Evidence from the field: missed opportunities for identifying and linking HIV-infected children for early initiation of ART

Dick Chamla[a], Dorothy Mbori-Ngacha[b], Morkor Newman[c], Scott E. Kellerman[d], Nandita Sugandhi[e], Anath Rwebembera[f], Peter Elyanu[g], Joseph Murungu[h], Charles Kiyaga[g], Chewe Luo[a], Craig McClure[a], The Child Survival Working Group of the Interagency Task Team on the Prevention, Treatment of HIV infection in Pregnant Women, Mothers, Child

AIDS 2013, **27** (Suppl 2):S139–S146

Introduction

The global plan to eliminate mother-to-child HIV transmission (eMTCT) and reduce HIV-related child mortality has made substantial progress since it was first announced in 2011 [1]. In low and middle-income countries (LMIC), where the majority of these infections occur, a 35% decline in new pediatric HIV infections has been observed between 2009 and 2012 [2]. Despite this progress, there is an estimated 210 000 infants born with HIV among the 21 eMTCT priority countries (where 90% of infections occur) in 2012 and challenges remain in identifying HIV-infected infants and linking them long-term care and treatment [3–6]. As of 2012, only 34% of treatment eligible children in LMIC countries were receiving ART [7] despite proven benefits of early initiation of antiretroviral treatment (ART) on child survival [8]. Without treatment, about 50% of HIV-infected children will die before their second birthday [9].

In most LMIC, early infant diagnosis (EID) of HIV using virological testing is recommended at 4–6 weeks of age, in line with WHO guidelines [10]. EID is usually implemented within PMTCT programs that are generally separate from both child health and ART services. However, coverage of EID remains suboptimal (see EID article in this series). Moreover, linking HIV-infected children and treatment services faces significant challenges [11]. HIV-infected children identified through PMTCT programs are often lost to follow-up and need to be identified elsewhere in order to be linked to care [11,12].

We reviewed routine EID laboratory and paediatric ART patient records to determine missed opportunities for optimizing EID and current status of linkage between EID entry points to paediatric ART initiation in Tanzania, Uganda and Zimbabwe. These are three countries with EID coverage of 22, 11 and 14%, respectively and ART coverage rates of 18, 16 and 32%, respectively [13]. We defined EID entry point as any service delivery point wherein a Dried Blood Spot (DBS) specimen for EID was collected whereas entry points for paediatric ART were defined as the last service delivery point located in the child's medical record that provided referral for HIV treatment and care.

This article examines the most likely delivery points for collection of blood samples for EID testing for infant and

[a]HIV Section, UNICEF, New York, USA, [b]Regional Office, Eastern and Southern Africa, UNICEF, Johannesburg, South Africa, [c]Inter-country Support Team, Eastern and Southern Africa, WHO, Harare, Zimbabwe, [d]Global HIV Technical Lead, Management Sciences for Health, Arlington, Virginia, [e]Global HIV Programme, Clinton Health Access, New York, USA, [f]National AIDS Control Programme, Ministry of Health, Dar-Es-Salaam, Tanzania, [g]National STD/AIDS Control Programme, Ministry of Health, Kampala, Uganda, and [h]National HIV Treatment Programme, Ministry of Health, Harare, Zimbabwe.

Correspondence to UNICEF, HIV Section, Programme Division, 3 UN Plaza, New York 10017 NY, USA.
Received: 26 September 2013; revised: 26 September 2013; accepted: 26 September 2013.

DOI:10.1097/QAD.0000000000000101

young children and the most likely referral points for ART initiation of HIV-infected children in these three countries. This data provides evidence of consistent missed opportunities for linking HIV-infected children identified during EID to early ART treatment. We also argue for expanding the provision of EID to other service delivery points beyond PMTCT platform and provide suggestions for better linkages from EID to care and treatment.

Methods

This was a facility-based, retrospective medical record review of routinely collected EID and paediatric ART data, which took place in the first 3 weeks of October 2012 in Tanzania, Uganda and Zimbabwe.

Data and study sites for early infant diagnosis

EID laboratory information systems were the primary source of EID data used in this study. Patient level EID records were abstracted from laboratory article-based systems present in the Muhimbili National Reference Laboratory in Dar es Salam, Tanzania and National Microbiology Reference Laboratory in Harare, Zimbabwe whereas an electronic system present in the Central Public Health Laboratory in Kampala in Uganda was used to download EID records. Trained data collectors were enlisted to manually abstract EID data in Tanzania and Zimbabwe from their article-based system while a national laboratory coordinator downloaded the records from the laboratory electronic system in the central laboratory in Uganda.

