PeRSEVERE: PRincipleS for handling end of participation EVEnts in clinical trials REsearch

Principles and explanation – September 2023

PeRSEVERE collaborative group*

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Summary of PeRSEVERE principles (key messages only)

Overarching principles (O)

- Everyone running or taking part in studies should be aware that participants may choose to change, reduce or stop their participation after they agree to join the study (principle **O1**).
- The nature and extent of participation changes should be the participant's decision to make, within the limits of what is possible for a given study. Their decision should be informed and freely-given (principle **O2**).
- Everyone running or taking part in studies should be aware that collecting as much as possible of a study's planned data can help a study reach a clear and reliable conclusion (principle **O3**).
- Loss of contact between a participant and researchers should not be considered the same as a participant saying that they want to stop study participation (principle **O4**).
- Study data collection should continue until a study participant explicitly tells researchers that they want it to stop (principle **O5**).
- Data collected for a study up to the point a study participant stops providing data should be used in the study analysis, and kept with the other study data until the study is over (principle **O6**).
- Stopping participation early does not affect participants' right to receive study-related information later on, if they want to receive it or if it could be important for them to have (principle **O7**).

Study Development and Participant Information (D)

- Studies should be designed and resourced to allow data collection to continue wherever possible, particularly for study outcome data (principle **D1**).
- Study protocols should include clear instructions on how participation changes should be practically managed (principle **D2**).
- Before participants agree to take part in a study, they should receive clear and balanced information about what will happen if they want to stop participating (principle **D3**).
- Participants should be informed, before they consent to join a study, about what will happen if contact is lost during the study (principle **D4**).
- Throughout each study, researchers should make reasonable efforts to check that participants are still willing and able to take part. Researchers should be prepared to discuss possible changes to participation, where these might allow participants who are still willing to make a contribution to the study to do so (principle **D5**).

- Everyone involved in running studies should be trained and supported to manage participation changes for the good of both the participants and the study (principle **D6**).

Data Management and Monitoring (M)

- Data about study participation changes should be recorded in a standardised way and include enough detail to usefully inform study management, analysis and reporting (principle **M1**).
- All those responsible for running and overseeing a study should, at appropriately regular intervals, review summarised data about participation changes in the study (principle **M2**).

Study Analysis and Reporting (R)

- When participation changes mean that not all the study data has been collected as planned, researchers should analyse the study in ways that give the best chance that the study will still have reliable results (principle **R1**).
- End of study reporting of participation changes should be done consistently within a study, showing any changes in level of participation, preferably split by treatment group (principle **R2**).

Introduction

Background and aims

All guidelines, policies and laws about clinical trials and other research with human participants (from here on referred to as 'studies') are clear that, before taking part in research, individuals[1] must voluntarily give informed consent, and that they can withdraw that consent at any time after having given it, without providing a reason and without negative consequences for them.[2] [3] [4] In real terms, study participants can therefore stop participating whenever they like.

Participation in a study may often be made up of different elements, for example undergoing the medical treatment that the study is evaluating, attending hospital visits for study-specific medical assessments, completing study-specific questionnaires, and so on. It is possible for some of these to stop while others continue (with some limitations – for example it would not be safe for a study participant to continue receiving study treatment while stopping medical assessments intended to monitor their safety).

We argue that the spirit of the right to withdraw consent suggests that individual study participants must stay in charge of their own destiny. It should therefore be they who decide which elements of study participation they are happy to continue and which they would like to stop, rather than being given an all-or-nothing choice. For example, if it is possible in a given study for participants to stop study-specific visits but continue providing relevant data from routine healthcare visits, participants should be given the choice to accept or refuse this arrangement, and they should be given adequate information to inform this choice. The only exception to this is where others need to take action to protect study participants, for example if those responsible for the participant's clinical care feel it is in their best interests for them to stop receiving study treatment.

The third principle of the ICH Guideline for Good Clinical Practice[3] says: "The rights, safety, and well-being of the [study participants] are the most important considerations and should prevail over interests of science and society." This points to the potential for conflict between the needs of individual study participants wanting to stop participating, and the needs of the study and the robustness of its results ("science and society"), which will be negatively affected by participants stopping participation earlier than was planned in the study protocol.

Despite this, we argue there is at least theoretically a way to prepare and run studies so that participants' rights are not compromised but *also* the negative impact on the study results is kept to a minimum (while not being completely eradicated).

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[1] Here, this means individuals with capacity to give informed consent – see 'Scope and limitations', below.
[2] Declaration of Helsinki: https://www.wma.net/policies-post/wma-declaration-of-helsinki-ethical-principles-for-medical-research-involving-human-subjects/
[3] ICH Guideline for Good Clinical Practice: https://www.ema.europa.eu/en/documents/scientific-guideline/ich-e-6-r2-guideline-good-clinical-practice-step-5_en.pdf
[4] 2001 EU Clinical Trials Directive: https://ec.europa.eu/health/sites/health/files/files/eudralex/vol-1/dir_2001_20/dir_2001_20_en.pdf

We must aim to achieve this for at least the following reasons: a) the results of clinical studies are used to inform and improve healthcare for the rest of society, so they must be as useful and reliable as possible, and b) when a study does not produce useful results (this means we don't learn anything *new* from the results, regardless of whether what we learn is 'positive' or 'negative'[5]), the study's participants have given their time and been exposed to any risks associated with study participation for no benefit to society.

The principles in this document have been developed through a project called PeRSEVERE (PRincipleS for handling end of participation EVEnts in clinical trials REsearch). They are intended to guide how study participants' right to withdraw their informed consent should be applied in practice so that we can achieve the following aims:

- **Do the best by individual study participants:** individual study participants should get the best possible information to inform their choices about ongoing study participation, and be as involved as possible in any decisions that are made about their participation. All decisions to change (or not change) the nature of their study participation must be informed and freely-made, in the same way as initial consent.
- **Do the best by the study, and by research and society in general:** the actual or perceived robustness of a study's results should not be impaired by individual study participants' decisions to stop participating unless it is completely unavoidable; this protects those patients in future whose treatment might be affected by the study's results. Studies should be transparently reported so that it is clear what changes in participation occurred, and how these changes were handled in the study analyses.

Our principles were initially developed through extensive discussion and debate within our collaborative group (see full list of contributors at the end of this document) which was formed through the UK CRC Registered Clinical Trials Unit Network[6] and which includes patients, statisticians, methodologists, clinical trial managers, data managers, and specialists in quality assurance, research regulation and bioethics. Our principles were then tested through a public consultation run in 2021, aiming in particular to gather additional feedback on the principles' clarity, feasibility, novelty and acceptability.

Throughout the process of developing our principles, we have been guided by the high-level principles of ethical research conduct (including good clinical practice), our knowledge and understanding of existing clinical research regulations and guidance, and our collective experience of designing, running, analysing, reporting on and participating in clinical trials and other research.

In general, we suggest it is best to be proactive in ensuring the above aims are achieved. This means designing studies and preparing to run them in the right way, rather than only reacting

[5] A trial could reliably show that a new treatment is *not* better than an existing treatment. This might be disappointing, but this would still be something new we had learned, and would be a useful result. The worst outcome from a trial is that the results are not reliable and so we have learned nothing new.
[6] https://ukcrc-ctu.org.uk

to problems as they occur. We aimed to keep this in mind as we have developed the principles.

Everyone within research teams can play a part in ensuring that studies are designed, prepared and run in the right way, but we suggest there may be particularly important roles for patients involved in running and overseeing a study (to ensure all actions taken and processes implemented are fair, appropriate and uphold study participants' rights) and statisticians, methodologists and trialists (to ensure that all actions and processes support the study objectives and uphold study integrity).

We acknowledge that some of our principles are already reasonably well-established in clinical research (at least in the UK). However, we consider it important to present them all as a complete, coherent set. We are not aware of any previous attempts to comprehensively define, as we have done here, how the ethical right of study participants to withdraw their consent should be put into practice.

Other relevant background information guiding our principles has included:

- The SPIRIT statement[7], which says what should be included in clinical trial protocols.
- The CONSORT statement[8], which says how clinical trials should be reported clearly and transparently.
- Revision 1 (R1) of the ICH guidance document E9: "addendum on estimands and sensitivity analysis in clinical trials to the guideline on statistical principles for clinical trials"[9], and other sources on the use of 'estimands' in clinical trials. The estimand concept is important in handling participation changes in clinical trials, as it requires researchers to describe a highly specific research question up front, and then design, conduct and analyse their study with this research question in mind.
- Current data protection laws in the European Union and UK (the EU and UK General Data Protection Regulation[10] [GDPR] and the UK 2018 Data Protection Act[11]). These give special protection to data used in research, including to allow researchers to keep data after a study participant decides to stop participating in a study, as long as certain conditions are met. These laws also mean that potential study participants must be clearly informed, before they join a study, about how their data will be used in the study, including about any limitations on their usual data protection rights and about any possible international data transfers.
- Laws governing how to run studies involving medicines[12] mandate that all data collected in a study must be kept for a long time after the end of the study (in some cases, as long as 25 years). This includes data about study participants who stopped participating early. This is so that it is possible for the regulatory authorities to check

[7] https://www.spirit-statement.org/
[8] http://www.consort-statement.org/
[9] https://www.ema.europa.eu/en/ich-e9-statistical-principles-clinical-trials
[10] https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32016R0679&from=EN
[11] http://www.legislation.gov.uk/ukpga/2018/12/pdfs/ukpga_20180012_en.pdf
[12] https://www.hra.nhs.uk/planning-and-improving-research/policies-standards-legislation/clinical-trials-investigational-medicinal-products-ctimps/

the results of the study are accurate at any time during this period. This is particularly important when a study led to changes in the standard of care for a particular health condition.

