

Clinical Review

Clinical Review identifies issues in the medical literature of interest to clinicians in Africa. Essential references are given at the end of each section

AIDS Review

Epidemiology of HIV/AIDS and scale up of antiretroviral therapy

The latest estimated numbers on the HIV/AIDS epidemic and the scale up of antiretroviral therapy (ART) in 2013 are provided through UNAIDS and the World Health Organization (WHO).^{1,2} By the end of 2013, there were an estimated 35.0 (33.2–37.2) million people living globally with HIV, a number similar to that reported for the previous year. Adults constituted 31.8 (30.1–33.7) million and children under the age of 15 years were 3.2 (2.9–3.5) million of the global total. In 2013, 2.1 (1.9–2.4) million people were newly infected with HIV and 1.5 (1.4–1.7) million people died from HIV/AIDS, both of these estimates being slightly lower than the previous year.

Sub-Saharan Africa continues to bear the brunt of this epidemic with 24.7 (23.5–26.1) million adults and children (71% of global total) living with HIV, 1.5 (1.3–1.6) million new HIV infections (71% of global total), and 1.1 (1.0–1.3) million deaths (73% of global total). Of children living with HIV, an estimated 2.9 million (91%) resided in sub-Saharan Africa, with 88% of new HIV infections and 95% of deaths in children occurring in this region. There is considerable variation in the severity of epidemics on the continent, with the southern African region still being the most severely affected, and the epidemic in South Africa continuing to be the largest in the world.

By the end of 2013, there were 11.7 million people from low- and middle-income countries on ART, representing 36% of people living with HIV in these countries. The additional 2 million people who started ART in 2013 marked the largest-ever annual increase in ART provision, and at current trends, the target of placing 15 million people on ART by 2015 in low- and middle-income countries will be exceeded. This surge in the numbers of people living with HIV accessing ART has been helped by many countries reacting swiftly to adopt the 2013 WHO ART Guidelines, and if fully implemented would increase the number of people eligible for ART to about 85% of all people living with HIV.

In sub-Saharan Africa there has been excellent progress, especially in the eastern and southern regions of the continent, with 9.1 million people on ART by the end of 2013, representing 37% of all people living with HIV. South Africa's ART programme is the largest in the world with just over 2.6 million people on ART. Despite these successes there are challenges. Children and adolescents lag behind adults in accessing ART

with the coverage gap continuing to grow. Men who are eligible for ART are less likely to start or be retained on ART compared with women. HIV services for key populations (including men who have sex with men, sex workers, transgender people and people who inject drugs) continue to be neglected.

Option B+, early ART and the impact on outcomes

Since the launch of the WHO 2013 ART Guidelines, several countries have adopted Option B+, a prevention of mother-to-child transmission strategy that involves starting HIV-infected pregnant or breastfeeding mothers on ART for life regardless of CD4 cell count or WHO clinical stage. Potential advantages of Option B+ include eliminating new paediatric infections by providing better protection for maternal health, and greater reduction in sexual transmission of HIV compared with other options. Malawi pioneered this strategy and commenced implementation in July 2011. Over a six-month period between October 2011 and March 2012, nearly 22 000 women in the country were enrolled to Option B+. Cohort monitoring of these women six months after ART initiation showed that 17% were lost to follow-up six months after ART initiation, with most losses occurring in the first three months of therapy.³ Risk factors associated with loss to follow-up included women who were well rather than needing ART for their own health, women who started ART during breastfeeding and women who commenced therapy on the day of diagnosis rather than after a period of group and individual counselling. These preliminary findings of high losses to follow-up emphasise the need to better understand the barriers to retention in care for women who start ART early under Option B+.

