# The cost-effectiveness of policies for the safe and appropriate use of injection in healthcare settings

Gerald Dziekan, <sup>1</sup> Daniel Chisholm, <sup>2</sup> Benjamin Johns, <sup>2</sup> Juan Rovira, <sup>3</sup> & Yvan J.F. Hutin <sup>1</sup>

**Objective** Poor injection practices transmit potentially life-threatening pathogens. We modelled the cost-effectiveness of policies for the safe and appropriate use of injections in ten epidemiological subregions of the world in terms of cost per disability-adjusted life year (DALY) averted.

**Methods** The incidence of injection-associated hepatitis B virus (HBV), hepatitis C virus (HCV), and human immunodeficiency virus (HIV) infections was modelled for a year 2000 cohort over a 30-year time horizon. The consequences of a "do nothing" scenario were compared with a set of hypothetical scenarios that incorporated the health gains of effective interventions. Resources needed to implement effective interventions were costed for each subregion and expressed in international dollars (I\$).

**Findings** Worldwide, the reuse of injection equipment in the year 2000 accounted for 32%, 40%, and 5% of new HBV, HCV and HIV infections, respectively, leading to a burden of 9.18 million DALYs between 2000 and 2030. Interventions implemented in the year 2000 for the safe (provision of single-use syringes, assumed effectiveness 95%) and appropriate (patients—providers interactional group discussions, assumed effectiveness 30%) use of injections could reduce the burden of injection-associated infections by as much as 96.5% (8.86 million DALYs) for an average yearly cost of I\$ 905 million (average cost per DALY averted, 102; range by region, 14–2293). Attributable fractions and the number of syringes and needles required represented the key sources of uncertainty.

**Conclusion** In all subregions studied, each DALY averted through policies for the safe and appropriate use of injections costs considerably less than one year of average per capita income, which makes such policies a sound investment for health care.

**Keywords** Injections/adverse effects; Equipment reuse/economics; Equipment contamination/prevention and control; Health policy; Syringes/adverse effects; Needles/adverse effects; Hepatitis B/etiology; Hepatitis C/etiology; HIV infections/etiology; Cost of illness; Cost-benefit analysis; Models, Theoretical; Cohort studies (*source: MeSH, NLM*).

**Mots clés** Injection/effets indésirables; Réutilisation matériel/économie; Contamination matériel/prévention et contrôle; Politique sanitaire; Seringue/effets indésirables; Aiguille/effets indésirables; Hépatite B/étiologie; Hépatite C/étiologie; HIV, Infection/étiologie; Coût maladie; Analyse coût-bénéfice; Modèle théorique; Etude cohorte (*source: MeSH, INSERM*).

**Palabras clave** Inyecciones/efectos adversos; Equipo reutilizado/economía; Contaminación de equipos/prevención y control; Política de salud; Jeringas/efectos adversos; Agujas/efectos adversos; Hepatitis B/etiología; Hepatitis C/etiología; Infecciones por VIH/etiología; Costo de la enfermedad; Análisis de costo-beneficio; Modelos teóricos; Estudios de cohortes (*fuente: DeCS, BIREME*).

الكلمات المفتاحية: مردودية، الحقن المأمون، الحقن الملائم، عوامل ممرضة، سنوات العمر المصححة باحتساب مدد العجز، التهاب الكبد سي، التهاب الكبد بي، العوز المناعي المكتسب، الرعاية الصحية، عبء الأمراض (المصدر: رؤوس الموضوعات الطبية، إقليم شرق المتوسط).

Bulletin of the World Health Organization 2003;81:277-285.

Voir page 283 le résumé en français. En la página 283 figura un resumen en español.

يمكن الاطلاع على الملخص بالعربية على الصفحة ٢٨٤.

## Introduction

Poor injection practices lead to infections with hepatitis B virus (HBV), hepatitis C virus (HCV), and human immunodeficiency virus (HIV) (1). In addition, unsafe injections have been important vectors for the introduction of HCV to patients in some countries, including Egypt and Pakistan (2–4). However, the burden of cirrhosis, hepatocellular carcinoma, and acquired immunodeficiency syndrome (AIDS) associated with unsafe injections is delayed and may not be directly apparent.

Although injection-associated infections constitute a silent epidemic, effective interventions are available to reduce injection use and unsafe practices (G. Dziekan & Y.I.F. Hutin,

unpublished data, 2002). First, information, education and communication (IEC) targeting prescribers, including patient—prescribers interactional group discussions, reduces injection use. Second, the provision of single-use injection equipment improves safety.

For national stakeholders faced with competing priorities, the availability of effective interventions to prevent a hidden epidemic might not be sufficient to justify investing in a policy for the safe and appropriate use of injections. Economic considerations also enter the debate. Accordingly, we set out to estimate the sectoral cost-effectiveness of policies for the safe and appropriate use of injections in terms of cost per disability-adjusted life year (DALY) averted.

Ref. No. 02-0444

<sup>&</sup>lt;sup>1</sup> Department of Blood Safety and Clinical Technology (BCT), World Health Organization, CH-1211 Geneva 27, Switzerland. Correspondence should be addressed to Dr Hutin (email: hutiny@who.int).

<sup>&</sup>lt;sup>2</sup> Global Programme on Evidence for Health Policy (GPE), World Health Organization, Geneva, Switzerland.

<sup>&</sup>lt;sup>3</sup> Health, Nutrition and Population Network, World Bank, Washington, DC, USA.

#### **Methods**

### **Study populations**

The six regions of WHO were separated into subgroups of countries on the basis of having similar rates of child and adult mortality. This resulted in 14 Global Burden of Disease 2000 epidemiological subregions characterized by the WHO region acronyms (AFR (African Region); AMR (Region of the Americas); EMR (Eastern Mediterranean Region); EUR (European Region); SEAR (South-East Asia Region); and WPR (Western Pacific Region)) and a letter for the mortality stratum (Table 1) (5). Four subregions in which the reuse of injection equipment in the absence of sterilization is negligible were excluded from the analysis (AMR A, EMR B, EUR A and WPR A).

#### **Effectiveness model**

We considered a theoretical cohort of the population living in the year 2000 in subregions where reuse of injection equipment has been reported (figures provided by the Global Burden of Disease study group). We first applied a current, "do nothing" scenario where persons were injected using contaminated needles and consequently acquired infections. Second, we applied a series of hypothetical intervention scenarios for the year 2000, taking into account the effect of these interventions on the incidence of infections.

