

Title of review article:

Adolescent transition among young people with perinatal HIV in high and low income settings

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Main text 2500 words maximum: current word count 2738

Abstract (200 words max) current word count 200

Purpose of review:

To summarise evidence for health outcomes among adolescents and young people living with HIV (AYLHIV) who have transitioned to adult care/adulthood, views of AYLHIV and providers on the transition process, and the effect of adolescent and youth friendly services (AYFS) on outcomes.

Recent findings:

Forty-three studies were identified (n= 13 high income countries (HIC), n=30 low/middle income countries (LMIC)). In HIC, around 75% of patients were retained in care at approximately 4 years post-transition. In LMIC retention worsened from older adolescence into young adulthood. Across both contexts, comparison of mortality, immunological and virological outcomes was hampered by limited number of studies and/or different definitions and study durations. AYLHIV and providers reported several factors which could aid transition and AYFS had generally positive outcomes.

Summary:

Overall, outcomes varied by study and context; direct comparison was severely hampered by the inclusion of different populations of AYLHIV (sometimes with small numbers and a lack of comparison groups), the use of different outcome definitions, varying follow-up duration, and the lack of a specific transition process in LMIC. Future studies need to consider harmonizing definitions and implementing unique patient identifiers and data linkage techniques to improve the evidence base on long-term outcomes.

Key words:

Adolescent, high income, low and middle income, transition, outcome, perinatal

INTRODUCTION

Transition to adult care, among adolescents and young people living with HIV (AYLHIV) in high income countries (HIC), is the process whereby children with perinatal HIV are generally seen in paediatric clinics and then transfer to adult clinics in the same or different hospitals. The model of care for adolescents with horizontal HIV may vary, with some seen in adolescent care before adult care. However in many low and middle income countries (LMIC), HIV-infected children are mostly seen with adults in completely integrated primary care clinics either from diagnosis or once stable on antiretroviral therapy (ART). While primary care clinics may have child or adolescent days, or specific health workers providing paediatric or adolescent care, providers are usually generalist clinicians who manage adults and children.[1,2] The shift from paediatric-focused to adult-focused care is therefore less pronounced in LMIC than in HIC, rarely involving moving to a different facility or even a different provider. Despite these varied definitions of transition, a key underlying theme is greater personal autonomy, including taking responsibility for one's own health, making one's own clinic appointments, and taking responsibility for ART adherence. Thus the broader issue of transition is relevant to all AYLHIV, and globally, in 2016 there were 1.3 million adolescents 15-19 years old (>80% in sub-Saharan Africa [SSA][3]) and 2.8 million young people 20-24 years old living with HIV.[4]

This review focuses on recent studies of adolescents and young adults mostly with perinatal HIV who have transitioned to adult care or adulthood and where key health outcomes have been measured. We also review papers assessing what young people themselves think of the transition process, provider perspectives and the effectiveness of adolescent and youth friendly services (AYFS) in improving outcomes. We searched PubMed and abstracts from major conferences in the field, and identified 43 studies, 13 from HIC [Table 1][5-19] and 30 from LMIC [Table 2].[20-49]

HEALTH OUTCOMES FOLLOWING TRANSITION IN HIC

Retention/ loss to follow-up and mortality

Three European[5-7] and three North American studies[8-10] described retention, loss to follow-up (LTFU) and/or mortality following transition (Table 1). Two, from Italy[5] and Canada,[8] were small, single centre

studies (n=24 and n=25 respectively) where patients transitioned at age 18 years. In both, three-quarters of patients were retained in care, around 4 years following transition. In larger multi-centre Spanish[6] and UK[7] studies, of 209 and 271 patients with perinatal HIV respectively, median age at transition was 18 years and 17 years, and 2% and 3% died. In Spain 14% were LTFU, not dissimilar to the Italian and Canadian studies' findings, although no timeframe was given for this estimate, but most patients were lost after the first year in adult care.

Transition from paediatric to adult care in the USA is later than in most other HIC, as patients <25 years generally enter paediatric care, and then transition to adult care at around 25 years of age. In Atlanta, 97% of 72 AYLHIV were linked to adult care, and 89% were retained in the first year, falling to 56% in the second year.[9] Outcomes for the 11 patients with perinatal HIV were not reported separately. In Baltimore, among 19 of 50 AYLHIV with perinatal HIV, 84% were linked to adult care, but only 11 (69%) of these were retained at 12 months, compared to 14 (52%) of the horizontally-infected group.[10]

Immunological and virological outcomes

Five of the studies above also reported immunological and/or virological outcomes post-transition,[5-9] in addition to two studies from Europe.[11,12] In the UK, CD4 was already declining pre-transition; post-transition it continued to decline in some groups but improved in others.[7] In the small Canadian study of 25 patients, CD4 decreased from a mean of 524 cells/mm³ pre-transfer to 370 cells/mm³ one year post-transfer (p=0.04).[8] In Italy, CD4 was higher at the end of follow-up than at transition, though the transition denominator included all patients and the follow-up denominator only those retained in care.