This need is even more pressing given the growing evidence of individual benefit from early ART. The landmark HPTN 052 randomised controlled trial published in 2011 had demonstrated that early ART was associated with a 96% reduction in HIV transmission, thus providing convincing evidence for the HIV prevention benefits of ART. Further analysis of patients in this same trial showed that those who started ART at median CD4 cell counts of 440 had a significant decrease in the incidence of new-onset AIDS events and tuberculosis compared with those starting ART at median CD4 cell counts of 230.⁴ Further work on the effect of ART on non-AIDS morbidity and mortality also suggests that early initiation of ART reduces the risk of non-AIDS death in people living with HIV to levels that are almost identical to those seen in HIV-uninfected individuals.⁵

Other ways of further reducing HIV-related morbidity and mortality

Cryptococcal meningitis is an important HIV-related opportunistic infection in Africa, and accounts for nearly one quarter of AIDS-related deaths. ART is essential for survival, but the optimal timing of therapy is still not known. A randomised trial in Uganda and South Africa showed that deferring ART for five weeks after the diagnosis of cryptococcal meningitis was associated with a significant reduction in mortality compared with starting ART at one to two weeks, especially amongst patients with few white

cells in the cerebrospinal fluid.⁶ These findings are similar to those observed in HIV-infected patients with tuberculosis meningitis, especially in those with low CD4 cell counts who are at particular risk of immune reconstitution inflammatory syndrome when ART is started soon after diagnosis. The development of this syndrome within the confined space of the central nervous system is dangerous as this leads to raised intracranial pressure with potentially fatal consequences. Deferred treatment with antiretroviral drugs appears to be the safest option.

Cotrimoxazole preventive therapy (CPT) administered before ART reduces morbidity and mortality in adults and children, but the current question in Africa is how long to continue with this adjunctive therapy. A randomised non-inferiority trial in Uganda and Zimbabwe in children and adolescents showed that continuing CPT after 96 weeks of ART was more beneficial than stopping prophylaxis with fewer hospitalisations for both malaria and non-malaria infections.⁷ Further evidence is now needed for adults, but these findings argue strongly for a policy of long-term CPT in conjunction with ART in children and adolescents in sub-Saharan Africa.

Ending the AIDS epidemic by 2030: the new '90-90-90' interim targets

As the post-2015 era draws closer, the global vision is to end the AIDS epidemic by 2030. To that end, UNAIDS has launched new ambitious treatment targets: by 2020, 90% of all people living with HIV will know their HIV status, 90% of all people with diagnosed HIV infection will receive sustained ART, and 90% of all people receiving ART will have viral load suppression.⁸ If this three-part target is achieved by 2020, at least 73% of all people living with HIV worldwide will be virally suppressed and modelling suggests this will enable the world to end the AIDS epidemic by 2030. Expansion of HIV testing, innovative approaches to testing and counselling services, better linkages to care, improved community empowerment, more cost-efficient drug regimens, and increased funding are some of the important interventions that will be needed to realise this dream.

To this end, in Malawi, a strategy of self-testing for HIV at home combined with home initiation of ART for those HIV-positive and eligible for treatment resulted in a greater number of persons initiating ART when compared with those who accessed facility-based services only.⁹ This may be one of the innovative ways of increasing HIV testing coverage in Africa that avoids the high transport and opportunity costs that patients often have to contend with in attending healthcare services. In terms of more cost-efficient ART regimens, a large multicentre, non-inferiority trial in 13 countries compared the efficacy of efavirenz 400 mg daily with the standard 600 mg dose in combination with tenofovir and emtricitabine as first-line treatment for HIV infection.¹⁰ The lower dose of efavirenz was not inferior in efficacy to the standard dose and was associated with a reduction in drug-specific adverse reactions. An interesting observation was that the recovery of CD4 cell counts was more pronounced at the lower dose of efavirenz compared with the higher dose, which may have something to do with the lower dose being associated with less host cell toxicity. A lower dose of efavirenz would

mean lower annual production in metric tonne of the drug for global consumption which in turn could lead to lower drug costs. More of these evidence-based simple interventions will be needed in the next few years to achieve the ambitious UNAIDS targets.

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Paediatrics Review

Two new growth standards for the foetus and newborn

In 2006 the World Health Organization Multicentre Growth Reference Study (WHO MGRS) published new infant and child growth standards from birth to 5 years old.¹ The objective was to describe how children *should* grow rather than *how* children grow. The design combined a longitudinal study from birth to 24 months with a cross-sectional study of children aged 18–71 months.² The pooled sample comprised infants and children from six countries: Brazil, Ghana, India, Norway, Oman and the United States. The study subpopulations had to have socioeconomic conditions (including education) favourable to optimal growth, *viz*, at least 20% of mothers practising breastfeeding, and all should adhere to MGRS feeding recommendations, absence of maternal smoking, single-term birth and no significant morbidity. For the longitudinal sample, mothers and their newborns were visited 21 times at home until 24 months of age. By April 2011, 125 countries had adopted the WHO growth standards, another 25 were considering their

