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The Risk of Blood-Borne Viral Infection due to Syringe Re-Use

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1. Introduction

Transmission of viral and bacterial infections through the practice of syringe re-use has been repeatedly documented (American Society of Anesthesiologists, 1999) and controlled experiments have demonstrated that a syringe barrel becomes contaminated with microbes after multiple re-uses (Lessard et al., 1988; Perceval, 1980).

In the fall of 2008, light was shed on the practice of syringe re-use occurring in western Canada (Government of Alberta, 2009). In this situation, syringes had been re-used between patients to administer sedating medication through patient intravenous (IV) lines (Government of Alberta, 2009). Later it was reported that other incidents of syringe re-use had occurred in Canada (CBC News-Edmonton, 2008a; CBC News-Edmonton, 2008b). The question arose of whether this practice may have resulted in the transmission of blood-borne pathogens to patients and, if so, how many and with what level of risk. To answer this question, a retrospective study involving approximately 1,400 patients was undertaken (Government of Alberta, 2009). However, questions were also raised as to whether estimates based on modeling scenarios could provide information to guide decisions on the need for look-backs.

Risk assessments have been carried out almost concurrently with the underlying study; they gave various and different conclusions (Population Health Branch-Saskatchewan Health, 2009; Sikora et al., 2010). Contrary to our study where we considered the Canadian nation as a whole, the Population Health Branch-Saskatchewan study looked at only a province-wide risk assessment for Saskatchewan based on the same methods in Sikora et al. (2010); they concluded that the blood-borne viral infection was negligible (Population Health Branch-

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Saskatchewan Health, 2009). The model in Sikora et al., (2010) is a multiplicative model of four probabilities. It also considers only the risk that one patient is imposing on one other patient without taking into account the number of times the syringe may have been re-used in between them.

A novel but simple probabilistic model is established in the underlying study to reflect more accurately the practical situation that is occurring. The risk of viral infection at any time of re-use depends not only on the prevalence and susceptibility but also the number of times the syringe barrel was re-used before that time. Uncertainty and sensitivity analyses were carried out here to incorporate the lack of knowledge about different parameters, e.g. probability of contaminating a syringe, and assess their influence on the risk.

2. Methods

Blood-borne diseases can be transmitted through contact with bodily fluids, most often blood; they include Hepatitis B (HBV), Hepatitis C (HCV) and Human Immunodeficiency Virus (HIV). A probabilistic model was designed for the purpose of assessing the risk of these three viral infections due to re-use of syringes on multiple patients. The values for multiple risk factor variables used in this quantitative risk assessment were obtained from the literature (where data existed), consensus of opinions from a nationally commissioned expert working group, (Public Health Agency of Canada, 2008; Public Health Agency of Canada, 2009) and from information extracted from recently documented cases of syringe re-use in Canada and other countries.

The risk assessment consisted of three main areas: 1) Issue identification, 2) Exposure and hazard assessment, and 3) Hazard and risk characterization.

2.1 Issue identification

There are many different types of IV apparatus systems, with possibly thousands of combinations of add-on auxiliary components. This assessment investigated the constituents of a basic IV administration apparatus, and the components of a generic disposable plastic syringe to choose a “most common method” used by health care workers to deliver medications to patients via the intravenous route. The apparatus chosen is described in the exposure and hazard assessment section below.