In Tanzania and Zimbabwe, data was collected for all HIV-exposed children 18 months and younger, receiving EID services between January and December 2010. For Uganda, data was abstracted for children 18 months and younger between the period of July 2010 and June 2011. As one of the goals of this study was to determine entry points for EID, our inclusion criteria was limited to those records with completed data on age, referral source, date of birth, and date of DBS collection and DNA-PCR test result. Records missing those variables were excluded. Data were then entered into a structured excel database for data analysis. As Uganda had a more advanced electronic laboratory system, it allowed for linking patient demographic information and entry points to EID and clinical variables. Data from Tanzania and Zimbabwe were collected manually which did not allow for the linking of variables.

Data and study sites for antiretroviral treatment initiation

For children receiving ART, the routine ART patient monitoring systems were the primary source of data. We purposively sampled and collected data from 47 ART facilities [Tanzania=15; Uganda=24; Zimbabwe=8]. For a wide representation in a variety of settings, the criteria for selecting these facilities were based on geographical location (urban/rural), caseload, facility level (tertiary, general hospital, health centres, and dispensary) and ownership (public/private). All sampled facilities covered the geographical areas where EID tests were sourced so as to ensure their comparability. Selected facilities from each country cumulatively initiated 500 or more children on ART aged less than 15 years of age in 2010 based on national ART reports. In Zimbabwe, as paediatric ART is initiated at district hospitals, eight hospital level sites were selected using the aforementioned criteria.

The routine ART patient monitoring systems of all three countries are based on WHO tools for enrolling and monitoring ART. For Uganda and Zimbabwe, the system was article-based; for Tanzania, both article and electronic systems were used (CTC-2 database). Data from ART registers and the CTC-2 database were abstracted from individual patient records of children aged less than 15 years who were newly initiated on ART from January to December 2010 for Tanzania and Zimbabwe respectively; and from July 2010 to June 2011 for Ugandan ART registers. Records with information on referral source, date of birth, and date of ART initiation were included and abstracted into a structured excel database.

Key variables

Study outcomes were identification of service delivery points for EID and referral sources for ART initiation for HIV-infected children aged less than 2 years as well as those aged 0–15 years. For Uganda, additional outcomes were EID service delivery points by HIV sero-status and by age group.

Statistical analysis

A de-duplicated list of records abstracted from patient records and entered into excel files were imported into STATA software version 11 [StataCorp, Texas, USA] for analysis. Given a limited number of variables in the laboratory system and the objectives of this article, our analysis was primarily descriptive.

Ethical considerations

All measures to ensure confidentiality and privacy of patient information including removal of personal identifiers were strictly adhered and cleared by relevant government bodies.

Results

Entry points for early infant diagnosis and HIV results

There were a total of 59 372 individual EID laboratory records from the central laboratories in Tanzania (14 250),

Zimbabwe (32 764) and Uganda (12 358) included in the analysis. As shown in Fig. 1, the ANC/PMTCT clinics collected the majority of DBS for EID for Zimbabwe (92.1%) and Tanzania (98.0%) while in Uganda, designated EID care points account for 30.4% of samples collected followed by ART sites (15.8%) and ANC/PMTCT sites (13%). The designated EID care points in Uganda were centres where HIV-exposed infants are referred and followed up for clinical care. A variety of other service delivery points provided some DBS samples such as immunization clinics (Uganda=10.1% and Zimbabwe=3.7%), in-patient departments (Uganda=0.5%, Zimbabwe=11.0%) and out-patient departments (Uganda=7.0% and Zimbabwe=2.5%). Data from Tanzania did not show these other service delivery points as among the entry points for EID.

Uganda was the only study country with an electronic laboratory information system allowing linkage of EID samples to their results. Figure 2 presents HIV test results by EID entry points in Uganda, depicting the percentages of HIV-exposed infants testing positive and the number of infants receiving EID in each service delivery point. The highest rates of HIV-infected samples were from in-patient departments (IPDs) (40.6%) and out-patient departments (OPD) (15.6%), but these only constituted 0.5% and 7.1% of all DBS samples respectively. In contrast, 5.6% and 9.1% of HIV-positive EID samples were from ANC/PMTCT and EID Care points respectively. Table 1 provides details on EID entry points by age category and shows the proportion of HIV-exposed infants aged less than 2 months accessing EID was 35.2% (4350/12358) of sampled records.

