Committed to making the world's scientific and medical literature a public resource

PLoS PUBLIC LIBRARY of SCIENCE

www.plos.org

Editor's Perspective: Publishing Results of Your RCT

EQUATOR Network Seminar – Getting Your Trial Published

Emma Veitch
Senior Editor, *PLoS Medicine;* Consulting Editor, *PLoS ONE*

PLoS
PUBLIC LIBRARY
of SCIENCE

Why do journal editors care about good reporting – and what can we do about it?

www.plos.org

PLoS
PUBLIC LIBRARY
of SCIENCE

Harms caused by mis-representation of trial findings in published papers (aka, bad reporting)

- Rofecoxib – omission of cardiovascular harms data from key company trial report in *NEJM*
- Rosiglitazone – FDA reanalysis of harms data, outcomes misclassified in *Lancet* postmarketing paper
- Paroxetine – systematic under-reporting of harms outcomes (suicidality, withdrawal problems) in trials
- Gabapentin – use of clinical trials in off-label marketing

- …the list goes on, and on, and on…

FDA Warning

An example

- Tsai et al in *PLoS Medicine* – what's the evidence base for aripiprazole in maintenance treatment for bipolar disorder?
- Initially approved for treatment of schizophrenia, subsequently approved and increasingly prescribed for use in bipolar disorder
- Tsai et al found a single manufacturer-sponsored trial supporting use in bipolar maintenance
- Problems extracting sufficient data from the published report to understand whether claims for efficacy were supported
- Report four key problems with the trial design which limit relevance for clinical practice – only one acknowledged in the report

RESEARCH ARTICLE OPEN ACCESS

Featured in *PLoS Hub for Clinical Trials*

Aripiprazole in the Maintenance Treatment of Bipolar Disorder: A Critical Review of the Evidence and Its Dissemination into the Scientific Literature

Article | Metrics | Related Content | Comments: 2

Alexander C. Tsai[1#*], Nicholas Z. Rosenlicht[2#], Jon N. Jureidini[3], Peter I. Parry[4], Glen I. Spielmans[5], David Healy[6]

1 Robert Wood Johnson Health and Society Scholars Program, Harvard University, Cambridge, Massachusetts, United States of America, **2** Department of Psychiatry, University of California at San Francisco and San Francisco Veterans Affairs Medical Center, San Francisco, California, United States of America, **3** Discipline of Psychiatry, University of Adelaide, Adelaide, South Australia, Australia, **4** Child and Adolescent Mental Health Service, Division of Mental Health, Flinders University, Adelaide, South Australia, Australia, **5** Department of Psychology, Metropolitan State University, St. Paul, Minnesota, United States of America, **6** Department of Psychological Medicine, Cardiff University, Cardiff, Wales, United Kingdom

To **add a note**, highlight some text. Hide notes

Make a general comment

Jump to

Abstract
Editors' Summary
Introduction
Methods
Results

The Bigger Picture: What Reporting-Related Biases are Out There?

- Nonpublication of entire studies – some estimates gauge perhaps ~50% of trials aren't published in full

- Outcome level reporting bias – may include any / all of the below
- Selective reporting of analyses
- Selective reporting on specific endpoints
- Selective reporting on specific timepoints
- Selective reporting of harms data

- Narrative Spin

- Studies of these phenomena suggest these forms of reporting bias are incredibly common…
- *Dissemination and publication of research findings: an updated review of related biases. Song et al, Health Technol Assess. 2010 Feb;14, 1-193*

PLoS
PUBLIC LIBRARY
of SCIENCE

Are journals still relevant?

