Title

Reporting of critical information in studies of pharmacists in HIV care

Journal

International Journal of Pharmacy Practice, 22(6)

ISSN

0961-7671

Authors

Cocohoba, Jennifer

Dong, Betty J

Johnson, Mallory O

et al.

Publication Date

2014-11-13

DOI

10.1111/ijpp.12096

Peer reviewed

Published in final edited form as:
Int J Pharm Pract. 2014 December ; 22(6): 375–385. doi:10.1111/ijpp.12096.

Reporting of critical information in studies of pharmacists in HIV care

Jennifer Cocohoba, Pharm.D, MAS, AAHIVP, BCPS,
Health Sciences Associate Clinical Professor, Department of Clinical Pharmacy, University of California San Francisco School of Pharmacy

Betty J. Dong, Pharm.D., FASHP, FCCP, AAHIVE,
Professor of Clinical Pharmacy, Department of Clinical Pharmacy, University of California San Francisco School of Pharmacy

Mallory O. Johnson, PhD, and
Professor of Medicine, Center for AIDS Prevention Studies, University of California San Francisco School of Medicine

Parya Saberi, Pharm.D., MAS, AAHIVE
Assistant Professor of Medicine, Center for AIDS Prevention Studies, University of California San Francisco School of Medicine

Abstract

Objective—To evaluate manuscripts documenting HIV pharmacist interventions and assess adequacy of reporting as defined by CONSORT and STROBE criteria.

Methods—PubMed, EMBASE, Cochrane Library, Web of Science, BIOSIS Previews, and PsycINFO databases were searched from inception-6/1/2011. Studies were included if pharmacists performed an intervention to improve HIV patient care, and the study evaluated the intervention's impact. Qualitative studies, non-English language reports, abstracts, and studies where the pharmacist did not intervene were excluded. Manuscripts were independently evaluated by two reviewers for the presence, absence, or lack of applicability of STROBE (observational studies) or CONSORT (randomized studies) criteria, for presence or absence of description of pharmacist's duties, CD4+ cell count, HIV viral load, and adherence measurement. Reviewers met to discuss the rationale behind their evaluation; a third arbiter was consulted when reviewers could not agree on a particular criterion.

Key findings—Twenty-two manuscripts met inclusion criteria. Observational studies of HIV pharmacists (n=19) included 56% of applicable STROBE criteria. Randomized studies of HIV

Corresponding Author: Jennifer Cocohoba, Pharm.D., MAS, AAHIVE, BCPS, 521 Parnassus Avenue, C-152, Box 0622, San Francisco, CA 94143-0622, Phone: (415) 514-0892, Fax: (415) 476-6632, cocohobaj@pharmacy.ucsf.edu.

Conflict of Interest: Authors declare no conflicts of interest with regard to this manuscript.

Authorship acknowledgement: All listed authors have contributed sufficient effort to the manuscript and had complete access to the study data in order to warrant authorship. Dr. Cocohoba designed the study, conducted data analysis, authored/edited drafts, and had the manuscript's final approval. Dr. Dong participated in data analysis, manuscript revisions, and the manuscript's final approval. Dr. Johnson participated in creation of the study design, manuscript revisions, and manuscript final approval. Dr. Saberi contributed to study design, data acquisition and analysis, manuscript revisions, and the final approval of the manuscript.

pharmacists (n=3) adhered more closely to CONSORT reporting guidelines (average 80% of applicable criteria). Manuscripts published after 2004 more consistently evaluated pharmacist impact on HIV outcomes such as CD4+ and viral load.

Conclusions—Thorough reporting increases the reader's ability to critically evaluate manuscripts of HIV pharmacist services. Increasing pharmacist awareness of manuscript guidelines such as CONSORT and STROBE may improve clarity of reporting in studies of HIV pharmacist interventions and clinical programs.

Keywords

clinical pharmacy; anti-infectives; research method; observation; RCT

Introduction

Complexities associated with antiretroviral therapy (ART) present unique opportunities for pharmacists to be closely involved in the care of patients with Human Immunodeficiency Virus (HIV).[1,2] Through formal HIV/AIDS pharmacy residencies, fellowships, credentialing certification programs and experience, dedicated pharmacists gain expertise in HIV pharmacotherapy and apply these skills to improve patient care.[3] Many manuscripts outlining these HIV clinical services and documenting HIV pharmacy interventions have been published.[4] Despite these strides, it is unclear whether manuscripts that comprise the body of published literature on HIV clinical pharmacy have included enough critical study information to be interpreted accurately and fairly. Recent treatment adherence guidelines published by the International Association of Physicians in AIDS Care (IAPAC) supported pharmacy-based medication management services for patients with HIV, but stated that the evidence was only of medium quality (IIIC) for this recommendation, based on available literature.[5] The quality of a study is determined by the rigor of its design, the appropriateness of its methodology, its generalizability, and other essential elements. Reporting is not a direct measure of quality. It simply notes whether these essential items were present or absent in the study manuscript. However, even if a study was well-conducted, poor reporting in the manuscript can influence a reader's perception of the quality of the study.