#### DALYs attributable to poor injection practices

We modelled the fraction of incident HBV, HCV, and HIV infections attributable to contaminated injections on the basis of the annual number of injections per person, the proportion of injections administered with equipment reused in the absence of sterilization, the probability of transmission following percutaneous exposure, the prevalence of active infection, the prevalence of immunity, and the incidence (6). The burden in DALYs for the years 2000–30 due to infections in the year 2000 was estimated on the basis of the natural history of viral infections (6), background mortality, Global Burden of Disease life tables (7), and the average duration and disability weights of acute hepatitis, cirrhosis, hepatocellular carcinoma, and AIDS — the four sequelae of interest (8). DALYs were age-weighted and 3% discounted (7).

#### Effectiveness of interventions

We examined interventions for reducing the unsafe use of injections, interventions for reducing injection use, and the effect of these two interventions when implemented jointly (G. Dziekan & Y.J.F. Hutin, unpublished data, 2002). For interventions to reduce the unsafe use of injections, we considered the effectiveness of interventions on the basis of provision of single-use injection equipment (9, 10). The effectiveness of interventions to reduce injection frequency was highly variable (1-53%) due to the variability in approaches and study designs (S. Luby, F. Hoodbhoy, A. Shah, unpublished data) (11-26). In our model, we used the estimate of effectiveness reported for interactional group discussions (30%) — a well-designed, well-evaluated intervention that has been used in developing countries (23). Interactional group discussions consist of moderated patientprescriber discussions on the topic of injection use, during which the prescribers are confronted with the actual absence of preference for injections among patients.

Our disease model was based on the number of contaminated injections — a product of the number of injections received and the proportion of these given with reused equipment. Thus, we assumed that the effectiveness of the combined interventions was a multiplication of the effect of the two. In the absence of evidence suggesting the contrary, we also assumed that intervention effectiveness did not differ with respect to the underlying magnitude of the burden under the "do nothing" scenario.

#### **Cost of interventions**

#### Quantification

First, we identified the activities required for each intervention at the national and subnational level for an implementation period of ten years (27) (Table 2). Each of these activities was assigned to the intervention to reduce injection use or to the intervention to reduce unsafe practices, or both (in the case of the latter, activities necessary in the two interventions were counted only once). We then estimated the quantity of fulltime-equivalent staff members and the material resources required to conduct these activities. Third, we estimated the needs of single-use syringe and needle sets on the basis of the number of injections administered and the proportion already given using sterile injection equipment (6). Fourth, the resources required for safe sharps waste collection and management was taken into account as part of the intervention. The needs quantified for 10 years were then averaged to obtain a yearly estimate that we used to cost the hypothetical intervention in the year 2000.

#### Costing

We estimated the average yearly programme cost for human resources and associated materials for the year 2000 by costing studies conducted in each subregion as part of the WHO-CHOICE (Choosing Interventions that are Cost Effective) project (27). The cost of injection equipment was calculated on the basis of international retail prices and the cost of distribution. First, we estimated international retail market prices among main international wholesalers. Second, we estimated international distribution costs on a standardized mark-up, taking into account the average difference between international free on board (FOB) and cost, insurance and freight (CIF) prices, as well as additional trade-related international distribution costs (28). Third, we estimated the cost of domestic distribution on the basis of a hexagon-shaped subregional distribution model that calculated the distances between the theoretical centre of a country with the highest population densities and a periphery with the lowest population density (29). The cost of personnel, capital, and fuel was estimated from a database to which fuel efficiency and maintenance cost was added (30). Finally, we used costing studies conducted by WHO to estimate the costs per syringe and needle set of sharps waste collection and disposal through incineration (Ulla Kou & Patrick Lydon, personal communication). All costs were expressed in international dollars (I\$) for the year 2000 (27). An international dollar has the same purchasing power as the US dollar has in the United States, and is derived via the application of purchasing power parity exchange rates. We assumed 100% coverage of all situations where injections were given in the formal public sector (e.g. hospitals, clinics).

Table 1. Contaminated injections in the year 2000, attributable and preventable burden of disease for the period 2000–30

	African Region		Region of E the Americas		astern Med terranean Region		European Region		South-East We Asia Region		fic All
	AFR D <sup>a</sup>	AFR E <sup>a</sup>	AMR B <sup>a</sup>	AMR D <sup>a</sup>	EMR D <sup>a</sup>	EUR B <sup>a</sup>	EUR C <sup>a</sup>	SEAR B <sup>a</sup>	SEAR D <sup>a</sup>	WPR B <sup>a</sup>	
Mortality in children	High	High	Low	High	High	Low	Low	Low	High	Low	
Mortality in adults	High	Very high	Low	High	High	Low	Low	Low	High	Low	
Injections per person per year <sup>b</sup>	2.2	2.0	1.7	1.9	4.3	5.2	11.3	2.1	4.0	2.4	3.4
Proportion of reuse (%) <sup>b</sup>	19	17	1.2	11	70	1.2	11	30	75	30	39.8
Total burden 2000–30 <sup>b</sup>	555 644	1 668 583	9 083	27 332	559 702	3 479	64 733	280 789	4 720 866	1 287 470	9 177 679
Preventable burden 2000–30 Reduction of injection use <sup>c</sup> Reduction of unsafe use <sup>d</sup> Combined interventions <sup>e</sup>	166 693 527 862 536 197	500 575 1 585 154 1 610 182	2 725 8 629 8 765	8 200 25 965 26 375	167 911 531 717 540 112	1 044 3 305 3 357	19 420 61 496 62 467	84 237 266 749 270 961	1 416 260 4 484 823 4 555 636	500 2	2 753 304 8 718 795 8 856 461

a Global Burden of Disease 2000 epidemiological subregions are characterized by the World Health Organization region acronym and a letter for the mortality stratum (5).

#### **Uncertainty analysis**

We first tested the upper and lower values of the attributable fraction of the comparative risk assessment (6). Second, we assumed that the effectiveness of interventions was only 7% for reducing injection use (the lowest effectiveness reported for an intervention targeting patients and providers) and 50% for reducing unsafe use of injections. Third, we ran the analysis using an upper value of the number of syringes and needle sets required. Fourth, we ran an analysis that did not take into account the additional cost of safe sharps waste collection and management. Finally, total estimated costs and effects (each simulated to have a truncated normal distribution and a coefficient of variation of 0.5) were entered into the software package MCLeague (31), which uses Monte Carlo simulation (1000 runs) to perform a stochastic uncertainty analysis of the probability that interventions represent a cost-effective use of resources given a specified budget constraint.

