HIV Care & PMTCT in Resource-Limited Settings

Monthly Intelligence Report
2010, Vol 6, Issue 4

Back Issues on Line

prepared by the Bordeaux Working Group

Members: Elise Arrivé, Renaud Becquet, Mathias Bruyand, François Dabis (Chair), Antoine Jaquet, Valérie Leroy, Charlotte Lewden, Evelyne Mouillet (Coordinator), Camille Ndondoki, Joanna Orne-Gliemann (Coordinator), Freddy Perez, Hapsatou Touré.

Number of citations selected for this issue: 18

Citation format (by alphabetical order of the authors): Author(s). Title. Source. Abstr. (Authors’ text) or Introduction (Authors’ text) or Selection (Selected sections of the paper) or Notes or Abstr. Edited (Written by the Bordeaux Working Group). Author Address, if available, Free Full Text, if available

**Abstr.** Background One of the critical clinical decisions made in antiretroviral therapy (ART) is when to switch from an initial regimen to another due to treatment failure. This complex process requires consideration of multiple factors including: (1) what type of monitoring (e.g., clinical, immunologic, virologic) is available to guide switching; (2) establishing criteria for treatment failure (e.g., viral load > 10,000 copies/mL); (3) integrating data from different types of monitoring; (4) making a decision; and, if possible, (5) follow-up and monitoring to determine patient outcomes. The initial step in this model of deciding when to switch is determining what type of monitoring for guiding when to switch is available and appropriate. This review seeks to find and summarize evidence on optimal monitoring strategies for guiding when to switch first-line regimens due to treatment failure among adults and adolescents living with HIV in low-resource settings. This review was one of a series of reviews prepared in 2009 at the request of the World Health Organization to inform the development of new guidelines on ART for adults and adolescents. Objectives To assess optimal monitoring strategies for guiding when to switch antiretroviral therapy regimens for first-line treatment failure among adults and adolescents living with HIV in low-resource settings. Search strategy We formulated a comprehensive and exhaustive search strategy in an attempt to identify all relevant studies regardless of language or publication status. In July 2009, we search the following electronic journal and trial databases: MEDLINE, EMBASE, CENTRAL. We also searched conference databases using NLM Gateway (for HIV/AIDS conference abstracts before 2005), abstract databases from the Conferences on Retroviruses and Opportunistic Infections, International AIDS Conferences, and International AIDS Society Conferences on HIV Pathogenesis, Treatment, and Prevention from 2005 to 2009, and the trials registers ClinicalTrials.gov, Current Controlled Trials, and Pan-African Clinical Trials Registry. We contacted researchers and relevant organizations and checked reference lists for all included studies. Selection criteria We selected studies which evaluated a monitoring intervention/strategy that helps guide when to switch ART. Study types included randomized controlled trials and observational studies (cohort and case-control) which included comparators. Data collection and analysis One author performed an initial screening. Two authors performed a detailed screening. Two authors independently assessed study eligibility, extracted data, and graded methodological quality. Differences were resolved by a third reviewer. Heterogeneity was assessed, and meta-analyses were performed where appropriate. Main results Two randomized trials were identified which were in abstract form only. Two cohort studies (both published) with comparators were identified. Of the evidence available, three comparisons were studied: clinical versus immunologic and clinical monitoring; clinical versus virologic, immunologic, and clinical monitoring; and immunologic and clinical monitoring versus virologic, immunologic, and clinical monitoring. Clinical vs. Immunologic and Clinical Monitoring: Based upon two randomized trials, clinical monitoring alone results in increased mortality (low-quality evidence), increased AIDS-defining illnesses and mortality as a composite endpoint (moderate), no difference in serious adverse events (low), increased numbers of unnecessary switches (low), and no difference in switches to second-line (low) compared to immunological and clinical monitoring. Clinical vs. Virologic, Immunologic, and Clinical Monitoring: Based upon a single randomized trial, clinical monitoring alone results in a trend toward increased mortality (low), increased AIDS-defining illnesses and mortality as a composite endpoint (low), increased unnecessary switches (low), no difference in virologic treatment failures (low), and a trend toward increased switches to second-line (low) compared to virologic, immunologic, and clinical monitoring. Immunologic and Clinical vs. Virologic, Immunologic, and Clinical Monitoring: Based upon a single randomized trial, immunologic and clinical monitoring results in no difference in mortality (low), no difference in AIDS-defining illnesses and mortality as a composite endpoint (low), no difference in unnecessary switches (very low), no difference in virologic treatment failures (low), and no difference in switches to second-line (low) compared to virologic, immunologic, and clinical monitoring. Observational studies appear to demonstrate that programs with virologic, immunologic, and clinical monitoring switch therapy more frequently (very low), earlier (very low), and at higher CD4 counts (very low) compared with programs that have immunologic and clinical monitoring alone.
Authors’ conclusions A limited number of studies were available to address this topic, and, of the two randomized trials identified, both were in abstract form only. Observational studies also were limited in number and were of lesser quality. Although the quality of the evidence varied from the randomized trials, ranging from very low to moderate, there appeared to be substantial benefits for key outcomes (e. g. mortality, AIDS-defining illness and mortality as a composite endpoint, and unnecessary switches) favoring both immunologic and clinical monitoring or virologic, immunologic, and clinical monitoring versus clinical monitoring alone. Very low-quality evidence from observational studies suggested that virologic, immunologic, and clinical monitoring led to more frequent switching, earlier switching, and switching at higher CD4 counts compared with immunologic and clinical monitoring. Further information on the studies currently reported in abstract form will provide insight. Ongoing studies addressing this topic likely will provide information to further clarify optimal monitoring strategies for guiding when to switch first-line therapy. Additionally, studies looking at different virologic monitoring frequencies and/or virologic monitoring at different times after ART initiation (e. g. after 2-3 years) would be informative. Finally, cost-analysis studies will lend further insights into the applicability of these findings to low-resource settings.

