Chapter 22

Contaminated injections in health care settings

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Summary

Injections given in health care settings with injection equipment reused in the absence of sterilization have been associated with infection with hepatitis B virus (HBV), hepatitis C virus (HCV) and HIV.

Input parameters included 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 age-specific prevalence of active infection, the prevalence of immunity (i.e. antibody to the hepatitis B core antigen or HbcAg [anti-HBc], anti-HCV and anti-HIV) and the incidence of HBV, HCV and HIV infections. We used mathematical models to transform diverse sources of data available into the prevalence of contaminated injections and the relative risk associated with these practices.

Four subregions[1] (AMR-A, EMR-B, EUR-A and WPR-A) where reuse of injection equipment in the absence of sterilization was negligible were assumed to have zero risk. In the remaining 10 subregions, the annual number of injections per person ranged from 1.9 to 11.3 and the proportion of injections administered with reused equipment ranged from 1.2% to 75%.

In 10 subregions, in 2000, injections caused an estimated 21 million HBV infections, two million HCV infections and 260 000 HIV infections, accounting for 32%, 40% and 5% of new infections, respectively. Thus, the burden in 2000 due to past and present exposure accounted for 501 000 deaths and 10 461 000 disability-adjusted life years (DALYs).

Injection overuse and unsafe practices are common worldwide and account for a high burden of infections with bloodborne pathogens. There is a need for policies and programmes for the safe and appropriate use of injections in countries where poor practices occur.

1. Introduction

During the twentieth century, injection use increased tremendously and today injections are probably the most common health care procedure (Drucker et al. 2001). Poor injection practices, including injection overuse and unsafe practices, have been reported in many developing and transitional countries (Simonsen et al. 1999). 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 needed (Reeler 1990; Simonsen et al. 1999). 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 22.1).

Unsafe injection practices constitute an important route of infection for bloodborne pathogens. Recently, a study suggested that the spread of HCV through unsafe injections in Egypt may represent the largest nosocomial outbreak ever reported (Frank et al. 2000). Epidemiological studies have reported an association between contaminated injections and infection with bloodborne pathogens, including HBV, HCV and HIV

Figure 22.1 Injection equipment soaked in tepid water before reuse in the absence of sterilization, Africa, 2000

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

(Simonsen et al. 1999). The causal nature of this association is supported by many criteria. First, transmission through unsafe injection practices is biologically plausible because all three viruses are present in blood and body fluids of infected individuals (Choo et al. 1989; Molina et al. 1994; Shikata et al. 1977). They can be transmitted by transfusion (Aach et al. 1991; Busch et al. 1996; Senior et al. 1974) and other percutaneous routes, including needle-stick injuries among health care workers (Cardo et al. 1997; CDC 1997; Seeff et al. 1978). Second, several studies in developing countries have demonstrated an association between receiving injections and infection with bloodborne pathogens. Third, the measures of association (e.g. odds ratios) often exceed 2 (Luby et al. 1997; Narendranathan and Philip 1993; Quigley et al. 2000) and show a dose–response relationship (Khan et al. 2000; Ko et al. 1991a; Quigley et al. 2000). Fourth, studies have also reported an association between recent, incident cases of infection with HBV (Hutin et al. 1999), HCV (El-Sakka 1997) and HIV (Quigley et al. 2000), and exposure to injections during the time period that patients were likely to have been infected, indicating that the exposure preceded the outcome.

The proportion of new infections with HBV, HCV and HIV attributable to unsafe injection practices in specific populations can be estimated from case–control and cohort studies. A total of 12 studies (Table 22.1) were identified to examine the association between HBV infection and injections, with population attributable fractions ranging between 21% and 61% (Anonymous 1998; Hsu et al. 1993; Hussain 2001; Hutin et al. 1999; Ko and Chung 1991; Ko et al. 1991a; Luby et al. 1997; Narendranathan and Philip 1993; Simard et al. 2000; Singh et al. 2000; Thuring et al. 1993; Val Mayans et al. 1990). Of these eight (67%) were based upon recent, incident cases. A total of 10 studies (Table 22.2) were identified to examine the association between HCV infection and injections, with population attributable fractions ranging between 20% and 84% (Chang et al. 1996; Chen et al. 1995; El-Sakka 1997; Ho et al. 1997; Khan et al. 2000; Luby et al. 1997; Mohamed et al. 1996; Sun et al. 1999, 2001; Thuring et al. 1993). Of these, three were based upon recent, incident cases. A total of four studies (Table 22.3) based upon recent, incident cases were identified to examine the association between HIV infection and injections, with population attributable fractions ranging between 8% and 45% (Bultreys et al. 1994; N'Galy et al. 1988; Quigley et al. 2000; Wawer et al. 1994). (Studies based upon prevalent cases of HIV infection are not included in this report as the high frequency of HIV transmission through sexual exposure raises the possibility of reverse causation.)

Two limitations were common among the studies of the association between injections and infections. A first limitation was that studies of persons with prevalent, chronic infections are generally unable to distinguish the direction of the causal relationship between injections and infection. While study subjects could have acquired infections because

Table 22.1 Studies examining the association between health care injections and HBV infection

Country or area	*Author(s)*	*Year of study*	*Study design*	*Types of cases*	*Attributable fraction (%)*
Cambodia	Thuring et al. (1993)	1990–1991	Survey	Prevalent	2–13
China (Province of Taiwan)	Hsu et al. (1993)	1994	Case–control	Prevalent	24.6
China (Province of Taiwan)	Ko and Chung (1991)	1984–1989	Cohort	Incident	43.1
China (Province of Taiwan)	Ko et al. (1991a)	1991[a]	Cohort	Incident	73.9
Gambia	Val Mayans et al. (1990)	1988	Cohort	Incident	*
Egypt	Anonymous (1998)	1994	Case–control	Incident	27.7
India	Narendranathan and Philip (1993)	1993[a]	Case–control	Incident	53.3
India	Singh et al. (2000)	1998	Case–control	Incident	49.7
Pakistan	Hussain (2001)	2000–2001	Case–control	Prevalent	52
Pakistan	Luby et al. (1997)	1994	Case–control	Prevalent	35–41
Romania	Hutin et al. (1999)	1998	Case–control	Incident	40
Republic of Moldova	Hutin et al. (1999)	1994–1995	Case–control	Incident	21, 52[b]

* No association found. However, only immunization injections were considered.

[a] Year of publication.

[b] 21% among children, 52% among adults.

Table 22.2 Studies examining the association between health care injections and HCV infection

Country or area	*Author(s)*	*Year of study*	*Study design*	*Types of cases*	*Attributable fraction (%)*
Cambodia	Thuring et al. (1993)	1990–1991	Survey	Prevalent	90.6
China (Province of Taiwan)	Chang et al. (1996)	1991	Survey	Prevalent	50.4
China (Province of Taiwan)	Chen et al. (1995)	1990–1994	Case–control	Incident	20.1
China (Province of Taiwan)	Ho et al. (1997)	1993	Case–control	Prevalent	51–88
China (Province of Taiwan)	Sun et al. (1999)	1992	Case–control	Prevalent	44
China (Province of Taiwan)	Sun et al. (2001)	1994	Case–control	Incident	36.4
Egypt	El-Sakka (1997)	1996–1997	Case–control	Incident	87.9
Egypt	Mohamed et al. (1996)	1996	Survey	Prevalent	9.9
Pakistan	Khan et al. (2000)	1995	Case–control	Prevalent	24.4–78.5
Pakistan	Luby et al. (1997)	1994	Case–control	Prevalent	1.4, 62.9[a]

[a] 1.4% for injections received during past year; 62.9% for injections received during the past 10 years.

Table 22.3 Studies examining the association between health care injections and HIV infection[a]

Country	*Author(s)*	*Year of study*	*Study design*	*Types of cases*	*Attributable fraction (%)*
Democratic Republic of the Congo	N'Galy et al. (1988)	1984–1986	Cohort	Incident	28
Rwanda	Bultreys et al. (1994)	1989–1993	Cohort	Incident	45
Uganda	Quigley et al. (2000)	1990–1997	Case–control	Incident	16, 41[b]
Uganda	Wawer et al. (1994)	1989–1990	Cohort	Incident	8

[a] Restricted to studies recruiting recent, incident cases of HIV infection.

[b] 16% among women, 41% among men.

they received injections, they could also have received injections as a result of complications of their infection. Studies examining risk factors for HCV and HIV infections are more often affected by this bias because recent, acute cases of infection with these two pathogens are difficult to identify. However, three elements suggest that reverse causation is unlikely. First, most case patients in these studies were asymptomatic and therefore unlikely to seek injections for treatment of their infection. Second, a study that included prevalent cases of infection and examined the association between injections received during different time periods reported that injections received in a distant past were more strongly associated with infection than those received in a recent past, precisely the opposite of what could be expected if the hypothesis of reverse causation were true (Luby et al. 1997). Third, studies that included incident, recent cases of infections have reported similar associations (Chen et al. 1995; El-Sakka 1997; Sun et al. 2001). This includes a prospective cohort study examining the risk factors for HCV infection that validated the results of a cross-sectional survey conducted in the same population (Sun et al. 2001).

A second limitation was that the association between injections and infections with bloodborne pathogens may have been confounded by a number of other exposures, including sexually transmitted infections (STIs). In some cases, the apparent association between injections and infection may be secondary to two hidden associations—between STIs and injections on the one hand, and between STIs and infection on the other. However, confounding is unlikely to explain the associations observed because most studies also examined risk factors other than injections, including STIs, and a number of studies used stratification and multivariate analysis to control for these potential confounders. Nonetheless, there is still a need for research to determine the degree to

which STIs and injections confound each other's relationship with bloodborne pathogens, particularly in the case of HIV infection.