#### Results

# Effectiveness of interventions Burden of disease attributable to

# contaminated injections in 2000

The number of injections per person per year was estimated to range from 1.7 in AMR B to 11.3 in EUR C, of which a proportion ranging from 1.2% in EUR B and 75% in SEAR D was administered with injection equipment reused in the absence of sterilization (Table 1). Overall, contaminated injections caused 21 million HBV infections, two million HCV infections and 260 000 HIV infections. These infections led to 49 000, 24 000, and 210 000 deaths, respectively, between the years 2000 and 2030, for a total of 9 177 679 discounted and age-weighted DALYs (non-discounted, unadjusted DALYs, 48 541 032). HIV infections accounted for the highest proportion of DALYs (63%), whereas HBV and HCV infections accounted for 34% and 4% of the total, respectively. Most of this burden was caused by early death rather than by disability.

#### Burden of disease preventable through interventions

We assumed the effectiveness of interactional group discussion to be 30% on injection use (23). This effectiveness translated directly into projected burden of disease reduction as the incidence of injection-associated infections in the present disease model was proportional to the annual number of injections per person and the proportion of injections given with reused equipment (6). Implementation of interventions to reduce injection use would lead to a reduction of 2753 304 DALYs. The effectiveness of provision of singleuse injection equipment was assumed to be 95% on the unsafe use of injections. Implementation of interventions to reduce the unsafe use of injections would lead to a reduction of 8718 795 DALYs. When combined, the two interventions would lead to a reduction of 8 856 461 DALYs.

#### **Costs of interventions**

The expected annual cost of the intervention to reduce injection use (Table 3) ranged from I\$ 1.1 million in AMR D to I\$ 26 million in WPR B (cost per capita, I\$ 0.009–0.024). The cost of the intervention to reduce the unsafe use of injections ranged from I\$ 2.5 million in AMR D to I\$ 459 million in SEAR D (cost per capita, I\$ 0.01–0.44). A high proportion of these costs (83–99% in all subregions other than AMR B and EUR B) consisted of injection equipment, including international retail price, international transport, and waste management. Overall, the international retail price accounted for 40% of the total injection equipment costs (Fig. 1). The estimated yearly cost of combined interventions ranged from I\$ 3 million in AMR D to I\$ 466 million in SEAR D (cost per capita, I\$ 0.03–0.45).

#### **Cost-effectiveness of interventions**

The average cost-effectiveness ratio (CER; total costs divided by total effects) for interventions to reduce injection use was I\$ 7 to I\$ 5124 per DALY averted according to the region (Table 3). The average CER for interventions to reduce unsafe use of injections, including waste management, was I\$ 12 to I\$ 1107 per DALY averted according to the region. The

 $<sup>^{\</sup>mbox{\scriptsize b}}$  "Do nothing" scenario.

<sup>&</sup>lt;sup>c</sup> Interactional group discussions between patients and providers to reduce injection use.

<sup>&</sup>lt;sup>d</sup> Provision of single-use, disposable syringes and needles for all injections.

<sup>&</sup>lt;sup>e</sup> Safe and appropriate use of injection policies combining the two interventions above.

Table 2. Activities included in interventions for the safe and appropriate use of injection<sup>a</sup>

Activity	Intervention	Timing	Level	Start-up	) <sup>b</sup>	<sup>b</sup> Years								
					1	2	3	4	5	6	7	8	9	10
National planning workshop	Appropriate use	Start-up	National <sup>c</sup>	Χ	-	-	_	_	-	-	-	-	_	_
Development of IEC <sup>d</sup> material	Appropriate use	Start-up	National <sup>c</sup>	Χ	_	_	_	_	_	_	_	_	_	-
Training of the trainers	Appropriate use	Start-up	National <sup>c</sup>	Х	-	-	-	_	_	-	-	-	-	-
Training of the procurement officer	Safe use	Start-up	National <sup>c</sup>	Χ	-	-	-	-	-	-	-	-	-	-
District planning workshops	Appropriate use	Start-up	Subnational	с Х	-	-	-	-	-	-	-	-	-	-
Supplying injection equipment <sup>e</sup>	Safe use	Post start-up	Subnational	c _	Χ	Χ	Χ	Χ	Χ	Χ	Χ	Χ	Χ	Χ
Annual national follow-up workshop	Appropriate use	Post start-up	National <sup>c</sup>	-	Χ	Χ	Χ	Χ	Χ	Χ	Χ	Χ	Χ	Χ
Interactional group discussions	Appropriate use	Post start-up	Subnational	c _	Χ	Χ	Χ	Χ	Χ	Χ	Χ	Χ	Χ	Χ
Annual monitoring surveys	Both <sup>f</sup>	Post start-up	Subnational	c _	Χ	Χ	Χ	Χ	Χ	Χ	Χ	Χ	Χ	Χ

<sup>&</sup>lt;sup>a</sup> The analysis considered the 3% discounted average yearly cost of a 10 year intervention. Safe and appropriate use interventions were considered separately and combined.

average CER for combined interventions for the safe and appropriate use of injections, including waste management, was I\$ 14 to I\$ 2293 per DALY averted according to the region. Incremental analysis (Table 3) suggested that in the six subregions in which the proportion of reuse of injection equipment exceeds 15% (Table 1), the intervention to reduce injection use represents the single most cost-effective strategy. In the four other subregions, the reduction of unsafe use was the most efficient strategy. However, in all regions, the average CER of the combined intervention strategy remained under the threshold of one year of average per capita income.

#### **Uncertainty analysis**

Five scenarios were assessed in the sensitivity analysis (Table 4). Higher attributable fraction reduced the average cost per DALY averted by 19-86% compared with the base case, but removing the costs of sharps waste management had little additional influence on baseline results (scenarios 1 and 2, with the latter representing the best case). Attribution of a lower fraction of injection-related infections raised the average cost per DALY averted (scenario 3). Using the minimum estimates for intervention effectiveness in addition to the lower attributable fractions increased CER ratios further, particularly for the intervention to reduce injection use (scenario 4). Finally, a scenario incorporating the lower attributable fraction, minimum effectiveness, and a doubled number of syringe and needle sets (scenario 5) resulted in a four- to ten-fold increase in the average cost per DALY averted, compared with initial baseline estimates. However, even in this worst-case scenario, the average cost-effectiveness ratio of all interventions remained below the threshold of average annual income per capita (Table 4). Inclusion of best- and worst-case total costs and effects in the stochastic uncertainty analysis showed that at very low levels of resource availability, reduction of injection use represents the most cost-effective strategy in most subregions (a small health gain, but achieved at a low cost). At higher levels

of resource availability, a combination approach would be the most efficient choice (considerably greater health gains at an increased but still cost-effective level of investment).