Address: Chang, Lw, Johns Hopkins Sch Med, Dept Med, Div Infect Dis, 1503 E Jefferson St, Room 116, Baltimore, Md 21287 USA. larrywillchang@gmail.com


Abstr. Objective To measure progress in implementing co-trimoxazole prophylaxis (CTXp) (trimethoprim plus sulfamethoxazole) and isoniazid preventive therapy (IPT) policy recommendations, identify barriers to the development of national policies and pinpoint challenges to implementation. Methods In 2007 we conducted by e-mail a cross-sectional survey of World Health Organization (WHO) HIV/AIDS programme officers in 69 selected countries having a high burden of infection with HIV or HIV-associated tuberculosis (TB). The specially-designed, self-administered questionnaire contained items covering national policies for CTXp and IPT in people living with HIV, current level of implementation and barriers to developing or implementing these policies. Findings The 41(59%) respondent countries, representing all WHO regions, comprised 85% of the global burden of HIV-associated TB and 82% of the global burden of HIV infection. Thirty-eight countries (93%) had an established national policy for CTXp, but only 66% of them (25/38) had achieved nationwide implementation. For IPT, 21 of 41 countries (51%) had a national policy but only 28% of them (6/21) had achieved nationwide implementation. Despite significant progress in the development of CTXp policy, the limited availability of co-trimoxazole for this indication and inadequate systems to manage drug supply impeded nationwide implementation. Inadequate intensified tuberculosis case-finding and concerns regarding isoniazid resistance were challenges to the development and implementation of national IPT policies. Conclusion Despite progress in implementing WHO-recommended CTXp and IPT policies, these interventions remain underused. Urgent steps are required to facilitate the development and implementation of these policies.

Address: Date, Aa, Ctr Dis Control & Prevent, Global Aids Program, Atlanta, GA 30333 USA. adate@cdc.gov


Introduction. In The Lancet today, Bradley Mathers and colleagues make a heroic effort—in fact, a systematic review—to document the coverage (services provided per individual in need of services) for HIV prevention and care for injecting drug users (IDUs) throughout the world. Whilst the problems in obtaining data and in assessing the quality of data that could be obtained were formidable, two conclusions can be safely drawn. First, there is great variation in coverage of HIV-related services for IDUs across different countries; and second, in much of the world, coverage is clearly inadequate. .