Six studies reported virological outcomes,[5-7,9,11,12] the largest in the UK[7] and Spain.[6] In the UK the proportion with viral suppression (VS) in the 12 months pre-transition was similar to 12 months post-transition (53%, 48% respectively). In Spain 86% of VS patients (denominator not given) pre-transition maintained suppression post-transition, and 70% with viral load (VL) >50 copies/mL pre-transition achieved VS post-transition.[6] In the Netherlands 59 AYLHIV (78% perinatal) transitioned to adult care across multiple clinics.[11] Viral failure peaked at age 18-19 years, which coincides with the timing of transition from paediatric to adult care in the Netherlands. Finally, in Atlanta, those seen more quickly in adult care

were more likely to have VS post-transition than those who took longer to have their first adult care appointment, though few patients in the study had perinatal HIV.[9]

Young people's views

Only two studies, from England[13] and Canada,[8] asked young people for their own views about transition. In England, of 120 young people, the majority in adult care rated adult care as better or no different to paediatric care for services and support offered.[13] Also adult care attenders were more likely than those in paediatric care to self-manage aspects of their care. However $\leq 50\%$ in each group could name their ART drugs or their most recent CD4 and viral load values. In the Canadian study of 25 patients, the majority felt that age 18 was too young for transition, and suggestions for improving the transition process included allowing young people to maintain ties to non-medical members of the paediatric team and other youth in the clinic, alternating appointments between the adult doctor and paediatrician until solid ties with the adult doctor had been established, and being provided with more information on adult care.[8]

Providers' views

Two European studies[14] and one USA study [15-17] captured provider views on transition. In France, health professionals reported making a clinical care distinction between young people with perinatal HIV and those infected horizontally, and applied different levels of care according to need.[14] Three major problems were identified: difficulties of young people in accepting their illness; difficulties linking young people with adult healthcare providers; and disorientation in the new adult care environment. Findings from the USA study were complementary,[15-17] with barriers to care falling into three groups: structural, including insurance eligibility, transportation and HIV stigma; clinical, including inter-clinic communication, and resource and personnel limitations; and individual including adolescent readiness to transition and developmental capacity. Four components were felt to be critical to successful transition: clinical outcomes, such as adherence and viral suppression; patients being able to self-manage their care; patients taking responsibility for treatment and health; and patient trust towards the adult clinic. Strategies for

connecting young people to adult care (e.g. adolescent clinic staff attending first adult care appointment) and approaches to evaluating longer term outcomes (data sharing) were recommended.

Impact of adolescent friendly services on outcomes

Only two studies within the review period, both from the USA, assessed the impact of adolescent and youth friendly services (AYFS) on outcomes post-transition.[18,19] In Baltimore, 54 patients with horizontal or perinatal HIV receiving care in a youth friendly clinic in adult care were less likely to have a 6 month gap in care (44% vs 59%, $p=0.10$) and more likely to have two appointments 90 days apart (83% vs 69%, $p=0.066$) compared to 78 receiving standard adult care.[18] In the other multi-centre study of 680 youth (35% perinatal or transfusion-acquired HIV), after adjustment for demographic and clinic factors, patients were more likely to be retained if they attended a clinic with a youth friendly waiting area, evening clinic hours, and providers with adolescent health training.[19]

HEALTH OUTCOMES FOLLOWING TRANSITION IN LMIC

Retention, loss to follow-up and mortality

Only three studies from LMIC reported mortality/LTFU following transition, with the number of participants ranging from 36-81 and similar transition age (17-18 years).[20-22] Study durations post-transition varied from approximately 6 months (Thailand) to 3 years (Dominican Republic), with corresponding mortality ranging from 0-6%; no studies reported rates for any outcomes.[20-22] LTFU was only reported for Dominican Republic (10%) where transition to a different site for adult care (vs staying at the same site) was associated with higher risk of death/LTFU ($p=0.042$).[21] Very high retention post-transition following a transition preparedness program was reported from Thailand.[22]

Two studies from SSA (South Africa,[23] Zimbabwe[24]) have examined outcomes as children age through late adolescence to young adulthood, in the context where transition to a different clinic does not routinely occur. Both studies found increased risk of LTFU when patients starting ART matured from young (10-14 years) to older adolescence (15-19 years), increasing further into young adulthood (20-24 years).

Three South African studies examined outcomes following transfer between different health facilities, however in this context transfer may not necessarily indicate transition to adult care.[25-27] Most commonly transfers are to decentralize care from hospital-based specialist pediatric clinics where patients initiated care to primary care clinics once stable on ART.[50] The proportion of patients successfully transferred in Cape Town (81%)[25] Durban (69-88%)[27] and Port Elizabeth (70%)[26] were broadly similar, despite differences in methods used.[25-27] However, only the Cape Town study, which linked datasets using unique identifiers, reported on retention post-transfer which declined from 90% to 84% from 1 to 3 years.[25]

Immunological and virological outcomes

Five studies[20-22,25,28] reported post-transition immunological/virological outcomes. In the Cape Town transfer study, the proportion with CD4 >500cells/ μ l did not change between transfer and 1, 2 and 3 years post-transfer, and VS only decreased slightly at 3 years.[25] However, VS and CD4 outcomes were worse in those transferring at older ages.[25] In Dominican Republic and Brazil, high proportions (>50%) of patients were not VS.[20,21] In contrast, in Thailand the STAY (Study of Transitioning Asian Youth) and transition training cohorts reported post-transition VS in 85% and 78% of patients respectively.[22,28]

Transition training/preparedness interventions

Two studies describe transition training with positive outcomes. In Thailand, the Happy Teen 2 (HT2) program (group education and individual counselling) increased median knowledge scores (45% to 95%) with overall high satisfaction.[29] In Malawi, a 6 week transition training program reported positive socio-behavioural outcomes (e.g. school re-enrolment), but impacts on transition were not reported.[30]

Young people's views

Seven studies [28,31-36] described AYLHIV's transition experience, and common transition challenges included fear of abandonment, loss of peer support, negative perceptions about adult care (longer wait times, unfavourable appointment days[32] and poorer quality of care),[31,33-35,51] and stigma.[31,34]

