# Health benefits, costs, and cost-effectiveness of earlier eligibility for adult antiretroviral therapy and expanded treatment coverage: a combined analysis of 12 mathematical models

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## Summary

**Background** New WHO guidelines recommend initiation of antiretroviral therapy for HIV-positive adults with CD4 counts of 500 cells per μL or less, a higher threshold than was previously recommended. Country decision makers have to decide whether to further expand eligibility for antiretroviral therapy accordingly. We aimed to assess the potential health benefits, costs, and cost-effectiveness of various eligibility criteria for adult antiretroviral therapy and expanded treatment coverage.

**Methods** We used several independent mathematical models in four settings—South Africa (generalised epidemic, moderate antiretroviral therapy coverage), Zambia (generalised epidemic, high antiretroviral therapy coverage), India (concentrated epidemic, moderate antiretroviral therapy coverage), and Vietnam (concentrated epidemic, low antiretroviral therapy coverage)—to assess the potential health benefits, costs, and cost-effectiveness of various eligibility criteria for adult antiretroviral therapy under scenarios of existing and expanded treatment coverage, with results projected over 20 years. Analyses assessed the extension of eligibility to include individuals with CD4 counts of 500 cells per μL or less, or all HIV-positive adults, compared with the previous (2010) recommendation of initiation with CD4 counts of 350 cells per μL or less. We assessed costs from a health-system perspective, and calculated the incremental cost (in US$) per disability-adjusted life-year (DALY) averted to compare competing strategies. Strategies were regarded very cost effective if the cost per DALY averted was less than the country's 2012 per-head gross domestic product (GDP; South Africa: $8040; Zambia: $1425; India: $1489; Vietnam: $1407) and cost effective if the cost per DALY averted was less than three times the per-head GDP.

**Findings** In South Africa, the cost per DALY averted of extending eligibility for antiretroviral therapy to adult patients with CD4 counts of 500 cells per μL or less ranged from $237 to $1691 per DALY averted compared with 2010 guidelines. In Zambia, expansion of eligibility to adults with a CD4 count threshold of 500 cells per μL ranged from improving health outcomes while reducing costs (ie, dominating the previous guidelines) to $749 per DALY averted. In both countries results were similar for expansion of eligibility to all HIV-positive adults, and when substantially expanded treatment coverage was assumed. Expansion of treatment coverage in the general population was also cost effective. In India, the cost for extending eligibility to all HIV-positive adults ranged from $131 to $241 per DALY averted, and in Vietnam extending eligibility to patients with CD4 counts of 500 cells per μL or less cost $290 per DALY averted. In concentrated epidemics, expanded access for key populations was also cost effective.

**Interpretation** Our estimates suggest that earlier eligibility for antiretroviral therapy is very cost effective in low-income and middle-income settings, although these estimates should be revisited when more data become available. Scaling up antiretroviral therapy through earlier eligibility and expanded coverage should be considered alongside other high-priority health interventions competing for health budgets.

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## Introduction

In July, 2013, WHO issued consolidated guidelines for the use of antiretroviral drugs for the treatment and prevention of HIV infection.[1] These guidelines recommended antiretroviral therapy for all HIV-positive adults whose CD4 count has fallen to 500 cells per μL or less, with treatment to be given irrespective of CD4 cell count for pregnant women, HIV-serodiscordant couples,

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and individuals with active tuberculosis or hepatitis-B-associated severe chronic liver disease. The decision to increase the threshold CD4 count from the 350 cells per µL recommended in 2010 was reached through a structured GRADE (Grading of Recommendations Assessment, Development and Evaluation) review process that assessed evidence for the clinical and epidemiological benefits of earlier HIV initiation.[2]

Evidence that antiretroviral therapy reduces HIV infectiousness[3,4] suggests that increasing the number of HIV-positive adults who are on treatment could have the potential to change the course of the epidemic in highly affected regions.[5,6] However, the resources necessary to implement these changes could be substantial.[1] The recommendation for earlier initiation of antiretroviral therapy comes at a time when progress towards implementation of antiretroviral therapy is varied: at the end of 2012 only an estimated 61% of HIV-positive individuals with CD4 counts of 350 cells per µL or less in low-income and middle-income countries were receiving treatment.[7] Even in settings where high coverage has been achieved, many patients start treatment late because of late HIV diagnosis and poor linkage to and retention in pre-antiretroviral care.[8–10]