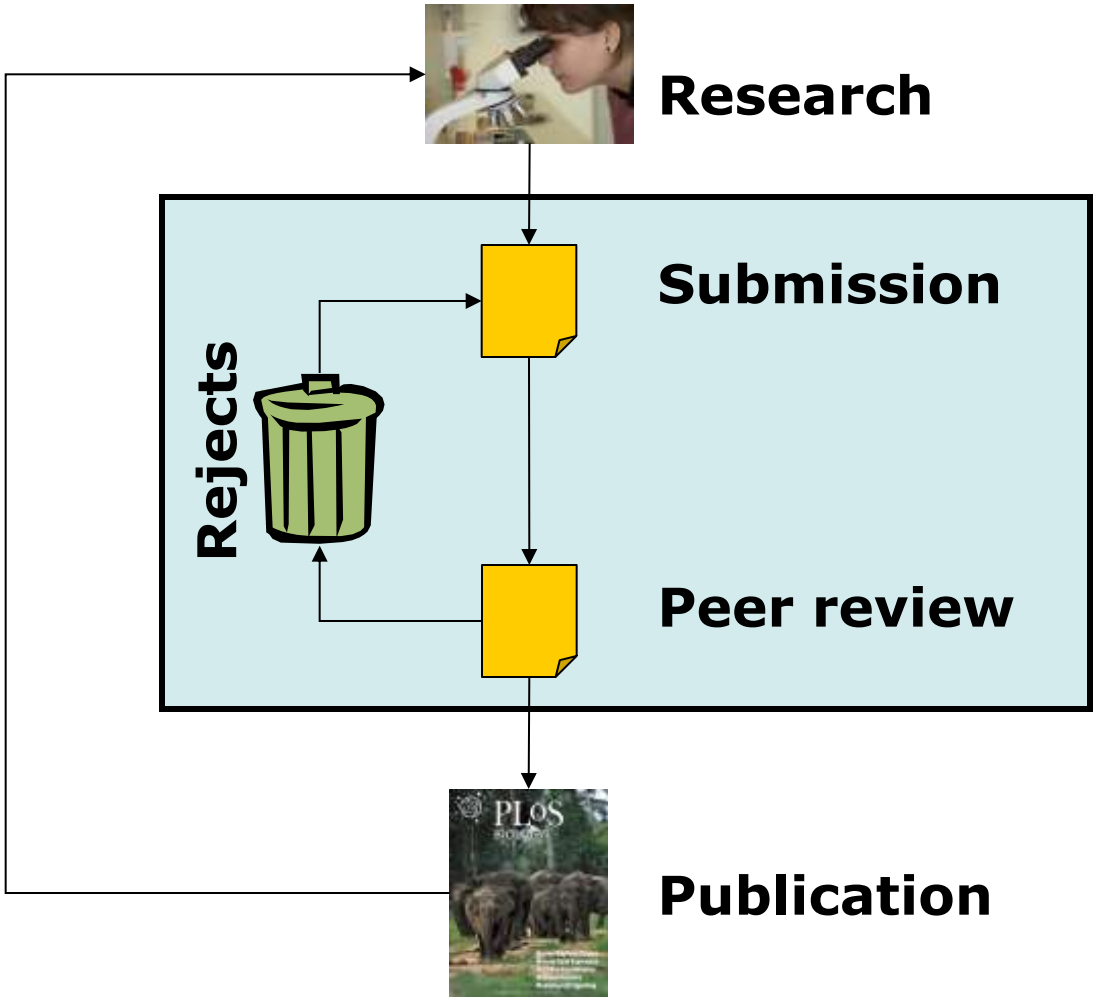
- Once, journals were (pretty much) the only mechanism for publishing results of trials and other studies
- Now - increasing focus on web registries – eg clinicaltrials.gov, company websites
- But journals still provide the main method of disseminating full details of trial design and results
- Investigators still want peer-reviewed journal publication as credit for what has been done
- Peer review and editorial process provides an important opportunity for achieving good quality reporting

What about journals' conflicts?

- Editors *can* act in ways which promote bias
- Want to publish new and "exciting" papers
- (Some) journals need to sell copies / reprints
- Most journals want to get (and maintain) a high impact factor so they can attract good papers
- "It is important for the industry to publish reports of large trials in prestigious journals, as such reports are essential for clinical decision making and for the sales of drugs and devices [2],[3]. However, journals not only stand to gain financially through the sales of reprints, but also publication of such trials may increase their impact factors, as a large number of reprints distributed to key clinicians by drug companies will likely increase citation rates."

