Evidence and Information for National Injection Safety Policies

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Table of contents

Table of figures

List of tables

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Summary

Background

The adverse consequences of poor injection practices have been reported for a few decades. However, key elements of evidence and information were lacking to allow decision-makers to formulate policies for the safe and appropriate use of injections. We conducted studies to (1) estimate the frequency of injection use and of poor injection practices, (2) estimate the consequences of poor injection practices in terms of death and disability, (3) formulate best infection control practices for intradermal, subcutaneous and intramuscular injections, (4) quantify the effectiveness of interventions to reduce unnecessary and unsafe use of injections and (5) estimate the cost-effectiveness of national policies for the safe and appropriate use of injections.

Methods

WHO's Global Burden of Disease project defined 14 regions based on geography and mortality patterns. The analysis excluded four regions (predominantly affluent, developed nations) where reuse of injection equipment in the absence of sterilization was assumed to be negligible.

To estimate the frequency of poor injection practices in the year 2000, data sources included published studies and unpublished WHO reports. Studies were reviewed using a standardized decision-making algorithm based upon the quality of the data to generate region-specific estimates of the annual number of injections per person and of the proportion of injections reused in the absence of sterilization.

To estimate the consequences of unsafe injections in the year 2000 in terms of death and disability for 2000-2030 as part of the 2000 update of WHO's Global Burden of Disease study, we modelled the fraction of new injection-associated HBV, HCV and HIV infections on the basis of the annual number of injections, the proportion of injections administered with reused equipment, the probability of transmission following percutaneous exposure, the prevalence of active infection, the prevalence of immunity and the total incidence. Infections in 2000 were converted into disability-adjusted life years (DALYs) in 2000-2030 using natural history parameters, background mortality, duration of disease, disability weights, age weights and a 3% discount rate.

A guideline development group summarized evidence-based best practices to prevent injection-associated infections in resource-limited settings. The development process included (1) a breakdown of the WHO reference injection safety definition into a list of potentially critical steps, (2) a review of the literature for each of these potentially critical steps, (3) the formulation of best practices and (4) the submission of the draft document to peer review.

To estimate the effectiveness of interventions to reduce the unnecessary and unsafe use of injections, we searched electronic databases. In addition, we reviewed WHO reports and unpublished assessments made available to WHO. We selected studies that contained quantitative and qualitative information on the effect of interventions and that provided information on study design, type of interventions, targeted participants and targeted behaviours.

To estimate the cost-effectiveness of national policies for the safe and appropriate use of injections, the consequences in 2000-2030 of a "do nothing" scenario for the year 2000 (as modelled for the Global Burden of Disease study) were compared to a set of counterfactual scenarios incorporating the health gains of effective interventions. Resources needed to implement effective interventions were costed for each sub-region and expressed in international dollars (I$).

Results

Four regions in the Global Burden of Disease study where reuse of injection equipment in the absence of sterilization was negligible were excluded from the analysis. In the 10 other regions, the annual ratio of injections per person was 3.4 (Range: 1.7 - 11.3) for a total of 16.7 thousand million injections received. Of these, 39.3% (Range: 1.2% - 75.0%) were administered with equipment reused in the absence of sterilization. Reuse was highest in the South East Asia region "D" (seven countries, mostly located in South Asia), the Eastern Mediterranean region "D" (nine countries, mostly located in the Middle East crescent) and the Western Pacific region "B" (22 countries) which together accounted for 88.4% of the 6.5 thousand million injections given in the year 2000 with equipment reused in the absence of sterilization. In 2000, contaminated injections caused an estimated 21 million HBV infections, two million HCV infections and 260 000 HIV infections, accounting for 32%, 40% and 5% respectively of new infections for a burden of 9 177 679 DALYs between 2000 and 2030.

Eliminating unnecessary injections is the highest priority to prevent injection-associated infections. However, when intradermal, subcutaneous or intramuscular injections are medically indicated, best infection control practices include (1) the use of sterile injection equipment, (2) the prevention of contamination of injection equipment and medication, (3) the prevention of needle-stick injuries to the provider and (4) the prevention of access to used needles.

We identified twenty-one articles, abstracts, unpublished reports and assessments containing information on the effectiveness of interventions aiming at reducing injection use (n=19) and at decreasing the unsafe use of injections (n=5). Studies showed a reduction in injection use ranging from 1% to 53% (gain over control groups: 3%-27%). Interventions aiming at reducing the reuse of injection equipment in the absence of sterilization reported an absolute decrease of 30%-82% in the intervention groups (relative decrease: 40-100%). Interventions implemented in the year 2000 for the safe (provision of single use syringes, assumed effectiveness: 95%) and appropriate use (patients-providers interactional group discussions, assumed effectiveness: 30%) 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$ million 905 (average cost-effectiveness per DALY averted: I$102, range by region: 14-2 293).

Conclusions

In 2000, in developing and transitional countries, 16 thousand million injections were administered for a ratio of 3.4 injections per person. More than a third of all these injections were administered with injection equipment reused in the absence of sterilization, accounting for a substantial burden of infection with bloodborne pathogens. Best infection control practices could make injections safer for the recipient, the health care workers and the community, all the more as effective interventions are available to reduce injection use and to achieve a safe use of injections. These interventions can also be considered very cost-effective on the basis of a cost per DALY averted that is below one year of average per capita income. Remaining areas of uncertainty include (1) the formulation of routine methods to describe injection use and to quantify needs of injection equipment, (2) the description of unsafe practices in greater detail to prevent all opportunities of transmission, (3) the need to generate better estimates of the proportion of HIV infections that may be attributed to unsafe health care injections, (4) the identification of the role of engineered technologies in policies to achieve injection safety, (5) the recovery of experience in the scaling-up of successful interventions and (6) the assessment of the cost-effectiveness of scaled-up national interventions.

Résumé

Contexte

Les conséquences délétères des mauvaises pratiques d'injection sont connues depuis plusieurs années. Cependant, des données scientifiques manquaient pour permettre de documenter des politiques pour l'utilisation sûre et appropriée des injections. Nous avons conduit des études dans le but de (1) estimer la fréquence des injections et des pratiques dangereuses, (2) estimer les conséquences des injections dangereuses en terme de décès et d'invalidité, (3) formuler des « bonnes pratiques » de lutte contre l'infection pour les injections intradermiques, sous-cutanées et intramusculaires, (4) quantifier l'efficacité des interventions pour réduire l'utilisation des injections et les pratiques dangereuses et (5) estimer le rapport coût/efficacité des politiques nationales pour l'utilisation sûre et appropriée des injections.

Méthodes

Le projet OMS de la charge globale de maladies définit 14 régions sur la base de la géographie et des profils de mortalité. L'analyse a exclu quatre régions, essentiellement riches et développées, où la réutilisation du matériel en l'absence de stérilisation a été considérée comme négligeable.

Pour estimer la fréquence des mauvaises pratiques d'injection pour l'année 2000, les sources d'information ont inclus des études publiées et des rapports OMS non publiés. Ces études ont été revues avec un algorithme de décision standardisé tenant compte de la qualité des données pour générer des estimations régionales du nombre annuel d'injections par personne et de la proportion d'injections administrées avec du matériel réutilisé en l'absence de stérilisation.

Pour estimer les conséquences des injections dangereuses au cours de l'année 2000 en termes de décès et d'invalidité en 2000-2030 dans le contexte de la mise à jour en 2000 de l'étude OMS sur la charge globale de maladies, nous avons modélisé la proportion des infections par le virus de l'hépatite B (VHB), le virus de l'hépatite (VHC) et le virus de l'immunodéficience humaine (VIH) sur la base du nombre annuel d'injections, de la proportion des injections administrées avec du matériel réutilisé, de la probabilité de transmission à la suite d'une exposition percutanée, de la prévalence des infections actives, de la prévalence de l'immunité et de l'incidence totale. Les infections en l'an 2000 ont été converties en années de vie ajustées pour l'invalidité pour 2000-2030 en utilisant les paramètres d'histoire naturelle des maladies, la mortalité par d'autres causes,

la durée de la maladie, les coefficients de pondération pour l'invalidité et pour l'âge et un taux d'escompte de 3%.

Un groupe de développement de règles directrices a utilisé les données disponibles pour résumer les meilleures pratiques pour prévenir les infections associées aux injections dans des contextes de ressources limitées. Le procédé de développement a inclus (1) une analyse de la définition OMS de référence pour la sécurité des injections pour obtenir une liste de points critiques, (2) une revue de la littérature pour chacun de ces points critiques, (3) la redaction de bonnes pratiques et (4) la soumission d'un premier document pour commentaires et suggestions.

Pour estimer l'efficacité des interventions pour réduire l'utilisation et l'utilisation dangereuse des injections, nous avons recherché des études dans des bases de données électroniques. De plus, nous avons revu des rapports OMS et des évaluations non publiées mises à disposition de l'OMS. Nous avons sélectionné des études contenant des informations quantitatives et qualitatives sur l'effet des interventions qui détaillaient le type d'étude, le type d'intervention, les participants ciblés et les objectifs en termes de comportement chez les patients et les soignants.

Pour estimer le rapport coût/efficacité des politiques nationales pour l'utilisation sûre et appropriée des injections, les conséquences pour 2000-2030 d'un scénario de « statu quo » pour l'année 2000 (tel qu'estimé pour l'étude de la charge globale de maladies) furent comparées à des scénarios alternatifs incorporant les gains pour la santé des interventions jugées efficaces. Les ressources nécessaires pour la mise en place d'interventions efficaces ont été estimées pour chaque région et exprimées en dollars internationaux (I$).

Résultats

Quatre régions de l'étude de la charge globale de maladies où la réutilisation de matériel injectable était négligeable ont été exclues de l'analyse. Dans les 10 autres régions, le ratio annuel d'injections par personne était de 3.4 (Extrêmes: 1.7 - 11.3) pour un total de 16.7 milliards d'injections reçues. Parmi celles-ci, 39.3% (Extrêmes: 1.2% - 75.0%) étaient administrées avec du matériel réutilisé sans stérilisation. La réutilisation était la plus fréquente dans la région d'Asie du Sud Est "D" (sept pays, surtout localisés en Asie du Sud), la région méditerranéenne orientale "D" (neuf pays, surtout localisés dans le croissant du Moyen Orient) et la région du Pacifique occidental "B" (22 pays) qui, ensemble, comptabilisaient 88.4% des 6.5 milliards d'injections données en l'an 2000 avec du matériel réutilisé sans stérilisation. En l'an 2000, les injections

contaminées ont causé 21 millions d'infections par le VHB, deux millions d'infections par le VHC et 260 000 infections par le VIH, représentant respectivement 32%, 40% et 5% des nouvelles infections pour une charge de 9 177 679 années de vie ajustées pour l'invalidité entre 2000 et 2030.

Eliminer les injections non nécessaires est la plus haute priorité pour prévenir les infections associées aux injections. Cependant, quand les injections intradermiques, sous-cutanées ou intramusculaires sont indiquées médicalement, les bonnes pratiques de contrôle des infections incluent (1) l'utilisation de matériel d'injection stérile, (2) la prévention de la contamination du matériel d'injection et des médicaments, (3) la prévention des piqûres chez les soignants et (4) la prévention de l'accès au matériel usagé et contaminé.

Nous avons identifié 21 articles, résumés et rapports non publiés contenant des informations sur l'efficacité des interventions pour réduire l'utilisation des injections (n=19) et pour réduire l'utilisation dangereuse des injections (n=5). Les études ont montré une réduction de l'utilisation de 1% à 53% (gain sur le groupe témoin: 3%-27%). Les interventions ciblant la réduction de la réutilisation du matériel injectable en l'absence de stérilisation ont rapporté une efficacité en valeur absolue de 30% à 82% dans les groupes d'intervention (efficacité en valeur relative: 40%-100%). Les interventions en 2000 pour l'utilisation sûre (distribution de matériel d'injection à usage unique, efficacité assumée: 95%) et appropriée (groupes de discussion patients-soignants, efficacité assumée: 30%) des injections pourraient réduire la charge de maladie due aux injections d'au moins 96.5% (8.86 millions d'années de vie ajustées pour l'invalidité) pour un coût moyen de 905 millions de dollars internationaux (Ratio moyen de coût/efficacité par année de vie ajustée pour l'invalidité: 102I$, extrêmes par régions: 14-2 293).

Conclusions

En l'an 2000, dans les pays en voie de développement et les pays en transition, 16 milliards d'injections ont été administrées pour un ratio de 3.4 injections par personne. Plus d'un tiers de ces injections a été administré avec du matériel réutilisé en l'absence de stérilisation, donnant lieu à une charge substantielle d'infections par les pathogènes liés au sang. La mise en place de bonnes pratiques de lutte contre les infections pourrait rendre les injections sûres pour les patients, les soignants et la population, d'autant plus que des interventions efficaces sont disponibles pour réduire l'utilisation des injections et pour assurer une utilisation sûre. Ces interventions peuvent aussi être considérées comme ayant un bon rapport coût/efficacité car le coût par année de vie

gagnée ajustée pour l'invalidité est inférieur à une année de revenu moyen par habitant. Les zones d'incertitude persistantes incluent (1) la formulation de méthodes de routine pour décrire l'utilisation des injections et pour quantifier les besoins en matériel d'injection, (2) la description plus détaillée des pratiques dangereuses afin de prévenir toutes les opportunités de transmission, (3) le besoin d'estimer plus précisement la proportion des infections par le VIH attribuables aux injections dangereuses, (4) l'identification du rôle des nouvelles technologies dans les politiques de sécurité des injections, (5) l'acquisition d'expérience dans la généralisation des interventions efficaces et (6) l'évaluation du rapport coût/efficacité des interventions étendues au niveau national.

"*Si tu sais que tu ne sais pas, tu sauras. Si tu ne sais pas que tu ne sais pas, tu ne sauras pas.*"

Hamadou Hampaté Bah

General introduction

Background

Unsafe injection practices have been increasingly recognized as a substantial source of infection with bloodborne pathogens, including hepatitis B virus (HBV) and hepatitis C virus (HCV). Similarly, standards of care have been raised in public health initiatives and the "first do no harm" principle is now at the heart of the delivery of key public health interventions, including immunization. As a consequence, WHO scaled up its activities for the safe and the appropriate use of injections in 1999 and created the Safe Injection Global Network (SIGN) alliance to ensure that this goal could be reached through the active participation of all public and private stakeholders.

The safe and appropriate use of injections was not conceptualized as an independent public health issue before 1999. In addition, WHO needed a basis of evidence to assist countries in the benchmarking, planning, assessment, implementation and evaluation of national injection safety policies. Thus, as part of the strategic planning for 2000-2003, resources were allocated to building an evidence base that could constitute the foundation of national policies for the safe and appropriate use of injections.

Goals and objectives

The goal of this work was to develop an evidence base upon which countries could make informed decisions regarding national policies for the safe and appropriate use of injections. The specific objectives included:

1. Describe injection practices worldwide in terms of (a) injection frequency and (b) injection safety (Chapter 1);
2. Estimate the global burden of disease associated with contaminated health care injections in terms of (a) attributable fractions for HBV, HCV and HIV infections and (b) secondary burden in terms of death and disability, as expressed in disability-adjusted life years (DALYs, Chapter 2);
3. Formulate best infection control practices for intradermal, subcutaneous and intramuscular injections (Chapter 3);
4. Review the effectiveness of interventions to reduce the use of injections and the unsafe use of injections (Chapter 4);

5. Estimate the cost-effectiveness of national policies for the safe and appropriate use of injections in terms of cost per DALY averted (Chapter 5).

Methods used to achieve the objectives

The methods used to reach the specific objectives included:

1. A review of studies using a standardized decision-making algorithm based upon the quality of the data to generate region-specific estimates of the annual number of injections per person and of the proportion of injections reused in the absence of sterilization (Chapter 1);

2. A model of the fraction of new injection-associated HBV, HCV and HIV infections on the basis of the annual number of injections, the proportion of injections administered with reused equipment, the probability of transmission following percutaneous exposure, the prevalence of active infection, the prevalence of immunity and the total incidence (Chapter 2);

3. The development of evidence-based best practices through (a) a breakdown of the WHO reference injection safety definition into a list of potentially critical steps, (b) a review of the literature for each of these potentially critical steps, (c) the formulation of best practices and (d) the submission of the draft document to peer review (Chapter 3);

4. A review of published studies, WHO reports and unpublished assessments made available to WHO containing quantitative and qualitative information on the effect of interventions and providing information on study design, type of interventions, targeted participants and targeted behaviours (Chapter 4);

5. A comparison of the consequences in 2000-2030 of a "do nothing" scenario for unsafe injections in the year 2000 with a set of counterfactual scenarios incorporating the health gains of effective interventions and estimating the resources needed to implement them in each sub-region using international dollars (Chapter 5).

The literature review was integrated to the respective chapters, as appropriate.

Chapter 1: Overuse and unsafe use of injections in health care settings worldwide, 2000

"La vida no es la que uno vivió, sino la que uno recuerda y como la recuerda para contarla."
Gabriel Garcia Marquez, "Vivir para contarla"

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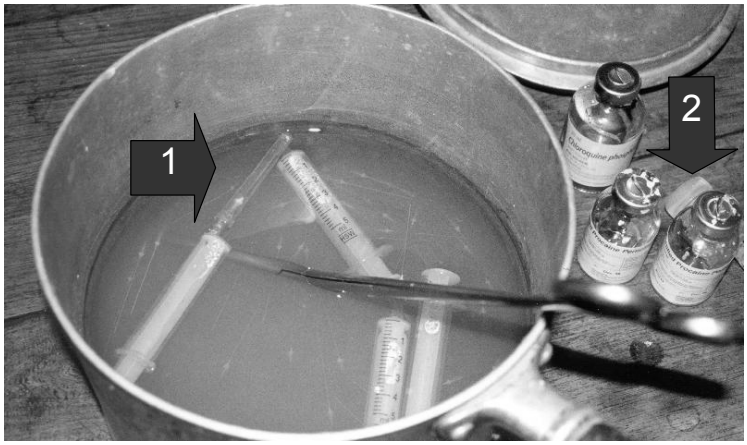
Introduction

Poor injection practices have been reported in health care settings worldwide. [1] During the twentieth century, injection use increased tremendously and today injection is probably the most common health care procedure. [2] Many injections given for curative purposes in developing and transitional countries are unnecessary as they are prescribed for the treatment of conditions that could be treated with oral drugs or for which medications are not indicated. [1,3] In addition to being unnecessary, many injections are unsafe. Of particular concern is the reuse of injection equipment in the absence of sterilization. A common practice consists of rinsing injection equipment between injections in a pot of tepid water (Figure 1).

Figure 1: Injection equipment soaked in tepid water before reuse in the absence of sterilization, Africa, 2000*



The combination of injection overuse and unsafe practices results in a major route of transmission for bloodborne pathogens. Epidemiological studies have indicated that unsafe injections commonly transmit hepatitis B virus (HBV, Abstract 7) [4] and hepatitis C virus (HCV). [5] The transmission of the human immunodeficiency virus (HIV) through unsafe health care injections has also been reported. [6] Other complications of unsafe injections include abscesses, [7,8] septicemia, [9] malaria [10] and infection with viral hemorrhagic fever viruses. [11,12]

As part of the Comparative Risk Assessment component [13] of the 2000 update of WHO's Global Burden of Disease study, [14] we have estimated the global burden of disease attributable to contaminated injections in health care settings. These estimates were based on mathematical models similar to those previously used to estimate the worldwide number of infections attributable to unsafe injections. [15,16] This paper summarizes the input parameters of this model in

* Note the disposable syringes rinsed in the tepid water (arrow 1) and the multi-dose medication vials (arrow 2).

terms of (1) the annual number of injections per person and (2) the proportion of injections administered with syringes and/or needles reused in the absence of sterilization. The results of the analysis suggest that four decades after the widespread availability of disposable injection equipment and two decades into the HIV pandemic, poor injection practices in health care settings remain an uncontrolled and dangerous vector of bloodborne and emergent pathogens.

Methods

Definitions

Health care injection

We defined a health care injection as a procedure that introduces a substance into the body through a piercing of the skin or of a mucosal membrane. This includes intradermal, subcutaneous, intramuscular and intravenous injections for curative or preventive health care purposes, whether administered in formal health care settings (e.g., clinics, hospitals) or other settings (e.g., homes, pharmacies). Injections of illicit drugs were not considered in this study.

Reuse of injection equipment in the absence of sterilization

We defined reuse of injection equipment in the absence of sterilization as the administration of an injection to a recipient with a syringe and or a needle that had been previously used on another person and that was reused in the absence of sterilization. In this paper, reuse of injection equipment in the absence of sterilization will simply be referred to as "reuse of injection equipment".

Sources of information used for the estimation of injection practice indicators

Regions used

The Global Burden of Disease 2000 regions used for this analysis were based upon the WHO regions, i.e., the American region (AMR), the African region (AFR), the Eastern Mediterranean region (EMR), the European region (EUR), the South East Asia region (SEAR) and the Western Pacific region (WPR).[17] These WHO regions were then subdivided into subgroups (Table 1) similar for selected vital statistics, including child and adult mortality. Subgroups were designated with a letter ("A" reflecting the lowest mortality and "E" reflecting the highest mortality).[17]

Table 1: Countries included in the Global Burden of Disease regions

Afr D includes: Algeria, Angola, Benin, Burkina Faso, Cameroon, Cape Verde, Chad, Comoros, Equatorial Guinea, Gabon, Gambia, Ghana, Guinea, Guinea-Bissau, Liberia, Madagascar, Mali, Mauritania, Mauritius, Niger, Nigeria, Sao Tome and Principe, Senegal, Seychelles, Sierra Leone, Togo. **Afr E includes**: Botswana, Burundi, Central African Republic, Congo, Côte d'Ivoire, Democratic Republic of the Congo, Eritrea, Ethiopia, Kenya, Lesotho, Malawi, Mozambique, Namibia, Rwanda, South Africa, Swaziland, Uganda, United Republic of Tanzania, Zambia, Zimbabwe. **Amr B includes**: Antigua and Barbuda, Argentina, Bahamas, Barbados, Belize, Brazil, Chile, Colombia, Costa Rica, Dominica, Dominican Republic, El Salvador, Grenada, Guyana, Honduras, Jamaica, Mexico, Panama, Paraguay, Saint Kitts and Nevis, Saint Lucia, Saint Vincent and the Grenadines, Suriname, Trinidad and Tobago, Uruguay, Venezuela. **Amr D includes:** Bolivia, Ecuador, Guatemala, Haiti, Nicaragua, Peru. **Emr D includes:** Afghanistan, Djibouti, Egypt, Iraq, Morocco, Pakistan, Somalia, Sudan, Yemen. **Eur B includes:** Albania, Armenia, Azerbaijan, Bosnia and Herzegovina, Bulgaria, Georgia, Kyrgyzstan, Poland, Romania, Slovakia, Tajikistan, The Former Yugoslav Republic of Macedonia, Turkey, Turkmenistan, Uzbekistan, Yugoslavia. **Eur C includes:** Belarus, Estonia, Hungary, Kazakhstan, Latvia, Lithuania, Republic of Moldova, Russian Federation, Ukraine. **Sear B includes:** Indonesia, Sri Lanka, Thailand. **Sear D includes:** Bangladesh, Bhutan, Democratic People's Republic of Korea, India, Maldives, Myanmar, Nepal. **Wpr B includes:** Cambodia, China, Cook Islands, Fiji, Kiribati, Lao People's Democratic Republic, Malaysia, Marshall Islands, Micronesia (Federated States of), Mongolia, Nauru, Niue, Palau, Papua New Guinea, Philippines, Republic of Korea, Samoa, Solomon Islands, Tonga, Tuvalu, Vanuatu, Viet Nam

Injection practice indicators

Four regions (European A, Eastern Mediterranean B, American A and Western Pacific A) representing mostly countries with high per capita gross national product were excluded as the proportion of reuse was considered negligible. To overcome the paucity of information available regarding injection practices in the published literature, we used exhaustive search strategies and unpublished reports. We searched published studies in MEDLINE and in the Index Medicus using "injection" as keyword. In addition, we searched WHO unpublished reports, including evaluations of the Expanded Programme of Immunization (EPI) and other reports circulated since 1999 through the electronic mail list server of the Safe Injection Global Network

(SIGN). [18,19] We also reviewed relevant references quoted in identified articles. We reviewed all studies using a standardized study abstraction instrument, appraised them, ranked them according to their quality and entered them in an electronic database.

To estimate the annual number of injections per person for each region, age, and gender stratum, we restricted our selection to (1) population-based surveys conducted for the purpose of estimating the frequency of injections and (2) other population-based data providing injection frequency estimates. Within each region, we averaged the estimates of all studies, corrected for the distribution of injections among male to female and/or among age groups if one of the studies in the region provided that information. Finally, we corrected for additional immunization injections among children under five years of age if the data source did not take this factor into account.

To estimate the proportion of reuse for each region stratum, we restricted our selection to (1) observational studies of injection practices using the WHO standardized injection safety assessment survey tool [20] and (2) studies of injection practices conducted using other, non-standardized methods. In the absence of data in some regions, we (3) back-calculated the proportion of reuse using a mass action equation [16] and the relative risks of infection with bloodborne pathogens associated with receiving injections in published analytical epidemiological studies. Within each region, we averaged the estimates of all studies. Estimates based upon non-standardized methods were excluded if assessments using the WHO standardized tool was available (Non-standardized assessments presented a number of limitations, including non-representative sampling, small sample size and the absence of observational data). Estimates based upon back-calculation were only considered if higher quality information was not available (except in the Eastern Mediterranean region where the injection safety assessment focused mostly on the informal private sector).

Uncertainty analysis

Lower and upper estimates were calculated for the annual number of injections per person and the proportion of reuse using standard error formulae for means and proportions. When the proportion of reuse was estimated on the basis of measures of association, the standard error was derived from the proportion and the sample size of the study as if the proportion had been obtained on the basis of a single random sampling of the individuals included in the study. For regions for which good quality data was available on injection frequency (injection frequency surveys) or injection safety (standardized or non-standardized injection safety surveys), the lower

and upper estimates were calculated on the basis of standard error (+/- 2 SE). For regions for which only lower quality data were available for injection frequency (other population-based injection frequency data) or injection safety (back-calculated estimates), an arbitrarily larger interval was used to account for added uncertainty (+/- 4 SE). For regions for which no data was available and for which inferences were made using other regions, an even larger interval was arbitrarily used to account for added uncertainty (+/- 6 SE).

Results

Regional estimates of the annual number of injections per person

A variety of sources of information were available to estimate the annual number of injections per person (Table 2). In eight regions, surveys had been conducted with the objective of estimating injection frequency, either as part of a large project supported in the early 1990s by the WHO global programme on AIDS to monitor exposures to potential risk factors for HIV infection [21] or with a more specific objective of assessing injection practices (Abstract 4). [22,23,24,25,26,27,28] In seven regions, other population-based information was obtained from control groups of case control studies that examined injection use as a potential risk factor for hepatocellular carcinoma, [29] paralytic polio, [30,31] HIV infection, [32,33,34] HCV infection, [35,5] HBV infection [36,37] and gluteal fibrotic contracture. [38] Final regional estimates were based upon (1) population-based injection frequency surveys (three regions), other population-based data (two regions) and a combination of these two methods (five regions). EUR C was the region with the highest injection frequency (11.3 injections per person and per year), followed by EUR B (5.2 injections per person and per year, Figure 2). The regions with the lowest annual number of injections per person were AMR B (1.7 injections per person and per year) and AMR D (1.9 injections per person and per year). Overall, we estimated that the 4.9 thousand million persons living in the 10 regions included in the study received 16.7 thousand million injections annually (lower and upper estimates: 15.2 and 18.1 thousand million, respectively) for a ratio of injections per person and per year of 3.4 (lower and upper estimates: 3.1 and 3.7, respectively).