Because information from epidemiological studies was too limited to permit estimation of the global burden of disease attributable to unsafe injections, a global mass action mathematical model was generated in 1995 (Aylward et al. 1995) and further developed to formulate regional estimates in 1999 (Kane et al. 1999). This model included input parameters reflecting injection frequency, injection safety, the percutaneous transmission potential of bloodborne pathogens and the epidemiology of infection with HBV, HCV and HIV. Results of this analysis suggested that each year, in the world, reuse of injection equipment in the absence of sterilization accounts for 8 to 16 million HBV infections, 2.3 to 4.7 million HCV infections and 80 000 to 160 000 HIV infections (Kane et al. 1999).

This mass action model had three main limitations. First, it did not address variations of input parameters (i.e. injection frequency, prevalence of immunity and incidence of HIV infection) across age and sex groups within subregions. Second, no systematic procedure was used to review the literature and generate subregional estimates for injection frequency and injection safety. In this work, we used a new mathematical model to estimate the global burden of disease from unsafe injection practices, which although based on the same general approach as Kane et al. (1999) improves on some of the data limitations. In our analysis, we considered only HBV, HCV and HIV infections because of the substantial information on their association with unsafe injections and because these pathogens probably account for the majority of injection-associated infections. Other complications of unsafe injections not included in this model include abscesses (Fontaine et al. 1984; Soeters and Aus 1989), septicaemia (Archibald et al. 1998), malaria (Abulrahi et al. 1997) and infection with viral haemorrhagic fever viruses (Fisher-Hoch et al. 1995; WHO 1976).

2. Methods

2.1 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, including intradermal, subcutaneous, intramuscular and intravenous injections, for curative or preventive health care purposes, whether administered in a formal health care setting (e.g. clinic, hospital) or other settings (e.g. homes, pharmacies). Injections of illicit drugs were not considered in this work (see chapter 13).

Reuse of injection equipment in the absence of sterilization

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

Choice of exposure variable contaminated injections

Reuse of injection equipment in itself would not be a risk factor in the absence of source patients infected with bloodborne pathogens. Thus, contaminated injections were the risk factor of interest. An injection contaminated with a bloodborne pathogen was defined as an injection given with a needle or a syringe used on an infected patient and reused on a second patient. The exposure under consideration for this study was defined as receiving at least one injection contaminated with HBV, HCV or HIV in one year. Exposure status would therefore depend on reuse of equipment, injection frequency and prevalence of active infection with HBV, HCV and HIV in the population. Persons receiving no contaminated injection in one year were considered unexposed. Four subregions (AMR-A, EMR-B, EUR-A and WPR-A) where reuse of injection equipment in the absence of sterilization was negligible were assumed to have zero risk.

Theoretical minimum level of exposure

The theoretical minimum level of exposure was zero contaminated injections per person and per year. This theoretical minimum is also an achievable goal as there are no reports of reuse of injection equipment in many industrialized countries.

2.2 Transmission model

Data on the risk associated with contaminated injections are generally not available as relative risks, especially since these can change from one place or time to another due to changes in background prevalence. Instead, information from diverse sources such as case–control studies, cross-sectional studies and observational studies of injection practices were brought together and integrated by means of mathematical models to develop internally consistent estimates of prevalence and hazard. The hazard estimates were based on the mass action principle, which states that

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

where p_s is the proportion of the population susceptible to infection (in most cases, 1 minus prevalence of antibody to the virus), p_t is the probability of transmission after percutaneous exposure to a particular

pathogen, 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. This model implicitly assumes that the whole population is equally likely to be currently infected or receive an injection. For HBV, HCV and HIV, the three pathogens under consideration, this incidence is small enough that the equation can be simplified to

$$I_u = p_s \times p_t \times p_r \times p_v \times n$$

which can be further reduced to

$$I_u = p_s \times p_t \times n_c$$

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

$$n_c = p_r \times p_v \times n$$

All parameters were assumed to be different for each of the three pathogens except the annual number of injections per person (n), which was assumed to be constant within a particular age, sex and subregional stratum and the probability of reuse of injection equipment (p_r), which was assumed to be constant within a particular subregion. 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 patient. For HBV, p_t was assumed to vary according to the proportion of the infected population that was negative for hepatitis B e-antigen (HBeAg), ($p_t = 0.06$), or HbeAg positive ($p_t = 0.3$), (Seeff et al. 1978). For HCV, p_t was assumed to be 0.018 (CDC 1997). For HIV, the generally accepted value of p_t of 0.003 (Cardo et al. 1997) for needle-stick injuries was too low, since most injuries on which this estimate was based were superficial and did not involve hollow-bore needles. At the same time, the estimated risk from a deep needle-stick injury that can be estimated from the same study, 0.021, was too high (it is higher than the estimated p_t for HCV) because time can elapse during which HIV can be inactivated between the initial use and the reuse of a syringe on a second patient. As a compromise, the mean of the estimates for superficial and deep injuries, 0.012, was used in the model as p_t for HIV.

2.3 Estimates of the proportion of the population exposed to contaminated injections from the mass action model

If $n_c < 1$ and each person in the population could receive only one injection, then the probability of receiving a contaminated injection, p_c, would equal n_c. However, it is possible for someone to receive two, three or more contaminated injections in any given year. Because contaminated

injections are small probability events (Table 22.6), it can be assumed that the number of contaminated injections per individual follows a Poisson distribution in the population with a mean of n_c per individual, then the probability of receiving zero injections 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, as noted above. 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.

2.4 Estimates of the relative risk from the mass action model

For the purposes of the model, we considered the total incidence of infection in the population, I_t, to be composed of two components: the incidence due to contaminated injections, I_u, and the baseline incidence, I_b, which can also be thought of as the incidence in the population if contaminated injections could be eliminated. I_t can be estimated from incidence or prevalence surveys and I_b can be estimated if I_t and I_u are known:

$$I_b = I_t - I_u$$

and the proportion of infections attributable to unsafe injections is

$$AF = I_u / I_t$$

As this proportion of infections would have occurred only among the exposed proportion of the population (p_c), the risk among the exposed relative to the unexposed, by back-calculation from attributable fraction (AF) relationship, would be:

$$RR_c = 1 + AF/(p_c \times (1 - AF))$$

In most situations where the necessary variables are available or can be estimated from existing data, this equation can estimate the relative risk. However, in situations where a substantial proportion of infections are attributable to contaminated injections (i.e. situations where I_u approaches I_t), this equation produces unstable estimates of the relative risk, and other methods were used, as below.

2.5 Estimates of relative risks from analytical epidemiological studies

Cohort and case–control studies that examined the association between injections and infection defined exposure as receiving at least one injection, contaminated or not, and the absence of exposure as receiving no injections. If RR_i is the estimate of relative risk from such a study and n_i is the average number of injections received by the cases, then $[1 + (RR_i - 1)/n_i]$ is the relative risk attributable to one injection. Only a portion $(p_r \times p_v)$ of the injections received are contaminated and persons who do not receive contaminated injections are at no increased risk. Therefore, the relative risk of infection in a person who receives only one contaminated injection is $[1 + (RR_i - 1)/(n_i \times p_r \times p_v)]$. In practice, this often underestimates the relative risk because persons who receive injections are more likely to have been infected in the past and are therefore less likely to be susceptible to infection. Because of this phenomenon, the calculated RR_i will be an underestimate of the true RR_i if nonsusceptible controls are not excluded from the relative risk calculation. To account for this phenomenon, we assumed that the number of injections received in the prior year was approximately proportional to the probability of having been previously infected, such that the relative risk from receiving a single contaminated injection is $[1 + (RR_i - 1)/(n_i \times p_r \times p_v \times p_s)]$. This method was used to estimate hazard in cases where a substantial proportion of infections was attributable to contaminated injections, as described above.

2.6 Data sources

Injection practice parameters

Sources of information available to estimate the annual number of injections per person (n) included, by decreasing order of data quality, population-based injection frequency surveys and other population-based data providing injection frequency estimates. Sources of information for estimating the proportion of reuse (p_{re}) included, by decreasing order of data quality, observational studies of injection practices using the World Health Organization (WHO) standardized injection safety assessment survey tool (WHO 2002), studies of injection practices conducted using other, non-standardized methods, and back-calculations in published analytical epidemiological studies using the mass action equation and the relative risks of infection with bloodborne pathogens associated with receiving injections.

Sources of information were obtained through Medline searches, searches in WHO unpublished documents, including evaluations of the Expanded Programme on Immunization (EPI) and unpublished reports made available through the electronic mail list server of the Safe Injection Global Network (SIGN) (Bass 2000; Hutin and Chen 1999). All studies were reviewed using a standardized study abstraction instrument

and entered in a database. Estimates were generated for each subregion for proportion of reuse (p_{re}) or number of injections per person for each age, sex and subregional stratum (n) using a standardized decision-making algorithm to use the best source of data available.

The frequency distribution of the annual number of injections per person that was available from two studies conducted in EUR-B (CDC 1999) and in EUR-C (WHO 1999) indicated that a small proportion of the population above the 90th percentile received more than 20 injections per year. To avoid overestimating the attributable fraction, we made the conservative assumption that those receiving such a high number of injections had already been infected and were already immune. Thus, for these two subregions (EUR-B and EUR-C) where the injection frequency distribution was available, we excluded those who had received more than 20 injections per year (approximately above the 90th percentile), thereby reducing the annual number of injections per year. For the other subregions, data were available in tabulated form in published reports. This format already eliminated the upper 10% of the frequency distribution and no adjustment was necessary (e.g. persons reporting more than seven injections per year were all considered to have received eight injections per year). When more than one source of information regarding injection frequency or reuse of equipment was available for one age, sex and subregion stratum, all were used to compute an estimate.