Notes: See below Mathers paper.

Address: Des Jarlais, Dc, Beth Israel Deaconess Med Ctr, New York, NY 10003 USA. dcdesjarla@aol.com
First-year lymphocyte T CD4(+) response to antiretroviral therapy according to the HIV type in the IeDEA West Africa collaboration. Aids 2010;24(7):1043-1050.

Abstr. Objective: To compare the lymphocyte T CD4(+) (CD4) response to combinations of antiretroviral therapy (ART) in HIV-1, HIV-2 and dually positive patients in West Africa. Design and setting: Collaboration of 12 prospective cohorts of HIV-infected adults followed in Senegal (2), Gambia (1), Mali (2), Benin (1) and Cote d'Ivoire (6). Subjects: Nine thousand, four hundred and eighty-two patients infected by HIV-1 only, 270 by HIV-2 only and 321 dually positive, who initiated an ART. Outcome measures: CD4 change over a 12-month period. Results: Observed CD4 cell counts at treatment initiation were similar in the three groups [overall median 155, interquartile range (IQR) 68; 249 cells/mu l]. In HIV-1 patients, the most common ART regimen was two nucleoside reverse transcriptase inhibitors (NRTIs) and one non-nucleoside reverse transcriptase inhibitor (NNRTI; N = 7714) as well as for dually positive patients (N 135). HIV-2 patients were most often treated with a protease inhibitor-based regimen (N 193) but 45 of them were treated with an NRTI-containing ART. In those treated with a NRTI-containing regimen, the estimated mean CD4 change between 3 and 12 months was significantly lower in HIV-2 (-41 cells/mu l per year) and dually positive patients (+12 cells/mu l per year) compared to HIV-1 patients (+69 cells/mu l per year, overall P value 0.01). The response in HIV-2 and dually positive patients treated by another regimen (triple NRTIs or protease inhibitor-containing ART) was not significantly different than the response obtained in HIV-1-only patients (all P values >0.30). Conclusion: An optimal CD4 response to ART in West Africa requires determining HIV type prior to initiation of antiretroviral drugs. NNRTIs are the mainstay of first-line ART in West Africa but are not adapted to the treatment of HIV-2 and dually positive patients. (C) 2010 Wolters Kluwer Health vertical bar Lippincott Williams & Wilkins.

Address: Thiebaut, R, Univ Bordeaux 2, Isped, Inserm Epidemiol & Biostat U897, 146 Rue Leo Saignat, F-33076 Bordeaux, France. rodolphe.thiebaut@isped.u-bordeaux2.fr


Abstr. Objective Clinical outcomes of HIV-infected children on antiretroviral treatment (ART) in a decentralised, nurse/counsellor-led programme. Design Clinical cohort. Setting KwaZulu-Natal, South Africa. Patients HIV-infected children aged <=15 years on ART, June 2004-2008. Main outcome measures Survival according to baseline characteristics including age, WHO clinical stage, haemoglobin and CD4%, was assessed in Kaplan-Meier analyses. Hazard ratios for mortality were estimated using Cox proportional hazards regression and changes in laboratory parameters and weight-for-age z scores after 6-12 months' treatment were calculated. Results 477 HIV-infected children began ART at a median age of 74 months (range 4-180), median CD4 count (CD4%) of 433 cells/mm3 (17%) and median HIV viral load of log 4.2 copies/ml; 105 (22%) were on treatment for tuberculosis and 317 (76.6%) were WHO stage 3/4. There were significant increases after ART initiation in CD4% (17% vs 22%; p=0.001), haemoglobin (9.9 vs 11.7 g/l; p<=0.001) and albumin (30 vs 36 g/l; p=0.001). 32 (6.7%) children died over 732 child-years of follow-up (43.7 deaths/1000 child-years; 95% CI 32.7 to 58.2), 17 (53.1%) within 90 days of treatment initiation; median age of death was 84 (IQR 10-181) months. Children with baseline haemoglobin <=8 g/l were more likely to die (adjusted HR 4.5; 95% CI 1.6 to 12.3), as were those aged <18 months compared with >60 months (adjusted HR 3.2; 95% CI 1.2 to 9.1). Conclusions Good clinical outcomes in HIV-infected children on ART are possible in a rural, decentralised service. Few young children are on ART, highlighting the urgent need to identify HIV-exposed infants.

