Model-based estimates of risks of disease transmission and economic costs of seven injection devices in sub-Saharan Africa[*]

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Objective To investigate and compare seven types of injection devices for their risks of iatrogenic transmission of bloodborne pathogens and their economic costs in sub-Saharan Africa.

Methods Risk assumptions for each device and cost models were constructed to estimate the number of new hepatitis B virus (HBV) and human immunodeficiency virus (HIV) infections resulting from patient-to-patient, patient-to-health care worker, and patient-to-community transmission. Costs of device purchase and usage were derived from the literature, while costs of direct medical care and lost productivity from HBV and HIV disease were based on data collected in 1999 in Côte d'Ivoire, Ghana, and Uganda. Multivariate sensitivity analyses using Monte Carlo simulation characterized uncertainties in model parameters. Costs were summed from both the societal and health care system payer's perspectives.

Findings Resterilizable and disposable needles and syringes had the highest overall costs for device purchase, usage, and iatrogenic disease: median US$ 26.77 and US$ 25.29, respectively, per injection from the societal perspective. Disposable-cartridge jet injectors and automatic needle-shielding syringes had the lowest costs, US$ 0.36 and US$ 0.80, respectively. Reusable-nozzle jet injectors and auto-disable needle and syringes were intermediate, at US$ 0.80 and US$ 0.91, respectively, per injection.

Conclusion Despite their nominal purchase and usage costs, conventional needles and syringes carry a hidden but huge burden of iatrogenic disease. Alternative injection devices for the millions of injections administered annually in sub-Saharan Africa would be of value and should be considered by policy-makers in procurement decisions.

Keywords Disease transmission; Iatrogenic disease/epidemiology; Injections/instrumentation/economics; Needles/adverse effects/economics; Syringes/adverse effects/economics; Injections, Jet; Hepatitis B/transmission; HIV infections/transmission; Risk factors; Costs and cost analysis; Models, Theoretical; Africa South of the Sahara (*source: MeSH, NLM*).

Mots clés Transmission maladie; Affection iatrogénique/épidémiologie; Injections/instrumentation/économie; Aiguille/effets indésirables/économie; Injections flash; Seringue/effets indésirables/économie; Hépatite B/transmission; HIV, Infection/transmission; Facteur risque; Coût et analyse coût; Modèle théorique; Afrique subsaharienne (*source: MeSH, INSERM*).

Palabras clave Transmisión de enfermedad; Enfermedad iatrogénica/epidemiología; Inyecciones/instrumentación/economía; Agujas/efectos adversos/economía; Jeringas/efectos adversos/economía; Inyecciones a chorro; Hepatitis B/transmisión; Infecciones por VIH/transmisión; Factores de riesgo; Costos y análisis de costo; Modelos teóricos; África al Sur del Sahara (*fuente: DeCS, BIREME*).

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Voir page 867 le résumé en français. En la página 867 figura un resumen en español.

Introduction

The Expanded Programme on Immunization has been increasingly successful in reducing the incidence of vaccine-preventable diseases in developing countries (*1*), where, unfortunately, a pattern of unsafe injection practices has been observed (*2*). Simonsen et al. estimated the prevalence of unsafe injections to range from 20% up to at least 50% in these countries. In 20–80% of health centres in sub-Saharan Africa there are insufficient supplies and equipment to guarantee safe injection (*3*). Incorrect injection practices include reuse of contaminated needles and syringes without sterilization between patients (*4*); incorrect disposal of used needles and syringes in the community (*5*); absence of swabbing with alcohol or acetone of the reusable nozzles of needle-free jet injectors between consecutive patients (*6*); and other unsafe practices, such as changing needles but not syringes between patients (*7*).

When not properly sterilized, or if contaminated, needles and syringes can produce local abscesses (*8, 9*) and can transmit bloodborne infections between patients (*10, 11*). Needlestick injuries can transmit infectious agents from patients to health care workers (*12–15*), while incorrect disposal can transmit disease to the community as a consequence of both needlestick injuries and improper reuse (*3*). Hepatitis B virus (HBV) (*16*) and human immunodeficiency virus (HIV) (*17*) are two of the most important bloodborne pathogens in terms of prevalence,

morbidity, and mortality, especially in many parts of the developing world (*4, 18*). Complications associated with HBV infection include chronic active hepatitis, cirrhosis of the liver, primary hepatocellular carcinoma, and premature death (*16*). HIV infection leads to the acquired immunodeficiency syndrome (AIDS), opportunistic infections, and premature death.

It is estimated that humans in health care settings receive each year between 8 and 12 billion parenteral injections, of which about one billion are for vaccines (*19*). In addition to routine immunizations for children, emergency campaigns in 1996 alone accounted for the administration of more than 240 million doses of vaccine (*20*). The plans for global measles control and eradication (*21*) can be expected to require billions more injections than are currently administered. As the number of vaccine injections increases, it may become increasingly difficult to ensure the safety of every injection, and thus to minimize risk for consequent iatrogenic disease (*7*).

Since 1997, WHO, the United Nations Children's Fund (UNICEF), and the United Nations Population Fund (UNFPA) have strongly recommended (*22–24*) the use of "auto-disable" needles and syringes (*25*) designed to prevent improper reuse. (Originally called "auto-destruct", these syringes were renamed because they still require proper disposal and destruction by incineration or other means.) The three agencies also agreed on a policy of "bundling", which requires donors of vaccine for developing countries also to supply a corresponding number of auto-disable needles and syringes along with "sharps" collection boxes to permit safe disposal.

The full risks and economic costs of conventional needles and syringes and alternative injection delivery technologies have not been adequately compared. We investigated the risks of iatrogenic disease transmission and the economic costs associated with various such devices for the parenteral administration of vaccines and other medications. Sub-Saharan Africa was selected as the setting for the model, because injection practices there are often unsafe, and severe financial barriers exist for the introduction of newer technologies.

Methods
The risk model
Three major categories of transmission of bloodborne infections by injection devices were modelled. First, patient-to-patient transmission can occur when a device is reused without sterilization or when it is incorrectly sterilized and transfers infected blood between patients. Second, transmission from patient-to-health care worker occurs when an accidental needlestick injury transfers infectious patient blood to the worker. Third, patient-to-community transmission may occur from improper disposal of needles and syringes, as when people scavenging waste dumps receive needlestick injuries. Devices "recycled" from dumps may also be reused unsterile, producing iatrogenic abscesses and transmission of pathogens.

A risk model was constructed for each of these routes of transmission, building on previous models (*4, 13, 26, 27*), in order to estimate the number of new HBV or HIV infections that might result from seven injection technologies. The general model is represented by the following equation:

Eq. 1. Expected number of new cases of HBV or HIV infections = (prevalence of HBV [or HIV]) x
(probability of blood exposure through:
A. reuse of non-sterile needle, or
B. vaccination by reusable-nozzle jet injector, or
C. needlestick injury to health care worker, or
D. probability of improper disposal x probability of needlestick injury or unsterile reuse in community) x
(probability of transmission of infection upon blood exposure to HBV [or HIV]) x
(proportion susceptible in population [1 − prevalence$_{HBV\ [or\ HIV]}$]).

In order to simplify Eq. 1 and because vaccines are administered mainly to young children, we ignored the decrease in susceptibility to HBV infection that occurs among groups of increasing age, due to immunity from incident HBV infections (as evidenced by the presence of hepatitis B core antibody).

We studied the use of seven devices for the parenteral delivery of vaccine and other medications (see Box 1) (*28–31*). Disease costs were totalled from the economic perspectives both of the health care system ("payer's" direct medical costs only) and of society (direct medical and lost productivity costs). The societal perspective allows a comprehensive assessment of the overall impact of different injection technologies on the economies of the countries concerned. The perspective of the health care system focuses on the narrower impact for national health care expenditures.

HBV and HIV prevalence
The prevalence of carriers of HBV surface antigen in the population of vaccinees whose blood might contaminate injection equipment was estimated at 10% (the "base case") for countries in sub-Saharan Africa, with a lower estimate of 5% and an upper of 15% used for sensitivity analysis (*16, 32, 33*) (Table 1). HIV seroprevalence was also estimated at 10% on the basis of reported rates exceeding 5% but less than 15% in 16 countries in the region (*17*). An HIV seroprevalence range of 2–25% was used for the sensitivity analysis. The 2% rate was estimated on the basis of data from the 19 countries in the region with the lowest reported values, ranging from 0.08% in Mauritius to 4.16% in Gabon (*17*). The 25% rate was based on data from eight countries with values ranging from 16% in Malawi to 36% in Botswana.