Prevalence and incidence of HBV, HCV and HIV infection

We used the prevalence of active infection in the general population to estimate the proportion of patients representing a source of contamination for reused syringes and/or needles (p_v). Therefore, we did not assume the prevalence of active infection to be higher in a health care setting, nor considered different strata according to selected settings (e.g. immunization vs clinic for the management of STIs) (see discussion). Estimates for the proportion of the population chronically infected with HBV, HCV and HIV were obtained from the WHO programmes on HBV (C. Nelson, personal communication, 2000) and HCV (D. Lavanchy, personal communication, 2000), and from the Joint United Nations Programme on HIV/AIDS (UNAIDS 2000). In the case of HBV and HCV, catalytic models in which the annual risk of infection was constant over time and over age groups were generated. These models were fitted so that annual risk of infection led to region-specific estimates of the prevalence of active infection. Once the annual risk of infection was obtained, it was used to estimate the age-specific prevalence of susceptibility and the total incidence of infection among susceptible individuals. In the case of HIV, incidence estimates were obtained from UNAIDS (2000).

2.7 Estimates of the proportion of the population exposed to contaminated injections

Proportion of reuse

Sources of information used to generate the estimates (Table 22.4) included observational studies of injection practices using the WHO standardized injection safety assessment survey tool (AFR-D, AFR-E and EUR-B), observational studies of injection practices conducted using non-standardized methods (SEAR-B, SEAR-D and WPR-D), back-calculations using the mass action equation and the relative risks of infection with bloodborne pathogens associated with receiving injections (EUR-C), and a combination of the second and the third methods (EMR-D). No quantitative data were available for six subregions. For two of them, AMR-B and AMR-D, there were qualitative reports of reuse. For AMR-B, these reports suggested that reuse was uncommon (Flaskerud and Nyamathi 1996; Ugalde and Homedes 1988; Villanueva et al. 1997). Thus, estimates from the other subregion 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 (Janszen and Laning 1993), estimates from EUR-C, with the second lowest frequency of reuse, were extrapolated. For EUR-A, EMR-B, AMR-A and WPR-A, representing mostly countries with high per capita gross national product, the proportion of reuse was considered negligible. Among subregions for which quantified estimates were available, SEAR-D had the highest proportion of reuse (75%), followed by EMR-D (70%) and WPR-B (30%). EUR-B had the lowest proportion of reuse (1.2%). (See Figure 22.2.)

Annual number of injections per person

Sources of information used to generate subregional input parameters (Table 22.5) included population-based injection frequency surveys, and other population-based studies that provided information about injection frequency. No injection frequency estimates were generated for those subregions for which reuse was considered negligible as no risk applied. Among subregions with quantified information available, EUR-C was the subregion 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) (CDC 1999; WHO 1999). However, when the top 10th percentile of injection frequency was removed, EMR-D was the subregion with the highest injection frequency (4.3 injections per person and per year), followed by SEAR-D (4 injections per person and per year). The subregions 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).

Table 22.4 Subregional estimates of the proportion of injections administered with reused equipment and data sources used, 2000

	AFR-D	*AFR-E*	*AMR-B*	*AMR-D*	*EMR-D*	*EUR-B*	*EUR-C*	*SEAR-B*	*SEAR-D*	*WPR-B*
Proportion of reuse (p_r) (%)	19	17	1.2	11	70	1.2	11	30	75	30
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	Burkina Faso, Chad, Gambia, Mauritania and Niger[a]	Eritrea, Ethiopia, Swaziland, Zambia and Zimbabwe[a]	NA	NA	NA	Kyrgyzstan[d]	NA	NA	NA	NA
Countries from which non-standardized injection safety surveys were used	NA	NA	NA	NA	Pakistan (Khan et al. 2000)	NA	NA	Indonesia (Kosen 1999)	India (Lakshman and Nichter 2000)	China (Schnurr et al. 1999)
Countries from which back-calculated injection safety estimates were used	NA	NA	NA	NA	Egypt (El-Sakka 1997)	NA	Republic of Moldova (Hutin et al. 1999)	NA	NA	NA
Use of other subregional data	NA	NA	EUR-B[b]	EUR-C[c]	NA	NA	NA	NA	NA	NA

NA Not applicable.

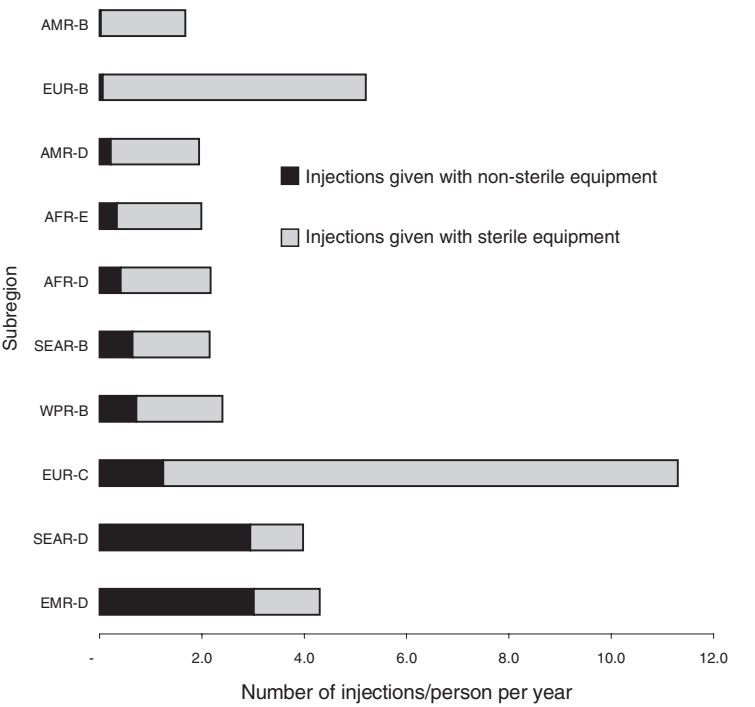
[a] Unpublished WHO reports.

[b] Qualitative information available on injection safety for AMR-B (Flaskerud and Nyamathi 1996; Ugalde and Homedes 1988; Villanueva et al. 1997) suggested occurrence of reuse in the absence of sterilization. To generate a conservative estimate, estimates for the subregion with the lowest proportion were extrapolated.

[c] Qualitative information available on injection safety for AMR-D (Janszen and Laning 1993) suggested occurrence of reuse in the absence of sterilization with a higher frequency than AMR-B. Thus, estimates for the subregion with the second lowest proportion were extrapolated.

[d] J. Fitzner, personal communication, 2002.

Figure 22.2 Number of injections per person and per year, and proportion of these administered with injection equipment reused in the absence of sterilization, by subregion, 2000[a]



[a] Crude injection frequency estimates. For the purpose of the model, estimates for EUR-B and EUR-C were used after subtraction of the 10 top percentiles.

Proportion of the population exposed to contaminated injections

The proportion of the population exposed to contaminated injections reflected the frequency of injections received, the frequency of reuse of injection equipment and the prevalence of active infection with HBV, HCV and HIV (Table 22.6). This estimate varied from 0.03% (AMR-B) to 13.33% (EMR-D) in the case of HBV, from less than 0.03% (AMR-B) to 16.73% (EMR-D) in the case of HCV, and from 0.00% (EUR-B) to 2.05% (AFR-E) in the case of HIV.

2.8 Estimates for the relative risks of infection for receiving contaminated injections

In the case of HIV, contaminated injections did not account for most new infections (i.e. I_u was not close to I_t). Thus, model-based estimates of relative risk were used for all subregions (Table 22.7[c]). In the case

Table 22.5 Subregional injection frequency estimates and data sources used, 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 (*n*)[a]	Crude	2.2	2.0	1.7	1.9	4.3	5.2	11.3	2.1	4.0	2.4
	Truncated[b]	NA	NA	NA	NA	NA	2.5	3.5	NA	NA	NA
Countries from which injection frequency surveys were used		Guinea-Bissau (Ferry 1995)	Central African Republic, Côte d'Ivoire, United Republic of Tanzania, Zambia, Burundi (Ferry 1995), Uganda (Priotto et al. 2001)	Brazil (Ferry 1995)	NA	Egypt (Talaat et al. 2001)	Romania (CDC 1999)	Republic of Moldova (WHO 1999)	Thailand (Ferry 1995; Reeler and Hematorn 1994) Indonesia (Ferry 1995; van Staa and Hardon 1996)	India (Anand et al. 2001; Ferry 1995)	NA

Countries from which other population-based data were used	Cameroon (Ferry 1995; Guyer et al. 1980) Nigeria (Otu et al. 2002)	United Republic of Tanzania (Grosskurth 1995; Quigley et al. 1997) Uganda (Quigley et al. 2000)	Latino communities in the USA (Flaskerud and Nyamathi 1996)	Haiti (Pape et al. 1985)	Pakistan (Luby et al. 1997)	NA	NA	NA	India (Deivanayagam et al. 1993)	China (Province of Taiwan) (Chang et al. 1996; Ko and Chung 1991; Ko et al. 1991a, 1991b)
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[c]	No[c]	No[c]	Yes	No[c]

NA Not applicable.

[a] Estimates age-adjusted using age group-specific population sizes to simplify data presentation. The model actually used age group and sex-specific estimates.

[b] Injections received by those receiving more than 20 injections per year excluded for the calculation of the burden of disease.

[c] Not applicable: age-specific injection frequency estimate takes into account immunization injections.