Nevertheless, many adolescents had positive transition expectations. Enabling factors included ongoing support from family, friends and providers,[33,36] maturity, financial security, early preparation, transitioning as a group and staying at the same facility after transition.[31,32] Adolescents frequently requested more time to transition, a formal transition program, involvement in decision-making, pre-transition contact with the adult team, and adolescent support groups in adult care.[31-34,52]

Four studies assessed AYLHIV's transition preparedness.[28,31,32,36] In Kenya, most adolescents (67% transitioned to adult care by 19 years) felt unprepared and experienced considerable anxiety.[31] In Cambodia 88% of pre-transition AYLHIV felt somewhat/very prepared for transition.[36] Several of these AYLHIV had undergone transition preparedness activities, and having a transition case manager, and transition counselling were strongly associated with better transition preparedness. In the Thai STAY cohort, 46% of post-transition AYLHIV were "very prepared" to transition and 91% were comfortable receiving adult care.[28]

Providers' views

Seven studies from SSA [37-43] and one from Dominican Republic [34] investigated provider perspectives on LMIC transition. There were few LMIC national guidelines or tools to support transition and very few facilities had transition protocols.[37,40,41] Transition age varied widely from 13-25 years; three studies reported using social signals (e.g. completion of secondary school, pregnancy) in addition to age to justify transition.[38-41]

Providers echoed transition challenges identified by AYLHIV. Common themes were: provider difficulty "letting go" of adolescents; patients preferring paediatric care; poor links between adult and paediatric providers; provider perceptions of adult clinics as depersonalized, overburdened, less comprehensive and not adolescent-friendly; and cessation of peer support groups.[34,37-43] While provider recommendations for transition were similar to those of adolescents including less abrupt transition, later transition age and adolescent support groups in adult care,[34] Kung et al (2017) reported that providers acknowledged that many HIC guidelines would not be feasible at scale in LMIC e.g. engagement of adult doctors pre-transition, transition case managers and post-transition paediatric follow-up.[40] Similarly, although nearly all facilities

in a survey recommended peer support during transition, only 50% provided this service.[37] There are, however, promising results from provider training programs aimed to strengthen adolescent services in Zimbabwe, with healthcare workers reporting improved linkage, retention and adherence subsequently.[43]

Impact of adolescent and youth friendly services or community adherence groups on outcomes

Three studies examined the impact of AYFS.[44-46] In South Africa, cross-sectional retention and VS in perinatally-infected adolescents were better in a Saturday “Teen Clinic” vs. standard clinic,[46] however in Kenya there was no difference in pre-ART or on-ART LTFU before and after implementation of AYFS for AYLHIV.[44] Post-transition VS increased among 32 adolescents in a Senegal Transition Support Programme but decreased in 15 receiving standard care, but results may be confounded as the standard care group included 4 pregnant women and 8 older youth previously refusing transition.[45] Results of previous studies are varied: Lamb et al (2014) found lower LTFU among adolescents initiating ART at clinics with sexual and reproductive health services and adolescent support groups,[53] while in Kenya there was no difference in LTFU between youth attending AYFS clinics (where 30% of patients were youth) and family-oriented clinics (3% youth).[54]

Three studies found positive outcomes of community-based care for AYLHIV, although again, none specifically examined transition outcomes. In South Africa 12-month retention was high among AYLHIV (median age 22.3 years) enrolled in adherence clubs.[47] In Uganda, LTFU was more than double in adolescents receiving clinic-based vs community-based ART.[48] In Zimbabwe, community based ART mentors positively impacted adolescent self-belief, esteem and adherence.[49]

CONCLUSIONS AND CHALLENGES FOR THE FUTURE

Across the 43 studies, outcomes varied by study and context, and direct comparison was severely hampered by the inclusion of different populations of AYLHIV (sometimes with small numbers and a lack of comparison groups), the use of different definitions of outcomes, varying periods of follow-up, and the lack

of a specific transition process in LMIC. Although health outcomes may differ between perinatally and behaviourally-infected AYHIV, mode of infection is often not routinely recorded or reported in studies, and there are limited disaggregated monitoring and evaluation data.[55,56] Recent analysis of UNAIDS estimates suggests that in 2016 about 60% of adolescents 15-19 years old in Southern and East Africa acquired HIV perinatally.[57] Additionally countries and regions are at different stages of transition through adolescence, and for many the bulk of adolescent transition is yet to come.[58] Studies in this review include some of the first cohorts of young people with perinatal HIV to transition, who may have particular challenges, including later ART start, exposure to sub-optimal ART regimens, and consequent persistent stunting, treatment failure and other comorbidities, particularly in LMIC.[58-60]

There is a lack of consensus on the most appropriate metrics to capture the process of transition and its outcomes, and it is hoped that a recent NIH-funded study will go some way towards defining a core set of variables for the global community. Long-term follow-up is hampered in many studies which rely on resource-intensive tracing or record reviews, often conducted as a one-off research endeavour, and point to the need for widespread implementation of unique identifiers and data linkage methods to enable longer term assessment of outcomes.[7,25]

Notwithstanding these limitations, in HIC, around 75% of patients were retained in care at approximately four years post-transition, few studies reported mortality and immunological outcomes, and different definitions hampered comparison of virological outcomes. In LMIC, studies of transition outcomes are limited to small cohorts, partly due to lack of a documented transition process in many settings, but suggest that LTFU increases from early through late adolescence and into young adulthood. Across both contexts, AYHIV and providers reported several factors which could aid transition. Only two studies described transition training interventions, and longer-term data on impact post-transition are needed. In general evidence suggested a positive impact of AYFS on outcomes across transition and/or adolescence, although assessment of quality and cost of services and addressing specific AYHIV needs may be required to improve outcomes in this group. Given the strong recommendation for peer support from both

adolescents and providers, differentiated care models such as community adherence groups may offer particular benefits for AYLHIV.[61,62]