The PeRSEVERE collaborator group is mostly based in the UK and we do not claim to be experts in laws and policies applying to research in other areas of the world. We are also conscious of the breadth of research activity globally, including settings and study types that none of us have experience of. We aimed for our principles to be general enough to be able to apply, at least in theory, to any setting. However, we certainly encourage others to apply our principles with some flexibility to account for each specific study, considering factors such as the patient group taking part in the study, the study's characteristics (e.g. the number of participants taking part, the study design and so on), and the study-specific risks to patient safety and study integrity.

Scope and limitations

1. Types of research: the PeRSEVERE principles are intended to apply to all health research with human participants that involves some active, ongoing participation from those participants. This means the individual participants have given informed consent before taking part, and that taking part lasts for a period of time (i.e. not a one-off contribution) and involves receiving medical treatment, completing questionnaires, undergoing medical assessments or otherwise actively providing data for use in the research. The principles are particularly relevant to clinical trials research (including randomised controlled trials), but can also apply to observational studies and other sorts of health research, if they include active, ongoing participation by individuals, as defined above.

The principles do not apply directly to research that involves only analysing biological samples that study participants have consented to be stored in a central location (for example a 'biobank') for research purposes, as this sort of research usually does not involve any active, ongoing participation from the individual participants (see also the related point below about storage and use of biological samples).

Similarly, the principles do not apply to research only involving data obtained from healthcare databases held by the UK National Health Service or similar public organisations. This sort of research also does not usually involve any active, ongoing participation from its participants. It sometimes may not be done on the basis of patients' consent[13], so issues of informed consent and its withdrawal will not apply (although patients can refuse this use of data via mechanisms such as the National Data Opt-Out[14]). Finally, it also often involves only

[13] An alternative route for conducting this sort of research in the UK is where access to confidential patient data for research is given via a 'section 251' approval. For more information see: https://digital.nhs.uk/services/data-access-request-service-dars/dars-guidance/data-sharing-standard-7b---duty-of-confidentiality

[14] https://digital.nhs.uk/services/data-access-request-service-dars/how-the-national-data-opt-out-affects-data-released-by-nhs-digital/national-data-opt-out-guidance-for-researchers/4-section-251-and-the-application-of-national-data-opt-outs

anonymous data, and as the researchers cannot tell who the data they have is about, there is no way for them to contact or otherwise 'involve' the individual research participants.

2. Types of participation change: our principles mainly address study participation changes that could lead to expected data being unavailable or not measured for study analysis, for example participants no longer taking part in study follow-up arrangements (whatever those might be). When participants only stop study treatment or intervention, but carry on with study follow-up arrangements, this should not lead to missing outcome data and is therefore mostly out of our scope. Our principles do not apply in cases where individuals' participation stops because the whole study is coming to a close earlier than planned.

a. Capacity to give informed consent: specific arrangements apply where potential study participants do not have the mental or legal capacity to give informed consent (for example due to being unconscious, having conditions such as dementia or being under the legal age of consent [16 for most situations in the UK]) or where study participants who gave valid informed consent later lose capacity to consent during the study. In the UK, the relevant laws include the Medicines for Human Use (Clinical Trials) Regulation[15] for most studies involving medicines, and for other studies the 2005 Mental Capacity Act[16] (applying in England and Wales) and the Adults with Incapacity (Scotland) Act 2000[17]. When dealing with these issues involving absence or loss of capacity to consent, researchers should follow the relevant local laws (including those in force outside the UK).

Although we acknowledge that understanding of the regulations in the UK may be limited,[18] we have decided that issues around loss or absence of capacity of consent are out of scope for this version of our principles, which are focussed on study participants making decisions for themselves. However, where necessary we have noted where issues of capacity to consent may be particularly relevant.

For similar reasons, the situation where an individual gains capacity to consent during their time taking part in a study (for example if they regain consciousness, or reach the age where they may consent for themselves) is also out of our scope. However if, after gaining capacity to consent, the individual does give informed consent to study participation, our principles will then apply.

[15] http://www.legislation.gov.uk/uksi/2004/1031/pdfs/uksi_20041031_en.pdf
[16] http://www.legislation.gov.uk/ukpga/2005/9/pdfs/ukpga_20050009_en.pdf
[17] http://www.legislation.gov.uk/asp/2000/4/pdfs/asp_20000004_en.pdf
[18] Shepherd V, Griffith R, Sheehan M, et al. Healthcare professionals' understanding of the legislation governing research involving adults lacking mental capacity in England and Wales: a national survey. Journal of Medical Ethics 2018;44:632-637.

b. Participants dying while the study is ongoing: if participants die while they are still participating in a study, clearly their active participation ends at that point.

However, death is inherently very different to other sorts of participation change. Many of our principles relate to activity or events that might take place after a participation change, and so these cannot apply in the case of participants' death. In theory, decision-making about aspects of study involvement that may continue (such as storage and use of samples or data) might pass to others, such as relatives or carers, after a participant's death. However, in the UK at least, an individual's consent given and not withdrawn (or affected by changes in capacity to consent) prior to their death is considered to persist after they die.[19] There is no existing obligation to inform relatives or carers about details of the participant's participation and which aspects of it might continue or not. There is also no clear argument that such disclosure would definitely be the right thing to do.

Considerations around consent and the possible involvement of relatives or carers in the case of participants dying while taking part in a study are likely to be complex and/or sensitive. It might be reasonable to suggest that additional guidance or policy is needed to clarify aspects of how these complexities and sensitivities should best be managed in practice. However, aside from a few specific places in our guidance, we have considered this issue to be out of our scope.

3. Improving retention: we are aware of efforts to understand how studies can be run to reduce the proportion of study participants who decide to stop participating early[20,21] (often referred to as 'improving retention'). This might be by offering ethically acceptable incentives to study participants, making study participation less burdensome, or through other means. This work is important and complementary to our principles, but also out of our scope. Instead, we are looking to achieve the aims outlined above, no matter what individual study participants decide to do.

We suggest that researchers designing and running studies should continue to follow evidence-based best practice around improving study retention, as it continues to develop. We also suggest that it should be routine (if it is not already) for researchers to consider, in discussion with involved patients, how to minimise the amount of time and effort taking part

[19] http://www.hra-decisiontools.org.uk/consent/principles-deceased.html

[20] Brueton, V. C., Tierney, J. F., Stenning, S., Meredith, S., Harding, S., Nazareth, I., & Rait, G. (2014). Strategies to improve retention in randomised trials: a Cochrane systematic review and meta analysis. BMJ Open, 4(2), e003821. https://doi.org/10.1136/bmjopen-2013-003821

[21] Brunsdon, D., Biesty, L., Brocklehurst, P., Brueton, V., Devane, D., Elliott, J., … Gillies, K. (2019). What are the most important unanswered research questions in trial retention? A James Lind Alliance Priority Setting Partnership: the PRioRiTy II (Prioritising Retention in Randomised Trials) study. Trials, 20(1), 593. https://doi.org/10.1186/s13063-019-3687-7

in the research will require of the participants. This includes limiting the amount of data collection to what is absolutely necessary.

4. Biological samples: we considered issues to do with storage and use of study participants' biological samples to be largely out of our scope (this means what happens to stored biological samples if a participant decides to stop participating in a study) unless we have specifically referenced them. However, our principles do apply to data that has been generated from analysing study participants' biological samples.

5. Privacy, confidentiality and consent to use personal data: informed consent, confidentiality and data use are usually closely linked. Participation in research often has implications for confidentiality, for example where more people than usual will see a patient's medical records or their name. In some jurisdictions and settings (though not often in the UK), participants' informed consent is the basis for researchers using personal data about them. These issues are broadly within scope for our principles, in particular where withdrawal of informed consent has implications for study participants' confidentiality and privacy and further data use. However, they are not our primary focus, so we have mentioned them only where they interact with the broader consent to participate in a research study.

There may also be additional considerations that we cannot realistically incorporate exhaustively into our guidance. For example, there are specific requirements around the reliance on consent to process personal data under EU and UK law,[22] and these requirements are quite separate to those around research consent. We therefore suggest that readers should use our guidance alongside any national and international laws and guidelines on confidentiality, privacy and personal data use.

[22] https://ico.org.uk/for-organisations/guide-to-data-protection/guide-to-the-general-data-protection-regulation-gdpr/lawful-basis-for-processing/consent/

Terminology and language: describing end of participation

In our experience, there can be confusion and ambiguity around terms commonly used to describe stopping study participation, such as ‘withdrawn’, ‘lost to follow-up’, ‘drop-out’ or ‘off-trial’.

In general, we aim in this document to describe participation ending or changing as plainly as we can, using language with explicit meaning which, as a result, can mean the same thing to everyone. Some suggestions for clearer terminology are outlined below. We suggest these, or similarly clear terminology, could be used in many situations when designing, running, analysing and reporting studies, including in study protocols, study reports, and in communications between researchers and study participants.

This level of detail may not be necessary in all situations. For example, by the time of a study’s final analysis, it may be useful to simply summarise which participants we have study outcome data for and which we do not. However, use of the suggested terminology below does not prevent this sort of summarisation taking place when it is needed.

Suggested terminology

- For aspects of study participation requiring ongoing commitment (for example receipt of intervention, attendance at clinic visits, completion of questionnaires):
    - When a participant decides to completely stop an aspect of participation before it was supposed to finish, we suggest using the phrase **"stopped … early".** For example "stopped study-specific visits early".
    - In some cases it might be useful to distinguish between participation changes following a participant’s decision and changes (particularly to medical treatment or procedures) guided by clinical decisions of a participant’s doctors. For example, if a participant’s doctor decided it was in their best interests to stop receiving a study treatment, they could be described as having “**stopped treatment early based on a clinical decision”.**
    - When a participant decides to *reduce* their level of commitment, without totally having stopped, we suggest using the term "**reduced…".** For example, "reduced frequency of study visits". This can also be used to describe changes in receipt of study treatment or intervention, but study protocols often make specific provisions around dose delays or modifications (if this is the case, the protocol’s terminology should be used).
    - When some alternative, specific arrangement has been made with a participant regarding their participation, we suggest this should be explicitly stated, for example “stopped study visits early; telephone follow-up only”. Alternatively, the general term **“changed…”** can be used, for example “follow-up changed from study visits to telephone follow-up only”.