Regional estimates of the proportion of reuse

Different types of studies and reports were available to estimate the proportion of reuse of injection equipment (Table 3). First, 11 observational injection safety surveys had been conducted using the standard WHO tool in three regions (WHO unpublished data). Second, four non-standardized observational injection safety surveys had been conducted in four regions. [39,40,41,42]

Third, two epidemiological studies were available to provide relative risks associated with receiving injections (Abstract 7).[4,43] Final estimates were based upon (1) standardized WHO injection safety assessments (three regions), (2) non-standardized injection practice surveys (three regions), (3) back-calculations using the mass action equation and the relative risks of infection with bloodborne pathogens associated with receiving injections (one region) and (4) a combination of the second and the third methods (one region). No quantitative data were available for six regions. For two of them, AMR B and AMR D, there were qualitative reports of reuse. For the AMR B region, these reports suggested that reuse was uncommon.[44,45,46] Thus, estimates from the other region with the lowest frequency of reuse (EUR B) were extrapolated. For AMR D, as qualitative reports suggested that reuse was more common than in AMR B,[47] estimates from the region with the second lowest frequency of reuse (EUR C) were extrapolated. For four regions (EUR A, EMR B, AMR A and WPR A), representing mostly countries with a high per capita gross national product, the proportion of reuse was considered negligible. Among regions for which quantified estimates were available, SEAR D was the region with the highest proportion of reuse (75%), followed by EMR D (70%) and WPR B (30%, Figure 2). The region with the lowest proportion of reuse was EUR B (1.2%). Overall, we estimated that among the 16.7 thousand million injections administered each year in the 10 regions included in the study, 6.7 thousand million (39.3%. Lower and upper estimates: 4.0 and 9.7 thousand million, respectively) were given with reused equipment.

Table 2: Regional injection frequency estimates and data sources used, by region, 2000

	AFR D	AFR E	AMR B	AMR D	EMR D	EUR B	EUR C	SEAR B	SEAR D	WPR B
Annual number of injections per person*	2.2	2.0	1.7	1.9	4.3	5.2	11.3	2.1	4.0	2.4
Lower and upper estimates	2.1-2.3	2.0-2.0	1.6--1.8	1.2-2.7	4.2-4.3	4.3-6.1	10.1-12.5	2.1-2.2	3.8-4.2	2.1-2.7
Countries from which injection frequency surveys were used	Guinea Bissau [21]	CAR Cote d'Ivoire Tanzania Zambia Burundi [21] Uganda [22]	Brazil [21]	-	Egypt [24]	Romania [27]	Moldova [28]	Thailand [21,23] Indonesia [25]	India [26]	-
Countries from which other population-based data were used	Cameroon [30] Nigeria [29]	Tanzania [33] Uganda [32]	Latino communities in the USA [46]	Haiti [34]	Pakistan [5]	-	-	-	India [31]	China, Province of Taiwan [38,35,36,37]
Use of different estimates for males and females	No	Yes	No	No	No	Yes	Yes	No	No	No
Addition of 0.5 injections per year among 1-4 years of age to account for immunization	Yes	Yes	Yes	Yes	Yes	No†	No †	No †	Yes	No †

* Estimates age-adjusted using age group-specific population sizes to simplify data presentation. The total estimate is based upon age- and gender-specific estimates.

† Not applicable: age-specific injection frequency estimate takes into account immunization injections.

Table 3: Regional estimates of the proportion of injections administered with reused equipment and data sources used, by region, 2000

	AFR D	AFR E	AMR B	AMR D	EMR D	EUR B	EUR C	SEAR B	SEAR D	WPR B
Proportion of reuse	19%	17%	1.2%	11%	70%	1.2%	11%	30%	75%	30%
Lower and upper estimates	15-23%	13-21%	0-8%	0-23%	58%-82%	0-4%	3-19%	23-37%	60-88%	0-63%
Methods used (See text)	Standard WHO survey	Standard WHO survey	Extrapolation	Extrapolation	Combination of methods	Standard WHO survey	Back-calculation	Non standard surveys	Non standard surveys	Non standard surveys
Countries from which WHO standardized injection safety surveys were used	Five countries in the region * †	Five countries in the region * †	-	-	-	Kyrgyztan †	-	-	-	-
Countries from which non standardized surveys were used	-	-	-	-	Pakistan [39]	-	-	Indonesia [39]	India [41]	China [42]
Countries from which back-calculated estimates were used	-	-	-	-	Egypt [43]	-	Moldova [4]	-	-	-
Use of other regions' data	-	-	EUR B‡	EUR C§	-	-	-	-	-	-

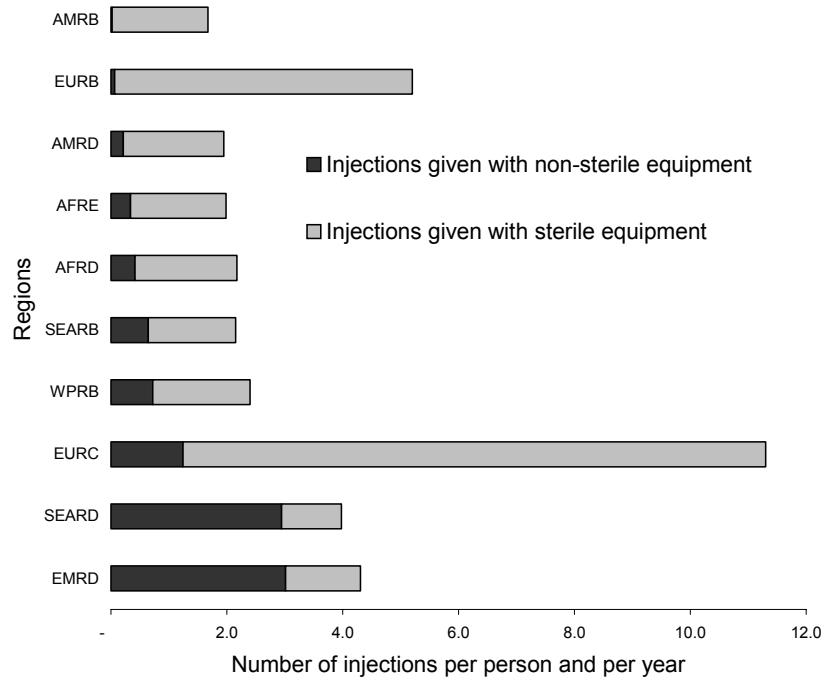
* Unpublished WHO reports. List of actual countries not available to the general public.

† Julia Fitzner, Department of Vaccine and Biologicals, WHO, personal communication.

‡ Qualitative information available on injection safety for AMR B [44,45,46] suggested occurrence of reuse in the absence of sterilization. To generate a conservative estimate, estimates for the region with the lowest proportion were extrapolated.

§ Qualitative information available on injection safety for AMR D [47] suggested occurrence of reuse in the absence of sterilization with a higher frequency than AMR B. Thus, estimated for the region with the second lowest proportion were extrapolated.

Figure 2: Number of injections per person and per year and proportion of these administered with injection equipment reused in the absence of sterilization, by region, 2000.



Discussion

The safe and appropriate use of injections remains elusive despite decades of knowledge about the consequences of poor injection practices. [48,49] Since the early 1990s, epidemiological studies have indicated that unsafe injections are a risk factor for new HBV, HCV and HIV infections. [1] Currently, almost five thousand million people live in regions where reuse of injection equipment occurs. According to the results of this analysis, persons in these regions receive an average of 3.4 injections each year, of which 39.3% are given with reused injection equipment. These figures constitute a call for action since effective and affordable interventions are available to reduce injection overuse and to achieve safe injection practices.

The high frequency of injections reported in developing and transitional countries contrasts with the paucity of data that is available to describe injection practices. In that respect, our study should be seen more as a first attempt to organize information in this field to raise awareness and underline the need for better quality data. Until recently, few standardized tools for assessment or evaluation were available to routinely collect information on injection frequency or injection safety. With respect to injection use, the WHO programme on essential drugs proposed the proportion of prescriptions including at least one injection as a critical indicator of rational drug

use.[50] This indicator has been widely used for initial assessments[51] or for the evaluation of interventions to improve the rational use of injections.[52] However, it does not provide a direct estimate of the annual number of injections per person as it does not take into account (1) the number of prescriptions per year, (2) the number of injections per prescription and (3) the injections prescribed or directly administered in the informal private sector. The Demographic and Health Surveys (DHS)[53] have included questionnaire items regarding injections received in some countries. Although the data are publicly available, the results of these analyses have not been published. With respect to injection safety, the Expanded Programme on Immunization (EPI) has conducted non-standardized injection safety surveys for a number of years. Since 2000, these assessments are conducted systematically and with a standardized tool.[20]

Our analysis indicates that there are over 16 thousand million injections each year in the 10 regions included in our study. Four of these regions stood out with particularly high estimates. The crude annual number of injections per person was the highest in the former Socialist economies of Europe and central Asia, reaching 5.2 and 11.3 in EUR B and EUR C, respectively. Most injections in these countries are administered in public health care facilities by physicians or nurses, with a high number of injections per prescription (Abstract 4).[27,28] While health care providers commonly emphasize patient demand as a major driver of injection overuse, the importance of this factor may be exaggerated. Surveys suggest that patients do not necessarily prefer injections for the administration of medications and that they are open to alternatives to injections (Abstract 4).[27,54] In fact, prescribers have a tendency to overestimate patients' preference for injections (Abstract 3).[55] They also often have false preconceptions about the effectiveness of injectable medications (Abstract 3)[55] and these preconceptions are sometimes supported by non evidence-based official treatment protocols.[56] Thus, prescribers' attitudes also contribute to injection overuse. Injection use was also high in the Middle East and in South Asia where the annual number of injections per person reached 4.3 in EMR D and 4.0 in SEAR D, respectively. In these regions, a high proportion of injections are administered by private providers who may have no formal medical qualification.[24,39,41] In such informal settings, health care providers' attitudes also drive injection overuse.[5,37,57] However, the reference to standard treatment guidelines is uncommon. Injections are frequently used on an "ad hoc" basis to administer mixtures of antibiotics, analgesics, vitamins or anti-histamines in the desire to meet what is believed to be the demand of the user.[39,57]

Reducing injection overuse would only be a matter of promoting rational drug use if injections were administered safely. However, our analysis indicates that injections are given in a way that

may harm the injection recipient. Determinants of these unsafe injection practices include the lack of supplies of new, single use injection equipment, [58] the lack of awareness among patients and providers regarding the risks associated with unsafe practices [39,26] and the absence of an efficient sharps waste management system to prevent recycling of contaminated equipment. [59] It is of interest that the results of our analysis suggest that injection practices are safer in sub-Saharan African (19% and 17% of reuse in AFR D and AFR E, respectively) than in the Middle East and South Asia (70% and 75% reuse in EMR D and SEAR D, respectively). The proportion of the population aware of the potential risk of HIV infection through unsafe injections was 24% in Pakistan in 1998, [60] 19% in India in 1999, [26] and 52% in Burkina Faso in 2001 (Abstract 12). [61] The social and economic consequences of the HIV pandemic have been perceived more acutely on the African continent than in Asia. Thus, a higher awareness regarding the risks of HIV infection associated with unsafe injections in sub-Saharan Africa [62] may partly explain this difference observed in the proportion of reuse.

This study has three main limitations. First, our injection frequency estimates may underestimate the total number of injections received in the population. The frequency distribution of the number of injections received in the population tends to be skewed to the right because of the small proportion of the population that receives a very high number of injections (e.g., diabetics). Some of the studies that we included may have had a sample size too small to include these rare individuals. This effect limits the usefulness of our estimates to forecast needs in injection devices although it does not affect their usefulness to compare regions. Second, publication bias could have led to an overestimate of the proportion of reuse if studies were initiated in response to a perception that injection practices were poor in a particular location (e.g., in Pakistan). This limitation may be of greater concern than potential observer-induced behaviour modifications among health care providers leading to better practices during health care facility surveys. Thus, overall, we may have overestimated the proportion of reuse. Third, the reuse of injection equipment that we used as a critical indicator is only a partial reflection of unsafe injection practices. It does not reflect other breaks in infection control practices that can also lead to infection, including unhygienic use of multi-dose medication vials [63] and cross contamination while preparing injections (Abstract 5) [64]. It also does not reflect the risk of needle-stick injuries among health care workers and the adverse health consequences of the poor management of sharps waste.

Policies for the safe and appropriate use of injections aim simultaneously to eliminate unnecessary injections and to achieve safe injection practices. Such initiatives should not

constitute separate programmes but should be integrated into other routine activities. [65] First, HIV prevention programmes should communicate the risks associated with unsafe injections to patients and health care workers. Second, essential drugs programmes should ensure access to sufficient quantities of single use, disposable injection equipment in each health care facility and build rational use of injections within the national drug policy. Third, donors and lenders who supply injectable substances (e.g., vaccines, contraceptives) should also fund adequate quantities of safe injection equipment to administer these. Fourth, health systems should manage sharps waste to prevent needle-stick injuries and the reuse of dirty equipment. Fifth, critical indicators of injection frequency and injection safety should be monitored as technical quality indicators of health system performance. Finally, the specific issue of injection overuse and poor practices among informal, providers may require specific targeted interventions. The "Injection practices: Rapid assessment and response guide (Appendix 1) " [66] recently developed by WHO proposes a list of such indicators together with instruments to collect the relevant information so that injection practices can be systematically assessed.

Chapter 2: The global burden of disease attributable to contaminated health care injections

"Toutes ces opinions passaient pour offenser Dieu; en fait, on leur reprochait surtout d'ébranler l'importance de l'homme."

Marguerite Yourcenar, "L'œuvre au Noir"

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Introduction

Injection overuse and unsafe practices have been reported in many countries.[1] Of particular concern is the reuse of injection equipment in the absence of sterilization.[2,3,67] In developing and transitional countries, persons receive an average of 3.4 injections per year of which 39.3% are administered with reused equipment (Chapter 1).

Unsafe injections lead to infections with bloodborne pathogens, including hepatitis B virus (HBV), hepatitis C virus (HCV) and human immunodeficiency virus (HIV). The causal nature of this association is supported by many causality criteria,[68,69,70,71,72,73,74,75,76] including the results of prospective studies that consistently indicated a strong association,[5,77,78] some of which reported a dose-response relationship[36,39,78] and a timing of infections that followed exposures (Abstract 7).[4,78,43]

Studies estimating the proportion of new infections with HBV (Abstract 2, Abstract 7),[4, 36,77,37,79,80,81,82,83,84,85] HCV,[5,35,37,43,81,86,87,88,89,90] and HIV[78,91,92,93] that are attributable to unsafe injections cannot be used directly to estimate the global burden of disease as they do not cover all world regions. Thus, as part of the Comparative Risk Assessment component[13] of the 2000 update of the Global Burden of Disease study,[14] we updated previous models[15,16] estimating the number of infections associated with unsafe injection practices and projected these infections into future death and disability. We considered only HBV, HCV and HIV infections because of the substantial literature documenting their association with injections and because these pathogens probably account for the majority of injection-associated infections. Other complications of unsafe injections were not addressed.[7,8,9,10,11,12]

Methods

Approach

Comparative Risk Assessment[13,94] collaborating groups were requested to define the exposure of interest and to estimate (1) its prevalence in the population and (2) the relative risk of disease among those exposed. These statistics were used to estimate attributable fractions in 14 regions (Table 1). For contaminated health care injections, we defined the exposure of interest as receiving one or more contaminated injections in a year. We used mathematical models to transform diverse sources of data available on unsafe injections and the risks associated with these practices into the necessary statistics.

Definitions

We defined health care injections as those given for curative or preventive purposes in health care facilities or other settings (e.g., homes, pharmacies). Injections of illicit drugs were not considered. We defined reuse of injection equipment as the administration of an injection with a syringe and or a needle that had been previously used on another person and that was reused in the absence of sterilization. A contaminated injection, the exposure of interest, was defined as an injection given with a needle or a syringe previously used on an infected patient and then reused.

Mass action model

The incidence of infection attributable to unsafe injection (I_u) was estimated in a "mass action" model that assumed

$$I_u = p_s [1 - (1 - p_t p_r p_v)^n]$$

in which p_s is the proportion of the population susceptible, p_t is the probability of transmission after percutaneous exposure, p_r is the probability that injection equipment will have been reused, p_v is the prevalence of active infection and n is the annual number of injections per person. The incidence of the three pathogens under consideration is small enough that the equation can be simplified to

$$I_u = p_s * p_t * n_c$$

in which n_c is the average annual number of contaminated injections.

$$n_c = p_r * p_v * n$$

The probability of transmission (p_t) was based upon studies estimating the risk of infection with HBV, HCV and HIV following a needle-stick exposure from an infected source-patient. For HBV, p_t was assumed to be 0.06 and 0.3 for hepatitis B e-antigen (HBeAg)-negative and HBeAg-positive source-patients, respectively. [71] For HCV, p_t was assumed to be 0.018. [72] For HIV, p_t was assumed to be 0.012, the mean of the average risk from needle-stick injuries (0.003) [73] and risk associated with deep needle-stick injuries (0.023). [73;95]

Mass action model-based estimates of the proportion of the population exposed

If each person in the population could receive only one injection then p_c, the probability of receiving at least one contaminated injection, would equal n_c. Assuming individuals can receive more than one contaminated injection per year and the number of contaminated injections per individual follows a Poisson distribution with an average of n_c per individual, then the probability of receiving no injection would be exp ($-n_c$), and the probability of receiving at least one injection would be

$$p_c = 1 - \exp(-n_c)$$

Thus when n_c is very small, p_c is approximately equal to n_c and each exposed person will receive on average only one contaminated injection per year. In most other situations, p_c will be slightly smaller than n_c and each exposed person will receive on average $n_c / (1 - \exp(-n_c))$ contaminated injections per year.

Estimates of the relative risk from the mass action model

Attributable fraction can be estimated from p_c and RR_c, the relative risk associated with exposure to at least one contaminated injection, with the following equation: [96]

$$AF = p_c * (RR_c - 1) / [1 + p_c * (RR_c - 1)].$$

Attributable fraction can also be estimated from the mass action model. The total incidence of infection in the population, I_t, is composed of the incidence due to contaminated injections, I_u, and the incidence in the population if contaminated injections could be eliminated, I_b. Thus, the attributable fraction is:

$$AF = I_u / I_t$$

Combining the two equations and solving for RR_c:

$$RR_c = 1 + I_u / (p_c * (I_t - I_u))$$

This equation was used to estimate relative risk from the mass action model except in regions in which I_u approached I_t, where the equation produced unstable estimates.

Estimates of the relative risk from epidemiological studies

In situations where I_u approaches I_t, relative risks were estimated using epidemiological studies estimating the association between injections and infection. Reported relative risks were adjusted for the frequency of contaminated injections among all injections. To avoid underestimating the relative risk because of non-susceptible controls, we assumed that the number of injections received in the prior year was proportional to the probability of having been previously infected.

Sources of information for input parameters

Injection practice parameters

The proportion of reuse (p_r) and the annual number of injections per person (n) were based upon a literature review (Chapter 1). To avoid overestimating the attributable fraction, we assumed that those receiving a number of injections above the 90th percentile were immune. This decision led to an adjustment of the input parameters for EUR B [27] (Abstract 4) and EUR C. [28] For the

other regions, estimates were calculated on the basis of data reported in tabulated form which already eliminated the upper 10% of the frequency distribution.

Prevalence and incidence of infections

Estimates for the proportion of the population chronically infected with HBV, HCV and HIV (p_i) were obtained from the WHO programmes on HBV and HCV [97] and from the United Nations Programme on HIV/AIDS (UNAIDS). [98] To estimate the incidence of HBV and HCV infection, catalytic models were generated using various hypothetical scenarios of annual incidence of infection that were applied uniformly to all age groups in the absence of any cohort effect (i.e., assuming equilibrium). The age-specific simulated estimates of the prevalence of susceptibility were then compared to the actual region-specific estimates of prevalence to identify which level of incidence led to the best fit. HIV incidence estimates were obtained from UNAIDS. [98]

Uncertainty analysis

Lower and upper estimates were generated for the injection practice parameters as described elsewhere (Chapter 1) and included in the equations to obtain lower and upper estimates of the proportion of the population exposed and the relative risks. Lower and upper estimates for the relative risks that were study-based were calculated on the basis of the confidence interval of the relative risk in the original studies.

Estimation of the Disability-Adjusted Life Years (DALYs)

HBV, HCV and HIV infections attributable to contaminated injections were converted into DALYs using theoretical cohorts of infected individuals followed for (1) background mortality and (2) disability and infection-associated deaths from acute hepatitis, hepatocellular carcinoma, end-stage liver disease and AIDS. We used standard average duration of disease and disability weights. [99] For HBV and HCV infection, natural history parameters included the rate of progression to chronic infection,[100,101] annual sero-reversion rates [102] and mortality rates associated with chronic liver disease among infected persons (Figure 3 and Figure 4). [101,103,104] In addition, for HBV, we took into account the risk of acute hepatitis and fulminant hepatitis. [100,105,106,107] We used parameters of progression of HIV infection to AIDS and death developed by WHO and UNAIDS (Neff Walker, UNAIDS, personal communication). DALYs were age-adjusted and 3% discounted. [108]

Results

Injection practices

In the regions considered, the annual ratio of injections per person was 3.4 (Range: 1.7 to 11.3) for a total of 16.7 thousand million injections received. Of these, 39.3% (Range: 1.2% - 75.0%) were administered with equipment reused in the absence of sterilization (Table 4). The exclusion of persons with injection frequencies above the 90th percentile lowered the estimated injection frequency in EUR B and EUR C from 5.2 and 11.3 to 2.5 and 3.5, respectively.

Fraction of new infections attributable to contaminated injections

In the regions where reuse of injection equipment was reported, the fractions of incident HBV, HCV and HIV infections attributable to contaminated injection were 31.9%, 39.9% and 5.4%, respectively (Table 4). For HBV, this proportion was highest in the EMR D region (58.3%) and lowest in the EUR B (0.9%) region. For HCV, this proportion was highest in the EMR D region (81.7%) and lowest in the EUR B region (0.9%). For HIV, this proportion was highest in the SEAR D region (24.3%) and lowest in the AMR B region (0%). In absolute numbers of infections, our analysis indicated that globally, in 2000, contaminated injections may have caused 20.6 million new HBV infections, 2.0 million HCV infections and 260 000 HIV infections.

Estimation of the burden in DALYs

The 21 million HBV infections in the year 2000 would lead to an estimated 26 492 deaths from fulminant hepatitis in the year 2000 and to 49 000 future additional early deaths from the consequences of chronic infection between 2000 and 2030 for a total burden of 3 114 539 DALYs (34% of the burden associated with contaminated injections, Table 5). The two million HCV infections in 2000 would lead to 24 000 future early deaths between 2000 and 2030 for a burden of 324 198 DALYs (4% of the burden associated with contaminated injections). Finally, 210 000 of the 260 000 persons infected with HIV through contaminated injections in 2000 are expected to die prematurely from AIDS between 2000 and 2030 for a burden of 5 738 942 DALYs (63% of the burden associated with contaminated injections). The total burden in 2000-2030 because of contaminated injections in 2000 amounted to 309 492 future early deaths and 9 177 679 DALYs.

Discussion

In the year 2000, four decades after the widespread availability of single use injection equipment and two decades into the HIV pandemic, contaminated injections account for close to one-third of new HBV infections, 40% of new HCV infections and 5% of new HIV infections. These infections translate to a substantial preventable burden of acute hepatitis, AIDS, hepatocellular carcinoma and end-stage liver disease.

HBV infection is the most common consequence of contaminated health care injections, with 20 million infections annually. Among the three pathogens examined, HBV is the most prevalent [109] and the one most easily transmitted through injections. [71] The fractions of new HBV infections attributable to injections were compatible with those reported in epidemiological studies, including 2% [81] to 73.9% [36] in WPR B (compared with 33.6% in our model), 49.7% [84] to 53.3% [77] in SEAR D (compared with 53.6% in our model) and 27.7% [82] to 52% [85] in EMR D (compared with 58.3% in our model). A number of other sources of infections, including perinatal exposure, horizontal transmission among children and unsafe sex explain the HBV infections that are not attributable to injections. Overall, the burden of injection-associated HBV infections in terms of DALYs is low in comparison to the number of infections. The 20 million HBV infections lead to three million DALYs. This was caused by the low rate of progression to chronic infections and the delay between infection and death during which infected persons may die from other causes of mortality.

In absolute numbers, HCV infection is the second most common consequence of contaminated injections with more than two million infections each year, about ten times less than for HBV. However, the fraction of new HCV infections attributable to contaminated injections was higher than that for HBV infection. The high attributable fractions that we modelled were compatible with those reported in epidemiological studies, including 20.1% [86] to 90.6% [81] in WPR B (compared with 37.6% in our model) and 9.9% [87] to 87.9% in EMR D [43] (compared with 81.7% in our model). Unlike HBV, HCV is primarily transmitted through percutaneous exposure to blood. [110] Perinatal transmission is relatively uncommon. [110] Transmission among sexual partners is not efficient, [110,111] although it may account for a higher proportion of infections in industrialized countries where percutaneous procedures are generally conducted using sterile equipment. [112,113] In some developing countries, including Egypt and Pakistan, unsafe health care injections have been major vehicles that transmitted HCV so that it reached high endemic levels in the community. [567] In terms of burden of disease, the conservative parameters that we used to describe the progression of HCV infection towards chronic liver disease and its consequences are

uncertain. The studies we used were conducted in industrialized countries and little is known regarding the risk of cirrhosis among infected patients beyond 20 years of follow-up. If the parameters used in our model are accurate, injection-associated HCV infections do not constitute a major avoidable burden of severe disease between 2000 and 2030. However, if we underestimated the severity of the natural history of HCV infection, then countries highly endemic for HCV will be confronted with the public health challenge of an ageing population with substantial mortality and morbidity related to HCV-associated liver disease during the 21st Century.

Historically, health care injections have not been viewed as a major vehicle of HIV infection. [114] However, the risk of HIV infection associated with health care exposures may have been underestimated in the past. [115] Most nosocomial outbreaks of HIV infection have been reported from countries with low prevalence of HIV infection. [1,6,116,117] In other countries where HIV infection and poor injection practices are more common, injection-associated HIV infections are likely to occur but they have rarely been detected or reported. Our analysis suggests that contaminated injections may cause 5.4% of new cases of HIV infections worldwide, representing 63% of the burden of disease. Few epidemiological studies were available to validate our estimates. [115] This lack of information represents a substantial source of uncertainty. In AFR E where prospective studies were available, [78,91,92,93] the lowest attributable fraction calculated on the basis of the data provided by the authors (8%) [92] exceeds our 2.5% modelled attributable fraction, suggesting that our estimate is conservative. In EMR D and in SEAR D, our model suggests that the attributable proportion could reach 7.1% and 24.3%, respectively. These high estimates are not validated by epidemiological studies and may be overestimated. Beyond concerns relating to attributable fractions, unsafe health care injections could transform dendritic HIV transmission networks into more effective cyclic ones (e.g., in the case of the unsafe use of injected antibiotics among commercial sex workers). [118,119] Studies assessing the risk factors for HIV infection should ensure that data are collected in a way that allows examination of the association between HIV infection and various types of injections. In the meantime, HIV prevention programmes should communicate the risk of HIV infection associated with health care injections, particularly in Asia where the high frequency of unsafe injection practices coincides with emerging HIV epidemics.