Transmission from patient to patient
For the base case, it was assumed that after every sterile injection with either a resterilizable needle and syringe (N&S) or a disposable N&S, non-sterile reuse would occur 30% of the time (range: 15–50% for the sensitivity analysis) (*2, 4, 26*) (Table 1). We assumed no risk to patients of blood exposure for the auto-disable N&S, auto-shielding N&S, and disposable-cartridge jet injector devices. For manual-shielding N&S devices, the base case assumed one non-sterile reuse 15% of the time (range: 1–30%) (*34*). For reusable-nozzle jet injector devices, we assumed a worst-case scenario in which health care workers did not swab the nozzle with alcohol or acetone between patients (*6*), contrary to the manufacturers' recommendations. On this basis we estimated a 1% probability (range: 0.1–5.0%) that the device would expose the next patient to transferred blood (*6, 35–37*).

The probability of newly acquiring HBV infection as a result of exposure to reuse of or to needlestick injury from an

Box 1. **Descriptions of injection devices compared in this study for the parenteral administration of vaccines**

Device	Description
Resterilizable N&S[a]	Conventional resterilizable (detachable) steel needle and resterilizable syringe (traditionally glass, but plastic also available).
Disposable N&S	Conventional plastic syringe with detachable, disposable, steel needle.
Auto-disable N&S[b]	Auto-disabling, single-use needle permanently fixed to a plastic syringe, designed to prevent inadvertent or intentional reuse.
Manual-shielding N&S[b]	Manually activated N&S in which, after injection, the user may activate a needle-shielding or needle-retracting mechanism to prevent needlestick injuries.
Auto-shielding N&S[c]	Hypothetical, automatically activated, single-use N&S with both needle-shielding or needle-retraction and auto-disabling features to prevent both needlestick injuries and inadvertent or intentional reuse.
Reusable-nozzle jet injector[b]	Needle-free jet injector for high-speed vaccination which feeds vaccine from multidose vials through reusable fluid chambers, pathways, and nozzles that are in contact with consecutive patients without intervening sterilization.
Disposable-cartridge jet injector[b]	Needle-free jet injector designed for disposable, single-use vaccine cartridges/nozzles.

[a] N&S = needle and syringe.
[b] Commercial examples and prototypes are mentioned in Annex Box A, available on the *Bulletin* web site: http://www.who.int/bulletin.
[c] No such commercial device is known to exist. A hypothetical device was therefore modelled, assuming the same purchase cost per unit as that of the manual-shielding N&S device.

unsterile injection device containing blood from an infected person was assumed to be 30% (range: 20–40%) (Table 1). For acquisition of HIV infection, 0.3% was used for the base case (range: 0.2–0.5%). These rates for HBV and HIV were based on empirical data from needlestick injury case series and surveillance (2, 38–43). We assumed that needles and jet injector nozzles contaminated with blood or tissue fluid from intramuscular or subcutaneous injections would transmit infection at rates similar to those observed in the above studies of injuries from needles used for drawing blood or other intravascular access.

Transmission from patient to health care worker
On the basis of data from the literature (2) and the observations in Côte d'Ivoire, Ghana, and Uganda (33, 51), we assumed a base-case frequency for needlestick injuries of 5% (range: 1–8%) for each use of the resterilizable N&S (which requires more handling to disassemble, clean, and sterilize), and 3% (range: 2–5%) for the disposable N&S (Table 1). Table 1 also provides the modelled probabilities for needlestick injuries for other devices (2, 29, 33, 34, 37, 51). The manual-shielding N&S carried some needlestick injury risk because of the possibility that health care workers would intentionally not activate the safety features, in order to reuse the device. The hypothetical

auto-shielding N&S and both types of jet injectors were assumed to have no risk of needlestick injury.

Transmission from patient to community
This route for acquiring infection is a consequence of improper disposal of sharps and needlestick injury outside the original health care setting where the device was originally used. In the model, the probabilities assumed for unsafe disposal (Table 1) are multiplied by those for needlestick injuries with various devices. Of course, the auto-shielding N&S and both types of jet injectors present no risk to the community. Because of the absence of data, we ignored possible patient-to-patient transmission from reuse of such disposed sharps salvaged in the community.

Economic costs
Costs of purchasing and using devices
For each injection device studied, data were collected from UNICEF (44) and WHO (45–48), device manufacturers (30, 49, 50), and the literature (5) for purchase prices of the items themselves, as well as the costs of necessary equipment (e.g. sterilizers, spare parts, supplies, and other consumables, including items for proper sharps disposal). In addition, the costs of labour for maintenance of necessary equipment and for actual administration of vaccine were estimated. The value of vaccine wasted in the routine use of some devices (e.g. purging air from reusable-nozzle jet injector) was also considered. All costs, including capital costs for equipment and reusable supplies, were amortized for the expected number of injections over the lives of the equipment or supplies, and converted to cost per injection. In order to account for uncertainties about such purchase and usage costs, in the sensitivity analysis the calculated base-case values were varied by factors of 25% for the lower estimate and 200% for the upper. Table 1 summarizes the overall total of such costs for each device. The individual component costs and details of the calculations, along with reference citations to the sources used (5, 30, 44, 45, 47–50) are provided in Annex Table A (available on the *Bulletin* web site: http://www.who.int/bulletin).

Direct medical care costs
Medical care costs were based upon data from original sources in Côte d'Ivoire, Ghana, and Uganda collected by the first author from June to December 1999 (33, 51). These direct costs for each new HBV and HIV infection were determined by modelling the reported costs, frequencies, coverage, and duration of outpatient visits, inpatient care, diagnostic tests, and occasional antiviral therapies for HBV (i.e. interferon in Côte d'Ivoire only) and for HIV (i.e. zidovudine, lamivudine, and indinavir). HBV infections were assumed to have been acquired in the first year of life as a result of unsafe vaccination or other injection. It was also assumed that the resulting direct medical costs would all be incurred in the year of the average age of premature death resulting from this disease (Côte d'Ivoire: 43 years, Ghana: 40 years, Uganda: 41 years). These direct medical costs were then discounted at 3% to present net values, using standard methods (52).

HIV infections from unsafe injection were also assumed to have been acquired in the first year of life. Using models and methods described by Over et al. (53) and Mansergh et al. (54), symptomatic AIDS and death were assumed to ensue among infected infants at a rate of 10% per year until, by the age of

Table 1. **Input parameters and assumptions for modelling costs and risks of alternative injection technologies and consequential disease from hepatitis B virus (HBV) and human immunodeficiency virus (HIV)**

Parameters	Base case	Lower estimate	Upper estimate	References
Prevalence of infection in vaccinated population				
HBV (surface antigen)	0.1	0.05	0.15	*16, 32, 33*
HIV	0.1	0.02	0.25	*17*
Patient-to-patient transmission[a]				
Probability of unsterile reuse/blood exposure [resterilizable N&S[b], disposable N&S]	0.3	0.15	0.5	*2, 4, 26*
Probability of unsterile reuse/blood exposure [auto-disable N&S, auto-shielding N&S, disposable-cartridge jet injector]	0	0	0	c
Probability of unsterile reuse/blood exposure [manual-shielding N&S]	0.15	0.01	0.3	*34*
Probability of blood exposure from routine use [reusable-nozzle jet injector]	0.01	0.001	0.05	*6, 35, 36*
Patient-to-health care worker transmission				
Probability of needlestick/blood exposure from:				
Resterilizable N&S	0.05	0.01	0.08	*2, 33*
Disposable N&S	0.03	0.02	0.05	*33*
Auto-disable N&S	0.01	0.001	0.02	*29, 33, 37*
Manual-shielding N&S	0.002	0.001	0.004	c
Auto-shielding N&S, reusable-nozzle jet injector, disposable-cartridge jet injector	0	0	0	c
Patient-to-community transmission[a]				
Probability of unsafe sharps disposal [resterilizable N&S, disposable N&S, auto-disable N&S, manual-shielding N&S, auto-shielding N&S]	0.05	0.01	0.1	*33*
Probability of unsafe sharps disposal [reusable-nozzle jet injector, disposable-cartridge jet injector]	0	0	0	c
Probability of needlestick injury [resterilizable N&S]	0.0002	0	0.0005	c
Probability of needlestick injury [disposable N&S, auto-disable N&S]	0.002	0.0005	0.004	*33*
Probability of needlestick injury [manual-shielding N&S, auto-shielding N&S, reusable-nozzle jet injector, disposable-cartridge jet injector]	0	0	0	c
Probability of infection upon blood exposure[a]				
HBV [resterilizable N&S, disposable N&S, manual-shielding N&S, reusable-nozzle jet injector]	0.3	0.2	0.4	*2, 38–42*
HIV [resterilizable N&S, disposable N&S, manual-shielding N&S, reusable-nozzle jet injector]	0.003	0.002	0.005	*2, 40–43*
Lifetime direct medical care costs, per infection[d] (US$)				
HBV	34.19	14.48	67.77	e
HIV	2 532	1 436	4 139	e
Cost of lifetime productivity loss, per infection[d] (US$)				
HBV	2 575	1 016	3 637	e
HIV	19 129	17 570	20 191	e
Device purchase and usage costs[f] (US$)				
Resterilizable N&S	0.0697	0.0174	0.1394	g
Disposable N&S	0.1016	0.0254	0.2031	g
Auto-disable N&S	0.1357	0.0339	0.2713	g
Manual-shielding N&S	0.5432	0.1358	1.0863	g
Auto-shielding N&S	0.5432	0.1358	1.0863	g
Reusable-nozzle jet injector	0.0393	0.0098	0.0786	g
Disposable-cartridge jet injector	0.3595	0.0899	0.7191	g

[a] Parameters are relevant only for the types of injection devices indicated in square brackets. See Box 1 for definitions of injection devices.

