Welcome to HIV this month! In this issue, we cover the following topics:

1. **Reduce sexual transmission**
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   - Childhood sexual violence and HIV risk in Tanzania
   - Testing for acute HIV infection feasible but impact remains uncertain
   - Effective, long-term programmes for alcohol and sexual risk reduction are yet to be shown
   - More rigorous evidence necessary on role of peers in adolescent sexual behaviour
   - Invitation plus tracing increases role of peers in adolescent sexual behaviour

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   - Relatedness, communication, and care of children living with HIV in eastern Uganda
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6. **Eliminate stigma and discrimination**
   - Peer support benefits MSM in Malawi

7. **Strengthening HIV integration**
- How many people have really died of HIV/AIDS in South Africa?
- Comparing strategies for HIV testing and counselling for children and adolescents

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HIV this month, published by UNAIDS, is a selective scan of new HIV-related information found in scientific journals. The Editors of HIV this month interpret original abstracts and provide editorial comment, so that information may be easily understood by people responding to the HIV epidemic in many diverse settings. The selection of material, its abridgement and other editorial changes, and also the original editorial comment are the responsibility of the Editors and do not represent any official statement of UNAIDS. It should be noted that (except for open access journals, e.g. PLoS) the authors and/or publishers retain copyright in the original published material to which HIV this month refers.
1. Reduce sexual transmission

HIV after 40 in rural South Africa: a life course approach to HIV vulnerability among middle aged and older adults.


South Africa has the highest number of people living with HIV in the world (over 6 million) as well as a rapidly aging population, with 15% of the population aged 50 and over. High HIV prevalence in rural former apartheid homeland areas suggests substantial aging with HIV and acquisition of HIV at older ages. We develop a life course approach to HIV vulnerability, highlighting the rise and fall of risk and protection as people age, as well as the role of contextual density in shaping HIV vulnerability. Using this approach, we draw on an innovative multi-method data set collected within the Agincourt Health and Demographic Surveillance System in South Africa, combining survey data with 60 nested life history interviews and 9 community focus group interviews. We examine HIV risk and protective factors among adults aged 40-80, as well as how and why these factors vary among people at older ages.

Abstract access

Editor’s notes: A growing body of work is documenting the importance of HIV in older age in East and southern Africa. This paper is a valuable addition to the literature. The authors look at how the risk of HIV infection, and the impact of living with HIV, affects women and men aged 40-80 years old. Forty is a relatively young age for a study of older people, but the age span covered by this paper does allow the authors to trace HIV vulnerability for people actively engaged in migrant labour to when they settle, as they age into their 60s and 70s. The finding that risk of HIV-infection and vulnerability to the impact of HIV vary across the life course, is not new. But the findings presented in this paper provide a compelling picture of changing risk. Indeed, the possibility that men in their 60s might be at particular risk of acquiring HIV because of their wives diminishing interest in sex highlights the importance of not assuming only people under 50 are ‘sexually active’. The authors also illustrate the risk that older women face who may prefer to remain celibate but cannot always refuse to have sexual intercourse with their husbands. One notable finding is that older men with a pension are attractive partners for younger women in what the authors describe as a poverty stricken area. The mixture of quantitative and qualitative data the authors use provide both breadth and depth to the findings presented making this both an interesting and informative paper.

HIV and childhood sexual violence: implications for sexual risk behaviors and HIV testing in Tanzania.


Prior research has established an association between sexual violence and HIV. Exposure to sexual violence during childhood can profoundly impact brain architecture and stress regulatory response. As a result, individuals who have experienced such trauma may engage in sexual risk-taking behavior and could benefit from targeted interventions. In 2009, nationally representative data were collected on violence against children in Tanzania from 13-24 year old respondents (n = 3739). Analyses show that females aged 19-24 (n = 579) who experienced childhood sexual violence, were more likely to report no/infrequent condom use in the past 12 months (AOR = 3.0, CI [1.5,
6.1], p = 0.0017) and multiple sex partners in the past 12 months (AOR = 2.3, CI [1.0, 5.1], p = 0.0491), but no more likely to know where to get HIV testing or to have ever been tested. Victims of childhood sexual violence could benefit from targeted interventions to mitigate impacts of violence and prevent HIV.

Abstract access

Editor’s notes: A growing body of evidence has established an association between sexual violence and increased vulnerability to HIV infection. Childhood sexual violence may increase HIV risk both directly (e.g. forced sex) and indirectly (e.g. through high-risk sex behaviours later in life). This paper examined two questions: is childhood violence exposure associated with (i) high-risk sexual behaviour in early adulthood and (ii) increased/decreased knowledge and uptake of HIV testing services.

A nationally representative sample of females aged 19-24 years were surveyed. Women were excluded from the analyses if they were not sexually active. Some 26.1% of 579 women reported childhood sexual violence (answering yes to one of four questions around unwanted touch / attempted rape / unwanted / coercive sexual intercourse before age 18 years). Childhood sexual violence was associated with (i) low / no condom use with someone other than husband / live in partner and (ii) >1 sexual partner, past 12 months. There was no association with knowledge or uptake of HIV testing services. These findings are consistent with research done elsewhere and suggest childhood sexual violence is associated with increased sexual risk taking behaviours in early adulthood. These findings present evidence for the importance of programmes to reduce childhood exposure to violence and focussed, adolescent-friendly sexual health services.

Incorporating acute HIV screening into routine HIV testing at sexually transmitted infection clinics and HIV testing and counseling centers in Lilongwe, Malawi.


Background and objectives: Integrating acute HIV infection (AHI) testing into clinical settings is critical to prevent transmission and realize potential treatment-as-prevention benefits. We evaluated acceptability of AHI testing and compared AHI prevalence at sexually transmitted infection (STI) and HIV testing and counseling (HTC) clinics in Lilongwe, Malawi.

Methods: We conducted HIV RNA testing for HIV-seronegative patients visiting STI and HTC clinics. AHI was defined as positive RNA and negative/discordant rapid antibody tests. We evaluated demographic, behavioral, and transmission-risk differences between STI and HTC patients and assessed performance of a risk-score for targeted screening.

