

Prioritized research questions for adolescent HIV testing, treatment and service delivery

The World Health Organization (WHO) and the Collaborative Initiative for Paediatric HIV Education and Research (CIPHER) of the International AIDS Society (IAS) have undertaken a global research prioritization process. This process is aimed at guiding research efforts and maximizing available resources to inform global policy change and improve outcomes for adolescents living with HIV.

The process was based on the Child Health and Nutrition Research Initiative (CHNRI) methodology¹ for setting priorities in health research. The priority research questions were identified through the collation of submissions from wide stakeholder outreach. The stakeholders who participated were then asked to score the collated lists of research questions against the following criteria: answerability, impact, implementation and equity.

To determine the ranking of the research questions, the Research Priority Score (RPS), a mean score given across criteria and scorers for each research question, was calculated according to this formula: $RPS = [(answerability \times .86) + (impact \times 1.56) + (implementation \times .77) + (equity \times .81)]/4^2$. The tables below present the results of the CHNRI process of ranked priority research questions and comprise a supporting annex to the final themes presented in the policy briefs.

An additional step, beyond the CHNRI approach, was undertaken to form the final research agenda. It involved an expert consultation of researchers, UN organizations, civil society and community representatives. They reviewed the top 10 ranked questions from the lists ranked in the tables in the context of ongoing research, published scientific literature and current WHO guidance. Themes, rather than questions, have been used for the final agenda.

For more information and access to the policy briefs, please visit: <https://www.iasociety.org/CIPHER>

TESTING

RESEARCH QUESTIONS		TOTAL RESEARCH PRIORITY SCORE
1	What are acceptable and effective strategies or interventions to improve access and uptake of HIV testing services by adolescents? <i>Consider different strategies for sub-groups such as young/older adolescents, urban/rural adolescents and adolescent girls and boys. Intervention or strategies may include, but are not limited to, stigma reduction, demand-creation activities, comprehensive sexuality education and mHealth.</i>	90.6
2	What individual, programmatic and structural factors enable or hinder newly diagnosed adolescents to link to HIV treatment and care? <i>Consider different sub-groups such as young/older adolescents, key populations, gender and sex.</i>	87.5
3	What strategies or interventions ensure timely linkage between HIV diagnosis and HIV treatment and care services for adolescents living with HIV? <i>Consider different strategies for sub-groups such as young/older adolescents, key populations, urban/rural adolescents and adolescent girls and boys. Interventions or strategies may include, but are not limited to, peer interventions, loss to follow up tracing, community based and mHealth.</i>	87.1
4	For adolescents from key populations, what are safe, acceptable and effective strategies or interventions to improve access and uptake of HIV testing services? <i>Consider different strategies for adolescents from different key population groups.</i>	86.8

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² Nagata JM, Ferguson JB, Ross DA. Research Priorities for Eight Areas of Adolescent Health in Low- and Middle-Income Countries. J Adolesc Health. 2016 Jul; 59(1): 50-60.

RESEARCH QUESTIONS		TOTAL RESEARCH PRIORITY SCORE
	<i>Intervention or strategies may include, but are not limited to, stigma reduction, demand creation activities, outreach and mHealth.</i>	
5	What are the individual, programmatic and structural factors that enable or hinder access and uptake of HIV testing services by adolescents? Consider different sub-groups such as young/older adolescents, key populations, gender and sex.	85.0
6	What consent policies and practices facilitate the access and uptake of HIV testing services among adolescents? <i>These may include, but are not limited to, lowering the age of consent, use of best-interest principles and policies, parent support interventions and protocols for providers.</i>	83.3
7	What strategies or interventions are effective for identifying adolescents at high risk of HIV for high yield testing, especially in low-HIV prevalence settings? <i>Interventions or strategies may include, but are not limited to, screening tools, index parent, partner testing and new innovations.</i>	82.4
8	Is self-testing a safe, acceptable and feasible HIV testing approach for adolescents?	77.9
9	Is self-testing effective in increasing the uptake of HIV testing and improving linkage to care among adolescents?	76.3
10	What is the acceptability, feasibility, sustainability and cost effectiveness of implementing school-based testing for adolescents?	76.3
11	What are the rates, predictors and correlates for HIV infection among adolescents?	74.1
12	What community-based approaches are effective at identifying undiagnosed HIV-positive adolescents?	51.8

