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Selection and reporting of usual care comparators when designing primary care trials of complex health interventions: a systematic review

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Abstract

Background: Many primary care trials evaluating complex health interventions use a 'usual care' comparator. As 'usual care' can vary across clinical sites, countries, and over time, impacting trial design and raising ethical considerations attention should be given to its content prior to a trial starting.

Aim: To understand how researchers select and describe usual care comparators when designing primary care trials of complex health interventions.

Design and setting: A systematic review of primary care trial or feasibility study protocols.

Method: Electronic databases were searched from 1 July 2020 to 20 June 2022.

Results: A total of 83 protocols were included. A range of terms such as usual care and care as usual were used to describe usual care. The description of usual care varied significantly between protocols in terms of the level of detail provided regarding its selection and content. We categorised these descriptions according to the amount of detail they provided as: basic (72%), moderate (16%) and comprehensive (12%). Few protocols justified the content of their usual care comparator, with most simply commenting that it was based on clinical guidelines or current practice.

Conclusion: Different terms are used to describe usual care and most primary care researchers provide limited details on the section and content of their usual care comparators when publishing study protocols. This has implications for transparency and replicability, and suggests researchers continue to give limited attention to the content of usual care when designing their trials.

Keywords

Randomised Controlled Trials, Usual Care, Comparator, Primary Care, Protocols, Feasibility studies

How this fits in

1. Many primary care trials are pragmatic in nature and use usual care as a comparator arm to assess the effectiveness of new treatments or practices.

2. It is known that usual care can vary between trial sites and practitioners, and that this variation can have methodological and ethical implications for a trial's design.

3. Researchers and reporting guidelines have emphasised the need for trials using a usual care comparator to describe it in detail, so it is clear what an intervention is being evaluated against and to allow researchers and practitioners to consider the trial's relevance to existing practices.

4. This review highlights that there is significant variability and the inadequate detail in the descriptions of usual care in protocols of primary care trials. Future research should establish what would be the most effective and efficient way of establishing what care is currently being delivered in practice, so that researchers can describe what usual care entails, prior to a trial starting, when using it as a comparator.

Background

Many primary care trials evaluating complex health interventions are pragmatic in nature and evaluate new or modified treatments or practices against a 'usual care' comparator. To ensure findings are relevant to clinical practice, the usual care comparator should replicate care given in everyday clinical practice.[1] This sounds simple, but usual care can vary for the same condition, across clinical sites, countries, and over time.[2] In addition, it is important that researchers designing trials know what it includes, as its content can affect methodological and ethical aspects of a trial, e.g., the sample size required,[3] and whether care provided at different trial sites is an acceptable standard.[4] The intensity and content of usual care could also affect between group-differences observed in a trial, and therefore how effective the trial determines the intervention to be.[3]

The potential heterogeneity of usual care and its impact on a trial's design means researchers should carefully consider its content when designing trials with usual care comparators, and document what it will include.[5] Whilst some researchers will define usual care as including the full range of treatments available in practice,[6,7] others have chosen to protocolise or restrict what usual care consists of when using it as a comparator arm.[8,9] Reasons for protocolising usual care include wanting to protect trial participants or to address variations across trial sites in terms of the quality of the care provided.[10]

Researchers have not consistently applied terminology when referring to usual care arms that include all treatments available in practice and may use, for example, terms such as 'usual care', 'treatment as usual' and 'standard care' interchangeably.[5]

When researchers have decided what their usual care comparator will included, they have used terms such as ‘protocolised’, ‘devised’ or ‘enhanced usual care’[5] but again terms have been used interchangeably.

There is growing recognition of the importance of defining and describing usual care prior to a trial starting and some reporting statements such as CONSORT[11] and TIDieR[12] request that both intervention and comparator arms are detailed. Currently we do not know to what extent researchers describe usual care comparators in protocols of primary care trials, why they use these comparator arms and what terms they use to refer to them. Thus, we conducted a systematic review to understand how researchers select and describe usual care comparators when designing primary care trials of complex health interventions.