To our knowledge, no studies have examined publications about HIV pharmacists to look for key, critical pieces of information that are desirable for inclusion in a manuscript. The purpose of our study is to examine the literature on HIV pharmacist interventions and assess the thoroughness of reporting in these studies.

Methods

Search strategy and selection of articles

In a previous study, a systematic review using the Cochrane Highly Sensitive Search Strategy was undertaken to identify articles which included any mention of pharmacists involved in HIV care.[4,6] The PubMed, EMBASE, Cochrane Library, Web of Science, BIOSIS Previews, and PsycINFO databases were searched from the date of inception of each database through June 1, 2011. References of publications were manually searched to

identify any additional relevant publications. A detailed description of this search strategy has been published.[4] Duplicate and irrelevant citations were removed by one author (PS). The abstracts of the remaining citations were independently reviewed by two authors (PS and JC) to identify relevant publications involving pharmacist care of HIV-positive adults. These publications were summarized and described in a narrative, systematic review.[4] During the process, we noted large inconsistencies in the amount of information included in these publications and the depth of description of key elements such as study methods. We sought to further explore these inconsistencies in reporting in a similar manner to prior studies.[7,8] The citations were further narrowed to include only the studies that were specifically designed to examine the pharmacist's interventions with HIV-positive individuals. Qualitative research studies were excluded from the systematic review because they documented value in a narrative fashion that was difficult to compare or contrast with the quantitative studies. We excluded conference abstracts because the STROBE and CONSORT criteria were designed to evaluate published manuscripts and abstracts lack the necessary data required for evaluation.[9,10] Lastly, if the pharmacist participated in the study intervention or objectives, but the research was not designed to examine the HIV pharmacist's contribution, the study was excluded. In these types of studies the pharmacist's involvement was often limited to antiretroviral dispensing only or dispensing directly observed therapy only.

Review of articles

The authors considered several tools to assess thoroughness of reporting in manuscripts and opted to apply STROBE criteria to observational studies and CONSORT criteria to randomized studies.[9,10] Criteria were rated as present (yes), absent (no), or not applicable to the study. Compound criteria which included multiple assessments were separated for consistency of evaluation. Authors held a preliminary discussion of each criterion in the STROBE and CONSORT checklists to guide the initial interpretation. A small list of additional criteria deemed important by the authors and relevant to studies of HIV pharmacists were assessed separately from STROBE or CONSORT criteria. These included concordance of the declared study design with Cochrane classifications, description of HIV pharmacist training or prior experience, and evaluation of key outcomes measures such as adherence, CD4+ cell count, and HIV-1 viral load.[6]

Each study was independently reviewed by two authors (JC/PS or JC/BD) for presence or absence of the required STROBE, CONSORT, or additional criteria. Inter-reviewer agreement on the criteria evaluated for each study was assessed using an unweighted kappa statistic, calculated for each study using STATA version 12.0 (StataCorp, College Station, TX).[11] If the two primary reviewers had different ratings (present vs. absent vs. not applicable) on a particular criterion within a manuscript, the reviewers met to see if the disagreement could be resolved through discussion. In the seven instances that a disagreement could not be resolved through discussion, a third author was asked to review the study and provide final input. Descriptive statistics were used to calculate the frequency at which studies satisfied various criteria and the overall proportion of criteria that each study satisfied. The criterion inclusion rate was summed across all observational studies and

divided by 19, or summed across all randomized studies and divided by three, to obtain an average inclusion rate.

Results

Of the initial 1,545 citations, 1,477 were discarded after abstract review because they were duplicate or irrelevant. The remaining 68 articles were reviewed by two authors (PS/JC). Review articles (n=3), abstract-only citations (n=11), qualitative studies (n=4), non-English language articles (n=3), articles which could not be categorized because they did not describe the pharmacist's activities (n=15), and manuscripts where the pharmacist's impact on the program or intervention was not evaluated (n=10) were excluded. The remaining 22 publications met eligibility criteria and were included in this analysis.[12-33] The majority of included studies were observational (n=19, 86%) and were evaluated using STROBE criteria. Three publications detailed experimental or quasi-experimental designs and were evaluated according to CONSORT criteria.[28,32,33] The reviewers' initial observed agreement on presence or absence of critical information in three randomized studies was high (observed agreement on all criteria for an individual study = 80-81%; kappa range = 0.56-0.68; all $p<0.001$). Reviewers had moderate to high agreement on the critical information presented in 19 observational studies (observed agreement on all criteria for an individual study 65-100%; kappa range = 0.39-1.00; all $p \leq 0.001$).

