landmark opportunity to work together to review our progress and renew our energies to make it happen.

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HAART's first decade: success brings further challenges

The initial benefits of highly active antiretroviral therapy (HAART)—restored or maintained immune function and markedly reduced risk of opportunistic disease and mortality[1]—were followed by several concerns: the large burden of pill taking, with possible effects on adherence; longer-term therapeutic toxicity, especially lipodystrophy;[2] increased cardiovascular risk;[3] and the potential effect of resistant virus on therapeutic choices.[4] The first decade of HAART met these challenges well, including the development of more potent regimens with lower pill burdens and reduced toxicity.[5]

However, have further therapeutic advances for HIV translated into continued declines in disease outcomes? In today's *Lancet*, The Antiretroviral Therapy (ART) Cohort Collaboration, involving 12 European and North American prospective cohort studies, addresses this issue by examining virological, immunological, and disease progression outcomes in more than 20 000 antiretroviral-naive individuals starting HAART in 1995–2003.[6] The major findings are that, despite improved initial HIV virological control (percentage <500 copies per mL at 6 months increased from 58% in 1995–96 to 83% in 2002–03), there were no significant improvements in early immunological response as measured by CD4-lymphocyte count, no reduction in all-cause mortality, and a significant increase in combined AIDS/AIDS-related death risk in more recent years. Importantly, the recent increase in AIDS risk seemed largely because of increased tuberculosis incidence.

Another major feature of the study, and the probable explanation for these somewhat paradoxical trends, was the changing characteristics of the study population: from 1995–96 to 2002–03, large increases in female (16% to 32%) and heterosexual (20% to 47%) proportions were balanced by a declining male homosexual proportion (56% to 34%). A major shift in antiretroviral class was also seen, with use of non-nucleoside reverse-transcriptase inhibitors increasing from 2% to 40% and regimens based on protease inhibitors declining from 95% to 45%.

Although data on country of birth were not available, given migration patterns to the countries involved, the increased incidence of tuberculosis probably reflected higher proportions of study participants born in regions with a high prevalence of tuberculosis. We have shown large contrasts in the spectrum of opportunistic disease by country of birth in the Australian HIV-infected population, especially the higher risk of tuberculosis in individuals born in Africa and Asia.[7] The greater contribution of tuberculosis as an AIDS event supports the strengthening of tuberculosis screening and prophylaxis initiatives, especially for individuals from regions with a high prevalence.[8]

An intriguing finding was a reduction in the median time to AIDS, with half of AIDS events in the 2000–03 cohort occurring in the first 2 months of the 12-month follow-up. The high initial AIDS incidence suggests that immune restoration syndrome is a contributing factor, and immune restoration syndrome tuberculosis[9] might

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partly explain the increasing risk of tuberculosis and AIDS in recent years. The trend towards lower CD4-lymphocyte count when starting HAART in recent years might have increased the risk of immune restoration syndrome, and is consistent with later HIV presentation in heterosexual and overseas-born groups in developed-country settings.[10] Undiagnosed active opportunistic infections at the start of HAART might be a further contributing factor. Screening for active opportunistic infection in individuals with more advanced immunodeficiency and enhanced characterisation of early events after HAART should provide a greater understanding of this important finding.

The lack of continued mortality declines in the ART Cohort Collaboration's population requires further exploration, including the effect of novel therapeutic strategies and the contribution of non-AIDS-related illness to mortality. Findings from the randomised SMART study showed higher mortality from interrupted than continuous antiretroviral therapy, and a large contribution of non-AIDS events to overall mortality in both arms.[11] A greater understanding of emerging patterns and pathogenesis of HIV-related morbidity and the development of strategies to reduce non-AIDS-related mortality are key challenges for the second decade of HAART.

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What does absorption capacity not measure?

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In today's *Lancet*, Chunling Lu and colleagues[1] analyse disbursal data from the Global Fund to Fight AIDS, Tuberculosis and Malaria (GFATM), and suggest that both political stability and relatively less developed health systems are important determinants of the fund's grant giving. As the authors acknowledge, these findings must be taken with the caveat that funding does not necessarily correlate with health effects or related outcomes.

Absorption capacity is variously defined but generally refers to the ability of a country or organisation to receive aid and use it effectively. The debate around absorption capacity largely stems from the work of World Bank economists[2,3] relating the experience of disbursals of external assistance to the level of monetary inflows and economic growth. Absorption capacity has several dimensions, ranging from the effect of assistance on the macroeconomic environment and fiscal management of funds, to the translation of these external funds into specific activities and service delivery.[4] Additional factors might also influence the outcome of assistance, such as demand-side constraints due to lack of family education and female empowerment.[5] Thus key questions about the assessments of GFATM grant performance also relate to the ability of local fund agents to equate disbursals and allocations with effective spending, programme coverage, and engagement by civic society in the process.

Several important additional limitations must be considered, especially those that relate to the ability of weak health systems to absorb funds. Unless there are concomitant data to lend support to the association of funding with health-system strengthening or performance indicators, mere expenditure might only reflect spending on procurements and infrastructure rather than programme content. The proportionate outlay