- When a participant has stopped an aspect of participation at the time that the study protocol specified it was supposed to stop, we suggest using "**completed…".** For example, "completed study visits".
- In some studies, there may not be a set period of time when participants get treatment/intervention. For example, participants may continue receiving treatment until it does not seem to be working any more. In these cases, the idea of stopping treatment 'early' might not be quite right, but nor might it be right to say they have 'completed' treatment. In these cases, we suggest the phase "**(permanently) stopped treatment because [of]…".** For example, "stopped treatment because it was no longer beneficial", or "stopped treatment because of side-effects".

- For aspects of study participation that do not require ongoing, active commitment[23] (for example clinical trials units getting additional data for the study from routine healthcare data providers like NHS digital, or biological samples being stored for future research projects) we will say "**no longer agrees to…".** For example, "the participant no longer agrees to have their biological sample stored for future research".

- Loss of contact:
  - We expect study protocols to specify how to manage loss of contact with participants (this means without them having expressed any explicit wish about stopping study participation). This should include a set process to follow, and criteria for judging when to stop trying to contact someone (or stop for the time being). At this point, we suggest describing the person as having **lost contact for now.** This implies that it should be possible to try again at a later date to contact them, for example prior to the final study analysis. The study protocol should specify when this later contact should be.
  - At the end of the study, there may be a group of participants who lost contact with the study without explicitly asking to stop participating and for whom no further data was ever obtained. We suggest these participants could be described as having **lost contact and never regained, with no further follow-up.**
  - If data about these participants is obtained through other sources (for example from routine healthcare data providers like NHS Digital, and always in line with participant consent), they might instead be categorised as having had **lost contact and never regained, but with some indirect follow-up.**

- **Change in participation status** or just **participation change**: general terms used to mean all instances where a participant makes a decision (or in some cases where a decision is made on their behalf) to end or reduce study participation.

[23] Where a piece of research only involves this sort of activity, it may not be within the scope of the PeRSEVERE principles; see 'Scope and limitations', above. The point here refers to cases where research involves these activities as well as others involving more ongoing, active commitment.

The terms above are not mutually exclusive, as ending or changing participation can be complex and specific to an individual's situation. The terms can be combined as appropriate with "but" or "and" in order to convey exactly what has stopped, reduced or still continues in each case. For example, "the participant stopped intervention early and is on reduced study visits, but still agrees to their data being accessed through routine healthcare data sources".

Glossary: other terms

- We have used the word '**study**' throughout this document as a generic word for all types of research that our principles apply to (see above).
- We have used the word '**participant**' throughout to mean people who take part in research, except where '**potential participant**' might be more appropriate (this means where we are referring to people who are only considering taking part in a study).
- We use '**researcher**' throughout the document as a general term to mean people who design, run, analyse or otherwise oversee research. We sometimes make an exception to mention specific roles or individuals. For example, in places we make a distinction between those with organisational responsibility for running studies (such as sponsors or clinical trials units) and those with clinical care responsibilities at clinical trial 'sites'. In these sorts of cases, we have specified who we mean, for example 'those with responsibility for participants' care'.
- We have generally used the word '**data**' to mean information that is used in study analysis or for running studies.
- We have generally used the word '**information**' to mean details provided verbally or in writing to (potential) study participants, including to inform their initial and ongoing consent.
- We have used the term '**data collection**' to refer to the act of adding relevant data onto study forms or systems. This therefore implies that this data will be available for running and analysing each study. We have not used this term to mean tests or procedures used to generate the data in the first place, although we accept that it is possible to imagine that data generation and data collection could be combined in some cases.

Overarching Principles

O1 Participation can stop, reduce or change: Everyone running or taking part in studies should be aware that participants may choose to change, reduce or stop their participation after they agree to join the study.

All language and communication about any participation changes should be clear about exactly what has changed, reduced or stopped, and what has not.

Explanation

In laws and other rules about research with human participants, 'withdrawal' of informed consent is described in all-or-nothing terms – participants have either given consent to participate, or they have withdrawn their consent and are not taking part in any aspects of the study anymore.

In reality, things are often more complex than that. Study participants might choose to completely stop only some aspects of study participation, for example taking study treatment, filling in study questionnaires, or attending study-specific hospital visits. Rather than stopping participation entirely, they might instead want to reduce participation, for example taking part less often.

If it is feasible and still fits with the study's aims, participants might also change *how* they take part, for example they might take part in study activities at the same times, but in a different way (for example, via telephone calls with their research nurse instead of going into a clinic for a visit). It may even be possible for participation to increase in some cases, for example if a participant were to change their mind about stopping aspects of participation and re-start them. Again, this can only happen if it is feasible and meets the study's aims.

It is important that everyone running and taking part in studies is aware of this complexity. We also need to use language that reflects this. Just describing study participants as 'withdrawn' or 'off-study' is unlikely to be useful in many cases, because we won't know exactly what participants' wishes are, or exactly what they want to stop.

See also:

- Unless a participation change needs to happen in order to protect a study participant (usually in relation to whether or not they continue taking a study treatment), all changes in participation should be decided by the participants themselves. See principle O2.
- See the principles about study development D1 (protecting study integrity by design) and D2 (protocol content) for more on preparing for participation changes during the study design stage. As per principle D1, any sort of reduced or alternative ways for

participants to keep taking part should only be allowed if they support the scientific integrity of the study.

- The issue of clear language and communication mentioned above affects many aspects of how studies are designed, run and reported. As well as study protocols (see principle D2), this is important in communication between researchers and study participants (see principles D3, D4 and D5), training of researchers running studies (see principle D6), data collection (principle M1), monitoring study progress (principle M2) and study reporting (R2).

Glossary:

- **Study protocol:** this is the document (or set of documents) that describes why a study is needed, what it aims to achieve and how it should be run.
- We use the term **"running" a study** here to mean all activity involved in making a study happen, including getting the relevant approvals to start the study, working with the NHS and other organisations to set up study sites where participants will be recruited, making decisions about the management of the study, collecting and processing study data, and so on.

O2 Participants decide how their participation changes: The nature and extent of participation changes should be the participant's decision to make, within the limits of what is possible for a given study. Their decision should be informed and freely-given.

The only exception to this is where aspects of participation need to change or be stopped by someone else in order to protect a participant's safety or well-being.

Explanation

When people are considering whether or not to take part in a research study, their decision about this is theirs to make. Their decision should be given freely, in that no one may put pressure on them to agree or to decline to take part. Their decision should also be informed by good information about what their choices are, and what the implications of these choices would be.

All of these things also apply when participation stops, reduces or changes. Participants should get clear and useful information about what their choices are, to help them understand the various advantages and drawbacks of the different options. Using this information, they should make their own decision (with the help or advice of others if they want) about how their participation will change. Their decision might be that they want to stop all aspects of their involvement in the study, but they might instead be happy to remain involved in some way.

Within each study, there will be limits to exactly how participation can change for a given participant. Researchers should consider this when they are designing a study, and where it might be useful for participants to know, researchers should make clear to participants what changes to participation are possible, and therefore which are not.

In some studies where participation involves a number of aspects, participants may theoretically have many options about how their participation can change. Researchers should consider how to avoid overloading participants with information and potential choices. This could involve organising the aspects of participation into 'layers' or 'tiers' to make participants' choices easier.

It is also important that the fact of participants having options and being asked to consider them should not act as any sort of barrier to participants stopping all aspects of participation, if that is what they want to do. It should therefore still be straightforward for them to communicate this sort of decision to the researchers.

An important exception where someone other than the participant decides how participation will change is where someone else – usually a doctor or another person responsible for the participant's care – will make a decision that it is in the participant's best interests for some aspects of participation to stop. This is often in the context of the participant stopping study treatment, if their doctor decides it is not safe for the participant to continue taking it. Study protocols often have specific rules about when treatment should stop, if it is showing signs of not being safe or not at least potentially beneficial for the participant. It is also possible that

those responsible for the participant's care, or the researchers, might decide that other aspects of participation should stop, if they feel that continuing them might not be in the participant's best interests.

These decisions by others should only apply to relevant aspects of participation, and not beyond these. For example, if a doctor decides it is best for a participant to stop study treatment, then the treatment should stop, but other aspects of participation should stop only if the participant wants them to.

Whenever a decision like this is made on behalf of the participant, or where a participant is keen to continue participating but cannot do so in a reduced or alternative way within the particular study, the decision should be communicated and explained to the participant, clearly and in a timely manner. The participant should also have the chance to ask questions of an appropriate person (for example, their doctor) so that they can understand why all or some aspects their participation has had to stop.

Other important considerations

Different considerations will apply in situations where individuals have lost capacity to give informed consent (or do not have capacity and have not since the study of the study). Applicable laws and guidance should be followed in these cases.

See also

- Information given to participants to guide their decision to change how they take part should include why, if they agreed to continue making a contribution to the study but with reduced commitment, this can be beneficial for the study results. See principle O3 for more on this.
- The situation where participants stop actively participating in a study without saying anything about what they want to do should be treated differently to a situation where they have expressed a wish to stop, reduce or change their participation. See principle O4.
- Study data collection is an example of an aspect of participation that can continue until a participant says they want it to stop, as long as all the conditions mentioned above are met. See principle O5.
- Participants should be made aware of the limits on their ability to have study data about them deleted, once it has been collected. See principle O6.
- Participants also have choices about what information they receive after they stop, reduce or change their participation. See principle O7.
- Researchers should decide when they are designing a study what choices will be available for reduced or altered participation, particularly focussing on allowing continued data provision with less participant commitment. See principle D1.

