Starter Packs Versus Full Prescription of Antiretroviral Drugs for Postexposure Prophylaxis: A Systematic Review

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Background. The provision of starter packs for human immunodeficiency virus postexposure prophylaxis (PEP) is practiced in many settings to facilitate rapid initiation by nonexperts and encourage adherence. However, the impact of starter packs on PEP completion rates has not been systematically assessed. We systematically reviewed the evidence on outcomes associated with starter packs for PEP compared to full prescriptions.

Methods. Four databases and 2 conference abstract sites were searched up to December 2013; this search was updated in 1 database in June 2014. PEP completion rates, stratified by prescribing practice, were pooled using random-effects meta-analysis.

Results. Fifty-four studies provided data on 11 714 PEP initiations. Thirty-seven studies, including 3 randomized controlled trials (RCTs) and 34 observational cohorts, provided information on starter packs (although none of the RCTs specifically assessed starter packs), and 17 studies, including 2 RCTs and 15 observational cohorts, provided information on full prescriptions. Overall, outcomes were better when participants were offered a full 28-day course of PEP at initial presentation to healthcare, with fewer refusals (11.4% [95% confidence interval {CI}, 5.3%–17.5%] vs 22% [95% CI, 16.7%–28.1%]) and higher completion rates (70% [95% CI, 56.7%–77.3%] vs 53.2% [95% CI, 44.4%–62.2%]). More than a quarter (28% [95% CI, 21.4%–34.5%]) of individuals provided with a PEP starter pack failed to return for their subsequent appointment and therefore defaulted prior to receiving a full course of PEP. The quality of the evidence overall was rated as very low.

Conclusions. The findings of this review suggest that starter packs do not improve adherence to PEP and may result in lower adherence and completion rates.

Keywords. adherence; completion; postexposure prophylaxis; starter packs; full prescriptions.

Postexposure prophylaxis (PEP) with antiretroviral drugs is a well-established and widely used intervention to prevent human immunodeficiency virus (HIV) infection. While the recommended duration of PEP (28 days) is generally consistent across guidelines, prescribing practices vary. In some settings the full 28-day course is provided at first visit, whereas in other settings an initial course of 3–5 days of antiretroviral drugs (commonly referred to as starter packs) is provided, with individuals required to return during 1 or more interim visits to collect the rest of their PEP course.

Reported reasons for using starter packs include facilitating rapid initiation of PEP by nonexperts [1], encouraging adherence [2], assessing toxicity and providing additional counseling [3], and pacifying anxious individuals with a view to discontinuing at next visit [4]. PEP starter packs may also be provided to high-risk individuals to take in case of subsequent exposure [5]. However, the impact of PEP starter packs on completion rates has not been systematically assessed.

To inform future World Health Organization (WHO) guidance on the provision of PEP, we systematically reviewed the evidence on outcomes associated with different PEP prescribing practices.

METHODS

Using a predefined protocol including a sensitive search strategy, 2 investigators (N. F., C. I.), working independently, scanned all abstracts, assessed potentially eligible studies as full text, and extracted outcomes in duplicate; in case of disagreement, a third investigator (Z. S.) was consulted. Medline via PubMed, Embase, the Cochrane Database of Systematic Reviews, and Lilacs was searched from inception to 1 December 2013; this search was updated in PubMed to 1 June 2014. Conference abstracts of all Conferences of the International AIDS Society were searched from 2010 to 2013, and the Conference on Retroviruses and Opportunistic Infections for 2014 (past conference sites being unavailable online) to identify recent studies that may not yet have been published as full text. Randomized trials and prospective observational cohort studies were eligible for inclusion if they reported outcomes on >10 individuals offered PEP irrespective of exposure type, and provide clear information about duration of PEP provided at baseline. No language or geographic exclusions were applied. The following key study characteristics were compared using χ^2 test and in the case of small numbers the Fisher exact test: exposure type, study population, number of drugs provided (2 vs 3), and whether the regimen included zidovudine or tenofovir. Point estimates and 95% confidence intervals (CIs) were calculated for the proportion of individuals reaching each step in the cascade of care, from eligibility determination to attendance of follow-up visit, and data were pooled using random-effects meta-analysis, following appropriate data transformation. The quality of the evidence was assessed using GRADE [6]. All analyses were conducted using Stata version 12.0 (StataCorp, College Station, Texas).