Results: Nearly two-thirds (62.8%, 9280/14 755) of eligible patients consented to AHI testing. We identified 59 persons with AHI (prevalence=0.64%) - a 0.9% case-identification increase. Prevalence was higher at STI (1.03% (44/4255)) than HTC clinics (0.3% (15/5025), p<0.01), accounting for 2.3% of new diagnoses, vs 0.3% at HTC. Median viral load (VL) was 758 050 copies/ml; 25% (15/59) had VL ≥10 000 000 copies/ml. Median VL was higher at STI (1 000 000 copies/ml) compared to HTC (153 125 copies/ml, p=0.2). Among persons with AHI, those tested at STI clinics were more likely to report genital sores compared to those tested at HTC (54.6% versus 6.7%, p<0.01). The risk score algorithm performed well in identifying persons with AHI at HTC (sensitivity=73%, specificity=89%).
Conclusions: The majority of patients consented to AHI testing. AHI prevalence was substantially higher in STI clinics than HTC. Remarkably high VLs and concomitant genital sores demonstrates the potential for transmission. Universal AHI screening at STI clinics, and targeted screening at HTC centers, should be considered.

Abstract access

**Editor’s notes:** Acute HIV infection (AHI) is defined as the time from HIV acquisition to the appearance of detectable antibodies. Individuals with AHI are highly infectious, at least partly due to high viral load. Effective strategies to identify and treat people with AHI could increase the impact of treatment as prevention strategies, although there continues to be debate around the contribution of AHI to HIV transmission at population level.

This study in Malawi was part of a clinical trial evaluating the impact of behavioural and antiretroviral programmes during AHI. The study was done in four high-volume urban facilities. Pooled HIV RNA testing was performed on blood from participants with negative or discordant rapid HIV tests, according to the routine testing algorithm (discordant defined as one positive and two negative tests). Overall participation rates were relatively low, with only one in three individuals with negative or discordant rapid HIV tests included. Most of the loss was due to potentially eligible persons not being screened. The reasons for this are not mentioned, although more than a third that were screened did not consent. Overall, one in 150 participants had AHI. This was higher, at one in 100, at the STI clinics. The proportion with AHI was lower than previous research in Malawi, which could reflect a decline in HIV incidence at population level.

The potential risk of HIV transmission during AHI is highlighted by the characteristics of the people with AHI. Almost half had HIV RNA $>6 \log_{10}$ copies/ml, a similar proportion had genital ulcers, and only one in five reported condom use at last sex. The algorithm for focussing AHI testing, previously developed in the same setting, had suboptimal performance across all sites.

This study adds to a body of evidence that suggests testing for AHI is feasible and will increase the overall yield of HIV testing by a small amount. We now need more evidence around whether programmatic implementation of AHI testing would have an impact on HIV transmission, and on the cost-effectiveness of different testing strategies. Data from treatment as prevention trials, none of which have included specific strategies to diagnose AHI, will also indirectly inform whether this should become a higher priority for public health programmes.

**HIV-alcohol risk reduction interventions in sub-Saharan Africa: a systematic review of the literature and recommendations for a way forward.**


Sub-Saharan Africa bears 69% of the global burden of HIV, and strong evidence indicates an association between alcohol consumption, HIV risk behavior, and HIV incidence. However, characteristics of efficacious HIV-alcohol risk reduction interventions are not well known. The purpose of this systematic review is to summarize the characteristics and synthesize the findings of HIV-alcohol risk reduction interventions implemented in the region and reported in peer-reviewed journals. Of 644 citations screened, 19 met the inclusion criteria for this review. A discussion of methodological challenges, research gaps, and recommendations for future interventions is included. Relatively few interventions were found, and evidence is mixed about the efficacy of HIV-alcohol risk reduction interventions. There is a need to further integrate HIV-alcohol risk reduction components into HIV prevention programming and to document
results from such integration. Additionally, research on larger scale, multi-level interventions is needed to identify effective HIV-alcohol risk reduction strategies.

Abstract access

**Editor’s notes:** Alcohol and risk of HIV have been shown to be linked, yet little is known about which programmes are best at reducing this risk. This paper features a systematic review updating a previous review published by the authors in 2011. While this update found several more programmes aimed at reducing risky behaviour caused by alcohol use and in more countries than just the one previously, South Africa, the results of the review are largely the same. Most programmes had limited follow-up time of participants and found a dissipating effect over time. Additionally, older models of behaviour change were primarily used as the frameworks upon which these programmes were built. These models focus only on individual behaviour and not on the structural factors further affecting consumption of alcohol and risky sexual behaviour. On a positive note, some studies found moderate success based on location of the programme, clinic versus bar or tavern setting for instance. This review clearly demonstrates the need for further efforts to integrate alcohol risk reduction components into HIV prevention programmes, particularly for populations in which alcohol consumption is common.

Is the sexual behaviour of young people in sub-Saharan Africa influenced by their peers? A systematic review.


Adolescents in sub-Saharan Africa are highly vulnerable to HIV, other sexually transmitted infections (STIs) and unintended pregnancies. Evidence for the effectiveness of individual behaviour change interventions in reducing incidence of HIV and other biological outcomes is limited, and the need to address the social conditions in which young people become sexually active is clear. Adolescents’ peers are a key aspect of this social environment and could have important influences on sexual behaviour. There has not yet been a systematic review on the topic in sub-Saharan Africa. We searched 4 databases to find studies set in sub-Saharan Africa that included an adjusted analysis of the association between at least one peer exposure and a sexual behaviour outcome among a sample where at least 50% of the study participants were aged between 13 and 20 years. We classified peer exposures using a framework to distinguish different mechanisms by which influence might occur. We found 30 studies and retained 11 that met quality criteria. There were 3 cohort studies, 1 time to event and 7 cross-sectional. The 11 studies investigated 37 different peer exposure-outcome associations. No studies used a biological outcome and all asked about peers in general rather than about specific relationships. Studies were heterogeneous in their use of theoretical frameworks and means of operationalizing peer influence concepts. All studies found evidence for an association between peers and sexual behaviour for at least one peer exposure/outcome/sub-group association. Of all 37 outcome/exposure/sub-group associations tested, there was evidence for 19 (51%). There were no clear patterns by type of peer exposure, outcome or adolescent sub-group. There is a lack of conclusive evidence about the role of peers in adolescent sexual behaviour in sub-Saharan Africa. We argue that longitudinal designs, use of biological outcomes and approaches from social network analysis are priorities for future studies.