In this context, decision makers have to consider whether resources should be devoted to implementing earlier eligibility, achieving high coverage and timely initiation of antiretroviral therapy for individuals with the greatest clinical need, or expanding other health programmes that might generate greater health gains. This decision should be based on assessment of the population-level benefits and costs of strategies to expand eligibility for antiretroviral therapy or increase coverage, accounting for the additional resources that would be needed. Whereas clinical trials can be used to assess the effect of expanded eligibility criteria for individuals, mathematical models can be used to project the long-term effects of policy decisions.[11] In the past decade, mathematical models have been useful for understanding the potential epidemiological effects, public health benefits, and costs of antiretroviral therapy in many populations.[5,11–14]

To better inform policy for antiretroviral therapy, we assembled 12 independently developed HIV epidemic models to generate estimates for the health benefits, costs, and cost-effectiveness of earlier eligibility for antiretroviral therapy using the most recent available evidence. We also assessed the cost-effectiveness of increasing HIV testing and linkage to care to improve coverage of antiretroviral therapy. The use of several models allows for the identification of conclusions that can be robustly reproduced across models, which is crucial in view of the wide range of results seen in previous analyses.[6] Because optimum strategies might be expected to differ in settings with different epidemic types, existing coverage of antiretroviral therapy, and income, we selected four countries with existing models of the effect of antiretroviral therapy as case studies in an effort to produce guidance applicable to a broad set of epidemic settings: South Africa (generalised epidemic, moderate antiretroviral therapy coverage), Zambia (generalised epidemic, high antiretroviral therapy coverage), India (concentrated epidemic, moderate antiretroviral therapy coverage), and Vietnam (concentrated epidemic, low antiretroviral therapy coverage).

## Methods

### Overview

We assessed the potential effect of changes to adult eligibility guidelines for antiretroviral therapy and improvements in HIV testing and linkage to care in four low-income and middle-income countries. We calibrated existing, independently developed mathematical models to epidemic settings in South Africa (seven models), Zambia (four models), India (three models), and Vietnam (one model). All models were dynamic HIV transmission models that simulate HIV transmission in populations and HIV disease progression, and incorporate both the therapeutic benefits of antiretroviral therapy for reducing HIV morbidity and mortality and the preventive benefits associated with reduced HIV infectiousness (table 1).

We used model outputs that describe changes in the use of health care to estimate changes in costs borne by the HIV programme and the broader health system. We estimated the effects of intervention strategies on HIV incidence, antiretroviral therapy costs and non-antiretroviral therapy health-care costs, and disability-adjusted life-years (DALYs) averted by comparing model projections of different antiretroviral therapy eligibility and access strategies over 20 years. We calculated incremental cost-effectiveness ratios (ICERs; reported as cost per DALY averted) to compare alternative strategies.

### Epidemiological modelling

The models represented three eligibility criteria by which antiretroviral therapy could be started for adult patients in care: HIV-positive adults with a CD4 count of 350 cells per µL or less (assumed to be the existing, baseline strategy); HIV-positive adults with a CD4 count of 500 cells per µL or less; and all HIV-positive adults. Each model simulated a baseline projection representing existing treatment coverage (ie, patterns of HIV testing, linkage to and retention in pre-antiretroviral care, and uptake of antiretroviral therapy), which we refer to as the status-quo access to HIV care.

All three eligibility criteria were simulated with the assumption of a continuation of status-quo access to HIV care—ie, patients started on antiretroviral therapy are those already being linked to HIV care programmes in accordance with existing patterns of access. Models also simulated each eligibility strategy with the assumption of substantial increases in routine HIV testing and linkage to care across the adult population, such that 80% of adults infected with HIV would be in care when they