3-2015

Assessing Usual Care in Clinical Trials

Judith A. Erlen
University of Pittsburgh School of Nursing

Lisa K. Tamres
University of Pittsburgh School of Nursing

Nancy Reynolds
Yale University

Carol E. Golin
University of North Carolina at Chapel Hill

Marc I. Rosen
Yale University

See next page for additional authors

Citation Details

Authors

Judith A. Erlen, Lisa K. Tamres, Nancy Reynolds, Carol E. Golin, Marc I. Rosen, Robert H. Remien, Julie W. Banderas, Neil Schneiderman, Glenn Wagner, David Bangsberg, and Honghu Liu

Assessing Usual Care in Clinical Trials

Judith A. Erlen[1], **Lisa K. Tamres**[1], **Nancy Reynolds**[2], **Carol E. Golin**[3], **Marc I.Rosen**[4], **Robert H.Remien**[5], **Julie W. Banderas**[6], **Neil Schneiderman**[7], **Glenn Wagner**[8], **David R. Bangsberg**[9], and **Honghu Liu**[10]

[1]Department of Health and Community Systems, University of Pittsburgh School of Nursing, Pittsburgh, PA

[2]School of Nursing, Yale University, New Haven, CT

[3]Division of General Medicine and Clinical Epidemiology, School of Medicine, Gillings School of Global Public Health University of North Carolina at Chapel Hill, NC

[4]School of Medicine, Yale University, New Haven, CT

[5]Department of Psychiatry, Columbia University, New York, NY

[6]Department of Medicine,UMKC School of Medicine, Kansas City, MO

[7]Department of Psychology, University of Miami, Coral Gables, FL

[8]RAND Corporation, Health Unit, Santa Monica, CA

[9]MGH Center for Global Health; Ragon Institute of MGH, MIT, and Harvard; Harvard Medical School, Boston, MA

[10]Division of Public Health & Community *Dentistry*, UCLA School of *Dentistry*, University of California Los Angeles, Los Angeles, CA

Abstract

Researchers designing clinical trials often specify usual care received by participants as the control condition expecting that all participants receive usual care regardless of group assignment. The assumption is that the groups in the study are affected similarly. We describe the assessment of usual care within the 16 studies in MACH 14, a multi-site collaboration on adherence to antiretroviral therapy. Only five of the studies in MACH 14 assessed usual care. Assessment protocols varied as did the timing and frequency of assessments. All usual care assessments addressed patient education focused on HIV, HIV medications, and medication adherence. Our findings support earlier work that calls for systematic assessments of usual care within the study design, inclusion of descriptions of usual care in reports of the study, and the influence of usual care on the experimental condition in clinical trials.

Keywords

Usual care; Intervention; Control condition; HIV; Adherence

Corresponding author: Judith A. Erlen, University of Pittsburgh School of Nursing, 415 Victoria Building, 3500 Victoria Street, Pittsburgh, PA 15261; jae001@pitt.edu; phone (412)624-1905; fax (412) 383-7293.

Investigators conducting clinical trials often specify that the usual health care provided to patients who participate in those trials is the control condition. A basic assumption underlying these trials is that all participants in the study, regardless of their study group assignment. continue to receive the usual care provided within the clinical setting. Differences detected in the outcomes at the end of the study are expected to be due to the experimental condition used in the study since that is what is different between the two or more groups (Hulley, Cummings, Browner, Grady, & Newman, 2007). However, during the study, when there is new evidence, there is the distinct possibility that health care providers may modify usual care. Thus, the assessment and influence of usual care become important considerations when examining the outcomes of a study.

Assessing Usual Care

Modifications in treatment guidelines in the clinical management of patients with HIV/AIDS have advanced because of drug discoveries and the emergence of new evidence regarding their effectiveness and impact on a patient's clinical outcomes (Panel on Antiretroviral Guidelines for Adults and Adolescents, 2013). Such changes in the delivery of usual care have the potential to affect the hypothesized outcomes in an ongoing study when the changes are introduced. All patients who participate in the study receive what is deemed to be usual care. However, these participants may not all receive the same usual care depending on the rate of adoption of the revisions to treatment guidelines at the study site, the level of adherence to the guidelines by the health care providers, and when the participants were recruited into the study. Clearly, usual care is a dynamic condition in which health care providers alter their management of patients based on the latest evidence.