- Protocol instructions about managing participation changes should include how researchers can help participants make an informed and freely-given decision about changing their participation, as well as details of the extent of, and limits on, participants' choices. See principle D2.
- Participants should get good information before they agree to take part in a study about what will happen if they later want to stop, reduce or change their participation, or if they stop actively participating without saying what they want to do. See principles D3 and D4 on these topics, respectively.
- Discussions between researchers and participants during the study and at the time of a participant deciding to change their participation can help the participant decide exactly what they want to do. See principle D5.
- Researchers should be adequately trained and supported to help participants make an informed and freely-given decision about changing their participation. See principle D6.

Glossary

- **Study protocol:** this is the document (or set of documents) that describes why a study is needed, what it aims to achieve and how it should be run.
- **Capacity** or **capacity to consent** means a person's ability to make decisions for themselves. In the context of research, it means a person's ability to give informed consent to take part in a study. Some people have a varying or reduced ability to make decisions for themselves, for example people with dementia. By law, children also do not have capacity to consent, so their parents or guardian need to consent (or not) on their behalf.

O3 The more data, the better: Everyone running or taking part in studies should be aware that collecting as much as possible of a study's planned data can help a study reach a clear and reliable conclusion.

This should be made clear to potential study participants using ethically-approved wording before they agree to take part in the study.

Explanation

Clinical trials and other studies are designed to answer research questions by collecting certain data about a specific number of study participants. If the study analysis includes fewer participants' data than planned, this can make study results less reliable. For example, it might mean results are unclear about whether or not a new treatment is better, when in reality it is better. For this reason, it is important that as much of the relevant data as possible is included in the study analysis. This is particularly the case for study outcome data, i.e. the data that will be used to answer the study's research questions.

Everyone running and designing studies should be aware of this, so that they can take appropriate action to make sure the study collects enough of the planned data to answer the main research question, wherever possible.

It is also important that study participants know how vital data collection is to the accuracy of study results. This information must not prevent study participants doing what is right for them – for example stopping study-specific hospital visits, or stopping data being collected entirely, if that is what they want to do. But they should be aware - before they join the study - of the effect of their data not being available for analysis, so that they can make an informed choice about any changes to their participation.

For example, it is sometimes possible for participants to stop study-specific visits but continue participating in the study in other ways that involve less commitment from them. Participants might like to do this, if they are given the choice. Studies should also be designed to allow this, where possible (see principle D1 on protecting study integrity by design).

Other important considerations

The amount of data collected for a study is not the only important thing. It is also important that the data is good 'quality', for example that it is accurate and contains the details that are needed to reliably answer the study's research questions.

Collection of quality data should be achieved through robust data collection and data management mechanisms. If any participants are happy to continue taking part but with reduced commitment, they should only be presented with options that will still provide reliable data to answer the study's research questions (see principle D1).

See also:

- The benefits of collecting as much as possible of the study's planned data should be communicated to potential study participants so that they can use this information to inform their decisions about stopping, reducing or changing their participation. See principle O2.
- Any forms of reduced participation, i.e. participants continuing to take part in some capacity but with reduced commitment, should be feasible and should not negatively affect the scientific integrity of a study. See principle D1.
- Participants should receive clear and balanced information, before they agree to take part in a study, about what will happen if they want to stop or change their participation later on. See principle D3 for more on this.
- Dialogue about study participation should be encouraged between researchers and participants throughout the study. See principle D5 for more on this. These discussions will be more productive if participants are as informed as they can be about the implications of their decision.

Glossary:

- We use the term **"running" a study** here to mean all activity involved in making a study happen, including getting the relevant approvals to start the study, working with the NHS and other organisations to set up study sites where participants will be recruited, making decisions about the management of the study, collecting and processing study data, and so on.
- **Data collection:** this means the act of adding relevant data onto study forms or systems, to make the data available for running and analysing each study. It does not refer to any separate tests or procedures used to generate the data in the first place.
- **Outcome data:** all research studies involve measuring something in order to reach conclusions. The thing being measured is the 'outcome', and data about it is the outcome data. For example, a healthcare study might give two groups of people different treatments, then measure how their health changes over time to see which treatment is better. The data about how the participants' health changes over time is the outcome data. Outcome data is particularly important, because without it, studies cannot reach clear conclusions.

O4 Losing contact: Loss of contact between a participant and researchers should not be considered the same as a participant saying that they want to stop study participation.

Explanation

Sometimes researchers might find that a study participant is no longer contactable, during the time they're still expected to take part in study activities. A loss of contact should not be considered the same as a participant deciding they don't want to take part in the study anymore.

While it is possible that the participant has decided to stop responding to researcher contact because they no longer want to take part in the study, this might not be the case. There may be other reasons why contact has been lost, and it might not be right to make a strong assumption in either direction. Therefore, unless there is a specific reason to think it is not appropriate, reasonable attempts can be made to regain contact with the participant to find out if they are happy to make further contributions to the study.

Researchers should make a plan, with patient involvement, when they are designing the study about what they will do in this situation. For example, they may wish to try to contact the participant directly or contact their GP to find out about their health and their whereabouts. Any further participant contributions must only be to support the aims of the study and researchers may decide that, for their particular study, it would not be useful or appropriate to make any attempts to get back in touch with participants. Methods to get back in touch must be carefully designed to minimise the risk that any participants perceive them as intrusive or unexpected.

Any further attempts researchers make to contact participants should still be done sensitively and without making the participant feel pressured. It is possible the participant did want to stop taking part in the study but did not feel able to express this to the researcher, for whatever reason.

Researchers might provide a simple way for participants to communicate that they want their involvement in the study to stop, without having to discuss with anyone. This might be in the form of an email address, online form or phone number for sending a text message.

Other important considerations

In some cases, there may be evidence to suggest that the participant should not be contacted again directly (for example if it was known that their health was deteriorating quickly before they lost contact with the study). In these cases, it is still acceptable to find out what might have happened from, for example, the participant's GP, as long as it is in line with the consent participants gave before they joined the study.

See also:

- Researchers should make a plan when they are designing their study for how they will deal with loss of contact with participants. See principle D2 for more about this.
- See principle D4 about the need to inform participants, before they agree to take part in a study, of what would happen if contact is lost between them and the research team.

O5 Continuing data collection: Study data collection should continue until a study participant explicitly tells researchers that they want it to stop.

This approach is valid and fair only if it is made clear to participants before they join the study, including how they can express a wish for stopping data collection, if that is what they want. Researchers should also make all reasonable efforts to find out exactly which aspects of study participation a participant wants to stop, if they express the wish to stop or reduce their participation. Any further data collection must still be done in line with the informed consent that participants previously gave.

This approach can also be applied to other aspects of participation, as long as those aspects are necessary and have a relatively low impact on participants, and as long as any further activity is done according to the conditions mentioned in this principle.

Explanation

If study participants want to stop their data being collected for the study, then it should stop. However, if they do not say they want it to stop, then it should not. This protects the quality of the research because the more of the relevant data about each participant is available for the study analysis, the better it is for the analysis.

When a participant says they want to stop taking part in a study, it could be because they do not want their data collected anymore, but it could be for other reasons. Stopping participation can mean a variety of things, and not all of these mean data collection needs to stop.

For example, a study might require a participant to attend extra hospital visits alongside some routine (non-study) visits that would happen anyway, even if they weren't in the study. After a while, a participant might find the study visits a burden and say that they no longer want to do them. They will continue to attend the routine visits as part of their usual care. Some data from the routine visits could be useful to the study.

If at all possible, the researchers should ask the participant if they are happy for their data from the routine visits to be used for the study. If the participant only says that they want to stop the study visits and doesn't say anything about not wanting their routine health data to be used for the study (even after having been asked their view on this), then the data should still be collected. They can still at any time say they don't want this to happen anymore.

If the participant does want data collection to stop, data from study visits or other events occurring before they made their decision can still be used for the study, as the participant had not yet made their decision at that point. Data from those previous points in time can also still be added to study forms or study databases, if this has not happened yet.

The details of this approach should be made clear to study participants before they agree to take part in a study. They should therefore be aware that until they say they want their data to stop being collected for the study, it will still be collected. However, it should also be clear that they can say they want data collection to stop at any time. Researchers must also make

all reasonable efforts to find out what participants want when they say they want to stop taking part in a study, including to find out if participants are happy for their data to be collected from routine healthcare visits. It may be fair to remind participants of any aspects of their participation that are still continuing at the time they stop or reduce their participation, if there is a suitable opportunity to do this.

It is possible for this sort of approach to be applied to other aspects of participation, meaning that those aspects can continue until a participant explicitly says they want them to stop. Any such aspects or activities must be necessary, for example in running the study, protecting study integrity or protecting the safety of patients in or outside the study. The activities must not involve unexpected or unwanted burden, intrusion or inconvenience to the participant, and they must continue to be done in the way described to participants when they previously gave informed consent. All the other conditions of using this approach (as mentioned above) must also be in place in order for it to be valid and fair.

The sorts of other study activities that might be suitable for this approach include continuing use and storage of biological samples, or continuing access for researchers to review participants' medical notes for the purposes of checking that the study has been run correctly (where this access is based on participants' initial consent).