[b] N&S = needle and syringe.

[c] Values estimated in the absence of published data or previous sources.

[d] Medical costs and productivity losses estimated at year 2000 prices, discounted by 3%.

[e] Sources and calculations of lifetime direct medical costs and indirect costs (productivity losses) for HBV and HIV detailed in Annex Table B (available on the *Bulletin* web site: http://www.who.int/bulletin).

[f] Base-case estimates for device purchase and usage costs were varied conservatively to 25% and 200% for the lower and upper estimates respectively. See Annex Table A (available on the *Bulletin* web site: http://www.who.int/bulletin) for details of calculation and ref: *5, 30, 44–50*.

[g] See Annex Table A footnotes (available on the *Bulletin* web site: http://www.who.int/bulletin) for references used in estimating device purchase and usage costs.

10 years, all had become symptomatic and died within a year. The direct medical costs attributable to HIV infection were discounted by 3% (conversion rate of 0.806) to the present value. Foreign currencies were converted to US$ at the year 2000 exchange rates (*55*). The arithmetic means of the present value totals of direct medical costs for the three countries were used as single sub-Saharan Africa estimates for the model. Additional details and assumptions for the input values and calculations of direct medical costs are described in Annex Table B (available on the *Bulletin* web site: http://www.who.int/bulletin).

Indirect costs — lost productivity

Lost productivity was the sole indirect cost considered for iatrogenic HBV and HIV diseases (Table 1) and was modelled

using an adaptation of the method of Over et al. for determining lost productivity from perinatal HIV transmission (*53*) (see footnote o in Annex Table B), available on the *Bulletin* web site: http://www.who.int/bulletin, for further explanation). Average annual earnings in public or private sectors collected from original sources in Côte d'Ivoire, Ghana, and Uganda (*33*) were adjusted for unemployment rates, and then applied to the years of life lost. This was calculated as the difference between average life expectancy at birth (51 years in Côte d'Ivoire, 57 in Ghana, 48 in Uganda) and the earlier average age of death due to HBV (Côte d'Ivoire: 43 years, in Ghana: 40 years, Uganda 41 years) or to HIV (6 years in all three countries).

As assumed by Over et al. (*53*), HIV-infected infants were assumed to have only 15% of average adult income during the "lost" years from 6 to 15 years (e.g. for tasks such as child care, wood gathering, and other domestic chores), and full income (100%) thereafter to the age of 50 years. From the ages of 51 to 65 years, income was adjusted to 85% of the average. For both HBV and HIV, the amounts of future lost income were discounted at 3% per year, standardized to US$ for the year 2000 exchange rates, and averaged among the three countries for the regional base-case amounts shown in Table 1. To avoid counting lost productivity in full years for both the year of premature death and year of death after normal life expectancy, only half of lost income was counted in those first and last years of the discounting model. Further details, input data, and the lost productivity discounting formula are provided in Annex Table B and Annex Box B (available on the *Bulletin* web site: http://www.who.int/bulletin).

Sensitivity analysis

In order to ascertain the degree of uncertainty inherent in the point estimates for the purchase and usage costs of each injection device and for the direct medical and indirect (lost productivity) costs of HBV and HIV disease, we performed multivariate sensitivity analyses using the Monte Carlo simulation sampling method (*56–58*).

For various base-case point estimates of input data in Annex Table B, lower and upper estimates were made and modelled in parallel runs. For example, in Uganda, the number of days of hospitalization for HIV disease averaged 14 days (lower and upper estimates 7 days and 31 days, respectively). In Ghana, the average number of follow-up doctors' visits for HIV care varied from two to 10, around a base case of four. In Côte d'Ivoire, the average cost of a laboratory test for hepatitis B surface antigen was US$ 42.14, with US$ 14.05 and US$ 84.27 set as the lower and upper estimates, respectively. Calculated device purchase and usage costs (Annex Table A, available on the *Bulletin* web site: http://www.who.int/bulletin) were varied by 25% and 200% to produce lower and upper estimates. Parallel runs of the model using such lower and upper cost estimates were used, along with the base-case estimates, to construct triangular probability distributions (*59*) for the Monte Carlo analyses (the triplicate input costs are provided in the final three sections of Table 1). The triangular probability distribution is often used in the absence of a large data set when the mean value is small and the standard deviation is large (*60*).

The simulations were conducted using @RISK software (Palisade Corporation, Newfield, NY, USA) (*61*), an add-in to Excel® spreadsheet software (Microsoft Corporation, Redmond, WA, USA). On each of 1000 simulation runs, a value for each parameter was drawn from its associated distribution and used to calculate risk and cost estimates for each injection device. For each device, the output of the simulation runs produced the mean, standard deviation, 5th, 50th (median), and 95th percentiles.

Results

Cost of device purchase and usage

The device with the highest purchase price and usage cost was the manual-shielding N&S, at US$ 0.54 each (Table 1, with input details provided in Annex Table A (available on the *Bulletin* web site: http://www.who.int/bulletin). The reusable-nozzle jet injector was the least expensive to buy and use, at US$ 0.04 per injection. The conventional disposable N&S was calculated to cost US$ 0.10 per injection.

Number of disease cases produced

Base-case point estimates for the predicted number of HBV and HIV infections resulting from one million injections with each of the modelled devices are shown in Table 2. The conventional resterilizable N&S caused the greatest number of iatrogenic infections per million injections ($n = 9545$), followed closely by the disposable N&S ($n = 9002$). The manual-shielding N&S incurred somewhat less then half this burden ($n = 4145$). In contrast, both the auto-disable N&S and reusable-nozzle jet injector produced relatively few HBV and HIV infections ($n = 276$ and $n = 273$ respectively). Of course, the reusable-cartridge jet injector and the hypothetical auto-shielding N&S produced no infections according to the model.

Costs of disease

The overall economic burdens of HBV and HIV disease resulting from the predicted iatrogenic infections are summarized in Table 3. The overall societal costs attributable to the resterilizable N&S and disposable N&S were US$ 26.71 and US$ 25.18 respectively, as the base case point estimates per injection (HBV and HIV costs combined). Each use of an auto-disable N&S was estimated to produce disease costs of US$ 0.77, which was nearly identical to the point estimates for the reusable-nozzle jet injector (US$ 0.76).

The Monte Carlo sensitivity analyses of these disease costs, also in Table 3, reveal medians that vary only slightly from the point estimates of each injection device for HBV disease, but somewhat more widely for HIV/AIDS. The 5th and 95th percentiles reveal modest ranges. For example, the resterilizable N&S ranged from US$ 11.71 to US$ 40.19 for HBV disease, and from US$ 0.90 to US$ 4.46 for HIV/AIDS.

Overall costs

Combining all costs for a societal perspective — device purchase and usage, medical costs, and lost productivity — it was estimated that the most expensive technology for administering vaccines is the resterilizable N&S, at US$ 26.77 per injection (Fig. 1). The next most expensive is the disposable N&S (US$ 25.29). The lowest costs were for the disposable-cartridge jet injector and auto-shielding N&S, at US$ 0.36 and US$ 0.54, respectively. Intermediate costs were found for the reusable-nozzle jet injector (US$ 0.80) and auto-disable N&S (US$ 0.91).

Looking only from the health care payer's perspective (Fig. 2), the relative overall costs of the various devices change.