Table 22.6(a) Proportion of the population (%) receiving injections contaminated with HBV annually, 2000[a]

		Age group (years)							
Subregion	*Sex*	*0–4*	*5–14*	*15–29*	*30–44*	*45–59*	*60–69*	*70–79*	*≥80*
AFR-D	Male	5.51	4.47	4.47	4.47	4.47	4.47	4.47	4.47
	Female	5.51	4.47	4.47	4.47	4.47	4.47	4.47	4.47
AFR-E	Male	4.72	3.31	3.31	3.31	3.31	3.31	3.31	3.31
	Female	4.72	4.20	4.20	4.20	4.20	4.20	4.20	4.20
AMR-B	Male	0.04	0.03	0.03	0.03	0.03	0.03	0.03	0.03
	Female	0.04	0.03	0.03	0.03	0.03	0.03	0.03	0.03
AMR-D	Male	0.52	0.41	0.41	0.41	0.41	0.41	0.41	0.41
	Female	0.52	0.41	0.41	0.41	0.41	0.41	0.41	0.41
EMR-D	Male	13.33	12.01	12.01	12.01	12.01	12.01	12.01	12.01
	Female	13.33	12.01	12.01	12.01	12.01	12.01	12.01	12.01
EUR-B	Male	0.28	0.12	0.09	0.15	0.15	0.15	0.15	0.15
	Female	0.28	0.13	0.16	0.19	0.19	0.19	0.19	0.19
EUR-C	Male	1.86	1.09	1.29	1.42	1.42	1.42	1.42	1.42
	Female	1.78	0.92	1.26	1.78	1.78	1.78	1.78	1.78
SEAR-B	Male	9.95	5.15	5.15	5.15	5.15	5.15	5.15	5.15
	Female	9.95	5.15	5.15	5.15	5.15	5.15	5.15	5.15
SEAR-D	Male	11.22	10.02	10.02	10.02	10.02	10.02	10.02	10.02
	Female	11.22	10.02	10.02	10.02	10.02	10.02	10.02	10.02
WPR-D	Male	11.74	7.84	7.84	7.84	7.84	7.84	7.84	7.84
	Female	11.74	7.84	7.84	7.84	7.84	7.84	7.84	7.84

[a] AMR-A, EMR-B, EUR-A and WPR-A excluded as reuse of injection equipment is negligible in these subregions.

Table 22.6(b) Proportion of the population (%) receiving injections contaminated with HCV annually, 2000[a]

		Age group (years)							
Subregion	*Sex*	*0–4*	*5–14*	*15–29*	*30–44*	*45–59*	*60–69*	*70–79*	*≥80*
AFR-D	Male	1.29	1.04	1.04	1.04	1.04	1.04	1.04	1.04
	Female	1.29	1.04	1.04	1.04	1.04	1.04	1.04	1.04
AFR-E	Male	1.12	0.78	0.78	0.78	0.78	0.78	0.78	0.78
	Female	1.12	0.99	0.99	0.99	0.99	0.99	0.99	0.99
AMR-B	Male	0.04	0.03	0.03	0.03	0.03	0.03	0.03	0.03
	Female	0.04	0.03	0.03	0.03	0.03	0.03	0.03	0.03
AMR-D	Male	0.62	0.49	0.49	0.49	0.49	0.49	0.49	0.49
	Female	0.62	0.49	0.49	0.49	0.49	0.49	0.49	0.49
EMR-D	Male	16.73	15.10	15.10	15.10	15.10	15.10	15.10	15.10
	Female	16.73	15.10	15.10	15.10	15.10	15.10	15.10	15.10
EUR-B	Male	0.09	0.04	0.03	0.05	0.05	0.05	0.05	0.05
	Female	0.10	0.05	0.06	0.07	0.07	0.07	0.07	0.07
EUR-C	Male	1.19	0.70	0.82	0.91	0.91	0.91	0.91	0.91
	Female	1.14	0.59	0.81	1.14	1.14	1.14	1.14	1.14
SEAR-B	Male	3.31	1.68	1.68	1.68	1.68	1.68	1.68	1.68
	Female	3.31	1.68	1.68	1.68	1.68	1.68	1.68	1.68
SEAR-D	Male	5.92	5.27	5.27	5.27	5.27	5.27	5.27	5.27
	Female	5.92	5.27	5.27	5.27	5.27	5.27	5.27	5.27
WPR-D	Male	3.28	2.16	2.16	2.16	2.16	2.16	2.16	2.16
	Female	3.28	2.16	2.16	2.16	2.16	2.16	2.16	2.16

[a] AMR-A, EMR-B, EUR-A and WPR-A excluded as reuse of injection equipment is negligible in these subregions.

Table 22.6(c) Proportion of the population (%) receiving injections contaminated with HIV annually, 2000[a]

		Age group (years)							
Subregion	*Sex*	*0–4*	*5–14*	*15–29*	*30–44*	*45–59*	*60–69*	*70–79*	*≥80*
AFR-D	Male	0.64	0.52	0.52	0.52	0.52	0.52	0.52	0.52
	Female	0.64	0.52	0.52	0.52	0.52	0.52	0.52	0.52
AFR-E	Male	2.05	1.43	1.43	1.43	1.43	1.43	1.43	1.43
	Female	2.05	1.82	1.82	1.82	1.82	1.82	1.82	1.82
AMR-B	Male	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01
	Female	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01
AMR-D	Male	0.13	0.11	0.11	0.11	0.11	0.11	0.11	0.11
	Female	0.13	0.11	0.11	0.11	0.11	0.11	0.11	0.11
EMR-D	Male	0.10	0.09	0.09	0.09	0.09	0.09	0.09	0.09
	Female	0.10	0.09	0.09	0.09	0.09	0.09	0.09	0.09
EUR-B	Male	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
	Female	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
EUR-C	Male	0.08	0.05	0.05	0.06	0.06	0.06	0.06	0.06
	Female	0.07	0.04	0.05	0.07	0.07	0.07	0.07	0.07
SEAR-B	Male	0.33	0.16	0.16	0.16	0.16	0.16	0.16	0.16
	Female	0.33	0.16	0.16	0.16	0.16	0.16	0.16	0.16
SEAR-D	Male	1.19	1.05	1.05	1.05	1.05	1.05	1.05	1.05
	Female	1.19	1.05	1.05	1.05	1.05	1.05	1.05	1.05
WPR-D	Male	0.06	0.04	0.04	0.04	0.04	0.04	0.04	0.04
	Female	0.06	0.04	0.04	0.04	0.04	0.04	0.04	0.04

[a] AMR-A, EMR-B, EUR-A and WPR-A excluded as reuse of injection equipment is negligible in these subregions.

Table 22.7(a) Relative risks associated with receiving injections contaminated with HBV, 2000[a]

		Age group (years)							
Subregion	*Sex*	*0–4*	*5–14*	*15–29*	*30–44*	*45–59*	*60–69*	*70–79*	*≥80*
AFR-D	Male	3.53	3.45	3.45	3.45	3.45	3.45	3.45	3.45
	Female	3.53	3.45	3.45	3.45	3.45	3.45	3.45	3.45
AFR-E	Male	3.47	3.37	3.37	3.37	3.37	3.37	3.37	3.37
	Female	3.47	3.43	3.43	3.43	3.43	3.43	3.43	3.43
AMR-B	Male	75.21	74.68	74.68	74.68	74.68	74.68	74.68	74.68
	Female	75.21	74.68	74.68	74.68	74.68	74.68	74.68	74.68
AMR-D	Male	25.43	24.78	24.78	24.78	24.78	24.78	24.78	24.78
	Female	25.43	24.78	24.78	24.78	24.78	24.78	24.78	24.78
EMR-D	Male	11.71	11.71	11.71	11.71	11.71	11.71	11.71	11.71
	Female	11.71	11.71	11.71	11.71	11.71	11.71	11.71	11.71
EUR-B	Male	6.49	6.44	6.43	6.45	6.45	6.45	6.45	6.45
	Female	6.49	6.45	6.46	6.47	6.47	6.47	6.47	6.47
EUR-C	Male	7.06	6.77	6.85	6.9	6.9	6.9	6.9	6.9
	Female	7.04	6.71	6.84	7.03	7.03	7.03	7.03	7.03
SEAR-B	Male	7.02	5.56	5.56	5.56	5.56	5.56	5.56	5.56
	Female	7.02	5.56	5.56	5.56	5.56	5.56	5.56	5.56
SEAR-D	Male	11.71	11.71	11.71	11.71	11.71	11.71	11.71	11.71
	Female	11.71	11.71	11.71	11.71	11.71	11.71	11.71	11.71
WPR-D	Male	7.86	6.28	6.28	6.28	6.28	6.28	6.28	6.28
	Female	7.86	6.28	6.28	6.28	6.28	6.28	6.28	6.28

[a] AMR-A, EMR-B, EUR-A and WPR-A excluded as reuse of injection equipment is negligible in these subregions.

