

Cost-effective prevention of HIV-related opportunistic infections

Summary

Cotrimoxazole prophylaxis, which prevents deaths and hospital admissions across all ages of individuals with HIV infection in resource-limited countries, is cheap. Economic research in adults in Uganda, and more recently in children in Zambia, has shown that Cotrimoxazole is highly cost-effective. Specific research in Zambia has even found that it could be cost saving: if all HIV-infected children in Zambia received Cotrimoxazole prophylaxis, the net effect could be savings to the health system in the range of US\$2.9 - 9.6 million per year.

Earlier research demonstrated that, in both adults and children with HIV infection not on antiretroviral therapy (ART), low dose Cotrimoxazole cuts deaths by nearly one half and hospital admissions by around one quarter. As a result of this research, WHO and UNAIDS issued statements in 2004, followed by updated WHO Guidelines in 2006, advocating the use of Cotrimoxazole prophylaxis as a key element of pre-ART care for children, adolescents and adults. However, there is evidence that this message is not being taken up. In 2006, UNAIDS figures estimate that only 4% of adults and 1% of children with HIV have access to Cotrimoxazole. Greater commitment is needed at national and international levels to ensure that this simple, life-saving drug is accessible to all who need it. This recent evidence of cost-effectiveness highlights that lives can be saved at very low cost.

The impact of opportunistic infections

Opportunistic infections are a leading cause of illness and death for adults and children living with HIV in resource-limited countries. Lung infections (pneumonia) and blood infections (septicaemia) caused by bacteria (for example, *Pneumococcus*, *Haemophilus Influenza*, *non-typhi Salmonella*, *Staphylococcus Aureus*) occur frequently in individuals with HIV because of poor immunity, particularly in young children. In very young children with HIV infection, a frequently fatal lung infection called *Pneumocystis Carinii* is very common. This occurs most frequently at around 3-6 months of age and is one of the major reasons why

nearly half of all children born with HIV infection die before their second birthday.

Where neither ART nor Cotrimoxazole prophylaxis are available, the impact of opportunistic infections makes HIV very expensive in terms of lives, economic costs to individuals, the health system and the economy as a whole. Preventing and treating opportunistic infections is vital to improving survival among those who do not have access to ART.

Cotrimoxazole prophylaxis to prevent opportunistic infections

Effective

There is strong evidence to support the use of Cotrimoxazole prophylaxis

in HIV-infected adults and children as well as in all infants born to HIV-infected mothers in the first year of life (HIV-exposed infants).

Key Points

- Cotrimoxazole prophylaxis saves lives and is highly cost effective and feasible
- Many who need it do not have access to it, making concerted action necessary

Cotrimoxazole Prophylaxis

Cotrimoxazole (trimethoprim-sulfamethoxazole) is a widely available, low cost, broad-spectrum antimicrobial drug and is given as a daily preventative therapy.

In adults, a meta-analysis of three African trials with both early and advanced HIV disease demonstrated a significant benefit of Cotrimoxazole prophylaxis, with a 31% reduction in mortality, 27% reduction in morbid events and 55% reduction in patients being hospitalised.

Cotrimoxazole is often used as full treatment for bacterial infections and this frequent use can result in high levels of resistance of bacteria to the drug. However, research examining the effect of Cotrimoxazole prophylaxis in HIV infected children older than 1 year of age in Zambia (a country with high Cotrimoxazole resistance) showed a 43% reduction in mortality, and hospital admission rates fell by 23% compared to children receiving no Cotrimoxazole.

Importantly, Cotrimoxazole prophylaxis given during the very early months of life almost completely prevents *Pneumocystis Carinii* in infants. Cotrimoxazole prophylaxis also reduces other diseases such as malaria and infections causing diarrhoea in children and adults.