Specific questions addressed were:

1) How have researchers defined usual care, standard care, treatment as usual (or other synonyms) in primary care trials?
2) How do researchers report and describe usual care in trial and feasibility protocols?
3) What information did they use to select and justify their usual care comparator, and how did they gather this information?

Methods

The protocol for this systematic review is registered with PROSPERO, (ID CRD42022347342). This review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines (PRISMA 2020).[13]

Search strategy and selection criteria

A comprehensive search strategy was developed and tested with support from an information specialist (SaD) (Supplementary Box S1). Searches included both MeSH and free text terms relating to usual care and synonyms, primary care, and randomised controlled trials, including pilot and feasibility studies. The electronic bibliometric databases MEDLINE, Embase, the Cochrane Library and PsycINFO were searched from 1 July 2020 to 20 June 2022 to capture recent practice and to keep the review manageable within the timeframe available for the study. No language restrictions were applied provided an English language abstract was available for initial screening (Table 1).

Screening

References were imported into Endnote and after deduplication they were imported into Rayyan.[14] Titles and abstracts were independently assessed for inclusion by two reviewers (SD and KT) using the pre-defined inclusion criteria (Table 1). The remaining study protocols were screened by one reviewer (SD) as inter-rater reliability was high (kappa coefficient=.84). 50% of full text was screened independently by two reviewers (SD, KT) and, due to high level of agreement (kappa coefficient= .77), the remaining full text was screened by one reviewer (SD). Any conflicts were resolved through discussion with a third reviewer (AH).

Data extraction

A customised data extraction form was developed in Microsoft Word and tested on a random sample of five papers. We consulted the TiDieR checklist[12] to identify important elements when reporting a trial arm namely a) rationale for the comparator

arm, b) components of usual care included, c) who delivered it and how, d) where they delivered it e) frequency and duration of usual care. Data were extracted by one reviewer (SD) and checked for accuracy by KT and AH. Discrepancies were resolved through discussion.

Risk of bias

Risk of bias of the included evidence was not determined as our aim was to review trial protocols to understand how researchers select and describe usual care when designing trials and not to assess the quality of the studies included.

Data synthesis

We used narrative synthesis using descriptive text and tables to summarise the data and identify similarities and differences within and between study protocols.[15]

Categorisation of usual care descriptions

Using a similar approach devised by Petersson et al. (2023)[16], we categorised usual care descriptions as 'basic', 'moderate' and 'comprehensive' according to the amount of detail they provided. To aid us and inform the definitions of these three categories, we read and re-read the descriptions we had extracted to consider what information they provided and therefore, what criteria or information we should use to decide whether, for example, a description was basic or moderate. Descriptions categorised as basic were those which described *usual care* as '*treatment as usual'* or '*provided according to a clinical or practice guideline*', and/or simply listed the treatments/procedures/materials included. No information was given about what the treatment(s) entailed, their delivery, dose, frequency, or duration. Descriptions

categorised as moderate included some information about what included treatments involved, the provider, location, and/or dose/frequency/duration. Comprehensive descriptions offered a detailed account of treatments/procedures/materials included provider, location and dose/frequency/duration. Comprehensive descriptions sometimes also provided information on mode of delivery. The use of reporting guidelines was recorded in all three categories to assess whether these had influenced the reporting of usual care.

Descriptions of usual care were categorised independently by SD, KT and AH. When there was uncertainty about how a description should be categorised, there was a team discussion and a 'best fit' agreed.

Patient and public involvement (PPI)

Prior to submitting the application for grant funding, the review was discussed with 7 PPI contributors. All 7 members viewed the study as important, agreed with the proposed design and suggested search terms for the review. In addition, one member of the group (TY) agreed to be a co-applicant on the grant. TY commented on the review protocol, attended three team meetings, and is a named author on this paper. Upon review completion, we conducted a PPI meeting with five PPI contributors (including TY) to share key findings and discuss how the findings should be disseminated. The group stated they understood the findings but suggested visual methods, such as infographics, should be used when disseminating to public audiences, as individuals working outside of trials might struggle to understand findings simply summarised in writing.