Table 2. **Numbers of iatrogenic hepatitis B virus (HBV) and human immunodeficiency virus (HIV) infections attributable to the use of injection devices, by route of transmission, per million injections[a]**

Type of injection device	No. of infections								
	Patient-to-patient transmission		Patient-to-health care worker transmission		Patient-to-community transmission		All-routes totals[b]		
	HBV	HIV	HBV	HIV	HBV	HIV	HBV	HIV	Both
Resterilizable N&S[c]	8100	81	1350	14	<1[d]	<1[d]	9450	95	9545
Disposable N&S	8100	81	810	8	3	<1[d]	8913	89	9002
Auto-disable N&S	0	0	270	3	3	<1[d]	273	3	276
Manual-shielding N&S	4050	41	54	1	0	0	4104	41	4145
Auto-shielding N&S	0	0	0	0	0	0	0	0	0
Reusable-nozzle jet injector	270	3	0	0	0	0	270	3	273
Disposable-cartridge jet injector	0	0	0	0	0	0	0	0	0

[a] Calculated from base-case assumptions in Eq. 1 (see text).
[b] Sum of cases for each route of transmission may not equal all-routes totals because of rounding errors.
[c] N&S = needle and syringe.
[d] Less than one infection expected per million injections.

The manual-shielding N&S takes the lead as the most expensive device at a median cost of US$ 0.81 per injection, followed by identical costs (US$ 0.67) for both the resterilizable N&S and disposable N&S. The disposable-cartridge jet injector moves up to fifth in order of cost (US$ 0.37), no longer being the lowest cost. The lowest cost is now for the reusable-nozzle jet injector (US$ 0.06). The auto-disable N&S becomes next to lowest, at US$ 0.16.

The multivariate sensitivity analyses found median costs to be similar to the base-case results (Table 3, Fig. 1). For example, the HBV disease cost attributable to each injection with the resterilizable N&S was US$ 24.66 in the base case and US$ 23.17 (94%) in the multivariate sensitivity analyses. For HIV disease, the corresponding values were US$ 2.05 and US$ 2.24 (109%) respectively. The 5th and 95th percentiles revealed modest ranges. For example, for the disposable N&S, the HBV disease cost ranged from US$ 11.45 to US$ 38.02 (around a base case of US$ 23.25, median US$ 22.09).

Discussion

Our modelling reveals that unsafe parenteral injection in sub-Saharan Africa causes a substantial health and economic burden from iatrogenic disease. Most of this cost is hidden because new infections are usually unrecognized, or cannot be linked to a causative injection, and because most of the disease sequelae are greatly delayed. We found that the most commonly used injection devices, resterilizable and disposable needles and syringes, actually cost around US$ 0.67 per injection in direct medical costs, and a staggering US$ 25 to US$ 27 in overall costs when lost productivity from premature death was included. These costs are high relative to estimated annual expenditures of US$ 33 per capita for all public and private health purposes by countries in sub-Saharan Africa (62).

Our input assumptions and findings are consistent with those of previous work on the incorrect use of injection devices (2, 4, 7, 26, 63). Another mathematical model assumed that a needle would be reused between one and four times (4). We assumed a probability of 0.3 (range: 0.15–0.5). An average of 33% of health centres in Chad, Côte d'Ivoire, Uganda, and Swaziland reused syringes or needles without sterilization (3). A macrolevel analysis by Kane et al. for the entire population of sub-Saharan Africa calculated the annual number of new HBV and HIV infections attributable to unsafe injection to be 780 052 and 51 208 respectively (26).

Our modelling exercise is limited by the numerous assumptions and input cost estimates that must be made, as there is a paucity of published, scientifically gathered sources for such data. Nevertheless, the risk and cost estimates used here are relatively conservative. They excluded the economic consequences of disease and premature death arising from other bloodborne pathogens that can be contracted by unsafe injection, e.g. hepatitis C, *Trypanosoma* sp., *Plasmodium* sp., and agents of haemorrhagic fever. We also ignored treatment costs for opportunistic infections associated with HIV/AIDS, such as tuberculosis, as well as burial costs, which can be substantial in developing countries (64, 65). Also excluded were the indirect costs for the time of others in caring for a patient. Thus, the *Bulletin* results are probably underestimates of the true costs of unsafe injection.

This problem is not peculiar to sub-Saharan Africa or other developing countries. A survey in Eastern Europe in 1992–93 revealed about half of health centres were administering unsafe injections (1). HBV and HIV spread widely in Romanian orphanages due to needle and syringe reuse (66–69), as did HBV in the Republic of Moldova (70). Fortunately, the problem is becoming increasingly recognized (19). In 1994, more than 50 African countries endorsed the Yamoussoukro Declaration on the safety of injections and its goal of 95% safe practice (1). As a result, the auto-disable N&S that cannot be reused is now the normative standard of care for developing country immunization programmes (22–24). We estimated US$ 0.14 per injection to buy and use them, plus an additional US$ 0.77 per injection for the medical costs of consequential needlestick injuries, which they do not prevent (Fig. 1).

Reusable-nozzle jet injectors are a needle-free vaccination technology formerly used in Africa for mass immunization

Table 3. **Overall direct and indirect costs[a] (societal perspective) estimated for iatrogenic hepatitis B virus (HBV) and human immunodeficiency virus (HIV) disease attributable to the use of various injection devices, in US$ equivalents, by route of transmission, per injection**

Type of injection device	Costs (US$)							
	Patient-to-patient transmission		Patient-to-health care worker transmission		Patient-to-community transmission		All-route totals[b]	
	HBV	HIV	HBV	HIV	HBV	HIV	HBV	HIV
Resterilizable N&S[c]	21.13 (20.05)[d] [10.30–34.51][e]	1.55 (1.94) [0.78–3.85]	3.52 (3.12) [1.41–5.68]	0.26 (0.30) [0.11–0.61]	0.001 (0.001) [<0.001–0.002]	<0.001 (<0.001) [<0.001–<0.001]	24.66 (23.17) [11.71–40.19]	2.05 (2.24) [0.90–4.46]
Disposable N&S	21.13 (20.05) [10.30–34.51]	1.55 (1.94) [0.78–3.85]	2.11 (2.04) [1.14–3.49]	0.15 (0.20) [0.08–0.37]	0.007 (0.007) [0.002–0.015]	0.001 (0.001) [<0.001–0.002]	23.25 (22.09) [11.45–38.02]	1.93 (2.14) [0.87–4.22]
Auto-disable N&S	0 (0)	0 (0)	0.70 (0.65) [0.25–1.30]	0.05 (0.06) [0.02–0.14]	0.007 (0.007) [0.002–0.015]	0.001 (0.001) [<0.001–0.002]	0.71 (0.65) [0.25–1.31]	0.06 (0.06) [0.02–0.14]
Manual-shielding N&S	10.57 (9.54) [3.56–19.42]	0.77 (0.92) [0.29–2.03]	0.14 (0.14) [0.07–0.26]	0.01 (0.01) [0.005–0.03]	0 (0)	0 (0)	10.71 (9.68) [3.63–19.69]	0.89 (0.94) [0.29–2.05]
Auto-shielding N&S	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Reusable-nozzle jet injector	0.70 (0.89) [0.22–2.34]	0.05 (0.08) [0.02–0.25]	0 (0)	0 (0)	0 (0)	0 (0)	0.70 (0.89) [0.22–2.34]	0.06 (0.08) [0.02–0.25]
Disposable-cartridge jet injector	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

[a] Estimated costs attributable to each injection device calculated as follows: (expected new cases of HBV [or HIV] infection) x (direct medical care costs for HBV [or HIV] + lost productivity costs for HBV [or HIV]. In each cell, the figure on the left is the base case-estimate.

[b] All-routes totals vary slightly from combined component amounts due to rounding in route-of-transmission columns.

[c] N&S = needle and syringe.

[d] Figures in parentheses are medians (50th percentiles) of the sensitivity analysis using 1000 Monte Carlo simulations, with input parameters in Table 1 set to triangular probability distributions.

[e] Figures in square brackets are ranges bound by the 5th and 95th percentiles of the sensitivity analysis using 1000 Monte Carlo simulations, with input parameters in Table 1 set to triangular probability distributions.

campaigns, such as control of meningococcal (71) and yellow fever (72) outbreaks. We calculated they cost only US$ 0.06 per injection from the health care payer's perspective. Such devices have delivered billions of injections in mass immunization campaigns and epidemic control activities since their introduction in the 1950s (73). However, their high initial capital cost and complex maintenance requirements make them unsuitable for routine immunization clinics. We therefore modelled them only for mass campaigns with an assumed usage of 1000 doses on each day of use (Annex Table A, available on the *Bulletin* web site: http:www.who.int/bulletin). The Program for Appropriate Technology in Health (PATH) estimated that low-volume use of such devices would result in a much higher direct cost of US$ 0.20 per injection (50).

In the mid-1980s, concern about the possibility of bloodborne disease transmission between consecutive vaccinees from reusable-nozzle jet injectors (Annex Box A, available on the *Bulletin* web site: http:www.who.int/bulletin) arose following an outbreak of hepatitis B in California, USA, caused by a Med-E-Jet® device (35, 74, 75). A 1990s study in Brazil identified contamination in 1–6% of ejectates collected immediately after the vaccination of patients (6). The Public Health Laboratory Service of the United Kingdom of Great Britain and Northern Ireland, with assistance from WHO, pioneered an animal model to identify and quantify blood at levels theoretically sufficient to transmit HBV in succeeding injections. The Public Health Laboratory Service found contamination of ejectates and/or transmission of HBV in the succeeding injection occurred with all devices tested (36). These and other unpublished studies formed the basis for the

Bulletin modelled base case assumption that these devices would transmit blood 1% of the time.