- *Lundh et al (2010) Conflicts of Interest at Medical Journals: The Influence of Industry-Supported Randomised Trials on Journal Impact Factors and Revenue – Cohort Study. PLoS Med 7(10): e1000354.*

The life cycle of a research article



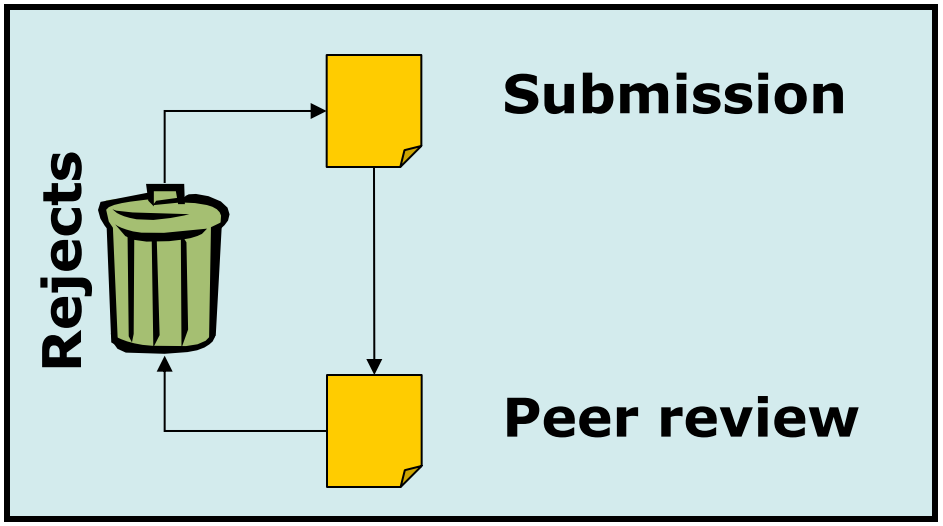
2-3 Experts

Is it rigorous?
Good enough?
Right audience?

Takes months/years

Journal name is key

What goes on in the black box called "peer review"?



At *PLoS Medicine*:

- Papers handled by in-house editor
- Additional advice from external academic editor (researcher / clinician)
- Around 90% papers rejected *before* peer review based on scope, quality, importance
- Typically 2-3 subject reviewers (eg in the clinical specialty)
- 1 statistical reviewer
- Around further 50% papers rejected *after* peer review

How *PLoS Medicine* uses CONSORT during the editorial process

- RCT submissions **must** include CONSORT flowchart and checklist to get through to editorial assessment
- These items also made available to academic editor, peer reviewers (including statistician)
- We encourage authors reporting non-randomized trials (eg single-arm) to use applicable parts of CONSORT guidance
- Editors and peer reviewers consider how well specific items in CONSORT have been reported
- Editors give further guidance / advice to authors on improving writeup if a revision is invited

PLoS journals – additional standards for trials reporting

- Trial registration: require prospective registration in WHO ICTRP approved registry
- Authors must also provide a copy of the original trial protocol
- Editors and peer reviewers check protocol and registry record for key items
- If there are differences between paper and protocol in outcomes reported, ask authors to add those data during a revision
- Encourage authors to be more upfront in describing changes from protocol in their paper

www.plos.org

What is outcome reporting bias ("ORB")?