Abstract Full-text [free] access
Editor's notes: This is the first quantitative systematic review of the role of peers in shaping young people’s sexual behaviour in sub-Saharan Africa. Each of the 11 higher-quality studies included found evidence for at least one association between a peer exposure and a sexual behaviour outcome. But overall, no clear patterns were found for the conditions in which peer exposures might, or might not, impact sexual behaviour. The mixed findings may highlight inherent difficulties with assessing such associations, such as reverse causation in cross-sectional studies (e.g. selection of peers based on established sexual behaviour), and reliance on self-reported sexual behaviour (likely to be a particular problem among adolescents). One interesting aspect of the paper was the classification of peer exposures into one of six types (including peer approval, peer connectedness, and status within peer networks). Given the likely importance of peers in adolescent behaviour, methods that collect information about specific peers and relationships such as social network analysis, rather than asking about peers in general, could help to identify peer effects.

Recruiting male partners for couple HIV testing and counselling in Malawi’s option B+ programme: an unblinded randomised controlled trial.


Background: Couples HIV testing and counselling (CHTC) is encouraged but is not widely done in sub-Saharan Africa. We aimed to compare two strategies for recruiting male partners for CHTC in Malawi’s option B+ prevention of mother-to-child transmission programme: invitation only versus invitation plus tracing and postulated that invitation plus tracing would be more effective.

Methods: We did an unblinded, randomised, controlled trial assessing uptake of CHTC in the antenatal unit at Bwaila District Hospital, a maternity hospital in Lilongwe, Malawi. Women were eligible if they were pregnant, had just tested HIV-positive and therefore could initiate antiretroviral therapy, had not yet had CHTC, were older than 18 years or 16-17 years and married, reported a male sex partner in Lilongwe, and intended to remain in Lilongwe for at least 1 month. Women were randomly assigned (1:1) to either the invitation only group or the invitation plus tracing group with block randomisation (block size=4). In the invitation only group, women were provided with an invitation for male partners to present to the antenatal clinic. In the invitation plus tracing group, women were provided with the same invitation, and partners were traced if they did not present. When couples presented they were offered pregnancy information and CHTC. Women were asked to attend a follow-up visit 1 month after enrolment to assess social harms and sexual behaviour. The primary outcome was the proportion of couples who presented to the clinic together and received CHTC during the study period and was assessed in all randomly assigned participants. This study is registered with ClinicalTrials.gov, number NCT02139176.

Findings: Between March 4, 2014, and Oct 3, 2014, 200 HIV-positive pregnant women were enrolled and randomly assigned to either the invitation only group (n=100) or the invitation plus tracing group (n=100). 74 couples in the invitation plus tracing group and 52 in the invitation only group presented to the clinic and had CHTC (risk difference 22%, 95% CI 9-35; p=0.001) during the 10 month study period. Of 181 women with follow-up data, two reported union dissolution, one reported emotional distress, and none reported intimate partner violence. One male partner, when traced, was confused about which of his sex partners was enrolled in the study. No other adverse events were reported.

Interpretation: An invitation plus tracing strategy was highly effective at increasing CHTC uptake. Invitation plus tracing with CHTC could have many substantial benefits if brought to scale.
Abstract access

Editor’s notes: A major challenge to the Option B+ prevention of mother-to-child-transmission programme is retaining women in HIV care. Lack of male partner support may be an important barrier to retention. Couples HIV testing and counselling (CHTC) can increase mutual disclosure, enhance behavioural HIV prevention, and ultimately improve maternal, child and male partner health outcomes. However, uptake of CHTC in antenatal settings remains low throughout most of sub-Saharan Africa. This randomised controlled trial illustrates that combining an invitation for the male partner to present to the antenatal clinic with active tracing of the partner by the study team greatly increased uptake of CHTC. A unique feature of the programme was that the invitation and tracing messages focused on general health during pregnancy, rather than on HIV, which may have improved acceptability. Even in the invitation alone arm, over half of the male partners presented for CHTC. Both strategies found that over half the men who tested were HIV positive, and the majority were unaware of their status. Women in the invitation plus tracing arm had higher retention in the Option B+ programme at one month than individuals in the invitation alone arm, and were more likely to report safer sex behaviour.

Although provider-based strategies for increasing couples testing are more expensive than patient-based strategies, they may be very cost-effective in settings of high HIV prevalence where few men are aware of their HIV status. Interestingly, most gains in partner uptake from tracing were a result of telephone contact, which is relatively low cost. Longer term follow-up is necessary to assess whether increases in retention are maintained over time but the results demonstrate the potential for provider-based strategies for increasing CHTC to help achieve UNAIDS 90-90-90 targets.

2. Prevent HIV among drug users

Hepatitis C and HIV incidence and harm reduction program use in a conflict setting: an observational cohort of injecting drug users in Kabul, Afghanistan.


Background: Armed conflict may increase the risk of HIV and other pathogens among injecting drug users (IDUs); however, there are few prospective studies. This study aimed to measure incidence and potential predictors, including environmental events and needle and syringe distribution and collection program (NSP) use, of hepatitis C virus (HCV) and HIV among IDUs in Kabul, Afghanistan.

Methods: Consenting adult IDUs completed interviews quarterly in year 1 and semi-annually in year 2 and HCV and HIV antibody testing semi-annually through the cohort period (November 2007-December 2009). Interviews detailed injecting and sexual risk behaviors, NSP service use, and conflict-associated displacement. Quarters with peak conflict or local displacement were identified based on literature review, and key events, including insurgent attacks and deaths, were reported with simple counts. Incidence and predictors of HCV and HIV were measured with Cox proportional hazards models.

Results: Of 483 IDUs enrolled, 385 completed one or more follow-up visits (483.8 person-years (p-y)). All participants were male with a median age of 28 years and a median duration of injecting of 2 years. Reported NSP use among the participants ranged from 59.9 to 70.5 % in the
first year and was 48.4 and 55.4 % at 18 and 24 months, respectively. There were 41 confirmed deaths, with a crude death rate of 93.4/1000 p-y (95 % confidence interval (CI) 67.9-125) and overdose as the most common cause. HCV and HIV incidence were 35.6/100 p-y (95 % CI 28.3-44.6) and 1.5/100 p-y (95 % CI 0.6-3.3), respectively. Changing from injecting to smoking was protective for HCV acquisition (adjusted hazard ratio (AHR) = 0.53, 95 % CI 0.31-0.92), while duration of injecting (AHR = 1.09, 95 % CI 1.01-1.18/year) and sharing syringes (AHR = 10.09, 95 % CI 1.01-10.3) independently predicted HIV infection.