Results

Overview of review process

We identified 6063 records and after de-duplication, 4077 titles and abstracts were screened. 293 study protocols were included for full-text screening and 83 were included in the review (Supplementary Figure S1). We have reported our findings in accordance with the PRISMA 2020 checklist[13]. Although none of the study team were clinicians, the approach, search strategy and findings were discussed with clinical colleagues working in primary care, to explore their views on its applicability to general practice and future primary care research.

Characteristics of included protocols

The 83 included study protocols were based in the UK (14),[17-30] USA (11),[31-41] Australia (7),[42-48] the Netherlands (7),[49-55] four studies each from Canada,[56-59] China[60-63] and Spain,[64-67] two studies each from Denmark,[68-69] Ethiopia,[70-71] Hong Kong,[72-73] Ireland,[74-75] Germany,[76-77] Pakistan,[78-79] Portugal,[80-81] Singapore,[82-83] and one study each from Tanzania and Uganda,[84] Bangladesh,[85] Botswana,[86] Chile,[87] Europe,[88] France,[89] Guatemala,[90] India,[91] Mexico,[92] Nepal,[93] Norway,[94] Papua New Guinea,[95] Uganda,[96] South Africa,[97] Poland,[98] and Zambia[99]. The study protocols described pilot (n=8), feasibility (n=5) or full randomised controlled trials (RCTs, n=70).

The study protocols detailed trials evaluating a wide range of health care interventions for mental and physical health (Supplementary Table 1). Overall, 55 of the 83 study protocols described using reporting guidelines: SPIRIT used on its own or with CONSORT or TIDieR (n=37), CONSORT (n=13), TIDieR (n=2), and one

each using CONSORT and TIDieR, CONSORT and Standards for Reporting Diagnostic accuracy studies (STARD or STARD-AI), and Consolidated Health Economic Evaluation Reporting Standards and guidelines from the Global Health Cost Consortium.

Usual care terms

A range of terms were used to describe usual care (Supplementary Table 2). Most of the included protocols used the term *usual care* or *care as usual* (n=36, 43.4%). Others used *control arm*, *control group* or *control condition* (n=10, 12%), *treatment as usual* (n=9, 11%), *standard care*, *standard practice* or *standard of care* (n=9, 11%), *routine care* or *usual routine clinical care* (n=3, 4%), *standard vertical care* (n=1, 1%) and *referral as usual* (n=1, 1%). The remaining protocols used context specific terms such as *enhanced care or boosted care* (n=7, 8.4%), *usual primary care* or *general practice care* (n=2, 2.4%), *standard nutrition care* (n=2, 2.4%), *routine antenatal care* (n=2, 2.4%) and *usual physiotherapy* (n=1, 1%). Where the terms usual care or routine care were used, it was apparent that in most cases they referred to existing standard practices. However, where authors referred to treatment as usual or standard care, there was considerable variation in what the usual care comparator included, as it could include standard practice or another intervention. The terms enhanced or boosted care were used to refer to standard practice, plus another intervention/treatment.

When viewing the data presented in Supplementary Table 1 and looking across the table, there appeared to be no relationship between country of publication, whether the protocol detailed a full RCT or a pilot or feasibility study, medical discipline, mode

of delivery or using a reporting guideline and how well usual care had been described.

Descriptions of the content of usual care

We categorised the protocols as basic, moderate or comprehensive as per our methods (Supplementary Table 2).

Study protocols with a basic description of usual care

60 study protocols were categorised as having a basic description of usual care [17-22,24-34,36-43,45,47,49,51,55-58,60-62,65,66,68,71-77,80,81,85-89,92-98] with four of these simply saying the comparator arm was *usual care*.[21,60,71,88] These protocols usually provided a very brief description what usual care entailed or gave a vague and broad description without further elaboration on what usual care actually entailed, or how it was chosen. 38 stated they had used a reporting guideline when writing the protocol.