- An area addressed by CONSORT that's receiving greater attention from journals and researchers
- ORB is a form of publication bias
- Occurs when statistically significant findings are more likely to be included in report
- Authors, reviewers and editors can all contribute to the problem (and help address it)
- Some journals – including PLoS journals – now ask for full protocols for submitted RCTs
- On PLoS Medicine – check outcomes reported in the paper against those in the protocol
- Frequently ask authors to add results for these outcomes to the paper and / or add explanations about outcome changes

- Dwan K, Altman DG, Arnaiz JA, Bloom J, Chan A-W, et al. (2008) Systematic Review of the Empirical Evidence of Study Publication Bias and Outcome Reporting Bias. PLoS ONE 3(8): e3081.

www.plos.org

Applying CONSORT guidance to real papers

- Many researchers think that once they have ticked the boxes in the checklist and filled out the numbers in the flowchart, salvation is theirs – they are "CONSORT compliant"

- I hope CONSORT group would agree: this is not true

- For reader (and those who want to use the findings) the devil is in the details!

In the real world – how should we decide which CONSORT to use?

- Lots of flavours of CONSORT…
- "Vanilla" (2-arm parallel design RCT)
- 8 extensions:
- Cluster RCT
- Non-inferiority / equivalence
- Pragmatic trials
- Herbal medicines
- Non-pharmacological
- Acupuncture
- Harms
- Abstracts

Using CONSORT and its extensions

- On *PLoS Medicine*, editors recommend taking a pragmatic view
- If multiple "flavours" of CONSORT apply to a study, we'd advocate trying to identify the one that is most relevant to your situation

Using CONSORT and its extensions

PLoS MEDICINE

a peer-reviewed open-access journal published by the Public Library of Science

Search art

Home Browse Articles About For Readers For Authors and Reviewers

RESEARCH ARTICLE OPEN ACCESS

Featured in *PLoS Hub for Clinical Trials*

Primary Prevention of Gestational Diabetes Mellitus and Large-for-Gestational-Age Newborns by Lifestyle Counseling: A Cluster-Randomized Controlled Trial

Article Metrics Related Content Comments: 0

Riitta Luoto[1,2*], Tarja I. Kinnunen[3], Minna Aittasalo[1], Päivi Kolu[1], Jani Raitanen[1,3], Katriina Ojala[1], Kirsi Mansikkamäki[1], Satu Lamberg[3], Tommi Vasankari[1,2], Tanja Komulainen[1], Sirkku Tulokas[4]

1 UKK Institute for Health Promotion Research, Tampere, Finland, 2 National Institute for Health and Welfare, Helsinki, Finland, 3 School of Health Sciences, University of Tampere, Finland, 4 Tampere University Central Hospital, Tampere, Finland

To **add a note**, highlight some text. Hide notes

Make a general comment

Jump to

Abstract

Editors' Summary

Introduction

Methods

Abstract Top

- Example – cluster trial with non-pharmacological intervention (and pragmatic aspects!)
- 4 CONSORT's apply
- Many of the complexities of this trial centre on the nature of the intervention and whether it can be replicated elsewhere
- So we advised the authors to use CONSORT for non-pharmacological extension as their main tool in reporting
- But also to make sure they considered CONSORT for cluster advice in the statistical components

www.plos.org

Using CONSORT and its extensions

PLoS MEDICINE

a peer-reviewed open-access journal published by the Public Library of Science

Search ar

Home Browse Articles About For Readers For Authors and Reviewers

RESEARCH ARTICLE OPEN ACCESS

Featured in *PLoS Hub for Clinical Trials*

A Multi-Country Non-Inferiority Cluster Randomized Trial of Frontloaded Smear Microscopy for the Diagnosis of Pulmonary Tuberculosis

Article Metrics Related Content Comments: 0

Luis Eduardo Cuevas[1,2*], Mohammed Ahmed Yassin[1], Najla Al-Sonboli[3], Lovett Lawson[4], Isabel Arbide[5], Nasher Al-Aghbari[6], Jeevan Bahadur Sherchand[7], Amin Al-Absi[6], Emmanuel Nnamdi Emenyonu[4], Yared Merid[8], Mosis Ifenyi Okobi[9], Juliana Olubunmi Onuoha[4], Melkamsew Aschalew[8], Abraham Aseffa[10], Greg Harper[1], Rachel Mary Anderson de Cuevas[1], Kristin Kremer[11], Dick van Soolingen[11], Carl-Michael Nathanson[2], Jean Joly[2], Brian Faragher[1], Stephen Bertel Squire[1], Andrew Ramsay[2]