2.2 Exposure and hazard assessment

To provide preliminary estimates of the level of exposure to viral pathogens via plastic syringe re-use, assumptions in the following categories were defined:

a. Assumptions of health care worker (HCW) practices

The precise number of times an HCW will re-use a syringe is unknown, and independent of the number of times the syringe was re-used previously.

b. Assumptions about medical device/instrument properties

Contamination of the syringe/tubing via fluid backflow was estimated based on the proximity of the medication injection site to the patient. A generic instrument set up

was used, which consisted of an infusion bag, and a length of tubing long enough to have a significant fluid flow/possibility of wash-out between two sites of injection; one proximal injection site at the bag, one distal at the catheter. No filters, locks or check valves were taken into account.

c. Assumptions on patient characteristics and needs

Patients treated are randomly selected from a high risk population on which the syringe could have been re-used; virus carriers can potentially infect any of the subsequent patients in a group before a syringe is disposed; and the events of source patient infection, virus contamination of the syringe and transmitting virus to subsequent patients are independent.

d. Assumptions on the nature of the viruses targeted

In accordance with worst case scenario, the presence of virus in the blood of a model patient is binary (either yes or no); the infectivity of the virus is 100%.

This assessment addresses only potential infection with re-used syringes. Other potential sources of contamination, in particular the contamination of multi-dose medicine vials, are not considered due to the lack of sufficient information in the literature.

2.3 Hazard and risk characterization

The model used probabilistic designed to assess the risk of HIV, HCV and HBV infection attributed to syringe re-use on multiple patients. The risk of viral contamination and subsequent patient infection only arises if the syringe is re-used. It is also changing with the number of syringe re-uses (S), or equivalently with the number of previous infectious patients on whom the syringe was re-used (R_1, R_2, R_3, \dots). The risk is lowered, but not completely eliminated, by a log reduction factor, if the syringe is flushed (this is known as “wash-out”).

If s patients were known to have been exposed to a re-used syringe, the risk of viral infection for the k^{th} patient in the sequence of s patients could be determined. The risk that the patient number k will contract the viral infection from one of the previous $k - 1$ patients is given by:

$$R_k = P^{(sus)} \times \left[1 - \prod_{j=1}^{k-1} (1 - Prev \times P^{(cont)} \times P_{k-j}^{(trans)}) \right], \text{ for } k = 2, \dots, s \quad (1)$$

with $R_1 = 0$, where $Prev$ is the prevalence, $P^{(cont)}$ is the probability of contaminating the syringe, $P^{(cont)}$ is the probability of being susceptible and $P_{k-j}^{(trans)}$ is the probability of transmitting the disease after $k - j - 1$ usages. The individual risk ($Risk$), or the risk imposed on a patient that underwent syringe re-use practice, is given by:

$$Risk = P(practice) \times \sum_{s=2}^{\infty} \frac{1}{s} \sum_{k=1}^s R_k \times P(S = s) \quad (2)$$

Here, S can be denoted as the number of injections until syringe replacement. The random variable S follows a geometric distribution with mean number of re-uses M given that $S \geq 2$. Thus, the individual risk is given by:

$$Risk = P(practice) \times \frac{1}{M-1} \times \sum_{s=2}^{\infty} \frac{1}{s} \sum_{k=1}^s R_k \times \left(1 - \frac{1}{M-1}\right)^{s-2}$$

(3)

where $P(practice)$ is the probability of syringe re-use practice. While the derivation of the three equations is straightforward, proofs are given in Appendix 1 for completion. Table 1 describes the model components and the values used to run the analysis.

Component	Variable	Range or Description	Probability Distribution*
Syringe re-use practice	$P(practice)$	2.2% - 60%	Pert (2.2%, 20%, 60%)
Wash-out factor	$r = 10^v$	Log-reduction	Uniform (1,2)
HBV immunity	Pro_{immu}	47% ¹	Triangular (46%, 47%, 48%)
HBV immunized but infected	$Pro_{immu \text{ and infected}}$	4% [†]	Triangular (3.5%, 4%, 4.5%)
# of patients in one group	S	Geometrically distributed	Discrete Triangular (2, 6,10)
Mean # of patients in one group	M	2-10	
Prevalence HIV HCV HBV	$Prev$	0.1% - 1.5% 2% - 4% 0.5% - 4%	Pert (0.1%, 0.4%, 1.5%) Pert (0.5%, 2%, 4%) Pert (0.5%, 1%, 3%)
Transmission HIV HCV HBV	$p_d^{(trans)}$	(0.3% - 0.5%) × (wash-out factor) ² (1% - 3%) × (wash-out factor) (10% - 30%) × (wash-out factor)	Triangular (0.3%, 0.4%, 0.5%) Triangular (1%, 2%, 3%) Triangular (10%, 20%, 30%)
Susceptibility HIV HCV HBV	$p^{(sus)}$	$1 - Prev$ $1 - Prev$ $1 - (Prev + Pro_{immu} - Pro_{immu \text{ and infected}})$	
Contamination Proximal Distal	$p^{(cont)}$	3.3% 0.3%	Triangular (2.3%, 3.3%, 4.3%) Triangular (0.2%, 0.3%, 0.4%)