Key points (3-5 key points/ sentences to summarise the article)

- Transition from paediatric to adult care occurs mainly in high income countries (HIC), whilst in low and middle income countries (LMIC) adolescents may stay with the same healthcare provider; however in both contexts adolescents are transitioning to adulthood and have greater autonomy for their health
- 43 studies across HIC and LMIC have reported evidence for health outcomes following transition to adult care or adulthood
- Outcomes varied by study and context, and direct comparison was severely hampered by the inclusion of different populations of AYLHIV (sometimes with small numbers and a lack of comparison groups), the use of different definitions of outcomes, varying periods of follow-up, and the lack of a specific transition process in LMIC
- Adolescents and young adults living with HIV and providers reported several factors which could aid transition in the future, and generally, adolescent and youth friendly services had positive outcomes
- Future studies need to consider harmonizing definitions and implementing unique patient identifiers and data linkage techniques to improve the evidence base on long-term outcomes.

Acknowledgements

None.

Financial support and sponsorship

A.J. receives support from NHS England and the PENTA Foundation. The Medical Research Council Clinical Trials Unit at University College London is supported by the Medical Research Council programme grant MC_UU_12023/26. M-A.D. receives support from the National Institutes of Health under Award Numbers U01AI069924 (International Epidemiologic Databases to Evaluate AIDS Southern Africa), R01HD080465 (B positive), R21HD089859 (GRADUATE), R24AI124872 (Harmonist) and the Wellcome Trust.

Conflicts of interest

A.J. and M-A.D. have no conflicts of interest.

TABLE 1: CHARACTERISTICS OF RESEARCH ARTICLES ON TRANSITION AMONG YOUNG PEOPLE WITH PERINATAL HIV

Studies are ordered firstly by the main outcome investigated, and then alphabetically by country within each geographical region

Author (year)	Country	Design			Mode of infection	Sample size	Median age	Participants			Main outcome	Main finding	Ref
		Qualitative/semi-struct	Cross-section	Cohort				Patients	Care-givers	Providers			
<i>Retention/ loss to follow-up and mortality outcomes, +/- other outcomes and +/- young people's views</i>													
Izzo (2017)	Italy			X	Perinatal	24	18 at transition	X			Retention (not defined), CD4, viral suppression, ART	100% retained 12m post-transition, and 76% 52 months later. 63% (75%) VL<50c/ml at transition (12 months post-transition). Median CD4 was 534 c/mm ³ at transition (n=24), 626 c/mm ³ 1 year later (n=24), and 716c/mm ³ 52 months later (n=19). Proportion taking integrase inhibitors increased post-transition.	[5]
Sainz (2017)	Spain			X	Perinatal	209	18 at transition	X			Loss to follow-up (not defined), mortality, viral suppression	14% loss to follow-up during or immediately after transition. 4 (2%) died post-transition. 86% who had VL<50c/ml pre-transition remained suppressed post-transition	[6]
Judd (2017)	UK			X	Perinatal	271	17 (last paed visit)	X			Mortality, CD4, viral suppression (two consecutive viral loads>400c/ml or one viral load >10,000 c/ml)	7 (3%) died post-transition. CD4 declined pre-transition, and continued to decline in some groups post-transition. Viral load suppression was similar in the 12 months pre-transfer and post-transfer (53%, 48%)	[7]
Kakkar (2016)	Canada	X		X	Perinatal	25	All transfer to adult care at 18. Mean 22 years at follow-up	X			Retention (≥1 clinic visit within 6 months of interview), CD4	76% were retained a mean of 3.6 years after transition from paediatric to adult care. Mean CD4 decreased from 524 c/mm ³ at transfer to 370 one year later. Participants felt that 18 years was too young an age to transfer.	[8]
Hussen (2017)	USA			X	15% perinatal 62.5% MSM 22% heterosexual	72	25 (first adult visit)	X			Retention (≥2 visits ≥3 months apart), viral suppression	89% (56%) retained in 1 st (2 nd) year after transition to adult care. Following transition, those seen sooner in adult care had higher viral suppression.	[9]
Ryscavage (2016)	USA			X	38% perinatal 62% horizontal	50	Perinatal 22 horizontal 25 at transition	X			Retention (≥2 visits over 12 months following linkage (1 st adult care visit))	86% were linked to adult care, of whom 58% were retained in adult care at 12 months. Retention was higher in those with perinatal HIV (69%) vs horizontal HIV (52%).	[10]