Researchers should still take a cautious approach to applying this principle – regarding further data collection or anything else. This might mean that, when there is no reliable information available about what the participant wants to do, researchers should assume that participants would want study activities to stop when continuing those activities would not reasonably be expected by the participant. There may also be sensitivities around particular scenarios (for example, related to worsening mental health or capacity to consent) that might lead researchers to conclude that it would not be appropriate to continue study activities without active confirmation that participants are happy with it.

Other important considerations

Different considerations will apply in situations where individuals have lost capacity to give informed consent: applicable laws and guidance should be followed in these cases.

There may also be cases where some data collection needs to continue even after a participant has said they would like study data collection to stop. For example, data about the safety of treatments needs to be collected by law in some drug studies (also known as clinical trials of 'investigational medicinal products', or 'CTIMPs') and this needs to continue even after a participant says they do not want their data to be collected for the study anymore. In studies where this sort of rule applies, it should be made clear to participants before they join the study and it should also be described in the study protocol.

See also:

- When a participant wants to stop or reduce their participation, this does not automatically mean they must stop all aspects of participation. In fact, participation can stop, reduce or change. See principle O1 for more on this.
- Participants' decisions about whether or not data collection continues should be informed by their knowledge of the consequences of their decision. See principle O2 for more about this.
- Participants should receive clear and balanced information, before they agree to take part in a study, about what will happen if they decide to stop or reduce their participation later on. This should make clear that data collection will continue until they ask for it to stop. See principle D3 for more on this.
- The discussions about the participant's wishes should form part of the ongoing dialogue about their participation. See principle D5 for more on this.

Glossary:

- **Data collection:** this means the act of adding relevant data onto study forms or systems, to make the data available for running and analysing each study. It does not refer to any separate tests or procedures used to generate the data in the first place.
- **Capacity** or **capacity to consent** means a person's ability to make decisions for themselves. In the context of research, it means a person's ability to give informed consent to take part in a study. Some people have a varying or reduced ability to make decisions for themselves, for example people with dementia. By law, children also do not have capacity to consent, so their parents or guardian need to consent (or not) on their behalf.
- **Study protocol:** this is the document (or set of documents) that describes why a study is needed, what it aims to achieve and how it should be run.

O6 Retaining data: Data collected for a study up to the point a study participant stops providing data should be used in the study analysis, and kept with the other study data until the study is over.

The data should also be made available for legitimate additional research in line with participant consent and appropriate approvals.

Explanation

Data collected for research studies up to the point a study participant stops providing data should be used in the study analysis, included in the reported study results and kept until the study is completely over. This includes the archiving period after the study analysis, when data is kept in case the results need to be checked.

If study participants could get the study data already collected about them deleted, or not used in the study analysis, this could seriously harm the study and its results. For example, it might mean the study no longer has enough data to be able to reliably answer the research question. This might mean that the study results are unclear about whether or not a new treatment is better, when in reality it is better. If lots of data was lost in this way from one of the treatment groups it might mean the study had misleading results.

This approach is allowed by laws about how people's data can be used in the UK and the EU. These laws recognise the need to protect research, particularly when it is being done in the public interest. Laws in other areas of the world may vary and should be followed appropriately.

While in many situations under UK and EU law, individuals can get organisations that hold data about them to delete that data, this right is limited when it comes to data that is being used for research. This limitation on participants' rights only applies to legitimate research with the appropriate ethical approvals (where required). It also only applies when the limitation has been clearly explained to participants before they joined the study.

Data collected for research studies is routinely made available to other researchers at the end of the study for additional research. This is only done for valid research with appropriate approvals (where required), and usually done in such a way that individual study participants cannot be identified by anyone outside the original study team. Collecting data for research studies takes a lot of time and effort, and this data sharing is one way to make the most of the effort involved. The data that is made available in this way should include data collected up to the point that an individual says they want to stop participating in a study, as long as this is in line with what they have consented to.

Other important considerations

In some specific and rare situations data already collected may need to be deleted for legal or other reasons. Some specific types of research (for example, interview-based 'qualitative'

research) sometimes give participants the option to have their data deleted for a period before the data is analysed, particularly if the data is about very sensitive topics.

In some other types of research study (for example in psychology), it is necessary to give participants false or misleading information during the study in order to carry out the research and obtain reliable results. These sorts of studies can only go ahead if an independent ethics committee agree that the deception is necessary for the research. In these studies, participants need to be told about the deception at the end, and they should be given the chance to have their data deleted by the researchers, if they want this.

Wherever possible, the potential for situations where data deletion could be allowed should be considered in advance (particularly in relation to the specific group of people who might take part in the study) and prepared for when the study is being designed.

In some research, data can be fully anonymised, so that it is no longer possible for anyone to say who the data is about. In these cases, it is no longer possible to delete individual participants' data, because it isn't possible to say which data is about them.

See also:

- This limitation on participants' rights to have data about them deleted may be easier for them to accept if they are aware that collecting less data than planned can have an impact on the quality of study results. See principle O3 for more on this.
- Participants must be informed of this limitation on their rights before they agree to take part in the study. Under UK and EU data protection law, it is also a legal requirement that they are informed of this. See principle D3 for more details.

Glossary:

- **Data collection:** this means the act of adding relevant data onto study forms or systems, to make the data available for running and analysing each study. It does not refer to any separate tests or procedures used to generate the data in the first place.
- **Treatment groups:** many types of research study involve comparing groups of participants taking different treatments, to see which treatment which might be better.
- **Qualitative research:** this term refers to research that collects and analyses data that is not made up of numbers and figures. It can often involve analysis of the contents of interviews with research participants, or of written texts.

O7 Information after stopping participation: Stopping participation early does not affect participants' right to receive study-related information later on, if they want to receive it or if it could be important for them to have.

Explanation

Participants may stop, reduce or change their participation in a study for a variety of reasons. The reason for participation changing may well have nothing to do with the participant losing interest in the study, or no longer supporting it. It is therefore not right to assume that, just because a participant is no longer actively contributing to a study, they do not want to receive study-related information and communications, or that they may not be offered these.

When participants stop taking part early or significantly reduce their contribution, they should be asked about their preferences for further contact about the study, including receiving study results. This should be recorded as part of the data that is collected about the participation change.

Researchers should respect participants' preferences, and also make sure that any later contact is appropriate to the participant's circumstances (for example, taking into account things like the participants' health having worsened in the meantime).

This principle also applies to participants who have lost contact with the researchers, although clearly in these cases it is not possible to find out participants' preferences for further contact because contact has been lost. Any further contact should therefore be in line with what participants were previously told about when they would be contacted, and with any contact preferences participants previously indicated. Before researchers make contact with these participants, they should also make sure it is appropriate to do so (based on the information the researchers have about the participant's circumstances), and that the participants' contact details are still likely to be correct.

There may be various kinds of information that participants might be interested to receive. This includes the final results and outcomes of the study, which should be offered to all participants in a research study, including those who stopped participating early. The participant might also be interested to receive other, more general updates on the study, such as study newsletters, if participants are offered these.

There may be other sorts of information that are important for participants to find out about, particularly where it could impact on participants' future treatment or care. This could include new information about the study treatment they received (for example, information on side-effects that the participant could still experience). It might also be important for participants to find out details of the treatment they received if they participated in a 'blinded' study where they were not told this at first (and at a time when researchers are happy that it will not affect the study integrity to share this information).

Finally, there may be information that is specifically relevant to participants who stop participating early because it is about their participation change. This can include clear

information about what will happen next regarding their care, or about exactly which elements of their participation have stopped. Participants stopping or reducing their participation in a study should get this information when they need it, to provide them with adequate support as their participation changes.

All information needs to be communicated to participants in a clear and careful way, and participants should be helped to understand the information and what it means for them.

Participating in research involves time and effort, and can involve some personal risk or inconvenience. All study participants should therefore be thanked and shown appreciation for the contribution they have made to improving healthcare for patients like them in future. This also applies to participants who stop study participation early.

Other important considerations

Some studies go on for a long time. It is therefore possible that some participants may die or lose the ability to make their own decisions between the time when they stop participating in a study, and the time when information (such as information about the study results) is available later on. Some other studies involve participants without capacity to consent from the outset (including studies where participants are children).

Decisions about whether or not the same information should be shared with the participant's family members or carers in these cases are complex and depend on the specific details of each study and each situation. It is beyond the scope of our guidance to provide comprehensive guidance on this topic.

However, we recommend that researchers make a plan, with patient involvement, for how they will manage the provision of information in studies where a large proportion of participants are at high risk of dying or losing the ability to make their own decisions during the time the study is active, or where participants will not have capacity to consent from the outset. The planning should include whether or not different sorts of information would be shared with relatives or carers, and a plan for whether or not this is raised with potential participants (or their relatives or carers) before they agree to take part in the study in the first place.

For other studies, it may still be sensible for researchers to have a planned approach, for example a way to decide the best thing to do for each specific participant given their circumstances. Whether or not to share information with relatives or carers may depend on how much prior involvement those individuals have had in the study, amongst other things. If it is not thought to be appropriate to contact relatives or carers directly, good public dissemination of information, such as the main study results, can still give those individuals the chance to find that information, if they want to.

See also:

- Participants should be informed, before they agree to take part in a study, about how they can get the results of the study when they are ready. They should also be informed that stopping participation early does not affect their right to receive information later on, including the study results if they want them. See principle D3 for more on this.
- Participants should be informed about whether there will be any further contact from researchers if participants and researchers lose contact with one another. See principle D4 for more on this.
- Participants' preferences for getting study results can be checked by researchers during ongoing discussions about participation. See principle D5 for more on this.
- Data about participants' preferences for further contact from researchers should be recorded along with other data about participation changes. See principle M1 for more about this.

Study Development and Participant Information

D1 Protecting study integrity by design: Studies should be designed and resourced to allow data collection to continue wherever possible, particularly for study outcome data.

