Management of HIV complications

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Interventions included in this evidence brief are:

1. HIV treatment (ART second-line)
2. Cotrimoxazole prophylaxis, HIV (children and pregnant mothers)

Description of condition and intervention

HIV is a major global public health problem, having claimed 36.3 million lives. In 2020, 6,80,000 people died from HIV related causes and 1.5 million people acquired new HIV infections. Human immunodeficiency virus (HIV) is an infection that attacks mainly the body's immune system. It attacks the white blood cells (WBCs) called CD4 cells. HIV destroys CD4 cells and weakens the immunity of a person. Infection of HIV leads to many opportunistic infections, such as tuberculosis, fungal infections, bacterial infections, and cancers (WHO 2021). Advanced stage of HIV infection is acquired immunodeficiency syndrome (AIDS). AIDS takes many years to develop, depending on the individual and treatment. The symptoms of HIV depend upon the stage of infection. People with HIV are more prone to infections in the first few months after being infected, many are unaware of their status until the later stages. The infection progressively weakens the immune system, other signs and symptoms can be developed, such as swollen lymph nodes, weight loss, fever, diarrhoea, and cough. Without treatment, they could also develop severe illnesses such as tuberculosis (TB), cryptococcal meningitis, severe bacterial infections, and cancers. (WHO 2020).

Early treatment of HIV can be managed by treatment regimens which are composed of 3 or more antiretroviral (ARV) drugs. The current antiretroviral therapy (ART) suppresses viral replication and allows and individual's immune system recovery to strengthen the capacity to fight with opportunistic infections and some cancers as well. WHO recommends that all people living with HIV should be provided with lifelong ART, including children, adolescents, adults and pregnant and breastfeeding women, regardless of clinical status or CD4 cell count (WHO 2021). Recent updated guidelines by WHO in 2019 recommend use of DTG (dolutegravir) as preferred ARV drug for second-line ART among adults, adolescents, and children, especially if a non-DTG based regimen has failed (WHO 2019). Provision of cotrimoxazole to HIV positive children to prevent opportunistic infections (PCP and toxoplasmosis). In this evidence brief, we discuss effectiveness for cotrimoxazole, assuming ART is already provided.

International guidelines

Organization	Indications/recommendations	Applicability in LIC & Lower MIC settings
WHO July 2021	Consolidated guidelines on HIV prevention, testing, Treatment, service Delivery and monitoring: Recommendations for a Public health approach	Yes
WHO 2014	Guidelines on post-exposure prophylaxis for HIV and the use of co-trimoxazole prophylaxis for HIV-related infections among adults, adolescents and children: recommendations for a public health approach 2014.	Yes

Intervention attributes

Type of interventions & Delivery platform

Table 1: Type of interventions & delivery platform

Intervention	Type	Delivery platform
1. HIV treatment (ART second line)	Chronic management	First level hospital

2. Cotrimoxazole prophylaxis, HIV (children and pregnant mothers)	Prevention	Community

Equity

In addition to considerations like cost-effectiveness and health systems factors, dimensions of equity can be relevant for priority setting. The opportunity for a long and healthy life varies according to the severity of a health condition that individuals might have, so there are inequities in individuals' opportunities for long and healthy lives based on the health conditions they face. Metrics used to estimate the severity of illness at an individual level can be used to help prioritize those with less opportunity for lifetime health. FairChoices: DCP Analytics Tool uses Health adjusted age of death (HAAD), which is a metric that estimates the number of years lived from birth to death, discounting years lived with disability. A high HAAD thus represents a disease less severe in terms of lifetime health loss, while a low HAAD represents a disease that is severe on average, causing early death or a long period of severe disability. It is also possible to estimate the distribution of HAAD across individuals with a health condition. FairChoices shows for each intervention an average HAAD value of the conditions that are affected by respective interventions that have health effects. Additionally, a plot shows HAAD values for around 290 conditions (Johansson KA et al 2020).

Time dependence

Moderate level of urgency. Treatment outcomes not highly affected by some days of delay.

Population in need of interventions

Table 2: Population in need of interventions

Intervention	Treated population		Affected population	
	Treated age	Treated fraction	Affected age	Affected fraction
HIV treatment (ART second line)	0 to 99 years	0.04 (Boettiger et al 2015)	0 to 99 years	Those with condition

Cotrimoxazole prophylaxis, HIV (children and pregnant mothers)	prevalence based			
Pregnant mothers	15 to 49 years	Annual incidence of pregnancy estimated as total fertility rate × prevalence of HIV/AIDS		
Infants (with HIV infection)	0 to 0 years	0.8 of new-borns adjusted to 1.2 to account for the 1.5 years treatment duration.		
Children	0 to 4 years	0.8 of children adjusted to 1.2 to account for the 1.5 years treatment duration.	0 to 4 years	0.8 of children adjusted to 1.2 to account for the 1.5 years treatment duration

Disease state addressed

The included interventions target HIV/AIDS condition. People with HIV/AIDS receive the intervention and the benefits of the interventions are considered in those with HIV/AIDS resulting in other diseases.