Referral to paediatric antiretroviral treatment initiation

In comparison to EID entry points presented in Fig. 1, the primary referral sources for paediatric ART initiation for children aged less than 2 years were IPD for Uganda and Zimbabwe (36.1 and 27.5% respectively) while in Tanzania, PMTCT sites were the most frequent place for ART initiation (42.2%) (Fig. 3). Children less than 2 years constituted 31.6% (154/487), 36.1% (426/1181) and 15.0% (83/552) of the total number of children 0–15 years of age newly initiated on ART in Tanzania, Uganda and Zimbabwe respectively during the study period.

Figure 4 illustrates the referral sites for ART initiation for all children aged 0–15 years included in the sample. Less than 15, 10 and 5% of children below the age of 15 years initiating ART were referred from ANC/PMTCT service delivery points in Tanzania, Uganda and Zimbabwe respectively. Most children initiating ART in these countries were referred from IPD (Uganda: 29.5%. Zimbabwe: 29.7%; Tanzania=11%); OPD (Tanzania: 10.3%. Uganda: 15.5%. Zimbabwe: 28.3%) and self-referrals from HIV testing sites (Tanzania: 41.6%; Uganda: 12.1%; Zimbabwe: 28.8%).

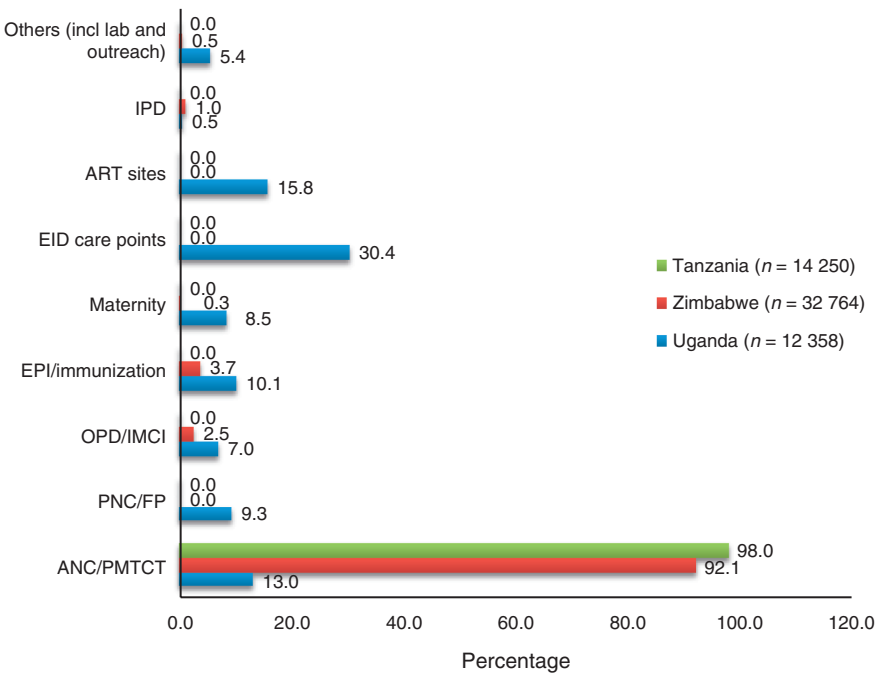

Fig. 1. Service delivery points for dried blood spot (DBS) collection for pediatric EID: Tanzania, Zimbabwe and Uganda, 2010–2011. ANC, antenatal care; ART, antiretroviral treatment; EID, early infant diagnosis; EPI, expanded programme on immunization; FP, family planning; IMCI, integrated management of childhood illness; IPD, inpatient department; OPD, outpatient department; PMTCT, prevention of mother to child transmission of HIV; PNC, postnatal care.