In 1997, liability risk led to manufacturer withdrawal of the Ped-O-Jet® from the market, followed by its recall by the United States military (76, 77). In 1998, WHO recommended that such injectors should not be used until testing demonstrated their safety (78). The United States Centers for Disease Control and Prevention recommended that public health authorities weigh the potential risk against the benefit in certain situations where the rapid vaccination of large numbers of people is required and the use of needles and syringes is not practical (79, 80). As a result, the world lacks a high-speed device of unquestioned safety for intramuscular or subcutaneous vaccination for use in influenza pandemics, measles eradication, response to biological terrorism, or other necessary mass immunization campaigns. This vulnerability will probably disappear when high-speed jet injectors with disposable cartridges are developed.

Low-workload jet injectors with disposable cartridges now exist (73, Annex Box A, available on the *Bulletin* web site: http:www.who.int/bulletin), but they are not affordable for use in the developing world because of the current expense of their cartridges — US$ 0.25–0.50 per injection. We modelled these at the lower cost. Also impeding their acceptance are their proprietary, non-interchangeable cartridges. Universal standards for a common cartridge might enhance market demand for such technology and reduce their costs through mass production. Another obstacle is the need for end users to fill the empty cartridges manually in the clinic. Vaccine manufacturer prefilling would be highly convenient and save users

Fig. 1. **Overall costs per injection from societal perspective for alternative injection technologies,[a] by base-case point estimates and by median (50th percentile) estimates from the Monte Carlo simulation sensitivity analysis (MC)**
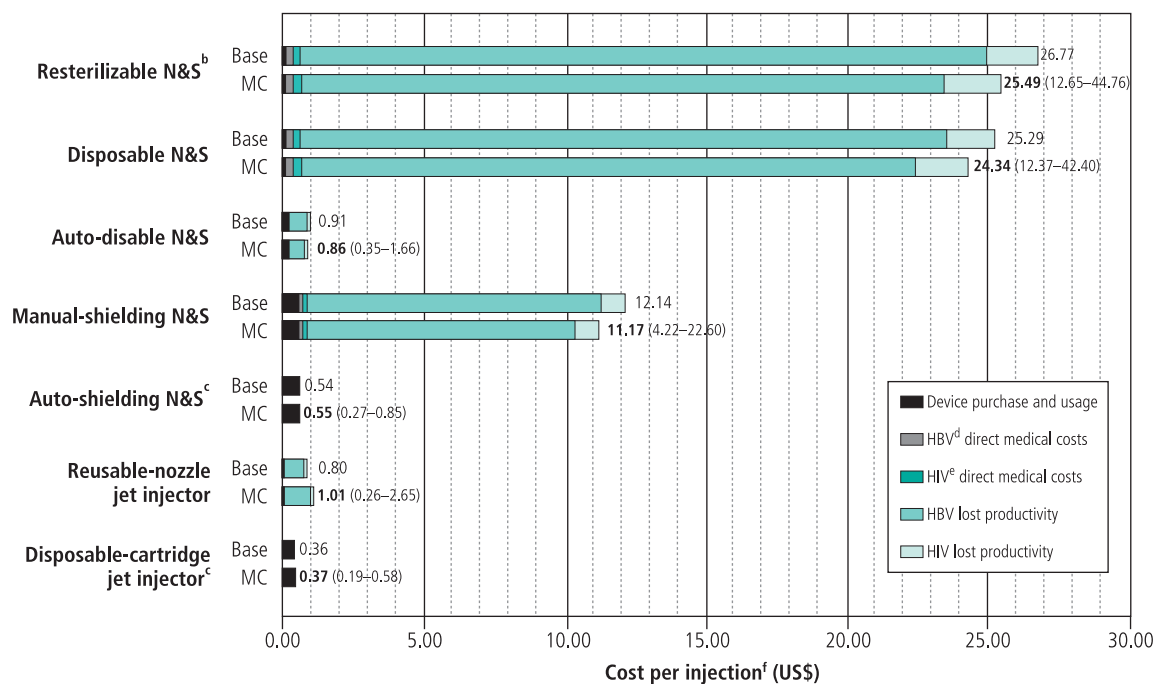
[a] See Box 1 for explanation of device types.

[b] N&S = needle and syringe.

[c] Disposable-cartridge jet injector and auto-shielding N&S were assumed to cause no iatrogenic HBV[d] or HIV[e] disease.

[d] HBV = hepatitis B virus.

[e] HIV = human immodeficiency virus.

[f] Costs in bold are the sum of the medians for the contributing values of the corresponding device. Ranges in parentheses represent the sums of the 5th and 95th percentile intervals from the Monte Carlo simulation.

WHO 02.164

Fig. 2. **Costs per injection from the health care payer's perspective only, for alternative injection technologies,[a] by median (50th percentile) estimates from the Monte Carlo simulation sensitivity analysis**
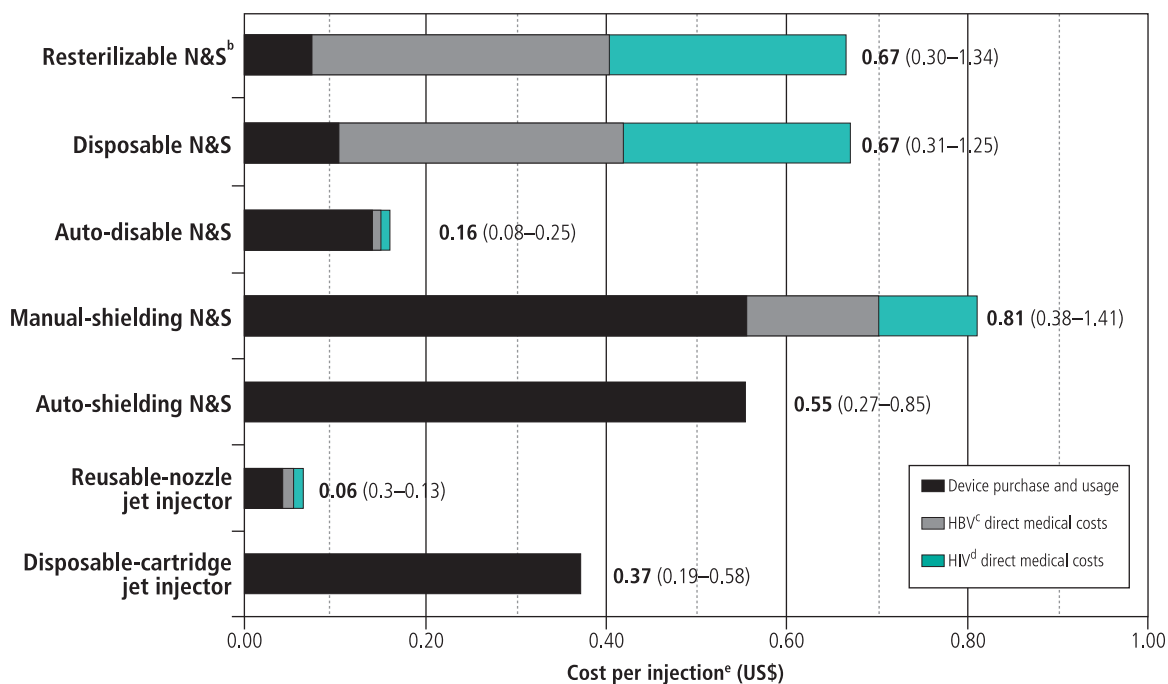
[a] See footnote a, Fig. 1.

[b] See footnote b, Fig. 1.

[c] See footnote d, Fig. 1.

[d] See footnote e, Fig. 1.

[e] See footnote f, Fig. 1.

WHO 02.165

the expense of purchasing empty cartridges. One such prefilled cartridge was successfully pilot tested in both industrialized and developing countries (*81–84*), but its further development was halted for unspecified reasons.

Needlestick injuries have been a focus of concern in both developing (*29*) and industrialized countries (*12–14, 85, 86*). In the USA, occupational safety regulations now require safer injection devices, such as the needle-shielding syringes and needle-free injectors we modelled (*87–89*). But needle-shielding syringes remain too expensive (modelled at US$ 0.54) for developing countries. Future needle-free vaccine technologies, such as mucosal (*90*) or transcutaneous (*91, 92*) immunization, would avoid the dangers of injection. However, they will probably take many years to be registered in developed countries and their costs may put them out of reach of developing countries for decades.