adoption and 30 had not adopted them.³

In 2008, the International Foetal and Newborn Growth Consortium for the 21st century (INTERGROWTH-21st) was launched.^{4,5} Sites selected for the studies were urban populations in eight countries; Brazil (Petotas), Italy (Turin), Oman (Muscat), UK (Oxford), USA (Seattle), China (Beijing), India (Nagpur) and Kenya (Nairobi). The study sites and groups were selected with the expectation of low-risk for impaired foetal growth based on the health and nutrition of the pregnant women and mothers.

The Newborn Cross-Sectional Study (NCSS), a component of the INTERGROWTH-21st project, undertook measurements of weight, length and head circumference of 20486 newborns and collected data prospectively on the pregnancy of their mothers and the perinatal period.⁴ For foetuses <14 weeks an estimate of gestational age was obtained by ultrasound measurement of crown-rump length and for those 14–24 weeks a biparietal diameter. A liberal practice of delayed cord clamping was recommended. To be eligible, a reliable ultrasound estimation of gestational age and delivery of one live infant with no congenital malformations was required. There had to be low levels of exposure to pollution, domestic smoke due to tobacco or cooking, radiation or other toxic substances. Measurements were undertaken at 12 hour intervals and each measurement was collected independently by two trained anthropologists. Enrolment was undertaken over a 4 year period (2009–13). Common reasons for exclusion were maternal age (<18 years or >35 years), maternal height (<153 cm), BMI (>30 or <18.5 kg/m²), current smoker, previous medical history, and obstetric complications. Mothers from India were the shortest and those from the UK and USA the tallest; body mass index values were similar across the eight study sites. Educational achievement was high in all sites. Caesarean section rate was highest in Brazil (65%) and lowest in Oman (14%) and the UK (18%). The infants were between 33 and 42 weeks gestation and only 82 were <34 weeks. Overall, boys were heavier, longer, and had larger head circumference than girls.

These international standards for weight, length, and head circumference have been welcomed as a complement to the 2006 Growth Standards 1–3 for measurement of infant size, and as a basis for the detection of early stunting. However, there have been two criticisms of the study.⁶ Birthweight decreases linearly during the first two days of life with a mean projected decrease in bodyweight of approximately 10–20 g/kg for a full-term infant after 12 hours; so the time of measurement could influence the birthweight. Also, delayed cord clamping (this practice was not uniform) can increase the birthweight by up to a mean of 1101 g.⁷

Reliable screening methods for fetal growth are an essential element of antenatal care and the detection of malformations and genetic disorders.⁸ Accurate detection of fetal growth restriction is important in decisions regarding timing of induction of labour and performing Caesarean section, and thus iatrogenic prematurity on the one hand and stillbirth on the other hand. However, there are major problems with standardisation of fetal biometric charts used ultrasounds.^{5,8,9} Some charts do not adhere to proper standards and also, clinicians have to rely on the charts uploaded to a particular ultrasound

machine. Thus, in the same institution charts may differ between which ultrasound machine is used.

The Foetal Growth Longitudinal Study (FGLS), which is part of the INTERGROWTH-21st Project, has produced international ultrasound standards for the growth and size of the foetus.⁵ The design of the study is similar to that described above for the NCSS study and was undertaken in the same eight countries. In total, 4607 pregnant women were eligible for the study. The following five measurements were undertaken every five weeks from 14 weeks to 42 weeks gestation: foetal head circumference, biparietal diameter, occipital diameter, abdominal circumference, and femur length. These were measured three times from three separately obtained ultrasound images for each structure. The median number of ultrasound scans in all the woman was 5.0 (range 1–7; mean (SD) 4.9 (0.8)). Charts were constructed for the 3rd, 5th, 10th, 50th, 90th, 95th and 97th centile curves according to gestational age. These are the first international standards for foetal growth and now are recommended for worldwide use, and hopefully will replace the inaccuracy and bias of some current charts.⁸