Table 22.7(b) Relative risks associated with receiving injections contaminated with HCV, 2000[a]

		Age group (years)							
Subregion	*Sex*	*0–4*	*5–14*	*15–29*	*30–44*	*45–59*	*60–69*	*70–79*	*≥80*
AFR-D	Male	19.74	18.88	18.88	18.88	18.88	18.88	18.88	18.88
	Female	19.74	18.88	18.88	18.88	18.88	18.88	18.88	18.88
AFR-E	Male	17.5	16.6	16.6	16.6	16.6	16.6	16.6	16.6
	Female	17.5	17.15	17.15	17.15	17.15	17.15	17.15	17.15
AMR-B	Male	31.36	31.28	31.28	31.28	31.28	31.28	31.28	31.28
	Female	31.36	31.28	31.28	31.28	31.28	31.28	31.28	31.28
AMR-D	Male	21.35	20.81	20.81	20.81	20.81	20.81	20.81	20.81
	Female	21.35	20.81	20.81	20.81	20.81	20.81	20.81	20.81
EMR-D	Male	27.77	27.77	27.77	27.77	27.77	27.77	27.77	27.77
	Female	27.77	27.77	27.77	27.77	27.77	27.77	27.77	27.77
EUR-B	Male	31.9	31.4	31.3	31.49	31.49	31.49	31.49	31.49
	Female	31.9	4.01	31.52	31.62	31.62	31.62	31.62	31.62
EUR-C	Male	31.9	31.4	31.3	31.49	31.49	31.49	31.49	31.49
	Female	31.9	4.01	31.52	31.62	31.62	31.62	31.62	31.62
SEAR-B	Male	38.0	23.86	23.86	23.86	23.86	23.86	23.86	23.86
	Female	38.0	23.86	23.86	23.86	23.86	23.86	23.86	23.86
SEAR-D	Male	37.64	26.72	26.72	26.72	26.72	26.72	26.72	26.72
	Female	37.64	26.72	26.72	26.72	26.72	26.72	26.72	26.72
WPR-D	Male	37.64	26.72	26.72	26.72	26.72	26.72	26.72	26.72
	Female	37.64	26.72	26.72	26.72	26.72	26.72	26.72	26.72

[a] AMR-A, EMR-B, EUR-A and WPR-A excluded as reuse of injection equipment is negligible in these subregions.

Table 22.7(c) Relative risks associated with receiving injections contaminated with HIV, 2000[a]

		Age group (years)							
Subregion	*Sex*	*0–4*	*5–14*	*15–29*	*30–44*	*45–59*	*60–69*	*70–79*	*≥80*
AFR-D	Male	14.05	13.84	5.57	5.57	5.57	5.57	5.57	5.57
	Female	14.05	13.84	3.39	3.39	3.39	3.39	3.39	3.39
AFR-E	Male	5.95	5.79	2.3	2.3	2.3	2.3	2.3	2.3
	Female	5.95	5.89	1.72	1.72	1.72	1.72	1.72	1.72
AMR-B	Male	122.12	121.85	21.03	21.03	21.03	21.03	21.03	21.03
	Female	122.12	121.85	41.1	41.1	41.1	41.1	41.1	41.1
AMR-D	Male	66.27	65.09	8.12	8.12	8.12	8.12	8.12	8.12
	Female	66.27	65.09	16.25	16.25	16.25	16.25	16.25	16.25
EMR-D	Male	1	1	64.41	64.41	64.41	64.41	64.41	64.41
	Female	1	1	135.38	135.38	135.38	135.38	135.38	135.38
EUR-B	Male	1	1	1	1	1	1	1	1
	Female	1	1	1	1	1	1	1	1
EUR-C	Male	1	1	6.48	6.48	6.48	6.48	6.48	6.48
	Female	1	1	31.5	31.7	31.7	31.7	31.7	31.7
SEAR-B	Male	198.4	150.67	26.01	26.01	26.01	26.01	26.01	26.01
	Female	198.4	150.67	43.86	43.86	43.86	43.86	43.86	43.86
SEAR-D	Male	213.52	166.26	16.61	16.61	16.61	16.61	16.61	16.61
	Female	213.52	166.26	33.35	33.35	33.35	33.35	33.35	33.35
WPR-D	Male	1	1	41.69	41.69	41.69	41.69	41.69	41.69
	Female	1	1	127.3	127.3	127.3	127.3	127.3	127.3

[a] AMR-A, EMR-B, EUR-A and WPR-A excluded as reuse of injection equipment is negligible in these subregions.

of HCV, contaminated injections did not account for most of new infections in all subregions apart from EUR-C, SEAR-D and EMR-D. For EUR-C and SEAR-D, model-based relative risks for EUR-B and WPR-B, which had similar prevalence patterns, were used. In EMR-D, the available study-based relative risk was used (Table 22.7[b]) (El-Sakka 1997). In the case of HBV, contaminated injections did not account for most of new infections in all subregions apart from SEAR-D and EMR-D. In EMR-D, the available study-based relative risk was used (Anonymous 1998). For SEAR-D, the study-based relative risk for EMR-D was used as this subregion had HBV prevalence patterns and injection practices close to those of EMR-D (Table 22.7[a]).

2.9 Progression of HBV, HCV and HIV infection to disability and death

Time interval between infection and the occurrence of disability and death

The majority of the burden of disease associated with infections with HBV, HCV and HIV is delayed in time. For HBV infection, a small proportion of acute infections lead to death through fulminant liver failure. However, most of the burden of disease is secondary to the long-term consequences of chronic HBV infection, including end-stage liver disease and hepatocellular carcinoma. For HCV infection, the death to case ratio for acute infections is negligible and all the burden of disease is secondary to the long-term consequences of chronic infection, including end-stage liver disease and hepatocellular carcinoma. For HIV infection, the burden of disease is secondary to the progression to AIDS and to death following AIDS.

To take into account the time interval between infection and the progression towards death and disability, two measures need to be distinguished. First, the attributable burden in 2000 includes the current burden in the year 2000 that is secondary to past and present unsafe injection practices. Second, the future burden due to current unsafe injection practices in 2000 includes the future long-term consequences in terms of end-stage liver disease, hepatocellular carcinoma and AIDS of the HBV, HCV and HIV infections acquired in 2000 because of contaminated injections.

Current burden due to past and present unsafe injection practices

In the absence of information regarding injection practices in the past, we were unable to model the fraction of HBV, HCV and HIV infection that was attributable to contaminated injections before the year 2000. Thus, we made the assumption that the fraction of HBV, HCV and HIV infections attributable to contaminated injections in the past was identical to the one modelled for the year 2000. We then applied these attributable fractions to the current burden in 2000 in terms of DALYs and

deaths that were associated with the consequences of HBV, HCV and infection (i.e. acute infections, hepatocellular carcinoma, end-stage liver diseases and HIV infection/AIDS).

Future burden due to current unsafe injection practices

To reflect the delay between infection and disease outcomes, the fraction of new infections with HBV, HCV and HIV attributable to contaminated injections was converted into years of life lost (YLL) using synthetic cohorts of infected individuals followed for mortality associated with HBV, HCV or HIV infection (AIDS or chronic liver disease) and background mortality. Background mortality was taken into account using age, sex and subregion-specific Global Burden of Disease (GBD) life tables.[2] To estimate the years of life lost secondary to HBV infections, the model parameters included:

- a rate of progression to chronic infection of 30% among persons infected under the age of 5 years and of 6% for persons infected at the age of 5 years or older (McMahon et al. 1985);
- an annual rate of clearance of infection (i.e. sero-reversion) of 1% following chronic infection (Alward et al. 1985); and
- an age-dependent yearly mortality rate associated with chronic liver disease among persons chronically infected with HBV (Figure 22.3) that was modelled on the basis of African and Asian studies (Gay et al. 2001).

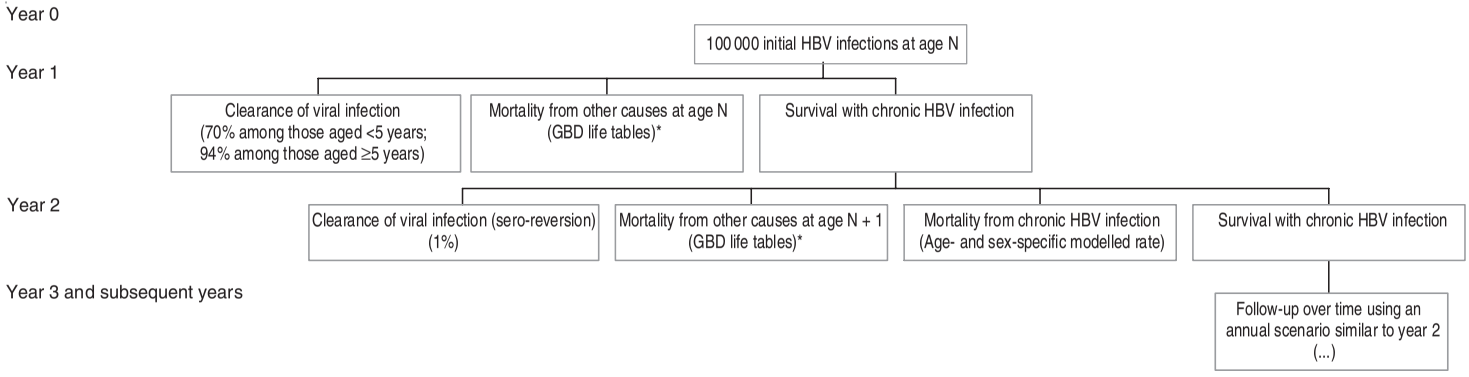
To estimate the years of life lost from HCV infections, two sets of assumptions were used according to the age of the individual at infection (Figure 22.4). For persons infected before the age of 40, the model parameters included:

- a rate of progression to chronic infection of 63%, the average of rates observed in two large studies conducted in this age group (Alter and Seeff 2000);
- a cumulated incidence rate of cirrhosis of 5% at 20 years among patients with chronic infection (Alter and Seeff 2000; Freeman et al. 2001); and
- a yearly mortality rate associated with hepatocellular carcinoma and chronic liver disease of 3.7% after the onset of cirrhosis, the average of two large studies (Alter and Seeff 2000).