Participants should be allowed to continue participating while making less commitment to the study, where this is feasible, safe and does not negatively affect the scientific integrity of the study.

Explanation

We know that in almost all studies, some participants will want to stop planned study activity before it was supposed to stop, so researchers designing studies should prepare for this.

Researchers should make sure there are adequate resources to complete all follow-up activity. This includes making sure research sites have enough funding to collect all the data required for a study.

It is also important, and in line with guidance and laws on both clinical research and data protection, that researchers designing studies should not ask for more data than is really needed. Researchers should aim to ensure that taking part in a study will involve as little burden on participants as possible.

If participants are finding the commitment of study visits too much but are still keen to make a contribution, it might be possible for them to reduce their active commitment but still provide data for the study. For example, a participant who has stopped study treatment but agreed to keep attending some study-specific hospital visits might be finding those visits difficult to keep attending, alongside the other commitments in their life. It might be possible for them to have occasional phone calls with their research nurse instead of going in for all the clinic visits. This could suit participants, because they can reduce their level of commitment but still contribute to the research. It can also suit the needs of the research, because data can still be collected.

It might not be appropriate or feasible in all cases to make adjustments like these. Where it is feasible and appropriate to make adjustments, researchers designing studies should plan for them in advance.

It might not be necessary or helpful to mention the adjustments to participants upfront (before they have agreed to take part in the study), as this might give participants a confusing message about what taking part in the study involves. In any case, the most suitable way that an individual participant's participation should change may depend on their specific circumstances (within the limits of what is possible for each study). Researchers should always make every effort to ensure that the standard level of participation will be as easy as possible for participants. They can then plan ways to help participants to make continued

contributions with reduced commitment, and be ready to offer these to participants who say they are struggling with the standard level of involvement.

There are a different set of considerations if study participants lose capacity to make decisions for themselves during their time on a study (see the Introduction to these principles for more on this).

See also:

- The study protocol should be written with the knowledge that participation can stop, reduce or change, so participants' wishes to reduce their participation might not need to result in them stopping all aspects of participation. See principle O1 for more on this.
- The available options for participants who want to stop or reduce their participation should be communicated to participants before and during the study when necessary. See principles D3 and D5 about this topic.
- Training and support for researchers should ensure they are aware of the options for participants who want to stop or reduce their participation. See principle D6 for more on this.

Glossary:

- **Data collection:** this means the act of adding relevant data onto study forms or systems, to make the data available for running and analysing each study. It does not refer to any separate tests or procedures used to generate the data in the first place.
- **Outcome data:** all research studies involve measuring something in order to reach conclusions. The thing being measured is the 'outcome', and data about it is the outcome data. For example, a healthcare study might give two groups of people different treatments, then measure how their health changes over time to see which treatment is better. The data about how the participants' health changes over time is the outcome data. Outcome data is particularly important, because without it, studies cannot reach clear conclusions.
- **Capacity** or **capacity to consent** means a person's ability to make decisions for themselves. In the context of research, it means a person's ability to give informed consent to take part in a study. Some people have a varying or reduced ability to make decisions for themselves, for example people with dementia. By law, children also do not have capacity to consent, so their parents or guardian need to consent (or not) on their behalf.

D2 Protocol content: Study protocols should include clear instructions on how participation changes should be practically managed.

This should include, where necessary, study-specific definitions for different types of participation change expected over the time the study will take place. Researchers should decide how these participation changes affect the specific research question they want to answer.

Protocols should also include a pre-defined plan, developed with patient involvement, for appropriate actions to take if study researchers lose contact with study participants.

Explanation

Study protocols should give clear instructions for the researchers running the study about how to practically manage different types of participation change. The instructions should be designed with the involvement of patient and public contributors, and approved by an independent research ethics committee before they are put into practice.

Instructions should include what to do when participants stop their study treatment and what information to give to a participant if they say they want to stop their study visits. They should also include what to do if the research team loses contact with a study participant, which is different to participants saying they want to stop taking part.

Instructions for researchers should say that when a participant says they want to stop taking part, the researchers should try to find out exactly which parts of the study the participant wants to stop and which they are happy to continue.

Researchers should be instructed to keep a written record (for example, in the participants' medical notes) of what the participant has said about how they want their participation to change. This record should be kept confidential, with access only for those who really need it. Any personal or sensitive details about the participant's changing circumstances (including their own reasons for changing their participation) should only be used for the study if they are relevant and the participant has agreed they can be used. However, it is important to keep a good record of the participant's wishes so that researchers can make sure they are doing what the participant wants.

In each study, the reasons why study participants might stop participating will vary, and this could be important to the study's research question. For example, if someone needs to stop receiving study treatment, this might be because the treatment has not worked. This would be important to know if we are looking at how well the treatment works.

Researchers designing studies should think about this before they start the study, and think about whether they need to prepare for any particular situations. They should also decide exactly what research question they are trying to answer, given the possible ways that participation could change. Researchers should define this by describing exactly what numerical value the study is aiming to estimate - also known as the 'estimand' – to answer the research question.

See also:

- The instructions about what to do in the case of lost contact should be written in the knowledge that researchers losing contact with participants is not the same as participants expressing a wish to stop taking part. See principle O4 for more on this.
- In line with principle O5 (data collection as default), data collection should only stop if participants want it to stop.
- As per principle D5, participants should be encouraged to keep in contact with the researchers about how they are getting on with their participation in the study.
- The instructions in the study protocol should be reinforced through relevant training and support. See principle D6 for more on this.
- Good record keeping about participation changes means researchers can collect clear and complete data about the participation changes, and keep an eye on any general problems with participation in the trial. See principles M1 and M2 for more on this.
- Researchers should consider the planned study analysis when they are initially writing the study protocol, and ensure that what is in the protocol is appropriate to the analysis. See principle R1 for more on this.

Glossary:

- **Study protocol:** this is the document (or set of documents) that describes why a study is needed, what it aims to achieve and how it should be run.
- We use the term **"running" a study** here to mean all activity involved in making a study happen, including getting the relevant approvals to start the study, working with the NHS and other organisations to set up study sites where participants will be recruited, making decisions about the management of the study, collecting and processing study data, and so on.
- **Estimand:** a description of exactly what numerical value a study is aiming to estimate in order to answer the study's specific research question.

D3 Participant information about stopping participation: Before participants agree to take part in a study, they should receive clear and balanced information about what will happen if they want to stop participating.

This should include information about how it is good for the study if participants can provide outcome data until the study ends. This way, participants can make an informed choice about initial and ongoing involvement.

Explanation

Before potential participants give consent to take part in a study, they should be informed about their right to stop participating and what this practically involves.

This information should communicate the advantages and the drawbacks of stopping or reducing their participation, both from their own point of view and from that of the study and its aims. Potential participants should be made aware that their data is important and is needed to help decide whether a treatment works or not, even if they have to stop taking the treatment for any reason. Having this balanced information helps participants make an informed choice about their initial and ongoing involvement in the study.

Potential participants should also get balanced information about giving a reason for changing their participation. It is important that participants have the right to stop participating in a study without giving a reason, and that they are aware of this right. Researchers must not put any pressure on participants to explain decisions about changing their participation. However, this does not mean that participants may not give a reason, if they are happy to. Knowing about reasons for participation changes can help researchers to reach more reliable conclusions when they analyse the study. Participants should get balanced information on what their options are, including the advantages and drawbacks of different choices. They should use this to make their own informed, freely-given decision about what they want to do.

In many studies, it may be possible for participants to continue contributing but with reduced commitment, instead of stopping all aspects of participation. The detailed information about exactly what choices participants have does not necessarily need to be given to participants before they agree to take part in a study. Potential study participants are already given lots of information to consider at that point. Information about options for reducing participation might also not be relevant at that early stage, and might give the potential participant a confusing message about what taking part in the study would involve for them. Instead, the details can be made available later on, at the time when participants are making a decision to stop, reduce or change their participation. Pre-study information could, however, mention the possibility of participation reducing or changing as opposed to completely stopping, and encourage participants to speak to the researchers if they ever want to discuss this.

Information given at the start of the study should make it clear that any data collected before someone stops some or all study activities will be kept and used as allowed by data protection laws (such as the UK and EU General Data Protection Regulations).

Other important considerations

Under data protection laws, anyone using data about individuals needs a good reason to use the data. This reason is known as the 'lawful basis'. In the UK, data in research studies is often used on the lawful basis that the research is being done in the public interest.

In other countries, data is sometimes used on the basis of individuals' consent. This means the data is only used when participants have agreed to their data being used, and if the participants change their mind then the data cannot be used anymore. In studies where data is used on the basis of consent, the information participants need to get before the start of a study will need to reflect this.

See also:

- Participants should be informed, before agreeing to take part in a study, about the importance of collecting as much of the planned study data as possible. See principle O3 for more on this.
- Participants should be informed about what would happen to data collection and to data already collected, if they decided to stop taking part in the study early. See principles O5 and O6 about this topic.
- Participants should be told, before they agree to take part in a study, how they can find out about the study results when they are ready. They should be told that stopping participation early will not affect their right to stay in touch with the study, if they want to. See principle O7for more on this.
- Participants should be informed about what would happen if contact between them and the researchers is lost. See principle D4 for more on this.
- Participants should be encouraged to talk to researchers as they progress through study about how they are getting on, and to highlight any challenges early. See principle D5 for more on this.
- Participants should be encouraged to tell researchers exactly what their wishes are if they later decide to stop or reduce their participation. They should also be informed about why it is helpful for them to explain their decision to change their participation, if they are happy to. These will help ensure there is good data about how and why their participation changed. See principle M1 for more on this.