## **Discussion**

The average cost of a policy by which single-use syringes and needles are used for all injections amounts to less than I\$ 0.50 per person per year. This may seem an unaffordable gold standard where sterilizable injection equipment is still in use, particularly because the benefits of safe injections in terms of death and disability prevented are far ahead in the future (32). However, in Burkina Faso, it was estimated that purchasing injection equipment in quantities that match injectable medicines increased essential drug expenditures by only 2.2% (WHO, unpublished data). Supplying sufficient quantities of single-use injection equipment is cost-effective. Implemented jointly with interventions to reduce injection use, injection safety interventions can prevent more death and disability while remaining a sound investment in public health. In addition, policies for the safe and appropriate use of injections can lead to savings in the cost of injectable medicines. These savings could be redirected to finance injection equipment for injectable medicines that are essential.

In all subregions analysed, the cost of each DALY averted through national policies for the safe and appropriate use of injections is considerably less than one year of average per capita income, which is the threshold for an intervention being highly cost-effective proposed recently by the WHO Commission on Macroeconomics and Health (33). When recently compared with other strategies to reduce leading risk factors for disease, the safe and appropriate use of injections was found to cause a modest reduction in DALYs but was one of the most cost-effective interventions (5). When compared with other modes of preventing HIV infection in sub-Saharan Africa, the cost-effectiveness ratio of policies for the safe and

<sup>&</sup>lt;sup>b</sup> Included in year one.

<sup>&</sup>lt;sup>c</sup> According to WHO-CHOICE (Choosing Interventions that are Cost Effective) methods (*5*).

<sup>&</sup>lt;sup>d</sup> IEC = Information, education, and communication.

<sup>&</sup>lt;sup>e</sup> With and without safe sharps waste management in the sensitivity analysis.

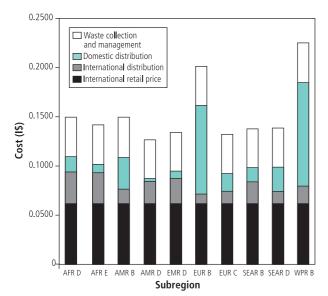
f This activity appears twice, once for the appropriate use and once for the safe use intervention, but is counted only once in the hypothesis of the combined intervention.

Table 3. Costs and cost-effectiveness of policies for the safe and appropriate use of injections<sup>a</sup>, 2000

	African Region		_	Region of Easte the Americas Mediterr Regi			pean gion	South- Re	Western Pacific Region	
	AFR D <sup>b</sup>	AFR E <sup>b</sup>	AMR B <sup>b</sup>	AMR D <sup>b</sup>	EMR D <sup>b</sup>	EUR B <sup>b</sup>	EUR C <sup>b</sup>	SEAR B <sup>b</sup>	SEAR D <sup>b</sup>	WPR B <sup>b</sup>
Total population (million) Gross domestic product per capita	294 1381	346 1576	431 7833	71 3837	343 2393	218 7294	243 6916	294 2545	1242 1449	1533 4186
Syringes/needles <sup>c</sup> Syringe/needle sets needed Syringe/needle costs	122 924 628 19 176 242	117 475 114 18 208 643	8 791 014 1 116 459	14 887 078 2 084 191	1 031 154 040 148 486 182	6 553 752 773 343	93 625 680 11 422 333	185 105 732 25 544 591	3 725 419 491 454 501 178	1 103 711 844 144 586 252
Programme costs <sup>d</sup> Reduction of injection use Reduction of unsafe use Combination	2 738 289 1 602 096 3 553 983	3 308 975 1 391 325 3 711 160	10 524 021 3 189 442 11 020 206	1 080 717 434 498 1 205 776	3 876 085 1 542 952 4 234 537	2 884 373	5 298 743 1 692 560 5 554 346	3 568 129 1 218 867 3 757 891	10 599 413 4 402 415 11 812 493	25 579 948 8 452 776 27 164 652
<b>Total cost per year</b> Reduction of injection use Reduction of unsafe use Combination	2 738 289 20 778 338 22 730 225	3 308 975 19 601 204 21 922 514	10 524 021 4 305 901 12 136 665	1 080 717 2 518 893 3 290 463	3 876 085 150 029 134 152 720 719	3 657 716	5 298 743 13 114 893 16 976 679	3 568 129 26 763 458 29 302 482	10 599 413 458 903 593 466 313 671	25 579 948 153 039 028 171 750 904
Average CER (I\$ per DALY averted) <sup>e</sup> Reduction of injection use Reduction of unsafe use Combination	16 39 42	7 12 14	3862 499 1385	132 97 125	23 282 283	5124 1107 2293	273 213 272	42 100 108	7 102 102	66 125 138
Incremental CER (I\$ per DALY averted) <sup>e,f</sup> Reduction of injection use Reduction of unsafe use Combination	16 50 234	7 15 93	- 499 57 579	– 97 1882	23  400	– 1107 77 666	- 213 3977	42 127 603	7 - 145	66 152 969

<sup>&</sup>lt;sup>a</sup> Costs are in international dollars (I\$).

Fig. 1. Total unit cost of syringes and needle sets according to various cost components, by subregion<sup>a</sup>



<sup>a</sup>Global Burden of Disease 2000 epidemiological subregions are characterized by the WHO region acronym and a letter for the mortality stratum (5). AFR = African Region, AMR = Region of the Americas, EMR = Eastern Mediterranean Region, EUR = European Region, SEAR = South-East Asia Region, WPR = Western Pacific Region.

WHO 03.32

appropriate use of injections remained under the threshold of I\$ 50 per DALY averted, which was in the range of the most cost-effective interventions for preventing HIV infection (e.g. blood safety, targeted condom distribution, and treatment of sexually transmitted diseases) (34).