This study is subject to a number of limitations. First, the transmission potentials of HBV, HCV and HIV through contaminated injections were obtained on the basis of studies that estimated the risk of infection associated with a needle-stick injury. Contaminated injections could have a different, either higher or lower, transmission potential. Second, our model only estimated the

incidence of infections with HBV, HCV and HIV caused by reuse of injection equipment on one patient. It did not take into account the fact that injection equipment can be reused on multiple patients,[1] the transmission associated with unhygienic use of multi-dose medication vials[120] and the transmission that may occur through cross-contamination while preparing injections (Abstract 5).[64] Third, in the absence of data, our analysis did not take into account any theoretical "close network effect" by which high injection frequencies and high probability of exposure to unsafe practices would not be distributed independently. However, we excluded persons presenting with high injection frequencies and adjusted the model for the possibility that persons receiving high numbers of injections could already be immune. All these limitations could have led to an underestimation or an overestimation of our attributable fractions. Thus, validation of these estimates with epidemiological studies is important. For HBV and HCV, the similar order of magnitude between the attributable fractions reported in epidemiological studies and those generated by the model suggests that our estimates can be used for decision-making. In the case of HIV, uncertainty remains are more information is needed.

The burden of disease associated with unsafe injections makes it necessary to eliminate unnecessary injections and to achieve safe injection practices. WHO proposes that national strategies for the safe and appropriate use of injections address behaviour change among health care workers and patients, provision of equipment and supplies and sharps waste management.[65] Such initiatives should not constitute separate programmes but should be integrated into other activities, including HIV prevention and care, essential medicines, immunization and health systems management. Finally, research is needed to address two key areas of uncertainty. First, cohort studies must be conducted to describe the long term natural history of HCV infection, particularly in developing countries. Second, epidemiological data are needed to better estimate the proportion of HIV infections attributable to contaminated injections in various regions of the world. These include (1) careful investigation of cases of HIV infection that could be associated to health care exposures and (2) prospective cohort and case-control studies examining all potential risk factors for recent HIV infection.

Table 4: Injection use, unsafe injection practices and proportion of new infections with HBV, HCV and HIV attributable to unsafe injections by region, 2000.

		Global Burden of Disease regions										
		African		American		Eastern Mediter-ranean	European		South East Asia		Western Pacific	
		AFR D	AFR E	AMR B	AMR D	EMR D	EUR B	EUR C	SEAR B	SEAR D	WPR D	World
Injections per person and per year		2.2	2.0	1.7	1.9	4.3	2.5 *	3.5 *	2.1	4.0	2.4	3.4
Proportion of reuse		19%	17%	1.2%	11%	70%	1.2%	11%	30%	75%	30%	39.8%
Proportion of infections due to unsafe injections †	**Hepatitis B virus**	10.9% (8.2%-13.9%)	9.2% (6.9%-11.5%)	2.3% (0.0%-16.3%)	9.3% (0.0%-26.9%)	58.3% (26.2%-82.4%)	0.9% (0.0%-3.3%)	7.7% (1.8%-15.0%)	22.4% (16.5%-28.7%)	53.6% (21.6%-79.9%)	33.6% (0.0%-79.0%)	31.9% (9.4%-56.9%)
	Hepatitis C virus	16.4% (12.3%-20.8%).	13.0% (9.8%-16.2%)	0.9% (0.0%-6.4%)	9.2% (0.0%-26.7%)	81.7% ‡ (52.1%-95.0%)	0.9% (0.0%-3.4%)	21.2% § (6.1%-34.7%)	30.8% (22.8%-39.2%)	59.5% ** (40.4%-93.6%)	37.6% (0.0%-89.8%)	39.9% (18.2%-66.7%)
	HIV	2.5% (1.9%-3.1%)	2.5% (1.9%-3.1%)	0.2% (0.0%-1.5%)	1.5% (0.0%-4.5%)	7.1% ‡ (5.7%-8.5%)	0.0% (0.0%-0.0%)	0.6% (0.2%-1.2%)	7.0% (5.2%-8.9%)	24.3% †† (18.3%-30.1%)	2.5% (0.0%-5.9%)	5.4% (3.9%-7.0%)

* Excludes injections received above the 90th percentile. Crude values are 5.2 and 11.3 for EUR B and EUR C, respectively.

† Lower and upper estimate into brackets

‡ Study-based relative risk from EMR D used.

§ Model-based relative risk from EUR B that has similar prevalence pattern used.

** Model-based relative risk from WPR B that has similar prevalence pattern used.

†† Study-based relative risk from EMR D that has similar injection practices and prevalence patterns used.

Table 5: HBV, HCV and HIV infections attributable to contaminated injections in 2000 (absolute numbers, lower and upper estimates) and secondary disability-adjusted life years (DALYs) projected for 2000 - 2030, by region.

		AFR D	AFR E	AMR B	AMR D	EMR D	EUR B	EUR C	SEAR B	SEAR D	WPR B	World
HBV	Number of infections	639 498 (478 834-814 351)	630 976 (474 379-792 536)	14 118 (112-98 872)	28 570 (16-82 490)	2 533 443 (1 140 352-3 580 611)	21 122 (156 78 639)	193 636 (46 035-378 229)	942 038 (694 606-1 205 102)	8 019 210 (3 237 944-11 954 579)	7 610 161 (2 126-17 868 925)	**20 632 772 (6 074 558-36 854 335)**
	DALYs	80 414	76 163	2 167	4 565	397 486	3 196	32 241	139 408	1 279 719	1 099 179	**3 114 539**
HCV	Number of infections	54 681 (41 078-69 402)	54 131 (40 819-67 794)	2 282 (18-15 985)	6 304 (4-18 215)	645 486 (412 078-750 452)	2 110 (16-7 729)	35 668 (10 287-58 378)	94 873 (70 235-120 979)	498 166 (338 548-784 474)	608 200 (172-1 454 478)	**2 001 901 (913 254-3 347 885)**
	DALYs	9 283	8 140	352	1 092	113 918	283	3 629	15 261	79 703	92 537	**324 198**
HIV	Number of infections	18 317 (13 765-23 243)	64 412 (48 520-80 759)	305 (2-2 132)	911 (1-2 626)	2 210 (1 775-2 668)	0 (0-0)	1 526 (374-2 903	6 260 (4 638-7 980)	156 663 (118 235-194 187)	5 549 (2-13 378)	**256 152 (187 312-329 877)**
	DALYs	465 948	1 584 279	6 564	21 674	48 297	0	28 863	126 120	3 361 444	95 753	**5 738 942**
Total DALYs		**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**

Figure 3: Decision tree for the theoretical cohort used for the calculation of the years of life lost (YLLs) from hepatitis B virus infection

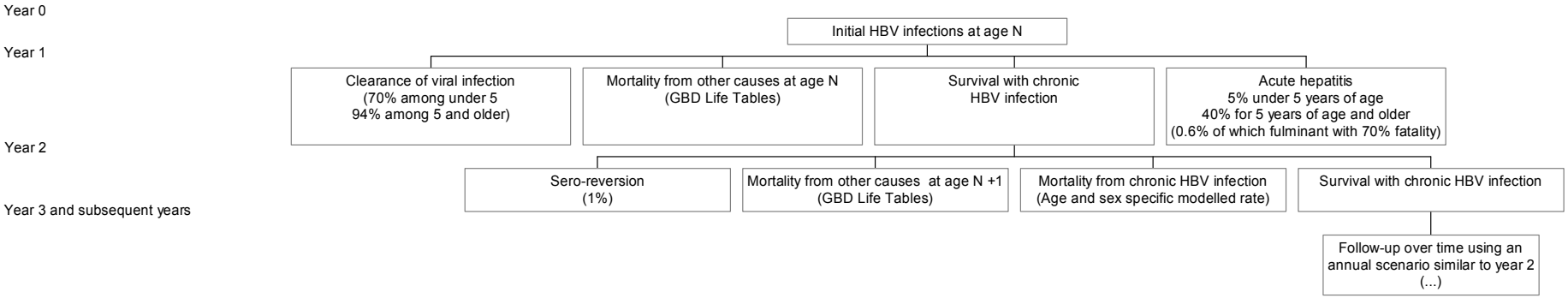
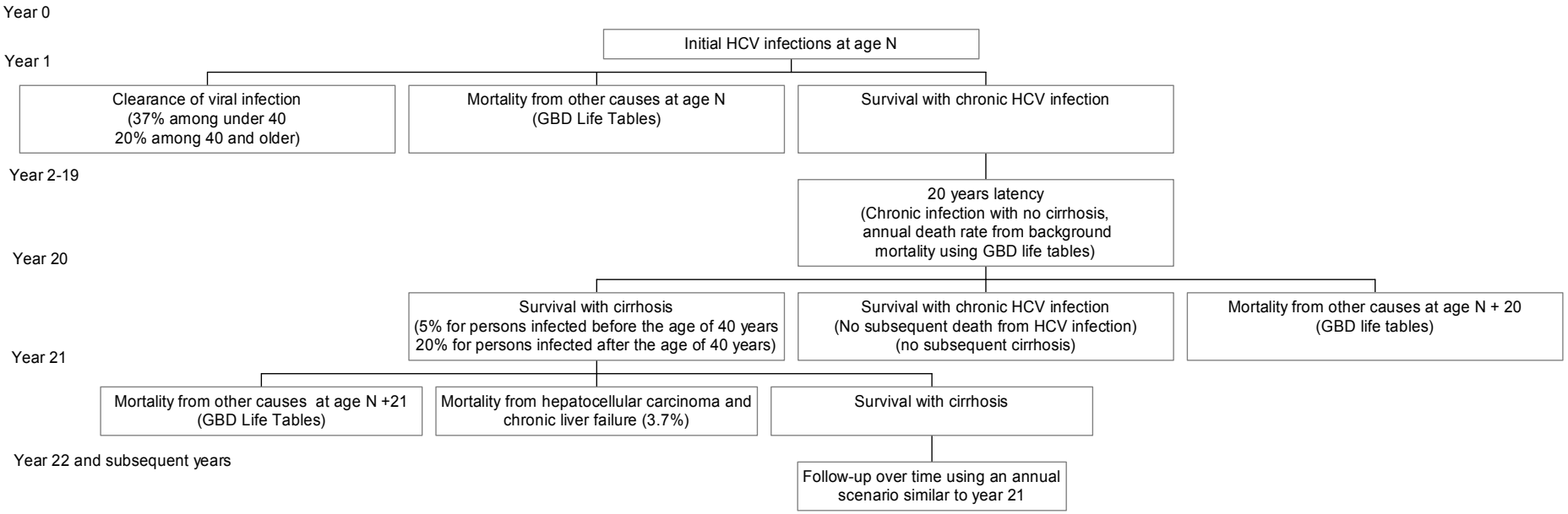


Figure 4: Decision tree for the theoretical cohort used for the calculation of the years of life lost (YLLs) from hepatitis C virus infection



Chapter 3: Best practices for injections

"Work every day, progress always."
Mao Zedong

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Introduction

In transitional and developing countries where unnecessary injections are common, the average annual number of health care injections per person was estimated to be 3.7 (this estimate includes all health care injections, including those given to diabetics for the administration of insulin, Chapter 1). In addition to being unnecessary, many injections are unsafe. Each year, in the world, reuse of injection equipment may cause 20 million infections with hepatitis B virus (HBV), two million infections with hepatitis C virus (HCV) and 250 000 human immunodeficiency virus (HIV) infections (Chapter 2). These chronic infections lead to a high burden of morbidity and mortality (Chapter 2).

No evidence-based guidelines are available to guide injection providers through the steps they should follow to prevent injection-associated infections. Thus, WHO developed best practices (Box 1) using the WHO recommended processes to formulate evidence-based guidelines.

Development process

Intended users

The primary audience includes public health professionals, clinicians and infection control practitioners. The secondary audience includes injection providers reached through training or communication material developed on the basis of these best practices.

Methods

Definitions

The development group defined an injection as a procedure that introduces a substance into the body through a piercing of the skin or of a mucosal membrane. Injections may be administered with a needle or with needleless devices, including jet injectors. However, for the purpose of these best practices, only needle injections were considered. WHO defines a safe injection as one that does not harm the recipient, does not expose the provider to any avoidable risk and does not result in waste that is dangerous to other people.

Analysis of the reference definition

The steering group broke down this reference definition into 24 potentially critical issues (Table 6).

Review of evidence

The steering group searched the English-language literature using MEDLINE with a list of key words. The search terms included injection(s), infection, sterilization, disinfection, vial, ampoule, medication, skin (preparation, cleaning, disinfection), hand hygiene, antisepsis, needle-stick(s), recapping, sharps (container, collection, disposal). Identified articles were used to select additional key and MeSH terms for further searches. Relevant references in identified articles and additional studies made available by members of the development group were also reviewed.

Table 6: Potentially critical issues to prevent infection among injection recipients, injection providers and the community

A. Prevention of infection among injection recipients		
Potential source of contamination	**Stage at which contamination may occur**	**Potentially critical issues**
• Injection equipment	• Sterilization	• Sterilization of injection equipment
	• Storage	• Duration and conditions of storage
	• Handling	• Handling of injection equipment
• Injected substance	• Before opening	• Type of medication
		• Medication and vial check
	• During opening	• Swabbing of stopper / neck
		• Filing and breaking of ampoules and vials
	• After opening	• Handling of multi-dose vials
• Skin of the recipient	• Introduction of the needle	• Site of injection administration
		• Skin preparation
• Environment	• Injection preparation	• Injection preparation area
		• Aseptic techniques
• Hands of the provider	• Injection preparation and administration	• Hand hygiene
B. Prevention of infection among injection providers		
Potential exposure source	**Stage at which exposure may occur**	**Potentially critical issues**
• Exposure to the injection recipient's blood through needle-stick injury	• During injection administration	• Patient preparation and / or restraint
	• Handling of injection equipment after use	• Recapping
		• Needle removal
		• Needle cutting
		• Rinsing and dissembling of sterilizable equipment
	• Collection of contaminated equipment	• Use of sharps containers
		• Quality of sharps containers
		• Improperly disposed of sharps
	• Sharps waste management	• Removal of containers used to collect used sharps
C. Prevention of infection in the community		
Potential exposure source	**Stage at which exposure may occur**	**Potentially critical issues**
• Exposure to the injection recipient's blood through needle-stick injury	• Sharps waste management	• Storage of containers used to collect used sharps
		• Terminal disposition of sharps waste

Formulation of best practices

The steering group formulated best practices for each of the potentially critical issues identified. Best practices strongly supported by well designed analytical, observational or intervention studies were characterized as category I (Box 1). Those supported by theoretical rationale and suggestive, descriptive evidence were characterized as category II. Those recommended on the basis of expert consensus and theoretical rationale were characterized as category III. For a number of other practice issues, best practices were not formulated. However, recommendations were formulated on the basis of expert consensus and theoretical rationale. The development

group then reviewed a draft and disseminated it for public comment through SIGNpost, the electronic forum of the Safe Injection Global Network (SIGN). All comments obtained from this peer review process were archived to keep a track of decisions made to modify, or not, the document. Finally, a summary was edited and reorganized so that it would be reader-friendly and separate the best practices from the other practice issues.

Analysis of available evidence

Prevention of infections among injection recipients

Best infection control practices to prevent infections among injection recipients include the use of sterile injection equipment and the prevention of contamination of injection equipment and medication.

Use of sterile injection equipment

Use of a sterile syringe and needle for each injection and to reconstitute each unit of medication is the most essential infection control measure to prevent infection among injection recipients. Reuse of injection equipment in the absence of sterilization has been reported from many countries (Chapter 1). These practices have been associated with infections (Chapter 2).

Use of a new, single use syringe and needle provides the highest level of safety to the recipient. However, unreliable and insufficient supplies may lead to reuse.[58] Even though boiling for 20 minutes does not achieve sterilization, [121] use of pans to boil single use injection equipment is common in developing and transitional countries. In many instances these pans are used as containers of tepid water where injection equipment is simply rinsed and soaked between injections.[39] While use of injection equipment taken from compromised packages has not been associated with infection, it is necessary to use injection equipment that is inspected before use for breaches in barrier integrity and discarded if punctured, torn or damaged.

When new single use injection equipment is not available, equipment designed for sterilization may be used. Sterilizable injection equipment is now made of plastic that can undergo steam sterilization. A steam sterilization procedure includes initial cleaning, is conducted according to WHO recommendations [122] and is controlled using Time, Steam and Temperature [TST] spot indicators. [121] Breakdowns in health systems lead to breaks in sterilization procedures.[58] Health systems using sterilizable injection equipment have poorer injection safety records than those using single use equipment [59] and use of sterilizable injection equipment has been specifically associated with infections. [86,77]

Prevention of contamination of injection equipment and medication

Work environment

It is important to prepare injections in a clean designated area, where blood or body fluid contamination is unlikely. HBV persists for up to seven days on surfaces, [123] potentially leading to environmental contamination. Environmental contamination is a potential source of HBV infection in chronic hemodialysis settings. [123] Factors that may facilitate HBV transmission among patients receiving chronic hemodialysis include (1) a high prevalence of HBV infection, (2) an environmental contamination with blood, (3) a high frequency of percutaneous procedures and (4) the presence of patients with high levels of viremia. These factors may be found in other health care settings because of (1) high HBV endemicity, (2) limited implementation of standard precautions, (3) overuse of injections and (4) presence of individuals (e.g., children) replicating HBV actively. In Romania, where some of these conditions were present, HBV infection was associated with receiving injections in 1998 (Abstract 2).[83] However, review of injection practices in the country suggested that single use syringes and needles were not reused and that HBV transmission was most likely related to preparation of injections in environments potentially contaminated with blood or body fluids (Abstract 5). [64,124] Preparation of injections in contaminated environments may also lead to bacterial infection [125] and cause infections among injection drug users (Abstract 6, Abstract 9). [126]

Multi-dose vials

It is important to use single-dose vials rather than multi-dose vials whenever possible. While preservatives decrease the survival of bacteria, [127] multi-dose vials remain prone to bacterial contamination. [125,128,129] Use of multi-dose vials were reported as a potential source of infection in 19 studies (Table 8, Abstract 8). [9,120,125,128,130,131,132,133,134,135,136,137,138,139,140,141,142,143] In two episodes, a needle had been left in the septum of the vial. [131,136] Needles left in the septum of multi-dose vials may facilitate use of the same syringe to repeatedly draw medications for one patient, a practice that may lead to vial contamination [129] and infections among subsequent patients. [136] Thus, if multi-dose vials must be used, it is essential to pierce the septum with a sterile needle and important not to leave any needle in place in the stopper.

Breaking of vials and ampoules

Injection providers may lacerate their hands while opening glass ampoules. [144] These lacerations may bleed and cause infections. [145] Thus, it is important to use pop-open ampoules rather than

ampoules that require the use of a metal file to open them, and to protect fingers with a clean barrier (e.g., small gauze pad) when opening ampoules that require a metal file to open.

Compromised packaging

Cracks and leaks represent a potential source of contamination for medications. [146] While the effectiveness of a visual examination of the vial is unknown, it is necessary to inspect for and discard medications with visible contamination or breaches of integrity (e.g., cracks, leaks) and to follow product-specific recommendations for use, storage and handling.

Aseptic techniques

Medical devices may be contaminated with bacteria if touched. Thus, it is necessary that a needle that has touched any non-sterile surface be discarded.

Other practice issues

Provider's hand hygiene and skin integrity

Hand hygiene (i.e., washing or disinfecting hands) is a standard procedure before preparing injection material. Injections have been administered in the absence of hand washing and without causing infection among diabetic patients. [147] The need for hand hygiene between each injection will vary based on the setting and whether there was contact with soil, blood or body fluids. Skin lesions and skin irritation are associated with bacterial contamination. [148] Thus, it is necessary to avoid giving injections if skin integrity is compromised by local infection or other skin conditions (e.g., weeping dermatitis) and to cover any small cut.

Swabbing vial tops or ampoules

Swabbing of vial tops or ampoules with an antiseptic or disinfectant is unnecessary. [125,149] Cotton balls and gauze stored wet in antiseptics may become contaminated and have contributed to infections among patients, particularly when benzalkonium chloride was used. [130,150,151] Thus, if swabbing with an antiseptic is selected for use, it is necessary to use a clean, single use swab and to maintain product-specific recommended contact time. Cotton balls stored wet in a multi-use container must not be used.

Skin preparation before injection

While skin that is visibly soiled or dirty must be washed, swabbing of the clean skin before giving an injection is unnecessary. Studies did not report an increased risk of infection when injections

are given in the absence of skin preparation (Table 7). [147,149,152,153,154,155] Bacteria from the skin flora may be introduced through skin piercing. [155] However, the majority of these bacteria are non-pathogenic and the number introduced is lower than the minimal infectious dose for pus formation. [156] Skin preparation protocols traditionally used, including wiping with 70% alcohol, may be insufficient to eliminate the skin flora because of a limited contact time [154,157] While the benefit of skin preparation is unclear, unsafe skin preparation protocols may be harmful. [150,151] Thus, if swabbing with an antiseptic is selected for use, it is necessary to use a clean, single use swab and to maintain product-specific recommended contact time. Cotton balls stored wet in a multi-use container must not be used.

Table 7: Studies reporting insulin injections given to diabetic patients with or without skin preparation*

Author	Follow-up	Study type	Physical examination of injection sites	Number of patients	Skin preparation protocol	Number of injections without skin preparation	Number of injections with skin preparation	Number of infections at injection site
Fleming [152]	0.5-59 years	Retrospective	No	21	N/A†	66 807‡	N/A†	0
Fleming [152]	20 weeks	Prospective	Yes	42	Alcohol	7,275‡	6445	0
McCarthy [153]	N/A	Prospective	Yes	50	1) Alcohol 2) Tap water	600§	1) 600§ 2) 600§	0
Borders [147]	1 week	Retrospective	Yes	47	N/A†	N/A†	N/A†	0
Stepanas [155]	≥ 1 week	Prospective	No	3	N/A†	N/A †	N/A†	0
Koivisto [154]	3-5 months	Prospective	Yes	13	70% alcohol	Over 1700	Over 1700	0

Prevention of infections among injection providers

Injuries from sharp devices have been associated with transmission of more than 40 pathogens, including HBV, HCV and HIV. [158,159]

Prevention of needle-stick injuries to the provider

Best infection control practices to prevent infections among injection providers address the prevention of patient movements, the prevention of unsafe recapping and the collection of contaminated sharps in puncture and liquid-proof containers.

* Assuming that 0.01% of injections with skin preparation would lead to infection, a power calculation suggests that the pooled data would allow the detection of a relative risk of 12.5 or higher with a power of 80% and an alpha risk of 5%.
† Not available.
‡ Injections given through clothing.
§ Individual patients reused their own injection equipment.

Patient movements

Needle-stick injuries during injections are usually attributable to abrupt patient movement during the procedure (Abstract 1). [159,160] Thus, it is important that providers anticipate and take measures to prevent sudden patient movement during and after injection. In some instances, physical assistance from other health care workers or family members may help in ensuring that the procedure is carried out under appropriate circumstances.

Recapping and other hand manipulation of used needles

Avoiding recapping and other hand manipulations of used needles (e.g., rinsing and dissembling of sterilizable equipment) is essential to prevent needle-stick injuries. In one study describing the epidemiology of needle-stick injuries, 2.8% of all injuries were attributed to cleaning of surgical equipment. [161] In countries where injection providers have to dissemble injection devices after use (e.g., Mongolia, Uzbekistan), needle-stick injuries are common. (Abstract 16, Jean Pierre Stamm, Swiss cooperation, personal communication) Also, high proportions of needle-stick injuries are attributable to two-handed recapping. [159] Teaching of the one-handed, scooping-resheathing-recapping technique was effective in reducing the risk of recapping-related needle-stick injuries in one study. [162] Thus, it is essential to use the single-handed scoop technique if recapping is necessary (e.g., in circumstances where a sharps container is not available).

Sharps collection

It is important to collect and properly contain syringes and needles at the point of use in a sharps container that is puncture- and leak-proof and that is sealed before completely full. Unsafe sharps waste collection causes between 5% and 28% of needle-stick injuries. [160,161] Puncture- and liquid-proof containers designed for the collection of contaminated sharps are associated with a lower risk of needle-stick injuries than regular cardboard boxes. [163] Presence of sharps containers close to the point of use reduces the incidence of recapping [164,165] and of recapping-related needle-stick injuries. [166,167] Interventions that combine provision of sharps containers and risk communications decrease the total number of needle-stick injuries. [160,168]

Other practice issues

Engineered technologies

Current hypodermic needles and syringes with safety features to prevent needle-stick injuries require a provider-dependent activation step. Their effectiveness is unclear. [169,170,171] None are able

to protect the provider when giving an injection as the safety feature is only activated after use. Reports on the effectiveness of other safer needle-bearing devices (e.g., intravenous catheters, phlebotomy needles) to protect health care personnel from needle-sticks are encouraging. [172,173,174,175] Thus, whenever possible, devices designed to prevent needle-stick injury that have been shown to be effective for patients and providers are preferable.

