Introduction

• The changing epidemiology of opportunistic infections (OIs) since the introduction of antiretroviral therapy (ART) has been well described in developed countries, where a greater than 50% reduction in AIDS-defining events has been reported.

• In low and middle income countries (LMIC), despite the global roll-out of ART since the mid-2000s with more than 8 million patients on ART, OIs continue to be the major driver of HIV-associated morbidity and mortality, accounting for most of the estimated 1.7 million deaths globally in 2011.

• We conducted a systematic review and meta-analysis to evaluate the impact of ART on the incidence of 15 key OIs in adults in low and middle-income countries (LMIC).

Materials and methods

• Eligible studies described the incidence of OIs and proportion on ART in Africa, Asia and Latin America from 1990 to January 2011, and were identified using PubMed and Global Health databases and conference abstracts.

• ART status was categorised as naïve (NA), early ART (eART) (<12 months), late ART (lART) (>12 months), and unspecified time on ART (uART). Studies where the proportion on ART was ≥10% or <80%, or which did not provide data on ART use were excluded. For studies that presented data from multiple time points, the earliest estimate within each category was used.

• Incident risk (IR) was calculated using random effects meta-analyses for OIs with reports from 10 or more studies, and estimates from ART subgroups compared using meta-regression to calculate an adjusted odds ratio (aOR).

• The number of OI cases averted annually was estimated using AIM modelling for those OIs with a significant impact of ART and where the cost per case was known, applying IRs from NA and eART to the estimated HIV population by region with CD4 counts<200.

Results

• We identified 4025 titles and abstracts, and 77 reports giving results from 57 cohorts or trials and comprising 157 684 people were included (fig. 1).

• Study size ranged from 54 to 61 105 participants (median 602, IQR: 215-1191). A CD4 count less than 200 cells/mm3, or a WHO stage III or IV were the main criteria for ART initiation in most studies.

• Incidence summary risks for fifteen OIs are shown in table 1.

• Most of the impact is seen in the first year of treatment.

• The most cases of OIs averted were oral candidiasis, herpes zoster, and pulmonary tuberculosis.

• The majority of the cases averted were in Sub-Saharan Africa.

Conclusions

• There was a potential decrease in the incidence of most OIs with ART use in LMIC (from 60% to 95%), comparable to rates seen in Europe and North America.

• This was greatest for oral candidiasis, toxoplasmosis, herpes zoster and Kaposi sarcoma, with a lesser reduction for Cryptococcal meningitis and Pneumocystis jirovecii infection.

• Most of the impact is seen in the first year of treatment.

• There was no impact on the incidence of genital ulcer diseaseHSV-2 or bacteriuria.

• The expansion of ART in LMIC has averted roughly 900 000 OIs annually, with yearly savings of at least 32 million dollars, excluding savings for pulmonary tuberculosis and toxoplasmosis which are likely considerable.

• There were significant gaps in data from Latin America, and the predominance of data from large cohorts in Uganda, Cote d’Ivoire, and South Africa.

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