A safe injection is defined as one that does not harm the recipient, the provider and the members of the community (35). Therefore, the costs of sharps waste collection and management were included as part of programme costs. However, the effect of safe sharps waste collection and management in terms of burden of disease secondary to needlestick injuries among healthcare workers or the community prevented could not be estimated. Thus, such a policy may be more cost-effective than the present results indicate. The sensitivity analysis indicates that the cost per DALY averted decreased by 36% to 39% if the costs of safe sharps waste collection and management were excluded to match costs and effects.

Policies for the safe and appropriate use of injections are natural additions to universal infant vaccination against hepatitis B in a national strategy to prevent HBV infection. Infant immunization against hepatitis B is probably more costeffective than safe and appropriate use of injections, with cost per life year saved ranging from I\$ 4 to I\$ 36 (36). When global efforts for universal vaccination of infants have reached adequate coverage for a sufficient period of time, high levels of

b Global Burden of Disease 2000 epidemiological subregions are characterized by the World Health Organization region acronym and a letter for the mortality stratum (5).

<sup>&</sup>lt;sup>c</sup> Syringes and needle costs include the international retail price, international transport, and waste management (domestic transport included under programme costs). Not applicable to intervention to reduce injection use.

<sup>&</sup>lt;sup>d</sup> Programme costs include personnel, transport, equipment, and supplies but exclude syringes and needles sets.

<sup>&</sup>lt;sup>e</sup> CER = cost-effectiveness ratio. DALY = disability-adjusted life year.

f Lowest value represents most cost-effective option relative to doing nothing; next-lowest value represents next most cost-effective option.

Table 4. Sensitivity analyses for the estimate of the average cost-effectiveness ratios of interventions for the safe and appropriate use of injections per DALY averted<sup>a</sup>

Sensitivity scenario	African Region		Region of the Americas		Eastern Mediterra- nean Regior	European Region		South-East Asia Region		Western Pacific Region
	AFR D <sup>b</sup>	AFR E <sup>b</sup>	AMR B <sup>b</sup>	AMR D	EMR D <sup>b</sup>	EUR B <sup>b</sup>	EUR C <sup>b</sup>	SEAR B <sup>b</sup>	SEAR D <sup>b</sup>	WPR B <sup>b</sup>
Higher attributable fraction <sup>c</sup>										
Reduction of injection use	13	5	523	44	17	1394	140	33	6	28
Reduction of unsafe use	32	10	68	33	210	301	109	79	78	53
Combination	34	11	187	42	210	624	139	85	78	59
Higher attributable fraction,										
no sharps waste management										
Reduction of injection use	13	5	523	44	17	1394	140	33	6	28
Reduction of unsafe use	20	6	61	22	127	276	71	49	47	33
Combination	23	7	181	31	129	599	102	55	48	39
Lower attributable fraction										
Reduction of injection use	22	9	NA	NA	45	NA	970	57	11	NA
Reduction of unsafe use	52	16	NA	NA	544	NA	758	136	156	NA
Combination	56	18	NA	NA	546	NA	967	146	156	NA
Lower attributable fraction,										
minimum effectiveness										
Reduction of injection use	93	37	NA	NA	191	NA	4159	245	49	NA
Reduction of unsafe use	99	31	NA	NA	1035	NA	1441	258	296	NA
Combination	106	34	NA	NA	1038	NA	1838	278	296	NA
Lower attributable fraction,										
minimum effect, double injection sets Reduction of injection use	93	37	NA	NA	191	NA	4159	245	49	NA
Reduction of injection use	190	60	NA NA	NA NA	2058	NA	2696	504	589	NA NA
Combination	190	62	NA NA	NA NA	2036	NA NA	3074	520	585	NA NA
Combination	130	UZ	IVA	IVA	2040	IVA	3074	320	202	IVA

<sup>&</sup>lt;sup>a</sup> Results are in international dollars (I\$). Not applicable (NA) refers to lower attributable fraction equals to zero; cost-effectiveness ratio (CER) cannot therefore be calculated. DALY = disability-adjusted life year.

immunity against HBV infection will ultimately protect populations from injection-associated HBV infection.

This study was not an attempt to compare various injection technologies. The present model did not consider the use of sterilizable injection equipment in any of the interventions because there are no data available to indicate that it can lead to safe injection practices. In fact, the use of sterilizable injection equipment has been specifically associated with infections with bloodborne pathogens (37-41), and health systems using sterilizable syringes have poorer practices than those using single-use equipment (42). No special reference was made to the use of autodisable (AD) injection equipment that inactivates itself after one use (43). AD syringes offer the highest level of safety and are now considered to be the standard for administering vaccines (44). However, immunization injections account for fewer than 10% of all injections (1). Thus, introducing AD syringes in immunization services will address only a small proportion of the burden of disease associated with unsafe injections. With respect to using AD syringes in curative services, although single-use syringes can be reused, effectiveness data indicating that AD syringes would be associated with safer injection practices compared with standard single-use syringes made available in sufficient quantities could not be identified. Nevertheless, AD syringes should be considered for use in settings where unsafe practices are common, particularly in the non-formal sector that is staffed with

unqualified health-care workers, specifically in South Asia (4, 45). In such cases, the results of our analysis could be easily extrapolated to AD syringes because they are now available at a cost that is very close to the one of standard single-use syringes. In 2002, the international retail price for an immunization AD syringe was five to seven US cents, whereas international retail prices for single use syringes ranged from four (2 ml) to eight (5 ml) US cents.

The present study presented several limitations. First, the model did not take into account any longer-term dynamic effects that reducing transmission of infection would have on the prevalence of infections with bloodborne pathogens. This could be a problem in the case of HCV infection because contaminated injections account for a high proportion of new infections. This limitation could also lead to an underestimation of the effect size, hence these interventions might be described as being less cost-effective than they really are. Second, the specific issues associated with working in the private sector were not addressed. The provision of sufficient quantities of single-use injection equipment and interactional group discussion might not be sufficient where the informal private sector accounts for a high proportion of healthcare services delivery. In such settings, demonstration projects should identify effective strategies, some of which might include the use of AD syringes in curative services or addressing financial incentives to overprescribing injections, or both.

b Global Burden of Disease 2000 epidemiological subregions are characterized by the World Health Organization region acronym and a letter for the mortality stratum (5).

c Attributable fraction refers to the fraction of new hepatitis B virus, hepatitis C virus, and human immunodeficiency virus infections attributable to contaminated injections.