Table 1 presents a summary of the critical information that was included in observational studies as evaluated by STROBE. Of the 19 studies evaluated, no single study reported all of the critical information suggested by the STROBE guidelines. If the non-applicable criteria for each study were discarded, then studies reported an average of 56% of the remaining criteria suggested by STROBE. These publications were most consistent at listing the key elements of study design (such as population, intervention, control, outcomes) early in the paper, described the settings and/or locations, defined basic study outcomes, described follow-up time, and included summary measures. Zero manuscripts stated their study design in the title or abstract or included a study flow diagram. Authors generally failed to address loss to follow up, any plans for handling missing data, sensitivity analyses, or the generalizability of their study results (included in 8%, 11%, 0%, and 11% of applicable studies, respectively).

The three randomized trials described in Table 2 each included an average of 80% of the information recommended by the CONSORT guidelines when criteria not-applicable to each study were discarded. Criteria that were less frequently met included describing how sample size was derived (0 studies), detailing additional subgroup or adjusted analyses (1 study), rigorous descriptions of study generalizability (0 studies), and providing information about access to the full study protocol and registration of the clinical trial (0 studies). Of note, one of the studies (Levy) was published prior to the time the International Committee of Medical Journal Editors issued their recommendation for all clinical trials to be registered prior to publication.[33,34]

Table 3 summarizes inclusion of additional criteria that were important to studies of HIV pharmacists, as deemed by the reviewers. All manuscripts provided a reasonable level of

detail (as agreed upon by the reviewers) on the HIV pharmacist's duties in the program or study intervention. Manuscripts published prior to 2004 tended not to specify a study design as they primarily described clinical programs. In the nine studies published after 2004 that did declare a study design, only in 5 cases did the listed study design agree with a study design that would have been ascribed using Cochrane Collaboration guidelines.[35] Over time, manuscripts about HIV pharmacists increasingly included CD4+ cell counts, HIV viral load, and adherence as outcome measures (15% in papers published prior to 2004 vs. 53% in papers published in 2004 and after). Manuscripts that measured adherence as an outcome typically described the adherence calculation well (8 of 9 studies) and most manuscripts provided some information about the study pharmacist's qualifications or background training (11 of 22 studies).

Discussion

Our search found that the majority of research studies evaluating HIV pharmacist interventions used pre-post observational study designs. After 2004, these observational studies also began to examine the impact of pharmacist services on HIV clinical outcomes such as CD4+ cell count and HIV viral load.[4] Despite this enhancement, published observational studies of HIV pharmacists failed to report a substantial amount of critical information as suggested by established manuscript guidelines. Randomized studies of HIV pharmacist interventions represent an even greater step forward towards demonstrating the value of HIV pharmacists. Yet there did not appear to be an increasing trend in publication of rigorous randomized studies of HIV pharmacists as only three of these studies were identified (2004, 2005, and 2010) and included in our evaluation. In general, the adequacy of reporting critical information was much improved in these three papers, and pertinent HIV clinical outcomes were often included as primary or secondary measures.

One limitation to our study is that most of the manuscripts we evaluated were published prior to the availability of the STROBE and CONSORT guidelines, or were published in journals which do not endorse these guidelines. Our review illustrates where HIV pharmacist literature stands under current reporting recommendations, and identifies areas where HIV pharmacist literature might continue to improve in reporting. This is a moving target because good reporting principles may evolve over time. Many of the observational studies we evaluated were descriptive and did not include a comparator group. STROBE criteria may be more applicable to observational cohorts with more than one group. Various tools to evaluate reporting in observational or non-randomized study designs exist, and our evaluation was limited only to STROBE. Though CONSORT guides the interpretation of its criteria with supportive explanations, STROBE criteria were more subject to interpretation. We attempted to ameliorate this issue by utilizing at least two reviewers per study, rather than relying on a single reviewer. STROBE criteria were published in 2007. Though STROBE criteria might be considered "usual elements" included in a paper, many observational studies we evaluated were published prior to the release of STROBE, and did not benefit from having this checklist in advance of their manuscript preparation. The GRADE criteria for systematic reviews were not applied because the studies appeared to be heterogeneous. The a priori goal of this review was to assess the thoroughness of reporting, rather than the quality of the evidence, though this would be the next step to take. A more

in-depth evaluation would evaluate the evidence to justify inclusion of pharmacists in HIV healthcare teams; however, this might turn out to be more favorable if the rigor of the study designs and their reporting increased. We did not contact the study authors as part of our methodology, so we cannot determine the reasons for missing information in the manuscripts. Our search strategy identified and evaluated papers which focused on HIV pharmacist interventions; other broader searches which included conference abstracts, foreign language reports or pharmacists peripherally involved in the care of HIV positive patients may have increased the adequacy of reporting found in the body of literature.