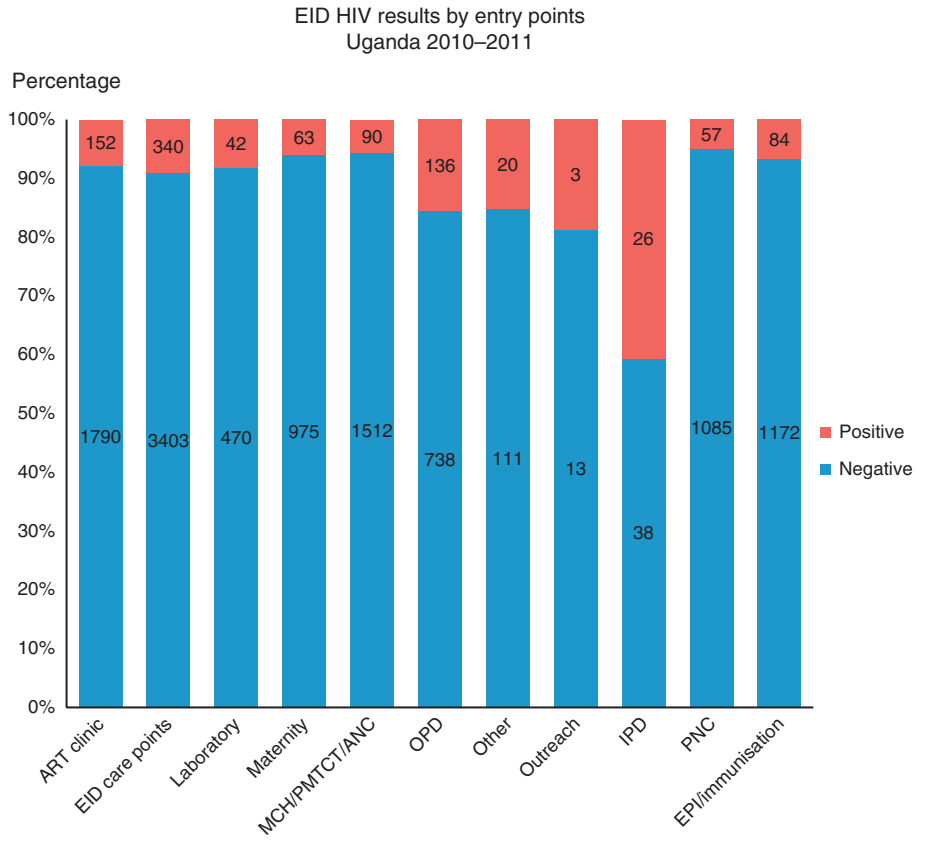

Fig. 2. EID HIV results by entry points Uganda 2010–2011. ANC, antenatal care; ART, antiretroviral treatment; EPI, expanded programme on immunization; IPD, inpatient department; MCH, maternal and child health; OPD, outpatient department; PMTCT, prevention of mother to child transmission of HIV; PNC, postnatal care.

Discussion

To our knowledge, this is the first study to analyse where HIV-exposed children accessed EID testing and the referral of those positive for treatment initiation, likely resulting in significant excess morbidity and mortality. The data indicates that there are multiple missed opportunities in which HIV-infected infants and children diagnosed in EID where not effectively referred for initiation of pediatric ART. Indeed, from the data, it is likely that significant delays occurred between diagnosis and referral to ART care and treatment following an IPD or OPD visit. Because these opportunities may have been missed for several years, other entry points for HIV-infected children into treatment programs have been used by caregivers to access life-saving ART; supported by the heterogeneity of EID entry points observed in all three study countries. Although current PMTCT programs in Tanzania and Zimbabwe provide most EID services, many HIV-infected children initiating treatment are not being tested in PMTCT programs. This is a tragic missed opportunity for early ART initiation despite clear guidance from the 2010 WHO guidelines which called for universal treatment of all infected children aged two and under. HIV-infected infants and children lost from the PMTCT cascade are identified later in other child health services, likely as a result of clinical signs or symptoms of HIV. The small proportion of children initiating ART that were referred from PMTCT programs in all three countries is consistent with other reports [14]. With the 2013 WHO treatment guidelines calling for universal treatment for all children under-5, it is incumbent on programs to accurately identify infected children and ensure that they are properly linked to care for ART initiation and retention (see Treatment 2.0 paper in this series).

In addition, the finding of low numbers of HIV-infected children identified in PMTCT and EID Care points suggests that EID (particularly at the 6–8 week time point) may not completely identify all HIV-infected children in need of treatment. As PMTCT programs continue to improve; becoming more comprehensive and contributing to decreasing vertical transmission rates in both the prenatal and postnatal periods, more children will remain negative. However, as more HIV-infected mothers survive and become pregnant, EID services will

Table 1. Entry points to early infant diagnosis by age, Uganda 2010/2011.