Poor injection practice is not a leading cause of disability and death worldwide. However, the safe and appropriate use of injection equipment represents an opportunity to avert a substantial number of DALYs at a relatively low cost. Improved injection practice can be recommended for implementation worldwide, particularly in settings where the reuse of injection equipment is common and where the HIV prevalence in the general population exceeds 1%. Such policies can be developed through a better coordination of already existing programmes to facilitate implementation. Finally, in addition to being cost-effective, the safe and appropriate use of injections is an attainable way of applying the "first do no harm" principle as part of the ethics of healthcare service delivery.

#### Acknowledgements

We are grateful to Andrew Creese, Majid Ezzati and Tessa Tan Tores for general guidance throughout this project; Niels Tomijima and Stephen Vanderhoorn for assistance in the calculation of the DALYs; and Ulla Kou and Patrick Lydon for the costing estimates for sharps waste collection and management.

**Funding:** This work was supported by a grant from the United States National Vaccine Program Office (NVPO), made available through WHO by the United States Agency for International Development (USAID).

**Conflicts of interest:** none declared.

#### Résumé

# Coût-efficacité des politiques en faveur de l'utilisation sûre et appropriée des injections dans les établissements de soins de santé

**Objectif** Des pratiques d'injection défectueuses sont à l'origine de la transmission d'agents pathogènes potentiellement mortels. Nous avons effectué une modélisation du rapport coût-efficacité des politiques en faveur d'une utilisation sûre et appropriée des injections dans dix sous-régions épidémiologiques du monde, les résultats étant exprimés en coût par année de vie ajustée sur l'incapacité (DALY) évitée.

**Méthodes** L'incidence des infections par le virus de l'hépatite B (VHB), le virus de l'hépatite C (VHC) et le virus de l'immunodéficience humaine (VIH) associées aux injections a été modélisée pour une cohorte de l'an 2000 sur une durée prospective de 30 ans. Les conséquences d'un scénario « statu quo » ont été comparées à une série de scénarios hypothétiques intégrant les gains, en termes de santé, d'interventions efficaces. Le montant des ressources nécessaires pour la mise en œuvre des interventions efficaces a été évalué pour chaque sous-région et exprimé en dollars internationaux (I \$).

**Résultats** A l'échelle mondiale, la réutilisation du matériel d'injection a été à l'origine, en 2000, de 32 %, 40 % et 5 %,

respectivement, des nouvelles infections par le VHB, le VHC et le VIH, ce qui conduirait à une charge de 9,18 millions de DALY entre 2000 et 2030. Des interventions mises en œuvre en 2000 en vue de l'utilisation sûre et appropriée des injections (grâce à la fourniture de seringues à usage unique, d'une efficacité supposée de 95 %, et à des groupes de discussion patients-dispensateurs de soins, d'une efficacité supposée de 30 %) pourraient réduire la charge des infections associées aux injections de 96,5 % (8,86 millions de DALY) pour un coût annuel moyen de I \$ 905 millions (rapport coût-efficacité moyen par DALY évitée: 102 ; intervalle selon les régions: 14-2293). Les principales sources d'incertitude concernaient la fraction attribuable et le nombre de seringues et d'aiguilles nécessaires.

**Conclusion** Dans toutes les sous-régions étudiées, chaque DALY évitée grâce à des politiques en faveur de l'utilisation sûre et appropriée des injections coûterait nettement moins d'une année de revenu moyen par habitant; ces politiques représentent donc un excellent investissement en termes de soins de santé.

#### Resumen

# Costoeficacia de las políticas de fomento del uso seguro y apropiado de las inyecciones en los entornos de atención de salud

**Objetivo** Las malas prácticas de inyección transmiten agentes patógenos potencialmente mortales. Procedimos a modelizar la costoeficacia de las políticas de fomento del uso seguro e idóneo de las inyecciones en diez subregiones epidemiológicas del mundo, teniendo en cuenta el costo de evitar la pérdida de un año de vida ajustado en función de la discapacidad (AVAD).

**Métodos** Se modelizó la incidencia de infecciones asociadas a inyecciones por virus de la hepatitis B (VHB), virus de la hepatitis C (VHC) y virus de la inmunodeficiencia humana (VIH) para una cohorte del año 2000 con un horizonte temporal de 30 años. Las consecuencias de un escenario de «inacción» se compararon con las de un conjunto de escenarios hipotéticos que incorporaban los beneficios sanitarios de las intervenciones eficaces. Se evaluaron para cada subregión los recursos necesarios para ejecutar las intervenciones eficaces, expresándolos en dólares internacionales (I\$).

**Resultados** A nivel mundial, la reutilización de material de inyección en el año 2000 representó el 32%, 40% y 5% de las infecciones nuevas por VHB, VHC y VIH, respectivamente, lo que

entrañaría una carga de 9,18 millones de AVAD entre 2000 y 2030. Las intervenciones llevadas a cabo en 2000 para fomentar el uso seguro (suministro de jeringas monouso, suponiendo una eficacia del 95%) y apropiado (discusiones de grupo interactivas pacientes-dispensadores, suponiendo una eficacia del 30%) del material de inyección podrían reducir la carga de infecciones asociadas a las inyecciones nada menos que en un 96,5% (8,86 millones de AVAD) por un costo anual promedio de I\$ 905 millones (costoeficacia promedio por AVAD evitado: 102; intervalo por regiones, 14–2293). Las fracciones atribuibles y el número de jeringuillas y agujas requerido son las principales fuentes de incertidumbre.

**Conclusión** En todas las subregiones estudiadas, cada AVAD evitado mediante las políticas de fomento de un uso seguro y apropiado de las inyecciones cuesta considerablemente menos que el promedio de un año de ingresos per cápita, lo que autoriza a considerar esas políticas como una sólida inversión en atención de salud.