It is possible that critical information was not inadvertently omitted in the manuscripts we evaluated. Authors might have been unfamiliar with reporting criteria, or information could be missing due to gaps in study design or analysis. Many of the earlier published manuscripts were descriptive observational studies with no comparator group. Those types of studies are not as rigorous in design and often do not collect information recommended for adequate reporting. Despite this, those studies still played the important role of broadening awareness of the important services HIV pharmacists provide when caring for patients: ameliorating drug-drug interactions, counseling patients on poor adherence, and detecting and preventing medication errors.[2,3] If critical information had been more strategically reported in those manuscripts, they may have been perceived by readers as more clear, rigorous, and generalizable.

Our study focused on the body of literature on HIV pharmacist interventions, yet it is likely that literature searches examining other pharmacist specialists' interventions might also yield low levels of reporting critical information. Pharmacy interventions need to be represented in well-designed research studies that adequately report critical information. For example, researchers should strive to increase the number of well-reported randomized studies that detail the efficacy of HIV pharmacist interventions in the literature. Randomized trials can be challenging to implement and conduct, however these studies provide the clearest evidence to support pharmacist clinical services.

One method to improve design and analysis of pharmacist intervention studies would be to encourage the training of pharmacists as clinical researchers. By enhancing research training in schools of pharmacy, fellowships, pharmacy association research training programs, and other degree programs pharmacists might become more intimately involved in conducting research on their clinical interventions and in improving reporting in manuscripts.[36-38] Interdisciplinary partnerships between clinical pharmacists and scientists rooted in epidemiology and interventional research design would also achieve similar results. It is important that all pharmacist authors familiarize themselves with reporting guidelines such as CONSORT and STROBE so that research is appropriately reported in the manuscripts. Lastly, an important burden lies on the editorial staff and peer reviewers of pharmacy and medical journals to select manuscripts that closely adhere to those reporting guidelines. By judiciously selecting papers that move forward to publication, editors can ensure that the body of literature evaluating pharmacists and their clinical interventions represents them in the clearest and most helpful manner possible.

Conclusion

Critical information is poorly reported in observational studies, but well-reported in the few randomized trials of HIV pharmacist interventions. Rigorously reported evidence supporting efficacy and expertise is essential to expand HIV pharmacist services. Future studies documenting the value of the HIV pharmacist specialist should consider the strengths and weaknesses of previous publications and should strive to adhere to established manuscript reporting guidelines. If an HIV pharmacist lacks research skills to evaluate their services, they should consider partnering with other scientists to improve the examination and documentation of their outcomes. Lastly, authors and journal editors should share the burden of complete and careful reporting of research findings on pharmacist programs or interventions in order to provide the most informative picture of the in-depth contributions of HIV pharmacists.

Acknowledgments

This publication is supported by funding from the National Institutes of Health National Institute of Mental Health K23MH087218 (Cocohoba), K24MH087220 (Johnson), and F32MH086323 (Saberi).

Funding: This project was supported by the National Institutes of Mental Health grants K23MH087218 (Cocohoba), K24MH087220 (Johnson), and F32MH086323 (Saberi).

References

1. ASHP statement on the pharmacist's role in the care of patients with HIV infection. Am J Health Syst Pharm. Oct 1; 2003 60(19):1998–2003. [PubMed: 14531248]
2. Tseng A, Foisy M, Hughes CA, et al. Role of the pharmacist in caring for patients with HIV/AIDS: clinical practice guidelines. Can J Hosp Pharm. Mar; 2012 65(2):125–145. [PubMed: 22529405]
3. Scott JD, Abernathy KA, Diaz-Linares M, Graham KK, Lee JC. HIV clinical pharmacists--the US perspective. Farm Hosp. Nov-Dec;2010 34(6):303–308. [PubMed: 20674431]
4. Saberi P, Dong BJ, Johnson MO, Greenblatt RM, Cocohoba JM. The impact of HIV clinical pharmacists on HIV treatment outcomes: a systematic review. Patient Prefer Adherence. 2012; 6:297–322. [PubMed: 22536064]
5. Thompson MA, Mugavero MJ, Amico KR, et al. Guidelines for improving entry into and retention in care and antiretroviral adherence for persons with HIV: evidence-based recommendations from an International Association of Physicians in AIDS Care panel. Ann Intern Med. Jun 5; 2012 156(11):817–833. [PubMed: 22393036]
6. Lefebvre, C.; Manheimer, E.; Glanville, J. Searching for Studies. In: Higgins, JP.; Green, S., editors. Cochrane Handbook for Systematic Reviews of Interventions: Cochrane Book Series. John Wiley & Sons, Ltd.; Chichester, UK: 2008.
7. Costa LO, Maher CG, Lopes AD, de Noronha MA, Costa LC. Transparent reporting of studies relevant to physical therapy practice. Rev Bras Fisioter. Aug-Sep;2011 15(4):267–271. [PubMed: 21975681]
8. Parsons NR, Hiskens R, Price CL, Achten J, Costa ML. A systematic survey of the quality of research reporting in general orthopaedic journals. J Bone Joint Surg Br. Sep; 2011 93(9):1154–1159. [PubMed: 21911523]
9. von Elm E, Altman DG, Egger M, Pocock SJ, Gotzsche PC, Vandenbroucke JP. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. Ann Intern Med. Oct 16; 2007 147(8):573–577. [PubMed: 17938396]