Intervention effectiveness and safety

Table 3: Effectiveness and safety of interventions for management of complications in HIV/AIDS

What happens?	No intervention	With intervention	Certainty of evidence	Transferability of evidence
Mortality Cotrimoxazole prophylaxis, HIV (children and mothers)	Based on Walker 2007, the efficacy is 25.3. The RCT looks at efficacy of adding cotrimoxazole (compared to placebo) to children with HIV under different circumstances (before ART is available, =no ART to children, and after ART is made available, =children get ART) in Zambia. Based on Figure 1 in this study, we only use numbers (deaths in the two groups - when ART is provided) - since we are mainly interested in added benefit of cotrimoxazole when children get ART (as this is the standard treatment in all countries today). Calculation from Figure 1 is then: ((1/120)/ (3/91) =0.253)			
ART (second-line)	Assumed to be 3/4th of efficacy of ART for first-line=0.52*(3/4) =0.39 reduction			

Model assumptions

Table 4: Summary of model parameters and values used in FairChoices – DCP Analytical Tool

Category	Model parameter	Notes
Intervention	HIV treatment (ART second line) Cotrimoxazole prophylaxis, HIV (children and pregnant mothers)	
Cost calculation		

Treated population	See Table 2	Epidemiological data from Global Burden of Disease Study 2019 for the health condition HIV/AIDS
Effect calculation		
Affected population	See Table 2	Epidemiological data from Global Burden of Disease Study 2019 for the health condition HIV/AIDS due to other illness
Affected fraction	See Table 2	
Comparison	No intervention	
Mortality Reduction (RRR) Cotrimoxazole prophylaxis, HIV (children and mothers) ART (second-line)	 0.747 0.39	 Walker et al 2007 Assumed

Intervention cost

The cost of Cotrimoxazole prophylaxis, HIV (children and mothers) is estimated to be $2.355 per person-year in specified population in 2006 USD in Zambia (Ryan et al 2008). The cost of Cotrimoxazole prophylaxis is calculated as the average of $1,57/year for ½X480 mg tablet and 3.14/year for 1X480 mg tablets.

The cost per patient per year for second-line treatment is estimated at 1037 in 2019 USD in South Africa, 71% of which is due to the cost of drugs (Long , Fox, Sanne, Rosen 2010).

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Appendix

Literature Review for effectiveness & safety

This literature search is an example of Level 1 search for intervention inputs taken from DCP3 or generated in an ad hoc manner (e.g., quick google search found one study of cervical cancer screening cost-effectiveness that was used to create an effectiveness parameter for that intervention).

Level of evidence of efficacy studies:

1. low (expert opinions, case series, reports, low-quality case control studies)
2. moderate (high quality case control studies, low quality cohort studies)
3. high (high quality cohort studies, individual RCTs)
4. very high (multiple RCTs, metaanalysis, systematic review, clinical practice guidelines)

An overview of interventions in this cluster with those included in this evidence brief highlighted in bold.

HIVSTI01	HIV population screening and early treatment
HIVSTI01-01	Community-based HIV education and testing services, including referral to care
HIVSTI01-02	HIV education and counselling for MARPS
HIVSTI01-03	Household HIV testing and linkage to ART
HIVSTI01-04	Provider HIV, STI, Hepatitis testing and linkage to care
HIVSTI01-05	HIV treatment
HIVSTI01-05-01	ART first-line
HIVSTI01-05-01-01	ART for HIV, no TB
HIVSTI02	**Management of HIV complications**
HIVSTI02-01	**Management of opportunistic infections associated with HIV/AIDS**
HIVSTI02-02	**HIV treatment (ART second-line)**

HIVSTI02-03	**Cotrimoxazole prophylaxis, HIV (children and mothers)**
HIVSTI03	HIV prevention
HIVSTI03-01	Mass media encouraging use of condoms, voluntary medical male circumcision, and STI testing
HIVSTI03-02	Voluntary medical male circumcision service in settings with high prevalence of HIV
HIVSTI03-03	Provision of condoms to MARPS
HIVSTI03-04	PrEP for discordant couples and others at high risk of HIV (in high prevalence settings)
HIVSTI03-05	Prevention of mother to child HIV transmission (PMTCT, option B+) and syphilis
HIVSTI04	IDU-HIV programs
HIVSTI04-01	IDU-HIV: outreach
HIVSTI04-02	IDU-HIV: needle exchange
HIVSTI04-03	IDU-HIV: opioid substitution therapy*
HIVSTI05	Syndromic management of common sexual and reproductive tract infections
HIVSTI05-01	Treatment of urinary tract infection (UTI)
HIVSTI05-02	Treatment of syphilis
HIVSTI05-03	Treatment of gonorrhea
HIVSTI05-04	Treatment of chlamydia
HIVSTI05-05	Treatment of trichomoniasis
HIVSTI05-06	Treatment of PID (Pelvic Inflammatory Disease)
HIVSTI05-07	Partner notification STIs (including HIV)