Prevention of infections in the community

Contaminated sharps are a potential source of biohazard to the community at large. To prevent these exposures, it is important to seal sharps containers for transport to a secure area in preparation for disposal. [176] After closing and sealing, sharps containers must not be opened, emptied, reused or sold. In South Asia, used injection equipment is sought for recycling, mostly for the plasticware industry (Abstract 15). [177] Such practices may lead to needle-stick injuries among waste pickers and can lead to illegal repackaging of syringes for reuse in health care settings. Finally, it is important to manage sharps waste in an efficient, safe and environment-friendly way. Contaminated sharps could be observed in the immediate surroundings of a high proportion of health care facilities in developing countries.[59] Such unsafe sharps waste management expose the community to needle-stick injuries. [178]

Discussion

We used WHO recommended processes to formulate best infection control practices for intradermal, subcutaneous and intramuscular injections and address the use of sterile injection equipment, the prevention of contamination of injection equipment and medication, the prevention of needle-stick injuries to the provider and the prevention of access to used needles. In addition, we addressed other practice issues of relevance to injection providers. Although we addressed the safety of injections from the perspectives of injection recipients, injection providers and communities, the burden of disease associated with unsafe injections is of a different magnitude among these three groups. In 2000, WHO estimated that contaminated injections may have caused 260 000 HIV infections among injection recipients (Chapter 2) while needle-stick injuries may have caused 1 000 HIV infections among injection providers. [179] No estimates are available regarding the burden of disease among the general population associated with unsafe sharps waste disposal; the low frequency of needle-stick injuries in this group suggests that it would be of an even lower magnitude. Thus, making injections safe to the injection recipients should be the first priority from a public health point of view. Sharps waste management

addresses a smaller burden of disease and may require the setting up of an infrastructure. Careful planning and integration throughout the health sector will limit costs and ensure sustainability.
The best practices do not constitute a standard for regulatory purposes or prescriptive guidelines. Rather, they distill critical steps believed to prevent injection-associated infections for resource-limited settings. While this approach removes some elements that could make them directly applicable to a particular setting, it allows adaptation by specific programmes or countries on the basis of practicality, feasibility or cost-effectiveness issues. For example, the recommendation to avoid multi-dose vials is not applicable in immunization services that make extensive use of them in developing countries. However, when multi-dose vials are used in immunization services, specific messages to providers will ensure their safe use.
These best practices did not address the use of specific engineered technologies, allowing the development group to avoid issues that could lead to actual or perceived conflicts of interest. Newer technologies supporting a safer use of injections have been developed. These include auto-disable (AD) syringes that inactivate themselves after one use (mostly for immunization and family planning services) and single use injection devices with other re-use prevention features (for therapeutic applications). A policy statement from WHO and UNICEF already recommends the exclusive use of AD syringes in immunization services. [180] For therapeutic applications, two research questions need to be addressed before best practices could recommend the generalized use of devices with reuse prevention features. First, there is a need to assess the user acceptability of these syringes in various settings. Second, their field effectiveness in eliminating re-use of injection equipment needs to be documented. Other safety mechanisms have been proposed to prevent needle-stick injuries. Policy decisions to recommend the use of these devices need to analyze in a cost-effectiveness evaluation (1) the probability of achieving safe practices in the absence of the device, (2) the effectiveness of the device in the setting where use is being considered and (3) the incremental cost involved.
These best practices do not include a recommendation to prepare the skin with an antiseptic. Skin preparation protocols have an influence on the risk of infection for intravenous catheters. [181] However, in this case, baseline rates of infections are higher and most infections are presumed to result from inward migration of bacteria from the insertion site. [181] Among injection drug users, skin cleaning may be associated with a lower risk of bacterial infections. [152]
These best practices have a number of limitations. First, the scope of the document was limited to intradermal, subcutaneous and intramuscular injections that constitute the majority of injections and that are homogeneous in terms of infection control requirements. Second, because

infections constitute the most common adverse effect associated with injections, the scope of these best practices was restricted to infection control and did not address other recommended practices (e.g., ensuring that the right dose of injection is given to the right patient, at the right time, etc.). Third, quality of medications and equipment was not addressed, as it depends upon national regulatory authorities rather than upon injection providers. Fourth, in the absence of data, the practice of removing needles after injections to collect sharps waste separately was not addressed. Disassembling injection equipment may cause needle-stick injuries. [159] In addition, it is unclear whether removing needles might produce splatters and aerosols as needle cutters do. [182] Thus, safety evaluations are needed before this practice can be recommended. In January 2004, WHO conducted an informal consultation to define the research agenda that is needed for WHO to address needle removers in a future revision of these best practices. Fifth, while calling for a reduction of injection overuse, our best practices do not provide details regarding the strategies proven effective in reducing the use of injections. Additional details regarding the rational use of injections may be obtained from the WHO Department of Essential Drugs and Medicine policy. WHO will promote the use of these best practices to prevent injection-associated infections. Pictograms (Figure 5) were developed to illustrate each of the steps. The best practices are also used as a reference for a WHO set of education tools and for a tool to assess injection safety in health care facilities. To ensure that these best practices continue to be useful, users of the document should continue reviewing scientific literature for new information and WHO will plan for revisions using the same methodology five years after the initial development, i.e. in 2005.

Figure 5: Three pictograms illustrating selected best practices, including (1) the use of new single use equipment, (2) the collection of dirty sharps in safety boxes and (3) the safe sharps waste management.

Table 8: Epidemiological studies reporting an association between infections and use of multi-dose vials

Author	Pathogen	Infection	Number infected	Type of study	Positive vial culture	Reported practices
Inman [133]	*Mycobacterium abscessus*	Abscess	12	Descriptive	N/A*	Reuse of syringes among different patients and decanting
Kothari [140]	*Pseudomonas*	Septic Arthritis	1	Descriptive	Yes	N/A*
Black [138]	*Streptococcus*	Abscess	1	Descriptive	Yes	N/A*
Borghans [131]	*Mycobacterium chelonei*	Abscess	47	Descriptive	N/A *	Permanent insertion of a needle, reuse of aspiration needle, reuse of injection needles after boiling, storage of residual vaccine for successive sessions and use of petroleum ether for skin preparation
Cabrera [134]	*Pseudomonas*	Bloodstream infection	5	Descriptive	Yes	Use of multi-dose vials of saline for preparation of injectable medications
Katzenstein [120]	HIV	HIV infection	1	Descriptive	N/A *	Use of multi-dose vials changed daily, repeated aspiration of medication for one patient followed by discarding of vial, aspiration needles discarded after use for individual patients
Kidd-Lungren [136]	HBV	HBV infection	2	Descriptive	N/A *	Permanent insertion of a needle and reuse of syringe to draw medication
Philipps [128]	*Streptococcus*	Peritonitis	1	Descriptive	Yes	Stopper wiped with antiseptic
Widell [137]	HCV	HCV infection	10	Descriptive	N/A *	N/A*
Widell [137]	HCV	HCV infection	9	Descriptive	N/A *	N/A*
Massari [138]	HCV	HCV infection	4	Descriptive	N/A *	Administration of medications in an IV line without an anti-reflux valve
Greaves [135]	*Streptococcus*	Abscess	7	Analytical	Yes	Skin preparation with cotton balls soaked in alcohol
Alter [63]	HBV	HBV infection	10	Analytical	N/A	Vials shared among patients †, medications prepared by patients and multi-dose vials not discarded at end of day

* Not available.

† In a hemodialysis unit.

Author	Pathogen	Infection	Number infected	Type of study	Positive vial culture	Reported practices
Archibald [9]	*Enterococcus*	Bloodstream infection	6	Analytical	N/A *	Stoppers wiped with povidone-iodine, introduction of needles before drying of povidone-iodine, no hand hygiene and cluttered work surfaces
Grohskopf [143]	*Serratia*	Bloodstream infection	20	Analytical	Yes	Pooling of residual medications for reuse
Krause [142]	HCV	HCV infection	4	Analytical	N/A *	N/A*
Nakashima [130]	*Serratia*	Arthritis	8	Analytical	Yes	Storage of filled syringes for use during next day, stoppers and skin wiped with cotton balls soaked in benzalkonium chloride, rinsing of storage canisters with tap water, no hand hygiene and no use of gloves
Oren [131]	HBV	HBV infection	5	Analytical	N/A *	Preparation of multi-dose heparin and saline solution, changed daily
Simon [125]	*Streptococcus*	Abscess	8	Analytical	N/A *	Handling in contaminated areas, stopper wiped with sterile cotton soaked in alcohol and use of sterile single use needles and syringes
Stelter [141]	*Streptococcus*	Abscess	12	Analytical	N/A *	Stopper and skin wiped with cotton balls soaked in alcohol
Stelter [141]	*Streptococcus*	Abscess	7	Analytical	Yes	Stopper and skin wiped with disposable alcohol swabs

Box 1: Summarized best infection control practices for intradermal, subcutaneous and intramuscular needle injections

Eliminating unnecessary injections is the highest priority to prevent injection-associated infections. When injections are medically indicated, they should be administered safely. These best practices are measures that have been determined through scientific evidence or expert consensus most effectively to protect patients, providers and communities.

1. Use sterile injection equipment *

- Use a sterile syringe and needle for each injection and to reconstitute each unit of medication. *
- Ideally, use a new, single use syringe and needle. * Inspect packaging for breaches in barrier integrity. Discard a needle or syringe if the package has been punctured, torn or damaged. ‡
- If single use syringes and needles are unavailable, use equipment designed for steam sterilization. Sterilize equipment according to WHO recommendations and document the quality of the sterilization process using Time, Steam, Temperature (TST) spot indicators. ‡

2. Prevent contamination of injection equipment and medication

- Prepare each injection in a clean designated area, where blood or body fluid contamination is unlikely. †
- Use single-dose vials rather than multi-dose vials. † If multi-dose vials must be used, always pierce the septum with a sterile needle. * Avoid leaving a needle in place in the stopper of the vial. †
- Select pop-open ampoules rather than ampoules that require use of a metal file to open. If using an ampoule that requires a metal file to open, protect fingers with a clean barrier (e.g., small gauze pad) when opening the ampoule. †
- Inspect for and discard medications with visible contamination or breaches of integrity (e.g., cracks, leaks). ‡ Follow product-specific recommendations for use, storage and handling. ‡ Discard a needle that has touched any non-sterile surface. ‡

3. Prevent needle-stick injuries to the provider

- Anticipate and take measures to prevent sudden patient movement during and after injection. †

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* Category I: Strongly recommended and strongly supported by well-designed experimental or epidemiological studies.
† Category II: Recommended on the basis of theoretical rationale and suggestive, descriptive evidence.
‡ Category III: Recommended on the basis of expert consensus and theoretical rationale.

- Avoid recapping and other hand manipulations of needles. If recapping is necessary, use a single-handed scoop technique. *
- Collect used syringes and needles at the point of use in an enclosed sharps container that is puncture- and leak-proof and that is sealed before completely full. †

4. Prevent access to used needles

- Seal sharps containers for transport to a secure area in preparation for disposal. After closing and sealing sharps containers, do not open, empty, reuse or sell them. †
- Manage sharps waste in an efficient, safe and environment-friendly way to protect people from voluntary and accidental exposure to used injection equipment. †

5. Other practice issues ‡

- **Engineered technology.** Whenever possible, use devices designed to prevent needle-stick injury that have been shown to be effective for patients and providers. Auto-disable (AD) syringes are increasingly available to prevent reuse of injection equipment in selected settings, including immunization services.
- **Provider's hand hygiene and skin integrity.** Perform hand hygiene (i.e., wash or disinfect hands) before preparing injection material and giving injections. The need for hand hygiene between each injection will vary based on the setting and whether there was contact with soil, blood or body fluids. Avoid giving injections if skin integrity is compromised by local infection or other skin conditions (e.g., weeping dermatitis). Cover any small cuts.
- **Gloves.** Gloves are not needed for injections. Single use gloves may be indicated if excessive bleeding is anticipated.
- **Swabbing of vial tops or ampoules.** Swabbing of clean vial tops or ampoules with an antiseptic or a disinfectant is unnecessary. If swabbing with an antiseptic is selected for use, use a clean, single use swab and maintain product-specific recommended contact time. Do not use cotton balls stored wet in a multi-use container.
- **Skin preparation before injection.** Wash skin that is visibly soiled or dirty. Swabbing of the clean skin before giving an injection is unnecessary. If swabbing with an antiseptic is selected for use, use a clean, single use swab and maintain product-specific recommended contact time. Do not use cotton balls stored wet in a multi-use container.

Members of the injection safety best practices steering group and development group

The steering group and the development group approved these best practices.

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Chapter 4: The effectiveness of interventions to improve injection use

"I am old and cannot sleep forever like the young, nor hope that death will be novelty but endless wakefulness. When I put down my work and go to bed: how much of what we did was good? Everything seems to move beyond our remedy. Come shield this wound. At this hour, nothing can be done, just before dawn the birds begin, the warblers who prefer the dark, the caged birds answering: to work. Outside this room, the chill of grace lies heavy on the morning grass. "
Chou En Lai final aria
"Nixon in China"
John Adams, composer
Alice Goodman, libretto

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Introduction

Poor injection practices, including injection overuse and unsafe techniques have been reported worldwide.[1] However, in developing and transitional countries, the cost associated with poor injection practices is particularly high. WHO's Global Burden of Disease study for the year 2000 suggests that each year reuse of injection equipment in the absence of sterilization may cause 22 million cases of hepatitis B virus (HBV) infections (30% of the total), two million cases of hepatitis C virus (HCV) infections (40% of the total) and 260 000 cases of HIV infection (five percent of the total, Chapter 2). In addition, epidemiological studies suggest that unsafe injections were a dominant vector for the introduction of HCV at high endemic levels in some countries, including Egypt and Pakistan.[67,5,39] According to the "first do no harm" principle, these infections associated with unsafe injections are unacceptable and should be prevented.

While the public health consequences of unsafe injection practices have become indisputable, the solutions that could be brought to the problem may appear unclear or difficult to achieve.[183] Injection overuse appears to many public health professionals as an overwhelming plague of health systems.[49] Studies have indicated that in most cultures, injecting a substance into the body has been re-interpreted according to the local social and anthropological context so that injections have become procedures that patients appreciate and ask for.[3] However, other studies clearly indicate that reduction of injection use is an attainable goal if communication between patients and health care providers is improved.[52] Similarly, safe injection practices, including the "one syringe, one patient" rule seemed so out of reach with standard single use syringes that innovative technological solutions were sought to design injection equipment that disables itself after a single use.[184] However, simple solutions, including ensuring universal access to sufficient quantities of single use injection equipment are underused (Abstract 5).[58]

To recommend successful strategies for national policies for the safe and appropriate use of injections, we identified, reviewed and produced a synthesis of studies that provided evidence regarding the effectiveness of interventions aimed at the reduction of injection use and the decrease in unsafe use of injections in various health systems.

Methods

Literature search

We searched electronic databases including “Medline” (1966 to 2001), “Healthstar” (1975 to 2001), "Embase Psychiatry" (1990 to 2001) and the “Cochrane” library. Cochrane Evidence

Based Medicine Reviews included the "Cochrane" Database of Systematic Reviews until 2001, ACP Journal Club (1991 to October 2001), the Database of Abstracts of Reviews of Effectiveness until 2001 and the "Cochrane" Controlled Trials Register until 2001. In addition, we included WHO reports and unpublished assessments made available to WHO through the International Network for the Rational Use of Drugs (INRUD).[185] Studies were included regardless of languages.

Selection of studies

We selected studies that contained quantitative and qualitative information on the effect of interventions on injection use and injection safety. In addition, we restricted the review to studies that provided information on study design, type of interventions, targeted participants and targeted behaviours.

Ranking of the quality of the evidence

We ranked all studies in four categories according to the level of evidence provided (Table 9). Category one (highest quality) included randomized controlled trials. Category two included non-randomized controlled trials, before-after comparisons with control groups and controlled interrupted time series. Category three included before-after comparisons and time series without control groups. Category four (lowest quality) included historical comparisons.

Table 9: Ranking of studies according to quality of evidence

Level of evidence *	Selected study designs	n (%)
Category 1	Randomized controlled trials	4 (19%)
Category 2	Non-randomized controlled trials	5 (24%)
	Before-after comparison with control groups	
	Controlled interrupted time series	
Category 3	Before-after comparison without control groups	9 (48%)
	Uncontrolled time series studies	
Category 4	Historical comparisons	2 (10%)

Information collected

We collected information on the characteristics of the interventions in an electronic database. Information abstracted included study identification, country, setting (e.g., facility or population based), study type, study objectives, sampling units, sampling methods, sample size, age group, gender, type and characteristics of interventions, frequency and duration of delivery of

* 1 denotes highest quality and 4 denotes lowest quality.

interventions, target population, coverage, time interval between two assessments, indicators used and change in these indicators. Interventions aiming at modifying the practices of health care workers were characterized as training or interactive communication. Interventions that aimed at educating the population or at increasing access to safe injection equipment were characterized as such.

To measure the effectiveness of interventions to reduce injection use, we used prescription-based indicators (e.g., the proportion of prescriptions including at least one injection) [186] and population-based indicators (e.g., the self-reported annual number of injections per person). To measure the effectiveness of interventions to reduce unsafe use of injections, we used the proportion of injections given with injection equipment reused in the absence of sterilization. We did not consider other practices that may also lead to a risk to the injection recipient (e.g., inappropriate use of multi-dose vials), the injection provider (e.g., unsafe sharps waste collection) and the community (e.g., unsafe sharps waste management).

The effect size in the intervention group was calculated as the difference between the value of the indicator before and after the intervention. In studies where a trial design or a before-after comparison with the control group was used, the effect size was calculated as the gain in the intervention group, i.e. the difference between the percent improvement in the intervention group and the percent improvement in the comparison group:

$$\text{Effect size} = (\%\text{after} - \%\text{before})_{\text{intervention}} - (\%\text{after} - \%\text{before})_{\text{control}}$$

Table 10: Summarized characteristics of studies assessing the effectiveness of interventions aimed at reducing injection use *

Author, Reference	Country	Year †	Characteristics of the intervention: Training of providers	Characteristics of the intervention: Interactive communication with providers	Characteristics of the intervention: Education of the population	Type of study (design)	Quality of evidence (Category) ‡	Indicator	Decrease in injection use in intervention group: Absolute impact	Decrease in injection use in intervention group: Gain over control group
Agyepong [188]	Ghana	1996	Continuous	Once	No	RCT §	1	Prescription-based ⌗	-4%	-7%
Bexell [187]	Zambia	1992	Multiple sessions	Multiple sessions	No	RCT §	1	Prescription-based ⌗	-3%	-7%
Kafle [189]	Nepal	1995	Continuous	Multiple sessions	No	RCT §	1	Prescription-based ⌗	-5%	-10%
Prawitasari [52]	Indonesia	1996	Once	Once	Once	RCT §	1	Prescription-based ⌗	-27%	-19%
Casado [193]	Spain	1993	Once	Continuous	No	Non-R CT §	2	Prescription-based **	-23%	-19%
Kafuko [192]	Uganda	1997	Continuous	Continuous	No	Before-after /control	2	Prescription-based ⌗	-6%	-7%
Ofori-Adjei [190] ††	Ghana	1995	Once	Once	No	Before-after /control	2	Prescription-based ⌗	-1%	0%
Thuo [191] §§	Kenya	1997	Multiple sessions	Multiple sessions	No	Before-after /control	2	Prescription-based ⌗	-3%	+3%
Widyastuti [194]	Indonesia	1997	No	Continuous	No	Before-after /control	2	Prescription-based ⌗	-39%	-27%
Ahmed [201] ‡	Pakistan	1999	Multiple sessions	Multiple sessions	Yes	Before-after	3	Population-based ***	-19%	N/A
Audi [196]	Kenya	1997	Once	Once	No	Before-after	3	Prescription-based ⌗	-4%	N/A

* By decreasing order of study quality.

† Year of publication.

‡ Ranking according to type of studies, quality of data and evidence (1=highest / 4=lowest quality); 1: randomized controlled trials; 2: non-randomized controlled trials, before-after comparisons with control group; 3: before-after comparisons and time series study without control group; 4: historical comparisons.

§ Randomized control trial.

** Proportion of prescriptions including at least one injected antibiotic.

†† Addressed injection use for the treatment of malaria.

⌗ OT8 indicator: Proportion of prescriptions including at least one injection.

§§ Addressed injection use in inpatient settings.

*** Proportion of the population reporting at least one injection in the last year.

Author, Reference	Country	Year	Characteristics of the intervention			Type of study (design)	Quality of evidence (Category) *	Indicator	Decrease in injection use in intervention group	
			Training of providers	Interactive communication with providers	Education of the population				Absolute impact	Gain over control group
Birrel [195]	Tanzania	2000	Once	Continuous	No	Before-after	3	Prescription-based ⌗	-3%	N/A
Brook [202]	USA	1976	Continuous	Once	No	Before-after	3	Prescription-based †	-25%	N/A
Christensen [197]	Uganda	1990	Once	Once	No	Before-after	3	Prescription-based ⌗	-9%	N/A
Luby [60] ‡	Pakistan	2002	No	No	Continuous	Before-after	3	Population-based §	-7%	N/A
Luby [200]	Pakistan	2002	Multiple sessions	Multiple sessions	No	Before-after	3	Population-based **	-14%	N/A
Ogwal-Okeng [198]	Uganda	1997	Continuous	Multiple sessions	No	Before-after	3	Prescription-based ⌗	-13%	N/A
Santoso [203]	Indonesia	1994	Multiple sessions	Multiple sessions	No	Time series	3	Prescription-based ⌗	-53%	N/A
Vos [199]	Tanzania	1998	Once	No	Continuous	Before-after	3	Prescription-based ⌗	-1%	N/A

* Ranking according to type of study, quality of data and evidence (1=highest / 4=lowest quality); 1: randomized controlled trials; 2: non-randomized controlled trials, before-after comparisons with control group; 3: before-after comparisons and time series study without control group; 4: historical comparisons.

† Number of injections prescribed per visit.

‡ Also addressed the reduction of unsafe use.

§ Proportion of the population reporting more than five injections in the last year.

** Proportion of the population reporting one injection in the last two weeks.

Results

We selected 21 studies for the review. This included 10 articles, three abstracts and eight unpublished reports. Nineteen studies reported information on the effectiveness of interventions aimed to reduce injection use (Table 10), five reported the effectiveness of interventions aimed to decrease the unsafe use of injections (Table 11) and three reported interventions that combined both objectives. Four studies (19%) presented category one evidence.[52,187,188,189] Five studies presented category two evidence (24%). [190,191,192,193,194] Nine studies (48%) presented category three evidence. [60,52,194,195,196,197,198,199,200,201,202,203] Two studies (10%) presented category four evidence.[64,204] Finally, we separately examined the effectiveness of an additional intervention that compared intervention and control areas after an intervention because measurement of effectiveness could not be directly compared with the others.[205]

Effectiveness of interventions aimed at reducing injection use

Interventions that aimed at reducing injection use were based upon communication strategies that included training of providers (n=17), interactive communication with providers (n=17) and education of the population (n=4, Table 10). Activities to train providers included the development and distribution of guidelines, workshops and seminars. Interactive communication with providers included interactive problem-based discussions, role play, focus group discussions to develop treatment norms, continuous assessment and feedback, monitoring of progress (including peer review systems to verify prescription against medical guidelines), on site visits for verbal case review and discussions during staff meetings. A unique intervention consisted in what was referred to as "interactive group discussions" that brought together patients and health care workers so that prescribers could be confronted with the absence of expressed preference for injections in the population.[52] Education of the population mostly consisted in health education programmes with production and distribution of Information, Education and Communication (IEC) material, announcements during religious gatherings and small group discussions. One single study used financial incentives to influence prescribers' behaviours through a link between use of injections and reimbursement policies.[202] Indicators used were prescription-based in 17 cases and population-based in two cases. The average length of follow-up was 12.2 months (Range: 3-48).

The reduction of injection use reported ranged from 1% to 53% with a gain in controlled studies ranging from 3% to 27%. This reduction in injection use was smaller for studies of better quality although the difference was not statistically tested (4%, 6% and 13% median reduction in

category 1, 2 and 3, respectively). The 15 interventions that solely targeted providers [187,188,189,190,191,192,193,194,195,196,197,198,200,202,203] reduced injection use by a median of 6% (range 1-53%). The four studies that targeted the general population in addition to providers [52,60,199,201] reduced injection use by a larger magnitude (median: 16%, range 7-27%). The two studies from industrialized countries (Spain and USA) reported a higher effectiveness for interventions to reduce injection use (median reduction: 24%) than the 17 studies from developing countries (median reduction: 7%, range: 1-53%). The additional study that could not be included in the table compared areas with and without an intervention that consisted in (1) seminars and (2) supply of drug ration kits restricting access to unnecessary injectable medications. The intervention area had a statistically significant lower proportion of prescriptions that included at least one injection (25%) than the control areas (58%). Interestingly, the authors concluded that the restriction of the range of drugs available in the drug ration kits probably had a greater influence than did training alone on improved drug use.[205]

Effectiveness of interventions aimed at reducing unsafe injection practices

Interventions aimed at reducing unsafe injection practices used communication strategies that included training and/or education of providers (n=3), provision of safe injection equipment (n=2) and education of the population (n=4). Indicators used were based upon patients' reports regarding the last injection received (n=2), observations of providers (n=2) and surveys of injection providers' practices (n=1).

The median absolute reduction in unsafe injection practices ranged from 30 to 82% (relative reduction ranging from 40 to 100%). Category three studies were mainly based upon communication activities. The reported reduction in unsafe injection practices ranged from 40 to 49%. Category four studies were mainly based upon provision of safe injection equipment. The reported relative reduction of unsafe injection practices ranged from 94 to 100%. The average length of follow up was 38 months (Range: 4-60).

Table 11: Summarized characteristics of studies assessing the effectiveness of interventions aimed reducing unsafe injection use

Author, Reference	Country	Year †	Characteristics of the intervention: Training of providers	Characteristics of the intervention: Provision of injection equipment	Characteristics of the intervention: Education of the population	Type of study	Quality of evidence ‡ (Category)	Indicator	Decrease in unsafe injections in intervention group *: Relative impact	Decrease in unsafe injections in intervention group *: Absolute impact
Luby [60]	Pakistan	2002	No	No	Continuous	Before-after	3	Patients' reports	-40.5%	-30%
Ahmed [201]	Pakistan	1999	Multiple	No	Yes	Before-after	3	Patients' reports	-48.9%	-35.9%
Vos [199]	Tanzania	1998	Once	No	Continuous	Before-after	3	Observations §.	-49.2%	-32%
Fitzner (Abstract 10) [204]	Burkina Faso	2000-2001	No	Yes	No	Historical comparison	4	Observations	-93.9%	-46.7%
CDC [64]	Romania	1993-2001	Continuous	Yes	Yes	Historical comparison	4	Survey of providers	-100%	-82%

* Proportion of injections given with used equipment, i.e. equipment reused in the absence of sterilization.

† Year of publication.

‡ Ranking according to type of studies, quality of data and evidence (Table 9).

§ Checklist included: Use of a sterile syringe and needle, no touch, disinfection of vial stoppers and use of a separate needle to draw medication and give injections.

Discussion

The issue of the safe and appropriate use of injections has received some attention from public health professionals in the last decades. Assessments were conducted,[58] policy statements were formulated [180] and alternative technologies were developed.[184] However, this interest did not always materialize in the form of interventions. We only identified a modest number of studies that included an initial assessment and a final evaluation. However, all demonstrated some degree of effectiveness in reducing injection use and/or unsafe injection practices. Interventions to reduce unsafe use of injections were more effective than interventions to reduce injection use, probably because they require a more modest change in behaviour (changing a type of syringe for another versus reducing injection use). Interestingly, the approach of the studies that examined the effectiveness of interventions to reduce injection use differed from the ones of those that examined the effectiveness of interventions to reduce unsafe use of injections (Table 12).

Table 12: Compared characteristics of interventions aiming at decreasing injection use and reducing unsafe injections

	Type of change needed	Public health benefit	Number of studies	Scientific quality	Coverage of intervention	Effectiveness	Key effective interventions
Interventions to reduce injection use	Substantial (Behaviour change of prescribers)	Improve rational use of injections	20	Higher	Small scale (Pilots selected districts)	-1 to - 53%	Communication and supervision with prescribers
Interventions to reduce unsafe injections	Limited (Replacement of a type of syringe by another)	Prevent HBV, HCV and HIV infection	5	Lower	Larger scale (Nationwide policy changes)	-30 to -82%	Supplying safe injection equipment

Reduction of injection use was usually addressed with well-conducted intervention studies usually conducted as part of interventions to improve the rational use of medicines. Improving the rational use of medicines is about changing the behaviour of prescribers, a highly educated target group. Interventions are often based upon revision of standard treatment guidelines and/or interactions with practitioners. Thus, a solid evidence base in the use of medicines is required to conduct and evaluate them. This may explain why the approach used to study the effect of interventions to reduce injection use has been largely academic. Compared to interventions to reduce unsafe use of injections, studies were available in a larger number and a higher proportion was of good quality (category one and two studies according to our ranking). However,

interventions to reduce injection use were mostly implemented on a small or pilot scale. Studies that attempted to influence the behaviour of the general population in addition to that of prescribers had a larger effect size. This suggests that patients may influence the choice of the medications that are prescribed to them. Among all these interventions to reduce injection use, interactional group discussions where prescribers were confronted with the actual lack of preference for injections among their patients stood out as a successful strategy that was both well described and well evaluated.