#### ىلخص

# مردودية سياسات الاستخدام الملائم والمأمون للحقن في مواقع الرعاية الصحية

مدد العجز بين عامي ٢٠٠٠ و ٢٠٣٠، ويمكن للتدخلات التي نفذت عام الفين من أجل الاستخدام المأمون للحقن (بتأمين محاقن تستعمل لمرة واحدة، والذي يفترض أن فعاليته تصل إلى ٩٥٪) ومن أجل الاستخدام الملائم للحقن (بإجراء مناقشات مع مجموعات متفاعلة من المرضى والقائمين على إيتاء الرعاية الصحية لهم، والذي يفترض أن فعاليته تصل إلى ٩٠٠٪) أن تنقص العبء الناجم عن حالات العدوى المصاحبة للحقن بنسبة تصل إلى ٩٦٠٪ (وهذا ما يعادل ٨,٨٦ مليون عام من سنوات العمر المصححة باحتساب مدد العجز) وتقدر التكلفة الوسيطة السنوية بد ٩٠٥ مليون دولاراً دولياً (باعتبار أن التكلفة الوسطية لضياع كل عام من سنوات العمر المصححة باحتساب مدد العجز ١٠٠ دولاراً دولياً، وهو ما يتراوح بين ١٠٤ دولاراً أمريكياً). وتُعَدُّ الأجزاء المتعلقة بالأوصاف وعدد المحاقن والإبر اللازمة من المصادر الرئيسية لعدم الثقة.

الاستنتاج: لقد وجد أنه في كل المناطق الفرعية التي درست ضياع كل عام من سنوات العمر المصححة باحتساب مدد العجز، فإن تكاليف سياسات الاستخدام الملائم والمأمون للحقن أقل بكثير من تكاليف سنة واحدة من وسطي الدخل للفرد الواحد، وهذا ما يجعل هذه السياسات من الاستثمارات القيمة في الرعاية الصحية.

الغرض: يمكن للمارسات السيئة في الحقن أن تنقل العوامل الممرضة المهددة للحياة، وقد وضعنا نماذج لحساب مردودية سياسات الاستخدام الملائم والمأمون للحقن في عشر من المناطق الإبيديميولوجية الفرعية في العالم مقدرة بتكاليف ما يضيع من سنوات العمر المصححة باحتساب مدد العحد.

الطريقة: وضعت نماذج لحساب معدلات انتشار العدوى المصاحبة للحقن بكل من فيروس التهاب الكبد بي وسي وفيروس العَوز المناعي المكتسب، وذلك خلال عام ألفين لدى الأتراب في ذلك العام وعلى مدى ٣٠ عاماً، وتمت مقارنة العواقب التي تنجم عن سيناريو يفترض عدم القيام بأي عمل مع عدد من السيناريوهات المفترضة التي تندرج فيها المكاسب الصحية التي قد تنجم عن التدخلات الفعّالة. وتم حساب التكاليف اللازمة لتغطية التدخلات الفعّالة اللازمة في كل منطقة فرعية مقدَّرة بالدولارات الدولية. المعودات: إن الاستخدام المتكرر لأدوات الحقن في عام ألفين كان مسؤولاً عن ٣٢٪ من حالات العدوى المستجدَّة بفيروس التهاب الكبد بي و٠٤٪ من حالات العدوى المستجدَّة بفيروس التهاب الكبد بي حالات العدوى المستجدَّة بفيروس التهاب الكبد مي عام عليروس حالات العدوى المستجدّة بفيروس التهاب الكبد عي عام عدد عنات عليروس التهاب الكبد عن عام الميون عام من سنوات العمر المصححة باحتساب عبء يصل إلى ٩,١٨ مليون عام من سنوات العمر المصححة باحتساب

#### References

- Simonsen L, Kane A, Lloyd J, Zaffran M, Kane M. Unsafe injections in the developing world and transmission of bloodborne pathogens. *Bulletin of* the World Health Organization 1999;77:789-800.
- Frank C, Mohamed MK, Strickland GT, Lavanchy D, Arthur RR, Magder LS, et al.
  The role of parenteral antischistosomal therapy in the spread of hepatitis C virus in Egypt. *Lancet* 2000;355:887-91.
- Luby SP, Qamruddin K, Shah AA, Omair A, Pasha O, Khan AJ, et al. The relationship between therapeutic injections and high prevalence of hepatitis C infection in Hafizabad, Pakistan. *Epidemiology and Infection* 1997;119: 349-56
- Khan AJ, Luby SP, Fikree FF, Karim A, Obaid S, Dellawala S, et al. Unsafe injections and the transmission of hepatitis B and C in a periurban community in Pakistan. *Bulletin of the World Health Organization* 2000;78:956-63.
- World Health Organization. Some strategies to reduce risk. In: World Health Report 2002: reducing risks, promoting healthy life. p. 101-44. Geneva: World Health Organization; 2002.
- Hauri AM, Armstrong GL, Hutin YJF. Contaminated injections in health care settings. In: Ezzati M, Lopez AD, Rodgers A, Murray CJL, editors. Comparative quantification of health risks: global and regional burden of disease attributable to selected major risk factors. Geneva: World Health Organization; 2003.
- World Health Organization, Global Program on Evidence for Health Policy. National burden of disease studies: a practical guide, 2nd ed. Geneva: World Health Organization: 2001.
- The Global Burden of Disease. A comprehensive assessment of mortality and disability from diseases, injuries and risk factors in 1990 and projected to 2010.
   Murray CJL, Lopez AD, editors. Boston, MA: Harvard School of Public Health on behalf of the World Health Organization and the World Bank; 1996.
- 9. Fitzner J, Aguilera JF. *Injection safety in Burkina Faso.* Geneva: World Health Organization; 2000 (unpublished document).
- Centers for Disease Control. Injection practices among nurses Valcea, Romania, 1998. Morbidity and Mortality Weekly Report 2001;50:59-61.
- Ofori-Adjei D, Arhinful DK. Effect of training on the clinical management of malaria by medical assistants in Ghana. Social Science & Medicine 1996;42:1169-76.
- Agyepong I, Anum P, Arhinful D, Ofori-Adjei D. The impact of group development of treatment norms on prescribing at primary health care levels in the greater Accra Subregion. Report to the Ministry of Health of Ghana: Accra, Ghana; 1996.
- Thuo HM, Gelders SF. Multi-feedback approach to rational drug use: using inpatient drug use indicators as an intervention tool. Presentation at the International Conference on Improving Use of Medicine, Chiang Mai, 1997. Available from: URL: http://www.who.int/dap-icium/