The hidden disease and economic cost of unsafe injections are enormous. Health ministries in sub-Saharan Africa, and the international agencies and initiatives that promote immunization and therapeutic injections should recognize this burden. To rephrase Hippocrates' *Epidemics*, in selecting injection technology, one should "do less harm". ■

Résumé

Estimations tirées de la modélisation du risque de transmission de maladies et du coût économique liés à sept dispositifs d'injection en Afrique subsaharienne

Objectif Etudier et comparer sept types de dispositifs d'injection du point de vue du coût économique et du risque de transmission iatrogénique de germes à diffusion hématogène en Afrique subsaharienne.

Méthodes Des hypothèses de risque et des modèles de coûts ont été établis pour chaque dispositif de manière à estimer le nombre de nouvelles infections par le virus de l'hépatite B (HBV) et le virus de l'immunodéficience humaine (VIH) à la suite d'une transmission d'un patient à l'autre, d'un patient à un agent de soins de santé et d'un patient à la communauté. Les coûts d'achat et d'utilisation des dispositifs ont été tirés des données publiées, tandis que les coûts des soins médicaux directs et de la perte de productivité associée à la maladie dans le cas des infections à HBV et à VIH ont été tirés de données recueillies en 1999 en Côte d'Ivoire, au Ghana et en Ouganda. Des analyses multivariées de sensibilité au moyen du modèle de Monte Carlo ont permis de caractériser l'intervalle d'incertitude des paramètres du modèle. Les coûts ont été additionnés du double point de vue de la société et du système de soins de santé.

Résultats Les aiguilles et seringues restérilisables et jetables avaient le coût global le plus élevé en ce qui concerne l'achat, l'utilisation et les maladies iatrogéniques, avec un coût sociétal médian par injection de US $26,77 pour le matériel restérilisable et US $25,29 pour le matériel jetable. Les injecteurs sans aiguille à cartouche jetable et les seringues à dispositif automatique de protection de l'aiguille avaient le coût le plus faible, soit respectivement US $0,36 et US $0,80. Les injecteurs sans aiguille à buse réutilisable et les aiguilles et seringues autobloquantes avaient un coût intermédiaire, soit respectivement US $0,80 et US $0,91 par injection.

Conclusion Malgré leur coût nominal d'achat et d'utilisation, les aiguilles et seringues conventionnelles comportent un risque non visible mais important de maladie iatrogénique. D'autres dispositifs d'injection utilisables pour les millions d'injections pratiquées chaque année en Afrique subsaharienne seraient intéressants et devraient être examinés par les responsables de l'élaboration des politiques lors des décisions d'achat.

Resumen

Estimaciones basadas en modelos de los riesgos de transmisión de enfermedades y el costo económico de siete dispositivos de inyección en el África subsahariana

Objetivo Investigar y comparar siete tipos de dispositivos de inyección en cuanto a su riesgo de infección iatrogénica por patógenos de transmisión hematógena y su costo económico en el África subsahariana.

Métodos Se elaboraron hipótesis de riesgos para cada dispositivo y modelos de costos para estimar el número de nuevas infecciones por los virus de la hepatitis B (VHB) y de la inmunodeficiencia humana (VIH) debidas a la transmisión entre pacientes, de paciente

a agente de salud, y de paciente a la comunidad. Los costos asociados a la compra y el uso de los dispositivos se calcularon a partir de información hallada en la literatura, mientras que los costos de la atención médica directa y de la productividad perdida como consecuencia de las infecciones por el VHB y el VIH se basaron en datos reunidos en 1999 en Côte d'Ivoire, Ghana y Uganda. Los intervalos de incertidumbre de los parámetros del modelo se determinaron mediante análisis de sensibilidad multifactoriales basados en el método de Monte Carlo. Se sumaron los costos obtenidos desde la perspectiva tanto de la sociedad como de los contribuyentes al sistema de atención de salud.

Resultados Las agujas y las jeringas reesterilizables y desechables se asociaron a los costos globales más altos en lo que atañe a la compra, el uso y las enfermedades iatrogénicas: medianas de US$ 26,77 y US$ 25,29, respectivamente, por inyección desde el punto de vista de la sociedad. Los costos más bajos correspondieron a los inyectores sin aguja con cartucho desechable y las jeringas con protección automática de la aguja: US$ 0,36 y US$ 0,80, respectivamente. Los inyectores de presión con boquilla reutilizables y las agujas y jeringas no reutilizables obtuvieron resultados intermedios, con US$ 0,80 y US$ 0,91, respectivamente, por inyección.

Conclusión A pesar de su costo nominal de adquisición y uso, las agujas y las jeringas convencionales comportan una carga oculta pero enorme de enfermedades iatrogénicas. El uso de dispositivos de inyección alternativos en los millones de inyecciones que se administran anualmente en el África subsahariana sería una medida inestimable, que debería ser tenida en cuenta por los formuladores de políticas en las decisiones de compra.

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Annex Box A. **Examples of commercial devices or prototypes modelled in the study**

Auto-disable needle and syringe (N&S)

Examples of auto-disabling, single-use needles permanently fixed to plastic syringes designed to prevent inadvertent or intentional reuse that meet WHO, the United Nations Children's Fund (UNICEF), and the United Nations Population Fund (UNFPA) criteria for safe injections in developing countries are: DestroJect® (DestroJect GmbH Medical Devices, Neumünster, Germany); SoloShot™ (*28, 29*) (Becton-Dickinson and Co., Franklin Lakes, NJ, USA); and UNIVEC Rx Ultra™ (Univec Inc., Farmingdale, NY, USA), among others.

Generic products are also available from: Atlas Medical Resources Corp. Inc., Ottawa, Ontario, Canada; Com Pro, Paris, France; and Pharmaplan GmbH, Bad Homburg, Germany, among others.

UniJect™ is an equivalent auto-disable device containing prefilled vaccine in a plastic blister with a fixed needle (Becton-Dickinson and Co.).

An updated list of auto-disable syringe manufacturers whose products are preliminarily approved by WHO and UNICEF is available from: URL: http://www.who.int/vaccines-access/injection_safety/Injections_Safety/Injection_Technology/ADsyringes_manu.html (accessed on 17 March 2002).

Manual-shielding N&S

The manually activated, needle-shielding N&S for the prevention of needlestick injuries modelled in the study was the VanishPoint® (Retractable Technologies Inc., Little Elm, TX, USA) (*30*). Similar devices are the SafetyGlide™ and Safety-Lok™ (Becton-Dickinson and Co.), MonoJect™ Safety Syringes (*31*) (Sherwood-Davis and Geck, St. Louis, MO, USA), and Needle-Pro® (Portex, Inc., Keene, NH, USA), among others.

All these devices require the health worker to perform an additional step (e.g. further depressing the plunger after injection is completed) in order to shield the needle and disable the device.

A database maintained by the State of California, USA, of needle-shielding devices and manufacturers is available from: URL: http://www.dhs.ca.gov/ohb/sharps/disclaim.htm (accessed on 17 March 2002).

Reusable-nozzle jet injector

The multiple-use nozzle jet injector devices modelled were the Ped-O-Jet® (Keystone Industries, Cherry Hill, NJ, USA) and the identical Am-O-Jet™ (American Jet Injector, Lansdale, PA, USA). Similar devices include the Med-E-Jet® (Evans Enterprises, Mayfield Heights, OH, USA), DermoJet® (Société AKRA DermoJet, Pau, France), Im-O-Jet® (Aventis Pasteur, formerly Institut Mérieux, Lyon, France), and BI-100™ (Felton International, Lenexa, KS, USA, and CADB/Medequip, Voronezh, Russian Federation).

Disposable-cartridge jet injector

The disposable-cartridge needle-free jet injector modelled represented a composite of the features of various marketed and investigational devices, including the Biojector 2000® (Bioject Inc., Portland, OR, USA); the INJEX™ (Equidyne Systems Inc., San Diego, CA, USA); the MEDiVAX™ (Vitajet Corporation and Program for Appropriate Technology in Health, Seattle, WA, USA); the SensaJet™ (Genesis Medical Technologies Inc., Denver, CO, USA); and the LectraJet™ (DCI Inc., East Syracuse, NY, USA).

A list maintained by the Centers for Disease Control and Prevention, Atlanta, GA, USA, of both reusable-nozzle and disposable-cartridge jet injectors is available from: URL: http://www.cdc.gov/nip/dev/jetinject.htm#devices (accessed on 17 March 2002).