In contrast to interventions to reduce the use of injections, interventions to reduce the unsafe use of injections were not conducted as academic studies. The public health benefit of these interventions consists essentially in the prevention of injection-associated infections with HBV, HCV and HIV. The approach used in interventions to improve injection safety was twofold. A number of interventions targeted the behaviour of providers and/or that of the general population. Others primarily focused on the provision of new single use injection equipment. Interventions to reduce unsafe use of injections have often been designed as policy changes. Thus, a smaller number have been published in peer-reviewed journals and those published were of lower quality (categories three and four according to our grading system). However, the practical rather than academic nature of interventions to reduce unsafe use of injections led to broader, nationwide coverage. Additional evidence supports the hypothesis that policy changes leading to increased availability of single use injection equipment improve injection practices. In Uzbekistan and in Mongolia, two countries that recently conducted injection safety assessments, reuse of injection equipment in the absence of sterilization was uncommon if observed at all [206] (Abstract 16, Jean Pierre Stamm, Swiss cooperation, personal communication). In these two countries, no historical reference was available to compare the current injection safety situation with the past one. However, anecdotal evidence suggested that the recent set-up of factories that produced single use syringes had a major impact to (1) eliminate the use of sterilizable injection equipment, (2) increase the availability of injection equipment and (3) improve injection practices. Overall, evidence suggests that provision of sufficient quantities of new, single use injection equipment is effective in reducing unsafe injection practices.

Our study suffered from four main limitations. First, we were not able to conduct a meta-analysis, the standard method for systemic reviews. The number of studies available was too small and the interventions examined were heterogeneous. Because of this limitation, we were not able to generate a weighted average effect size and its confidence interval. Second, the information provided in these studies did not allow us to estimate the quantity or the quality of

the resources invested in the communication activities conducted to reduce injection use or to reduce unsafe use of injections in these various interventions. Third, a number of studies using communication activities to target injection use and/or unsafe injections were conducted as pilot studies involving highly qualified and highly motivated staff. Thus, it is unclear what additional or alternative efforts would be needed to achieve similar levels of effectiveness at the national level. Fourth, we compared various studies using different indicators. Some of these could overestimate effectiveness (e.g., prescription-based indicators that do not take into account injections received outside of the formal health care setting). Some others could underestimate effectiveness (e.g., population-based injection frequency indicators that take into account all injections received, including those received in settings not targeted by the intervention). However, all indicators tended to measure the same outcome and all studies were consistent in documenting a higher effectiveness of interventions to reduce unsafe use of injections than interventions to reduce injection use.

While interventions to reduce injection use and to reduce the frequency of unsafe injections have mostly been conducted separately, they have all demonstrated some degree of effectiveness and they should be recommended for wider use. Conducting them together may yield additional benefits in terms of effectiveness. Thus, national drug policies should (1) promote rational use of injections through communication activities targeting providers and patients and (2) improve access to safe injection equipment to ensure that all injections are administered safely. Restricting access to unnecessary injectable medications may also contribute to the reduction of injection use. [205] Beyond the national drug policy, programmes for the prevention and care of HIV infection should communicate the risk of HIV infection associated with unsafe injections and the health system should manage sharps waste. Implementation of such national policies for the safe and appropriate use of injections will generate substantial benefits, not only in terms of rational use of drugs but also in terms of prevention of infection with bloodborne pathogens.

Chapter 5: The cost-effectiveness of the safe and appropriate use of injections

"Jumping is the cheapest way to go to the moon. However, we don't do it, because it does not work".
Mark Kane

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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 were an important vector for the introduction of HCV in some countries, including Egypt and Pakistan. [67,5,39] However, the burden of cirrhosis, hepatocellular carcinoma and Acquired Immunodeficiency Syndrome (AIDS) associated with unsafe injections is delayed in time and may not be directly apparent.

While injection-associated infections constitute a silent epidemic, effective interventions are available to reduce injection use and unsafe practices (Chapter 4). First, Information, Education and Communication (IEC) targeting prescribers, including patient/prescribers interactional group discussions, reduces injection use. Second, 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 may not be sufficient to justify an investment in a policy for the safe and appropriate use of injections. Economic considerations also enter the debate. Accordingly, we set out to estimate the cost-effectiveness of policies for the safe and appropriate use of injections in terms of cost per Disability Adjusted Life Year (DALY) averted. In so doing, we adopted a broad, sectoral approach to cost-effectiveness analysis, using the perspective of the health system, the goal of which is maximization of health.

Methods

Study populations

The six regions of the World Health Organization (WHO) were subdivided into subgroups of countries sharing similar rates of child and adult mortality. This gives rise to 14 Global Burden of Disease 2000 epidemiological sub-regions characterized by the WHO region acronym and a letter for the mortality stratum (Table 1). [207] Four sub-regions (AMR A, EMR B, EUR A and WPR A) where reuse of injection equipment in the absence of sterilization is negligible were excluded from the analysis.

Effectiveness model

We considered a theoretical cohort of the population living in the year 2000 in sub-regions where reuse of injection equipment is reported. We first applied a current, "do nothing" scenario where

persons were exposed to contaminated injections and acquired infections. Second, we applied a series of "counterfactual" 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 (Chapter 1 and Chapter 2). The burden in DALYs for the years 2000-2030 because of infections in the year 2000 were estimated on the basis of the natural history of viral infections, background mortality, life tables [108] and the average duration and disability weights of acute hepatitis, cirrhosis, hepatocellular carcinoma and AIDS, the four sequelae of interest.[99] DALYs were age-weighted and 3% discounted (Chapter 2).

Effectiveness of interventions

We examined interventions to decrease unsafe use of injections, interventions to reduce injection use and the effect of these two interventions implemented jointly. For interventions to decrease unsafe use of injections, we considered the effectiveness of interventions based upon provision of single use injection equipment (Abstract 5).[204,64] Interventions to decrease injection frequency reported a large variation of effectiveness (1-53%) due to variable approaches and study designs.[52,188,191,192,60,197,195,200,198,201,189,196,187,199,203,194] We used the effectiveness reported for interactional group discussions, an intervention developped, implemented and evaluated in Indonesia. [52] Interactional group discussions consist of moderated patient/prescriber 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 upon the number of contaminated injections, a direct product between 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 addition, in the absence of evidence suggesting another scenario, we assumed that the effectiveness of the intervention was identical irrespective of the magnitude of the problem in the "do nothing" scenario.

Cost of interventions

Quantification

First, we identified the activities required for each intervention at the national and sub-national level for an implementation period of 10 years of intervention (Table 13).[207] Each of these activities was assigned to the intervention to reduce injection use, to the intervention to reduce unsafe practices or to both (in the case of the latter, activities necessary in the two interventions were only counted once). Second, we estimated the fractions of full time-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 with sterile injection equipment (Chapter 1). Fourth, the resources required for safe sharps waste collection and management was taken into account as part of the intervention.

Table 13: Activities included in interventions for the safe and appropriate use of injections *

					Years									
Activities	Intervention	Timing	Level	Start-up†	1	2	3	4	5	6	7	8	9	10
National planning workshop	Appropriate use	Start-up	National ‡	X	-	-	-	-	-	-	-	-	-	-
Development of IEC§ material	Appropriate use	Start-up	National ‡	X	-	-	-	-	-	-	-	-	-	-
Training of the trainers	Appropriate use	Start-up	National ‡	X	-	-	-	-	-	-	-	-	-	-
Training of the procurement officer	Safe use	Start-up	National ‡	X	-	-	-	-	-	-	-	-	-	-
District planning workshops	Appropriate use	Start-up	Sub-national ‡	X	-	-	-	-	-	-	-	-	-	-
Supplying injection equipment **	Safe use	Post start-up	Sub-national ‡	-	X	X	X	X	X	X	X	X	X	X
Annual national follow-up workshop	Appropriate use	Post start-up	National ‡	-	X	X	X	X	X	X	X	X	X	X
Interactional group discussions	Appropriate use	Post start-up	Sub-national ‡	-	X	X	X	X	X	X	X	X	X	X
Annual monitoring surveys	Both ††	Post start-up	Sub-national ‡	-	X	X	X	X	X	X	X	X	X	X

* The analysis considered the 3% discounted average yearly cost of a 10-year intervention. Safe and appropriate use interventions were considered both separately and combined.

† Included in year one.

‡ According to WHO CHOICE methods. [207]

§ Information, Education and Communication.

** With and without safe sharps waste management in the sensitivity analysis.

†† 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.

Costing

We estimated the average yearly programme cost for human resources and associated materials for the year 2000, based on costing studies conducted in each sub-region as part of the WHO CHOICE project.[207] 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.[208] Third, we estimated the cost of domestic distribution on the basis of a hexagon-shaped sub-regional distribution model that calculated distances between the theoretical centre of a country with highest population densities and a periphery with lowest population density.[209] The cost of personnel, capital and fuel was estimated from a database to which fuel efficiency and maintenance cost were added.[210] 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 and Patrick Lydon, personal communication). We assumed 100% coverage of all situations where injections were given in the formal public sector.

Uncertainty analysis

We first tested the lower and upper values of the attributable fraction of the Comparative Risk Assessment (Chapter 2). Second, we assumed that the effectiveness of interventions was only 7% for reduction of injection use (the lowest effectiveness reported for an intervention targeting patients and providers) and 50% for reduction of 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, we entered total baseline costs and effects into an analytical software package (MCLeague) for a stochastic analysis using Monte Carlo simulation for 1 000 runs using a truncated normal distribution. [211]

Results

Effectiveness of interventions

Burden of disease attributable to contaminated injections in 2000

We estimated that the number of injections per person per year ranged 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 14). Overall, contaminated injections caused 22 million HBV infections, two million HCV infections and 260 000 HIV infections. These infections lead to 49 000, 24 000 and 210 000 deaths between the years 2000 and 2030, respectively, 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%) while HBV and HCV infections accounted for 34% and 4% of the total, respectively. Most of this burden is caused by early death rather than by disability.

Burden of disease preventable through interventions

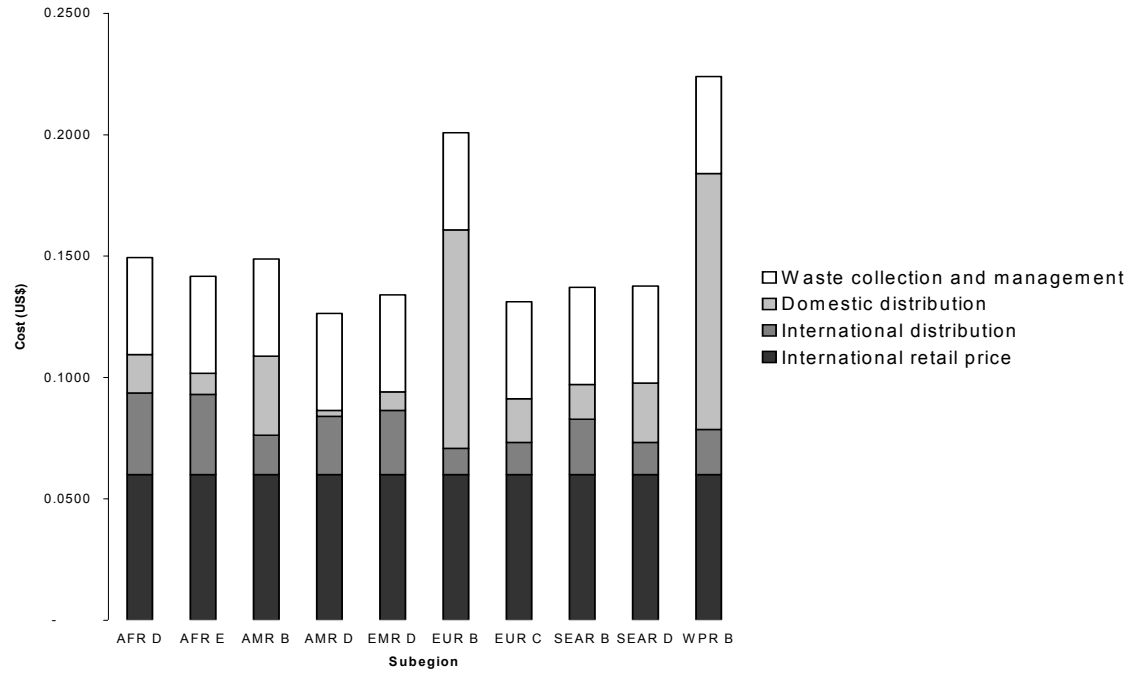
We assumed the effectiveness on injection use of interactional group discussion to be 30%. [52] This effectiveness translated directly into projected burden of disease reduction, since in our disease model the incidence of injection-associated infections was proportional to (a) the annual number of injections per person and (b) the proportion of injections given with reused equipment (Chapter 2). Implementation of interventions to reduce injection use would lead to a reduction of 2 753 304 DALYs. The effectiveness on the unsafe use of injections of provision of single use injection equipment was assumed to be 95%. Implementation of interventions to reduce unsafe use of injections would lead to a reduction of 8 718 795 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 15) 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 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 sub-regions 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 (Figure 6). 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).

Figure 6: Total unit cost of syringes and needle sets according to various cost components, by sub-region.



Cost-effectiveness of interventions

The average cost-effectiveness ratio (CER; total costs divided by total effects) for interventions to reduce injection use ranged from I$7 to I$5 124 per DALY averted according to the region (Table 15). The average CER for interventions to reduce unsafe use of injections, including waste management, ranged from I$ 12 to I$1 107 par DALY averted according to the region. The average CER for combined interventions for the safe and appropriate use of injections, including waste management, ranged from I$14 to I$ 2 293 per DALY averted according to the region. Incremental analysis (Table 15) suggested that in the six sub-regions where the proportion of reuse of injection equipment exceeds 15% (Table 15), the intervention to reduce injection use represents the single most cost-effective strategy. In the four other sub-regions, reduction of unsafe use is the most efficient strategy. However, in all regions, the combined interventions remained under the threshold of one year of average per capita income.

Uncertainty analysis

Five scenarios were assessed in the sensitivity analysis (Table 16). Higher attributable fraction reduced the average cost per DALY averted by 19-86% compared to the base case, but removal

of sharps waste management costs 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 to initial baseline estimates. However, even under this worst-case scenario, the average cost-effectiveness ratio of all interventions remained below the threshold of average annual income per capita (Table 16). 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 sub-regions for a small health gain achieved at a low cost. At higher levels of resource availability, a combination approach would be the most efficient choice for considerably greater 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 appear an unaffordable gold standard where sterilizable injection equipment is still in use, particularly in view of the fact that safe injections yield benefits in terms of death and disability prevented far ahead in the future.[212] However, in Burkina Faso, it was estimated that purchasing injection equipment in quantities that match injectable medicines only increased essential drug expenditures by 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 on the cost of injectable medicines that may be redirected to finance injection equipment for those injectable medicines that are necessary.

In all sub-regions analyzed here, each DALY averted through national policies for the safe and appropriate use of injections costs 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. [213] When recently compared with other

strategies to reduce leading risk factors for disease, safe and appropriate use of injections leads to a modest reduction in DALYs but was one of the most cost-effective interventions. [207] When compared with other modes of HIV infection prevention in sub-Saharan Africa, the cost-effectiveness ratio of policies for the safe and appropriate use of injections remained under the threshold of I$ 50 per DALY averted, in the range of the most cost-effective interventions to prevent HIV infection (e.g., blood safety, targeted condom distribution and treatment of sexually transmitted diseases).[214] Policies for the safe and appropriate use of injections are a natural addition to universal infant vaccination against hepatitis B in a national strategy to prevent HBV infection. Infant immunization against hepatitis B is probably more cost-effective than the safe and appropriate use of injections with cost per life year saved ranging from I$ 4 to I$ 36.[215] However, when global efforts for universal vaccination of infants will have reached sufficient coverage for a sufficient period of time, high levels of immunity against HBV infection will ultimately protect populations from injection-associated HBV infection.

A safe injection is defined as one that does not harm the recipient, the provider and the members of the community at large (Chapter 3).[216] To take this into account, we included the costs of sharps waste collection and management as part of programme costs. However, we were not able to estimate the effect of safe sharps waste collection and management in terms of burden of disease prevented secondary to needle-stick injuries among health care workers or the community. Thus, such a policy may be more cost-effective than our results suggest. Our 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.

This study was not an attempt to compare various injection technologies. Our model did not consider the use of sterilizable injection equipment in any of the interventions. There is no data available to indicate that the use of sterilizable injection equipment can lead to safe injection practices. In fact, the use of sterilizable injection equipment has been specifically associated with infections with bloodborne pathogens [86,77,88,37] and health systems making use of sterilizable syringes have poorer practices than those making use of single use equipment.[59] We did not make any special reference to the use of auto-disable (AD) injection equipment that inactivates itself after one use.[184] AD syringes offer the highest level of safety and are now considered the standard for the administration of vaccines. However, immunization injections only account for less than 10% of all injections (Chapter 1). Thus, introduction of AD syringes in immunization services will only address a small proportion of the burden of disease associated with unsafe injections. With respect to use of AD syringes in curative services, while single use syringes can be reused,

we were unable to identify effectiveness data indicating that when compared with standard single use syringes made available in sufficient quantities, AD syringes would be associated with safer injection practices. Nevertheless, AD syringes should be considered for use in settings where unsafe practices are common, particularly in the informal sector, specifically in South Asia.[39,41] In such cases, the results of our analysis could be easily extrapolated to AD syringes since 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 while international retail prices for single use syringes ranged from four [2 ml] to eight [5 ml] US cents. Our study presented a number of limitations. First, our model did not take into account any longer term dynamic effects that the reduction of transmission would have on the prevalence of infections with bloodborne pathogens. This may be a problem in the case of HCV infection as contaminated injections account for a high proportion of new infections. This limitation could also have led to an underestimation of the effect size that in turn would lead us to describe these interventions as less cost-effective than they really are. Second, we did not address the specific issues associated with working in the private sector. Provision of sufficient quantities of single use injection equipment and interactional group discussion may not be sufficient where the informal private sector accounts for a high proportion of health care services delivery. In such settings, demonstration projects should identify effective strategies, some of which may include the use of AD syringes in curative services and/or addressing financial incentives to over-prescribing injections. Because we did not have information on the proportion of injections administered in the private sector, we were unable to include this factor in our sensitivity analysis. Third, we used interactional group discussions as a template to estimate the cost and the effectiveness of interventions to reduce injection use. Interactional group discussion was the best scenario to use as (1) they have been well evaluated and (2) they represent a substantial investment in human resources that could be invested in other types of interventions to reduce injection use. However, interactional group discussions have only been used in Indonesia. In addition, they only represent one of various strategies that may be used to reduce injection use. Thus, the effetiveness reported in Indonesia may not be generalizable to a model that assumes their scaled-up implementation in other developing and transitionnal countries. Fourth, the effectiveness of interventions to supply single-use injection devices was estimated on the basis of studies that were of lower scientific quality (e.g., before-after comparison without control groups and historical comparisons, Chapter 4). Thus, the estimates is subject to uncertainty and the lower estimate used for the worst case scenario was chosen arbitrarily.

Poor injection practice is not a leading cause of disability and death worldwide. However, safe and appropriate use of injections 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 reuse of injection equipment is common and where the HIV epidemic is generalized. 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 health care service delivery.

Table 14: Contaminated injections in the year 2000, secondary attributable and avertable burden of disease for the period 2000-2030

		AFRICA		THE AMERICAS		EASTERN MEDI-TERRANEAN	EUROPE		SOUTH EAST ASIA		WESTERN PACIFIC	
		AFR D	**AFR E**	**AMR B**	**AMR D**	**EMR D**	**EUR B**	**EUR C**	**SEAR B**	**SEAR D**	**WPR B**	**ALL**
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 *		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 *		19%	17%	1.2%	11%	70%	1.2%	11%	30%	75%	30%	39.8%
Total burden 2000-2030 *		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 2000-2030	**Reduction of injection use** †	166 693	500 575	2 725	8 200	167 911	1 044	19 420	84 237	1 416 260	386 241	2 753 304
	Reduction of unsafe use ‡	527 862	1 585 154	8 629	25 965	531 717	3 305	61 496	266 749	4 484 823	1 223 096	8 718 795
	Combined interventions §	536 197	1 610 182	8 765	26 375	540 112	3 357	62 467	270 961	4 555 636	1 242 408	8 856 461

* "Do nothing" scenario.

† Interactional group discussions between patients and providers to reduce injection use.

‡ Provision of single use, disposable syringes and needles for all injections.

§ Safe and appropriate use of injection policies combining the two interventions above.

Table 15 Costs and cost-effectiveness of policies for the safe and appropriate use of injections (in international dollars (I$)), 2000

Region	AFR D	AFR E	AMR B	AMR D	EMR D	EUR B	EUR C	SEAR B	SEAR D	WPR B
Total population (million)	*294*	*346*	*431*	*71*	*343*	*218*	*243*	*294*	*1,242*	*1,533*
Gross domestic product (GDP) per capita (I$)	*1,381*	*1,576*	*7,833*	*3,837*	*2,393*	*7,294*	*6,916*	*2,545*	*1,449*	*4,186*
Syringes /needles *										
Syringe/needle sets needed	122,924,628	117,475,114	8,791,014	14,887,078	1,031,154,040	6,553,752	93,625,680	185,105,732	3,725,419,491	1,103,711,844
Syringe/needle costs (I$)	19,176,242	18,208,643	1,116,459	2,084,191	148,486,182	773,343	11,422,333	25,544,591	454,501,178	144,586,252
Programme costs (I$) †										
Reduction of injection use	2,738,289	3,308,975	10,524,021	1,080,717	3,876,085	5,349,039	5,298,743	3,568,129	10,599,413	25,579,948
Reduction of unsafe use	1,602,096	1,391,325	3,189,442	434,498	1,542,952	2,884,373	1,692,560	1,218,867	4,402,415	8,452,776
Combination	3,553,983	3,711,160	11,020,206	1,205,776	4,234,537	6,922,989	5,554,346	3,757,891	11,812,493	27,164,652
Total cost per year (I$)										
Reduction of injection use	2,738,289	3,308,975	10,524,021	1,080,717	3,876,085	5,349,039	5,298,743	3,568,129	10,599,413	25,579,948
Reduction of unsafe use	20,778,338	19,601,204	4,305,901	2,518,893	150,029,134	3,657,716	13,114,893	26,763,458	458,903,593	153,039,028
Combination	22,730,225	21,922,514	12,136,665	3,290,463	152,720,719	7,696,332	16,976,679	29,302,482	466,313,671	171,750,904
Average CER (I$ per DALY averted)										
Reduction of injection use	16	7	3,862	132	23	5,124	273	42	7	66
Reduction of unsafe use	39	12	499	97	282	1,107	213	100	102	125
Combination	42	14	1,385	125	283	2,293	272	108	102	138
Incremental CER (I$ per DALY averted) ‡										
Reduction of injection use	16	7	-	-	23	-	-	42	7	66
Reduction of unsafe use	50	15	499	97	-	1,107	213	127	-	152
Combination	234	93	57,579	1,882	400	77,666	3,977	603	145	969

* Syringes and needle costs include the international retail price, international transport and waste management (domestic transport included under programme costs). Not applicable to interventions to reduce injection use.

† Programme costs include personnel, transport, equipment and supplies but exclude syringes and needles sets.

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

Table 16: Sensitivity analyses for the estimate of the average cost-effectiveness ratios of interventions for the safe and appropriate use of injections (expressed in international dollars (I$)) per DALY averted *

Sensitivity scenario	AFR D	AFR E	AMR B	AMR D	EMR D	EUR B	EUR C	SEAR B	SEAR D	WPR B
1. Higher attributable fraction †										
Reduction of injection use	13	5	523	44	17	1,394	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
2. Higher attributable fraction, no sharps waste management										
Reduction of injection use	13	5	523	44	17	1,394	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
3 Lower attributable fraction										
Reduction of injection use	22	9	N/A	N/A	45	N/A	970	57	11	N/A
Reduction of unsafe use	52	16	N/A	N/A	544	N/A	758	136	156	N/A
Combination	56	18	N/A	N/A	546	N/A	967	146	156	N/A
4. Lower attributable fraction, minimum effectiveness										
Reduction of injection use	93	37	N/A	N/A	191	N/A	4,159	245	49	N/A
Reduction of unsafe use	99	31	N/A	N/A	1,035	N/A	1,441	258	296	N/A
Combination	106	34	N/A	N/A	1,038	N/A	1,838	278	296	N/A
5. Lower attributable fraction, minimum effect, double injection sets										
Reduction of injection use	93	37	N/A	N/A	191	N/A	4,159	245	49	N/A
Reduction of unsafe use	190	60	N/A	N/A	2,058	N/A	2,696	504	589	N/A
Combination	196	62	N/A	N/A	2,046	N/A	3,074	520	585	N/A

* Not applicable (N/A) refers to lower attributable fraction equals to zero; CER cannot therefore be calculated.

† Attributable fraction refers to the fraction of new HBV, HCV and HIV infections attributable to contaminated injections.

Conclusion

1. Context of this work and main objectives

In 1999, a review of the literature suggested that poor injection practices required more attention from public health policy-makers.[1] This review drew three main conclusions. First, high rates of injection use were reported from many developing and transitional countries. Second, a substantial proportion of these injections was administered under non-sterile circumstances. Third, epidemiological studies conducted in selected countries suggested that receiving health care injections could transmit HBV and HCV on a large scale and was associated with HIV infection. However, a number of elements were missing. No regional estimates were available for the frequency of injections and the proportion of injections given with injection equipment reused in the absence of sterilization. The proportion of new HBV, HCV and HIV infections attributable to contaminated health care injections was not estimated. There was no evidence-based international consensus over what constituted a safe injection. More importantly, it was unclear what strategies were effective at reducing injection use or the unsafe use of injections. Finally, no economic analysis was available to determine whether investing in the safe and appropriate use of injections was a cost-effective use of financial resources in countries where poor injection practices occur.

The goal of this work was to constitute an evidence base that would support national policies for the safe and appropriate use of injections. First, we estimated the annual number of injections per person and the proportion of injections given with a syringe and or a needle reused in the absence of sterilization in selected regions of the world (Chapter 1). Second, we participated in the Comparative Risk Assessment component of the 2000 update of the Global Burden of Disease study and used mathematical models to estimate the proportion of HBV, HCV and HIV infections that were attributable to contaminated health care injections in the year 2000 (Chapter 2).[94] Third, we reviewed the evidence available on infection control practices with respect to administering injections to formulate evidence-based best infection control practices for intradermal, subcutaneous and intramuscular injections using the new WHO proposed framework to formulate evidence-based guidelines (Chapter 3). Fourth, we reviewed evidence available on the effectiveness of interventions to reduce injection use and to achieve safe injection practices to estimate their effectiveness and identify successful prevention strategies (Chapter 4). Finally, we participated in the WHO CHOICE project to estimate the cost-effectiveness of national policies for the safe and appropriate use of injections in terms of cost

per DALY averted (Chapter 5). None of these studies provide a final answer to the research questions that they tried to address and uncertainty remains. However, our conclusions summarized below allow us to propose a conceptual framework to benchmark, assess, plan, implement and evaluate national policies for the safe and appropriate use of injections (Appendix 1).