Wagner and Kanouse (2003) in their seminal discussion offered three reasons to assess usual care when conducting clinical trials designed to examine the effect of an intervention on adherence to antiretroviral therapy (ART) prescribed for HIV infected patients. First, describing usual care, as well as the intervention is necessary for another practice setting to determine whether the tested intervention has the potential to be adopted and effective within a different setting. This is particularly important given the current focus on translating research into practice (Glasziou et al., 2010). Additionally, in a multi-site study differences in usual care may provide the explanation for the site differences that occurred in regard to the outcomes. However, this explanation can only be offered when usual care is consistently monitored at each of the participating sites. Lastly, health care providers who are also the researchers may begin to change the management of patients in their practice and knowingly or unknowingly provide different care to the participants in the usual care arm. Although, Wagner and Kanouse (2003) focused their comments on ART adherence research, they did not limit the monitoring of usual care to only those trials; they emphasized the need to assess usual care in other studies that include a behavioral intervention.

In 2009, de Bruin, Viechtbauer, Hospers, Schaalma, and Kok called for investigators to report usual care to improve the accuracy of the assessment of change that occurred as a result of a behavioral intervention being tested within a clinical trial. Williams (2010) supported this position stating that the components and processes occurring during usual

care are important to the overall conduct of the clinical trial. When usual care is based on the latest evidence, it may include components that are also within the behavioral intervention that is being tested in the trial such as health teaching to promote better medication management (de Bruin et al., 2010). The meta-analysis conducted by de Bruin and colleagues (2010) showed that the intervention arm performed better when there was a lower level of usual care provided. As the level of usual care increased and included more of the components in the intervention, there was less effect demonstrated by the intervention being tested (de Bruin et al., 2010; Williams, 2010).

Yet, investigators do not typically describe the usual care condition within the methods section of a published paper raising questions regarding what is actually included in usual care, whether usual care was monitored for any changes in delivery during the study, and how changes in usual care may have affected the hypothesized outcomes (de Bruin et al., 2009). Without this information the internal validity of the study is threatened (Polit & Beck, 2012). Descriptions of usual care are even more problematic when a study uses multiple sites because of possible variation in usual care across clinics and differences in practices based on geographic location (Freedland, Mohr, Davidson, & Schwartz, 2011). Also, whether individuals within a site or sites are randomized within a study needs to be considered.

Despite the need for and value of assessing usual care, only a few methods for monitoring the control condition in a study have been described (Carroll, 1997; Garland, Hurlburt, Brookman-Frazee, Taylor, & Accurso, 2010). The use of a Theory Coding Scheme designed to capture the components of the theory that are present in the interventions that are delivered in an RCT could be extended to the systematic assessment of usual care (Michie, Prestwich, & de Bruin, 2010). Similarly, the importance of assessing adherence to treatment guidelines cannot be overlooked. Another possible usual care assessment, the Session Report Form developed for a larger clinical trial, has been suggested by Kelley, Vides de Andrade, Sheffer, and Bickman (2010). The form is completed by health care providers at the end of a usual care session designed for youth being seen for mental health conditions to inform the content addressed and the context in which usual care occurred. Possibly patients could be informants about usual care; however, they may be unable to differentiate the usual care provided to all patients in the clinic setting from the individualized care that they are receiving.

Purpose

Although systematic assessment of usual care has clear advantages in clinical trials with a behavioral intervention, usual care does not necessarily lend itself to rigorous, reliable, or feasible assessment. To our knowledge no standard form for assessing usual care is described in published studies. Additionally, there are few reports available to inform how best to monitor usual care. This paper describes the assessment of usual care within the 16 studies of the MACH 14 (Multi-site Adherence Collaboration in HIV among 14 institutions) collaborative group (Liu et al., 2013) and offers insight into current research practice using those studies as examples when conducting and reporting results from clinical trials.

Methods

Design

Data for this descriptive study examining the practice of assessing usual care were provided by the sample of principal investigators within the MACH 14 collaboration and were collected after the studies had ended. MACH 14 includes 16 NIH-funded studies conducted at 14 different sites in various regions of the United States from 1997 to 2009. Each study focused on medication adherence in patients with HIV/AIDS in which the outcome of adherence in both the usual care/control and intervention arms was assessed using electronic event monitors (Liu et al., 2013). All studies in MACH 14 received approval from their respective organization's institutional review board.