Author (year)	Country	Design			Mode of infection	Sample size	Median age	Participants			Main outcome	Main finding	Ref
		Qualitative/semi-struct	Cross-section	Cohort				Patients	Care-givers	Providers			
Immunological and virological outcomes													
Weijsenfeld (2016)	Netherlands			X	78% perinatal	59	19 at transition	X			Virological, social	Proportion with viral failure increased during transition to adult care vs pre-transition paediatric care. Low education attainment and less autonomy of ART adherence predicted failure.	[11]
Westling (2016)	Sweden			X	91% perinatal	34 at baseline, 29 2 years later	19 at transition	X			Virological, ART	2 years after transfer from paediatric to transition clinic, 90% of 29 were on ART, of which 61% took integrase inhibitors, and 92% had viral load <50c/ml	[12]
Young people's views													
Judd (2017)	UK		X		Perinatal	120	n=38 in paediatric care: 16 yrs n=82 in adult care: 20 yrs	X			Rating of adult care vs paediatric care; readiness to self-manage care	Most rated adult care as better or no different to paediatric care for services and support offered. Those in adult care were better able to self-manage their care.	[13]
Provider views													
Le Roux (2017)	France	X			Perinatal	18	N/A			X	Transition practices	Adult care providers attempted to adapt their practice to YP with perinatal HIV transferring from paediatric to adult care. Practice depended on the needs of each patient.	[14]
Tanner (2017) Philbin (2017) Philbin (2017)	USA	X			Perinatal, horizontal	58	N/A			X	Transition processes, barriers and facilitators; definitions of successful transition	Providers identified components of successful transition from adolescent to adult care. Several structural, clinical and individual factors were identified as transition barriers. Collaborative process of transition from adolescent to adult clinics was recommended to facilitate uninterrupted care	[15-17]
Adolescent and youth friendly services													
Griffith (2016)	USA			X	Perinatal, horizontal	132 16/54 receiving youth-targeted care were PHIV	25	X			Retention (≥6 month gap in care; ≥2 visits ≥90 days apart) at 12 months in youth-targeted care vs adult clinic	A lower proportion of those receiving youth-targeted care had a 6 month gap in care (44% vs 59%) and a higher proportion had 2 appointments ≥90 days apart (83% vs 69%).	[18]

Author (year)	Country	Design			Mode of infection	Sample size	Median age	Participants			Main outcome	Main finding	Ref
		Qualitative/semi-struct	Cross-section	Cohort				Patients	Care-givers	Providers			
Lee (2016)	USA		X		19% heterosexual. 44% MSM, 35% perinatal or transfusion-acquired	680	25% 15-19 75% 20-24	X			Retention in care (≥ 2 HIV care visits ≥ 90 days apart within 12 months) stratified by "youth friendly" clinic factors	85% were retained overall. After adjustment for demographic and clinical factors, retention was higher in clinics with youth-friendly waiting areas, evening clinic hours, and providers with adolescent health training.	[19]

TABLE 2: CHARACTERISTICS OF RESEARCH ARTICLES ON TRANSITION AMONG YOUNG PEOPLE WITH PERINATAL HIV (LMIC)

Studies are ordered firstly by the main outcome investigated, and then alphabetically by country within each geographical region

Author (year)	Country	Design			Mode of infection	Sample size	Median age	Participants			Main outcome	Main finding	Ref
		Qualitative/semi-struct	Cross-section	Cohort				Patients	Care-givers	Providers			
<i>Retention/ loss to follow-up and mortality outcomes, +/- other outcomes and +/- young people's views</i>													
Carvalho Freitas 2016	Brazil			X		41	18 at first adult visit	X			Characteristics of youth in transition to adult care (last 2 yrs in paediatric and first 2 yrs in adult care) Adherence failure (defined as either reported in medical records, missed prescription refills, or missed appointments.	At transition: Median CD4: 250 cells/ μ l; 54% VL>400 copies/ml 1 death post-transition Adherence failure high both in final 2 yrs of paediatric care and first 2 yrs of adult care	[20]
Abreu-Perez 2017	Dominican Republic		X		>95% perinatal	81	18 (range: 13-26) at transition; 21 (range: 15-29) at analysis	X			Mortality, LTFU (not defined), VL	6% died; 8% LTFU, 9% discontinued ART. Transitioned to a different site for adult care vs staying at same site associated with death/LTFU (p=0.042) Median VL 1759 copies/ml	[21]
Sricha-roenchai 2017	Thailand		X		98% perinatal	158; (36 post-transition)	20 (range 16-23) at transition	X			Satisfaction with and barriers to transition in adolescents 12 months after completing the Happy Teen 2 (HT2) Transition Training Program	12 months after program, 23% had transitioned – 33% at same and 67% at different hospital 94% of transitioned participants completed all adult clinic appointments At median 6.6 months post-transition: 78% had VL <40 copies/ml; median CD4 count =520 (range:24-1,357) cells/ μ l. 94% satisfied with adult HIV care <u>Training program:</u> Helpful for transition (97%); Provided good guidance for adult clinics (92%); Promoted confidence in the transition (100%) <u>Transition barriers:</u> Perceived quality of adult care; Adult providers unfriendly; Adult clinics disorganized, long wait time, long distance to the clinic.	[22]
Marcus 2017	South Africa			X	NR; Children and adolescents aged 5-19 at ART start	555	NR; 5-9 yrs: 174 10-14 yrs: 100 15-19 yrs: 281	X			LTFU (not defined)	Using age-updated analysis, current older adolescents (15-19 yrs) and young adults (20-24 yrs) had higher LTFU than children 5-9 yrs (aHR 7.16; CI 3.25; 15.76 and aHR 7.46; CI 3.16; 17.58 respectively), but those currently 10-14 years had lower LTFU (aHR 2.78; CI 1.19; 6.51).	[23]