Annex Table A. **Purchase and usage cost estimates[a] for seven vaccine delivery technologies**

Device type[b] and component costs	Cost per unit (US$)	No. of injections per unit	Cost per injection (US$)
Resterilizable needle and syringe (N&S)			
Glass or (sterilizable) plastic syringe purchase[c]	0.730	100	0.007 30
Needle purchase[d]	0.050	45	0.001 11
Sterilizer purchase[e]	107.760	50 000	0.002 16
Hard-water pad for sterilizer[f]	20.730	25 000	0.000 83
Spare parts for sterilizer[g]	14.420	15 000	0.000 96
Steam sterilization indicators[h]	261.190	750 000	0.000 35
Cleaning and sterilization[i]	0.016	1	0.016 00
Resharpening needle[j]	0.075	10	0.007 50
Safety box for used N&S[k]	0.966	10 000	0.000 10
Incineration of safety box[l]	0.850	10 000	0.000 09
Labour[m]	1.500	45	0.033 33
Total cost			
Base case			**0.069 72**
Lower estimate[n]			0.017 43
Upper estimate[n]			0.139 44
Disposable N&S			
Disposable syringe purchase[o]	0.039	1	0.039 40
Disposable needle purchase[p]	0.019	1	0.019 00
Safety box for used N&S[k]	0.966	100	0.009 66
Incineration of safety box[l]	0.850	100	0.008 50
Labour[m]	1.500	60	0.025 00
Total cost			
Base case			**0.101 56**
Lower estimate[n]			0.025 39
Upper estimate[n]			0.203 12
Auto-disable N&S			
Auto-disable N&S purchase[q]	0.093	1	0.092 50
Safety box for used N&S[k]	0.966	100	0.009 66
Incineration of safety box[l]	0.850	100	0.008 50
Labour[m]	1.500	60	0.025 00
Total cost			
Base case			**0.135 66**
Lower estimate[n]			0.033 92
Upper estimate[n]			0.271 32
Manual-shielding N&S and Auto-shielding N&S			
Device purchase[r]	0.500	1	0.500 00
Safety box for used N&S[k]	0.966	100	0.009 66
Incineration of safety box[l]	0.850	100	0.008 50
Labour[m]	1.500	60	0.025 00
Total cost			
Base case			**0.543 16**
Lower estimate[n]			0.135 79
Upper estimate[n]			1.086 32
Reusable-nozzle jet injector			
Device purchase[s]	2 300.000	1 000 000	0.002 30
Spare parts kit[t]	275.000	50 000	0.005 50
Cleaning and sterilization[u]	3.250	1 000	0.003 25
Routine maintenance[v]	0.250	200	0.001 25
Overhaul[w]	153.000	100 000	0.001 53
Training[x]	45.000	100 000	0.000 45
Three-dose vaccine waste on purge[y]	0.900	60	0.015 00
Labour[z]	1.500	150	0.010 00
Total cost			
Base case			**0.039 28**
Lower estimate[n]			0.009 82
Upper estimate[n]			0.078 56

Device type[b] and component costs	Cost per unit (US$)	No. of injections per unit	Cost per injection (US$)
Disposable-cartridge jet injector			
Device purchase[aa]	250.000	25 000	0.010 00
Maintenance and cleaning[bb]	3.000	200	0.015 00
Safety box for used cartridges[k]	0.966	400	0.002 42
Incineration of safety box[l]	0.850	400	0.002 13
Labour[cc]	1.500	60	0.025 00
Vaccine vial transfer devices[dd]	0.550	10	0.055 00
Disposable cartridges[ee]	0.250	1	0.250 00
Total cost			
Base case			**0.359 54**
Lower estimate[n]			0.089 89
Upper estimate[n]			0.719 08

[a] Lower and upper estimates of costs were varied from 25% to 200% of the base-case calculation. Sources: ref. *44–46*, unless indicated otherwise.

[b] See Box 1 for classification and description of device types.

[c] Resterilizable syringe modelled: glass, 2 ml capacity (United Nations Children's Fund (UNICEF) catalogue item no. 078 3500). An average of 100 uses were assumed before breakage or disposal (*47*).

[d] Resterilizable needle modelled: stainless steel, 0.7 mm x 32 mm (UNICEF catalogue item no. 075 0500). An average of 45 uses were assumed before disposal (*47*).

[e] Sterilizer modelled: double rack, steam pressure, fuel, kit B (with accessories), 84-syringe/100-needle capacity (UNICEF catalogue item no. 990 8100). Assumed a useful life of 10 years, 100 sterilizations per year at 60% of capacity (50 syringes). Useful life estimate source: M. Lainejoki, J. Lloyd, M. Zaffran, personal communications, 1998, 1999.

[f] Hard-water pad modelled: item 015 7118. Average 5-year life assumed, 100 sterilizations per year at 60% of capacity (50 syringes). Useful life estimate source: M. Lainejoki, M. Zaffran, personal communications, 1998.

[g] Replacement parts modelled: gasket (UNICEF catalogue item no. 015 7115, US$ 4.01), handle (UNICEF catalogue item no. 015 7117, US$ 3.10), pressure valve (UNICEF catalogue item no. 015 7113, US$ 4.36), safety valve (UNICEF catalogue item no. 015 7116, US$ 2.95). Average 3-year life assumed, 100 sterilizations per year at 60% of capacity (50 syringes).

[h] Sterilization confirmation indicators modelled: Temperature-Steam-Time (TST) indicator spots, at US$ 261.19 for 50 boxes with 300 spots per box (plus record sheets), assuming one test spot per load at 60% of capacity (50 syringes).

[i] Includes cost of disinfectants for cleaning and fuel for sterilizer. Cost estimate source: ref. *48*.

[j] Assumed sharpening required for 3 minutes (at US$ 1.50/hour labour) after every 10 injections. Time estimate source: ref. *50*.

[k] Sharps box modelled: UNICEF catalogue item no. 078 2208, capacity 100 syringes (or 400 disposable needle-free cartridges of approximately 25% of size of average N&S). Resterilizable syringes deposited after average of 100 injections each; other syringes and needle-free cartridges deposited after being used once.

[l] Assumed cost of US$ 0.85 to incinerate one safety box. Cost source: ref. *5*.

[m] Assumed 80 seconds to assemble, fill, and administer each injection for resterilizable syringes (45/hour at US$ 1.50/hour labour), 60 seconds for disposable, auto-disable, and retractable-needle syringes (60/hour). Time estimates source: ref. *50*.

[n] Lower and upper estimates used in Monte Carlo sensitivity analyses.

[o] Disposable syringe modelled: plastic, 5 ml capacity (UNICEF catalogue item no. 078 2405, US$ 3.94 per 100).

[p] Disposable needle modelled: 0.7 mm x 32 mm (UNICEF catalogue item no. 074 7440).

[q] Auto-disable N&S device modelled: 0.5 ml capacity, fixed needle (UNICEF catalogue item no. 078 2207).

[r] Retractable needle syringe modelled: VanishPoint® (see Annex Box A) (*30*).

[s] Reusable-nozzle jet injector modelled: Ped-O-Jet®, model POJ (foot-operated) unit (*49*). Assumed 50 days per year of use for mass immunization campaigns, 1000 vaccinations per day, device lifespan 20 years.

[t] Spare parts kit no. J6000A includes sufficient replacement seals, springs, valve balls, and other wearable items needed for field maintenance during 50 000 injections (one year) (*49*; J. Stengel, R. Harrington, personal communications, 1998).

[u] Assumed 1.5 hours per day of 1000 vaccinations (at US$ 1.50/hour labour) for device disassembly, sterilization, and reassembly, plus US$ 1.00 for autoclave sterilization, including fuel.

[v] Assumed maintenance of 10 minutes per 200 vaccinations for clearing clogged nozzles, freeing jammed check valves, etc. (at US$ 1.50/hour labour). Time estimate source: ref. *50*. Not included are costs of a second backup injector kept on hand to keep a mass vaccination programme on schedule in case of failure of the primary device.

[w] Assumed major rebuild overhaul every 100 000 injections (2 years) by trained national technician (1 hour at US$ 3.00/hour labour), plus average US$ 150.00 cost of replacement parts and factory shipping.

[x] Assumed training time of 10 hours each for trainee (at US$ 1.50/hour labour) and trainer (at US$ 3.00/hour labour), required biannually (every 100 000 injections). Time estimate source: ref. *50*.

[y] Reusable-nozzle jet injectors feed vaccine from multi-dose vials into internal fluid chambers, and must be purged of air when changing vaccine vials and at end of vaccination session. Assumed loss of three doses (at US$ 0.30 each) for every 60 injections.

[z] Assumed average 150 injections per operator per hour (at US$ 1.50 per/hour labour).

[aa] Low workload, disposable-cartridge/nozzle jet injector modelled as a composite of various commercial and prototype models (see Methods and Annex Box A). Assumed 20 injections/day for 250 days per year for 5 years useful lifespan. Cost estimate source: ref. *50*.