Glossary:

- **Outcome data:** all research studies involve measuring something in order to reach conclusions. The thing being measured is the 'outcome', and data about it is the outcome data. For example, a healthcare study might give two groups of people different treatments, then measure how their health changes over time to see which

treatment is better. The data about how the participants' health changes over time is the outcome data. Outcome data is particularly important, because without it, studies cannot reach clear conclusions.

- **Data collection:** this means the act of adding relevant data onto study forms or systems, to make the data available for running and analysing each study. It does not refer to any separate tests or procedures used to generate the data in the first place.

D4 Participant information about losing contact: Participants should be informed, before they consent to join a study, about what will happen if contact is lost during the study.

If any participants might feel that the ways that researchers may try to get back in touch are intrusive, participants should have the chance to provide freely-given, informed consent to allow these contact methods to go ahead. Researchers may not carry out these attempts at further contact if participants have not given consent.

Explanation

While some study participants actively say they no longer want to participate, others more passively lose contact with the researchers by missing visits, not returning questionnaires or not answering calls, letters or emails. This may be a sign that they do not want to take part anymore. However, it might also be due to changes in a range of personal circumstances, for example moving home, or developing new physical or mental health problems. When they are designing a study, researchers should decide, with patient involvement, what they will do in this situation.

Before potential participants agree to join a study it is important they know what activities will continue unless they ask for them to stop, for example data being taken straight from medical records.

The information given to participants should contain clear information about how to get back in touch with the researchers, so that this is easy for participants to do, if they want to do it. This can include more than one way of getting in touch with the researchers, in case participants prefer a particular method of contact. It could also include more than one person's details, in case the participant would like to speak with someone outside the main research team, for any reason. Researchers might also provide a simple way for participants to communicate that they want their involvement in the study to stop, without having to discuss with anyone. This might be in the form of an email address, online form or phone number for sending a text message.

If applicable, participants should also be told how the researchers might try to regain contact with them. This might include using a different contact method (telephone, mail and so on), contacting the participant's GP, or contacting family, friends or caregivers (if they have agreed to be contacted).

Some methods of trying to regain contact may require participants to give consent first, if these methods could be considered by any participants to be intrusive. Ethics committees can advise on which ways of making contact might require participants' consent.

See also:

- Loss of contact between participants and researchers is not the same as participants saying they want to stop participating. See principle O4 for more about this.

- Participants should be made aware, before they agree to take part, that data collection will continue until they say they want it to stop. See principles O5 and D3 for more about this.
- Study protocols should include a plan for what action to take if researchers and participants lose contact. See principle D2 for more on this.
- Participants should be encouraged to discuss with the researchers if they are having problems taking part in the study, or if they know about something that might prevent them taking part until the end of the study. See principle D5 for more about this.
- Researchers should be adequately trained and supported to deal with situations where contact is lost. See principle D6 for more about this.
- Researchers with responsibility for overseeing the progress of a study should keep an eye on the number of cases of lost contact, to see if any changes might be needed to the way the study is run. See principle M2 for more on this.

D5 Encouraging dialogue: Throughout each study, researchers should make reasonable efforts to check that participants are still willing and able to take part. Researchers should be prepared to discuss possible changes to participation, where these might allow participants who are still willing to make a contribution to the study to do so.

Participants should be encouraged to contact the researchers at the earliest opportunity if they are experiencing difficulties with any part of the study or if their circumstances may be changing in ways that will make taking part more difficult.

Explanation

Consent is an ongoing process and study participants can stop their involvement at any time. Researchers should make reasonable efforts throughout the study to check that participants are still willing and able to take part in the study in the same way as they currently are. The nature and frequency of this sort of checking should depend on the study and on the relationship between the researchers and the participant.

The checking should not be burdensome, intrusive or off-putting for the participant, but should make them feel supported during their time taking part, and remind them that their participation remains voluntary. The checking might not need to be in the form of a direct question to participants, if researchers can establish whether or not participants are happy to keep taking part through routine discussion. The checking should also not be burdensome for researchers, in terms of extra documentation or anything else.

Participants should be encouraged from the outset to talk to the researchers about any challenges completing study activities as they emerge, or any changes in their circumstances that might affect their participation. This allows for an open discussion of the issues and the potentially acceptable solutions that may allow participants to continue making a contribution to the study, if they want to.

For example, there may be alternative methods of data collection that might be less intrusive and more acceptable for the participant, such as reduced study visits or only using data collected from routine healthcare activities. Or if participants are planning to move home, it might be possible for them to continue participating in the study at a different study site, if they want to.

Participants can be offered the chance to discuss their participation with someone outside the main researcher team, if they might like more independent advice on their options.

See also:

- When they discuss, both participants and researchers should be as well informed as possible about participants' rights, but also about why it is important for studies to collect as much of the planned data as possible. See principle O3 for more on this.

- If a participant is thinking about stopping or reducing their participation, they should be reminded that data collection will continue until they want it to stop, and encouraged to express their wishes about whether data collection can continue or not. See principle O5 for more about this.
- Any potential alternative methods of collecting data that would allow the participant to stay in the study should be specified in advance in the study protocol. See principle D1 for more on this.
- Researchers who are in direct contact with participants should be appropriately trained and supported to have these discussions. See principle D6 for more on this.

Glossary:

- **Data collection:** this means the act of adding relevant data onto study forms or systems, to make the data available for running and analysing each study. It does not refer to any separate tests or procedures used to generate the data in the first place.

D6 Training and support: Everyone involved in running studies should be trained and supported to manage participation changes for the good of both the participants and the study.

This should be done in line with applicable regulations and include an understanding of the importance of continuing study data collection wherever possible. Training should acknowledge that satisfying participants' wishes for less involvement in a study may not need to result in their participation stopping altogether.

Explanation

Every member of staff involved in research studies should have clear training and guidance about managing participation changes. We should recognise that helping participants do what is best for them, while also trying to do the best for the study, is a challenging task. The nurses, doctors and other staff who run studies (particularly those who interact directly with study participants) should be given help and support in order to do this.

As well as reminding research staff about participants' right to stop participating in the study at any point, without giving a reason and without negative consequences, the training should mention the importance of continuing study data collection (especially the data needed to answer the research questions of the study) until participants say they want it to stop. It should also focus on understanding that if a participant wants to reduce their participation (for example only attend for routine clinic visits) this does not mean that they need to stop taking part in the study completely.

See also:

- Researchers should be aware, through their training, that researchers and participants losing contact with one another is not the same as participants saying they want to stop taking part in a study. See principles O4 and D4 for more on this.
- Researchers should be aware that study data collection should continue until a participant says they want it to stop. When a participant says they want to stop or reduce their participation in a study, the researchers should be trained and supported to make all reasonable efforts to find out whether or not the participant wants data collection to continue. See principle O5 for more on this.
- Training should make researchers aware of any ways for participants to continue contributing but with less commitment, so that they can discuss this with participants who are thinking about stopping participation. See principle D1 for more on this.
- Researchers should be trained and supported to have proactive discussions with participants about their participation. See principle D5 for more on this.
- Researchers should be trained and supported to collect complete and accurate data about how and why participation has changed. See principle M1 for more about this.

Glossary

- We use the term **"running" a study** here to mean all activity involved in making a study happen, including getting the relevant approvals to start the study, working with the NHS and other organisations to set up study sites where participants will be recruited, making decisions about the management of the study, collecting and processing study data, and so on.
- **Data collection:** this means the act of adding relevant data onto study forms or systems, to make the data available for running and analysing each study. It does not refer to any separate tests or procedures used to generate the data in the first place.

Data Management and Monitoring

M1 Informative data collection about participation changes: Data about study participation changes should be recorded in a standardised way and include enough detail to usefully inform study management, analysis and reporting.

Data should include, when available, meaningful information about when and why the participant has reduced or stopped their participation. Collected data should also clearly communicate the participant's wishes, including which elements of study participation they want to stop, and which they have agreed to continue.

Explanation

There are several reasons why researchers running a study should collect good quality data about the number and nature of participation changes occurring while the study is ongoing.

Good quality data is essential for study analyses. It is also important for clear reporting of studies and so that researchers running and overseeing studies can keep an eye on any trends in participation changes. Collecting data in a standardised way where possible is important, so that data from different places (within a study or even between studies) can be more easily used, combined and compared.

It can be particularly important for study analyses to know *why* participation changes have occurred. This is so that researchers analysing the data can understand how the participation changes might have affected the study results. We know that study participants have the right to stop participating without giving a reason, and so don't always give one. However, when participants have made an informed, freely-given decision to provide a reason to the researchers, this should be collected and used to inform study analyses, possibly based on some sort of standardised list. Information about reasons for participation changes can be sensitive and personal. Researchers should therefore only collect as much detail as necessary for the purposes of analysing and reporting on the study.

Whenever the participation change is the participant's choice, a clear record of participants' wishes allows clarity for researchers about what further study activity will take place for a participant, if any. Researchers running studies should make reasonable efforts to find out exactly what a participant wants when they say they want to stop or reduce their participation. If, despite these efforts, the participant has not given detailed information about their wishes, the data recorded for study purposes should make this clear. This can be important when thinking about, for example, whether any data from routine healthcare visits could be collected for use in the study.

Researchers should also check and make a note of whether or not the participant wants to find out the results of the study when they are available (as well as any other updates that might be available later in the study), regardless of whether the participant completed all parts of the study or not.

Researchers should only collect as much data and as much detail as they need for the purposes mentioned above. They should decide what data they need to collect for their specific study, in line with reporting guidelines, core outcome sets and other agreed approaches.