TREATMENT

RESEARCH QUESTIONS		TOTAL RESEARCH PRIORITY SCORE
1	What are effective strategies or interventions to improve adherence among adolescents on ART? <i>These may include, but are not limited to, mHealth, mental health interventions, treatment strategies, peer interventions and financial and social incentives.</i>	89,3
2	What is the safety, efficacy and acceptability of novel drug delivery systems to improve treatment outcomes for adolescents? <i>These include, but are not limited to, long-acting or extended release delivery systems, for example, a single-dose regimen (injection) or continuous dosing regimen (implant, transdermal patch, optimization of oral formulations, etc.).</i>	88.0
3	What are the individual, programmatic and structural factors that enable or hinder adherence among adolescents taking ART?	87.2
4	What simplified screening tools can be developed and validated to assess the risk of non-adherence and treatment failure among adolescents on ART?	84.1
5	How do we optimize the prevention and/or clinical management of co-infections, particularly tuberculosis, for adolescents living with HIV to improve clinical outcomes?	83.5
6	What are the optimal 1st, 2nd, and 3rd regimens and formulations to maximize adherence and treatment outcomes for adolescents living with HIV?	83.4

RESEARCH QUESTIONS		TOTAL RESEARCH PRIORITY SCORE
7	What is the impact of HIV infection and/or ART exposure on long-term outcomes among adolescents living with HIV? <i>These include, but are not limited to, prevalence and outcomes of non-communicable disease (cardiovascular, respiratory, metabolic), developmental outcomes (physical, neuro, psycho and sexual development), disease progression and mortality, quality of life, and psychosocial and educational outcomes.</i>	83.3
8	What are the risk factors for non-communicable diseases among adolescents living with HIV and the optimal simplified screening tools to identify them?	82.3
9	What are the rates and correlates of virological suppression and treatment failure among adolescents on ART?	81.9
10	What is the optimal frequency of viral load monitoring to prevent and identify virological failure among adolescents on ART?	80.0
11	What simplified screening tool can be developed and validated to assess neurocognitive development and mental health disorders among adolescents living with HIV?	79.4
12	What are the patterns and correlates of HIV drug resistance among adolescents living with HIV?	79.2
13	What is the prevalence of opportunistic and coinfections among adolescents living with HIV, especially tuberculosis and hepatitis?	76.3
14	What is the prevalence of ARV-related side effects among adolescents on ART? <i>These may include, but are not limited to, renal and physical changes – skin lipoatrophy, lipo-hypertrophy, dyslipidaemia.</i>	74.7
15	What are the best immunization strategies for adolescents living with HIV? <i>These may include, but are not limited to, revaccination, novel vaccinations and standard vaccination procedures.</i>	70.6
16	What are the levels of adherence by age and population (such as route of infection and high-risk group) among adolescents on ART?	70.5
17	How does the age at ART initiation impact clinical and programme outcomes for those infected during adolescence?	69.0

SERVICE DELIVERY

RESEARCH QUESTIONS		TOTAL RESEARCH PRIORITY SCORE
1	What are effective interventions to improve retention in care among adolescents living with HIV? <i>Consider sub-groups such as younger adolescents, key populations and gender. Interventions may include, but are not limited to, outreach, community- or school-based, adolescent-friendly health services, peer interventions, mHealth, tracking loss to follow up, financial and social incentives, and those addressing structural barriers.</i>	92.4
2	Among adolescents living with HIV, what are effective strategies or interventions to improve sexual and reproductive health (SRH) outcomes? <i>These may include, but are not limited to, interventions to reduce SRH risk-taking behaviours, increase use and uptake of SRH information and services, and reduce rate of sexually transmitted infections.</i>	87.8
3	What strategies or interventions are effective in supporting pregnant adolescents living with HIV to improve the health outcomes of the mother-baby pair?	87.5