[bb] Assumed 2 hours labour (at US$ 1.50/hour) required every 200 injections for routine maintenance and cleaning.

[cc] Assumed 60 injections per operator per hour (at US$ 1.50 per/hour labour), to transfer vaccine from vial to cartridge, load injector, and administer injection.

[dd] Disposable transfer device (or other system) attaches to multi-dose or unit-dose vials to measure and transfer vaccine into injection cartridge, without needing additional syringe or needle. Assumed transfer vial cost of the INJEX® vial adaptor (see Annex Box A), i.e. US$ 0.55 each (quantities above 5000; L. Petersen, personal communication, 1999). Assumed transfer device disposed after use with one 10-dose vial. Other injector systems may have a different means of effecting transfer into disposable cartridges, if not prefilled by vaccine manufacturer.

[ee] Assumed disposable cartridges to be filled in clinic immediately before injection (instead of prefilling by vaccine manufacturer); base price set at actual price for INJEX® brand of ampoules (see Annex Box A), i.e. US$ 0.25 each for quantities exceeding 5000 (L. Petersen, personal communication, 1999). Reduction in price to the lower (25%) estimate of US$ 0.065 each is considered feasible if several millions of ampoules were used per year.

C

Annex Table B. **Input data and cost assumptions,[a] attributable to HBV[b] and HIV[c] disease, as used for base-case estimates of corresponding direct medical costs[d] and indirect (lost productivity)[e] costs in representative sub-Saharan African countries**

Costs[f] (US$)	Côte d'Ivoire		Ghana		Uganda	
	HBV	HIV	HBV	HIV	HBV	HIV
Direct medical costs						
Outpatient care						
Average cost of first doctor visit	7.02	7.02	0.59	0.85	3.04	6.92
Average cost of follow-up visits	3.51	2.81	0.28	0.34	1.82	2.74
Average number of follow-up visits per lifetime	4	4	3	4	4	4
Lab test(s) for HBsAg[g] or HIV	42.14	3.51	0.94	0.94	6.08	2.13
Total travel costs for care	2.81	2.81	0.47	0.47	2.13	2.13
Disease-related drugs						
Average cost of interferon for HBV, lifetime[h]	7.94	NA[i]	NA	NA	NA	NA
Average cost for 1 month's drug(s) for HIV[j]	NA	173.96	NA	308.99	NA	308.99
Average months/year on HIV therapy[k]	NA	4.31	NA	1.50	NA	1.50
Average number of years on HIV therapy	NA	5	NA	5	NA	5
Inpatient hospitalization						
Average cost per day hospitalized	27.29	35.68	1.84	2.58	6.34	15.60
Average days hospitalized per lifetime	7.0	20.0	9.5	21.0	8.4	14.4
Subtotal: lifetime direct costs, undiscounted[l]	265	4487	20.34	2375	71.88	2564
Total: lifetime direct costs, 3% discounted[m, n]	**75.00**	**3616**	**6.24**	**1914**	**21.33**	**2067**
Indirect (lost productivity) costs						
Average life expectancy from birth (in years)	51	51	57	57	48	48
Average age at death from disease acquired in infancy (in years)	43	5	40	5	41	5
Average annual earnings	3 259	3 259	79.40	79.40	1 105	1 105
Average unemployment rate (%)	10	10	20	20	20	20
Adjusted annual adult earnings	2 933	2 933	64	64	884	884
Subtotal: productivity loss, undiscounted[o]	23 463	109 545	1 080	2 696	6 187	30 495
Total: productivity loss, 3% discounted	5 814	43 779	248	1 014	1 664	12 595

[a] Data collected in late 1999 from original sources in the countries listed (*33, 51*).

[b] HBV = hepatitis B virus.

[c] HIV = human immunodeficiency virus.

[d] Lifetime direct medical care costs = (initial outpatient visit cost) + ((follow-up visit cost) x (number of follow-up visits)) + (lab tests cost) + (travel costs) + [(lifetime HBV therapy cost) or (1-month HIV drug costs) x (months per year on HIV drugs) x (years on HIV drugs)] + [(daily inpatient hospital cost) x (average inpatient days)].

[e] Lifetime indirect (lost productivity) costs = sum of adjusted expected earning in future years between the average age of premature death from HBV or HIV and the life expectancy otherwise, adjusted for unemployment and age group. See Annex Box B for calculation formula.

[f] Costs collected in local currencies have been converted to US$ at the following year 2000 exchange rates for US$ 1.00: Côte d'Ivoire, 712 CFA; Ghana, 5322 Cedis; Uganda, 1645 Ugandan shillings (*55*).

[g] HBsAg = hepatitis B surface antigen.

[h] Reported per-patient cost in Côte d'Ivoire of 1 130 400 CFA (US$ 1588) for interferon treatment for chronic HBV infection was reduced by the assumed proportion among all HBV-infected who become chronic carriers (10%) and then by the estimated proportion of such carriers who will receive such interferon later in life (5%). This yields an average cost of US$ 7.94 for each new HBV infection.

[i] N/A = not applicable.

[j] Assume average child weight of 18 kg and surface area of 0.72 m^2. Côte d'Ivoire: paediatric triple-drug therapy modelled using available zidovudine (AZT, 200 mg/day), lamivudine (3TC, 140 mg/day) and indinavir (1080 mg/day), representing 40%, 48%, and 45% respectively of adult doses, and costing a proportionate US$ 173.96 of the total adult dosage costs of 286 290 CFA (US$ 402) per month. Ghana: HIV drugs available at the time only from Ugandan source; Ugandan costs applied. Uganda: same drugs and dosages assumed as in Côte d'Ivoire; zidovudine (three 200 ml bottles per month of 10 mg/ml syrup, costing 40 500 Ugandan shillings (US$ 24.62) per bottle); lamivudine (1.75 240 ml bottles per month of 10 mg/ml solution, costing 63 000 Ugandan shillings (US$ 38.30) per bottle); and indinavir (45% (US$ 168.10) of adult monthly dosage cost of 614 500 Ugandan shillings (US$ 373.56)).

[k] Estimated average months per year for what ideally should be year-round, triple-drug, antiretroviral therapy. This reflected both intermittent receipt and non-receipt of drug therapy by substantial proportions of HIV-infected children.

[l] Subtotals vary slightly from individual components listed due to rounding.

[m] HBV direct costs are assumed incurred during the final year of life at the average age of (premature) death resulting from infection acquired from unsafe injection, and discounted back at 3% to the first year of life (year 0). Totals for each country produce an arithmetic mean amount of US$ 34.19 used in the model for each new HBV infection (see Table 1).

[n] HIV direct costs discounted at 3% back to year 0 from the assumed probability of 10% per year of developing AIDS and dying within 12 months among those HIV-infected during the first year of life, using a discounting factor of 0.801 (*53, 54*). Totals for each country produce arithmetic mean amount of US$ 2533 used in the model for each new HIV infection (see Methods and Table 1).

[o] HBV: adjusted annual adult earnings x number of years between average age of death due to HBV disease and average life expectancy of uninfected people. HIV: adjusted annual adult earnings x number of years from age 16 years to average life expectancy of uninfected people, plus 15% of annual adult earnings from the average age of death (6 years) to the age of 15 years.

Annex Box B. **Formula used for calculating indirect costs of iatrogenic HBV[a] or HIV[b] disease resulting from lost productivity**

$$L = 0.5 \left(E_t\, W_{gt}\, (1+r)^{-t} \right) + \sum_{n=t+1}^{T-1} E_n\, W_{gn}\, (1+r)^{-n} + 0.5 \left(E_T\, W_{gT}\, (1+r)^{-T} \right)$$

where:

L = loss of earnings attributable to premature death resulting from HBV or HIV disease

n = future year of age for which the value in the first year of life (age 0) is being determined

t = assumed age of premature death, in years, for HBV or HIV infections acquired in infancy

T = assumed average age of death (life expectancy at birth), in years

E_n = average per capita annual earnings of employed adults in public and private sectors, adjusted for unemployment, in the year n (t, t +1,..., T-1, T). (The current year 0 value for earnings is assumed for each future year n.)

W_{gn} = age-weighting factor for adjustment of earnings of individuals of age group g in the year of age n

   (W_{gn} = 0 when age group g is 0–5 years,

   W_{gn} = 0.15 when age group g is 6–15 years,

   W_{gn} = 1.0 when age group g is 16–50 years,

   W_{gn} = 0.85 when age group g is 51–65 years,

   W_{gn} = 0.25 when age group g is $\geqslant$ 66 years)

r = assumed annual interest rate 3% for discounting the future value of money to the present time

$(1+r)^{-n}$ = discount factor for calculating the present value of future earnings

[a] HBV = hepatitis B virus.

[b] HIV = human immunodeficiency virus.