Address: Ruth M Bland, Africa Centre for Health and Population Studies, University of KwaZulu-Natal, PO Box 198, Mtubatuba, KwaZulu-Natal, 3935, South Africa. r bland@africacentre.ac.za

Free Full Text: http://adc.bmj.com/content/95/6/414.full.pdf


Abstr. Background. Patients with human immunodeficiency virus (HIV) infection and tuberculosis have an increased risk of death, treatment failure, and relapse. Methods. A systematic review and meta-analysis of randomized, controlled trials and cohort studies was conducted to evaluate the impact of
duration and dosing schedule of rifamycin and use of antiretroviral therapy in the treatment of active tuberculosis in HIV-positive patients. In included studies, the initial tuberculosis diagnosis, failure, and/or relapse were microbiologically confirmed, and patients received standardized rifampin-or rifabutin-containing regimens. Pooled cumulative incidence of treatment failure, death during treatment, and relapse were calculated using random-effects models. Multivariable meta-regression was performed using negative binomial regression. Results. After screening 5158 citations, 6 randomized trials and 21 cohort studies were included. Relapse was more common with regimens using 2 months rifamycin (adjusted risk ratio, 3.6; 95% confidence interval, 1.1-11.7) than with regimens using rifamycin for at least 8 months. Compared with daily therapy in the initial phase (patients from 35 study arms), n = 3352 thrice-weekly therapy (n = 211 patients from 5 study arms) was associated with higher rates of failure (adjusted risk ratio, 4.0; 95% confidence interval, 1.5-10.4) and relapse (adjusted risk ratio, 4.8; 95% confidence interval, 1.8-12.8). There were trends toward higher relapse rates if rifamycins were used for only 6 months, compared with >= 8 months, or if antiretroviral therapy was not used. Conclusions. This review raises serious concerns regarding current recommendations for treatment of HIV-tuberculosis coinfection. The data suggest that at least 8 months duration of rifamycin therapy, initial daily dosing, and concurrent antiretroviral therapy might be associated with better outcomes, but adequately powered randomized trials are urgently needed to confirm this.

Address: Menzies, D, Mcgill Univ, Ctr Hlth, Montreal Chest Inst, 3650 St Urbain,Rm K1-24, Montreal, Pq H2x 2p4, Canada. dick.menzies@mcgill.ca


Abstr. Background: Southern Africa is witnessing the emergence of an epidemic of long-term survivors of vertically acquired human immunodeficiency virus (HIV) infection presenting with untreated HIV as adolescents. Dermatologic conditions, common in both HIV-infected adults and children, have not been described in this age-group. We investigated the prevalence and spectrum of skin conditions in adolescents admitted to hospitals in Zimbabwe. Methods: A total of 301 consecutive adolescents admitted to 2 central Harare hospitals, underwent a dermatologic examination. Clinical history, HIV serology, and CD4 lymphocyte counts were obtained. Herpes simplex virus-2 serology was used as a surrogate marker for sexual activity. Results: A total of 139 (46%) patients were HIV-1 antibody positive, of whom only 2 (1.4%) were herpes simplex virus-2 antibody positive. The prevalence of any skin complaint among HIV-infected and uninfected participants was 88% and 14%, respectively (odds ratio: 37.7, 95% confidence interval: 19.4-72). The most common HIV-related conditions were pruritic papular eruptions (42%) and plane warts >5% of body area (24%). Having 3 or more skin conditions, a history of recurrent skin rashes and angular cheilitis were each associated with CD4 counts <200 cells/μL (P < 0.03, P < 0.01, and P < 0.05, respectively). Conclusions: Skin disease was a common and striking feature of underlying HIV-infection in hospitalized HIV-infected adolescents in Zimbabwe. In resource-poor settings with maturing epidemics, the presence of skin disease should be regarded as a strong indication for HIV testing and especially as it may reflect advanced immunosuppression. The high frequency of multiple plane warts has not previously been described, and may be a feature that distinguishes vertically-infected from horizontally-infected adolescents.