- Kafuko JM, Zirabumuzaale C, Bagenda D: Rational drug use in rural health units of Uganda: effect of national standard treatment guidelines on rational drug use. Final report. Kampala, Uganda: UNICEF; 1996.
- Christensen RF. A strategy for the improvement of prescribing and drug use in rural health facilities in Uganda. Report for the Ministry of Health, Uganda: Uganda Essential Drugs Management Programme; 1990.
- 16. Birrel G, Birrel KG. Assessment of a 1-year teaching programme in Zanzibar, Tanzania. *Lancet* 2000;356:1084.
- Luby S, Yaidi N, Rehman S, Northrup R. Improving private practitioner sick-child case management in two urban communities in Pakistan. *Tropical Medicine* & International Health 2002;7:210-9.
- Ogwal-Okeng JW, Anokbonggo WW, Birungi H. Prescribing audit with feedback intervention in six subregional hospitals and Mulago referral/teaching hospital (Uganda). Presentation at the International Conference on Improving Use of Medicine, Chiang Mai, 1997. Available from: URL: http://www.who.int/dap-icium/
- Ahmed ST. Reducing use of injetions for IMCI diseases by primary care providers. HANDS report, Karachi, Pakistan, 1999.
- Kafle KK. Intervention test of training and supervision of prescribing practices. Report to USAID/RPM/JSI, Kathmandu, Nepal, August 1995.
- 21. Audi M, Gatobu A, Gitau L. Drug use studies and the impact of small group in-service training on improving the use of drugs: A case study of three mission hospitals in Kenya. Presentation at the International Conference on Improving Use of Medicine, Chiang Mai, 1997. Available from: URL: http://www.who.int/dap-icium/
- Bexel A, Lwando E, Tembo S, von Hofsten B, Diwan V. Does information improve prescribing practices and patient management in primary care? Report from an intervention study carried out at 16 health centres in Lusaka, Zambia. Report from Management Sciences for Health to the Essential Drug Programme. Zambia: Ministry of Health; 1992.
- Prawitasari Hadiyono JE, Suryawati S, Danu SS, Sunartono, Santoso B.
   Interactional group discussion: results of a controlled trial using a behavioural intervention to reduce the use of injections in public health facilities. Social Science & Medicine 1996:42:1177-83.
- Vos J, Gumodoka B, van Asten HA, Berege ZA, Dolmans WM, Borgdorff MW. Improved injection practices after the introduction of treatment and sterility guidelines in Tanzania. *Tropical Medicine & International Health* 1998; 3:291-6
- 25. Santoso B. From research to action: The Gunungkidul experience. *Essential Drug Monitor* 1995;20:21-2.

- Widyastuti S, Dwiprahasto I, Andajaningsih, Bakri Z. The impact of problembased rational drug use training on prescribing practices, cost re-allocations and savings in primary care facilities. Presentation at the International Conference on Improving Use of Medicine, Chiang Mai, 1997. Available from: URL: http://www.who.int/dap-icium/
- Johns B, Baltussen R, Adam T, Hutubessy R. Programme costs in the economic evaluation of health interventions. Cost Effectiveness and Resource Allocation 2003;1:6. Available from: URL: http://www.resource-allocation.com
- Liamo N, Venebles AJ. Infrastructure, geographical disadvantage, transport costs, and trade. World Bank Economic Review 2001;15:451-79.
- Gusein-Zade. Comments on "A Note on the Location of Medical Facilities" by
   Drezner. Journal of Subregional Sciences 1992;32:229-31.
- 30. Nancollas S. Transport in primary health care. A study to determine the key components of a cost effective transport system to support the delivery of health care services. Composite report by Abt associates, Bill and Melinda Gates Children's Vaccine Programme at PATH and the World Health Organization, August 2001.
- Hutubessy RC, Baltussen RM, Evans DB, Barendregt JJ, Murray CJ. Stochastic league tables: communicating cost-effectiveness results to decision-makers. Health Economics 2001;10:473-7.
- Battersby A, Feilden R, Nelson C. Sterilizable syringes: Excessive risk or cost effective option? Bulletin of the World Health Organization 1999;77:812-9.
- 33. Report of the WHO Commission on Macroeconomics and Health. Geneva: World Health Organization; 2001.
- Creese A, Floyd K, Alban A, Guinness L. Cost-effectiveness of HIV/AIDS interventions in Africa: a systematic review of the evidence. *Lancet* 2002;359:1635-42.
- 35. Hutin Y, Hauri A, Chiarello L, Catlin M, Stilwell B, Ghebrehiwet T, et al. Best infection control practices for intradermal, subcutaneous, and intramuscular injections. *Bulletin of the World Health Organization* (forthcoming).
- Miller MA, McCann Laura. Policy analysis of the use of hepatitis B, haemophilus influenzae type B-, Steptococcus pneumoniae-conjugate and rotavirus vaccines in national immunization schedules. *Health Economics* 2000;9:19-35.

- Chowdhury A, Santra A, Chaudhuri S, Ghosh A, Banerjee P, Mazumder DN. Prevalence of hepatitis B infection in the general population: a rural community based study. *Tropical Gastroenterology* 1999;20:75-7.
- 38. Chen TZ, Wu JC, Yen FS, Sheng WY, Hwang SJ, Huo TI, et al. Injection with nondisposable needles as an important route for transmission of acute community-acquired hepatitis C virus infection in Taiwan. *Journal of Medical Virology* 1995;46:247-51.
- 39. Narendranathan M, Philip M. Reusable needles a major risk factor for acute virus B hepatitis. *Tropical Doctor* 1993;23:64-6.
- Ho M-S, Hsu C-P, Yuh Y, King CC, Tsai JF, Mau YC, et al. High rate of hepatitis C virus infection in an isolated community: persistent hyperendemicity or period-related phenomena? *Journal of Medical Virology* 1997;52:370-6.
- Ko YC, Chung DC. Transmission of hepatitis B virus infection by iatrogenic intramuscular injections in an endemic area. *Kaohsiung Journal of Medicine* 1991;7:313-7.
- 42. Hofmann CA. *The WHO injection safety assessment tool: first results.*Presentation made at the annual meeting of the Safe Injection Global Network, 30-31 August 2002, New Delhi, India. Geneva: World Health Organization. WHO document WHO/BCT/DCT/01.04.
- Nelson CM, Sutanto A, Suradana IG. Use of SoloShot autodestruct syringes compared with disposable syringes, in a national immunization campaign in Indonesia. *Bulletin of the World Health Organization* 1999;77:29-33.
- Safety of Injection: WHO-UNICEF-UNFPA joint statement on the use of autodisable syringes in immunization services. Geneva: World Health Organization, 1999. WHO document WHO/V&B/99.25.
- 45. Lakshman M, Nichter M. Contamination of medicine injection paraphernalia used by registered medical practitioners in south India: an ethnographic study. *Social Science & Medicine* 2000;51:11-28.