Age in months/ *n* (%)	ART clinic	EID care points	MCH-PMTCT-ANC	Maternity	PNC	EPI/ immunization	OPD	IPD/ paediatric ward	Laboratory	Outreach	Other	Total
<2	584 (13.4)	1133 (26.1)	742 (17.1)	476 (10.9)	575 (13.2)	509 (11.7)	154 (3.5)	9 (0.2)	125 (2.9)	2 (0.1)	41 (0.9)	4350 (100)
2–5	473 (14.9)	1064 (33.6)	318 (10.0)	255 (8.0)	257 (8.1)	361 (11.4)	236 (7.4)	18 (0.6)	151 (4.8)	3 (0.1)	34 (1.1)	3170 (100)
6–11	417 (17.1)	756 (30.9)	313 (12.8)	126 (5.2)	168 (6.9)	219 (9.0)	266 (10.9)	22 (0.9)	128 (5.2)	7 (0.3)	24 (1.0)	2446 (100)
12–18	473 (19.8)	799 (33.4)	238 (9.9)	186 (7.8)	144 (6.0)	170 (7.1)	222 (9.3)	15 (0.6)	108 (4.5)	4 (0.2)	33 (1.4)	2392 (100)
Total	1947 (15.8)	3752 (30.4)	1611 (13.0)	1043 (8.4)	1144 (9.3)	1259 (10.2)	878 (7.1)	64 (0.5)	512 (4.1)	16 (0.1)	132 (1.1)	12358 (100)

ANC, antenatal care; ART, antiretroviral treatment; EPI, expanded programme on immunization; IPD, inpatient department; MCH, maternal and child health; OPD, outpatient department; PMTCT, prevention of mother to child transmission of HIV; PNC, postnatal care.

remain vital for identifying all exposed and infected infants as early as possible for evaluation and initiation on ART as needed. The initiation of paediatric ART and the sites where HIV-infected children are referred deserves further study as this may improve linkage and retention by better aligning infant treatment to other sectors of the health system. This is particularly true as more countries move towards a B/B+ model, in which pregnant HIV-infected women are offered ART for the duration of pregnancy and breastfeeding or for life, irrespective of their CD4 cell count [15,16]. The family care model for paediatric HIV and integration of MCH and paediatric ART can be one-stop care points, where integrated services are provided to entire families or mother–baby pairs. These models can improve the often overlooked issues of linkage and retention in care for infants and children following an HIV diagnosis [17].

The findings further suggest that optimizing availability of EID using various child survival entry points may be more effective than relying solely on PMTCT or other vertical platforms as has been previously argued [18]. However as integration is the goal for many health programs, the consequences of providing all services everywhere may not be the most efficient model. A missed opportunities study using enhanced programmatic data may help to determine not only that linkage opportunities are missed as we've shown here, but also why they were missed and perhaps how to mitigate these circumstances with the goal of providing earlier initiation of HIV-infected children on ART.

The IPD, OPD and self-referrals from voluntary counselling and testing sites were found to be the most common referral points for paediatric ART initiation in all three countries. This counters the prevailing belief that most infected children are diagnosed and subsequently referred for ART initiation from the PMTCT program. Children attending these clinics present with a variety of childhood illnesses including HIV/AIDS-related diseases. In high prevalence countries, provider-initiated testing and counselling (PITC) for sick children who present for health services for growth monitoring, pneumonia, diarrhoea and malaria is an effective approach for identifying HIV-infected children (see Case Finding article in this series) [19]. Offering routine HIV testing in these settings is feasible and has shown excellent uptake in similar settings [20]. These child survival entry points allow capture of HIV-infected children born to women who did not benefit from or access PMTCT programs while pregnant, and children infected postnatally during breastfeeding. Our study did not evaluate other potential entry points for EID or serologic testing such as tuberculosis clinics and malnutrition rehabilitation centres though these were also identified as referral sources for ART. Use of these services for EID may further increase the identification of HIV-infected children while improving delivery of treatment for both

