



**Systematic reviews and economic evaluation of HIV
behavioural interventions in China**

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ABSTRACT

China has experienced a dramatic increase in the number of HIV infections, with newly infected cases increasing by 70,000 (range 60,000-80,000) per year¹. Prevention is a central element in AIDS control. This thesis focuses particularly on behavioural interventions for preventing sexual transmission of HIV. The international literature on the evaluation of this type of intervention largely originates from developed countries and from Africa. Developing countries as China, where the AIDS epidemic is growing rapidly, lack rigorous evaluation studies to determine the effectiveness of HIV prevention activities in their local settings.

Thus, I have developed a model to inform decision-making based on evidence generated in settings other than those for which policy is being developed. This model has been illustrated through two case studies in China, the first on HIV/AIDS prevention strategies targeting young people, and the second on men who have sex with men (MSM). To begin with, systematic reviews of all published experimental and quasi-experimental studies of HIV behavioural interventions for these two populations were conducted to inform decision-makers about the effectiveness of the intervention of interest. However, since HIV behavioural interventions are complex and dependent on the context in which they are implemented, I argue that systematic reviews should be context-specific. Therefore, in addition to the standard methods of systematic reviews, it has been necessary to add an analysis of whether the evaluated

¹ UNAIDS/WHO. New HIV data show growing AIDS epidemic in China. http://www.who.int/mediacentre/news/releases/2006/china_hiv_aids/en/index.html (accessed 4 December 2006)

interventions could be implemented in China (applicability) and whether the effectiveness of the intervention detected in the original evaluation could be transferred to the Chinese setting (transferability).

The effectiveness of an intervention, on its own, does not justify resource allocation, given that resources are inevitably scarce. Therefore, economic evaluations were conducted for the interventions found to be effective and applicable in order to determine the extent to which they represent value for money. Decision-analytic models were developed to estimate the cost-effectiveness of these interventions when implemented over one-year. The extent of uncertainty in the transferability of all the evaluated interventions was examined in threshold analyses. The cost-effectiveness of long-term interventions for MSM was also estimated using a Markov model.

The study indicates that well designed and implemented community-based peer education and HIV voluntary counselling and testing (VCT) programs targeting MSM are applicable to the Chinese setting and cost-saving, compared with “no active intervention”. By contrast, although they pass the test of applicability, the incremental cost per disability-adjusted life-year saved of HIV VCT for the general population and school AIDS education for young people who have a general risk level are International \$29,621 and International \$2,413,971 respectively, and so are not cost-effective based on a threshold recommended by the World Health Organization. Sensitivity analyses show that these results are robust to the likely range of variation for most variables and assumptions.

I conclude that, at the current stage of the AIDS epidemic in China, intervention strategies that target high-risk population groups like MSM should be a priority area for public funding. Although the interventions analysed are not comprehensive, the model established in this study could be used to evaluate other interventions. This study has shown a way forward for bridging gaps between evidence-based public health and its relevance to developing countries.

DECLARATIONS

This work contains no material which has been accepted for the award of any other degree or diploma in any university or other tertiary institution and, to the best of my knowledge and belief, contains no material previously published or written by another person, except where due reference has been made in the text.

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PUBLICATIONS DURING PhD STUDY

Journal articles/letters

1. Wang S, Moss JR, Hiller JE. Applicability and transferability of interventions in the evidence-based public health. *Health Promot Int*, 2006, 21(1):76-83.
2. Wang S, Moss JR, Hiller JE. Assessment of generalisability of health interventions should be context specific. Published online 9 September 2006. <http://bmj.bmjournals.com/cgi/eletters/333/7563/346> (letter)

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Conference proceedings

1. Wang S, Moss J, Hiller J. Cost-effectiveness of HIV behavioural interventions in China. 3rd Annual Meeting Health Technology Assessment International, 2nd-5th July 2006. Adelaide, Australia.
2. Wang S, Hiller JE, Moss JR. Applicability and transferability of interventions in evidence-based public health: HIV/AIDS prevention programs in China. The Fourth Asia-Pacific Conference on EBM, 15th-17th April, 2006. Chengdu, China.
3. Wang S, Moss JR, Hiller JE. Cost-effectiveness of HIV behavioural interventions for men who have sex with men in China: a decision analytic model. Australasian Epidemiological Association Annual Conference, 10th -12th October, 2004, Adelaide.
4. Wang S, Moss JR, Hiller JE. Cost-effectiveness of HIV voluntary counseling and testing for men who have sex with men in China. South Australian PHAA/AFPHM conference, 9th October, 2004, Adelaide.
5. Wang S, Moss JR, Hiller JE. Effective behavioural interventions for young people to reduce sexually transmitted HIV/AIDS. The 18th World Conference on Health Promotion & Health Education, 26th-30th April, 2004, Melbourne.
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ABBREVIATIONS

AIDS	Acquired Immune Deficiency Syndrome
CD4	Cluster of differentiation 4, a glycoprotein expressed on the surface of T helper cells
CDC	Centers for Disease Control and Prevention
CEA	Cost-effectiveness analysis
CRD	Centre for Reviews and Dissemination
DALY	Disability-adjusted life-year
DDM	Data for Decision-making
DEBI	Diffusion of Effective Behavioral Interventions
ELISA	Enzyme-linked immunosorbent assay
HIV	Human immunodeficiency virus
ICER	Incremental cost-effectiveness ratio
IDU	Injecting drug user
LY	life-year
MSM	Men who have sex with men
NHMRC	Australian National Health and Medical Research Council
NHS	National Health Service (UK)
NMB	Net monetary benefit
NICE	National Institute for Health and Clinical Excellence (UK)
PBAC	(Australian) Pharmaceutical Benefits Advisory Committee
PPP	Purchasing power parity
QALY	Quality-adjusted life-year
RCT	Randomised controlled trial
REP	Replicating Effective Programs
STD	Sexually transmitted disease
STI	Sexually transmitted infection
UAI	Unprotected anal intercourse
UN	United Nations
UNAIDS	The Joint United Nations Programme on HIV/AIDS
VCT	Voluntary counselling and testing
WHO	World Health Organization
WTP	Willingness to pay
YLL	Years of life lost due to premature death
YLD	Years of life lost due to disability