Sample

Twelve of the 16 studies (75%) in MACH 14 were intervention studies Liu et al., 2013). The length of the interventions within these studies varied from 5 to 23 weeks. The experimental condition focused on improving medication adherence and directly or indirectly targeted the participant's behavior. The interventions included one or more of the following components: directly observed therapy, problem solving, counseling, feedback to the participant, peer counseling, and feedback to the physician. Theories and models supporting the interventions incorporated social cognitive theory, contingency management, self-regulation, and motivational interviewing.

Data Collection

MACH 14 investigators initially provided a brief written summary of their intervention and usual care/control study groups. Because these descriptions were rather general, we sought more specific information regarding the assessment of usual care in the 16 studies. We developed a questionnaire for the MACH 14 researchers to complete. If the researchers answered "yes" that they monitored usual care, we asked them to describe how usual care was assessed, when usual care was assessed, the frequency of the assessments, who provided the assessment data, how the data were obtained, and the specific clinical practices within usual care that were assessed. We also invited investigators to provide any additional comments relevant to the assessment of usual care in their particular clinical settings.

Data Analysis

We reviewed each of the general descriptions of usual care provided by the MACH 14 researchers to get a sense of their use of the term "usual care". We summarized the data from the questionnaires using descriptive statistics, for example, frequencies and percents.

Results

The initial written descriptions showed that two-thirds (n=10) of the investigators identified usual care as the "procedures provided to all patients". However, when referring to the control condition in their clinical trials, the researchers used diverse terms such as usual care, standard clinic care, standard patient education, or comparison condition. While there

was agreement regarding the definition of usual care, there was variability in how the control condition was defined. Usual care was one example of the control condition.

Our findings showed that only one-third of the studies in Mach 14 (n=5) assessed usual care. Responses to how usual care was assessed demonstrated that investigators in four of the studies developed a study-specific form for assessing usual care. However, in the fifth study, the researchers who were also the health care providers in that setting, stated that they were familiar with the usual care practices and therefore did not conduct regular assessments of usual care.

The frequency of the assessments of usual care varied. Four studies assessed usual care at both the beginning and at the end of the study. Two of those four studies also monitored usual care at 3 or 6 month intervals throughout the study. One study assessed usual care only at the beginning; this study was the one where the health care porviders were also the researchers. The investigators collected usual care data by telephone, face to face, electronically, or mail. Most informants providing usual care assessment data were direct care providers within the practice site. For the longitudinal studies that collected usual care data more often, different personnel within the setting provided the information. Thus, there was not continuity across informants.

The clinical practices within usual care that were assessed included HIV medical care (referrals, laboratory monitoring, and physical examinations) and patient education related to HIV infection, HIV medications, and medication adherence. Another practice in the setting that was assessed was a patient's level of medication adherence when that individual was seen for their clinic appointment.

Discussion

Recognizing the importance of the role of usual care in clinical trials, we set out to describe the manner in which usual care was assessed within the 16 studies included in the MACH 14 collaboration as a means of showing the current research practice when conducting clinical trials. The MACH14 sample included both intervention and non-intervention studies from across the United States; these studies spanned nearly 15 years (Liu et al., 2013). During that time there were new drug discoveries that changed antiretroviral treatment guidelines potentially altering the usual care provided to patients with HIV participating in these longitudinal studies (Panel on Antiretroviral Guidelines for Adults and Adolescents, 2013).

The findings available in this report demonstrate that there was limited systematic monitoring of usual care in the trials included in MACH 14. MACH 14 was a convenience sample of studies that assessed adherence to antiretroviral therapy using electronic event monitors, as well as other bio-behavioral measures. The assessment of usual care was not a criterion for a study's inclusion in MACH 14. The five studies monitoring usual care were all intervention trials and each had assessments at the beginning of those studies; most assessed usual care at the end of the study. Only a few studies assessed usual care at intervals throughout the course of the study. Researchers in MACH 14 conducting non-

intervention studies did not monitor usual care. However, the significance of usual care in observational studies is no less important.