Conclusion: There is high HCV incidence and high numbers of reported deaths among male Kabul IDUs despite relatively consistent levels of harm reduction program use; peak violence periods did not independently predict HCV and HIV risk. Programming should increase awareness of HCV transmission and overdose risks, prepare clients for harm reduction needs during conflict or other causes of displacement, and continue efforts to engage community and police force support.

3. 15 million accessing treatment

Abacavir, zidovudine, or stavudine as paediatric tablets for African HIV-infected children (CHAPAS-3): an open-label, parallel-group, randomised controlled trial.


Background: WHO 2013 guidelines recommend universal treatment for HIV-infected children younger than 5 years. No paediatric trials have compared nucleoside reverse-transcriptase inhibitors (NRTIs) in first-line antiretroviral therapy (ART) in Africa, where most HIV-infected children live. We aimed to compare stavudine, zidovudine, or abacavir as dual or triple fixed-dose-combination paediatric tablets with lamivudine and nevirapine or efavirenz.

Methods: In this open-label, parallel-group, randomised trial (CHAPAS-3), we enrolled children from one centre in Zambia and three in Uganda who were previously untreated (ART naive) or on
stavudine for more than 2 years with viral load less than 50 copies per mL (ART experienced). Computer-generated randomisation tables were incorporated securely within the database. The primary endpoint was grade 2-4 clinical or grade 3/4 laboratory adverse events. Analysis was intention to treat. This trial is registered with the ISRCTN Registry number, 69078957.

Findings: Between Nov 8, 2010, and Dec 28, 2011, 480 children were randomised: 156 to stavudine, 159 to zidovudine, and 165 to abacavir. After two were excluded due to randomisation error, 156 children were analysed in the stavudine group, 158 in the zidovudine group, and 164 in the abacavir group, and followed for median 2.3 years (5% lost to follow-up). 365 (76%) were ART naive (median age 2.6 years vs 6.2 years in ART experienced). 917 grade 2-4 clinical or grade 3/4 laboratory adverse events (835 clinical [634 grade 2]; 40 laboratory) occurred in 104 (67%) children on stavudine, 103 (65%) on zidovudine, and 105 (64%), on abacavir (p=0.63; zidovudine vs stavudine: hazard ratio [HR] 0.99 [95% CI 0.75-1.29]; abacavir vs stavudine: HR 0.88 [0.67-1.15]). At 48 weeks, 98 (85%), 81 (80%) and 95 (81%) ART-naive children in the stavudine, zidovudine, and abacavir groups, respectively, had viral load less than 400 copies per mL (p=0.58); most ART-experienced children maintained suppression (p=1.00).

Interpretation: All NRTIs had low toxicity and good clinical, immunological, and virological responses. Clinical and subclinical lipodystrophy was not noted in those younger than 5 years and anaemia was no more frequent with zidovudine than with the other drugs. Absence of hypersensitivity reactions, superior resistance profile and once-daily dosing favours abacavir for African children, supporting WHO 2013 guidelines.

Abstract Full-text [free] access

Editor’s notes: Since 2013, the World Health Organization (WHO) has recommended abacavir as the preferred first-line nucleoside reverse transcriptase inhibitor (NRTI) in children. This recommendation was largely based on expert opinion, observational studies and issues such as cost and availability as a fixed dose combinations (FDC).

The CHAPAS-3 open-label trial is the only trial in African children that has conducted a direct head-to-head comparison of the three most relevant NRTIs (abacavir, stavudine and zidovudine) used for paediatric treatment. These were co-formulated in non-NRTI/NRTI generic fixed-dose combination paediatric tablets, with dosing based on WHO drug ratios and weight bands. The other drugs in the triple regimen were lamivudine with either efavirenz or nevirapine.

The primary aim of the trial was a comparison of the toxicity profile of the three NRTIs. The trial found no major difference in any adverse event or toxicity endpoint during nearly two and a half years of follow-up in both ART-naive and ART-experienced children. There were no hypersensitivity reactions to abacavir, in agreement with other studies that have reported its rarity in Africans. Haemoglobin increased regardless of the NRTI and severe anaemia occurred no more frequently in children who received zidovudine versus children who received either of the two other drugs. This should reassure clinicians that zidovudine substitution is rarely necessary for anaemia among children on ART. However, an important caveat is that severe anaemia was an exclusion criteria in the trial. Clinical lipodystrophy was also rare. This is in contrast to older children and adolescents where lipodystrophy is much more common. At least in young children, stavudine could be safely used if other alternatives are not available, supporting WHO guidelines that stavudine for children should not be discontinued completely.

Overall, CHAPAS-3 demonstrates that children respond well to all NRTI/non-NRTI recommended FDCs with minimal toxicity. Unlike previous trials, there was no difference in immunological or
virologic outcomes between the three drugs. Importantly, choice of the NRTI backbone should not be a barrier to widening treatment access globally for HIV-positive children. Children receiving abacavir in their first-line regimen who had unsuppressed viral load at the end of the study were less likely to have resistance mutations compromising second-line NRTIs. In addition to its excellent tolerability profile, abacavir is the only NRTI available as a once-daily FDC licenced for children. This would support WHO recommendation of abacavir as the first choice NRTI in children. However, it does remain more expensive than the other two NRTIs and further price reductions will be required if abacavir use is to be widened.

Communication in the context of family caregiving: an exploratory study of Ugandan children on antiretroviral therapy.

It is important to consider the complexities of family dynamics when deciding when and how to communicate with HIV-infected children about their illness and treatment. Previous research has focused on providers' and caregivers' perspectives on whether, when and how to disclose HIV/AIDS diagnosis and treatment to HIV-infected children. From the perspective of HIV-infected children, communication does not mean just giving information about illness and treatment, but also encompasses emotional and material care. This paper places communication within the broader framework of caregiving in family situations. This exploratory study was conducted in Jinja district, Uganda, between November 2011 and December 2012. Through participant observation and in-depth interviews, communication by, and with, HIV-infected children in the context of family situations was explored from the perspectives of 29 HIV-infected children aged 8-17 years on antiretroviral therapy (ART) using content thematic analysis. Children's communication with caregivers about their illness and treatment varied depending on whom they were living with and the nature of caregiving. Although a mother's care was considered best, children described others who cared 'like a mother'. For some, caregiving was distributed among several relatives and non-relatives, while others felt they had hardly anyone to care for them. Caregiving from the children's perspective involved emotional support, expressed verbally and explicitly in messages of concern, encouragement conveyed in reminders to take medicines, attention when sick and confidential conversations about the challenges of having HIV and taking ART. Caregiving was also communicated implicitly in acts of provision of food/drinks to take with medicines, counting pills to confirm they had taken the medicines and accompanying children to treatment centres. Children's communication about their health and medicines and the care they received was to a large extent shaped by the nature of their relatedness to their caregivers, the extent to which caregiving was dispersed among several people and who else in the household was infected with HIV and on medication.