To **add a note**, highlight some text. Hide notes

Make a general comment

Jump to

Abstract

Editors' Summary

Introduction

Methods

- Example – cluster trial of diagnostic regimens, non-inferiority framework, also fairly pragmatic!
- 3-4 CONSORT's apply, plus STARD (reporting guideline for diagnostics)
- We thought the diagnostics issues were really important here, so advised authors to use vanilla CONSORT, and also refer to STARD

www.plos.org

Using CONSORT in publication

- Optional template for authors, using CONSORT items as headings for structured writeup of the paper
- Available for authors on all PLoS journals but most heavily used on *PLoS Medicine, PLoS ONE*
- Sent to authors when a revision is invited
- Authors can use components that work for them – in addition to the CONSORT checklist and flowchart
- Works best for primary papers (ie reporting main results of RCT); less so for exploratory / ancillary papers
- For published papers, CONSORT flowchart, checklist and protocol all included alongside as figures / supporting information

www.plos.org

OPEN ACCESS Freely available online

PLoS one

Effect of Peer Health Workers on AIDS Care in Rakai, Uganda: A Cluster-Randomized Trial

Larry W. Chang[1]*, Joseph Kagaayi[2], Gertrude Nakigozi[2], Victor Ssempijja[2], Arnold H. Packer[3], David Serwadda[2], Thomas C. Quinn[1,4], Ronald H. Gray[5], Robert C. Bollinger[1], Steven J. Reynolds[1,4]

1 Division of Infectious Diseases, Johns Hopkins School of Medicine, Baltimore, Maryland, United States of America, 2 Rakai Health Sciences Program, Kalisizo, Uganda, 3 Johns Hopkins University, Baltimore, Maryland, United States of America, 4 Laboratory of Immunoregulation, Division of Intramural Research, National Institute for Allergy and Infectious Diseases, National Institutes of Health, Bethesda, Maryland, United States of America, 5 Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland, United States of America

Abstract

Background: Human resource limitations are a challenge to the delivery of antiretroviral therapy (ART) in low-resource settings. We conducted a cluster randomized trial to assess the effect of community-based peer health workers (PHW) on AIDS care of adults in Rakai, Uganda.

Methodology/Principal Findings: 15 AIDS clinics were randomized 2:1 to receive the PHW intervention (n = 10) or control (n = 5). PHW tasks included clinic and home-based provision of counseling, clinical, adherence to ART, and social support. Primary outcomes were adherence and cumulative risk of virologic failure (>400 copies/mL). Secondary outcomes were virologic failure at each 24 week time point up to 192 weeks of ART. Analysis was by intention to treat. From May 2006 to July 2008, 1336 patients were followed. 444 (33%) of these patients were already on ART at the start of the study. No significant differences were found in lack of adherence (<95% pill count adherence risk ratio [RR] 0.55, 95% confidence interval [CI] 0.23–1.36; <100% adherence RR 1.10, 95% CI 0.94–1.30), cumulative risk of virologic failure (RR 0.81, 95% CI 0.61–1.08) or in shorter-term virologic outcomes (24 week virologic failure RR 0.93, 95% CI 0.65–1.32; 48 week, RR 0.83, 95% CI 0.47–1.48; 72 week, RR 0.81, 95% CI 0.44–1.49). However, virologic failure rates ≥96 weeks into ART were significantly decreased in the intervention arm compared to the control arm (96 week failure RR 0.50, 95% CI 0.31–0.81; 120 week, RR 0.59, 95% CI 0.22–1.60; 144 week, RR 0.39, 95% CI 0.16–0.95; 168 week, RR 0.30, 95% CI 0.097–0.92; 192 week, RR 0.067, 95% CI 0.0065–0.71).