RESEARCH QUESTIONS		TOTAL RESEARCH PRIORITY SCORE
4	What peer interventions or models are effective in improving health outcomes for adolescents along the HIV cascade? <i>These may include, but are not limited to, peer navigators, peer networks, peer support groups or clubs, peer outreach workers, peer health providers, camps and mHealth.</i>	87.5
5	What are effective psychosocial support strategies or interventions for adolescents living with HIV to improve health, wellbeing and programmatic outcomes? <i>Consider sub-groups such as key populations and pregnant adolescents, and different delivery settings. Interventions may include, but are not limited to, peer interventions, support groups, counselling and mHealth.</i>	86.9
6	What are effective, acceptable, feasible and cost-effective models for perinatally HIV-infected adolescents as they transition from paediatric to adult ART services? <i>These may include, but are not limited to, transitional clinics, joint paediatric/adult care before transition, peer interventions and mHealth.</i>	86.7
7	What differentiated service delivery models are appropriate and effective in improving health and programmatic outcomes for adolescents living with HIV? <i>Consider different sub-population groups such as younger adolescents, pregnant adolescents and adolescents from key populations.</i>	86.7
8	What are the individual, programmatic and structural factors that enable or hinder adolescents living with HIV to be retained in services?	85.5
9	What are effective prevention, promotion and treatment strategies or interventions to improve mental health outcomes among adolescents living with HIV?	85.0
10	What service delivery models are effective in improving the health and programmatic outcomes of adolescents along the HIV cascade? <i>Consider sub-groups such as key populations. Interventions may include, but are not limited to, adolescent clinics, decentralized primary health clinics and mobile- and community-based services.</i>	84.4
11	What are the sexual and reproductive health needs, characteristics and their associated outcomes of adolescents living with HIV? <i>Consider current sexual activity, age of sexual debut, fertility desires, partner numbers and status, and risk-taking behaviours.</i>	84.4
12	How can effective adolescent-friendly health services be best implemented in decentralized healthcare settings for adolescents living with HIV, taking into consideration cost effectiveness, feasibility and sustainability?	84.3
13	How can effective peer interventions for adolescents living with HIV be implemented at scale, taking into consideration cost effectiveness, feasibility, sustainability and acceptability?	83.3
14	What are effective strategies or interventions to reduce stigma and discrimination, including self-stigma, experienced by adolescents living with HIV? <i>Consider interventions in different settings such as community, home, health facilities and education system.</i>	82.5
15	How can effective retention strategies or interventions be implemented in different settings at scale, taking into consideration cost effectiveness, feasibility and sustainability?	81.4
16	How can effective psychosocial support strategies or interventions be implemented at scale, taking into consideration cost effectiveness, feasibility and sustainability?	81.4
17	What strategies or interventions are appropriate and effective in supporting self-efficacy and resilience among adolescents living with HIV?	80.1
18	What are the outcomes and characteristics of perinatally HIV-infected adolescents transitioning from paediatric to adult ART services?	80.0
19	What are the rates, predictors and correlates of loss to follow up among adolescents living with HIV?	79.8

RESEARCH QUESTIONS		TOTAL RESEARCH PRIORITY SCORE
20	What are effective strategies or interventions to support the development of relationships and communication skills for parents and caregivers to improve health and programmatic outcomes for adolescents living with HIV?	79.4
21	Among adolescents living with HIV, what are the literacy, knowledge and understanding levels regarding HIV, ART and sexual and reproductive health, and how can they be improved?	79.3
22	What school-based strategies or interventions are effective, appropriate and feasible to support the health and educational outcomes of adolescents living with HIV?	78.8
23	What are the rates, correlates and impact of mental health disorders among adolescents living with HIV? <i>Consider sub-groups such as young/older adolescents, sex and gender identity, key populations and mode of infection.</i>	78.1
24	What is the level of stigma and discrimination experienced by adolescents living with HIV in different settings and its impact on health and wellbeing, and educational and programmatic outcomes?	78.0
25	What strategies or interventions can be implemented to support late disclosure to adolescents living with HIV? <i>Consider interventions for adolescents, parents and caregivers and/or health providers etc.</i>	76.6
26	What individual, programmatic, societal and structural factors enable or hinder the improvement of self-efficacy and resilience among adolescents living with HIV?	76.6
27	What models of health provider capacity building are effective, feasible and sustainable in improving health and programmatic outcomes for adolescents living with HIV? <i>Models may include, but are not limited to, routine supervision, mentoring, audits with feedback and continuous quality improvement etc.</i>	75.6
28	What strategies or interventions are effective in supporting adolescents to disclose to others? <i>Consider family, sexual partners, friends, teachers and work colleagues.</i>	75.0
29	Among adolescents living with HIV, what are rates and influencing factors of disclosure/nondisclosure to others? <i>Consider family, sexual partners, friends, teachers and work colleagues.</i>	74.7
30	What are the pregnancy rates of adolescents living with HIV, and what are the characteristics and outcomes of pregnant adolescents living with HIV?	73.8
31	What is the impact of different types of violence on the health outcomes of adolescents living with HIV?	72.1
32	What are rates, influencing factors and outcomes of late disclosure among adolescents living HIV?	71.4

Prioritized research questions for paediatric HIV testing, treatment and service delivery