Abstract access

Editor's notes: The majority of children who acquire HIV are infected perinatally. This makes HIV unique among paediatric conditions to the extent that mothers may be ill or deceased. The family plays a vital role in the treatment and care of children, including individuals living with HIV. The family context is an important consideration when supporting children to adhere to care. It also affects decisions on how and when to communicate with children about their illness and treatment. The authors argue that for children living with HIV, communication is not just the transmission of factual information, but also the conveying of concern, feelings of affection and implicit messages of support,
as well as their opposites. This is particularly important in the context of loss and family disruption; stigma and discrimination; and dislocation from siblings and other family when children are cared for by new carers.

This qualitative paper draws on ethnographic data collected between 2011 and 2012 in eastern Uganda through in-depth interviews and participant observation. A total of 29 children living with HIV aged between eight and 17 years and on ART were followed up for one year. Children were purposively sampled to include different ages, sexes and family status (residence, orphan status), education levels and disclosure statuses.

The study draws on the concept of ‘relatedness’ in order to understand the meaning of communication in the context of family caregiving. It highlights that communication by, and with children living with HIV, extends beyond the transmission of information to being structured around a much broader relationship of care. This has important implications for treatment centres as the person that a child lives with may not always be their main caregiver. This framing incorporates a broader understanding of caregiving to include both emotional and material support which may be delivered both explicitly and implicitly through words and deeds.

The effectiveness of routine opt-out HIV testing for children in Harare, Zimbabwe.


Objective: HIV testing is the entry point to access HIV care. For HIV-infected children who survive infancy undiagnosed, diagnosis usually occurs on presentation to health care services. We investigated the effectiveness of routine opt-out HIV testing (ROOT) compared to conventional opt-in provider-initiated testing and counselling (PITC) for children attending primary care clinics.

Methods: Following an evaluation of PITC services for children aged 6 to 15 years in six primary health care facilities in Harare, Zimbabwe, ROOT was introduced through a combination of interventions. The change in the proportion of eligible children offered and receiving HIV tests, reasons for not testing, and yield of HIV positive diagnoses were compared between the two HIV testing strategies. Adjusted risk ratios for having an HIV test in the ROOT compared to the PITC period were calculated.

Results: There were 2831 and 7842 children eligible for HIV testing before and after the introduction of ROOT. The proportion of eligible children offered testing increased from 76% to 93% and test uptake improved from 71% to 95% in the ROOT compared to the PITC period. The yield of HIV diagnoses increased from 2.9% to 4.5%, and a child attending the clinics post intervention had a 1.99 increased adjusted risk (95% CI 1.85-2.14) of receiving an HIV test in the ROOT period compared to the pre-intervention period.

Conclusion: ROOT increased the proportion of children undergoing HIV-testing, resulting in an overall increased yield of positive diagnoses, compared to PITC. ROOT provides an effective approach to reduce missed HIV diagnosis in this age-group.

Abstract access

Editor’s notes: The policy and practice of HIV testing in high HIV prevalence settings has evolved over the years, from a more cautious approach in the early years of the HIV epidemic to a more proactive one with the scale up of antiretroviral therapy (ART). Despite a marked increase in HIV
testing following the introduction of provider-initiated testing and counselling (PITC) in clinical settings, coverage remains suboptimal. Routine opt-out testing (ROOT) describes a strategy of HIV testing as part of the routine clinical ‘work-up’, unless a person explicitly refuses to test. To date, ROOT has been confined to specialist clinical services, such as prevention of mother-to-child HIV transmission programmes, sexual health clinics and tuberculosis services.

This study in primary care facilities in Harare compared the effectiveness of ROOT with PITC in children aged six to 15 years, a group for whom opportunities to receive HIV testing have been limited. The authors found that a 22% increase in the proportion of eligible children offered testing following the introduction of ROOT; a 34% increase in the proportion of HIV test uptake; and a 55% increase in proportion of children testing HIV positive (yield). Importantly, the increase in proportion of children to whom testing was offered, test uptake and yield compared to opt-in PITC was sustained over the 1.5 years follow-up period. Factors postulated to have resulted in improved testing and uptake included the removal of the decision of whether to test from the guardian and healthcare worker and decreased stigma associated with opt-out testing. The authors also acknowledge that investment in training and human resource capacity likely contributed to improvements seen. Further, as stated by the authors, HIV testing must be accompanied by effective strategies to ensure linkage to care in order to improve health outcomes in this population.

Age in antiretroviral therapy programmes in South Africa: a retrospective, multicentre, observational cohort study.


Background: As access to antiretroviral therapy (ART) expands, increasing numbers of older patients will start treatment and need specialised long-term care. However, the effect of age in ART programmes in resource-constrained settings is poorly understood. The HIV epidemic is ageing rapidly and South Africa has one of the highest HIV population prevalences worldwide. We explored the effect of age on mortality of patients on ART in South Africa and whether this effect is mediated by baseline immunological status.

Methods: In this retrospective cohort analysis, we studied HIV-positive patients aged 16-80 years who started ART for the first time in six large South African cohorts of the International Epidemiologic Databases to Evaluate AIDS-Southern Africa collaboration, in KwaZulu-Natal, Gauteng, and Western Cape (two primary care clinics, three hospitals, and a large rural cohort). The primary outcome was mortality. We ascertained patients' vital status through linkage to the National Population Register. We used inverse probability weighting to correct mortality for loss to follow-up. We estimated mortality using Cox's proportional hazards and competing risks regression. We tested the interaction between baseline CD4 cell count and age.