See also:

- Data collection should be planned with the knowledge that participation can stop, reduce or change, and the data collected should reflect this complexity. See principle O1 for more about this.
- Data collection about participation changes should make a difference between participants saying they want to stop taking part, and researchers losing contact with participants. See principle O4 for more on this.
- Clear data about participants' wishes is important so that researchers know if participants are happy for data collection to continue or not. See principle O5 for more on this.
- Data collection should be informed by the study protocol and the statistical planning. See principles D2 and R1 about this.
- Collection of good quality data about participation changes relies on researchers being trained and supported to collect it. See principle D6 for more on this.
- Good quality data about participation changes is essential for oversight of studies while they are ongoing, and for clear reporting of studies when they are finished. See principles M2 and R2 about this.

Glossary

- **Data collection:** this means the act of adding relevant data onto study forms or systems, to make the data available for running and analysing each study. It does not refer to any separate tests or procedures used to generate the data in the first place.
- We use the term **"running" a study** here to mean all activity involved in making a study happen, including getting the relevant approvals to start the study, working with the NHS and other organisations to set up study sites where participants will be recruited, making decisions about the management of the study, collecting and processing study data, and so on.
- **Reporting guidelines:** these give researchers expert guidance about how to share results of their studies in a clear and consistent way.
- **Core outcome sets:** these are things that experts have agreed should always be measured in similar sorts of studies, and included in the results of these sorts of studies.

M2 Monitoring: All those responsible for running and overseeing a study should, at appropriately regular intervals, review summarised data about participation changes in the study.

This allows them to identify common issues or developing trends in study participation, and reasons for these trends, so that timely and targeted action can be taken.

Those running and overseeing studies should also consider reviewing information about the participation changes of individual study participants, if this might be important for their study.

Explanation

Those responsible for running and overseeing how a study is run routinely look at all aspects of how well the study is progressing. The frequency of these reviews depends on the nature and risks of each study.

These regular reviews should include useful, consistently-collected data about study participants stopping or reducing their participation and why this is happening. This data should be presented separately for the different treatment groups, where this would be helpful and where those reviewing the data are allowed to see information split up in this way.

Reviewing this data might show that some action is needed, for example if lots of study participants are stopping study participation early, or if there is a big difference in the number of participants stopping early in the different treatment groups. Decisions about what action to take should be made by those responsible for running the study, with the help of study statisticians and patient involvement contributors. Proactive changes could benefit participants by, for example, making the study less burdensome to take part in.

Any changes made to the way the study is run should be designed to benefit the research by helping to ensure as much relevant and accurate data as possible is available for the study analyses. This in turn can help make the study results as reliable as possible. Additional data reviews later on can help show whether the actions taken have had any positive impact.

Those responsible for running and overseeing studies should also consider, before they start a study, whether or not it might be useful to review more detailed information about individual participation changes. They can do this by, for example, reviewing participants' medical notes. When they are deciding whether or not to do this sort of check, they should consider things like the nature of the study and its participants, the study design, and the risks to participants' rights and to the study's integrity.

Review of detailed information about individual participants can help them to check that participants' wishes about how they want their participation to change have been correctly recorded and carried out. They can also check that participation changes have generally been handled in ways that do the best by individual participants and by the study.

Other important considerations

Data collected and reviewed while the study is still ongoing should be interpreted with caution as it may not yet represent a full picture of participation changes in the study.

See also:

- The actions taken in response to review of the data might include new or different training for study researchers. See principle D6 for more on this.
- This ongoing review of studies is dependent on having good quality data about participation changes. See principle M1 for more on this.
- The monitoring activity and actions taken in response to any findings should be guided by statistical considerations in the study. See principle R1 for more on this.

Glossary

- We use the term **"running" a study** here to mean all activity involved in making a study happen, including getting the relevant approvals to start the study, working with the NHS and other organisations to set up study sites where participants will be recruited, making decisions about the management of the study, collecting and processing study data, and so on.
- **Data collection:** this means the act of adding relevant data onto study forms or systems, to make the data available for running and analysing each study. It does not refer to any separate tests or procedures used to generate the data in the first place.
- **Treatment groups:** many types of research study involve comparing groups of participants taking different treatments, to see which treatment which might be better.

Study Analysis and Reporting

R1 Analysing studies with participation changes: When participation changes mean that not all the study data has been collected as planned, researchers should analyse the study in ways that give the best chance that the study will still have reliable results.

The analysis should be done using methods that are planned in as much detail as possible before the study starts, and that follow current best practice for the specific research questions in the study.

Explanation

We know that in almost all studies, some participants will want to stop planned study activity before it was supposed to stop. Study participation can change, stop or reduce in various ways.

In some cases, for example if a participant wants to stop any further data being collected about them for a study, participation changes will lead to data being missing from study analyses. This means that the things the study is looking to measure in order to find out how successful a new treatment is (for example, participants' health status or quality of life) will be unavailable or not known. If study analyses are not done in ways that correctly take account of these unavailable and unknown measurements (sometimes called 'missing data' by researchers), the study results might be misleading or unreliable.

Researchers responsible for analysing the data, including appropriately trained and experienced statisticians, should therefore analyse the study in ways that take account of any unavailable or unknown measurements. The methods available for doing this always rely on making some assumptions, so it is not possible to guarantee that the study results will be totally reliable. However, researchers should aim to use methods that give the best chance of reliable study results.

Researchers should plan the key aspects of how they will analyse the study data before the study starts, and they should have all details planned before they start the analysis. This planning can be documented in the study protocol or statistical analysis plan, or in related documents. Researchers should document and report the assumptions they make when doing this planning, and they should follow best practice (for example, using evidence and guidance in published scientific journal articles) to help decide the best statistical methods to use.

When they do their statistical planning, researchers should think about how they will deal with the fact that some participants will have stopped some or all of their participation earlier than expected, as well as how the analysis might be affected if any study participants die while taking part in the study. Researchers designing each study should decide exactly what their research question is, given the possible ways that participation could change (researchers should define by describing exactly what numerical value the study analysis is aiming to

estimate – also known as the 'estimand' – to answer the research question). The methods used in the analysis should be appropriate to their specific research question.

Analysis planning before the start of a study should also include details of which groups of participants to include in each analysis, the overall approach that will be used to dealing with the missing data, and whether or not data about reasons for participation changes will be used to check the assumptions the researchers have made. When they are designing the study, researchers should also consider any possible implications for the number of participants the study will need to have in order to produce reliable results.

If it is available, researchers should use data from previous studies to inform their planning, for example data about how many participants in previous, similar studies stopped taking part early.

See also:

- The statistical planning and analysis should be done in the knowledge that study participation may stop, reduce or change. See principle O1 for more on this.
- When writing the study protocol, researchers should decide exactly what their research question is, given the possible ways that participation may change. This will then influence the way that the analysis is done later on. See principle D2 for more on this.
- The study analysis needs good quality data about participation changes. See principle M1 for more about this.
- The statistical planning and details of exactly what was done to analyse participation changes in a study should be reported clearly at the end of the study. Planning the design and analysis of future studies is also highly reliant on good reporting of what participation changes took place in previous studies. See principle R2 for more on these topics.

Glossary:

- **Data collection:** this means the act of adding relevant data onto study forms or systems, to make the data available for running and analysing each study. It does not refer to any separate tests or procedures used to generate the data in the first place.
- **Missing data:** data that was planned to be collected might not be included in a study analysis because researchers do not have access to it, or because it does not exist. All the planned data that is not included in study analysis is collectively called missing data.
- **Study protocol:** this is the document (or set of documents) that describes why a study is needed, what it aims to achieve and how it should be run.

- **Statistical analysis plan:** this explains exactly how the study data will be analysed. It is important that this is written before the statisticians have seen any study data.
- **Estimand:** a description of exactly what numerical value a study is aiming to estimate in order to answer the study's specific research question.

R2 Consistent and complete reporting: End of study reporting of participation changes should be done consistently within a study, showing any changes in level of participation, preferably split by treatment group.

This helps with the assessment of the quality of the study and of the reliability of the results. It can also inform the size, design and conduct of future studies. Methods used to handle missing data should also be described, to allow interpretation and replication of results.

Explanation

When reporting a study's results, it is essential that researchers present the level of, and reasons for, missing data due to changes in participation. This helps the reader to assess the quality of the study and reliability of the results. It should be clear what happened to all study participants, including whether they completed all aspects of the study or had to stop any of them early, including reasons why they stopped, where reasons are available.

The level of detail presented can depend on the nature and design of the study, as well as the format of the report, but should be enough to meet the aims described in this principle. Adoption of this principle, in accordance with the Consolidated Standards of Reporting Trials (CONSORT) guidance, will help ensure consistency across studies.

If any participants stopped taking part in some or all aspects of the study before the end, this should be taken into account when analysing the study data. The analysis methods used should be reported, so that anyone reading the study results knows what has been done and why.

Complete reporting allows researchers planning future studies to learn how often and why participation changes during studies. This means they can make evidence-based adjustments to sample size calculations and adjust their study design to improve participation. Consistent and complete reporting allows other researchers to use the results for further research, for example in a 'meta-analysis', where results from several studies are combined to get an overall result.

See also:

- Reporting of data on participation changes should be done in the knowledge that participation can stop, change or reduce. See principle O1 for more on this.
- There should be separate data reported about participants who said they wanted to stop and those who lost contact with the research team. See principle O4 for more on this.
- Clear reporting is reliant on good quality data collected during the study about participation changes. See principle M1 for more about this.

Glossary:

- **Treatment groups:** many types of research study involve comparing groups of participants taking different treatments, to see which treatment which might be better.
- **Missing data:** data that was planned to be collected might not be included in a study analysis because researchers do not have access to it, or because it does not exist. All the planned data that is not included in study analysis is collectively called missing data.
- **Sample size:** before a study starts, researchers need to work out the minimum number of participants they will need in order for the study to reach a clear conclusion. This number is called the sample size. The number should not be much more than this minimum number, because once there is a clear conclusion, people outside the study (that is, patients receiving routine healthcare) should benefit from the study results.