Some protocols reported usual care had been defined according to practice guidelines but did not always reference the guidelines or detail what care was included.[74] Other protocols reported usual care was provided in accordance with usual practice in the region or based on national/international/condition-specific guidelines, but again the content of usual care was not described.[86,97] Some protocols detailed what treatments or support participants would not receive, rather than detailing the ones they would receive.[98]

Only one protocol which acknowledged variation in usual care delivered across sites.[81]

Study protocols with a moderate description of usual care

13 study protocols were categorised as having a moderate description of usual care.[23,35,44,52,53,63,69,70,79,83,90,91,99] Typical examples included information of usual care, along with some information on who delivered it and, in some cases, timing of follow-up and/or duration of the treatment. 11 of the 13 protocols stated they had used a reporting guideline.

Most protocols did not offer any justification for the content of usual care in this category. In one protocol, justification included the need to match the intervention group and maintain community trust.[35] In some protocols, justifications included following relevant guidelines or basing the content of usual care on clinical guidelines along with the description of usual care.[52,53]

Study protocols with a comprehensive description of usual care

10 study protocols were categorised as having a comprehensive description of usual care.[46,49,50,54,59,64,67,78,82,84] Descriptions in this category included who provided the treatment, where, duration, type of treatment, frequency and follow up. Six of the 10 protocols stated they had used a reporting guideline.

Justification for the content of usual care comparator included following the same care provided in the region/clinical practice guideline for the condition.[49]

Discussion

Summary

Researchers designing primary care trials use a range of terms to refer to their usual care comparator. Irrespective of the term used, the content of a usual care

comparator could range from standard practice or a single intervention the researchers had chosen to represent usual care. When usual care had been enhanced, this was sometimes reflected in the term used but this was not always the case.

72% of the included protocols gave only a basic description of usual care. There was little evidence of researchers establishing what usual care included prior to starting a trial, or ensuring it would be similar across trial sites or that it met the standards of clinical guidelines. A small number of studies provided a justification for the content of their usual care comparator but most simply stated it was based on local/national clinical guidance or current practice. Whilst researchers stated they had used reporting guidelines, there was little evidence that such guidelines had resulted in detailed descriptions of the usual care arm.

Strengths and limitations

Databases were searched from 1 July 2020 to 20 June 2022, limiting the timeframe of the review and including protocols that were published during the Covid-19 pandemic. This 2-year timeframe, however, meant we reviewed recent practice and, whilst the pandemic will have affected how trials were delivered during this period, there was no evidence in any of the included protocols that it had affected how usual care had been selected and described in the trials they detailed. Although some of the included protocols were difficult to assign to the categories we developed, and their allocation was subjective, this allowed us to gauge what proportion of protocols

only provide a basic description and what proportion describe usual care in a way that enables the reader to know what it included and how it was delivered.

Limitations were that we only included studies published in English. As the term 'usual care' is not used consistently, we might not have identified all relevant articles. However, our search strategy with designed with input from an information scientist (SaD), a researcher experienced in trial methodology (KT), a PPI co-applicant and other trialists.

Comparison with existing literature

Others have commented on researchers limited descriptions of usual care comparators in different settings.[16,100,101] Given that usual care arm has a critical role to play in ethical and methodological aspects of a trial, it is surprising that there has been minimal consideration given to its content. This could be because our comprehension of trials is constrained by the notion that the experimental arm is 'the' intervention, while the usual care control is merely a necessary framework for the trial.[5,102]