RESULTS

Study Characteristics

From an initial screen of 3259 titles (Supplementary Appendix), 54 studies were taken through for review: 37 studies (5997 PEP initiations) across 17 countries reported outcome data for individuals provided with a PEP starter pack at first visit [2, 4, 5, 7–40], and 17 studies (5717 initiations) across 9 countries reported outcome data for individuals provided with a full PEP course [41–57]. Studies reporting on starter packs included 3 randomized controlled trials (RCTs) and 34 observational cohorts, whereas studies on full prescriptions included 2 RCTs and 15 observational cohorts. None of the RCTs were designed to specifically assess the impact of starter packs (3 assessed adherence support interventions [7, 28, 43] and 2 assessed drug safety [38, 57]). Only 1 cohort study that reported PEP outcomes following sexual assault in South Africa provided a direct comparison of completion rates before and after a policy change from starter

Table 1. Pooled Proportion of Postexposure Prophylaxis Outcomes by Prescribing Practice

Outcomes	Partial Course	Full Course
Refused PEP	22.4% (16.7%–28.1%)	11.4% (5.3%–17.5%)
Stopped: exposed HIV positive	0.3% (.1%–.6%)	0.6% (.1%–1.1%)
Stopped: source HIV negative	8.2% (6.3%–10.1%)	11.2% (5.3%–17.0%)
Stopped because of adverse drug reaction	6.8% (5.1%–8.4%)	4.2% (1.6%–6.8%)
Defaulted on incomplete course	28.0% (21.4%–34.5%)	0[a]
Completed PEP	53.2% (44.4%–62.2%)	70% (56.7%–77.3%)

Data are presented as proportions (95% confidence intervals).

Abbreviations: HIV, human immunodeficiency virus; PEP, postexposure prophylaxis.

[a] All patients received the 28-day course at baseline.

packs to the full 28-day PEP [58]. The provision of a full course of PEP at initial visit was more common for occupational exposures (35.1% vs 17.7%), but differences were not significant (P = .2). There were no apparent differences in study characteristics with respect to other exposures, population, or number or type of drugs used.

The overall quality of the evidence contributing to the systematic review was rated as very low. Most data were contributed by small observational studies, leading to imprecision in the pooled estimates for all outcomes, and no direct contemporaneous comparisons were available for analysis.

Review Findings

Where starter packs were given, the duration of the first course varied from 1 day to 14 days, with the most common course being a 3-day (47% of studies) or 5-day course (17%). Details of included studies are provided in the Supplementary Appendix.

Overall, outcomes were better when participants were offered a full 28-day course of PEP, with fewer refusals (11.4% [95% CI, 5.3%–17.5%] vs 22% [95% CI, 16.7%–28.1%]) and higher completion rates (70% [95% CI, 56.7%–77.3%] vs 53.2% [95% CI, 44.4%–62.2%]) vs starter packs. More than a quarter (28% [95% CI, 21.4%–34.5%]) of individuals provided with a PEP starter pack failed to return for their subsequent appointment and therefore defaulted prior to receiving a full course of PEP. A similar proportion of people had PEP discontinued either because of adverse drug reactions or because it was considered unnecessary (Table 1). In the one study that assessed PEP completion rates before and after a policy change from starter packs to full prescriptions, patients given a full course of drugs on first visit were significantly more likely than those

given a starter pack with follow-up appointments to have taken PEP for 28 days (71% vs 29%, respectively) [58].

DISCUSSION

This review assessed outcomes for starter packs compared with full prescriptions of PEP across 54 studies, including 5 RCTs and 1 pre–post study, and found that starter packs did not improve adherence to PEP, and may result in lower adherence and completion rates.

Starter packs may have a role in specific clinical settings, such as emergency departments, that are not adequately prepared to support patients in need of PEP and instead provide starter packs as part of the referral process. However, a recent study from the United States that reported low rates of PEP completion following referral from emergency departments suggested that patients presenting to emergency departments should be provided with extended or full courses of PEP to provide patients an opportunity to take PEP even if they do not adhere to scheduled clinic follow-up [9]. In South Africa, long distances and travel costs have been suggested as a reason why women are unable to return to care to receive a full course of PEP following sexual assault [13], and preference has been expressed to receive a full course of treatment at first visit [59].

Strengths of this review include a broad search strategy that allowed for the analysis of >11 000 PEP initiations across a range of settings and exposures. The main limitation of this review is the lack of high-quality studies directly comparing different prescribing practices, and there may be important differences in patient and program characteristics between studies that provided starter packs and those that provided full prescriptions. We were only able to identify 1 study that compared the 2 approaches within the same cohort; this was a before–after study in which multiple programmatic changes were made during the reporting period. This reflects a general lack of high-quality evidence to support policy for PEP [60]. High-quality studies that directly compare starter packs and full prescriptions are needed.

The latest WHO guidelines for antiretroviral therapy recommend that nonphysician health workers can initiate antiretroviral therapy, and this recommendation can be extended to PEP. The use of less-toxic drugs and a simplified approach to risk stratification will facilitate PEP provision such that the use of starter packs to support PEP provision by nonspecialists may no longer be relevant. The findings of this review suggest that while starter packs may be a useful strategy in specific settings, there is no evidence to suggest they result in improved outcomes. Although referrals for counseling and advice may still be needed, PEP providers should consider providing a full 28-day course of drugs at the outset. These findings support the recommendation by WHO to provide a full 28-day course of PEP at initial presentation [61].

Supplementary Data

Supplementary materials are available at *Clinical Infectious Diseases* online (http://cid.oxfordjournals.org). Supplementary materials consist of data provided by the author that are published to benefit the reader. The posted materials are not copyedited. The contents of all supplementary data are the sole responsibility of the authors. Questions or messages regarding errors should be addressed to the author.

Notes

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