Address: Owe, S, Upton Hosp, Garden Clin, Berkshire E Primary Care Nhs, Sexual Hlth Serv, Slough Sl1 2bj, Berks, England. saralowe@fastmail.fm


Abstr. Background Previous reviews have examined the existence of HIV prevention, treatment, and care services for injecting drug users (IDUs) worldwide, but they did not quantify the scale of coverage. We undertook a systematic review to estimate national, regional, and global coverage of HIV services in IDUs. Methods We did a systematic search of peer-reviewed (Medline, BioMed Central), internet, and grey-literature databases for data published in 2004 or later. A multistage
process of data requests and verification was undertaken, involving UN agencies and national experts. National data were obtained for the extent of provision of the following core interventions for IDUs: needle and syringe programmes (NSPs), opioid substitution therapy (OST) and other drug treatment, HIV testing and counselling, antiretroviral therapy (ART), and condom programmes. We calculated national, regional, and global coverage of NSPs, OST, and ART on the basis of available estimates of IDU population sizes. Findings By 2009, NSPs had been implemented in 82 countries and OST in 70 countries; both interventions were available in 66 countries. Regional and national coverage varied substantially. Australasia (202 needle syringes per IDU per year) had by far the greatest rate of needle syringe distribution; Latin America and the Caribbean (0.3 needle syringes per IDU per year), Middle East and north Africa (0.5 needle syringes per IDU per year), and sub-Saharan Africa (0.1 needle syringes per IDU per year) had the lowest rates. OST coverage varied from less than or equal to one recipient per 100 IDUs in central Asia, Latin America, and sub-Saharan Africa, to very high levels in western Europe (61 recipients per 100 IDUs). The number of IDUs receiving ART varied from less than one per 100 HIV-positive IDUs (Chile, Kenya, Pakistan, Russia, and Uzbekistan) to more than 100 per 100 HIV-positive IDUs in six European countries. Worldwide, an estimated two needle syringes (range 1-4) were distributed per IDU per month, there were eight recipients (6-12) of OST per 100 IDUs, and four IDUs (range 2-18) received ART per 100 HIV-positive IDUs. Interpretation Worldwide coverage of HIV prevention, treatment, and care services in IDU populations is very low. There is an urgent need to improve coverage of these services in this at-risk population.

Notes: See above Des Jarlais comment.
Address: Mathers, Bm, Univ New S Wales, Natl Drug & Alcohol Res Ctr, Sydney, Nsw 2052, Australia. b.mathers@unsw.edu.au

Notes: See above Des Jarlais paper.
Address: Infectious Diseases Division, Miriam Hospital, Providence, Rhode Island 02906, USA. kenneth_mayer@brown.edu
Free Full Text: http://www.journals.uchicago.edu/doi/pdf/10.1086/651475

Abstr. Background. In women, single-dose nevirapine for prophylaxis against mother-to-child transmission of human immunodeficiency virus type 1 (HIV-1) selects for nevirapine-resistant HIV-1, which subsequently decays rapidly. We hypothesized that the selection, acquisition, and decay of nevirapine-resistant HIV-1 differs in infants, varying by the timing of HIV-1 infection. Methods. We conducted a prospective, observational study of 740 Mozambican infants receiving single-dose nevirapine prophylaxis and determined the timing of infection and concentrations of nevirapine-resistant HIV-1 over time. Results. Infants with established in utero infection had a high rate (87.0%) of selection of nevirapine-resistant HIV-1-1 mutants, which rapidly decayed to undetectable levels. The few without nevirapine resistance received zidovudine with single-dose nevirapine and/or their mothers took alternative antiretroviral drugs. Infants with acute in utero infection had a lower rate (33.3%; P = .006, compared with established in utero infection), but mutants persisted over time. Infants with peripartum infection also had a lower rate of nevirapine-resistant HIV-1-1 (38.1%; P = .001, compared with established in utero infection) but often acquired 100% mutant virus that persisted over time (P = .017, compared with established in utero infection). Conclusions. The detection and persistence of nevirapine-resistant HIV-1 in infants after single-dose nevirapine therapy vary by the timing of infection and the antiretroviral regimen. In infants with persistent high-level nevirapine-resistant HIV-1, nevirapine-based antiretroviral therapy is unlikely to ever be efficacious because of concentrations in long-lived viral reservoirs. However, the absence or decay of nevirapine-resistant HIV-1 in many infants suggests that nevirapine antiretroviral therapy may be effective if testing can identify these individuals.
Address: Frenkel, Lm, 1900 9th Ave, Seattle, WA 98101 USA. lfrenkel@u.washington.edu
Free Full Text: http://www.journals.uchicago.edu/doi/pdf/10.1086/651475