Author (year)	Country	Design			Mode of infection	Sample size	Median age	Participants			Main outcome	Main finding	Ref
		Qualitative/semi-struct	Cross-section	Cohort				Patients	Care-givers	Providers			
Kranzer 2017	Zimbabwe			X	"mostly perinatal" except for older age group	2273	NR; 5-9 yrs: 1013 10-14 yrs: 875 15-19 yrs: 385				LTFU (> 60 days late for scheduled visit) when moving to next age group	Patients starting ART as young adolescents and older adolescents had higher LTFU when moving to next age group (ARR:1.54; CI: 0.94; 2.55 and 1.79; CI: 1.05–3.07 respectively)	[24]
Davies 2017	South Africa			X	NR; adolescents aged 10-19 years on ART who transferred out	460	At transfer: 10-14 yrs; 72% 15-19 yrs 28%	X			1) Successful transfer (visit at new health facility after transfer) identified using record linkage to visit, laboratory and pharmacy data 2) Post-transfer retention, VL<400 copies/ml, CD4 >500 cells/µl	81% transferred successfully Retention decreased from 1-3 yrs post-transfer (90-84%). Proportion with VL<400 copies/ml & CD4>500 cells/µl post-transfer was lower in those transferring at 15-19 vs 10-14 yrs.	[25]
Teasdale 2017	South Africa			X	NR; Aged 0-15 years at ART start	199 aged >10 yrs	NR – all >10 years	X			Successful transfer (using clinic records) and outcomes in patients LTFU during transfer using community tracing and laboratory data	70% successfully transferred using clinic records. No predictors of successful transfer. Using community tracing and laboratory data 40% of those LTFU during transfer were in care at time of study but most had a care interruption at time of transfer	[26]
Ramirez-Avila 2017	South Africa		X		NR; Visit at age 11-18 years from May-June 2012	309 surveyed; 90% of 341 transferred	13 (IQR 12-15) at transfer	X	X		Caregivers report of patient linkage to care post transfer validated with clinic records in 10%	Using cross-sectional survey and clinic validation data 88% (CI: 77-97) of patients linked to transfer clinic. 52% transferred to assigned transfer clinic; 48% transferred to an alternate clinic; Although 35% assigned to hospital-based clinic, 46% actually linked to hospital-based care.	[27]
Immunological and virological outcomes													
Sohn 2017	Thailand		X		93% perinatal	83	20 (IQR: 19-21) at study	X			Post-transition VL and transition preparedness of a transitioned cohort	85% had VL<40 cpm at median post-transition time of 4.7 mos since first adult visit or 7.4 mos since last paediatric visit. 46% very prepared to transfer 42% were very and 49% somewhat comfortable receiving care at adult clinics.	[28]
Transition training/preparedness interventions													

Author (year)	Country	Design			Mode of infection	Sample size	Median age	Participants			Main outcome	Main finding	Ref
		Qualitative/semi-struct	Cross-section	Cohort				Patients	Care-givers	Providers			
Lolekha 2017	Thailand			X	perinatal	161	17 (range: 14-22) at study	X			Effect of Happy Teen 2 programme (HT2) (mix of group education and individual counselling sessions) on youth knowledge scores	Median knowledge score increased from 45% to 82% and 95% after 12 & 18 mos respectively Better knowledge scores in those with tertiary education and not double orphans Overall high satisfaction with the HT2 sessions HT2 participants who transferred to adult clinic (18%) said knowledge from program was helpful in transition process.	[29]
Mc-Kenney 2016	Malawi		X		NR; aged 18-24 yrs in T2 program	100 (of 105 T2 graduates)	"average" 20 years;	X			Evaluation of Transition Training (T2) program which aims to equip young adults with life and self-care skills 6-week program meeting twice weekly.	45% re-enrolled in school/enrolled in tertiary education or found work/internship 36% are ALHIV program mentors 24% disclosed their HIV status to a friend or partner 83% had good adherence by pill count; 86% had VL <150 copies/ml compared to clinic suppression rates of 77%	[30]
Young people's views													
Grewal 2017	Kenya	X	X		NR; aged 15-24 yrs	96 (survey); 38 adolescents + 11 key informants (in-depth interviews)	NR	X		X	Proportion transitioned; Barriers and Facilitators	67% transitioned by 19 yrs Most participants felt unprepared for transition and had anxiety during transition <u>Transition challenges:</u> Fear of letting go of the bond formed with pediatric providers; Stigma and discrimination in adult clinic; Differences in care between pediatric and adult clinics; Poor preparedness <u>Transition enablers:</u> Independence and having sense of responsibility; Early preparation; Transitioning as a group; Supportive system from caregivers and providers	[31]
Massavon 2016	Uganda	X			NR; aged 17-28 yrs attending adolescent clinic	132	20.1 (mean) at study	X			Challenges and enablers to transition	65% had accepted transfer; 8% currently attend adult clinic <u>Transition challenges:</u> Loss of peer support; Unfavourable appointment days; Long clinic hours; Stigma from adults <u>Transition enablers:</u> maturity; financial security; support structures; same clinic or staff & peer support networks	[32]