10. Moher D, Hopewell S, Schulz KF, et al. CONSORT 2010 explanation and elaboration: updated guidelines for reporting parallel group randomised trials. BMJ. 2010; 340:c869. [PubMed: 20332511]
11. Viera AJ, Garrett JM. Understanding interobserver agreement: the kappa statistic. Fam Med. May; 2005 37(5):360–363. [PubMed: 15883903]
12. Walji N, Beardsell A, Brown G. Pharmacists' activities in monitoring zidovudine therapy in an AIDS clinic. Can J Hosp Pharm. Feb; 1992 45(1):29–32. [PubMed: 10117360]
13. Geletko SM, Segarra M, Copeland DA, Teague AC. Pharmaceutical care for hospitalized HIV-infected patients compared to infectious diseases consult patients without HIV infection. Journal of Infectious Disease Pharmacotherapy. 1996; 2(1):45–57.
14. Bozek PS, Perdue BE, Bar-Din M, Weidle PJ. Effect of pharmacist interventions on medication use and cost in hospitalized patients with or without HIV infection. Am J Health Syst Pharm. Jun 1; 1998 55(11):1151–1155. [PubMed: 9626378]
15. Garey KW, Teichner P. Pharmacist intervention program for hospitalized patients with HIV infection. Am J Health Syst Pharm. Dec 15; 2000 57(24):2283–2284. [PubMed: 11146973]
16. McPherson-Baker S, Malow RM, Penedo F, Jones DL, Schneiderman N, Klimas NG. Enhancing adherence to combination antiretroviral therapy in non-adherent HIV-positive men. AIDS Care. Aug; 2000 12(4):399–404. [PubMed: 11091772]
17. Geletko SM, Poulakos MN. Pharmaceutical services in an HIV clinic. Am J Health Syst Pharm. Apr 15; 2002 59(8):709–713. [PubMed: 11977854]
18. Segarra-Newnham M. Preventing Medication Errors with a "Pharmacy Admission Note" for HIV-Positive Patients. Hospital Pharmacy. 2002; 37(1):34–37.
19. Foisy MM, Akai PS. Pharmaceutical care for HIV patients on directly observed therapy. Ann Pharmacother. Apr; 2004 38(4):550–556. [PubMed: 14990778]
20. Castillo E, Palepu A, Beardsell A, et al. Outpatient pharmacy care and HIV viral load response among patients on HAART. AIDS Care. May; 2004 16(4):446–457. [PubMed: 15203413]
21. De Maat MMR, De Boer A, Koks CHW, et al. Evaluation of clinical pharmacist interventions on drug interactions in outpatient pharmaceutical HIV-care. J Clin Pharm Ther. 2004; 29(2):121–130. [PubMed: 15068400]
22. Sterling ES, Romanelli F, Martin CA, Hoven AD, Smith KM. Impact of a pharmacy-initiated HIV admission note on medication errors within an academic hospital. Hosp Pharm. 2005; 40(10):874–881.
23. Heelon M, Skiest D, Tereso G, et al. Effect of a clinical pharmacist's interventions on duration of antiretroviral-related errors in hospitalized patients. Am J Health Syst Pharm. Oct 1; 2007 64(19): 2064–2068. [PubMed: 17893418]
24. March K, Mak M, Louie SG. Effects of pharmacists' interventions on patient outcomes in an HIV primary care clinic. Am J Health Syst Pharm. Dec 15; 2007 64(24):2574–2578. [PubMed: 18056946]
25. Horberg MA, Hurley LB, Silverberg MJ, Kinsman CJ, Quesenberry CP. Effect of clinical pharmacists on utilization of and clinical response to antiretroviral therapy. Jaids-Journal of Acquired Immune Deficiency Syndromes. Apr; 2007 44(5):531–539.
26. Horace A, Philips M. Identification and prevention of antiretroviral medication errors at an academic medical center. Hosp Pharm. 2010; 45(12):927–933.
27. Ma A, Chen DM, Chau FM, Saberi P. Improving adherence and clinical outcomes through an HIV pharmacist's interventions. AIDS Care. Oct; 2010 22(10):1189–1194. [PubMed: 20640958]
28. Krummenacher I, Cavassini M, Bugnon O, Spirig R, Schneider MP. Antiretroviral adherence program in HIV patients: a feasibility study in the Swiss HIV Cohort Study. Pharm World Sci. Dec; 2010 32(6):776–786. [PubMed: 20862544]
29. Henderson KC, Hindman J, Johnson SC, Valuck RJ, Kiser JJ. Assessing the effectiveness of pharmacy-based adherence interventions on antiretroviral adherence in persons with HIV. AIDS Patient Care STDS. Apr; 2011 25(4):221–228. [PubMed: 21323566]
30. Carcelero E, Tuset M, Martin M, et al. Evaluation of antiretroviral-related errors and interventions by the clinical pharmacist in hospitalized HIV-infected patients. HIV Med. Mar 13.2011 12:494–499. [PubMed: 21395966]