Conclusions/Significance: A PHW intervention was associated with decreased virologic failure rates occurring 96 weeks and longer into ART, but did not affect cumulative risk of virologic failure, adherence measures, or shorter-term virologic outcomes. PHWs may be an effective intervention to sustain long-term ART in low-resource settings.

Trial Registration: ClinicalTrials.gov NCT00675389

Citation: Chang LW, Kagaayi J, Nakigozi G, Ssempijja V, Packer AH, et al. (2010) Effect of Peer Health Workers on AIDS Care in Rakai, Uganda: A Cluster-Randomized Trial. PLoS ONE 5(6): e10928. doi:10.1371/journal.pone.0010928

Editor: Patricia Kissinger, Tulane University, United States of America

Received December 30, 2009; **Accepted** May 12, 2010; **Published** June 2, 2010

Funding: This study was funded by the Doris Duke Charitable Foundation, The Division of Intramural Research, The National Institute for Allergy and Infectious Diseases, National Institutes of Health, and a National Institutes of Health Training Grant (2 T32-AI07291) and Career Development Grant (1 K23-MH086338). The funders had no role in the study design, data collection and analysis, decision to publish, or preparation of this manuscript.

Competing Interests: The authors have declared that no competing interests exist.

* E-mail: lchang88@jhmi.edu

Introduction

The provision of antiretroviral therapy (ART) in low-resource settings entails substantial challenges due to human resource limitations [1]. One of the main strategies advocated by the World Health Organization (WHO) and the United States President's Emergency Plan for AIDS Relief (PEPFAR) to address this crisis is through task shifting, the rational redistribution of tasks among health workforce teams from higher trained providers to those who require less training [2]. Community health workers (CHWs) are a key cadre to whom tasks can be shifted; however, there is limited trial-based evidence on their effectiveness in improving AIDS care outcomes [2,3].

Community-based peer health workers (PHWs) are people living with HIV (PLHIV) and may potentially be a valuable type of CHW. Peers have been used effectively in HIV/AIDS programs in low-resource settings, typically as peer educators [4], and psychosocial support using peers has been recommended by the WHO for all PLHIV [5]. However, PHWs could deliver more care-oriented services in addition to counseling, education, and social support, and may therefore provide one strategy to mitigate the human resource crisis.

The Rakai Health Sciences Program (RHSP) is located in the rural Rakai District in southwest Uganda. Since June 2004, PEPFAR has enabled RHSP to provide ART via a decentralized, mobile clinic approach. In an operational and implementation research effort to evaluate the role of task shifting with PHWs at RHSP [6,7], we conducted a cluster-randomised trial of the effect of PHWs on adult AIDS care outcomes [8]. Descriptive pilot data were previously presented [9], and this study reports trial

Where are CONSORT items reported?

- Trial registration (item 23)
- Funding (item 25)

www.plos.org

PLoS

PUBLIC LIBRARY of SCIENCE

outcomes. Our primary hypothesis was that, compared to patients in control communities, patients on ART in communities with PHWs will have improved adherence and fewer virologic failures.

Methods

The protocol for this trial and supporting CONSORT checklist are available as supporting information; see Protocol S1 and Checklist S1.

Ethics Statement

The trial was approved by institutional review boards at the Uganda Virus Research Institute, the Uganda National Council for Science and Technology, Johns Hopkins University, and the Western Institutional Review Board (Olympia, WA). Informed consent was not obtained for this study as the institutional review boards agreed that (i) PHWs were program staff performing routine care functions, and (ii) only de-identified programmatic data would be analyzed by community of randomization, and therefore informed consent was not required.

Study Setting

The Rakai district in southwestern Uganda has a population of approximately 460,000 persons in an area of about 5000 square kilometers. In June 2004, RHSP/PEPFAR began providing ART through a mobile clinic program operating in 15 non-overlapping catchment areas (clusters) throughout the district. The mobile clinic model consisted of medical staff traveling from a central facility to designated government health clinics in each catchment area biweekly. In between clinic days (13 out of 14 days), patients' options for accessing care were limited and included traveling to a central facility, calling an RHSP mobile phone hotline (with call cost paid by caller) or toll-free warmline (similar to a hotline but staffed only during clinic hours), or visiting non-RHSP care facilities and providers [10].