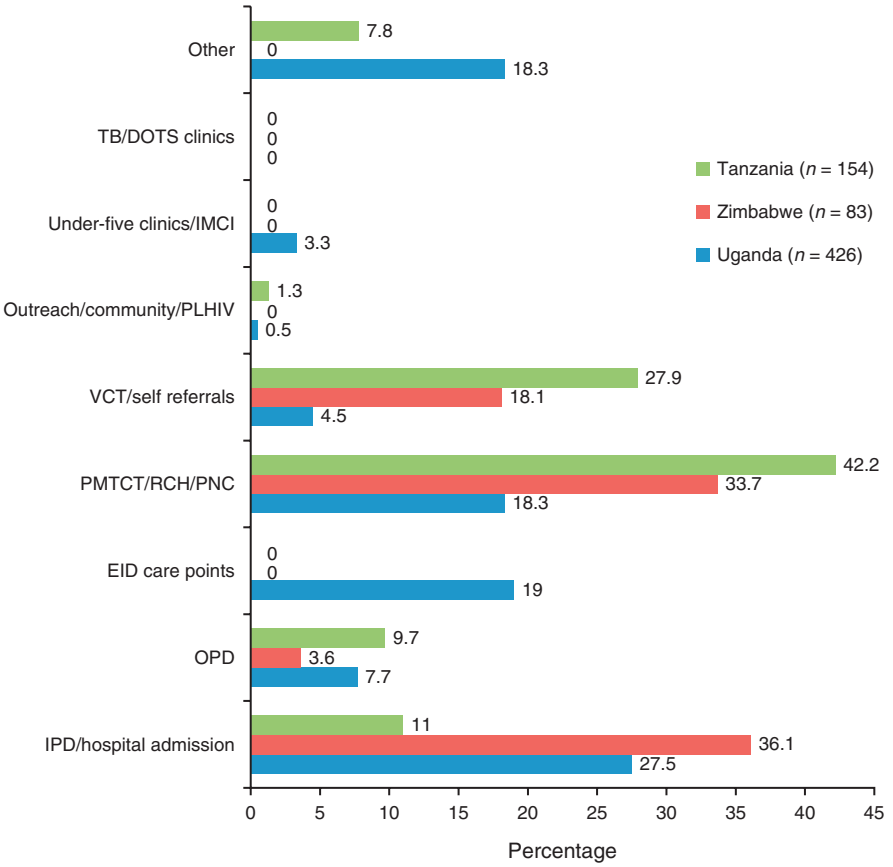

Fig. 3. Entry points to antiretroviral treatment (ART) initiation among children less than 2 years in Tanzania, Uganda and Zimbabwe, 2010/11. DOTS, direct observed therapy short course; EID, early infant diagnosis; FP, family planning; IMCI, integrated management of childhood illness; IPD, inpatient department; OPD, outpatient department; PLHIV, people living with HIV; PMTCT, prevention of mother to child transmission of HIV, PNC; postnatal care; RCH, reproductive healthcare; TB, tuberculosis; VCT, voluntary counselling and testing.

tuberculosis (TB) and HIV, although the capacity of these different sites varies widely by country. However, the challenges of diagnosing childhood TB [21] suggest that identifying paediatric TB/HIV co-infections in most high burden countries will remain a challenge. Increasing need for infant testing services will also require addressing additional challenge in EID programs (see EID article in this series). Finally, as more HIV-infected women survive because of advances in treatment and care such as earlier initiation of ART, more children will be born exposed to HIV and likely subject to the insults specific to exposure, an area about which data is only beginning to emerge (see HIV-Exposed Uninfected Infant article in this series).

Implications

At the macro level, the results of this study affirm the need for renewed global discourse on framing paediatric HIV services within PMTCT and child survival programs. Opportunities for such integration can be reinforced through collaborations with existing initiatives such as a global commitment to improving child survival by the year 2032 – a Promise Renewed to child survival [22]. At the program level, initiatives such as integrated community case management for sick children (iCCM) [23], immunization and other child care points such as OPD and IPD depicted by this study provide further opportunities to increase communication about the importance of testing and treatment, uptake, and retention in paediatric HIV care. In addition, with the current pace of introduction of point-of-care (PoC) diagnostics, these results can support better strategies on identifying service delivery points where PoC EID diagnostics can be positioned to maximize early identification and referral to care.

Limitations

Our findings have some limitations, which are likely to affect the generalizability and interpretation of results. The use of routine patient information is dependent on recording practices and quality of data, which varied among study countries. Laboratory-facility linkage data was only available for Uganda and while the rate of positivity from samples collected at different service points could not be determined for the other two