In summary these two newly published growth standards^{4,5} extend the WHO MGRS to cover foetal and newborn life. Together, with on-going construction of further growth standards, they will describe: (1) foetal growth assessed by clinicians and ultrasound measures; (2) postnatal growth of term and preterm infants up to 2 years of age; and (3) the relationship between birthweight, length and head circumference, gestational age, and perinatal outcomes.¹⁰

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Family Medicine Review

Palliative care

Palliative care is a critical issue in developing countries and rural areas of developed countries, not least in Africa. In South Africa, Campbell and Amin¹ used in-depth qualitative methods to understand the experi-

ences of four palliative care nurses and 17 home-based care workers as palliative caregivers in rural homes. They found that the patients these healthcare workers (HCWs) cared for valued traditional rituals connected to illness and dying. The HCWs proposed that traditional healers should be included in palliative care training programmes as they could offer appropriate psychological, cultural, and spiritual care, because of their knowledge of patients' spiritual needs, and cultural practices relating to illness, death, dying, and bereavement. This may be particularly important where there are cultural differences or opposing world views between healthcare providers and patients, as it would facilitate the provision of appropriate care.

Interprofessional collaborative practice (ICP) should be a central element of palliative care. Much has been written on models of and competencies for ICP. Key elements of successful ICP have been described as shared decision-making and responsibility, efficient and effective coordination, and communication, mutual trust, and respect of other disciplines' professional opinions, confidence to express one's own perspectives, and autonomy of individual care providers.² However, given the fact that there are differences in the use of caregiver services,³ with rural patients using healthcare services more than social services, probably due to access and availability, which would be applicable in many areas of Africa, it is important to understand how this applies in resource-constrained environments. Recently published research looked at how this applies in the setting of rural palliative care.⁴ The authors found these key elements were an important part of the ICP of rural palliative care teams, but the rural environments proved to be distinctive in the way the elements were manifested, indicating the importance of context to practice. Included in the findings was the fact that collaboration usually pre-dated palliative care; collaboration is established almost automatically between rural practitioners, mainly because there are a limited number of healthcare and social service providers in such communities, so they are mostly already used to working together in facing the major resource challenges of providing care to their patients.

While the role of the team is critical, adequate analgesia is a major need in palliative care. Oral morphine is recognised by the World Health Organization (WHO) as the first-line drug for treatment of moderate to severe cancer pain. A recent study from Tanzania demonstrated the effectiveness of palliative care teams in reducing patients' pain and in increasing other positive life qualities in the absence of morphine; at the same time, it describes the distress of caregivers, trained in morphine delivery, who have to watch their patients suffering and in extreme pain, because of the limited availability of the drug.⁵ There is thus a need for clinicians to advocate for increased availability and use of oral morphine in such settings in addition to palliative care services.

Chronic diseases

Given the ever-increasing global burden of chronic illness – including non-communicable diseases, chronic communicable diseases (such as HIV-AIDS), and mental illness – and the increasing time and attention that is being (and needs to be) given to these conditions in pri-

mary care, it is important to revisit this subject regularly.

Patient-centred care has been acknowledged as vital in the management of patients with chronic conditions. Patient-centred care has been found to be associated with improved patient outcomes, including improved self-management, patient satisfaction, and medication adherence.⁶ Motivational interviewing and shared decision making are practical methods to accomplish patient-centred care. A recent article in the *Annals of Family Medicine* discusses shared decision making and motivational interviewing as tools that focus on engaging patients to explore their views and opinions, including options for treatment or management approaches from patients' perspectives, suggesting that clinicians could benefit from integrating both approaches in assisting patients, particularly in the context of chronic illness.⁷ The authors explain that motivational interviewing addresses ambivalence to change, seeking to explore and understand a patient's responses to change before making an action plan, while shared decision making seeks to clarify treatment options in order to assist patients in making informed, well-considered decisions. They give an example of using this in counselling for long-term conditions such as diabetes, as well as for behavioural changes, such as weight loss.