Participants

This trial was conducted between May 2006 to July 2008 and comprised adult patients at the 15 mobile clinic sites who were either already on ART at the start of the trial or were started on ART at any time during the trial. About half (53%) of these patients were referred to the clinic from previous or current RHSP studies. All of these studies have recruited participants representative of Rakai District as a whole [11]. The remaining participants (47%) were "walk-ins" as any Rakai resident could come to these clinics and receive HIV counseling, testing, and care. Eligibility criteria for starting ART was a CD4 count ≤250 or WHO Stage IV illness [12]. All care and medications were provided free of charge.

PHW Intervention (Arm A)

In addition to the usual standard of care at all clinic sites, Arm A clinics received the PHW intervention. The general approach to the design and implementation of this intervention was pragmatically-oriented, meaning that a general framework for PHW recruitment, training, tasks, and monitoring was developed, but the intervention was allowed to adapt to needs and problems which arose, e.g. arranging for a home visit to occur at a workplace if so requested by a patient [8]. Criteria for becoming a PHW included being a PLHIV on ART, good ART adherence for at least six months, and literacy. PHWs were nominated by fellow patients at each clinic site with final approval by RHSP staff if they met all qualifications. PHWs received a two day residential training on basic HIV pathogenesis, prevention, treatment, adherence counseling, performing pill counts, protecting patient confidentiality, and filling out a home visit form. Trainers included RHSP staff and experienced PHWs from an urban-based Ugandan ART program [13]. At the clinic, PHW tasks included providing ART counseling and support in group and individual sessions. For their home visit tasks, PHWs were initially assigned about 15 patients each who were visited biweekly. At these visits, PHWs were tasked to record on a standardized form a review of symptoms, a patient self-report of adherence, and to perform and record a pill count. PHWs were asked to counsel and educate their patients on ART adherence and general HIV/AIDS-related issues during these home visits. If patients were thought to need urgent care, PHWs were asked to alert RHSP staff and facilitate transfer to a higher level of care. PHWs submitted completed forms to subsequent clinic sessions where they were added to patient charts for provider review. To assist with their duties and encourage retention, PHWs were each given a bicycle, identifying t-shirts, basic supplies, and an initial monthly allowance of about 12.5 USD. Day-to-day supervision of PHW activities was largely performed by a single RHSP staff member working part-time.

Control Group (Arm B)

The control arm continued with the usual standard of care. However, standard of care did change over the study period, as a number of changes unrelated to the PHWs were subsequently implemented by RHSP in both the PHW and control arms. These programmatic changes included a peer educator program to promote use of preventive care services in mid-2006, the use of viral load results to guide care in late 2006, more focused ART-related health messaging in early 2007, and the use of enhanced adherence counseling, chart stickers to help identify patients failing virologically, and second-line ART provider talks in mid- to late 2007.

Mobile Phone Support Intervention Substudy (Arm A^1 and A^2)

As a substudy, PHW intervention areas were also randomized 2:1 to receive a mobile phone support intervention (Arm A^1, n = 4 clusters) or not (Arm A^2, n = 6 clusters). PHWs randomized to the mobile phone intervention were each given a mobile phone and, in addition to their usual responsibilities, were tasked to use text messaging to send home visit data back to the central clinic to be reviewed by centralized staff. PHWs could also call providers with questions or concerns [10]. Detailed results from this substudy will be presented elsewhere.

Procedures

We used an unrestricted randomization process. The 15 mobile clinic sites were randomized 2:1 to receive the PHW intervention (Arms A, n = 10 clusters) or control (Arm B, n = 5 clusters). We assigned clusters using unmatched, unrestricted random allocation by a drawing of lots. Study investigators (LWC, JK) generated the allocation sequence and implemented the randomization. This study was open label and unblinded.

