period.

12. Baseline withdrawal (ABA)

This quasi-experimental research design usually consists of three phases: 1) baseline phase with measurement, 2) phase in which the intervention is applied with a measurement, 3) another non-intervention phase with a measurement. This setup assesses the effect of the intervention on the dependent variable (outcome measure).

The design should take into account the sensitivity of the outcome measure to change and the frequency of measurements (the HbA1c measurement in diabetes, for example, gives a picture of blood sugar levels over a longer period and is not determined frequently).

Advantages

Research participants act as their own control. Therefore, this research design can even be used in an individual case study.

Disadvantages

The lack of a control group may require relatively long measurement periods and/or large groups to achieve statistical significance. It sometimes takes quite some time before there is clarity, particularly when measurements are infrequent (e.g. only annual measurements as in controls of patients with cardiovascular risk factors).

13. Regression discontinuity

In this form of quasi-experimental research, study participants are assigned to the intervention condition or the control condition based on the outcome of a measurement. Anyone with an outcome above a predefined cut-off value is assigned to one group; anyone with an outcome below this value enters the other group. This creates groups that are fairly comparable around the cut-off value, differing only in the intervention allocation (for example, patients with a systolic blood pressure of 120 mm Hg do not differ substantially from patients with a blood pressure of 121).

Advantages

No randomisation is required, while still avoiding bias in the allocation to one of the two groups.

Disadvantages

This design provides less information the more individuals have an outcome that is further from the cut-off value (for example, when blood pressure is measured, this creates a comparison between patients with low/normal blood pressure and patients with high blood pressure, two groups that are likely to differ on many variables).

14. Randomised controlled trial

A randomised controlled trial (RCT) is an experimental research design in which two or more groups of individual participants are compared. For example, one or more interventions may be compared with a control condition. This control condition can be normal healthcare or a placebo condition, e.g. general psychoeducation on the subject of the study. Participants are randomly assigned to one of the study groups (arms). The effect is measured by comparison between the outcomes of a pre-measurement and one (or more) post-measurement(s) in all arms of the study.

Advantages

The allocation to the study groups is not influenced by (unmeasured) differences between study participants. Differences between these groups are based purely on chance (randomisation). Due to the lot-drawing procedure, factors such as the preference of the researcher/practitioner or the patient also do not play a significant role. This is especially true for interventions such as drug administration that can be given 'double-blind', in other words none of the parties involved know which participant will be administered which treatment (or placebo). In lifestyle interventions, a double-blind design is not possible.

Disadvantages

An RCT is expensive and laborious, especially if large groups are needed to measure statistically significant differences. RCTs are therefore rarely conducted to evaluate more complex interventions such as (long-term) psychosocial interventions aimed at behavioural change. Because a double-blind design is impossible, researcher bias and patient disappointment may play a role. An RCT measures group effects; it is not always possible to generalise to other populations. It is also not easy to control for environmental and seasonal effects.

15. Cluster RCT

A cluster randomised controlled trial (cRCT) is an experimental research design that randomises at the level of groups (clusters) rather than individual participants. Each cluster is randomly assigned to either an intervention or control group. The effect is measured at the level of each individual participating patient by comparison between the outcomes of a pre-measurement and one (or more) post-measurement(s) in all arms of the study. Individual outcomes are adjusted for clustering, as patients within a cluster tend to be more alike.

Advantages

For lifestyle interventions, this design has the advantage that the practitioner, working in one cluster, can follow the same approach in all patients, allowing for more consistency in implementation. This is a clear advantage, especially for more complex interventions that require extensive instruction. Because of this homogeneity, practitioner and patient preferences will also have less influence than in an ordinary RCT. From an organisational perspective, it may also be more feasible to conduct a comparative study at the level of groups, e.g. healthcare facilities, municipalities or residential areas.

Disadvantages

The number of individuals that need to participate to reach statistical significance is usually larger, so a cluster RCT is often even more expensive than a conventional RCT. Differences between the clusters that have nothing to do with the intervention can affect the outcomes, especially if the correlation of outcomes within each cluster is not carefully considered or if there are large differences between the number of included patients per cluster.

16. Patient preference trial

A patient preference trial is an experimental research design comparing two or more groups of individual participants. Allocating participants into intervention or control groups depends (in part) on participants' preferences. The effect is measured by comparing the outcomes of a pre-measurement and one (or more) post-measurement(s) in all arms of the study.

Advantages

In lifestyle interventions in particular, adherence is often a limiting factor. If participants are not motivated to carry out the intervention for an extended period of time, they are likely to drop out. This problem is (somewhat) mitigated by assigning participants according to their own preferences. Respecting patients' preferences could improve generalisability, especially in behavioural interventions, where personality traits play a role. If the intervention works or does not work in people who choose this intervention, it is presumably also predictive of others who choose this intervention. In implementation research, an advantage is that this design fits well with practice, in which, after all, patient preference is taken into account in the decision (shared decision making).