2. Key conclusion points

2a) In developing and transitional countries, 16 thousand million injections are administered each year for a ratio of 3.4 injections per person that suggests a gross overuse of injections

In the 10 of the 14 global burden of disease regions included in our study, over 16 thousand million injections are administered each year, for an average of 3.4 injections per person (Chapter 1). However, we were unable to estimate the distribution of these injections received between various injection providers, indications and health care settings. The heterogeneity of injection frequency across regions and the high number of injections per person suggest that injections are grossly overused in most developing and transitional countries. However, studies were not available in sufficient numbers to allow the estimation of the proportion of these injections that are unnecessary. Unnecessary injections represent a major wastage of health care resources. This wastage is distributed among four expenses. First, the cost of injectable medications (the median international retail price of the injectable medications on the WHO model essential drugs list is US$ 0.5 per dose). Second, the cost of injection equipment (the average international retail price of a new syringe and needle set is US$ 0.05). Third, the prescriber's fee for service. Fourth, the injection provider's labour. These expenses that are often incurred out of patients' pockets probably sustain injection overuse through provision of a financial incentive to physicians, pharmacists and nurses to prescribe, dispense and administer injectable medicines. Injection overuse is commonly attributed to the preference for injections among patients. Qualitative assessments and Knowledge, Attitude and Practices (KAP) studies conducted among patients and health care providers suggest that while perceptions that injectable medicines are more effective or work faster are prevalent in general populations,[3] most patients do not prefer injectable medications for the treatment of common ailments (Abstract 4, Abstract 13).[217,27,28] In fact, health care providers overestimate patients' preference for injections (Abstract 3).[55,52] Thus, in contrast to what many public health specialists may think, injection overuse is driven to a large

extent by health care providers on the basis of financial incentives and inaccurate perceptions of their patients' preferences.[52]

2b) In developing and transitional countries, approximately one third of all injections are administered with injection equipment reused in the absence of sterilization

Reducing injection overuse would only be a matter of promoting rational use of essential medicines if injections were administered safely. However, the results of our analysis indicate that injections are given in a way that may harm the injection recipient. Overall, the proportion of injections administered with equipment reused in the absence of sterilization was 39.3%, ranging from 1.2% in Latin America to 75% in South Asia (Chapter 1). Determinants of these unsafe injection practices include the lack of supplies of new, single use injection equipment, the lack of awareness among patients and providers regarding the risks associated with unsafe practices and the absence of an efficient sharps waste management system to prevent illegal re-processing for re-packaging of used injection equipment.

2c) In the year 2000, the combination of injection overuse and unsafe practices may have accounted for one third of new HBV infections, 40% of new HCV infections and 5% of new HIV infections

In the year 2000, four decades after the widespread availability of single use injection equipment and two decades into the HIV pandemic, contaminated injections may still account for close to one third of new HBV infections, 40% of new HCV infections and five percent of new HIV infections. Injection-associated HBV, HCV and HIV infections acquired in the year 2000 will translate into 9 177 679 discounted and age-adjusted disability-adjusted life years (DALYs) between 2000 and 2030 because of fulminant hepatitis, AIDS, hepatocellular carcinoma and end-stage liver disease (Chapter 2). This burden of disease accounts for less than one percent of the total burden attributable to 20 main risk factors to health that are avoidable.[94] Thus, contaminated injections in health care settings are not a leading cause of death and disability worldwide. However, in contrast to some other risk factors responsible for a higher burden of disease (e.g., tobacco use, hypertension), interventions to achieve the safe and appropriate use of injections may be simpler to conduct and more effective. A majority of the burden of disease associated with contaminated health care injections (63%) is secondary to injection-associated HIV infections (Chapter 2). Thus, the fraction of HIV infections attributable to contaminated health care injections and the uncertainty around its estimate is a key element in apprehending the burden of disease secondary to this public health problem.

2d) Best infection control practices could make injections safer for the recipient, the health care worker and the community

The proportion of injections administered with a syringe and or a needle reused in the absence of sterilization was a key input parameter in our burden of disease model (Chapter 2) and is used as a critical indicator of injection safety.[20] Reuse of injection equipment is the focus of much attention as it leads to more burden of disease (260 000 HIV infections worldwide annually, Chapter 2) than needle-stick injuries among injection providers (1 000 HIV infections worldwide annually).[179] However, a safe injection is one that should be completely safe to the patient, the health care worker and the community. Thus, in addition to using new, single use injection equipment, additional infection control steps are needed to make injections safe for the recipient and to prevent needle-stick injuries. Eliminating unnecessary injections is the highest priority towards preventing injection-associated infections (Chapter 3). However, when injections are medically indicated, evidence-based best infection control practices for intradermal, subcutaneous or intramuscular injections include (1) the use of sterile injection equipment, (2) the prevention of contamination of injection equipment and medication, (3) the prevention of needle-stick injuries to the provider and (4) the prevention of access to used needles (Chapter 3). These best practices may be achieved if injection providers are trained in these safe techniques and if sufficient quantities of injection equipment (i.e., single use syringe and needle sets) and infection control supplies (i.e., puncture- and liquid- proof containers for the collection of sharps waste) are made available. Engineered technologies have been developed to support safer injection practices. These include auto-disable syringes that make the reuse of injection equipment difficult or impossible through plunger blocking, plunger breaking or needle retraction and safety syringes that prevent needle-stick injuries.

2e) Effective interventions are available to reduce injection use and to achieve a safe use of injections

While the danger of injection overuse and unsafe practices has been underlined for a few decades, the safe and appropriate use of injections remains elusive. This lead to a widespread perception among public health policy makers that poor injection practices are a chronic plague of health systems and that no effective interventions are available. The data does not support that complacency. In our review of studies that allowed the estimation of the effectiveness of interventions to reduce injection use and achieve safe practices, all studies demonstrated some degree of effectiveness. The effectiveness of interventions to reduce injection use ranged from

1% to 53% (Chapter 4). While interventions targeting providers are keys to change prescribing practices, interventions that targeted providers and the general population achieved a higher median effectiveness than interventions targeting providers alone. Among all these interventions, patient/provider interactional group discussions (IGD) to change prescribing behaviours stood out as a successful strategy that was well described and well evaluated.[52] The effectiveness of interventions to reduce unsafe use of injections ranged between 30% and 82% (Chapter 4). Among the interventions to improve injection safety, provision of sufficient quantities of new, single use injection equipment was highly effective in reducing unsafe injection practices. Interventions to reduce injection use and to reduce the frequency of unsafe injections can be recommended for wider use. Implementing them as a joint safe and appropriate use of injection strategy may generate opportunities for synergy and reinforce messages to yield additional effectiveness benefits.

2f) Interventions for the safe and appropriate use of injections can be considered very cost-effective on the basis of a cost per DALY averted that is below one year of average per capita income

We evaluated the cost-effectiveness of interventions for the safe (i.e., provision of new, single use injection equipment) and appropriate use of injections (i.e., interactive, patient-provider group discussions) separately and in combination in the regions where the burden from unsafe injections is substantial. Reducing unnecessary use of injections will have a lower total impact on population health than reducing reuse of injection equipment without sterilization (Chapter 5). The effect of doing both at the same time is less than additive, although doing both together does improve population health to a greater extent than doing simply one. In approximately half the sub-regions, reducing reuse is also the most cost-effective option. However, in the other regions, behavioural interventions to reduce overuse are more cost-effective than interventions to reduce reuse, which require large quantities of injection equipment. In all regions, combined interventions for the safe and appropriate use of injections had a cost-effectiveness ratio well below the cut-off point of one gross domestic product per capita for each DALY averted (Chapter 5). On that basis and according to the criteria proposed by the WHO report of the commission on macroeconomics and health,[213] the safe and appropriate use of injections may be considered a very cost-effective intervention.

3. Remaining areas of uncertainty

The relative frequency of injection use can be compared across world regions. Similarly, injection safety assessments provide a good understanding of the worldwide distribution of reuse of injection equipment in the absence of sterilization. Best infection control practices for intradermal, subcutaneous and intramuscular injections are well characterized. Interventions that are successful in decreasing injection use or unsafe use injection are identified and economic evaluations suggest that these constitute a very cost-effective use of health care resources. However, uncertainty remains in the understanding of unsafe injection practices, their determinants and their consequences. First, injection frequency estimates do not translate easily into figures that can be used to forecast needs in injection equipment. Second, breaks in infection control practices other than reuse of injection equipment are not well described. Third, the proportion of HIV infection attributable to contaminated health care injections is uncertain. Fourth, the role of engineered technologies in interventions to achieve injection safety is unclear. Fifth, experience is limited in scaling up interventions for the safe and appropriate use of injections. Finally, cost-effectiveness models need to be validated through real-size economic analysis of in-country interventions. We will now review these areas of uncertainty.

3a) Routine methods are needed to describe injection use and quantify needs of injection equipment

The population-based surveys and the prescription reviews that we used allowed the generation of estimates of the annual number of injections per person and per year. This indicator can be used to document high levels of injection use, suggest injection overuse and compare injection frequency across regions. However, it is unclear whether the mean number of injections per person and per year obtained using our methods can be used to forecast needs in injection equipment. Within a population, the frequency distribution of the number of injections received is heterogeneous. There is a small proportion of the population in which injection use is clustered and where the number of injections received is high (e.g., diabetics, patients hospitalized in surgery or in intensive care). The studies that we reviewed may have had too small a sample size to include these rare individuals in sufficiently large numbers to describe injection practices among them. Thus, the results of our analysis may underestimate the total number of injections received in the population. To account for this uncertainty, we ran a sensitivity analysis in our cost-effectiveness model where we multiplied by two the number of syringe and needle sets needed (Chapter 5). In practice, for supply management purposes, two approaches have been

used to estimate injection equipment needs. First, epidemiologists who tend to be population-focused have conducted population-based injection frequency surveys based upon the self-reported number of injections received. However, this approach does not capture well the high level of injection use that is clustered in specific settings. Second, marketing specialists who tend to be device-focused have studied the number of syringes and needles sold in a country. However, this approach does not capture well the number of times that a syringe and needle set may be reused. These two types of approaches should be combined to ensure appropriate forecasting of injection equipment needs. Studies could compare (1) population-based injection frequency estimates with (2) market data on the consumption of injection equipment, which could include specific consumption surveys in programmes and settings where injection use is particularly high. Collaboration between the private and the public sector may be useful in that regard. Procurement units in Ministries of Health could benefit from these accurate forecasting methods to provide injection equipment in quantities that are sufficient to prevent shortages. [227]

3b) Unsafe injection practices need to be described in greater detail to prevent all opportunities of bloodborne pathogen transmission

The reuse of injection equipment in the absence of sterilization is an indicator that is somewhat arbitrary and that does not reflect the variety of breaks in infection control practices that may occur in health care settings. These include the immediate reuse of a syringe and needle set on a second patient, the reuse of a syringe and needle set on multiple patients, the reuse of a syringe although the needle has been changed, the reuse of injection equipment after rinsing in a pot of tepid water, the reuse of injection equipment after an inappropriate or incomplete sterilization procedure (e.g., boiling), the reuse of injection equipment on a same patient in combination with the use of a multi-dose medication vial, the preparation of injections in areas potentially contaminated with blood and body fluids and the reuse of injection equipment to administer intravenous medications to hospitalized patients in intravenous catheters in which reflux may occur. Thus, tools developed to assess [20] or to supervise [218] injection practices should use the checklist proposed by the best infection control practices for intradermal, subcutaneous and intramuscular injections (Chapter 3) to ensure that all breaks of infection control practices are identified, quantified and prevented.

3c) Better estimates of the proportion of HIV infections that may be attributed to unsafe health care injections are needed

In the case of HBV and HCV infection, epidemiological studies assessing the association between injections and infections are available to validate the results of our estimates of the proportion of HBV and HCV infections attributable to injections. In contrast, in the case of HIV, epidemiological studies are limited to sub-Saharan Africa where they suggest that our estimate is conservative. In Asia, our high attributable fractions are not validated by epidemiological studies and may be overestimated. At the end of the 1980s, the consensus among public health officials involved in the prevention of HIV infection evolved towards the concept that unsafe health care injections only account for a small proportion of all HIV infections.[219] Since then, the achievement of safe health care injections has not received a high level of attention in HIV prevention and care programmes,[220] often because of a fear of "diluting the message" that sex is the main driver of the HIV epidemic. In addition, most epidemiological studies estimating the relative importance of various potential sources of HIV infection in developing and transitional countries have not fully examined the role of health care injections in HIV transmission. Questionnaire items were either missing or not adapted. When data were collected, they were often not analyzed or not reported. Today, the uncertainty around the proportion of HIV infections attributable to unsafe health care injections has generated a controversy.[95] Researchers reviewed prevalent and incident analytical epidemiological studies to suggest that the fraction of HIV infection attributable to health care injections could be as high as 20-40% in sub-Saharan Africa.[95] Others argue that reverse causation is possible as most of the evidence available is based upon cross-sectional studies that do not disentangle health care injections as an exposure from a variety of confounding factors, including sexually transmitted infections that may lead to health care visits. This unresolved issue will have to be addressed through prospective case control and cohort studies examining the risk of HIV infection associated with health care exposure in a way that allows for the control of confounding factors. In the meantime, progress has been achieved in that irrespective of the fraction of HIV attributable to unsafe health care injections, it is considered that unsafe health care injections should not occur. Communication of the results of the Global Burden of Disease study within WHO has led the department of HIV/AIDS to make a number of key decisions. First, the safe and appropriate use of injections is now considered one of the 10 key elements of a national strategy for the prevention and care of HIV infection along with health care worker protection.[221] Second, a time-bound milestone now proposes that by 2005, all supplies of injectable substances,

including vaccines and essential medicines should be delivered with matching quantities of single use injection equipment.[222] Third, a meeting of consultants held at WHO on 13 March 2003 reviewed all data available regarding the proportion of HIV infections that may be attributable to unsafe health care injections. While the majority of HIV infections in sub-Saharan Africa are clearly attributable to unsafe sex, strategies to prevent HIV infection should include strategies to achieve the safe and the appropriate use of injections and adapted epidemiological methods should monitor injection practices as part of HIV prevention indicators.[223]

3d) The role of engineered technologies in policies to achieve injection safety is unclear

The best infection control practices for intradermal, subcutaneous and intramuscular injections as we defined them do not address the use of specific safety injection devices, allowing the development group to avoid issues that could lead to actual or perceived conflicts of interest. Newer technologies supporting a safer use of injections have been developed.[184] Auto-Disable (AD) syringes are engineered to inactivate themselves by plunger blocking, plunger breaking or needle retraction to prevent reuse of injection equipment. Other safety mechanisms have been engineered to prevent needle-stick injuries among health care workers (Chapter 3). WHO, UNICEF and UNFPA formulated a policy statement in 1999 to recommend the exclusive use of auto-disable injection equipment in immunization services by the end of 2003. [180] However, in curative services, the effectiveness of these engineered technologies in preventing specific unsafe practices is unknown. In the absence of evidence, a policy statement cannot be formulated to recommend their wide-scale use. Well-monitored comparative field studies will need to determine whether auto-disable syringes lead to safer injection practices than single use syringes provided in sufficient quantities. Such field studies will need to be conducted in a variety of geographical settings and health systems, including the informal private sector. Identification of independent funding sources may help prevent actual or perceived conflicts of interest in the financing of such studies. In practice, to ensure that such studies are conducted, as the results of our research suggest they should be, the industry needs the expression of a sufficient level of interest in curative-size auto-disable syringes to develop products and make them available for evaluation. Thus, to facilitate research and development, open a market for the industry and make products available for broader assessment in curative health care services, WHO made the strategic choice to recommend the use of curative size auto-disable syringes in selected donor- or lender-supported programmes making use of injections (e.g., tuberculosis treatment with streptomycin in the context of the Global TB Drug Facility of the Stop TB alliance). This initial support to the

introduction of auto-disable syringes through programmes funded through donors and lenders will provide opportunities to recover experience associated with the use of auto-disable syringes in curative services through systematic assessments. This experience will ultimately generate the body of evidence upon which a future policy decision will be based.

3e) More experience is needed in the scaling-up of successful interventions to reduce injection use and achieve safe injection practices

WHO proposes that national policies for the safe and appropriate use of injections be based upon (1) behaviour change among patients and health care workers to decrease injection overuse and achieve safe injection practices, (2) provision of sufficient quantities of injection equipment and infection control supplies and (3) sharps waste management.[65] The three interventions recommended as components of this strategy have been conducted individually or on a pilot level. However, limited experience is available on the implementation of multidisciplinary national strategies for the safe and appropriate use of injections that include these three elements. Interventions to reduce injection use, including interactional group discussions, have mostly been conducted as well-evaluated, pilot research projects but have rarely been scaled up as national policies (Chapter 4). In contrast, provision of sufficient quantities of single use injection equipment to improve injection safety has mostly been implemented as national policies that have not always been evaluated prospectively (Chapter 4). There are two challenges to overcome to successfully scale up national policies for the safe and appropriate use of injections. First, cross-departmental collaborations within the Ministry of Health need to integrate the multidisciplinary interventions required in the routine of health care service delivery. While a national strategy for the safe and appropriate use of injections should not be implemented as a separate programme, let alone a vertical one, integration raises additional difficulties as tasks and responsibilities need to be distributed, coordinated and evaluated across health programmes and services. Second, there is a need to address the overuse and unsafe use of injections in the informal, private sector, particularly in South Asia [39,41] where these providers account for a high proportion of health care services delivery. Interventions in the informal, private sector may require specific strategies, including mechanisms to address the financial incentives for injection overuse and the introduction of auto-disable syringes. Scaled-up national demonstration projects in selected countries in various regions of the world would assist in overcoming these two challenges. Such demonstration projects would generate an experience that could be recovered to

offer practical guidance to other countries regarding the steps and processes to follow for a successful scale-up.

3f) Cost-effectiveness assessment of scaled-up national interventions are needed to validate the results of our cost-effectiveness estimates

We generated our cost-effectiveness estimates using mathematical models based upon a number of assumptions, including the proportion of HIV infections attributable to unsafe health care injections, the assumed effectiveness of selected interventions and the theoretical costing exercises that WHO conducted as part of the CHOICE project.[207] This approach remains subject to a number of limitations (Chapter 5). A stronger confidence in the cost-effectiveness of national policies for the safe and appropriate use of injections may be obtained through a cost-effectiveness analysis conducted on the basis of the evaluation of a scaled-up national demonstration project. As a practical next step, implementation of this approach on scale in a single high-burden country in a region where the model generated a high cost-effectiveness ratio would allow to evaluate the assumptions of this model. To achieve this, costs and effects will need to be closely monitored throughout a study design that will have to be integrated into the intervention itself. Thus, better cost-effectiveness estimates will be both a direct consequence of the first scaled-up national interventions and the condition for implementation of similar policies in additional countries.

4. Recommendations for prevention strategies

From evidence to policy

Throughout our work, we provided evidence indicating that the combination of injection overuse and unsafe practices transmit HBV, HCV and HIV on a large scale worldwide, causing substantial death and disability. To prevent the consequences of unsafe injections, we formulated best practices, identified the interventions that are successful in implementing them and estimated the cost-effectiveness of these prevention strategies. Evidence and information need to translate into public health action that may be implemented more effectively if it is seen as a quality cycle.

The injection safety planner

A national policy for the safe and appropriate use of injections should not be seen as a static document. Rather, it is a process by which a standard is developed, the current situation is

assessed, a plan is made, actions are implemented and an evaluation measures progress. This "quality cycle" that includes five steps is outlined below and developed further in the injection safety planner ("Managing an injection safety policy", see Figure 7, Appendix 1).

Setting a national standard ("Benchmarking")

Benchmarking defines the ideal system and its indicators. WHO best infection control practices for intradermal, subcutaneous and intramuscular injections may be used as a template for a national standard that can be defined through an involvement of all stakeholders.

Assessing practices

Assessment will determine how the current system differs from the ideal one on the basis of selected indicators (Abstract 10). A set of input, process and outcome indicators identified as key to estimating the burden of disease associated with unsafe injections were developed together with rapid assessment tools to collect them (See Table 17 in Appendix 1).

Planning for change

A planning process will set the objectives and targets to reach the ideal system. Ideally, a template plan should include five key elements:

1. HIV prevention and care programme to communicate the risk of HIV infection associated with poor injection practices;
2. National drug policy to prevent injection overuse;
3. Essential drug system supplies to make syringes and sharps boxes available in every health care facility;
4. Immunization and family planning to deliver injectable substances with auto-disable syringes and sharps boxes;
5. Health care system to manage sharps waste.

Implementing multidisciplinary interventions

Implementation will conduct interventions to reach the targets and improve the system.

Evaluating impact

Evaluation will measure progress towards the objectives and targets. A supervision process based upon the best practices will facilitate evaluation and provide guidance through reinforcing good practices and proposing strategies to improve weak ones.

Convincing finance committees to invest in injection safety

The approach proposed in the injection safety planner has never been attempted in real size at country level. This lack of experience is a substantial barrier to securing funds for implementation. A national programme would require a specific budget to cover the various components of the recommended multidisciplinary approach. Governments of low income country have several budgetary constraints, including a limited capacity to collect revenues and extreme competition for resources. Cost-effectiveness estimates are unlikely to be sufficient to convince finance committees of the need to invest in an intervention that addresses less than one percent of the burden of disease. While international donors and lenders might have some interest in this issue because of the cost-effectiveness ratio, external ongoing support for these initiatives in priority countries is unlikely. Thus, the remaining challenge is to acquire practical experience in the mechanisms that would reduce the costs of the intervention (e.g., financing single-use injection devices through a cut in purchases of unnecessary injectable medicines) and that would break down these costs into smaller manageable pieces that could be spread over essential components of various routine programmes (e.g., Behaviour change campaigns of HIV/AIDS prevention and care programmes, essential medicines procurement, training and supervision in immunization services and health care waste management within health care services delivery).

The elephant, the mouse and the wise old owl

The elephant and the mouse who had wanted to get married in spite of the resentment of their families had been most happy with the advice from the wise old owl of the forest a year beforehand. At that time, she suggested that they listen to their hearts to move forward with what, to the best of their awareness, was a good move. When they went to see her again in the forest the following year looking for more words of wisdom to build a family, she replied with the most humble tone:

- *"Uh-Oh! I am sorry, I am an expert in policy, but not in implementation."*

Table of appendices (including abstracts)

Appendix 1: Managing an injection safety policy

A framework to benchmark, assess, plan, implement and evaluate a national strategy for the safe and appropriate use of injections

Introduction

Rationale

Unsafe injection practices are common worldwide (see Chapter 1).[1] Due to the overuse of injections in many countries, unsafe injections cause a substantial proportion of infection with bloodborne pathogens.[16] At risk of infection are injection recipients and health care workers through contaminated needles and syringes and the community at large through exposure to contaminated sharps waste. A mathematical model has been used to estimate the burden of disease from unsafe injections in various regions (see Chapter 2). According to its estimates, unsafe injections accounted for 32% of hepatitis B virus infection, 40% of hepatitis C virus infection, 28% of liver cancer, 24% of cirrhosis and 5% of HIV infections in the year 2000 (Chapter 2). Overall, about 500 000 deaths per year are attributable to contaminated injections in health care settings worldwide (Chapter 2).

What is the objective of this document?

This guide is designed to assist in benchmarking, assessing, planning, implementing and evaluating a national strategy for the safe and appropriate use of injections.

Who should use this document?

This framework is to be used – and adapted – by national public health managers and their national and international partners.

Elements of a national strategy for the safe and appropriate use of injections

A national strategy for the safe and appropriate use of injections should be viewed as a process by which a national standard is developed, the current situation is assessed, a plan is made, actions are implemented under continuous monitoring and an evaluation is done to measure progress. In fact, public health strategies can be seen as a "quality cycle" that includes five steps (Figure 7):

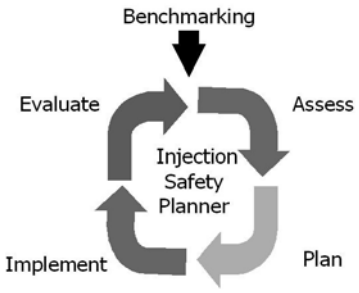


Figure 7: The quality cycle

Standard setting (benchmarking)

Benchmarking defines and re-defines the standard (the ideal system) and its indicators.

Assessing

Assessing consists of determining how the current system differs from the ideal one on the basis of selected indicators.

Planning

Planning allows the setting of objectives and targets to reach the ideal system.

Implementing

Implementing is about conducting interventions to reach the targets and improve the system.

Evaluating

Evaluating is done through measuring progress towards the objectives and targets.

1. Setting a national standard ("Benchmarking")

Rationale

Before engaging on an assessment of injection practices, it is useful to set a national standard. Injection practices may be described using a set of key indicators. Each of these indicators has an ideal value (see Table 17). The national standard will define a target value and the assessment determines how much the current situation differs from this target.

Objective

A national standard for injection practices is defined that addresses (1) injection overuse, (2) injection safety, (3) the type of injection equipment to be used and (4) safe sharps waste management.

Who should set the national standard?

Setting a national standard requires the participation of all stakeholders,[224] including professional associations of health care workers (who prescribe and give injections, e.g., physicians and nurses), infection control practitioners (who define infection control standards), health system managers (who define standards of care) and procurement units (who purchase necessary equipment and supplies).

How to make it happen?

Injection use

National standard treatment guidelines may be used to define the clinical situations for which injections are justified.

Injection safety

The best practices may be used as a basis to describe the steps that make an injection safe or unsafe (Chapter 3).

Injection equipment to be used

The choice of injection equipment to be recommended (sterilizable, single use or auto-disable) may be an issue for which consensus is difficult to reach. Two elements should be taken into consideration. First, WHO best practices recommend single use injection equipment (standard or

auto-disable) for all injections (Chapter 3). Second, WHO, UNICEF, UNFPA and IFRC recommend that immunization services should exclusively use auto-disable injection equipment by the end of 2003. [180] Sterilizable injection equipment should only be considered if (1) sufficient quantities of single use injection equipment cannot be made available and (2) if the quality of the sterilization is documented in registers with Time, Steam and Temperature (TST) spot indicators for all injections. Experience in many developing and transitional countries indicates that the latter condition is rarely met and that only single use injection equipment made available in sufficient quantities can ensure the safety of injections.

Table 17: Key indicators to describe injection practices in a country *

PROGRAMME INDICATORS (INPUT)	IDEAL VALUE	TARGET VALUE
I.1. HIV/AIDS prevention and care programme communicating the risk of HIV infection associated with injections	Yes	
I.2. National drug policy discouraging injection overuse	Yes	
I.3. Number of injectable medications on the national essential drug list	Lowest possible †	
I.4. Essential drugs programme supplying syringes, needles, diluent and safety boxes in quantities matching supplies of injectable medications	Yes	
I.5. Donor or lender-funded programmes such as immunization or family planning services supplying AD syringes and needles in quantities matching supplies of injectables	Yes	
I.6. Health care waste management plan established within the health care system	Yes	
DETERMINANTS OF INJECTION PRACTICES (PROCESS)	**IDEAL VALUE**	**TARGET VALUE**
Injection Use		
P.1. Proportion of the population reporting a preference for injections in the case of fever	< 15 %	
P.2. Proportion of prescribers reporting a preference for injections among patients in the case of fever	< 15% ‡	
P.3. Proportion of the population recalling that the last injection received has been given at home	< 10%	
Injection Safety		
P.4. Proportion of the population spontaneously reporting the risk of HIV infection associated with unsafe injections	100%	
P.5. Proportion of prescribers spontaneously reporting the risk of hepatitis C virus infection associated with unsafe injections	100%	
P.6. Proportion of health care facilities using sterilizable injection equipment	0%	
P.7. Proportion of health care facilities using single use injection equipment	100%	
P.8. Proportion of health care facilities using auto-disable injection equipment	100%	
P.9. Proportion of health care facilities with sufficient stocks of single use injection equipment (in the facility or in a nearby public or community pharmacy)	100%	
P.10. Proportion of injections administered by unqualified or family providers	0%	
INJECTION PRACTICES (OUTCOME)§	**IDEAL VALUE**	**TARGET VALUE**
Injection Use		
O.1. Proportion of prescriptions including at least one injection **	Lowest possible †	
O.2. Average number of injections per prescription (for prescriptions containing at least one injectable medication)	Variable †	
O.3. Average number of injections per person and year	< 1	
Injection Safety		
O.4. Proportion of health care facilities where injections are always given with a sterile syringe and needle	100%	
O.5. Proportion of health care facilities where used injection equipment can be observed in places where they expose health care workers to needle-stick injuries	0%	
O.6. Annual number of needle-stick injuries per injection provider	0	
O.7. Proportion of health care facilities where used injection equipment can be seen in the surrounding environment	0%	

* The difference between the national target value and the observed value from the assessment will determine the objectives of the national injection safety strategy.