Findings: Between Jan 1, 2004, and Dec 31, 2013, 84 078 eligible adults started ART. Of these, we followed up 83 566 patients for 174 640 patient-years. 8% (1817 of 23 258) of patients aged 16-29 years died compared with 19% (93 of 492) of patients aged 65 years or older. The age adjusted mortality hazard ratio was 2.52 (95% CI 2.01-3.17) for people aged 65 years or older compared with those 16-29 years of age. In patients starting ART with a CD4 count of less than 50 cells per µL, the adjusted mortality hazard ratio was 2.52 (2.04-3.11) for people aged 50 years or older compared with those 16-39 years old. Mortality was highest in patients with CD4 counts of less than 50 cells per µL, and 15% (1103 of 7295) of all patients aged 50 years or older starting ART were in this group. The proportion of patients aged 50 years or older enrolling in
ART increased with successive years, from 6% (290 of 4999) in 2004 to 10% (961 of 9657) in 2012-13, comprising 9% of total enrolment (7295 of 83 566). At the end of the study, 6304 (14%) of 44 909 patients still alive and in care were aged 50 years or older.

Interpretation: Health services need reorientation towards HIV diagnosis and starting of ART in older individuals. Policies are needed for long-term care of older people with HIV.

Abstract access

Editor’s notes: This article reports on a retrospective cohort analysis that examined the effect of age on mortality of people starting antiretroviral therapy (ART) in South Africa. Previous studies already illustrated higher mortality and lower risk of loss to follow-up in older people compared to younger adults on ART. Older people on ART also experience poorer immunological recovery on ART.

The investigators used data from six South African cohorts. Their dataset, with more than 80 000 people who started ART between 2004 and 2013, included much larger numbers of older adults than previously reported, particularly in low and middle income countries. This enabled the investigators to look at baseline characteristics of older people at ART initiation, such as CD4 count, and their association with mortality, which may not have been possible in analysis of single cohorts.

The authors found increasing proportions of people older than 50 years, initiating ART in successive years, from 6% in 2004 to 10% in 2013. They affirmed findings from previous studies that mortality increased with age at ART initiation, while loss to follow-up did not. They also affirmed that immunological recovery was diminished in older people, with smaller gains in CD4 cell count at older age than at younger ages.

Interestingly they found that the effect of age on mortality was strongest among individuals with the lowest baseline CD4 cell counts (lower than 50 cells/mm$^3$). Older people were 2.5 times more likely to die compared to younger people in this group. In people with higher CD4 cell counts (more than 200 cells/mm$^3$) the effect of age at ART initiation was less strong. Moreover some 15% of people aged 50 years or older started ART at CD4 cell counts of less than 50 cells /mm$^3$, and should thus be prioritised as a key group of people requiring additional attention in ART programmes.

The lack of HIV prevention and testing strategies for older people may be one of the reasons for delayed diagnosis and late ART initiation. In addition, health care workers are less likely to consider an HIV diagnosis in older people.

The authors suggest that some of these older people may be long-term survivors despite the absence of ART, and further research into this could be valuable.

4. Avoid TB deaths

Causes of hospital admission among people living with HIV worldwide: a systematic review and meta-analysis.


Background: Morbidity associated with HIV infection is poorly characterised, so we aimed to investigate the contribution of different comorbidities to hospital admission and in-hospital mortality in adults and children living with HIV worldwide.
Methods: Using a broad search strategy combining terms for hospital admission and HIV infection, we searched MEDLINE via PubMed, Embase, Web of Science, LILACS, AIM, IMEMR and WPIMR from inception to Jan 31, 2015, to identify studies reporting cause of hospital admission in people living with HIV. We focused on data reported after 2007, the period in which access to antiretroviral therapy started to become widespread. We estimated pooled proportions of hospital admissions and deaths per disease category by use of random-effects models. We stratified data by geographical region and age.

Findings: We obtained data from 106 cohorts, with reported causes of hospital admission for 313 006 adults and 618 2 children living with HIV. For adults, AIDS-related illnesses (25 119 patients, 46%, 95% CI 40-53) and bacterial infections (14 034 patients, 31%, 20-42) were the leading causes of hospital admission. These two categories were the most common causes of hospital admission for adults in all geographical regions and the most common causes of mortality. Common region-specific causes of hospital admission included malnutrition and wasting, parasitic infections, and haematological disorders in the Africa region; respiratory disease, psychiatric disorders, renal disorders, cardiovascular disorders, and liver disease in Europe; haematological disorders in North America; and respiratory, neurological, digestive and liver-related conditions, viral infections, and drug toxicity in South and Central America. For children, AIDS-related illnesses (783 patients, 27%, 95% CI 19-34) and bacterial infections (1190 patients, 41%, 26-56) were the leading causes of hospital admission, followed by malnutrition and wasting, haematological disorders, and, in the African region, malaria. Mortality in individuals admitted to hospital was 20% (95% CI 18-23, 12 902 deaths) for adults and 14% (10-19, 643 deaths) for children.

Interpretation: This review shows the importance of prompt HIV diagnosis and treatment, and the need to reinforce existing recommendations to provide chemoprophylaxis and vaccination against major preventable infectious diseases to people living with HIV to reduce serious AIDS and non-AIDS morbidity.
prevent the complications of advanced HIV disease. It also underscores the need for better coverage of screening for tuberculosis and preventive therapy for people without active disease.

Effect of an integrated community-based package for maternal and newborn care on feeding patterns during the first 12 weeks of life: a cluster-randomized trial in a South African township.


Objective: To analyse the effect of community-based counselling on feeding patterns during the first 12 weeks after birth, and to study whether the effect differs by maternal HIV status, educational level or household wealth.

Design: Cluster-randomized trial with fifteen clusters in each arm to evaluate an integrated package providing two pregnancy and five postnatal home visits delivered by community health workers. Infant feeding data were collected using 24 h recall of nineteen food and fluid items.

Setting: A township near Durban, South Africa.

Subjects: Pregnant women (1894 intervention and 2243 control) aged 17 years or more.