No consistent form for assessing usual care was used across the studies; each study developed its own form. Only particular aspects of usual care within a practice setting may have been included on the assessment form thus limiting the amount of information that was obtained and that could be used to determine the role of usual care on the study outcomes. While these studies attempted to capture any changes in usual care, having more objective measures is preferred and makes tracking changes over time more precise.

Who provided the information about usual care may have affected the information that was collected and made it challenging for the researcher to obtain objective and nonbiased data about current clinic practices. There may have been a "Hawthorne effect" or a social desirability effect when reporting data on usual care practices.

Because participants in some of the studies within MACH 14 were enrolled for 12 months or longer and the interventions lasted between 5-23 weeks, there was the distinct possibility that the usual care provided to participants may have differed by the time all participants were enrolled into and completed a particular study. When usual care is monitored only at the start of the study, it is not possible to know if any changes occurred in patient care practices over the length of the investigation or whether the usual care began to include aspects of the experimental condition. If participants are recruited from the community, as well as clinics, it is not possible to gather data on usual care from all the practices where participants received their care. Thus, the usual care received by participants recruited from the community is unknown.

Our limited findings show that usual care assessments occurred intermittently, even those that occurred at multiple time points within a study. With intermittent monitoring assessments may not be done at the time an evidenced-based practice change was introduced. Additionally, summarizing the common elements within usual care when there are multiple health care providers in the practice setting is difficult as all providers may not manage their patients in the same way. The variability of the available services and what individual patients are offered and receive is difficult to capture within a standardized usual care assessment form.

This brief report demonstrates the limited assessment of usual care within both clinical trials and observational studies in MACH 14 supporting findings from earlier meta-analyses, as well as commentaries calling for the need to assess usual care. How the assessment data was used in the analyses within these studies is unknown. Assessing usual care is important to understand the potential impact of changes in clinical practice during the length of a study. A description of the usual care provided to study participants needs to be included when reporting the study findings. Without a clear depiction of usual care, it becomes difficult to make comparisons across studies and conduct systematic reviews or meta-analyses (de Bruin et al., 2009).

This report suggests that there is a need to develop a protocol within the study to systematically assess usual care throughout the study. Regardless of the research design a

process similar to that for monitoring intervention fidelity should be considered (Wickersham et al., 2011; Glasziou et al., 2010). Monitoring usual care throughout a study and incorporating those data into the analysis will assist researchers to include the influence of usual care on the outcomes of the study and offer changes in usual care as a potential explanation for the findings in the study. Refer to Table 1 for the categories of assessment and recommendations for monitoring usual care.

Acknowledgements

References

Carroll KM. Manual-guided psychosocial treatment: A new virtualrequirement for pharmacotherapytrails? Archives of General Psychiatry. 1997; 54:923–928. doi:10.1001/archpsyc. 1997.01830220041007. [PubMed: 9337772]

de Bruin M, Viechtbauer W, Hospers HH, Schaalma HP, Kok G. Standard care quality determines treatment outcomes in control groups of HAART-adherence intervention studies: Implications for the interpretation and comparison of intervention effects. Health Psychology. 2009; 28:668–674. doi:10.1037/a0015989. [PubMed: 19916634]

de Bruin M, Viechtbauer W, Schaalma HP, Kok G, Abraham C, Hospers HJ. Standard care impact on effects of highly active antiretroviral therapy adherence interventions: A meta-analysis of randomized controlled trials. Archives of Internal Medicine. 2010; 170:240–250. doi:10.1001/archinternmed.2009.536. [PubMed: 20142568]

Freedland KE, Mohr DC, Davidson KW, Schwartz JE. Usual and unusual care: Existing practice control groups in randomized controlled trials of behavioral interventions. Psychosomatic Medicine. 2011; 73:323–335. doi: 10.1097/PSY.0b013e318218e1fb. [PubMed: 21536837]

Garland AF, Hurlburt MS, Brookman-Frazee L, Taylor RM, Accurso EC. Methodological challenges of characterizing usual care psychotherapeutic practice. Administration and Policy in Mental Health and Mental Health Services Research. 2010; 37:208–220. doi 10.1007/s10488-009-0237-8. [PubMed: 19757021]

Glasziou P, Chalmers I, Altman DG, Bastian H, Boutron I, Brice A, Williams JW. Taking healthcare interventions from trial to practice. British Medical Journal. 2010; 341:c3582. doi:10.1136/bmjc3852. [PubMed: 20610503]

Hulley, SB.; Cummings, SR.; Browner, WS.; Grady, DG.; Newman, TB. Designing clinical research. 3rd ed.. Lippincott Williams & Wilkins; Philadelphia, PA: 2007.