Author (year)	Country	Design			Mode of infection	Sample size	Median age	Participants			Main outcome	Main finding	Ref
		Qualitative/semi-struct	Cross-section	Cohort				Patients	Care-givers	Providers			
Machado 2016	Brazil	X			perinatal	16	17 at study	X			Adolescent perspectives on process of transitioning from paediatric to adult care via a Transition Adolescent Clinic (TAC) in paediatric services	<p><u>Transition challenges:</u> Strong bond between adolescent and the paediatric team with feelings of abandonment at leaving paediatrics; Unprepared to address own health needs; Negative beliefs about adult care</p> <p><u>Transition Facilitators:</u> Resilience and positive expectations of adult care;</p> <p><u>Transition recommendations:</u> More time to adapt to transition; Contact with adult team before transition</p>	[33]
Pinzon-Iregui 2017	Dominican Republic	X			NR	7 post-transition adults; 8 pre-transition adolescents 7 providers in paediatric and adult care; 7 caregivers	17.8 mean; range 13-23) at study	X	X	X	Transition challenges and recommendations from 4 focus group discussions	<p><u>Transition challenges:</u> Fear of loss of relationships and social isolation; Reduced support from caregivers after transition; Not being part of decision-making; Lack of familiarity with adult providers; Long wait times in adult clinic; Stigma as more easily identified as HIV+ when attending adult clinic;</p> <p><u>Transition recommendations:</u> Transitioning with cohort; Formal transition program with recognition through graduation ceremonies; Encourage caregivers to accompany to adult clinic visits; Logistic planning of first adult visit; Text-messages to support retention and adherence; Transition less abrupt</p>	[34]
De Souza 2016	Jamaica	X			NR; adolescent in paediatric care	18 adolescents 21 providers	NR	X		X	Perspective of adolescents and providers on transfer process	<p><u>Transition challenges:</u> Psychosocial benefits associated with paediatric care; Better quality of care in paediatrics; Rootedness in the pediatric clinic and apprehension about transfer.</p>	[35]
Yi 2017	Cambodia		X		79% perinatal	223	15.8 (mean) at study	X			Level of preparedness for transition measured through structured questionnaire	<p>13% self-reported being "very" and 75% "somewhat" prepared for transition.</p> <p>58% were "very" and 12% somewhat dissatisfied with the transition process</p> <p>84% preferred care in paediatric clinic</p> <p>53.3% had high level of transition preparedness when formally assessed</p> <p>Higher level of transition preparedness independently associated with older age (AOR 2.44, CI 1.34–4.46), family having received social support for their health (AOR 5.32, CI 1.97–14.36), knowing the kind of treatment they received (AOR 12.67, CI 2.91–15.19), trust in friends/ family for HIV treatment (AOR 7.82, 95% CI 1.13–8.89), receiving counseling on transition (AOR 3.17, CI 1.15–8.76), having a 'Case Manager' (AOR 3.89, CI 1.08–13.96), and satisfaction with transition preparation process (AOR 0.35, CI 0.03–0.87).</p>	[36]

Author (year)	Country	Design			Mode of infection	Sample size	Median age	Participants			Main outcome	Main finding	Ref
		Qualitative/semi-struct	Cross-section	Cohort				Patients	Care-givers	Providers			
Provider views													
Mark 2017	SSA (23 countries)		X		NR	218 facilities	N/A			X	Facility-level situational analysis of adolescent HIV treatment and care services	50% had no transition protocols 63% provide counselling to support transition Age of transition varied widely Peer support recommended by all but only offered by half of facilities	[37]
Gillespie 2016	Botswana; Lesotho; Malawi; Swaziland Tanzania; USA		X		"almost all" perinatally infected	7 clinics		X		X	Characteristics and current healthcare transition practices	<u>Transition challenges:</u> Patient/family reluctance; Concerns regarding transition-readiness of patient; Lack of support services in adult clinic; Concern about quality of care in adult clinic	[38]
Rakhmanina 2016	Kenya, Zambia, Swaziland Lesotho	X			X	4 countries	N/A			X	Approaches for transition to adult care.	No national guidelines for age of transition Standard practice ranges from 15 (Zambia) to 21 (Swaziland) Only Kenya's National Adolescent Package of Care included standardized national tools for transition.	[39]
Kung 2016	South Africa	X	X		Mostly perinatal providers	43 survey 7 interviews	NA			X	Current state of transition, barriers and facilitators, and components of transition models	No clinics had a systematised transition process No national guidelines Signals used to justify transition incl: age (16-25); completion of schooling, request to move, traditional circumcision, pregnancy <u>Transition challenges:</u> Providers' difficulty in letting go of their relationships with adolescent patients; Patient and caregiver attachment to paediatric providers/clinic environment; Poor links between adult and paediatric providers; Feared transferring adolescents to judgemental, depersonalised and overburdened environment; Mental health problems and neurocognitive delay; Stigma especially if moving to township clinic <u>Transition recommendations:</u> Adolescent support groups in adult clinics; Later transition age	[40]
Frigati 2016	South Africa		X		perinatal	7 facilities				X	Survey of transition approaches	Only 1 site had a formal transition guideline Reasons for transition were age, school completion, return from traditional circumcision, adolescent or caregiver request, defaulted clinic attendance, pregnancy	[41]
Chekata Inzaule 2016	Uganda	X			NR	33 providers; 5 expert clients				X	Challenges to long term adherence	Stigma in boarding schools; Cessation of adolescent peer groups and decreased clinician support when transition to adult care	[42]
Willis 2016	Zimbabwe	X			NR	N/A				X	Describes program to strengthen provider capacity	66 adolescent support groups established Saturday clinics & community adolescent	[43]