A crucial principle in the management of chronic illnesses is continuity of care.⁸ Korean researchers recently looked at the impact of continuity of care on mortality, costs, and health outcomes in patients with newly diagnosed cardiovascular risk factors, viz. hypertension, diabetes, or hypercholesterolaemia.⁹ A total of 47 433 patients were included in their study. The evidence was unequivocal: greater continuity of care was associated with lower overall and cardiovascular mortality, lower incidence of cardiovascular events, and reduced healthcare utilisation and costs. This was true even after controlling for potential confounders such as comorbidities and total number of visits to clinicians. They argue that doctors who see the same patients regularly are likely to have better knowledge of them, to recognise problems earlier, and to provide higher quality of care, while patients who have continuity are more likely to adopt better self-management behaviours, and to demonstrate increased adherence to medication. Continuity of care is hard work, and requires individual commitment and system change, but it clearly is of great benefit to our patients.

Village health workers, as they are known in many parts of the world, and their equivalents, offer a huge potential for community-based care, and support of patients with chronic illness. Recognising that support of self-management is the cornerstone in the control of chronic illness, these workers offer a bridge between healthcare providers and patients in achieving this goal. A study from Cape Town, South Africa, explored the role of Community Health Workers (CHWs) in the management of non-communicable diseases (NCDs).¹⁰ The authors described multiple roles that are played by CHWs in the care of NCDs, acting as health educators, advisors, rehabilitation workers, and support group facilitators. They also screen for complications of illness and assist community members to navigate the health system. They point out the potential enhanced role for

CHWs in distribution of medication in the community, which would be enhanced if CHWs advise on improving adherence and provide education relating to medication for the management of NCDs, as currently occurs with patients on HIV and tuberculosis treatment.

Eye health

One of the complications associated with a number of NCDs, and diabetes in particular, is visual impairment and blindness. A study was conducted in government healthcare facilities in Limpopo province, South Africa, to assess risk factors for visual impairment and blindness amongst 225 African patients aged 40 years and older, who had diabetes mellitus.¹¹ Of the 225 participants, 41.3% had visual impairment and 3.6% were blind, with cataracts (76.8%) and diabetic retinopathy (7.1%) being the most common causes. Risk factors that were associated with these conditions were increasing age and lower monthly income. The authors argue that interventions need to include population-based education about early detection of problems, and ensuring that refraction and cataract surgical services are available and accessible to such populations.

The relationship between eye problems and age was also discussed in a study on presbyopia (loss of accommodation of the crystalline lens with increasing age) in a rural community in Nigeria.¹² This was driven by a concern that, with presbyopia, doing near work becomes associated with headache and eye strain, and reading and writing become a challenge, thus causing frustration and social isolation in the elderly. The authors examined 585 people aged older than 35 years, and found a prevalence of presbyopia of 63.4%, increasing with age. Of greater concern, the unmet presbyopia need was 45.8%. Thus healthcare providers should be aware of the problem and take every opportunity to educate older patients about the availability of corrective lenses, while service providers and health administrators should ensure that affordable eyecare is made available to poorer communities.

The need to provide eyecare for rural African communities, and to educate patients about this, was illustrated by other research from Nigeria, which mapped the initial pathways to eyecare in a rural population in the south-east of the country.¹³ Questionnaires were administered to 501 participants regarding eye health-seeking behaviour for major eye diseases such as cataract, glaucoma, diabetic retinopathy, refractive error, and eye infection. The preferred initial responses were to consult a patent medicine dealer (35.0%), to consult an ophthalmologist (33.0%), and to self-medicate (125; 25.0%). The main reasons for not consulting an ophthalmologist were poor access (67.9%), ignorance (56.5%), and cost (59.2%). The article makes the case for greater accessibility to and subsidisation of eyecare services, integration of alternative eyecare providers into the healthcare system, and eye health literacy campaigns.

Research methods

Although this is a clinical review, good clinicians should be engaged in research – whether this is less formal research such as quality improvement projects, clinical governance activities, etc., or more formal research, for academic or other purposes. I thus want to commend to readers

the recently published series of articles on primary care research in Africa, published by the *African Journal of Primary Health Care and Family Medicine*.¹⁴ While the ten articles focus on building capacity of faculty members and postgraduate students in departments of family medicine and primary care in Africa, they provide useful guides for all potential or novice primary care researchers in Africa. The articles focus on common methods such as surveys using questionnaires, qualitative research, participatory action research, quality improvement cycles and programme evaluation, as well as providing guidance on how to write a research proposal and a research report. Go to <http://www.phcfm.org/> to access the articles.

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