Introduction. In patients with HIV-1 infection who are starting combination antiretroviral therapy (ART), the incidence of immune reconstitution inflammatory syndrome (IRIS) is not well defined. We did a meta-analysis to establish the incidence and lethality of the syndrome in patients with a range of previously diagnosed opportunistic infections, and examined the relation between occurrence and the degree of immunodeficiency. Systematic review identified 54 cohort studies of 13 103 patients starting ART, of whom 1699 developed IRIS. We calculated pooled cumulative incidences with 95% credibility intervals (CrI) by Bayesian methods and did a random-effects metaregression to analyse the relation between CD4 cell count and incidence of IRIS. In patients with previously diagnosed AIDS-defining illnesses, IRIS developed in 37.7% (95% CrI 26.6-49.4) of those with cytomegalovirus retinitis, 19.5% (6.7-44.8) of those with cryptococcal meningitis, 15.7% (9.7-24.5) of those with tuberculosis, 16.7% (2.3-50.7) of those with progressive multifocal leukoencephalopathy, and 6.4% (1.2-24.7) of those with Kaposi’s sarcoma, and 12.2% (6.8-19.6) of those with herpes zoster. 16.1% (11.1-22.9) of unselected patients starting ART developed any type of IRIS. 4.5% (2.1-8.6) of patients with any type of IRIS died, 3.2% (0.7-9.2) of those with tuberculosis-associated IRIS died, and 20.8% (5.0-52.7) of those with cryptococcal meningitis died. Metaregression analyses showed that the risk of IRIS is associated with CD4 cell count at the start of ART, with a high risk in patients with fewer than 50 cells per μL. Occurrence of IRIS might therefore be reduced by initiation of ART before immunodeficiency becomes advanced.

Address: Egger, M, Univ Bern, Ispm, Iedea, Finkenhubelweg 11, Ch-3012 Bern, Switzerland. egger@ispm.unibe.ch


Abstr. Objective: We describe medium-term outcomes for young children receiving antiretroviral therapy (ART) in resource-limited countries. Methods: Analyses were conducted on surveillance data for children <5 years of age receiving ART (initiated April 2002 to January 2008) in 48 HIV/AIDS treatment programs in Africa and Asia. Primary outcome measures were probability of remaining in care, probability of developing World Health Organization stage 4 clinical events, rate of switching to second-line ART, and drug toxicity, compared at 6, 12, 24, and 36 months of ART. Results: Of 3936 children (90% in Africa) initiating ART, 9% were <12 months, 50% were 12 to 35 months, and 41% were 36 to 59 months of age. The median time of ART was 10.5 months. Probabilities of remaining in care after 12, 24, and 36 months of ART were 0.85, 0.80, and 0.75, respectively. Compared with children 36 to 59 months of age at ART initiation, probabilities of remaining in care were significantly lower for children <12 months of age. Overall, 55% and 69% of deaths and losses to follow-up occurred in the first 3 and 6 months of ART, respectively. Probabilities of developing stage 4 clinical events after 12, 24, and 36 months of ART were 0.03, 0.06, and 0.09, respectively. Only 33 subjects (0.8%) switched to second-line regimens, and 151 (3.8%) experienced severe drug toxicities. Conclusions: Large-scale ART for children <5 years of age in resource-limited settings is feasible, with encouraging clinical outcomes, but efforts should be increased to improve early HIV diagnosis and treatment.