For persons infected at the age of 40 years or older, the model parameters included:

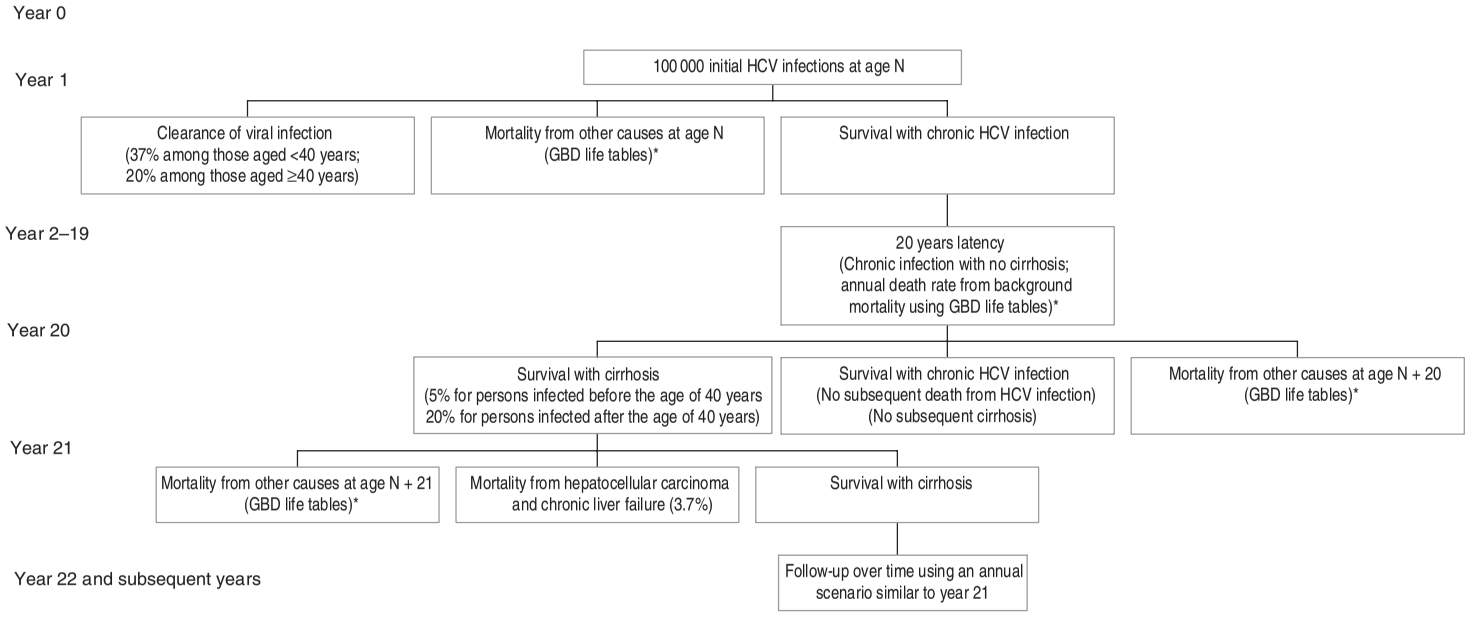
- a rate of progression to chronic infection of 80% (Alter and Seeff 2000);

Figure 22.3 Decision tree for the theoretical cohort used for the calculation of the years of life lost (YLL) secondary to hepatitis B virus infection



* GBD life tables prepared for *World health report 2001* (WHO 2001).

Figure 22.4 Decision tree for the theoretical cohort used for the calculation of the years of life lost (YLL) secondary to hepatitis C virus infection



* GBD life tables prepared for *World health report 2001* (WHO 2001).

- a cumulated incidence rate of cirrhosis of 20% at 20 years (Alter and Seeff 2000; Freeman et al. 2001); and
- a yearly mortality rate associated with chronic liver disease of 3.7% after the onset of cirrhosis, as in the younger age group.

Disability and death attributable to acute viral hepatitis were considered negligible for HBV and HCV in comparison with the disability and death secondary to chronic infection. In the case of HIV, parameters of progression of HIV infection to AIDS and death developed by WHO and UNAIDS were used (N. Walker, personal communication, 2002).

Uncertainty analysis

Standard errors were calculated for selected key input parameters, including the annual number of injections per person and the proportion of reuse. Standard formulae for the calculation of confidence intervals for means and proportions were used. In the specific case of the proportion of reuse estimated on the basis of measures of association, total sample size was assumed to be the total number of study participants included in the study.

For subregions for which good quality data were available on injection frequency (injection frequency surveys) or injection safety (standardized or non-standardized injection safety surveys), a 95% confidence interval was calculated for the input parameter on the basis of the standard error (±2 SE). For subregions for which only lower quality data were available for injection frequency (other population-based injection frequency data) or injection safety (back-calculated estimates), an arbitrary larger interval was used to account for added uncertainty (±4 SE). For subregions for which no data were available and inferences were made using other subregions, an even larger interval was arbitrarily used to account for added uncertainty (±6 SE).

Lower and upper bounds of the 95% confidence intervals for the proportion of the population exposed and for relative risk estimates were obtained by including the values for lower and upper bounds of the input parameters in the model equations. Confidence intervals for the relative risks that were study-based rather than model-based were calculated on the basis of the confidence interval of the relative risk in the original epidemiological studies. See section 4 for further discussion of sources of uncertainty.

3. Results

3.1 Fraction of infections attributable to contaminated injections in 2000

Globally, the fractions of incident HBV, HCV and HIV infections attributable to contaminated injections in the subregions where reuse of injec-

tions was reported were 31.9%, 39.9% and 5.4%, respectively (Table 22.8). For HBV, this proportion was highest in EMR-D (58.3%) and lowest in EUR-B (0.9%). For HCV, this proportion was highest in EMR-D (81.7%) and lowest in EUR-B (0.9%). For HIV, this proportion was highest in SEAR-D (24.3%) and lowest in AMR-B (0.00%). In absolute numbers of infections, our analysis indicated that globally, in 2000, contaminated injections may have caused 20.6 million cases of new HBV infections, 2.0 million cases of HCV infections and 260 000 cases of HIV infections.

3.2 Current burden due to past and present unsafe injection practices

The current burden in 2000 due to past and present unsafe injection practices reached 501 000 deaths, with the majority of deaths occurring in Asia (39% and 31% in WPR-B and SEAR-D, respectively) (Table 22.9) and among persons aged ≥15 years (n = 444 000, 88%). When death and disability were combined, the burden reached 10 461 000 DALYs, with a similar predominance in Asia (27% and 39% in WPR-B and SEAR-D, respectively) and adults (n = 8 419 000, 81% of DALYs among persons aged ≥15 years). Taken together, viral hepatitis B and C and their chronic consequences accounted for 74% and 61% of the deaths and DALYs, respectively, and HIV accounted for the remainder. There were no substantial differences in the distribution of death and disability by sex.

3.3 Future burden due to current unsafe injection practices

Models of natural history and background mortality allowed estimation of the burden of disease attributable to contaminated injections received in 2000. This analysis suggested that the 20.6 million HBV infections in the year 2000 would lead to 26 492 deaths in 2000 from fulminant hepatitis and an additional 49 000 early deaths from the consequences of chronic infection between 2000 and 2030. With respect to HCV infection, we estimated that the two million infections in 2000 would lead to 24 000 early deaths between 2000 and 2030. 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. While our analytic horizon did not go beyond year 2030, it is anticipated that persons infected with HBV and HCV because of contaminated injections in 2000 would continue to develop long-term complications leading to death beyond this date.

4. Discussion

While the consequences of poor injection practices have been recognized for many decades (Anonymous 1945; Wyatt 1984), the safe and

Table 22.8 HBV, HCV and HIV infections attributable to contaminated injections (attributable fraction and absolute numbers, lower and upper estimates), 2000

	HBV		*HCV*		*HIV*	
Subregion	*Attributable fraction (%)*	*Number of infections*	*Attributable fraction (%)*	*Number of infections*	*Attributable fraction (%)*	*Number of infections*
AFR-D	10.9 (8.2–13.9)	639 498 (478 834–814 351)	16.4 (12.3–20.8).	54 681 (41 078–69 402)	2.5 (1.9–3.1)	18 317 (13 765–23 243)
AFR-E	9.2 (6.9–11.5)	630 976 (474 379–792 536)	13.0 (9.8–16.2)	54 131 (40 819–67 794)	2.5 (1.9–3.1)	64 412 (48 520–80 759)
AMR-B	2.3 (0.0–16.3)	14 118 (112–98 872)	0.9 (0.0–6.4)	2 282 (18–15 985)	0.2 (0.0–1.5)	305 (2–2 132)
AMR-D	9.3 (0.0–26.9)	28 570 (16–82 490)	9.2 (0.0–26.7)	6 304 (4–18 215)	1.5 (0.0–4.5)	911 (1–2 626)
EMR-D	58.3 (26.2–82.4)	2 533 443 (1 140 352–3 580 611)	81.7 (52.1–95.0)	645 486 (412 078–750 452)	7.1 (5.7–8.5)	2 210 (1 775–2 668)
EUR-B	0.9 (0.0–3.3)	21 122 (156–78 639)	0.9 (0.0–3.4)	2 110 (16–7 729)	0.0 (0.0–0.0)	0 (0–0)
EUR-C	7.7 (1.8–15.0)	193 636 (46 035–378 229)	21.2 (6.1–34.7)	35 668 (10 287–58 378)	0.6 (0.2–1.2)	1 526 (374–2 903)
SEAR-B	22.4 (16.5–28.7)	942 038 (694 606–1 205 102)	30.8 (22.8–39.2)	94 873 (70 235–120 979)	7.0 (5.2–8.9)	6 260 (4 638–7 980)
SEAR-D	53.6 (21.6–79.9)	8 019 210 (3 237 944–11 954 579)	59.5 (40.4–93.6)	498 166 (338 548–784 474)	24.3 (18.3–0.1)	156 663 (118 235–194 187)
WPR-B	33.6 (0.0–79.0)	7 610 161 (2 126–17 868 925)	37.6 (0.0–89.8)	608 200 (172–1 454 478)	2.5 (0.0–5.9)	5 549 (2–13 378)
World	31.9 (9.4–56.9)	20 632 772 (6 074 558–36 854 335)	39.9 (18.2–66.7)	2 001 901 (913 254–3 347 885)	5.4 (3.9–7.0)	256 152 (187 312–329 877)