Kelley SD, Vides de Andrade AR, Sheffer E, Bickman L. Exploring the black box: Measuring youth treatment process and progress in usual care. Administration and Policy in Mental Health and Mental Health Services Research. 2010; 37:287–300. doi: 10.1007/s10488-010-0298-8. [PubMed: 20238155]

Liu H, Wilson IB, Goggin K, Reynolds N, Simoni JM, Golin CE, Bangsberg DR. MACH 14: A multi-site collaboration on ART adherence among 14 institutions. AIDS and Behavior. 2013; 17:127–141. doi: 10.1007/s10461-012-0272- 4. [PubMed: 22864921]

Michie S, Prestwich A, de Bruin M. Importance of the nature of comparison conditions for testing theory-based interventions: Reply. Health Psychology. 2010; 29:468–470. doi: 10.1037/a0020844.

Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents. 2013. Retrieved from http://aidsinfo.nih.gov/contentfiles/lvguidelines/AdultandAdolescentGL.pdf

Polit, DF.; Beck, CT. Nursing research: Generating and assessing evidence for nursing practice. 9th ed.. Wolters Kluwer Health; Philadelphia, PA: 2012.

Wagner GJ, Kanouse DE. Assessing usual care in clinical trials of adherence interventions for highly active antiretroviral therapy. Journal of Acquired Immune Deficiency Syndromes. 2003; 33:276–280. [PubMed: 12794566]

Wickersham K, Colbert A, Caruthers D, Tamres L, Martino A, Erlen JA. Assessing fidelity to an intervention in a randomized controlled trial to improve medication adherence. Nursing Research. 2011; 60:264–269. doi:10.1097/NNR.0b013e318221b6e6. [PubMed: 21677597]

Williams DM. Importance of the nature of comparison conditions for testing theory-based interventions: Comment on Michie and Prestwich. Health Psychology. 2010; 29:467. doi: 10.1037/a0019597. [PubMed: 20836599]

Table 1

Recommendations for Assessing Usual Care in Clinical Trials

Focal area	Recommendations
Study specific instrument	Develop a study specific form or modify a form so that it is specific to the study *a priori*
	Consider developing a more detailed form rather than one that has broad categories in order to collect relevant information
	Include space for dates for any changes in clinic practices; provide space for identifying the changes
	Include space for frequencies of ongoing events such as labs and follow-up appointments
Content	Include questions related to:
	Clinic visits including initial vs. follow-up, laboratory tests, physical examinations
	Usual frequency of clinic visits
	Referral services such as psychiatric -mental health or social service
	Special programs that are offered such as peer support groups
	Educational services such as review of medications, medication management/adherence, nutrition
	Programmatic and/or clinic changes including the nature of the change and date when the change occurred
	Other regular occurrences within the clinical management of patients
Study data collector	Identify usual care data collection as a specific position responsibility for a member of the research staff
	Ensure that staff member has a clinical background
	Prepare a study specific protocol for collecting usual care data
	Provide training regarding the protocol for collecting usual care information
	Conduct periodic quality assessments of usual care data collection
	Conduct ant retraining of study staff, as necessary
Clinic Informant	Identify one consistent person from the healthcare agency/clinic who is knowledgeable about the clinic's practices
	Provide training for the designated informant in order to ensure accurate and complete data collection
Timing	Collect data at the beginning, end, and at intervals during the study
	Track the date for each usual care data collection
	Arrange a convenient date and time with the clinic informant for collecting usual care data
Mechanism	Collect data using an on-site face to face interview (preferred approach at least for the initial data collection)
	Use telephone interview or electronic/mail data collection if unable to use on-site approach
	Enter data into a database as soon after the data collection as possible
	Contact the clinic informant to obtain any missing data or to clarify any of the information