Address: Epicentre, Paris, France. delphsauvageot@hotmail.com


Abstr. Although the mother-to-child transmission (MTCT) contributes only 5% of transmission of HIV infection, its impact has reversed the decline in infant and child mortality rates. With antenatal service coverage of over 90%, the integration of prevention of MTCT (PMTCT) of HIV infection into the Reproductive and Child Health (RCH) services in Tanzania, this is likely to overstretch the staff capacity and undermine the already compromised quality of health care services. A retrospective study was conducted to assess the impact of integrating and scaling-up PMTCT of HIV infection into routine RCH services, on the magnitude of staff workload in RCH clinics. The study was conducted in 60 health facilities identified from five regions that had participated in the pilot phase of PMTCT.
implementation in the Mainland Tanzania. The average staff workload was calculated from staff-load obtained from attendance records and activity-time obtained by direct observation; and staff-time from records that were kept at the clinic. The average staff workload was found to be 50.5% (8-147%) for facilities providing PMTCT of HIV infection and 37.8% (11-82%) for facilities without PMTCT services. The average staff workload was computed on the assumption that all clients attending various antenatal clinics received PMTCT services from trained staff only and the result revealed staff workload of 87.2%. This study concludes that services for PMTCT of HIV infection can easily be scaled-up and integrated into RCH services using the already existing staff. In the wake of the human resource crisis in the health sector in developing countries, strategies to address the problem will need to go beyond numbers to address issues of staff productivity and their distribution.

Address: Simba, D, Muhas, Sch Publ Hlth & Social Sci, Dept Community Hlth, Po 65015, Dar Es Salaam, Tanzania. dsimba@muchs.ac.tz


Introduction. Diarrhoea is the second leading killer globally of children under five (after pneumonia), responsible for nearly one in five childhood deaths (~1.5 million each year). Around 40% of these deaths occur in Africa. Outcomes may be even worse for those children who have fallen through the cracks of programmes to prevent vertical transmission of HIV. Many young children with undetected HIV, like Thandi, first present for care with persistent diarrhoea (it is one of the several clinical features that is suggestive of HIV infection).


Abstr. Objective: Despite World Health Organization recommendations, concerns about promoting resistance have impeded implementation of isoniazid preventive therapy (IPT) for tuberculosis (TB). We describe characteristics of TB in individuals previously exposed to IPT as part of ‘Thibela TB’, a cluster-randomized trial of community-wide IPT in gold miners in South Africa. Design: Case series including participants who were dispensed IPT, attended at least one follow-up visit and were subsequently treated for TB. Methods: TB episodes were detected through surveillance and through follow-up if IPT was stopped early. Drug susceptibility data were compared with TB episodes detected through surveillance in control clusters (where IPT use was minimal) and a laboratory substudy of mycobacterial sputum culture from TB suspects in control clusters. Results: Among 126 eligible individuals (125 men, median age 43 years), median time from starting IPT to TB treatment was 316 days (interquartile range 174-491). Ninety-four of the 126 (75%) were first episodes. Eighty-nine of 103 (86%) tested HIV-infected, with the median CD4 cell count of 196 cells/μl (n = 51). Sixty-four of 108 (59%) with known treatment outcomes were cured or completed treatment. Among 71 isolates with drug susceptibility results available, 12.1% [95% confidence interval (CI) 5.0-23.3] and 7.7% (95% CI 0.2-36.0) from first and retreatment episodes, respectively, had isoniazid resistance, compared with 6.0% (95% CI 3.1-10.2) and 18.7% (95% CI 10.6-29.3) in control clusters and 11.8% (95% CI 8.2-16.3) among first TB episodes in the laboratory substudy. Conclusion: TB after recent IPT has prevalence of drug resistance similar to background and treatment outcomes typical of this setting. These data support wider implementation of IPT.