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TESTING

RESEARCH QUESTION		TOTAL RESEARCH PRIORITY SCORE
1	What is the optimal placement and the impact of point-of-care early infant diagnosis on the rates of ART initiation among infants and children living with HIV?	89.4
2	What interventions ensure timely linkage between HIV diagnosis and treatment and care for infants and children living with HIV?	87.7
3	What are novel diagnostic tools that are optimized for point of care (such as smaller size and battery compatible) that can be developed and validated to provide accurate results for birth testing and recent infection of HIV-exposed infants?	87.3
4	What interventions or strategies improve access and uptake of early infant diagnosis for infants living with HIV? <i>These may include, but are not limited to, m-health platforms, family testing, integrated services and community engagement.</i>	87.0
5	What community-based approaches are effective in identifying undiagnosed HIV-positive infants and children?	84.7
6	What factors enable or hinder timely initiation of ART among infants and children infected with HIV and subsequent linkage to care?	83.9
7	What testing strategies at entry points other than antenatal care (ANC) and the labour ward are effective, feasible and acceptable in identifying undiagnosed HIV-positive infants and children in different epidemic settings? <i>Strategies may include, but are not limited to, screening tools for targeted testing, HIV testing integration with birth registration, vaccination and preschool services.</i>	82.8

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RESEARCH QUESTION		TOTAL RESEARCH PRIORITY SCORE
8	What strategies or interventions are effective at improving uptake and retention in care of HIV-exposed uninfected infants and children?	81.9
9	What is the effectiveness, acceptability and feasibility of routine birth testing on the identification of undiagnosed HIV-positive infants and their initiation on ART?	80.0
10	What are the factors that enable or hinder access and uptake of HIV testing services by parents and caregivers (including those from key populations) for infants and children exposed to HIV? <i>Factors may include, but are not limited to, age, gender, distance from the health facility, disclosure status and service entry points.</i>	78.9
11	In the context of maternal ART during pregnancy and breastfeeding, what is the sensitivity and specificity of early infant testing approaches on the identification of undiagnosed HIV-positive infants?	78.5
12	What clinical management, monitoring and surveillance strategies for HIV-exposed uninfected infants and children are effective in improving health and programmatic outcomes?	77.7
14	In the context of maternal ART, do HIV-exposed uninfected children have a higher risk of adverse short-, medium- and long-term health outcomes compared with HIV-non-exposed children? <i>These may include, but are not limited to, effects on short- to medium-term outcomes such as growth and early child development and effects on long-term outcomes such as non-communicable diseases, metabolic syndromes, neurocognitive development and fertility, in addition to quality of life and psychosocial and educational outcomes.</i>	69.8
15	How can parents or caregivers be supported to effectively deliver HIV self-tests to their children (>18 months of age) who may be at high risk of HIV infection from mother to child transmission (MTCT)?	69.5
16	In the context of maternal ART, what are the rates and correlates of mortality and morbidity outcomes (short and long term) among HIV-exposed uninfected children compared with non-exposed children? <i>Consider underlying biological and immunological mechanisms.</i>	69.1
17	In the context of maternal ART, what are correlates of HIV infection among infants and children? <i>These may include, but are not limited to, transmission patterns, incidence of HIV infection, geographic differences and late maternal seroconversions.</i>	67.6

TREATMENT

RESEARCH QUESTION		TOTAL RESEARCH PRIORITY SCORE
1	What are the safety, efficacy and pharmacokinetic profiles of new antiretroviral drugs, drug classes and formulations to be used in infants and children living with HIV? <i>Consider addressing specific issues such as maternal/transmitted HIV drug resistance, harmonization with maternal ARV regimens, acceptability and feasibility of paediatric formulations in low- and middle-income countries and ARV central nervous system penetration.</i>	87.6
2	What are effective strategies or interventions to improve adherence among infants and children on ART? <i>These may include, but are not limited to, mental health tools, monitoring strategies, family-focused health systems and innovative technologies such as mobile phone platforms.</i>	86.8