31. Krummenacher I, Cavassini M, Bugnon O, Schneider MP. An interdisciplinary HIV-adherence program combining motivational interviewing and electronic antiretroviral drug monitoring. AIDS Care. May; 2011 23(5):550–561. [PubMed: 21271406]
32. Rathbun RC, Farmer KC, Stephens JR, Lockhart SM. Impact of an adherence clinic on behavioral outcomes and virologic response in the treatment of HIV infection: A prospective, randomized, controlled pilot study. Clin Ther. Feb; 2005 27(2):199–209. [PubMed: 15811483]
33. Levy RW, Rayner CR, Fairley CK, et al. Multidisciplinary HIV adherence intervention: a randomized study. AIDS Patient Care STDS. 2004; (12):728–735. http://www.mrw.interscience.wiley.com/cochrane/clcentral/articles/022/CN-00503022/frame.html. [PubMed: 15659884]
34. de Angelis C, Drazen JM, Frizelle FA, et al. Clinical trial registration: a statement from the International Committee of Medical Journal Editors. N Engl J Med. Jun 21.2004 351:1250–1251. 2012. [PubMed: 15356289]
35. Reeves, BC.; Deeks, JJ.; Higgins, JP.; Wells, GA.; The Cochrane Collaboration. Chapter 13: Including non-randomized studies. In: Higgins, JPT.; Green, S., editors. Cochrane Handbook for Systematic Reviews of Interventions Version 5.0.2. 2009.
36. Fagan SC, Touchette D, Smith JA, et al. The state of science and research in clinical pharmacy. Pharmacotherapy. Jul; 2006 26(7):1027–1040. [PubMed: 16803427]
37. Bauman JL, Evans WE. Pharm.D.-only investigators are critical to the profession: let's preserve the fellowship as an equally important way to prepare future clinical pharmaceutical scientists or the case against the "all-Ph.D.". Pharmacotherapy. Feb; 2009 29(2):129–133. [PubMed: 19170582]
38. Blouin RA, Pollack GM. Training clinical pharmaceutical scientists in today's highly competitive times: it's time to commit to change. Pharmacotherapy. Feb; 2009 29(2):134–137. [PubMed: 19170583]

Table 1

Presence or absence of critical information reported in observational studies evaluating the impact of HIV clinical pharmacists

		Walji (1992)[12]	Geletko (1996)[13]	Bozek (1998)[14]	Garey (2000)[15]	McPherson-Baker (2000)[16]	Geletko (2002)[17]	Segarra-Newnham (2002)[18]	De Maat (2004)[21]	Foisy (2004)[19]	Castillo (2004)[20]	Sterling (2005)[22]	Heelon (2007)[23]	March (2007)[24]	Horberg (2007)[25]	Horace (2010)[26]	Ma (2010)[27]	Krummenacher (2011)[31]	Henderson (2011)[29]	Carcelero (2011)[30]
1a	Is the study design indicated in the title or abstract? *a*																			
1b	Does the abstract present an informative and balanced summary of what was done and what was found?																			
2	Does the study explain the scientific background and rationale? *b*																			
3a	Does the study state specific objectives? *c*																			
3b	Does the study include any pre-specified hypotheses?																			
4	Are key elements of study design presented early in the paper? *d*																			
5a	Does the paper describe the setting and locations?																			
5b	Does the paper describe the relevant dates, including periods of recruitment?																			
5c	Does the paper describe the relevant dates, including periods of exposure, follow-up, and data collection?																			
6a	Does the study include eligibility criteria and describe follow-up? *e,f*																			
6b	Does the study include sources and methods of selection of participants? *g*																			
6c	For matched cohort studies does the study give matching criteria and the number of exposed and unexposed? *e*																			
7a	Does the study clearly define all outcomes?																			
7b	Does the study clearly define all exposures and predictors? *h*																			
7c	Does the study clearly define all potential confounders, effect modifiers, and diagnostic criteria (if applicable)? *h*																			
8	For each variable of interest, does the study give sources of data and details of methods of assessment, and describe comparability of assessment methods if there is more than one group?																			
9	Does the study describe any efforts to address potential sources of bias? *h*																			
10	Does the study explain how the study size was arrived at? *h*																			
11	Does the paper explain how quantitative variables were handled in the analyses? If applicable, does it describe which groupings were chosen and why?																			