Implications for research and practice

This descriptive systematic review is a sister publication to a methodology review that aimed to summarise current thinking about what should inform the content of usual care comparators.[5] We identified various drivers that should inform this decision, including establishing what care is currently being provided in practice, prior to a trial starting. We appreciate this will take time and resources. We also realise given the potential heterogeneity of usual care, defining usual care could be

challenging. Establishing the most effective way to do this is still unknown, however, many trialists conduct feasibility studies prior to a main trial and such studies would allow researcher to establish what usual care includes. In addition, with the development of NHS digital, and the potential for trials and routinely collected NHS data to become more integrated in the future, there are opportunities to understand usual care in greater depth. Furthermore, it might be possible to analyse routinely collected electronic health record patient data via, for example, the Clinical Practice Research Datalink (CPRD) database. CPRD collects these data from UK-based GP practices and provides patient-level information on various aspects of care, such as the administrative nature of consultations (frequency, length, staff member, continuity of care), diagnosis, investigations, medications prescribed, other clinical interventions (e.g. reviews), and referrals made.

Primary care researchers use a range of terms to refer to their usual care comparator. Usual care remains poorly described in protocols describing primary care trials, despite growing recognition of the need to define this trial arm and the requests from reporting guidelines to do so. In addition, researchers provide limited justification for the content of their usual care comparator; most simply indicated it was based on local or national guidelines or current practice. These have implications for transparency, replicability and reproducibility. Journal editors and reviewers should make it a requirement that reporting guidelines are followed, and researchers should be encouraged to view usual care comparators as complex interventions that will affect how a trial is designed and interpreted, and therefore need to be fully considered and documented before a trial starts. Uncertainty remains about how best to decide the content of a usual care comparator, but our

recent methodology review indicated what might drive its content and what steps researchers could take to inform their decision.[5]

Declarations

Data availability statement

All data presented in the manuscript are from publicly available papers as they are all published. Extracted data are available as tables in the manuscript.

Ethics statement

Ethical approval was not required as it involved working with already published data.

Competing interests

None to declare.

Funders statement

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Table 1: Criteria for inclusion

	Inclusion	Exclusion
Types of studies included	Feasibility studies and protocols of primary care trials evaluating complex health interventions that include a usual care comparator arm, and feasibility and developmental studies informing the design of such trials.	
Population	Any population in primary care	NA
Intervention	Any health care provision in a primary care trial of a complex health intervention described as usual care (or synonym) which acts as a control or comparator arm. The MRC's (2021) definition of complex interventions was used: interventions that are complex due to their properties, such as the number of components involved, range of behaviours targeted, expertise and skills required to deliver/receive it, number of groups/settings/levels targeted, permitted level of flexibility of the intervention or its components.	We excluded trials of interventions evaluating medicines (e.g. drugs or pills) that are focused only on treatment outcomes and not, for example, improving adherence.
Comparator	The trial arm which is viewed as reflecting current practice i.e., usual care or standard care, or usual care plus intervention (enhanced usual care or boosted usual care)	Waitlist or drugs or another intervention that does not represent usual clinical practice
Outcomes	1. How usual care (and its synonyms) is defined and described in primary care feasibility studies and trial protocols of complex health interventions to improve patient outcomes when used as a control/comparator arm. 2. What steps and information researchers have used to inform what their usual care comparator includes. 3. Any justification given for having a usual care comparator or for what this trial arm includes. Our review indicates how and to what extent trialists have defined usual care comparators when designing primary care trials, giving clinicians insight into how these comparator arms are designed and allowing them to consider how they could apply trial findings to improve patient health outcomes.	
Setting	Primary care trials of complex health and health care interventions that include a usual care comparator. The World Health Organisation's definition of primary health care was used: 'PHC is a whole-of-society approach to health that aims at ensuring the highest possible level of health and well-being and their equitable distribution by focusing on people's needs and as early as possible along the continuum from health promotion and disease prevention to treatment, rehabilitation and palliative care, and as close as feasible to people's everyday environment.' (Primary	

	health care (who.int). We used this definition as it is internationally recognised but we are aware it is very broad, so we only included studies that were undertaken in a primary care setting and/or involved primary care practitioners.	