Outcomes

The primary outcomes included adherence (pill counts) and cumulative risk of virologic failure (any failure during follow-up period equaling failure). Secondary outcomes were virologic failure at each 24 week time point up to 192 weeks of antiretroviral therapy, mortality, lost to follow-up, and CD4 change at 24 and 48 weeks of ART. A summary clinic pill count was calculated by dividing the number of pills taken over the study period by the sum

Where are CONSORT items reported?

Study setting (item 4b)

Participants (item 4a)

Interventions (item 5)

Outcomes (item 6a)

Journal experiences of CONSORT

- *PLoS Medicine* is a CONSORT endorser (and we try hard to be an implementer!)
- But making sure that every paper we publish fully adheres to CONSORT is another matter
- Despite the simplicity and usability of CONSORT, substantial work – from authors, peer reviewers and editors - is often needed to promote full adherence to CONSORT during the peer review and revision process
- CONSORT instruments (checklist, flowchart) now well accepted and used by authors
- Some reluctance to report that "not all went as planned" eg conduct, outcome changes during the trial
- We want to encourage researchers that this is OK, and we won't reject a paper just because it didn't all go to plan

Using CONSORT: what are the advantages and opportunities?

For authors:

- Adhering to CONSORT upfront means your paper will go straight through to the editor's desk
- (Anecdotally) - clearly reported papers go through peer review faster and with fewer revisions. Quicker, easier trip through copyediting
- We can't guarantee the decision will be different (as this may well hinge on the importance of the question and quality of the study)

For editors / guideline developers:

- How do we encourage better reporting of exploratory or ancillary sub-studies?
- How do we encourage better reporting for non-randomized trials?

How are things changing? Beyond published papers

BMJ 2011;342:c7258 doi:10.1136/bmj.c7258 (Published 11 January 2011)
Cite this as: BMJ 2011;342:c7258

Analysis

Ensuring safe and effective drugs: who can do what it takes?

Tom Jefferson, researcher[1], **Peter Doshi**, doctoral student[2], **Matthew Thompson**, senior clinical scientist[34], **Carl Heneghan**, clinical reader and director CEBM[3], **Cochrane Acute Respiratory Infections Group**

+ Author Affiliations

Correspondence to: P Doshi pnd@mit.edu

Accepted 7 November 2010

*Drawing on their experience in producing a Cochrane review of neuraminidase inhibitors for influenza, **Tom Jefferson and colleagues** discuss how to improve the reliability of systematic reviews*

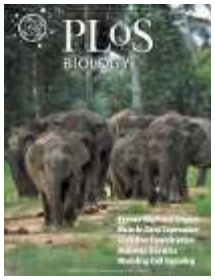
In the midst of the H1N1 flu "pandemic," the Australian and UK governments commissioned an update of our longstanding Cochrane review on neuraminidase inhibitors for influenza in (otherwise) healthy adults. The review had first been published in 1999 with updates in 2006 and 2008. While preparing the 2009 update, we received a comment from a Japanese paediatrician. He questioned our conclusion that oseltamivir (Tamiflu) reduces the risk of complications (such as pneumonia) and pointed out that the evidence underlying this conclusion in our 2006 review was based on a single paper—a manufacturer funded meta-analysis [1] of 10 manufacturer trials, of which only two had been published in the peer reviewed literature. [2 3] To verify the quality and reliability of our previous conclusions, we wrote to the lead author of the

- *Jefferson et al:*
- *To get a full picture of all the evidence on a particular drug, we need access to:*
- *Full clinical study reports*
- *Regulatory documents*
- *Full datasets for individual trials*
- *Original protocols*
- *Emphasis on understanding entire trial programme, not just individual trials*

"We do not yet know whether sound scrutiny is feasible with a journal's resources…" **www.plos.org**

PLoS
PUBLIC LIBRARY
of SCIENCE

PLoS Biology
October, 2003



PLoS Medicine
October, 2004

PLoS Community Journals

June-September, 2005

October, 2007

PLoS ONE
December, 2006

www.plos.org