		Walji (1992)[12]	Geletko (1996)[13]	Bozek (1998)[14]	Garey (2000)[15]	McPherson-Baker (2000)[16]	Geletko (2002)[17]	Segarra-Newnham (2002)[18]	De Maat (2004)[21]	Foisy (2004)[19]	Castillo (2004)[20]	Sterling (2005)[22]	Heelon (2007)[23]	March (2007)[24]	Horberg (2007)[25]	Horace (2010)[26]	Ma (2010)[27]	Krummenacher (2011)[31]	Henderson (2011)[29]	Carcelero (2011)[30]
12a	Does the paper describe all statistical methods, including those used to control for confounding?																			
12b	Does the paper describe any methods used to examine subgroups and interactions? [h]																			
12c	Does the paper explain how missing data were addressed?																			
12d	For cohort studies - does the paper explain how loss to follow-up was addressed? If a cross-sectional study, (and if applicable) does the study describe analytical methods taking account of sampling strategy? [e,h]																			
12e	Does the study describe any sensitivity analyses? [h]																			
13a	Does the study report the numbers of individuals at each stage of the study – e.g. numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing followup and analyzed?																			
13b	Does the paper give reasons for non-participation at each stage? [h]																			
13c	Does the study include a flow diagram?																			
14a	Does the paper give characteristics of study participants (e.g. demographic, clinical, social) and information?																			
14b	Does the paper indicate the number of participants with missing data for each variable of interest?																			
14c	Does the paper summarize follow-up time (e.g. average and total amount)? [i]																			
15a	Does the study report numbers of outcome events or summary measures over time (cohort studies)? Do the authors report numbers of outcome events or summary measures (cross sectional studies)? [e]																			
16a	Does the study give unadjusted estimates? [h]																			
16b	Does the study give confounder-adjusted estimates and their precision (e.g. 95% confidence interval)? [h]																			
16c	If confounder-adjusted estimates are given, does it make clear which confounders were adjusted for and why they were included? [h]																			
16d	Does the study report category boundaries when continuous variables were categorized?																			
16e	If relevant, does the study translate estimates of relative risk into absolute risk for a meaningful time period?																			
17	Does the study report any other analyses done – e.g. analyses of subgroups and interactions, and sensitivity analyses?																			
18	Does the study summarize key results with reference to study objectives?																			
19a	Does the paper discuss the limitations of the study?																			
19b	Does the paper take into account sources of potential bias or imprecision, as well as both direction and magnitude of any																			

		Walji (1992)[12]	Geletko (1996)[13]	Bozek (1998)[14]	Garey (2000)[15]	McPherson-Baker (2000)[16]	Geletko (2002)[17]	Segarra-Newnham (2002)[18]	De Maat (2004)[21]	Foisy (2004)[19]	Castillo (2004)[20]	Sterling (2005)[22]	Heelon (2007)[23]	March (2007)[24]	Horberg (2007)[25]	Horace (2010)[26]	Ma (2010)[27]	Krummenacher (2011)[31]	Henderson (2011)[29]	Carcelero (2011)[30]
	potential bias? [h]																			
20	Does the paper give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence?																			
21	Does the study discuss the generalizability (external validity) of the results?																			
22	Does the paper give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based?																			

Legend: Grey = yes; White = no; Black = not applicable

[a] For this criteria a specific research design had to be specified. Stating “prospective” or “retrospective” without a specific design (e.g. cohort, cross-sectional) was marked “no”

[b] If the background was not specific or relevant to study, the category was marked “no”

[c] The study was marked “yes” even if it didn’t specifically say “purpose”, “objective”, or “aim”, but alluded to a gap or need that the study was filling.

[d] “Key elements” were defined as population, intervention and control (if applicable), outcomes. “Early” was defined as anywhere prior to the results section.

[e] Additional criteria are given for case-control studies, however there were no case-control studies evaluated in this review.

[f] A study was marked “yes” for this category if it contained eligibility criteria (at minimum)

[g] If a study suggested that consecutive sampling was performed (e.g. stated “all patients were included”) then the study was marked “yes” for this category.

[h] If a manuscript was descriptive (did not analyze a comparator group), this category was considered not applicable.