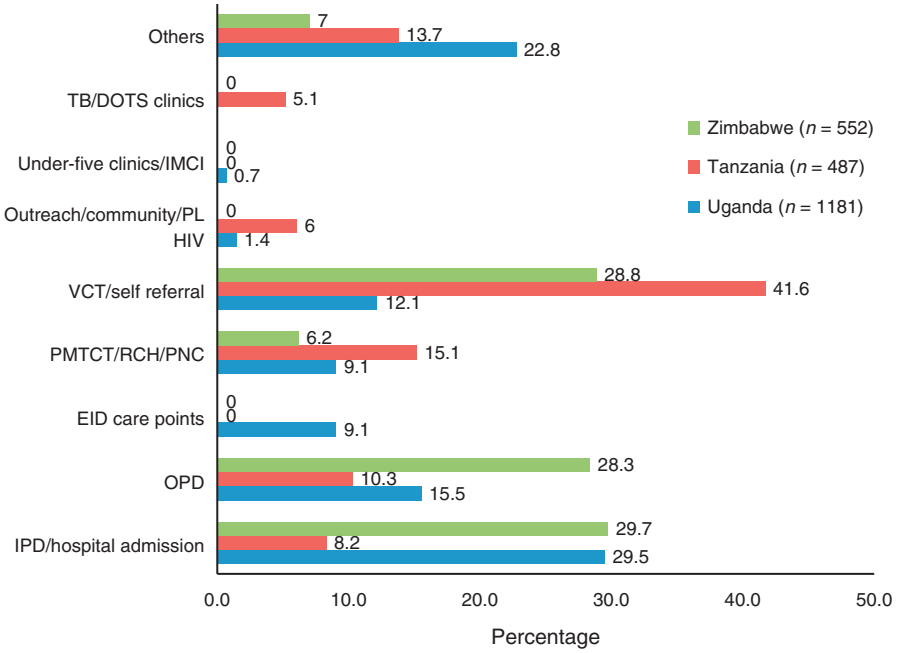

Fig. 4. Entry points to antiretroviral treatment (ART) initiation among children less than 15 years in Tanzania, Uganda and Zimbabwe, 2010/11. DOTS, direct observed therapy short course; EID, early infant diagnosis; FP, family planning; IMCI, integrated management of childhood illness; IPD, inpatient department; OPD, outpatient department; PLHIV, people living with HIV; PMTCT, prevention of mother to child transmission of HIV; PNC, postnatal care; RCH, reproductive healthcare; TB, tuberculosis; VCT, voluntary counselling and testing.

countries, it is hypothesized that given similar patterns in referral points for initiation, a similar trend would be seen in the Tanzania and Zimbabwe. The purposeful sampling of ART facilities also limits the representation of the findings, however there was wide geographical and facility level representation of the facilities selected. Despite these limitations, the consistency in the results from all three countries and conformity with published literature increase the validity of our results and warrants further study and consideration for policy review and adjustment. The importance of strengthening systems in order to capture longitudinal data on exposed infant outcomes will be critical in developing optimal programs to ensure that services provided meet the needs of mother and children requiring access to EID and early initiation of treatment.

Conclusion

The approach to the diagnosis, care and treatment of children with HIV should be enhanced beyond PMTCT settings to incorporate a wider child survival platform. Improving linkage between EID and treatment calls for different approaches; one size may not fit all. With successful PMTCT programs, child health programs such as immunization, OPD, IPD and community-level interventions can be critical platforms for early identification and initiation of life-saving ART for HIV-infected children. What is clear from this data is that existing PMTCT programming in the study countries may be able to identify HIV-exposed and HIV-infected children, but are not able to consistently refer, link and retain those children who are infected in appropriate ART care and treatment. Undoubtedly, the success of any model should depend on the available evidence on approaches that are effective in identifying infected infants and linking them to care and treatment.

Acknowledgements

Special thanks to

Christine Chakanyuka, WHO, Harare

Joyce Mphaya, UNICEF Harare

Richard Banda, WHO Tanzania

Florence Kitabira, UNICEF Swaziland

Conflicts of interest

There are no conflicts of interest.

Disclaimer: The findings and conclusions in this article are those of the authors and do not necessarily represent the official position of the World Health Organization or

the U.S. government including the U.S. Centers for Disease Control and Prevention and Agency for Toxic Substances Disease Registry and the United States Agency for International Development. The authors acknowledge the support of UNICEF and the Canadian International Development Agency (CIDA) whose financial assistance made this series possible and the U.S. President's Emergency Plan for AIDS Relief for support of contributing staff time.