Results: Twelve weeks after birth, 1629 (intervention) and 1865 (control) mother-infant pairs were available for analysis. Socio-economic conditions differed slightly across intervention groups, which were considered in the analyses. There was no effect on early initiation of breast-feeding. **At 12 weeks of age the intervention doubled exclusive breast-feeding** (OR=2.29; 95 % CI 1.80, 2.92), **increased exclusive formula-feeding** (OR=1.70; 95 % CI 1.28, 2.27), **increased predominant breast-feeding** (OR=1.71; 95 % CI 1.34, 2.19), **decreased mixed formula-feeding** (OR=0.68; 95 % CI 0.55, 0.83) and **decreased mixed breast-feeding** (OR=0.54; 95 % CI 0.44, 0.67). **The effect on exclusive breast-feeding at 12 weeks was stronger among HIV-negative mothers than HIV-positive mothers (P=0.01), while the effect on mixed formula-feeding was significant only among HIV-positive mothers (P=0.03).** The effect on exclusive feeding was not different by household wealth or maternal education levels.

Conclusions: A perinatal intervention package delivered by community health workers was effective in increasing exclusive breast-feeding, exclusive formula-feeding and decreasing mixed feeding.

Abstract access

**Editor’s notes:** This trial assesses the provision of an integrated package of motivational interviewing-based counselling during home visits by systematically supervised, remunerated full-time community health workers on breastfeeding practices. It found stronger effects among HIV negative mothers than mothers living with HIV. This is particularly important in the context of a setting where exclusive breast feeding is practised by only 8% of mothers and where messages have been mixed about the safety of breastfeeding among mothers living with HIV. The smaller effect among mothers living with HIV may be a legacy of the free provision of formula to these mothers from 2002 to 2011, and cultural feeding practices. Exit interviews with the community health workers revealed that no mothers had exclusively breast-fed their babies, and this may have influenced their delivery of the programme. Further work is necessary to communicate messages on the need for exclusive breast feeding among mothers living with HIV.
5. Close the resource gap

Costs of HIV/AIDS treatment in Indonesia by time of treatment and stage of disease.


Background: We report an economic analysis of Human Immunodeficiency Virus (HIV) care and treatment in Indonesia to assess the options and limitations of costs reduction, improving access, and scaling up services.

Methods: We calculated the cost of providing HIV care and treatment in a main referral hospital in West Java, Indonesia from 2008 to 2010, differentiated by initiation of treatment at different CD4 cell count levels (0-50, 50-100, 100-150, 150-200, and >200 cells/mm$^3$); time of treatment; HIV care and opportunistic infections cost components; and the costs of patients for seeking and undergoing care.

Discussion: Before antiretroviral treatment (ART) initiation, costs were dominated by laboratory tests (>65 %), and after initiation, by antiretroviral drugs (≥60 %). Average treatment costs per patient decreased with time on treatment (e.g. from US$580 per patient in the first 6 month to US$473 per patient in months 19-24 for those with CD4 cell counts under 50 cells/mm$^3$). Higher CD4 cell counts at initiation resulted in lower laboratory and opportunistic infection treatment costs. Transportation cost dominated the costs of patients for seeking and undergoing care (>40 %).

Conclusions: Costs of providing ART are highest during the early phase of treatment. Costs reductions can potentially be realized by early treatment initiation and applying alternative laboratory tests with caution. Scaling up ART at the community level in certain high prevalence settings may improve early uptake, adherence, and reduce transportation costs.

Abstract Full-text [free] access

Editor’s notes: There is a growing evidence base on the costs of HIV treatment and care, however much of the evidence to date is from sub-Saharan African settings. A review conducted by Siapka et al. in 2014 found 31 studies reporting unit costs for antiretroviral therapy, only 10 of which were outside of Africa and only four of which were set in Asia and the Pacific. This study provides necessary evidence on ART costs in Indonesia. This will be important for Indonesian policy makers as they seek to scale up HIV treatment - especially in the context of recent guideline reforms for ART provision.

Findings from this study largely confirm what has been found elsewhere. Antiretroviral drug costs are primary cost drivers, followed closely by treatment of opportunistic infections. Costs of ART provision are therefore highest during the treatment initiation phase, and drop off as people are established on care. For the same reason, this study also found that costs for treating people with a CD4 count > 200 were significantly lower than costs for treating people with a CD4 count < 200.

Unit costs per person per year range from $1699 to $2346. This is higher than previously published costs from studies in Thailand, Viet Nam and India, as reported by Siapka et al. It is difficult to tell whether it is representative of ART costs generally in Indonesia as this is the first study reporting costs from this country.

The authors note that delivering HIV treatment at the community level may reduce costs. It is difficult to tell from the results of this study whether this is indeed the case, as costs are estimated for only one health facility (the largest public referral hospital in West Java province). However, it poses an
interesting question for further research. Further evidence on costs for provision of HIV treatment and care across a variety of settings in Indonesia would improve policy relevance and help decision-makers identify potential avenues for improving efficiency.

6. Eliminate stigma and discrimination

Feasibility of a combination HIV prevention program for men who have sex with men in Blantyre, Malawi.


Introduction: The use of combination HIV prevention interventions (CHPI) now represent the standard of care to minimize HIV acquisition risks among men who have sex with men (MSM). There has been limited evaluation of these approaches in generalized HIV epidemics and/or where MSM are stigmatized. A peer-based CHPI program to target individual, social, and structural risks for HIV was developed for MSM in Blantyre, Malawi.

Methods: To test the feasibility of CHPI, adult MSM were followed prospectively from January 2012 to May 2013. Participants (N = 103) completed sociobehavioral surveys and HIV testing at each of the 3 follow-up study visits.

Results: Approximately 90% of participants attended each study visit and 93.2% (n = 96) completed the final visit. Participants met with peer educators a median of 3 times (range: 1-10) in the follow-up visits 2 and 3. Condom use at last sex improved from baseline through follow-up visit 3 with main (baseline: 62.5%, follow-up 3: 77.0%; P = 0.02) and casual male partners (baseline: 70.7%, follow-up 3: 86.3%; P = 0.01). Disclosure of sexual behaviors/orientation to family increased from 25% in follow-up 1 to 55% in follow-up 3 (P < 0.01).

Discussion: Participants maintained a high level of retention in the study highlighting the feasibility of leveraging community-based organizations to recruit and retain MSM in HIV prevention and treatment interventions in stigmatizing settings. Group-level changes in sexual behavior and disclosure in safe settings for MSM were noted. CHPI may represent a useful model to providing access to other HIV prevention for MSM and aiding retention in care and treatment services for MSM living with HIV in challenging environments.