RESEARCH QUESTION		TOTAL RESEARCH PRIORITY SCORE
3	How do we optimize ARV dosing for infants and children living with HIV? <i>These may include, but are not limited to, validation of fixed-dose combination dosing (FDC) and current modelling approaches, as well as the impact of drug interactions and health status (such as malnutrition or diarrhoeal disease) on efficacy.</i>	86.2
4	What is the safety, efficacy and acceptability of novel drug delivery systems to improve treatment outcomes in infants and children living with HIV? <i>These include but, are not limited to, long-acting or extended release delivery systems, for example, a single-dose regimen (injection) or continuous-dosing regimen (implant, transdermal patch, optimization of oral formulations, etc.).</i>	86.1
5	How do we optimize the prevention and/or clinical management of co-infections, particularly tuberculosis, for infants and children living with HIV to improve clinical outcomes?	84.3
6	What are the individual, family, programmatic and structural factors that enable or hinder adherence and virological suppression (or treatment failure) among infants and children on ART?	81.0
7	What is the impact of HIV infection and/or ART exposure on short- to long-term outcomes among infants and children living with HIV? <i>These may include, but are not limited to, prevalence and outcomes of non-communicable disease outcomes (cardiovascular, respiratory, metabolic), developmental outcomes (physical, neuro, psycho and sexual development), disease progression and mortality, in addition to quality of life and psychosocial and educational outcomes.</i>	80.6
8	What is the optimal frequency of viral load monitoring to prevent and identify virological failure among children on ART?	79.5
9	What are the patterns and correlates of HIV drug resistance among infants and children living with HIV?	78.5
10	What are the short- and long-term virologic and immunologic response outcomes of starting treatment early in infants living with HIV?	78.2
11	What simplified screening tools can be developed and validated to assess the risk of treatment failure among infants and children living with HIV?	78.2
12	What are the surrogate markers of HIV reservoirs and the innovative therapeutic strategies to control HIV reservoirs in order to achieve a functional cure for infants living with HIV?	77.0
13	What are the optimal approaches to treatment sequencing for children living with HIV?	76.8
14	What are the best immunization strategies for infants and children living with HIV? These may include, but are not limited to, revaccination, novel vaccinations or maintaining standard vaccination strategies.	76.6
15	What are the optimal screening tools and effective strategies or interventions to prevent and minimize the impact of non-communicable diseases among infants and children living with HIV?	75.8
16	What is the prevalence of opportunistic and co-infections among infants and children living with HIV? <i>This is especially with regards to tuberculosis and hepatitis.</i>	70.5
17	What are the strategies to control immune activation among infants and children living with HIV?	70.4
18	What are the markers and correlates of immune activation and their impact on clinical outcomes?	69.0
19	How does the age of ART initiation affect and predict short- and long-term outcomes? <i>These may include, but are not limited to, non-communicable disease incidence, neurodevelopment, co-morbidities, mortality, survival, retention and adherence.</i>	67.7
20	What is the impact of planned treatment interruption (weekends off/ treatment holidays) on clinical outcomes for children living with HIV, and what strategies allow for safe treatment interruption?	67.6

RESEARCH QUESTION		TOTAL RESEARCH PRIORITY SCORE
21	What are the key characteristics and determinants of paediatric elite controllers and how can they be identified and managed?	65.0

SERVICE DELIVERY

RESEARCH QUESTIONS		TOTAL RESEARCH PRIORITY SCORE
1	What are effective strategies or interventions to improve access, uptake and retention in care among infants and children living with HIV? <i>Consider strategies or interventions at the programmatic, facility, individual and community level for different age groups.</i>	89.7
2	What service delivery models are effective in improving the health and programmatic outcomes of infants and children (including orphans) along the HIV cascade? <i>Service delivery models may include, but are not limited to, decentralization, specialized paediatric clinics, family-centred care models, community-based delivery and differentiated service delivery.</i>	85.7
3	What are effective family support strategies or interventions that ensure appropriate care and support of infants and children living with HIV? <i>These may include, but are not limited to, social protection and economic support, training and skills development.</i>	84.2
4	What are effective psychosocial support strategies or interventions for children living with HIV to improve health, wellbeing and programmatic outcomes?	82.0
5	What are the rates and patterns of loss to follow up and the factors that enable or hinder infants and children living with HIV to access, uptake and be retained in services? <i>Consider individual, structural and programmatic factors.</i>	78.9
6	What strategies or interventions can be implemented to improve and support parents, caregivers and healthcare providers to facilitate HIV disclosure to children living with HIV?	78.5
7	What are the factors that enable or hinder HIV disclosure to children living with HIV?	78.3
8	How do we effectively integrate comprehensive HIV treatment and care into the MCH services delivery platforms to improve outcomes among infants and children living with HIV?	77.9
9	What are effective strategies or interventions to reduce stigma and discrimination experienced by children living with HIV and their caregivers? <i>Consider different settings such as community, home, health facilities and education system.</i>	77.5
10	What is the prevalence of disability, including learning disabilities, among children living with HIV and what interventions or strategies can effectively improve their health outcomes?	76.8
11	What is the level of stigma and discrimination experienced by children living with HIV and their caregivers in different settings and its impact on child health, educational and programmatic outcomes? <i>Consider settings such as the community, home, health facilities and education system.</i>	74.8
12	What are the knowledge, attitudes and practices of healthcare providers in providing comprehensive treatment, care and support to infants and children living with HIV?	71.7
13	What are the optimal nutritional supplementations to improve health outcomes among infants and children living with HIV?	69.8
14	What is the impact of different types of violence on the health outcomes of children living with HIV, and how can these be appropriately and effectively addressed?	68.2