[i] Studies were marked “yes” if there was mention of the duration during which patients were followed, even if there was no specific calculation of person-years

Table 2

Presence or absence of critical information reported in randomized $ CS studies evaluating the impact of HIV clinical pharmacists

		Levy (2004)[33]	Rathbun (2005)[32]	Krummenacher (2010)[28]
1a	Does the study identify as a randomized trial in the title?			
1b	Is there a structured abstract which summarizes trial design, methods, results, and conclusions?			
2a	Is there a section in the introduction which reviews the scientific background and explains rationale?			
2b	Are there specific objectives or hypotheses stated?			
3a	Is there a description of trial design (such as parallel, factorial) including allocation ratio?			
3b	If applicable, does the study list important changes to methods after trial commencement (such as eligibility criteria), with reasons?[a]			
4a	Does the paper state eligibility criteria for participants?			
4b	Does the paper describe the settings and locations where the data were collected?			
5	Does the paper describe the interventions for each group with sufficient details to allow replication, including how and when they were actually administered?			
6a	Does the paper include completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed?			
6b	If applicable, were any changes to trial outcomes which happened after the trial commenced described, with reasons?[a]			
7a	Does the study state how the sample size was determined?			
7b	When applicable, was there an explanation of any interim analyses and stopping guidelines?[a]			
8a	Does the paper describe the method used to generate the random allocation sequence?			
8b	Does the paper describe the type of randomization including details of any restriction (such as blocking and block size)?			
9	Does the paper describe the mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned			
10	Does the paper include who generated the random allocation sequence, who lenrolled participants, and who assigned participants to interventions?			
11a	If applicable, does the paper describe who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how?			
11b	If relevant, does the paper provide a description of the similarity of interventions?			
12a	Does the paper describe the statistical methods used to compare groups for primary and secondary outcomes?			
12b	Does the paper describe methods for additional analyses, such as subgroup analyses and adjusted analyses?			
13a	Does the study include (for each group), the numbers of participants who were randomly assigned, received intended treatment, and were analyzed for the primary outcome?			
13b	Does the study outline (for each group) losses and exclusions after randomization, together with reasons?			
14a	Does the study provide dates defining the periods of recruitment and follow-up?[b]			
14b	Does the study describe why the trial ended or was stopped?			
15	Does the paper include a table showing baseline demographic and clinical characteristics for each group?			
16	Does the study state (for each group), the number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups?			
17a	Does the paper describe, for each primary and secondary outcome, the results for each group and the estimated effect size and its precision (such as 95% confidence interval)?			

		Levy (2004)[33]	Rathbun (2005)[32]	Krummenacher (2010)[28]
17b	If the paper includes binary outcomes, was there a presentation of both absolute and relative effect sizes?[a]			
18	Are the results of any other analyses performed included, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory?			
19	Are all important harms or unintended effects in each group described?[c]			
20	Does the paper discuss trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses?			
21	Does the paper discuss the generalizability (external validity, applicability) of the trial findings?			
22	Is the interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence?			
23	Does the paper include registration number and name of trial registry?			
24	Does the study list where the full trial protocol can be accessed, if available?			
25	Does the study list sources of funding and other support (such as supply of drugs) and the role of such funders?			

Legend: Grey = yes; White = no; Black = not applicable

[a]Though CONSORT states “not applicable” is “compliant”, was maintained as “not applicable” for this analysis.

[b]If the recruitment period could be calculated using information reported in the study about follow-up or vice versa, the study was marked “yes”.

[c]Harms were guided by definitions listed in CONSORT

Table 3

Additional assessment criteria for manuscripts evaluating the impact of HIV clinical pharmacists

	Walji (1992)	Geletko (1996)	Bozek (1998)	Garey (2000)	McPherson-Baker (2000)	Geletko (2002)	Segarra-Newnham (2002)	De Maat (2004)	Foisy (2004)	Castillo (2004)	Levy (2004)	Sterling (2005)	Rathbun (2005)	Heelon (2007)	March (2007)	Horberg (2007)	Horace (2010)	Krummenacher (2010)	Ma (2010)	Krummenacher (2011)	Henderson (2011)	Carcelero (2011)
Was a study design specified?																						
Does the specified study design agree with Cochrane's categorization?[a]																						
Was the role of the pharmacist well described?																						
Was there any description of pharmacist HIV training or HIV experience?																						
Was adherence included as an outcome?																						
If adherence was an outcome, was the calculation method well described?																						
If adherence was calculated, was the calculation method referenced in prior literature? [b]																						
Was adherence presented as a continuous variable in the study? [b]																						
Was HIV viral load included as an outcome measurement?																						
Was CD4+ cell count included as an outcome measurement?																						

Legend: Grey = yes, White = no, Black = not applicable

[a] As defined by Table 13.2.a and 13.2.b in the Cochrane Handbook for Systematic Reviews of Interventions. Available at http://www.cochrane-handbook.org/, last updated 3/2011.

[b] If adherence was not studied or calculated, category was not applicable