Abstract access

Editor’s notes: Gay men and other men who have sex with men are a key, difficult-to-reach population in many parts of sub-Saharan Africa. Stigma and criminalization of same-sex practices cause many challenges in improving access to HIV prevention and treatment services. This study tested the feasibility of a combination HIV prevention programme for gay men and other men who have sex with men in Malawi. The programme worked at three levels. At the individual level peer educators provided outreach to increase use of condoms, lubricants and other prevention methods. The health sector level provided training for doctors and nurses, to improve access to services. The community level built capacity to advocate in national HIV strategies and support decriminalisation of homosexuality. Study participants were identified by respondent-driven sampling. Retention was very high in the cohort, and over 16 months, participants reported improved behaviour-associated outcomes. This study was implemented by a community-based organisation and peer educators, and used several methods to protect participant confidentiality and privacy which can be adopted by
others working in stigmatising settings. Overall, the study demonstrates that HIV prevention programmes for gay men and other men who have sex with men can be implemented if security measures and awareness of the social and political situation are well maintained.

7. Strengthening HIV integration

HIV/AIDS in South Africa: how many people died from the disease between 1997 and 2010?


Objectives: Empirical estimates of the number of HIV/AIDS deaths are important for planning, budgeting, and calibrating models. However, there is an extensive misattribution of HIV/AIDS as an underlying cause-of-death. This study estimates the true numbers of AIDS deaths from South African vital statistics between 1997 and 2010.

Methods: Individual-level cause-of-death data were grouped according to a local burden of disease list and source causes (i.e. causes under which AIDS deaths are misclassified) that recorded a rapid increase. After adjusting for completeness of registration, mortality rate of the source causes, by age and sex, was regressed on lagged HIV prevalence to estimate the rate of increase correlated with HIV. Background trends in the source-cause mortality rates were estimated from the trend experienced among 75-84 year olds.

Results: Of 214 causes considered, 19 were identified as potential sources for cause misattribution. High proportions of deaths from tuberculosis, lower respiratory infections (mostly pneumonia), diarrhoeal diseases, and ill-defined natural causes were estimated to be HIV-related, with only 7% of the estimated AIDS deaths being recorded as HIV. Estimated HIV/AIDS deaths increased rapidly, then reversed after 2006, totalling 2.8 million deaths over the whole period. The number was lower than model estimates from UNAIDS and the Global Burden of Disease Study.

Conclusion: Empirically based estimates confirm the considerable loss of life from HIV/AIDS and should be used for calibrating models of the AIDS epidemic which generally appear too low for infants but too high for other ages. Doctors are urged to specify HIV on death notifications to provide reliable cause-of-death statistics.

Abstract access

Editor’s notes: In many countries, the true number of HIV-associated deaths is significantly under-reported in national vital registration data making it difficult to monitor the epidemic trends from this source. This study describes new estimates of HIV-associated mortality based on empirical vital registration data which aimed to provide accurate estimates of the numbers of HIV-associated deaths in South Africa. The study estimates that, from 1997-2010, 2.86 million deaths in South Africa were due to HIV – over one-third of all deaths. However, relatively few deaths, 7%, were registered as HIV-associated. At the peak of the epidemic in 2006 the vital registration derived estimates show lower trends than other models. All models estimated a decline in the number of HIV-associated deaths post-2008, a finding which is consistent with the extensive roll-out of antiretroviral therapy in South Africa, and with trends reported from verbal autopsy data for all deaths in rural South African demographic surveillance sites. This paper highlights the importance of reporting accurate causes for HIV-associated deaths in the death registration process - however, without de-stigmatisation of HIV, this is going to be difficult to achieve.
Uptake and yield of HIV testing and counselling among children and adolescents in sub-Saharan Africa: a systematic review.


Introduction: In recent years children and adolescents have emerged as a priority for HIV prevention and care services. We conducted a systematic review to investigate the acceptability, yield and prevalence of HIV testing and counselling (HTC) strategies in children and adolescents (5 to 19 years) in sub-Saharan Africa.

Methods: An electronic search was conducted in MEDLINE, EMBASE, Global Health and conference abstract databases. Studies reporting on HTC acceptability, yield and prevalence and published between January 2004 and September 2014 were included. Pooled proportions for these three outcomes were estimated using a random effects model. A quality assessment was conducted on included studies.

Results and discussion: A total of 16 380 potential citations were identified, of which 21 studies (23 entries) were included. Most studies were conducted in Kenya (n=5) and Uganda (n=5) and judged to provide moderate (n=15) to low quality (n=7) evidence, with data not disaggregated by age. Seven studies reported on provider-initiated testing and counselling (PITC), with the remainder reporting on family-centred (n=5), home-based (n=5), outreach (n=5) and school-linked HTC among primary schoolchildren (n=1). PITC among inpatients had the highest acceptability (86.3%; 95% confidence interval [CI]: 65.5 to 100%), yield (12.2%; 95% CI: 6.1 to 18.3%) and prevalence (15.4%; 95% CI: 5.0 to 25.7%). Family-centred HTC had lower acceptance compared to home-based HTC (51.7%; 95% CI: 10.4 to 92.9% vs. 84.9%; 95% CI: 74.4 to 95.4%) yet higher prevalence (8.4%; 95% CI: 3.4 to 13.5% vs. 3.0%; 95% CI: 1.0 to 4.9%). School-linked HTC showed poor acceptance and low prevalence.

Conclusions: While PITC may have high test acceptability priority should be given to evaluating strategies beyond healthcare settings (e.g. home-based HTC among families) to identify individuals earlier in their disease progression. Data on linkage to care and cost-effectiveness of HTC strategies are needed to strengthen policies.

Abstract Full-text [free] access

Editor’s notes: In sub-Saharan Africa children and adolescents are a priority group for HIV prevention and care services. Children and adolescents living with HIV are less likely than adults to know their HIV status, to access treatment and to achieve virologic suppression. As with adults, the first essential step to managing HIV in children and adolescents is to provide appropriate HIV testing and counselling services. This is the first systematic review to assess HIV testing and counselling strategies in this age group, 5-19 years. One key finding is the lack of data on testing and counselling services for this age group. Most services replicate strategies developed for adults with little consideration for the specific needs of children and adolescents. The studies illustrated that health care facility-based provider-initiated testing and counselling had relatively high acceptance, yield and linkage-to-care, but tended to identify individuals at a late stage of disease. In contrast, community-based approaches had the potential to diagnose asymptomatic children. Further work on innovative approaches, family-centred and mobile-based, should be assessed.