† Will vary according to many factors including health care settings, standard treatment guidelines, severity of illnesses when patients seek care.

‡ The value of P.2 should not exceed the value of P.1.

§ Estimation of the incidence of infection-associated infections as outcome indicator of a strategy for the safe and appropriate use of injections requires substantial epidemiological expertise and resources.

** Also referred to as "OT8 indicator" to monitor essential medicine policies.

2. Assessing practices

Rationale

A base of evidence is needed to define the most common and important problems related to injection practices so that the plan of action can be developed and adapted to the local situation.

Objective

Stakeholders are engaged in a process by which they describe injection practices on the basis of up-to-date evidence.

Who should conduct the assessment?

Stakeholders' involvement in all steps of the assessment process will facilitate planning. However, the data collection step requires expertise in the design, implementation, analysis and interpretation of surveys.

How to make it happen?

Key indicators (Table 17) include programme indicators (input), determinants of injection practices (process) and indicators of injection practices (outcome). Two main tools are available to obtain information on these indicators: The "Rapid assessment and response guide" and the "Tool for the assessment of injection safety" (see Table 18). The methods they propose may be combined.

The rapid assessment guide for injection practices [66] aims at engaging stakeholders in launching a planning process through the provision of a simple description of injection practices, their determinants and their consequences. It is based upon combined sampling of injection prescribers, injection providers and the general population. It offers a range of sampling strategies according to the level of precision required and resources available (Abstract 16).

The WHO tool to assess injection safety [20] aims at estimating the proportion of health care facilities engaging in safe injection practices in a standardized way. It is based on a cluster sample of 80 health care facilities and provides representative data on injection practices predominantly in immunization and curative public health care services (Abstract 10, Abstract 11).

Table 18: Compared characteristics of the two WHO assessment tools available

	Rapid assessment and response guide	Tool for the assessment of injection safety
Aim	• Engage stakeholders to launch a planning process	• Estimate the proportion of safe injections as the basis for planning
Focus	• Injection frequency • Injection safety	• Injection safety
Groups surveyed	• General population • Injection prescribers (e.g., physicians) • Injection providers (e.g., nurses)	• Formal health care facilities, most often in the public sector
Precision	• According to sampling strategy	• ± 10% around the estimate
Representativity	• According to sampling strategy	• Good
Qualitative component	• More qualitative	• More quantitative
Potential users	• National essential medicine policy-makers • Injection safety committee	• Expanded Programme on Immunization • Injection safety committee
Cost	• Around US$ 10 000	• Around US$ 20 000

3. Planning for change

Rationale

A successful strategy to achieve safe injection practices requires making deliberate efforts to engage all national programmes and services involving injections. Such a strategy will contain three elements (See "Aide mémoire" for a national safe and appropriate use of injection policy [65]):

1. **Behaviour change** among patients and health care workers to reduce unnecessary injections and achieve safe practices (e.g., through interactional patient-provider group discussions);
2. **Equipment and supplies:** Provision of sufficient quantities of new, single use injection equipment and infection control supplies;
3. **Sharps waste management:** Safe collection and management of sharps waste.

Objective

Different national programme areas establish plans of action based on the assessment results in which they incorporate the three elements of the strategy for the safe and appropriate use of injections. These plans form the blueprint for the implementation of interventions.

Who should formulate the national plan?

Key Ministry of Health departments (including HIV prevention and care, essential medicines, immunization, family planning and health care system) and partners can gather in an initial national workshop. Its participants can then establish a multidisciplinary national committee on injection safety that meets regularly to follow up on the national policy and its implementation through the plan of action.

How to make it happen?

Template agenda for the national workshop

The national workshop can set priorities and define a plan of action on the basis of the assessment results.

Template national plan

A template may be used to generate a national plan of action (see Table 20). The proposed outline makes reference to specific programmes implementing specific activities. Behaviour change activities may be best conducted by the programmes on HIV prevention and care and the

programme on essential medicines. Equipment and supplies may be best provided through the programme on essential medicines and the immunization and family planning programmes. Sharps waste management may be best implemented within the broader health care system. National blood transfusion services will monitor the prevalence of hepatitis B and C viruses and of HIV infection and ensure safe blood donations. Other potential entry points include legislation, regulation and financing of health care services, quality management programmes, human resources training and health promotion. In practice, the actual distribution of tasks may differ according to the organizational chart of the Ministry of Health and the local situation. What matters is that all these activities are conducted regardless of who takes the lead in implementation so that health care workers and the general public receive consistent messages from all programmes.

Setting a timeline

Once a plan is formulated, setting a timeline with designated, time-bound milestones for progress will assist in implementation and monitoring.

Costing, budgeting and financing

Cost estimates for each area of work will facilitate the inclusion of the required elements in the budgets of the various ministries (such as Ministries of Health, Education, Law, Environment) and programmes (e.g., HIV, essential medicines, immunization and health care services). Proper costing (Table 19) and budgeting will also help in identifying sources of funds.

Table 19: Costing elements of a plan of action for the safe and appropriate use of injections

INPUT	Activities					
	Behaviour change		Supplies		Waste management	
	US$	% total	US$	% total	US$	% total
Capital costs						
Information, education and communication material development						
Curriculum development of training materials						
Good manufacturing practices and technology transfer to local producers of injection equipment and safety boxes						
Equipment for waste treatment (e.g. incineration) and waste disposal						
Total capital costs						
Recurrent costs						
Capacity building to use new equipment through pre-service and in-service training						
Revision of standard treatment guidelines and the essential drug list						
Appropriate injection equipment and safety boxes						
Supervision and in-service training on updating skills						
Transport for delivery of supplies and collection of waste						
Contracts for treatment and disposal of contaminated waste						
Fuel and supplies for incinerators						
Information, education, communication and mass media activities						
Interactional group discussions between patients and health care providers						
Total recurrent costs						
TOTAL COSTS						

For calculation of costs of injection equipment and injection control supplies refer to "Procuring single use injection equipment and safety boxes: a practical guide". In countries not yet providing safe injection equipment to all programmes and services, costs for equipment will likely be the major cost elements of a plan of action for the safe and appropriate use of injections.

Option appraisal

A comprehensive option appraisal should present both quantified and non-quantified costs and benefits. Besides the financial implications of a plan of action, other issues to be considered include the technical feasibility, the legal and administrative constraints and the long-term

sustainability in terms of managerial and financial resources. Wider effects of an intended change on the traditional, social or power structure of communities, on employment, equity and gender as well as possible environmental effects need to be equally appraised.

Table 20: Template for a plan of action for the implementation of the national policy for the safe and appropriate use of injections

1. BEHAVIOUR CHANGE			
HIV PREVENTION AND CARE PROGRAMME TO COMMUNICATE THE RISK OF HIV INFECTION ASSOCIATED WITH POOR INJECTION PRACTICES			
Objectives	**Core interventions**	**Beneficiaries / Target groups**	**Indicators**
Achieve safe injection practices	**Create consumer demand for new, single use injection equipment** • Education materials • Mass media	• Patients	• Proportion of the population spontaneously reporting the risk of HIV infection associated with unsafe injections (Indicator P.4)
	Ensure use of new, single use injection equipment • Pre-service and in-service training	• Injection providers (e.g., nurses)	• Proportion of health care facilities where injections are always given with a sterile syringe and needle (Indicator O.4)
	Protect health care workers from needle-stick injuries • Endorsement of best practices by medical and nursing association • Pre-service and in-service training	• Injection providers (e.g., nurses)	• Proportion of health care facilities where used injection equipment can be observed in places where they expose health care workers to needle-stick injuries (Indicator O.5)
NATIONAL DRUG POLICY TO PREVENT INJECTION OVERUSE			
Objectives	**Core interventions**	**Beneficiaries / Target groups**	**Indicators**
Reduce injection overuse	**Promote oral medication** • Education materials • Mass media	• Patients	• Proportion of the population reporting a preference for injections in the case of fever (Indicator P.1)
	Reduce prescription of injectable medications • Standard treatment guidelines • Policy statement from medical association • Interactional group discussions • Reduce financial incentive to provide injections	• Injection prescribers (e.g., physicians, medical assistants, including in the private sector)	• Proportion of prescriptions including at least one injection (Indicator O.1. also referred to as OT8)
	Reduce access to injectable medications • Remove unnecessary injectable medications from the essential drug list	• Health facilities, pharmacies and depots	• Number of injectable medications on the essential drug list (Indicator I.3)

2. EQUIPMENT AND SUPPLIES			
ESSENTIAL MEDICINE PROGRAMME TO MAKE SYRINGES AND SHARPS BOXES AVAILABLE IN EVERY HEALTH CARE FACILITY			
Objectives	**Core interventions**	**Beneficiaries / Target groups**	**Indicators**
Ensure universal access to safe injection equipment and safety boxes	**Deliver injectable medications with matching quantities of injection equipment and injection control supplies when procuring and distributing essential drugs** • Procure syringes, needles, diluents and safety boxes for the collection of sharps • Strengthen the national regulatory authority to ensure the quality of injection equipment	• Public and private health care facilities	• Proportion of health care facilities with sufficient stocks of single use injection equipment (in the facility or in a nearby public or community pharmacy) (Indicator P.9)
IMMUNIZATION AND FAMILY PLANNING PROGRAMMES TO DELIVER INJECTABLES WITH AUTO-DISABLE SYRINGES AND SAFETY BOXES			
Objectives	**Core interventions**	**Beneficiaries / Target groups**	**Indicators**
Make all injectable vaccines and contraceptives available with matching quantities of injection equipment and safety boxes	**"Bundle" injectable vaccines and contraceptives procured by donors and lenders with essential injection equipment and supplies, including:** • Auto-disable syringes and needles • Appropriate diluents • Safety boxes	▪ Immunization services (EPI programme) ▪ Family planning services	• Donor or lender-funded programmes such as immunization or family planning services supplying AD syringes and needles in quantities matching supplies of injectables (vaccines or contraceptives) (Indicator I.5)
3. SHARPS WASTE MANAGEMENT			
HEALTH CARE SYSTEM TO PROPERLY MANAGE SHARPS WASTE			
Objectives	**Core interventions**	**Beneficiaries / Target groups**	**Indicators**
Integrate sharps waste management into a comprehensive national health care waste management plan	**National health care waste management plan** • National policy with regulatory framework • Plan from waste production to disposal • Training at all levels • Procurement of waste treatment options	• Health care facilities • Injection providers • Communities	• Proportion of health care facilities where used injection equipment can be seen in the surrounding environment (Indicator O.7)

4. Implementing multidisciplinary interventions

Rationale

Interventions to decrease both the unnecessary use (i.e., through patient-providers interactional group discussions) and the reuse (i.e., through provision of single use equipment) of injections have been shown to be a very cost-effective investment in health (cost-effectiveness less than the annual gross domestic product per capita, Chapter 5). Implementation of the strategy for the safe and appropriate use of injections across all programmes or services involved in injections will achieve the required consistency in the practices of health care workers.

Objective

Positive changes towards the safe and appropriate use of injections are brought about through (a) effective communication and behaviour change interventions, (b) the sufficient and continuous provision of injection equipment and infection control supplies and (c) an appropriate sharps waste management that eliminates contaminated sharps from the environment.

Who can assist in implementation?

1. Communication and behaviour change will require communication experts to formulate a communication strategy, photographers, graphic designers, writers and other public relations experts to design information, education and communication materials;
2. Provision of supplies will require pharmacists or administrators familiar with procurement procedures;
3. Sharps waste management will require health system specialists to manage the plan, engineers for the construction of the waste treatment options and logisticians for implementation.

How to make it happen?

1- Communication and behaviour change strategy

WHO designed a template communication and behavioural change strategy for the safe and appropriate use of injections. This strategy proposes to develop six essential behaviours among patients, prescribers and injection providers (see
Table 21). Further tools and details to implement the proposed communication strategy may be found in the "Communication strategy for the safe and appropriate use of injections". [225]

Table 21: Communication strategy for the safe and appropriate use of injections

Four problems	*Three participant groups*	*Six key actions*
THERAPEUTIC INJECTION OVERUSE	PRESCRIBERS	1. Prescribe oral medications wherever possible
	PATIENTS	2. If prescribed an injection, ask if medication can be given orally instead
REUSE OF INJECTION EQUIPMENT WITHOUT STERILIZATION		3. Demand that a syringe and needle be taken from a new, sealed and undamaged package
	INJECTION PROVIDERS (Health Care Workers)	4. Use a syringe and needle from a new, sealed and undamaged package for every injection
UNSAFE SHARPS COLLECTION		5. Without recapping, place syringes and needles in a safety box immediately after use
UNSAFE MANAGEMENT OF INJECTION WASTE		6. Manage injection waste safely and appropriately

2- Provision of equipment and supplies

a) Curative health care system

Since a lack of supplies of injection equipment leads to unsafe practices,[58] the WHO expert committee for essential medicines recommended that "those who supply injectable medications should also procure the equipment to administer them safely"(Abstract 14) .[226] Thus, national procurement officers purchasing pharmaceuticals should ensure that orders and deliveries of injectable substances also include matching quantities of (1) single use syringes and needles, (2) single-dose vials of diluents and (3) safety boxes for the collection of sharps waste. In some settings characterized by a high level of reuse of injection equipment, auto-disable syringes may be required instead of standard, single use syringes. Key steps to facilitate the procurement of equipment and supplies required to ensure injection safety are summarized in Table 22 and described in more detail in "Procurement single use injection equipment: A practical guide". [227]

b) Immunization, family planning and other donor- and lender-supported programmes

In the immunization field, the "bundling"* policy statement recommends that donors and lenders who supply injectable vaccines should also supply auto-disable syringes and safety boxes for the collection of sharps. Family planning services, tuberculosis control and other donor- and lender-supported programmes making use of injections should also procure the equipment to administer

* "Bundling" refers to the inclusion of the costs of auto-disable syringes and safety boxes in the costs of good quality vaccines provided by donors and lenders as described in the WHO/UNICEF/UNFPA/IFRC 1999 policy statement [5]. "Bundling" has no physical connotation and does not imply that items must be "packaged" together.

injections safely. These programmes can use the immunization "bundling" policy statement as a template for the formulation of their own injection safety policy. [180]

Table 22: Steps to follow to procure injection equipment and safety boxes at country level

Step	Objective	Tasks
Step1	**Select products**	Select the type of injection equipment and safety boxes required to be procured according to the purpose of use
Step 2	**Estimate injection equipment needs**	• Estimate needs of injection equipment and sharps boxes in preventive and curative services • Calculate costs and funds required
Step 3	**Prepare for procurement**	• Define procurement or tender specifications • Establish injection equipment specifications • Prepare bidding documents • Select potential suppliers
Step 4	**Process tender**	• Choose a tender format • Prepare bidding documents for selective tender • Solicit and receive offers for selective tender • Select suppliers • Issue contract • Assess contract performance • Evaluate product performance

3- Sharps waste management

While sharps waste constitutes a small proportion of all health care waste, it is associated with one of the highest hazards. Management of sharps waste within the broader context of health care waste management, as described in the "Aide mémoire" for safe health care waste management [228] improves effectiveness and sustainability. The key to success is the locally adapted combination of the managerial (see Table 23 and technology aspects (see Table 24).

Table 23: Key elements of safe health care waste management

National policy for safe health care waste management

- Designation of responsible authority
- Regulatory framework and guidelines
- Initial assessment
- Integration into overall waste management plan
- Monitoring and evaluation

Comprehensive system of health care waste management

- Assignment of waste management responsibilities to personnel
- Allocation of resources
- Minimization of waste
- Segregation of waste
- Safe collection, handling and storage
- Safe treatment and disposal

Awareness and training

- Inclusion of waste management in the curricula of health care personnel
- National training package
- Train the trainers programme
- Education on health risks
- Education on safe practices

Selection of options for the management of health care waste

- Review of available options (see Table 8)
- Checks of safety and environment-friendliness
- Ensure workers' safety
- Evaluation of sustainability
- Assessment of acceptability
- Monitoring of safety and efficiency

Table 24: Comparison of various methods for processing/disposal of sharps waste

Method	Strengths	Weaknesses
Waste burial pit or encapsulation	• Simple • Inexpensive • Low tech • Prevents sharps-related infections/injuries to waste handlers/scavengers	• Potential of being unburied • No volume reduction • No disinfection of wastes • Pit may fill quickly • Not adapted for non-sharp infectious wastes • Presents a danger to community if not properly buried • Inappropriate in areas of heavy rain or if water table is near the surface
Burning (< 400°C), including: Brick oven burners Drum burners Pit burning	• Relatively inexpensive • Minimum training required • Reduction in waste volume • Reduction in infectious material	• Incomplete combustion • May not completely sterilize • Results in heavy smoke • May require fuel or dry waste to start burning • High potential for toxic emissions (e.g., dioxins and furans), if waste stream is not properly managed
Incineration (≥ 800°C)	• Almost complete combustion and sterilization of used injection equipment • Reduces risk of toxic emissions • Greatly reduces volume of sharps waste • Greater compliance with local environmental laws	• Relatively expensive to build, operate and maintain • Requires trained personnel to operate • May require fuel or dry waste to start burning • Some potential for toxic emissions (e.g., dioxins and furans) if waste stream is not properly managed.
Needle removal/ Needle destruction	• Reduces occupational risks to waste handlers and scavengers • Plastic and steel may be safely recycled for other uses after treatment • Manual technologies available	• Potential risk of needle-stick injuries • Fluid splash back may create opportunities for bloodborne pathogen transmission • Used needles/syringes need further treatment for disposal • Safety profile is not conclusively established
Plastic recycling	• Environmentally friendly • Makes use of prevailing market mechanisms • Provides revenue to local private sector (e.g., production of buckets and coat hangers)	• Needs to be preceded by use of a safe needle removal system • Potential risk of needle-stick injuries during processing • Requires estimation of financial viability under different scenarios and contexts
Melting in industrial ovens	• Greatly reduces volume of sharps waste	• Expensive • Requires electricity
Autoclave steam sterilization followed by shredding	• Sterilizes used injection equipment • Environmentally friendly • May reduce waste volume	• High capital and operational costs • Requires electricity • High maintenance requirements • Less volume reduction than incineration

Further information on sharps waste management is available at http://www.healthcarewaste.org.

5. Monitoring and evaluating impact

Rationale

Monitoring and evaluation are required to document progress towards the targets laid out in the national standard for injection practices and to adapt implementation of interventions accordingly.

Objective

The implementation of the national plan for the safe and appropriate use of injections is regularly monitored and intermittently evaluated using a combination of input, process and outcome indicators to obtain evidence of the progress achieved and a basis for the new planning process.

Who should conduct monitoring and evaluation?

The easiest way to ensure monitoring and evaluation is to incorporate injection practice indicators into sets of indicators routinely used to monitor the technical quality of health systems.

How to make it happen?

Indicators

The indicators to be used for evaluation are identical to the ones used for the initial assessment (see Table 17). The subset of indicators mentioned in the plan of action (see Table 20) are particularly suitable for monitoring purposes.

Input indicators

Input indicators reflect the human and financial and planning resources invested in the national strategy for the safe and appropriate use of injections.

Process indicators

Process indicators reflect the status of implementation of the various action points proposed in the national strategy for the safe and appropriate use of injections.

Outcome indicators

Outcome indicators reflect the evolution of injection practices in terms of frequency and safety following the implementation of the national strategy for the safe and appropriate use of injections.

Data collection

Data regarding these indicators may be collected regularly in the Ministry of Health and in different programme offices, during supervisory visits in health care facilities, in separate surveys and/or as part of the process of accreditation of health care facilities. In the latter case, the proposed indicators may be adapted. Additional resources regarding the use of supervision visits to monitor injection practices are available in the "Guide to supervising injection providers". [218]

Appendix 2: Abstracts of other publications and presentations on injection safety

Abstract 1: Transmission of Hepatitis C Virus Infection Associated with Home Infusion Therapy for Hemophilia

CDC publication with primary responsibility. Morb Mortal Wkly Rep 1997; 46:597-9.

Report

Transmission of hepatitis C virus (HCV) and other bloodborne viruses between household members who are not sex partners presumably results from unapparent percutaneous or permucosal exposures, such as sharing articles that may be contaminated with microscopic quantities of blood. The risk for nonsexual household transmission is extremely low, and no cases of such transmission have been documented (1); direct percutaneous exposures (e.g., injecting drugs) have been identified as the major risk factor for infection (1). This report summarizes the investigation of a newly acquired case of HCV infection in a child with hemophilia, after a preliminary investigation identified several household members with HCV infection. The findings suggest the child-acquired infection through percutaneous exposure to the mother's HCV-infected blood during infusion of clotting-factor concentrate.

On September 12, 1996, a case of seroconversion of antibody to HCV (anti-HCV) in a 4-year-old child with moderate factor VIII deficiency was reported to the Seroconversion Surveillance Project, a surveillance system maintained jointly by the Food and Drug Administration, CDC, and the National Hemophilia Foundation. The child tested positive for anti-HCV on August 29, 1996, after testing negative in June 1994 and August 1995. Serum drawn on the same day (August 29) tested negative for human immunodeficiency virus (HIV) antibody. With the exception of the 14 days after birth, the child had always received recombinant clotting-factor concentrate for treatment of bleeding episodes.

Testing of serum samples from six household members indicated that three were anti-HCV-positive, including the patient's mother, an older sibling, and an aunt who had stayed in the household for 6 weeks during September-October 1995. The mother and aunt had histories of having injected illicit drugs but had not been tested previously for anti-HCV. The sibling, aged 11 years, had moderate factor VIII deficiency and was anti-HCV-positive when first tested in 1992. Until November 1994, the child was treated for bleeding episodes at a local emergency department with recombinant clotting-factor concentrate brought from home. Beginning in

November 1994, the patient's mother administered clotting-factor concentrate to him at home after receiving training from a nurse employed by a home health care company. Follow-up consisted of an annual visit to a hemophilia treatment center. During February 1995-June 1996, the period during which the child probably became infected, the patient's mother administered factor VIII concentrate to him on 13 occasions. She reported that, until May 1996, three other persons were required to restrain the child during infusions because the child was combative and resistant. Infusions usually were administered through a vein in the foot because of reported difficulties in accessing a vein in the upper arm, and up to 3 hours were required for infusion. The mother recalled that, on at least two occasions, she pricked her finger with the needle while attempting an infusion and drew a visible quantity of blood, but she could not remember whether she continued to use the same needle for the infusion. Before learning in September 1996 that she was infected with HCV, she did not use gloves when infusing clotting-factor concentrate. No other family members assisted in administering factor concentrates.

The child and the mother shared a bed. Although each household member had his or her own toothbrush, bath towels were shared. All household members were negative for or denied recent histories of dermatitis, open wounds, injury, or external bleeding episodes. Sequence analysis of the HCV strains of the child and the HCV-infected family members indicated that the strain isolated from the mother and the child was identical in a sequence of 220 nucleotides in the NS5b region of the genome. Viral sequences in this region isolated from the aunt and brother differed by four and 10 nucleotides, respectively, from the child's strain.

Reported by: L Finelli, PhD, Acting State Epidemiologist, EA Gursky, ScD, Senior Assistant Commissioner, New Jersey Dept of Health and Senior Svcs. Hematologic Diseases Br, Div of AIDS, STD, and TB Laboratory Research, and Hepatitis Br, Div of Viral and Rickettsial Diseases, National Center for Infectious Diseases, CDC.

Editorial Note

Editorial Note: The results of the investigation described in this report suggest that the child acquired HCV infection through percutaneous exposure to the mother's HCV-infected blood during infusion of clotting-factor concentrate. The mother was responsible for infusing factor concentrate and reported incurring needle-sticks during some of these infusions. Therefore, blood-to-blood contact may have resulted either from use of a contaminated needle to administer an infusion or by contamination of the infusion site. In addition, analysis of the sequences of the segments of HCV strains isolated from the mother and child indicated the strains were closely

related. Because the time of initial infection of the mother could not be documented, the possibility that the child acquired infection from another unrecognized source and was the subsequent source of infection for the mother cannot be excluded. However, the mother had been a long-term injecting-drug user before birth of the child and may have acquired HCV infection through sharing needles and syringes. Surveys indicate that up to 90% of long-term injecting-drug users test positive for anti-HCV (1).

Among persons with hemophilia who were heavily infused with clotting-factor concentrates before the development of viral inactivation methods, the prevalence of anti-HCV exceeds 90% (1). The safety of plasma-derived clotting-factor concentrates has been improved by instituting measures that include screening for serologic markers of bloodborne pathogens in donated plasma used in the manufacture of these products and the incorporation of viral inactivation steps (e.g., dry heating, pasteurization, and solvent detergent treatment) (2). Transmission of HCV or other viral agents has not been reported in association with receipt of genetically engineered factor concentrates or of albumin, the only human plasma-derived material present in these recombinant products (3,4). Based on these considerations, clotting-factor concentrate was an unlikely source of infection in the case described in this report because the child had received only recombinant product during the period in which infection was likely to have been acquired.

Home infusion therapy is a convenient and cost-effective alternative to treatment of hemophilia in the health care setting (5). However, if proper infection control procedures are not followed, patients and household members may be at risk for exposure to bloodborne pathogens during home infusion therapy. In one study, 18% of household members who assisted HIV-infected hemophilia patients with the infusion process reported having sustained at least one needle-stick injury (6), and HIV infection has been acquired through percutaneous exposure during home treatment of acquired immunodeficiency syndrome (7) and hemophilia (8).

CDC recommends that patients and families who are eligible for home infusion therapy be informed of the potential risks for infection with bloodborne pathogens and be assessed for their ability to use adequate infection-control practices consistently. Patients and families should receive training with a standardized curriculum that includes appropriate infection-control procedures before initiation of home infusion therapy, and infection-control practices should be regularly evaluated at home through follow-up visits by health care professionals with specific training in such practices. Routine testing of caregivers for bloodborne pathogens is not recommended; all caregivers should follow the universal precautions recommended for all persons who infuse blood products. Gloves should be worn by persons who prepare or infuse

blood products and during disposal of infusion equipment and waste. A needle that has broken the skin should not be reused, and used needles should never be recapped. Used needles should be placed in a sharps container in a location inaccessible to children. Needle-stick incidents occurring during home infusion therapy should be reported to the health care professionals supervising home treatment. All household and sexual contacts of patients with chronic hepatitis B virus infection should receive hepatitis B vaccine.