Disadvantages

Following patients' preferences creates groups that are not comparable in all respects. In the effectiveness study, an outcome may therefore (partly) be caused by differences in the natural process and differences in other (lifestyle) factors that are not part of the intervention. Participant choice partly depends on the information provided prior to the study and how this is done. The (unconscious) bias of the researcher/healthcare provider can thus influence the composition of the groups and thus the outcomes of an effect measurement.

17. Trial of intervention principles (TIPs)

A trial of intervention principles (TIPs) is an experimental research design comparing two or more groups of individual participants, where the intervention under study may change over the course of the study. This design tests theoretical concepts (behavioural change techniques) underlying the intervention. An intervention that is being further developed, e.g. an e-health application, can also be studied. The underlying principles (type of strategy, type of intervention, goal, outcome measures) are defined beforehand and do not change. Adjustments are made only when they do not conflict with these established basic principles. In concrete implementation, several approaches are possible, including sequential sub-trials, after which even re-randomisation or reclassification of participants based on intermediate outcomes is possible.

Advantages

The great advantage of this approach is its flexibility. Relevance increases enormously as a result, particularly in the study of e-health applications. After all, with a rigid RCT approach, there is a risk that the results are no longer relevant when the study is completed because the application has since been renewed or replaced by a better programme. A study of the underlying principles remains relevant even if the application changes.

Disadvantages

The analysis of the results is more complex and requires sound statistical and methodological knowledge. Healthcare professionals and health insurers will look extra critically at the outcomes of a TIPs study, so careful explanation of the methodology followed is all the more important. After all, flexibility and adjustment based on interim outcomes may raise concerns about potential bias. Detailed documentation in advance and clear agreements on what can and cannot be adjusted should prevent this.

4. Quality of evidence: from research to contracting in the basic health insurance package

Methods | Effectiveness research | References

In the Netherlands, the National Health Care Institute (Zorginstituut Nederland, ZIN) is responsible for the package management of insured healthcare within the basic insurance. This means that the institute assesses which care is eligible for reimbursement under the Health Insurance Act (Zorgverzekeringswet, Zvw). An important part of this assessment is use of an appropriate research design to demonstrate the effectiveness of an intervention. However, this is only one aspect of the overall assessment. The fact that an intervention is effective according to scientific research does not automatically mean that it will actually be reimbursed under the Zvw.

The National Health Healthcare Institute states that not only must there be scientific evidence, but that the intervention must also be in line with current scientific knowledge and practice. This means that the effectiveness of the intervention must be generally accepted within the professional group. In addition, the ZIN looks at the efficiency of the intervention: the ratio between the costs and the benefits must be justified. Only when all these conditions have been met will an intervention be considered for inclusion in the insured basic package.

The ZIN (Dutch language) documents *'Beoordeling stand van de wetenschap en praktijk, 2023'* (Zorginstituut Nederland, 2023), *'Rapport - Pakketbeheer in de praktijk 4 | Rapport | Zorginstituut Nederland'* (Zorginstituut Nederland, 2023) and *'Wegwijzer 'Leefstijlinterventies: van initiatief naar basisverzekering'* (Zorginstituut Nederland, 2022) explain this assessment process in more detail. These publications make it clear that the inclusion of healthcare in the basic insurance package requires careful and comprehensive consideration of multiple criteria. Those who would like to know more about the assessment and authorisation of interventions for the basic health insurance package can find additional information on the ZIN website.