In 2004 a joint UNAIDS/WHO/UNICEF statement was issued on the use of Cotrimoxazole as prophylaxis in HIV exposed and HIV infected children. Building on this, in 2006 WHO issued detailed updated recommendations advocating the use of Cotrimoxazole prophylaxis in resource-limited settings in all HIV-exposed infants from around 6 weeks of age until shown not to be infected, all symptomatic HIV-infected adults and children, all HIV-infected asymptomatic children and asymptomatic adults with mild to moderate immune suppression.

Although we need more information about the need to keep taking Cotrimoxazole prophylaxis once ART has been started, the evidence so far suggests that benefit may continue, especially in children. WHO recommends that all children on ART continue to take Cotrimoxazole prophylaxis.

Practical

Cotrimoxazole prophylaxis is a low-technology intervention that is widely available as both solid and, though more expensive, syrup formulations. Children and babies can simply take either low-dose tablets or half or one quarter of an adult tablet which is cheaper and easier to transport and administer than syrups. It is made locally in most countries in Africa

“If all HIV-infected children in Zambia received cotrimoxazole prophylaxis, this would generate up to US\$9.6 million of savings to the health system per year”

and other resource-limited countries and can be implemented at the local health centre level. For the patient and carer, this reduces travel costs and time spent away from employment. Approaches to ensuring accessibility and regular supply in some countries could include deregulating the

Cost-effective

WHO have recommended that an intervention may be considered highly cost-effective if the cost per outcome, e.g. cost per DALY, is less than the Gross Domestic Product (GDP) per capita in that country.

Cost-saving

An intervention may be considered cost-saving if the savings generated are greater than the total cost associated with implementing the intervention.

prescribing of Cotrimoxazole prophylaxis so that nurses and healthcare assistants are able to dispense it, and linking Cotrimoxazole to special supply chains established for ART.

Cheap and highly cost-effective

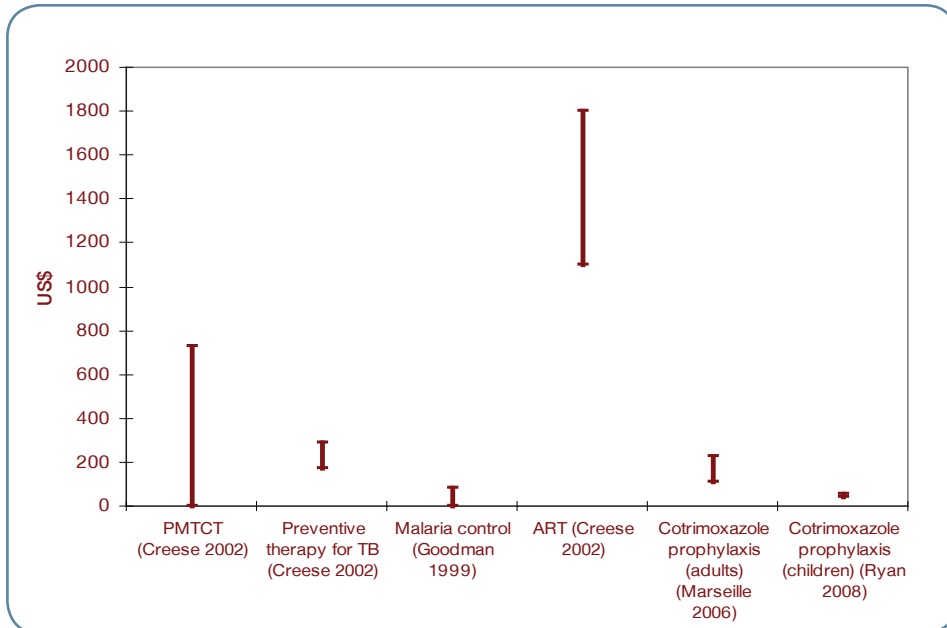
Cotrimoxazole is an inexpensive drug, with cheap generic versions available. Based on prices in Zambia, Cotrimoxazole prophylaxis costs as little as US\$1.57 per year for children under five and US\$3.14 per year for those over five years.