Author (year)	Country	Design			Mode of infection	Sample size	Median age	Participants			Main outcome	Main finding	Ref
		Qualitative/semi-struct	Cross-section	Cohort				Patients	Care-givers	Providers			
										for AYLHIV services	treatment supporters (CATS) introduced; Providers described improved linkage, retention, adherence and mental health in adolescents & high acceptance of CATS		
Adolescent and youth friendly services or community adherence groups													
Teasdale 2016	Kenya			X	NR; AYLHIV age 10-24 at enrolment	2321; 730 (AYFS); 2321 (standard care)	21 (IQR:19-23) at enrolment	X			LTFU before and after implementation of AYFS	Pre-ART and on-ART LTFU similar before and after implementation of AYFS e.g. pre-ART LTFU 33.2% (CI: 28.6; 37.9) vs 25.2% (CI: 20.4; 30.3) at 12 months; p=0.15 on ART LTFU 11.9% (CI: 7.5; 17.3) vs 17.0% (CI: 10.4; 25.0) at 6 months; p=0.19	[44]
Ndiaye 2017	Senegal			X	Perinatal	47; 32 in Transition support Program (TSP) vs 15 in Standard Care (SC)	18.3 (IQR: 17.1-19.7) in TSP; 20.4 (IQR: 18.4-22.1) in SC	X			Virologic suppression (VS) (not defined) before and after TSP In TSP, transfer to adult care preceded by 2 years of joint visits with adult & pediatric clinician and community support groups. SC: preparation sessions in pediatric clinic with direct transfer to adult care	Transition duration longer in TSP vs SC (median [IQR] 27 months [17-40] vs 7 [6-8]) VS increased in TSP (61%-81%) but decreased in SC (73%-60%).	[45]
Zanoni 2016	South Africa			X	perinatal	254; 88 (Teen Clinic [TC]) 153 (standard care [SC])	NR	X			Cross-sectional retention (picked up meds <3 mos ago) and viral suppression at Teen Clinic (Saturday) vs standard care (weekday paediatric clinic)	Higher retention in TC vs SC (aOR =9.6; p=0.004) Higher viral suppression in TC vs SC (aOR = 4.1; p=0.004).	[46]
Wilkinson 2016	South Africa			X	NR; age 12-25	337	22.3 (IQR 20.3-23.7) at enrolment	X			Retention at 12 months (visit in the 3 months before database closure)	Retention at 12 mos by category: ART ineligible: 52.9% (CI:40.0-64.2) Newly started ART: 86.4% (CI:78.7-91.4) Stable on ART: 94.3% (CI:85.4-96.8)	[47]
Okoboi 2016	Uganda			X	NR: aged 10-19 at ART start	617	55% 10-14 yrs	X			Retention (not defined)	Non-retention at 12 months significantly associated with clinic-based (vs. community-based) ART delivery (a HR2.58, CI: 1.26-5.29)	[48]
Kamusiya 2016	Zimbabwe	X			NR	172	NR	X			Description of Community Based ART Mentors to support adolescents on ART.	Adherence to treatment increased to 95-100%; Community Based ART Mentors enhanced the adolescent self-belief and esteem	[49]

Note: all ages are reported in years; All Confidence intervals are 95% confidence intervals; aHR = adjusted Hazard Ratio; aOR = adjusted Odds Ratio; aRR = adjusted Risk Ratio; ART = antiretroviral therapy; AYLHIV = adolescents and youth living with HIV; CI: Confidence Interval; IQR: Interquartile Range; mos = months; N/A = not applicable; NR = not reported; yrs = years; SSA = sub-Saharan Africa

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Papers of particular interest, published within the annual period of review, (the last 2 years) have been highlighted as:

- of special interest
- of outstanding interest

The following papers will have •:

- Sainz[6]
Multicentre Spanish study of 209 adolescents with perinatal HIV transitioning to adult care, measuring LTFU, mortality and VS
- Hussen[9]
Study of 72 AYLHIV (15% perinatal) in a clinic in Atlanta, USA, who transfer to adult care at median 25 years of age
- Ryscavage[10]
Study of 50 AYLHIV (38% perinatal) in a clinic in Baltimore, USA, who transfer to adult care in their early/mid- 20s
- Weijnsfeld[11]
Nationwide study of 59 AYLHIV (78% perinatal) who transferred to adult care, exploring virological and social outcomes
- Westling[12]
Follow-up study of 34 AYLHIV (91% perinatal) transferring to adult care in the largest HIV outpatient clinic in Sweden
- Kung[40]
This study describes provider views on the transitions process in South Africa.
- Davies[25]
Study of post-transfer outcomes in 460 adolescents in South Africa using linkage across health services based on unique identifiers.
- Judd[7]
Assessment of mortality, virological and in particular immunological outcomes among 271 patients transferring to adult care in the UK
- Lolekha[29]
Description of a Thailand transition training programme and assessment of outcomes in 161 AYLHIV with perinatal HIV.
- Machado[33]
Qualitative study of adolescent perspectives on process of transitioning from paediatric to adult care via a Transition Adolescent Clinic (TAC) in paediatric services
- Zanoni[46]
Study of 254 adolescents with perinatal HIV showing better outcomes among those attending a "Teen Clinic" compared to those in standard care.
- Okoboi[48]
Ugandan study of 617 AYLHIV indicating better retention with community-based vs. facility based ART delivery.

The following papers will have ••:

- Kakkar[8]
Although a small study of 25 patients, the investigators not only measured engagement and immunological outcomes, but also patient perspectives on the transition process
- Tanner[15]
One of three papers from the same comprehensive study of healthcare providers' views on the transition process
- Griffith[18]
A study of 132 youth with HIV, suggesting a beneficial effect of youth-targeted care compared to standard of care on retention
- Lee[19]
Study of 680 youth with HIV, suggesting a beneficial effect of certain youth-friendly structures of care on retention
- Kranzer[24]
Study of 2273 children and adolescents in Zimbabwe showing that patients starting ART as young adolescents and older adolescents had higher LTFU when moving to next age group.
- Yi[36]
Study of 223 AYLHIV in Cambodia describing transition preparedness and the effect of different transition activities on preparedness for transition.
- Teasdale[44]
Study of 2321 AYLHIV enrolling in care before or after implementation of AYFS, suggesting no impact on LTFU after implementation of AYFS.

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