Table 22.9 Current burden in 2000 due to past and present contaminated injections

		AFR-D	*AFR-E*	*AMR-B*	*AMR-D*	*EMR-D*	*EUR-B*	*EUR-C*	*SEAR-B*	*SEAR-D*	*WPR-B*	*World*
Deaths	HBV and HCV	6	6	1	1	41	1	10	25	88	193	372
(000s)	HIV/AIDS	10	44	0	0	4	0	0	3	66	1	129
	Total	16	51	1	2	44	1	10	28	154	194	501
DALYs	HBV and HCV	106	111	15	22	721	13	162	413	2007	2781	6349
(000s)	HIV/AIDS	325	1436	2	10	106	0	3	99	2094	38	4112
	Total	430	1547	17	31	826	13	165	512	4100	2819	10461

appropriate use of injections remains a target that has not been reached in most developing and transitional countries. Since the early 1990s, epidemiological studies of new HBV, HCV and HIV infections have indicated that unsafe injections are a risk factor for each disease (Simonsen et al. 1999). In most transitional and developing countries where HBV and HCV lead to a high burden of chronic liver disease, unsafe injections account for a high proportion of these infections (Hutin et al. 1999; Khan et al. 2000; Luby et al. 1997; Narendranathan and Philip 1993).

This chapter made use of the best available evidence regarding the rates of injection use, the frequency of reuse and the association between injections and infections. Use of a mass action model was needed for the communicable nature of outcomes and lack of transferability of hazard from across populations. The results indicate that in 2000, four decades after the widespread availability of disposable injection equipment and two decades into the HIV pandemic, contaminated injections accounted for close to a third of new HBV infections, 40% of new HCV infections and 5% of new HIV infections globally. The burden of disease in 2000 due to past and current infections reached 501 000 deaths and 10 461 000 DALYs, with the majority of deaths occurring among adults, mostly in Asia.

Using available studies, we described injection practices worldwide in terms of safety and frequency. Our analysis indicated high rates of injection worldwide, with marked subregional variations, for a total exceeding 16 thousand million injections in the 10 (of 14) subregions that were included in our study. This order of magnitude is validated by the market analysis suggesting that in Japan, the United States of America and western Europe, 17.5 thousand million syringes are sold annually (Kaninda 2001).

Four subregions 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 11.3 and 5.2 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 (CDC 1999; WHO 1999). While patients' demand is commonly quoted by health care providers as a major driver of injection overuse, knowledge, attitude and practice (KAP) surveys find that health care providers have a tendency to overestimate patients' preference for injections and that the population is open to alternatives to injected medications (CDC 1999; Vong et al. 2002). In fact, KAP surveys conducted among physicians indicate that prescribers have false preconceptions about the effectiveness of injectable medications and that these preconceptions are sometimes supported by non-evidence-based official treatment protocols. Thus, prescribers' attitudes also contribute to injection overuse (Stoica et al. 1999).

Injection use was also high in the Middle East and in south Asia where the annual number of injections per person reached 4.3 and 4.0 in EMR-

D and SEAR-D, respectively. In these countries, a high proportion of injections are administered by private providers who, in some cases, are not medically qualified (Khan et al. 2000; Kosen 1999; Talaat et al. 2001). In such settings, health care providers' attitudes also drive injection overuse (Khan et al. 2000; Luby et al. 1997). However, practices are different. The reference to any guideline is uncommon. Injections are frequently used on an ad hoc basis to administer mixtures of antibiotics, analgesics, vitamins or antihistamines in the desire to meet what is believed to be the demand of the user (Khan et al. 2000).

Reducing injection overuse would only be a matter of promoting rational drug use if injections were administered safely. Unfortunately, our analysis indicated 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, sterile, single-use, disposable injection equipment (Dicko et al. 2000), the lack of awareness among patients and providers regarding the risks associated with unsafe practices (Anand et al. 2001; Khan et al. 2000), and the absence of an efficient sharps waste management system to prevent recycling of contaminated equipment (Hofmann 2001). Of interest, our analysis suggests that injection practices are safer in sub-Saharan Africa (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 (Luby et al. forthcoming), 19% in India in 1999 (Anand et al. 2001) and 52% in Burkina Faso in 2001 (Logez 2001). In addition, 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 (Birungi 1998) may partly explain this difference observed in the proportion of reuse.

HBV infection was the most common consequence of unsafe injection practices in the world, with more than 20 million cases of infection annually. Among the three pathogens that we examined, HBV is the most prevalent globally (Maynard et al. 1989) and the one most easily transmitted through unsafe injections (Seeff et al. 1978). The subregion-specific fractions of new HBV infections attributable to contaminated injections were compatible with those reported in analytical studies, including 2% (Thuring et al. 1993) to 73.9% (Ko et al. 1991a) in WPR-B (compared with 33.6% in our model), 49.7% (Singh et al. 2000) to 53.3% (Narendranathan and Philip 1993) in SEAR-D (compared with 53.6% in our model) and 27.7% (Anonymous 1998) to 52% (Hussain 2001) in EMR-D (compared with 58.3% in our model). Because attributable fractions were also high among children aged <5 years, a substantial proportion of unexplained transmission of HBV among preschool children may thus be attributed to unsafe injections

(Davis et al. 1989). Such infections would entail a substantial burden of disease and death in the future since the long-term consequences of HBV infections are most severe among persons infected during childhood (McMahon et al. 1985). The natural history of the infection is well described for HBV and there was relatively little uncertainty around the disease progression parameters that we used.

The burden of disability and death secondary to injection-associated HBV infections was estimated to be low in comparison to the number of infections because of the low proportion of progression to chronic infections and the delay between infection and death. This delay between initial infection and death reduced the burden because of the 30-year horizon of this work and because background mortality would lead infected persons to die from other causes during this time interval. In addition, the burden of disease avoidable through the control of contaminated injections as a risk factor is limited because universal childhood immunization against hepatitis B is being increasingly introduced in resource-poor countries with the support of the Global Alliance for Vaccines and Immunization (GAVI). If high vaccination rates are indeed reached in the future, as in our assumptions for 2030, herd immunity will progressively reduce the incidence of injection-associated infections through a high prevalence of immunity and a low prevalence of active infection (Wittet 2001).

HCV infection was estimated to be the second most common consequence of contaminated injections worldwide, with more than two million infections each year. Injection-associated HCV infection was less common than injection-associated HBV infection because of the lower prevalence of HCV infection (WHO 2000a) and the lower percutaneous transmission potential of HCV (CDC 1997). However, the fraction of new HCV infection attributable to contaminated injections was high among all age groups, including adults, and was higher than for HBV infection. These high attributable fractions are compatible with those reported in analytical studies, including 20.1% (Chen et al. 1995) to 90.6% (Thuring et al. 1993) in WPR-B (compared with 37.6% in our model), and 9.9% (Mohamed et al. 1996) to 87.9% (El-Sakka 1997) in EMR-D (compared with 81.7% in our model).

HCV is primarily transmitted through percutaneous or permucosal exposure to blood (Alter 1995). Transmission among sexual partners occurs but is not efficient (Alter 1995), occurring mostly among individuals engaging in high-risk sexual behaviour that may expose them to blood, or body fluids contaminated with blood (Williams et al. 1999). Sexual transmission may account for a higher proportion of HCV infections in industrialized countries, where contaminated health care injections and other unsafe percutaneous procedures are uncommon (Alter et al. 1999). However, in developing and transitional countries, the exposures most likely to transmit HCV include unsafe injections, transfusion of blood, blood components and blood products, and other unsafe

percutaneous exposures conducted in medically-related and other settings (e.g. dental care, surgery, circumcision, shaving).

The risk of HCV infection following transfusion of contaminated blood—about 92% (Aach et al. 1991)—greatly exceeds the risk of HCV infection following a contaminated injection. However, transfusion of blood, blood components and blood products is an infrequent exposure in comparison with injections. Annually, worldwide, it is estimated that over 75 million blood donations occur (WHO 2000b). Our analysis suggested that for developing and transitional countries alone, more than 16 thousand million injections might occur annually. Thus, despite a lower risk associated with each unsafe event, the higher frequency of injections explains why, globally, our analysis suggested that a high proportion of HCV infection was attributable to contaminated injections. While percutaneous exposures other than injections have been associated with HCV infection in epidemiological studies, they rarely explain a high proportion of infections (Wasley and Alter 2000).

HCV infection is currently not preventable through immunization and, in contrast to HBV infection, its long-term consequences may be more severe among persons infected during adulthood than among persons infected during childhood (Alter and Seeff 2000; Vogt et al. 1999). To estimate the burden of disease secondary to current injection-associated HCV infections, we used conservative estimates for the parameters describing the progression of HCV infection towards chronic liver disease and its consequences. However, there is substantial uncertainty as to whether these estimates obtained from studies conducted in industrialized countries are representative of the natural history of HCV infection in developing and transitional countries as environmental factors could influence the risk of progression to chronic liver diseases and its consequences. In addition, because the parameters that we selected assume that infected patients only die after 20 years, the 30-year analytic horizon of this work only captured a small proportion of the future early deaths. Nevertheless, if the parameters used in our model were indeed representative, our analysis would suggest that injection-associated HCV infections would not constitute a major avoidable burden of disease between 2000 and 2030. If we underestimated the severity of the natural history of HCV infection, then the burden of chronic liver disease and death secondary to injection-associated HCV infection that could be avoided in the future, particularly in countries highly endemic for HCV, would be estimated as substantial.