Recent cost-effectiveness analysis of trial data from Zambia demonstrates that children who receive Cotrimoxazole prophylaxis spent less inpatient days in hospital and had lower inpatient costs than children

not receiving Cotrimoxazole. This research showed that Cotrimoxazole prophylaxis in HIV-infected children is highly cost-effective, when taking into account all HIV related outpatient and inpatient care. This found that there was a cost of US\$53 per Disability Adjusted Life Year (DALY) averted, based on care at a tertiary care hospital. Once the costs of transportation to hospital and lost carer productivity were factored in these costs fell to US\$38 per DALY averted. Basing the costs on local health clinics, Cotrimoxazole prophylaxis appears even more attractive, with a cost of US\$3 per DALY averted. For children of 9 years or older, Cotrimoxazole prophylaxis is cost-saving.

Other studies in Côte D'Ivoire and Uganda arrived at similar conclusions of cost-effectiveness for Cotrimoxazole prophylaxis in

Cost Per DALY Averted



HIV-infected African adults. These cost-effectiveness ratios compare favourably with other health interventions considered cost-effective in the African setting, as figure 1 illustrates.

In the Zambian trial, a simple budget impact analysis, which examined the cost of drug and outpatient monitoring minus the cost of inpatient care, suggests that Cotrimoxazole prophylaxis may even be cost-saving. The total cost of Cotrimoxazole prophylaxis in Zambia could result in a saving of US\$35.75 per patient year. If all HIV-infected children in Zambia (HIV prevalence range from 1.5% to 5%) received prophylaxis, this could generate savings to the health system in the range of US\$2.9 - 9.6 million per year.

Still not accessible to all

Despite all the evidence of the benefits of Cotrimoxazole prophylaxis for HIV infected people, the drug has not yet been incorporated into the Essential Healthcare Packages

“Globally only 4% of adults and 1% of children living with HIV have access to Cotrimoxazole”

of many countries and widespread implementation of Cotrimoxazole prophylaxis at the local health centre level has not taken place. UNAIDS estimates that in 2006 globally only 4% of adults and 1% of children living with HIV had access to Cotrimoxazole.

Policy recommendations

Recommendations for national governments

Policy

- Implement Cotrimoxazole prophylaxis, a cost-effective intervention, as an integral component of the HIV chronic care package and as a key element of pre-ART care
- As currently recommended, continue Cotrimoxazole prophylaxis after initiation of ART

Fig. 1 Cost-effectiveness of health interventions in resource poor settings

Disability Adjusted Life Year (DALY)

The Disability Adjusted Life Year is a health gap measure that extends the concept of potential years of life lost due to premature death to include equivalent years of 'healthy' life lost in states of less than full health, broadly termed disability. One DALY represents the loss of one year of equivalent full health.

(Source: WHO)

Implementation

- Ensure local health care providers are aware of the WHO recommendations around the provision of Cotrimoxazole, and have access to guidelines and training to implement effectively national policy on Cotrimoxazole prophylaxis
- Enhance decentralisation of Cotrimoxazole provision to increase access
- Offer Cotrimoxazole prophylaxis at no cost or free at the point of delivery

Supply

- Facilitate uninterrupted supply chains through existing distribution systems and integrate Cotrimoxazole with other related services
- Assist pharmacies with support in drug forecasting

Recommendations for others

- Advocate for government commitment to the actions outlined above
- Provide funding for programmes that deliver Cotrimoxazole prophylaxis, in particular using locally made drugs which have been quality-assured
- Support systematic surveillance of Cotrimoxazole supply chains



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* = Recommended readings

Credits

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on HIV treatment and care systems

About Evidence for Action

Evidence for Action is an international research consortium with partners in India, Malawi, Uganda, UK and Zambia, examining issues surrounding HIV treatment and care systems.

The research is organised in four key themes:

1. What "package" of HIV treatment and care services should be provided in different settings?
2. What delivery systems should be used in different contexts?
3. How best should HIV treatment and care be integrated into existing health and social systems?
4. How can new knowledge related to the first three questions be rapidly translated into improved policy and programming?

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