References

1. UNAIDS, The Global Plan towards the elimination of New HIV Infection among children by 2015 and keeping their mothers alive. UNAIDS Publications, 2011.
2. UNAIDS, 2013 Progress Report on the Global Plan: towards the Elimination of new HIV Infection among Children by 2015 and keeping their Mothers Alive. UNAIDS Publications, 2013.
3. Binagwaho A, Mugwaneza P, Irakoze AA, Nsanzimana S, Agbonyitor M, Nutt CT, *et al*. **Scaling up early infant diagnosis of HIV in Rwanda, 2008–2010.** *J Public Health Policy* 2013; **34**:2–16.
4. Boender TS, Sigaloff KC, Kayiwa J, Musiime V, Calis JC, Hamers RL, *et al*. **Barriers to Initiation of Pediatric HIV Treatment in Uganda: A Mixed-Method Study.** *AIDS Res Treat* 2012; **2012**:817506.
5. Meyers T, Moultrie H, Naidoo K, Cotton M, Eley B, Sherman G. **Challenges to pediatric HIV care and treatment in South Africa.** *J Infect Dis* 2007; **196 (Suppl 3)**:S474–S481.
6. Chatterjee A, Tripathi S, Gass R, Hamunime N, Panha S, Kiyaga C, *et al*. **Implementing services for Early Infant Diagnosis (EID) of HIV: a comparative descriptive analysis of national programs in four countries.** *BMC Public Health* 2011; **11**:553.
7. WHO, Global Update on HIV Treatment 2013: Results, Impact and Opportunities. WHO Publications, 2013.
8. Violari A, Cotton MF, Gibb DM, Babiker AG, Steyn J, Madhi SA, *et al*., CHER Study Team. **Early antiretroviral therapy and mortality among HIV-infected infants.** *N Engl J Med* 2008; **359**:2233–2244.
9. Newell ML, Coovadia H, Cortina-Borja M, Rollins N, Gaillard P, Dabis F. **Ghent International AIDS Society (IAS) Working Group on HIV Infection in Women and Children. Mortality of infected and uninfected infants born to HIV-infected mothers in Africa: a pooled analysis.** *Lancet* 2004; **364**: 1236–1243.
10. WHO, Antiretroviral therapy of HIV infection in infants and children: towards universal access: recommendations for a public health approach: 2010 revision. WHO Publications, 2010.
11. Ahoua L, Ayikoru H, Gnauck K, Odaru G, Odar E, Ondoa-Onama C, *et al*. **Evaluation of a 5-year programme to prevent mother-to-child transmission of HIV infection in Northern Uganda.** *J Trop Pediatr* 2010; **56**:43–52.
12. Ioannidis JP, Taha TE, Kumwenda N, Broadhead R, Mtimavalye L, Miotti P, *et al*. **Predictors and impact of losses to follow-up in an HIV-1 perinatal transmission cohort in Malawi.** *Int J Epidemiol* 1999; **28**:769–775.
13. UNAIDS, Global Report: UNAIDS Report on Global AIDS Epidemic, 2010. 2010, United Nations Joint Programme on AIDS: Geneva.
14. McNairy ML, Lamb MR, Carter RJ, Fayorsey R, Tene G, Mutabazi V, *et al*., Identifying Optimal Models of HIV Care and Treatment in Sub-Saharan Africa Consortium. **Retention of HIV-infected children on antiretroviral treatment in HIV care and treatment programs in Kenya, Mozambique, Rwanda, and Tanzania.** *J Acquir Immune Defic Syndr* 2013; **62**:e70–e81.
15. Kellerman S, Jay JS, Quick JD. **Is Option B+ the best choice?** *Lancet* 2014; **381**:1273.
16. Thyssen A, Lange JH, Thyssen E, Reddi A. **Toward an AIDS-free generation with option B+: reconceptualizing and integrating prevention of mother to child transmission (PMTCT) with pediatric antiretroviral therapy initiatives.** *J Acquir Immune Defic Syndr* 2013; **62**:127–128.
17. Betancourt TS, Abrams EJ, McBain R, Fawzi MC. **Family-centred approaches to the prevention of mother to child transmission of HIV.** *J Int AIDS Soc* 2010; **13 (Suppl 2)**:S2.
18. Kellerman S, Essajee S. **HIV testing for children in resource-limited settings: what are we waiting for?** *PLoS Med* 2014; **7**:e1000285.
19. Mutanga JN, Raymond J, Towle MS, Mutembo S, Fubisha RC, Lule F, Muhe L. **Institutionalizing provider-initiated HIV testing and counselling for children: an observational case study from Zambia.** *PLoS One* 2012; **7**:e29656.
20. Kankasa C, Carter RJ, Briggs N, Bulterys M, Chama E, Cooper ER, *et al*. **Routine offering of HIV testing to hospitalized pediatric patients at university teaching hospital, Lusaka, Zambia: acceptability and feasibility.** *J Acquir Immune Defic Syndr* 2009; **51**:202–208.
21. Pearce EC, Woodward JF, Nyandiko WM, Vreeman RC, Ayaya SO. **A systematic review of clinical diagnostic systems used in the diagnosis of tuberculosis in children.** *AIDS Res Treat* 2012; **2012**:401896.
22. UNICEF. *Committing to child survival: a promise renewed.* UNICEF Publications; 2012.
23. de Sousa A, Tiedje KE, Recht J, Bjelic I, Hamer DH. **Community case management of childhood illnesses: policy and implementation in Countdown to 2015 countries.** *Bull World Health Organ* 2012; **90**:183–190.