Historically, health care injections have not been viewed as a major vehicle of HIV infection and the promotion of safe injection practices has not held a high priority in HIV prevention programmes. However, most nosocomial outbreaks of HIV infection have been reported from countries with low prevalence of HIV infection, including Colombia (Shaldon 1995), the Libyan Arab Jamahiriya (Yerly et al. 2001), Romania (Hersh et al. 1993) and Ukraine (Simonsen et al. 1999). In

other countries where HIV infection and poor injection practices are more common and where sexual transmission accounts for the majority of infections, injection-associated HIV infections are likely to occur but they have rarely been reported or suspected.

Our analysis suggests that contaminated injections may cause 5.4% of new cases of HIV infection worldwide, representing the largest burden of disease that could be avoided through safe and appropriate use of injection policies. Few epidemiological studies are available with which to validate our estimates, either because transmission through injections was not examined or because these studies were not based upon recent, incident HIV infections. This lack of information represents a substantial source of uncertainty. In AFR-E where several studies were available (Bultreys et al. 1994; N'Galy et al. 1988; Quigley et al. 2000; Wawer et al. 1994), the lowest attributable fraction (8%) calculated on the basis of the data provided by Wawer et al. (1994) largely exceeded our estimate of 2.5%. In EMR-D and SEAR-D, the model suggests that the attributable fraction could reach 7.1% and 24.3%, respectively. These estimates are not validated by epidemiological studies and may be overestimated because the epidemic is still concentrated, violating the assumptions made in the mass action model about the distribution of contaminated injections. Despite large uncertainty in attributable fractions in these two subregions, the high frequency of unsafe injection practices coinciding with emerging HIV epidemics must lead to urgent preventive measures.

In the future, studies of 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 injections. In the meantime, HIV prevention programmes should communicate the risk of HIV infection associated with health care injections since safe and appropriate use of injection policies constitute effective interventions against HIV infection (CDC 2001; Logez 2001; Prawitasari Hadiyono et al. 1996).

While much emphasis was put on gathering the best available data from published and unpublished sources, this analysis has a number of limitations due to data scarcity.

- Our model was constrained by the limited number of studies with adequately described injection practices. Moreover, some of these studies employed non-standardized methodologies, which could not be used. The high frequency of injections reported in developing and transitional countries contrasts with the paucity of data available to describe practices. Until recently, few standardized tools for assessment or evaluation were available to routinely collect information on injection frequency or safety. However, WHO has recently developed new assessment tools that utilize standardized methods, which will prospectively generate information of appropriate quality. This should

allow future revisions of these burden of disease estimates to be based upon data of better quality.

- The transmission potential of HBV, HCV and HIV through percutaneous exposure was obtained on the basis of epidemiological studies that estimated the risk of infection with bloodborne pathogens among health care workers following a needle-stick injury. Although these figures are based upon many well-conducted studies that included a large number of study participants, they estimated a different risk: infection associated with a needle-stick injury. Factors that could cause the risk from contaminated injections to be higher than the risk from needle-stick injuries include the liquid flow rinsing the needle that occurs during an injection and the potential survival of HBV and HCV in the pots of tepid water often used to rinse injection equipment between injections. Factors that could cause the risk from contaminated injections to be lower than the risk from needle-stick injuries include a longer time interval between injections that could cause inactivation of some virus particles and a dilution effect in the pots of tepid water when injection equipment is reused.
- Our model only estimated the incidence of infections with HBV, HCV and HIV secondary to the reuse of injection equipment on one patient. It did not take into account the transmission secondary to the reuse of equipment on multiple patients, the transmission associated with unhygienic use of multi-dose medication vials and the transmission that may occur through cross-contamination while preparing injections. Failure to address these specific unsafe practices may have led to an underestimation in our results.
- Our analysis did not take into account any transmission networks by which injection frequencies, background prevalence of infection or probability of exposure to unsafe practices, were assessed. As a result, exposure to contaminated injections would not be distributed independently, thus creating various population subgroups with different bloodborne pathogen transmission dynamics. This would be particularly important in settings with concentrated groups of infected persons (e.g. persons with HIV in SEAR-D). However, we excluded persons presenting with very high injection frequencies to calculate the subregional injection frequency input parameters and adjusted the model for the possibility that persons receiving a high number of injections could already have immunity against infection with bloodborne pathogens. Further a potential network effect could involve percutaneous and sexual transmission (e.g. use of injected antibiotics among commercial sex workers), thereby transforming a dendritic transmission network into a more effective cyclic one (Potterat et al. 1999; Rothenberg et al. 1998).

Safe and appropriate use of injection policies aims to eliminate unnecessary injections and achieve safe injection practices. Such initiatives should not constitute separate programmes but should be integrated with other activities (WHO 2000c) to provide more effective interventions including:

- communication of risks associated with unsafe injections to patients and health care workers through disease prevention programmes such as HIV prevention;
- ensuring access to sufficient quantities of single-use, disposable injection equipment in health care facilities; and
- management of sharps waste to prevent reuse of dirty equipment and needle-stick injuries.

This study generated initial estimates of the burden of disease that could be avoided through the implementation of such policies. Further studies will address sources of uncertainty that remain in the natural history of HCV infection and in the proportion of HIV infections attributable to contaminated injections.

5. Projections of future levels of exposure

The future prevalence of exposure to contaminated injections and the future relative risk of HBV, HCV or HIV infection associated with contaminated injections were calculated by including different input parameters into the same model. Assumptions regarding the injection practice parameters in 2030, including the annual number of injections per person and proportion of reuse, were generated through a survey of nine experts from four of the six WHO regions. These projections took into account the high effectiveness of planned or implemented interventions aimed at improving the safety of injections, the moderate effectiveness of interventions aimed at decreasing injection overuse, the prospective for future increased access to health care in sub-Saharan Africa (which could lead to an increase in injection use), and the potential for health care reform in the former socialist countries of eastern Europe and central Asia (which could lead to a decrease in injection overuse). Assumptions regarding the expected number of injections per person and the proportion of reuse were compatible with a slight decrease of injection frequency and a marked improvement of injection safety, although subregions were expected to remain heterogeneous (Table 22.10).

Epidemiological parameters of HBV infection were modified to account for the expected increased use of hepatitis B vaccine secondary to the accelerated introduction of this vaccine into immunization programmes supported by GAVI: the three-dose vaccine coverage was assumed to be 90% among persons aged <15 years and 50% among persons aged 15–29 years. The prevalence of active infection in the pop-

Table 22.10 Assumptions regarding projected injection practices in 2030

	AFR-D	*AFR-E*	*AMR-B*	*AMR-D*	*EMR-D*	*EUR-B*	*EUR-C*	*SEAR-B*	*SEAR-D*	*WPR-B*
Proportion of reuse (%)	8	7	0	4	25	0	4	8	17	9
Annual no. of injections per person	2.3	2.2	1.2	1.9	3.0	1.6	2.2	1.7	2.4	1.8

ulation was assumed to be 2% in all subregions, except for AMR-B and AMR-D, where it was assumed to be 0.5%. The annual incidence among susceptible individuals was assumed to be 0.1% in all subregions, except for AMR-B and AMR-D where it was assumed to be 0.01%. In the absence of available epidemiological projections, the incidence and the prevalence of HCV and HIV were assumed to remain constant. Changes in parameters were assumed to be linear between 2000 and 2030.

Our projections into the future of the risk of infection with bloodborne pathogens associated with exposure to contaminated injections did not take into account the dynamic effect of new injection-associated infections on the prevalence of infection with bloodborne pathogens. Our model, a Bernoulli risk projection model, is more adapted to the estimation of the current and past incidence of injection-associated infections. In the case of HIV, where contaminated injections account for only a small proportion of new infections and the pandemic continues to be largely driven by sexual transmission, this limitation is unlikely to substantially affect our results. In the case of HBV, contaminated injections account for a substantial proportion of new infections. The impact of prevention policies on the future burden of disease is likely to be underestimated because prevented cases of HBV infection will reduce the pool of chronically infected persons who constitute sources of infection. However, in countries of intermediate or high HBV endemicity, age-specific prevalence of infection and historical data suggest that the endemicity level has not substantially changed over the past decades, and there is no evidence of injection practices playing a major role in the introduction of HBV in a community.

In contrast, in the case of HCV, where the proportion of infections attributable to injections is high, the effect of this limitation is likely to be considerable. In addition, there is evidence that in some countries, including China (Province of Taiwan) (Sun et al. 1999), Egypt (Frank et al. 2000) and Pakistan (Luby et al. 1997), HCV was recently introduced,

largely through contaminated injections, and rapidly reached high prevalence levels. In fact, in some of these countries, the prevalence is heterogeneous and areas persist where the virus has not been widely introduced (Mujeeb et al. 2000; Sun et al. 1999). In subregions where reuse of injection equipment is common but the prevalence of HCV infection is not yet high (e.g. SEAR-D), there is an opportunity at present to prevent future community-wide outbreaks of HCV infections. Our model does not reflect this opportunity.

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Notes

1 See preface for an explanation of this term.

2 Prepared for *World health report 2001* (WHO 2001).

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