References

1. Skivington K, Matthews L, Simpson SA, Craig P, Baird J, Blazeby JM, Boyd KA, Craig N, French DP, McIntosh E, et al. A new framework for developing and evaluating complex interventions: update of Medical Research Council guidance. *BMJ* (2021)n2061. doi: 10.1136/bmj.n2061
2. van Lanen A, Kok DE, Wesselink E, Derksen JWG, May AM, Smit KC, Koopman M, de Wilt J, Kampman E, van Duijnhoven FJB. Associations between low- and high-fat dairy intake and recurrence risk in people with stage <scp>I–III</scp> colorectal cancer differ by sex and primary tumour location. *Int J Cancer* (2024) 155:828–838. doi: 10.1002/ijc.34959
3. Pourhabibi-Zarandi F, Kahrizsangi MA, Eskandarzadeh S, Mansouri F, Vali M, Jalali S, Heidari Z, Shateri Z, Nouri M, Rashidkhani B. Dietary quality index and the risk of breast cancer: a case-control study. *BMC Womens Health* (2023) 23:469. doi: 10.1186/s12905-023-02588-6
4. Strombotne KL, Lum J, Ndugga NJ, Utech AE, Pizer SD, Frakt AB, Conlin PR. Effectiveness of a ketogenic diet and virtual coaching intervention for patients with diabetes: A difference-in-differences analysis. Diabetes Obes Metab (2021) 23:2643–2650. doi: 10.1111/dom.14515
5. Xu W, Ouyang M, Peng D, Jiang Z. Bidirectional Mendelian randomization explores the causal relationship between dietary habits and rheumatoid arthritis. *Medicine (Baltimore)* (2024) 103:e39779. doi: 10.1097/MD.0000000000039779
6. Wongsala M, Rosendahl S, Manasatchakun P, Anbäcken E-M. Applying the PDSA cycle to a group activity promoting lifestyle change for the active ageing of older Thai adults - a focused ethnography. *BMC Geriatr* (2022) 22:117. doi: 10.1186/s12877-022-02775-4
7. Schutte BAM, Haveman-Nies A, Preller L. One-Year Results of the BeweegKuur Lifestyle Intervention Implemented in Dutch Primary Healthcare Settings. *Biomed Res Int* (2015) 2015:484823. doi: 10.1155/2015/484823
8. Nieuwenhuijse EA, Vos RC, van den Hout WB, Struijs JN, Verkleij SM, Busch K, Numans ME, Bonten TN. The Effect and Cost-Effectiveness of Offering a Combined Lifestyle Intervention for the Prevention of Cardiovascular Disease in Primary Care: Results of the Healthy Heart Stepped-Wedge Trial. *Int J Environ Res Public Health* (2023) 20: doi: 10.3390/ijerph20065040
9. Stuber JM, Mackenbach JD, de Bruijn G-J, Gillebaart M, Hoenink JC, Middel CNH, de Ridder DTD, van der Schouw YT, Smit EG, Velema E, et al. Real-world nudging, pricing, and mobile physical activity coaching was insufficient to improve lifestyle behaviours and cardiometabolic health: the Supreme Nudge parallel cluster-randomised controlled supermarket trial. *BMC Med* (2024) 22:52. doi: 10.1186/s12916-024-03268-4
10. Tian Y, Ma Y, Fu Y, Zheng J-S. Application of n-of-1 Clinical Trials in Personalized Nutrition Research: A Trial Protocol for Westlake N-of-1 Trials for Macronutrient Intake (WE-MACNUTR). *Curr Dev Nutr* (2020) 4:nzaa143. doi: 10.1093/cdn/nzaa143
11. Connolly EL, Liu AH, Radavelli-Bagatini S, Shafaei A, Boyce MC, Wood LG, McCahon L, Koch H, Sim M, Hill CR, et al. Cruciferous vegetables lower blood pressure in adults with mildly elevated blood pressure in a randomized, controlled, crossover trial: the VEgetableS for vaScular hEaLth (VESSEL) study. *BMC Med* (2024) 22:353. doi: 10.1186/s12916-024-03577-8
12. Li Y, Babazono A, Jamal A, Liu N, Fujita T, Zhao R, Maeno Y, Su Y, Liang L, Yao L. The impact of lifestyle guidance intervention on health outcomes among Japanese middle-aged population with metabolic syndrome: A regression discontinuity study. *Soc Sci Med* (2022) 314:115468. doi: 10.1016/j.socscimed.2022.115468

13. van den Burg EL, Schoonakker MP, van Peet PG, van den Akker-van Marle EM, Lamb HJ, Longo VD, Numans ME, Pijl H. Integration of a fasting-mimicking diet programme in primary care for type 2 diabetes reduces the need for medication and improves glycaemic control: a 12-month randomised controlled trial. *Diabetologia* (2024) 67:1245–1259. doi: 10.1007/s00125-024-06137-0
14. Lean ME, Leslie WS, Barnes AC, Brosnahan N, Thom G, McCombie L, Peters C, Zhyzhneuskaya S, Al-Mrabeh A, Hollingsworth KG, et al. Primary care-led weight management for remission of type 2 diabetes (DiRECT): an open-label, cluster-randomised trial. *Lancet* (2018) 391:541–551. doi: 10.1016/S0140-6736(17)33102-1
15. Iannuzzelli K, Suzuki S, Karavolos K, Powell LH. Patient Preferences for Lifestyle Management in a Multi-site Randomized Lifestyle Trial for Remission of the Metabolic Syndrome. *Int J Behav Med* (2024) doi: 10.1007/s12529-024-10278-2
16. Fitzsimmons-Craft EE, Taylor CB, Graham AK, Sadeh-Sharvit S, Balantekin KN, Eichen DM, Monterubio GE, Goel NJ, Flatt RE, Karam AM, et al. Effectiveness of a Digital Cognitive Behavior Therapy–Guided Self-Help Intervention for Eating Disorders in College Women. *JAMA Netw Open* (2020) 3:e2015633. doi: 10.1001/jamanetworkopen.2020.15633

Coalitie
Leefstijl in de Zorg

Authors
Prof. dr. Jessica Kiefte (LUMC)
Dr. Myrthe Boelens (LUMC)
Dr. Rimke Vos (LUMC)
Drs. Pieter van Megchelen
Drs. Marjo Knapen (NFU)
Dr. Jolanda van Bilsen (TNO)

In opdracht van
Coalition for Lifestyle in Healthcare, Research Team
Dr. Jolanda van Bilsen, Drs. Marjo Knapen