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Abstract 2: Using Surveillance Data to Monitor Key Aspects of the Epidemiology of Hepatitis B Virus (HBV) Infection in Romania

Y. J. F. Hutin*, D. Craciun, N. Ion-Neldelcu, E. E. Mast, M.J. Alter, H. S. Margolis.

Abstract presented at the annual meeting of the Infectious Diseases Society of America, Denver, CO, November 1998.

Early childhood transmission and unsafe injection practices are major determinants of high levels of HBV transmission in Romania. Universal childhood hepatitis B (HB) vaccination was implemented in October 1995, and surveillance for acute viral hepatitis in children under five

years old was initiated in July 1997. Patients identified with physician-diagnosed acute hepatitis were tested for HB surface antigen (HBsAg), IgM antibody to HB core antigen, and IgM antibody to hepatitis A virus. Potential exposures and HB vaccine doses received were ascertained for all cases. To measure HB vaccine efficacy among children born after October 1995, the vaccination status of HBsAg-positive children who had acute hepatitis was compared with that of HBsAg negative children who had hepatitis A. To measure the association between acute HB and injections among children who had received fewer than three doses of HB vaccine, the injection history in children who had acute HB was compared with that of HBsAg-negative children who had hepatitis A. Of 10 HBsAg-positive children, four (40%) had received three doses of vaccine, compared with 57 (92%) of the 62 controls (vaccine efficacy = 94%, 95% confidence interval [CI]: 65-99). Of 32 children with acute HB, 15 (47%) received an injection, compared with 33 (11%) of the 288 controls (odds ratio = 6.8, 95% CI: 2.8-16, population attributable risk = 40%). In Romania, HB vaccine efficacy and the association between HB and injections can be estimated using acute hepatitis surveillance data in children under five years of age, providing an opportunity to monitor essential prevention programmes.

Abstract 3: Attitudes of Physicians Regarding the Use of Therapeutic Injections, Arges District, Romania

A. Stoica, Y.J.F. Hutin, M. Paun, E.E. Mast, H.S. Margolis. Abstract presented at the annual meeting of SHEA, San Francisco, April 1999.

Background:

In Romania, a high proportion of the population receives therapeutic injections every year, unsafe injection practices have been reported, and studies indicate an association between acute hepatitis B and recent injections. Although anecdotal reports suggest a preference for injections among patients, no information is available regarding physicians' prescribing practices.

Methods:

A simple random sample of 200 clinically active physicians in Arges District was selected using the physician association list. Data regarding demographic characteristics and attitudes regarding therapeutic injections were collected on a standardized questionnaire.

Results:

Of the 200 physicians recruited, 26% were male; 18% were < 35 years old, 45% were 35 to 44 years old, 33% were 45 to 59 years old, and 4% were > 60 years old. The majority (69%) was involved in outpatient

care. Most physicians (64%) accurately perceived that injections were more frequently used in Romania than in Western Europe, but 40% reported that the use of injections was not excessive in Romania. Criteria reported as frequent reasons for choosing injections to administer medications included inability of the patient to take oral medications (72%), more rapid effect of injected medications (72%), poor intestinal absorption of the drug (72%), stronger effect of injected medications (64%), desire to directly observe therapy (60%), and observance of recommendations from university professors (50%).

Conclusion:

Physicians' attitudes may be an important determinant of injection overuse in Romania. Initiatives to prevent injection-associated transmission of bloodborne pathogens should include education programmes to reduce the use of therapeutic injections by physicians

Abstract 4: Therapeutic Injections in Romania: A Population Survey in Four Districts

C. M. Dentinger, Y.J.F. Hutin, S. A. Fisher-Owens, E. E. Mast, H.S. Margolis, N. Ion-Nedelcu. Poster presented at the SHEA annual meeting, April 1999, San Francisco.

Background:

Acute hepatitis B is one of the most common reportable diseases in Romania and the prevalence of chronic hepatitis B virus (HBV) infection is high. Recent analysis of surveillance data demonstrates that therapeutic injections are associated with acute hepatitis B among unimmunized children under 5 years old. Anecdotal reports suggest that patients request injectable medications from physicians; however, little is known about injection frequency or the determinants of injection use.

Methods:

We conducted a population-based survey of 300 households in each of four selected districts. Information was collected from each household member on the number of therapeutic injections received in the last 12 months. Knowledge and attitudes regarding the use of injections were assessed from one randomly selected adult in each household.

Results:

An estimated 50%, 32%, 36%, and 33% of the population in the districts of Hunedoara (n = 904), Iasi (n = 964), Mures (n = 879), and Prahova (n = 932), respectively, reported receiving at least one therapeutic injection in the last 12 months. Among those who received injections, the

median number received was 10, seven, six, and five in the four districts, respectively. Of 1,200 adults interviewed, 75% reported that injectable medications were stronger than oral medications; however, a lower proportion indicated a preference for injections for the treatment of diarrhea (18%), fever (28%), upper respiratory infections (29%), or for vitamin supplementation (42%).

Conclusions:

A high proportion of the Romanian population receives injections each year; however, a minority of patients indicated a preference for injected medications for common medical conditions. Additional information regarding prescribing practices of physicians is needed to develop a programme to reduce injection use.

Abstract 5: Injection Practices in Romania: Progress and Challenges

C. Dentinger, L. Pasat, M. Popa, Y.J.F. Hutin, EE Mast. Infect Cont Hosp Epidemiol 2004; 25:30-35.

Background:

In Romania, a high proportion of the population receive therapeutic injections each year, and studies indicate an association between recent injections and acute hepatitis B. However, no information is available on nursing infection-control practices that might lead to hepatitis B virus (HBV) transmission through injections.

Methods:

We surveyed a systematic sample (n=180) of the 1,906 nurses in Vilcea District, Romania. Interviewers used standardized questionnaires to collect information on nurses' knowledge and practices regarding injection use and adherence to Universal Precautions (UP) for the prevention of transmission of bloodborne pathogens.

Results:

The median age of the 180 nurses was 44 years, 91% were female, the median years of practice was 22, 94% worked full-time, and 91% (95% Confidence Interval [CI] = 86-95%) reported UP training. A total of 38% (95% CI = 31-45%) of nurses accurately reported that HBV remains infectious for as long as 1 week in the environment, and 4% (95%CI=1-8%) knew that HBV is transmitted percutaneously more efficiently than human immunodeficiency virus. No nurse reported reuse of syringes or needles on different patients, but 2% (95% CI = 0.6-6%) reported they would reuse a syringe or needle on the same patient in an emergency. Almost half (47%

[95%CI =39-66%]) of nurses reported preparing injections where blood-contaminated items were also handled. Infection-control supply shortages, including sharps containers, disinfecting solutions, and gloves, were reported by 72% (95%CI = 65-79%), 53% (95% CI = 45-60%), and 60% (95% CI = 51-68%) of respondents, respectively.

Conclusions:

Most nurses in Vilcea were trained in UP, and none reported needle or syringe reuse; however, knowledge deficiencies, unsafe practices, and infection-control supply shortages exist and might facilitate injection-associated HBV transmission.

Abstract 6: Identifying Target Groups for a Potential Vaccination Programme during a Hepatitis A Communitywide Outbreak

Y.J. Hutin, B.P. Bell, K.L. Marshall, C.P. Schaben, M. Dart M, M.P. Quinlisk, C.N. Shapiro. Am J Pub Health 1999; 89:918-21.

Objectives:

This study sought to identify groups for targeted vaccination during a communitywide hepatitis A outbreak in 1996.

Methods:

Residents of the Sioux City, Iowa, metropolitan area reported with hepatitis A between September 1995 and August 1996 were sampled and compared with population-based controls.

Results:

In comparison with 51 controls, the 40 case patients were more likely to inject methamphetamine, to attend emergency rooms more often than other health care facilities, and to have a family member who used the Special Supplemental Nutrition Programme for Women, Infants, and Children.

Conclusions:

Groups at increased risk of hepatitis A can be identified that might be accessed for vaccination during communitywide outbreaks.

Abstract 7: Injections Given in Healthcare Settings as a Major Source of Acute Hepatitis B in Moldova

Y.J. Hutin, R. Harpaz, J. Drobeniuc, A. Melnic, C. Ray, M. Favorov, P. Iarovoi, C.N. Shapiro, B.A. Woodruff. Int J Epidemiol 1999; 28:782-6.

Background:

Reported rates of acute hepatitis B are high in many former Soviet Union republics and modes of transmission are not well defined.

Methods:

Two case-control studies were undertaken in Moldova to identify risk factors for acute hepatitis B in people aged 2-15 years (children) and > or =15 years (adults). Serologically confirmed acute hepatitis B cases occurring between 1 January 1994 and 30 August 30 1995, were matched on age, sex, and district of residence to three potential controls who were tested for hepatitis B markers to exclude the immune. Stratified odds ratios (SOR) were calculated using bivariate and multivariate methods.

Results:

In multivariate analysis, compared with the 175 controls, the 70 adult cases (mean age 25 years, 66% male) were more likely to report receiving injections in the 6 months before illness during a dental visit (SOR = 21; 95% CI: 3.7-120), a hospital visit (SOR = 35; 95% CI: 7.2-170), or a visit to the polyclinic (SOR = 13; 95% CI: 2.4-74). Among children, receiving injections during a hospital visit (SOR = 5.2; 95% CI: 1.2-23) was the only exposure reported significantly more often by the 19 cases (mean age 8 years, 68% male) compared with the 81 controls.

Conclusion:

These results, along with reported unsafe injection practices in Moldova, suggest that injections are a major source of hepatitis B virus transmission and highlight the importance of proper infection-control procedures in preventing transmission of bloodborne infections.

Abstract 8: An Outbreak of Hospital-Acquired Hepatitis B Virus Infection among Patients Receiving Chronic Hemodialysis

Y. J. Hutin, S.T. Goldstein, J.K. Varma, J.B. O'Dair, E.E. Mast, C.N. Shapiro, M.J. Alter. Infect Cont Hosp Epidemiol 1999; 20:731-5.

Objective:

To investigate a cluster of hepatitis B virus (HBV) infections between December 1995 and May 1996 among chronic hemodialysis patients in one county.

Setting:

Two dialysis centers (A and B) and a hospital (C) in one county.

Patients:

Six case-patients who were dialyzed in one of two centers, A and B, and had all been hospitalized between January and February 1996 at hospital C.

Methods:

Patient 1, usually dialyzed in center A, sero-converted to hepatitis B surface antigen (HBsAg) in December 1995 and could have been the source of infection for the others, who seroconverted between March and April 1996. Two cohort studies were conducted: one among patients dialyzed in center A, to determine where transmission had occurred, and one among patients dialyzed at hospital C at the time patient 1 was hospitalized, to identify factors associated with infection.

Results:

Four (15%) of the 26 susceptible patients dialyzed at center A became infected with HBV. Hospitalization at hospital C when patient 1 was hospitalized was associated with infection (P = .002). A cohort study of the 10 susceptible patients dialyzed at hospital C during the time patient 1 was hospitalized did not identify specific risk factors for infection. However, supplies and multidose vials were shared routinely among patients, providing opportunities for transmission.

Conclusion:

When chronic hemodialysis patients require dialysis while hospitalized, their HBsAg status should be reviewed, and no instrument, supplies, or medications should be shared among them.

Abstract 9: Multiple Modes of Hepatitis A Virus Transmission among Methamphetamine Users

Y.J. Hutin, K.M. Sabin, L.C. Hutwagner, L. Schaben, G.M. Shipp, D.M. Lord, J.S. Conner, M.P. Quinlisk, C.N. Shapiro, B.P. Bell. Am J Epidemiol 2000; 152:186-92.

Methamphetamine users are at increased risk of hepatitis A, but modes of transmission are unclear. The authors conducted a case control study among methamphetamine users during an outbreak in Iowa in 1997. Twenty-eight reported, laboratory-confirmed, hepatitis A cases did not differ from 18 susceptible controls with respect to age, sex, or number of doses used. When compared with controls in multivariate analysis, case-patients were more likely to have injected methamphetamine (odds ratio (OR) = 5.5, 95% confidence interval (CI): 1.1, 27), to have used methamphetamine with another case-patient (OR = 6.2, 95% CI: 0.95, 41), and to have used brown methamphetamine (OR = 5.5, 95% CI: 0.51, 59). Receptive needle sharing was reported by 10 of the 20 case-patients who injected. Methamphetamine use with another case-patient was also associated with hepatitis A in an analysis restricted to noninjectors (OR = 17, 95% CI: 1.0, 630). During this outbreak, hepatitis A may have been transmitted from person to person among methamphetamine users through the fecal-oral and the percutaneous routes. Methamphetamine users should be vaccinated against hepatitis A and should be given immune globulin if they used methamphetamine with a case-patient in the last 2 weeks. Persons who intend to continue using methamphetamine should be advised about safer practices.

Abstract 10: Pilot Testing the Injection Safety Assessment Tool in Burkina Faso

J.F.Aguilera. Presentation given at the annual SIGN meeting, 23-24 September 2000, Cairo, Egypt.

Unsafe delivery and overuse of injections are responsible for numerous transmissions of hepatitis B virus, hepatitis C virus and HIV in the developing world. Following a report suggesting that in 1995-96 only 11% of injections in rural health centres in Burkina Faso were performed with sterile equipment, in 1996 communities were given the responsibility of supplying injection equipment. Stocks of new disposable injection equipment were then established in each community to be sold to patients when needed. The aim of the present study was to estimate the frequency of unsafe injection practices in Burkina Faso. A two-stage cluster sample methodology was used to select eight clusters with probability proportional to population size. In each cluster, 10 health centres were randomly selected. Information was collected in June 2000 through (1) structured observation of injection equipment supplies and injection practices and (2) staff interviews. Confidence intervals for proportions were calculated taking into account design effect (DE) using Epi-Info software. A total of 116 injections were observed in 52 of the 80 centres visited. In 50 centres (96% CI [85-99], DE=1.03) injections were given with a new

disposable syringe and in 51 (98% [85-99], DE= 1.03) with a new disposable needle. All centres had a community stock to provide new disposable syringes and needles. In 29 centres (56% [36-74], DE=1.98), health staff recapped needles using two hands. In 71 centres of the 80 centres visited, staff remembered suffering accidental needle-stick injuries in the last 12 months. Used needles were discarded in open containers in 66 centres (83% [55-96], DE=4.56) and found in the environment of 46 centres (57% [32-80], DE=4.66). The increased availability of injection equipment in communities may have contributed to the increase in the use of sterile injection equipment observed between 1995 and 2000 in Burkina Faso. However, unsafe sharps waste collection and disposal persist, placing health care workers and patients at risk of infection. To achieve safe injection practices in Burkina Faso, recommendations have been made for policy development in health care waste management and for increased availability of sharps containers.

Abstract 11: Unsafe Injection Practices, Niger, 2000

J.A. Painter, Y. Hutin. Presentation given at the 2001 EIS conference, Atlanta, GA, USA, April 2001.

Background:

Unsafe injection practices transmit bloodborne pathogens on a large scale worldwide. To better direct prevention efforts in Niger, we assisted the Ministry of Health in conducting an assessment of injection safety in August 2000.

Methods:

We conducted interviews and observations of injection practices in a sample of health clinics in Niger. First, eight clusters were selected from 25 regions with a probability proportional to population size. Second, 10 clinics were randomly selected within each cluster. Information was collected through an inventory of available equipment, structured observations, and staff interviews.

Results:

Of the 80 clinics selected, 79 provided partial or complete responses. During the previous year, clinics reported insufficient disposable syringes at 24 (46%) of 52 clinics and insufficient energy for sterilization at 13 (25%) of 52 clinics. We observed attempts to inject patients with nonsterile equipment in 5 (11%) of 45 clinics before tactful interruption by the assessment team. Contaminated sharps waste were observed in open containers in 73 (95%) of 77 clinics and in the

environment surrounding 43 (61%) of 70 clinics. Health care workers reported experiencing at least one needle-stick injury in the previous year at 56 (72%) of 77 clinics.

Conclusions:

Lack of supplies, unsafe behaviours, and poor sharps waste management lead to unsafe injection practices in Niger, exposing patients, health care workers, and the community to bloodborne infections. A coordinated strategy to increase supplies of both disposable syringes and fuel sources for sterilizers, train health care workers, and encourage proper disposal of sharps is required to prevent injection-associated infections in Niger.

Abstract 12: Increased Access to Injection Equipment in Burkina Faso: When Essential Drug Programmes Improve Injection Safety

S. Logez. Presentation given at the annual SIGN meeting, 30-31 August 2001, New Delhi, India.

The objective was to evaluate the impact of a National Drug Policy on injection safety between 1992 and 2001. The methodology was a two-stage cluster sample of health care facilities. Compared to widespread reuse of injection equipment that exceeded 50% of health care facilities in 1995, reuse of equipment was observed in 4% of health care facilities in June 2000. Sharps were found in open containers in 83% of settings and found around 57% of health care centres. The national drug policy provided a framework for improved availability of essential drugs and injection equipment in Burkina Faso. Inclusion of disposable injection equipment in the national essential drug list allowed tax exemptions. At district level, wholesalers and supervisory teams were set up. Community pharmacies provided supplies at the health care facility level using a cost recovery scheme that made drugs and injection equipment available at low cost to the population. The proportion of health care facilities that had access to a community pharmacy increased from 5% in 1992 to 95 % in 2000 in Burkina Faso. The number of 5 ml syringes sold in the country increased from 884 000 in 1996 to 1 840 000 in 2000. The price of new 5 ml syringe is 10 cents and remained stable. Injection equipment is judged affordable by 88% of pharmacists and 55% of buyers. Thus, availability and affordability of injection equipment may have contributed to improved injection practices in Burkina Faso between 1995 and 2000. However, the most dramatic change observed was an improved geographical access since the price of injection equipment remained stable. Recommendations of the assessment included that access could be improved by monitoring prices and profit margins. Improved access to sharps boxes could occur through cost recovery and inclusion in essential drug lists since this mechanism was successful in the case of syringes and needles.

Abstract 13: Determinants of High Frequency of Therapeutic Injections, Chisinau, Republic of Moldova, 1998

S. Vong, J. Perz, Y. Hutin, J. Drobeniuc, B. Bell & 1998 International Field Epidemiology Course Participants. Presentation given at the 2002 EIS conference, Atlanta, GA, USA, April 2002.

Background:

In many countries where hepatitis B is highly endemic, overuse of therapeutic injections and unsafe practices account for a large proportion of infections. We conducted a population-based survey in Chisinau, Moldova, an area of high hepatitis B endemicity, to determine factors associated with receiving injections.

Methods:

We sampled 704 households in 32 clusters in which one person ≥15 years was randomly selected and interviewed regarding frequency of injections received in the last 12 months and related knowledge, attitudes and practices.

Results:

Of 700 persons interviewed, 385 (55%) had received >1 injection (median 10, range 1-720). Persons receiving injections were similar to those who did not in terms of age (median 44 vs. 41 years), sex (35% vs. 40% male), education (median 12 vs. 12 years), and awareness of hepatitis B and its consequences (45% vs. 46%). Compared to persons not receiving injections, persons receiving them were more likely to report a preference for injections to treat colds (Odds Ratio [OR]=1.72, 95% Confidence Interval [CI]=1.15–2.57) or fever (OR=1.58, 95% CI=1.08–2.31), and to request injections when oral treatments were prescribed (OR=1.84, 95% CI=1.19–2.85). However, none of these preferences were reported by more than 30% of participants. Most participants reported knowing about risks from syringe reuse, but persons who received injections were less likely to have this knowledge (60% vs. 68%; OR=1.41, 95% CI=1.01–1.96).

Conclusion:

Despite a general awareness of their potential for bloodborne pathogen transmission, therapeutic injections were common among Chisinau residents. However, a minority of them reported attitudes favorable to injection use. Interventions to decrease injection overuse should include promoting alternative modes of therapy to both health care providers and the public.

Abstract 14: Could the WHO Model List of Essential Medicines do more for the safe and appropriate use of injections?

S. M.D. Logez, Y.J.F. Hutin, K. Holloway, R. Gray, H.V. Hogerzeil. J Clin Pharmacol 2004; in press.

Background:

A national drug policy addressing the safe and appropriate use of injections is an important element to prevent overuse and unsafe use of injections. Because the WHO Model List of Essential Medicines is a keystone of national drug policies, we examined the way it addresses injection practices.

Methods:

We reviewed the eleventh WHO Model List of Essential Medicines to collect information on (1) injectable drugs, (2) diluents and (3) the recommendations regarding injection equipment procurement.

Results:

Of 306 active ingredients on the list, 135 (44%) are mentioned in injectable form. Of these, 41 (30%) need diluents for reconstitution. The list does not mention the need to procure appropriate diluents, injection equipment and safety boxes in quantities that match the quantities of injectable medicines. In addition, the list provides limited information that can be used to forecast the needs of injection equipment to administer the injectable medicines that are included in the list.

Conclusions:

Future revisions of the WHO Model List of Essential Medicines should attempt to reduce the number of injectable references on the basis of evidence. In addition, the list should specify that when injectable medicines are being supplied, diluents, single use syringes and safety boxes should be supplied. The volume of necessary syringes should be specified to facilitate the forecasting of injection equipment needs.

Abstract 15: Recycling of Injection Equipment in Pakistan

S.A. Mujeeb, M.A. Malik, A. Altaf, Y. Hutin, S. Luby. Recycling of injection equipment in Pakistan. Infect Cont Hosp Epidemiol 2003; 24:145-6.

The prevalence of hepatitis C virus (HCV) infection is high in the general population in Pakistan, ranging from 2% to 6%.1 Reuse of injection equipment in the absence of sterilization is common, particularly in health care facilities that serve low-income populations. Studies have identified unsafe injection practices as a major route of transmission of HCV in Pakistan. Changing the behaviour of injection providers so that they would use new freshly-opened disposable syringes would improve injection safety in Pakistan. However, frequent reports of recycling of injection equipment in the local media question the safety of apparently new syringes. Clinical laboratories are one of the major sources of production of used syringes. To evaluate the resale of used syringes, we followed the course of used syringes from their initial use to their final destination.

Abstract 16: Rapid Assessment of Injection Practices in Mongolia, 2001

S.M.D. Logez, G. Soyolgerel, R. Fields, S. Luby, Y. J.F. Hutin. Am J Infect Cont Pract 2004; 2004; 32 :31-7.

Background:

Anecdotal reports of unsafe practices and a high prevalence of HCV infection suggest that unsafe use of injections may transmit bloodborne pathogens in Mongolia. To achieve safe and appropriate use of injections, the Ministry of Health of Mongolia conducted a rapid assessment.

Methods:

Information on injection practices, their determinants and their consequences was collected through interviews and observations of a small convenience sample of prescribers, injection providers and members of the general population.

Results:

The 65 members of the general population reported receiving an average of 13 injections per year. New, locally produced, disposable injection equipment was used in the 20 health care facilities visited. There were breaks in infection control practices while administering injections, including observations of 500 ml intravenous infusion bottles used as multi-dose diluent vials and eight of the 28 providers (28%) reporting reusing syringes and/or needles for the same patient. Injection providers reported an average of 2.6 needle-stick injuries per year. Contaminated sharps were burned in a drum, without any incinerator. Among persons interviewed, 19 of the 21

prescribers (90%) and 49% of the population was aware of the potential risk of HIV transmission through unsafe injections.

Conclusions:

A multi-disciplinary initiative is necessary to achieve safe and appropriate use of injections in Mongolia through (1) development of key behaviours among patients and health care workers to reduce injection overuse and to ensure safe practices, (2) increasing availability and affordability of injection equipment and sharps boxes and (3) appropriate sharps waste management.

Curriculum vitae

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Education

1990-1991:

London School of Hygiene & Tropical Medicine, London, UK: MSc course in Clinical Tropical Medicine.

1982-1988:

University of Nancy, France: Medical school.

Diplomas

1995:

Diploma of Specialized Studies (DES) in **hepatology and gastroenterology** (Paris, France).

1992:

MD (Faculty Xavier Bichat, Paris, France).

1991:

MSc of Clinical Tropical Medicine (University of London, UK).

1988:

CSCT -- **Qualification** (Nancy University, France).

1982:

Baccalaureat C (BS, France)

Residency (Paris, France) 1988-1995

One semester of Chest Medicine, three semesters of Infectious Diseases and Tropical Medicine and four semesters of Hepato-gastroenterology.

Licences and board certifications

60165 (Ordre National des Médecins, 60 Bd Latour Maubourg, 75 007 Paris, France).
Board certified in hepatology and gastroenterology in France, August 95.

Professional experience

1999- Pst:

Safe Injection Global Network (SIGN) project leader, World Health Organization Headquarters, Geneva, Switzerland. Assistance to member states in assessing, planning, implementing and evaluating safe and appropriate use of injection policies, coordination of the Secretariat of the SIGN alliance and leveraging of international efforts for the safe and appropriate use of injections worldwide.

1998 - 1999:

Medical epidemiologist, Hepatitis Branch, Centers for Disease Control and Prevention, Atlanta, GA, USA. International activities for hepatitis B prevention, injection safety in Romania and supervision of EIS officers during outbreak investigations.

1996- 1998:

Epidemic Intelligence Service (EIS) Officer, Hepatitis Branch, Centers for Disease Control and Prevention, Atlanta, GA, USA. Outbreak investigations, evaluation of surveillance systems, long-term research projects and teaching in epidemiology.

1995- 1996:

Medical Epidemiologist at EPICENTRE, Paris, France, based in Kampala, Uganda. Coordination of a clinical trial, rapid assessments in refugee settings, international health, evaluation of public health programmes, outbreak investigations and surveillance.

1992- 1993:

National Service as Medical Epidemiologist, Service d'Epidémiologie, de Statistique et d'Information Sanitaire (OCCGE: Organization of Coordination and Cooperation for the

Control of Major Endemic Diseases), Bobo-Dioulasso, Burkina Faso, West Africa. Surveillance, surveys and evaluation.

Teaching experience

2002:

Instructor in Epidemiology for the Chinese Field Epidemiology Training Programme (C-FETP), Beijing, China.

2001-2002:

Faculty at the Advanced Vaccinology Course, Annecy.
Facilitator at the WHO Lyon course to strengthen the capacity of laboratories. Development of a case study on cholera.

1998:

Coordinator of an international field epidemiology course, Chisinau, Moldova.

1994- 2000:

Instructor for the International Lecture of Epidemiology and Biostatistics (I.D.E.A.), Veyrier du Lac, France (on a yearly basis).

1995:

Instructor in Epidemiology for the first Interafrican EPIGEPS lecture (epidemiology and health planning and financing), Yamoussoukro, Ivory Coast, West Africa.

Memberships of societies/awards

2000:

Nakano citation, Centers for Disease Control and Prevention, Atlanta, GA, USA.

1991:

Frederick Murgatroyd Award, London School of Hygiene and Tropical Medicine, London, UK.

1991:

Member of the **Société de Pathologie Exotique de l'Institut Pasteur**, Paris, France.

1990:

Fellow of the **Royal Society of Tropical Medicine and Hygiene**, London, UK.

MD thesis

Hutin YJF. Epidémiologie des diarrhées à Clostridium difficile au cours de l'infection VIH: une étude cas-témoin dans une unité spécialisée. MD Thesis, Faculty Xavier Bichat, Paris VII, 1992

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