Address: Van Halsema, Cl, Univ London London Sch Hyg & Trop Med, Dept Infect & Trop Dis, Clin Res Unit, Keppel St, London WC1E 7HT, England. claretaylor@doctors.org.uk


Abstr. Background Co-trimoxazole prophylaxis can reduce mortality from untreated HIV infection in Africa; whether benefits occur alongside combination antiretroviral therapy (ART) is unclear. We estimated the effect of prophylaxis after ART initiation in adults. Methods Participants in our observational analysis were from the DART randomised trial of management strategies in HIV-infected, symptomatic, previously untreated African adults starting triple-drug ART with CD4 counts
lower than 200 cells per μL. Co-trimoxazole prophylaxis was not routinely used or randomly allocated, but was variably prescribed by clinicians. We estimated effects on clinical outcomes, CD4 cell count, and body-mass index (BMI) using marginal structural models to adjust for time-dependent confounding by indication. DART was registered, number ISRCTN13968779. Findings: 3179 participants contributed 14,214 years of follow-up (8128 [57%] person-years on co-trimoxazole). Time-dependent predictors of co-trimoxazole use were current CD4 cell count, haemoglobin concentration, BMI, and previous WHO stage 3 or 4 events on ART. Present prophylaxis significantly reduced mortality (odds ratio 0.65, 95% CI 0.50-0.85; p=0.001). Mortality risk reduction on ART was substantial to 12 weeks (0.41, 0.27-0.65), sustained from 12-72 weeks (0.56, 0.37-0.86), but not evident subsequently (0.96, 0.63-1.45; heterogeneity p=0.02). Variation in mortality reduction was not accounted for by time on co-trimoxazole or current CD4 cell count. Prophylaxis reduced frequency of malaria (0.74, 0.63-0.88; p=0.0005), an effect that was maintained with time, but we observed no effect on new WHO stage 4 events (0.86, 0.69-1.07; p=0.17), CD4 cell count (difference vs non-users, 3 cells per μL [-12 to 6]; p=0.50), or BMI (difference vs non-users, 0.04 kg/m² [-0.20 to 0.13]; p=0.681).

Interpretation: Our results reinforce WHO guidelines and provide strong motivation for provision of co-trimoxazole prophylaxis for at least 72 weeks for all adults starting combination ART in Africa.

Notes: See above Anglaret editorial.

Address: Walker, As, Mrc, Clin Trials Unit, 222 Euston Rd, London Nw1 2da, England. asw@ctu.mrc.ac.uk


Abstr. A cross-sectional study was conducted in HIV-1-infected patients receiving lamivudine-containing antiretroviral therapy (ART) to determine the prevalence and risk factors of hepatitis B virus drug resistance (HBV-DR). HBV DNA and HBV genotypic resistance test were performed. Patients were categorized into two groups: with and without HBV-DR. There were 84 patients with a mean age (standard deviation [SD]) of 42.2 (10.2) years and 77% were males. Median (range) duration of ART and lamivudine use was 46 (3-177) and 40 (3-140) months, respectively. Median (range) CD4 cell count was 352 (49-790) cells/mm³. Of all, 19 (23%) had HBV-DR with a median (range) HBV DNA of 2.56 x 10⁷ (0.01-2.3 x 10⁹) IU/mL. In univariate analysis, there were no differences in age, gender, ART regimen, liver function test, anti-HBc antibody, anti-HCV antibody between the two groups. Patients with HBV-DR had a higher proportion of positive HBeAg (68.4% versus 3.8%, p<0.001). In multivariate analysis, positive HBeAg (odds ratio [OR] 16.64; 95% confidence interval [CI] 3.31-83.60) and duration of lamivudine use [per 6-month increment, OR 1.24; 95% CI, 1.06-1.36] were significant risk factors for HBV-DR. All 19 patients with HBV-DR had lamivudine resistance with the mutations as follows: M204V/I (95%), L180M/A181T (95%), L80V/I (47%), V173L (32%), and N236T (21%). Of these, 95%, 84%, 32%, and 0% of patients had HBV-DR to telbivudine, entecavir, adefovir, and tenofovir, respectively. HBV-DR is common in HBV/HIV-1 coinfected patients receiving lamivudine-containing ART without tenofovir. Positive HBeAg and longer duration of lamivudine use are risk factors for HBV-DR. In addition to lamivudine resistance, cross-resistance to other anti-HBV drugs is also frequently observed.

Address: Sungkanuparph, S, Mahidol Univ, Ramathibodi Hosp, Fac Med, Div Infect Dis, Dept Med, 270 Rama 6 Rd, Bangkok 10400, Thailand. rasuy@mahidol.ac.th