* Pert (min, most likely, max), Triangular (min, most likely, max) and Uniform (min, max)

Table 1. Model components with the values and distributions used for the MCS analysis

Monte Carlo Simulations (MCS) were necessary to incorporate uncertainties surrounding syringe re-use practice. MCS sometimes requires specific computational software and platforms. In this study, we have used Monte Carlo Simulations implemented on the R statistical software (R Development Core Team, 2010).

¹ Refer to Table 2.

² The efficiency of transmission is calculated by multiplying transmission percentage by log reduction (wash-out) factors.

The parameter “ Pro_{immu} ” represents the percentage of individuals who display HBV immunity after having received HBV vaccination. The immunogenicity of the HBV vaccine is not 100%, and requires multiple dosing to achieve protective antibody levels (≥ 10 IU/L) (Mackie et al., 2009). The primary determinant of seroprotection is the age at which an individual is vaccinated. The average HBV seroprotection rates as described by the Canadian Immunization Guide (Public Health Agency of Canada, 2006) are outlined in Table 2.

Age Range (years)	Seroprotection Rates
>2	95%
5-15	99%
20-29	95%
30-39	90%
40-49	86%
50-59	71%
≥ 60	50% to 70%

Table 2. Seroprotection rates based on age groups following HBV vaccination, data from The Canadian Immunization Guide (Public Health Agency of Canada, 2006)

Recipient factors other than age also affect the rate of seroprotection in vaccinated individuals. For example, the antibody response is lower in patients with diabetes mellitus (range: 70% to 80%), renal failure (range: 60% to 70%) and chronic liver disease (range: 60% to 70%). Based on these factors, as well as vaccination uptake in the population, the expert group working on this assessment concluded that approximately 47% (range: 46% to 48%) of the general population is susceptible to HBV infection due to the absence of protective levels of antibodies to HBV in the year 2008 (Mackie et al., 2009; Public Health Agency of Canada, 2006).

The parameter “ $Pro_{immu\ and\ infected}$ ” represents the percentage of individuals who are HBV infected, and who have also been vaccinated against HBV, as of the year 2008. The value was determined through expert consensus of a nationally organized working group (Public Health Agency of Canada, 2008).

Finally, a set of input distributions needed to be created for each variable, in order to run the MCS analysis. Using information provided by health care experts (Public Health Agency of Canada, 2009), we arrived at a set of distributions to address the uncertainty involved in syringe re-use (Table 1).

3. Results

Scenario analysis was conducted for each blood-borne viral infection using different input values and distributions (Table 1). For the three blood-borne viral infections, the model was most sensitive to changes in disease prevalence. For example, changing the prevalence of HIV from 0.004 to 0.015 increased the individual risk by about 4 times (0.161 and 0.596, respectively) for a value of average syringe re-use of 4 and a wash-out factor of 100. Similarly for HBV, increasing the prevalence from 0.005 to 0.030 increased the individual risk from 6.911 to 43.60, when using an average value of syringe re-use of 4 and a wash-out factor of 100. The increase in risk is almost linear in the disease prevalence, which is supported by the sensitivity analysis (Appendix 2).

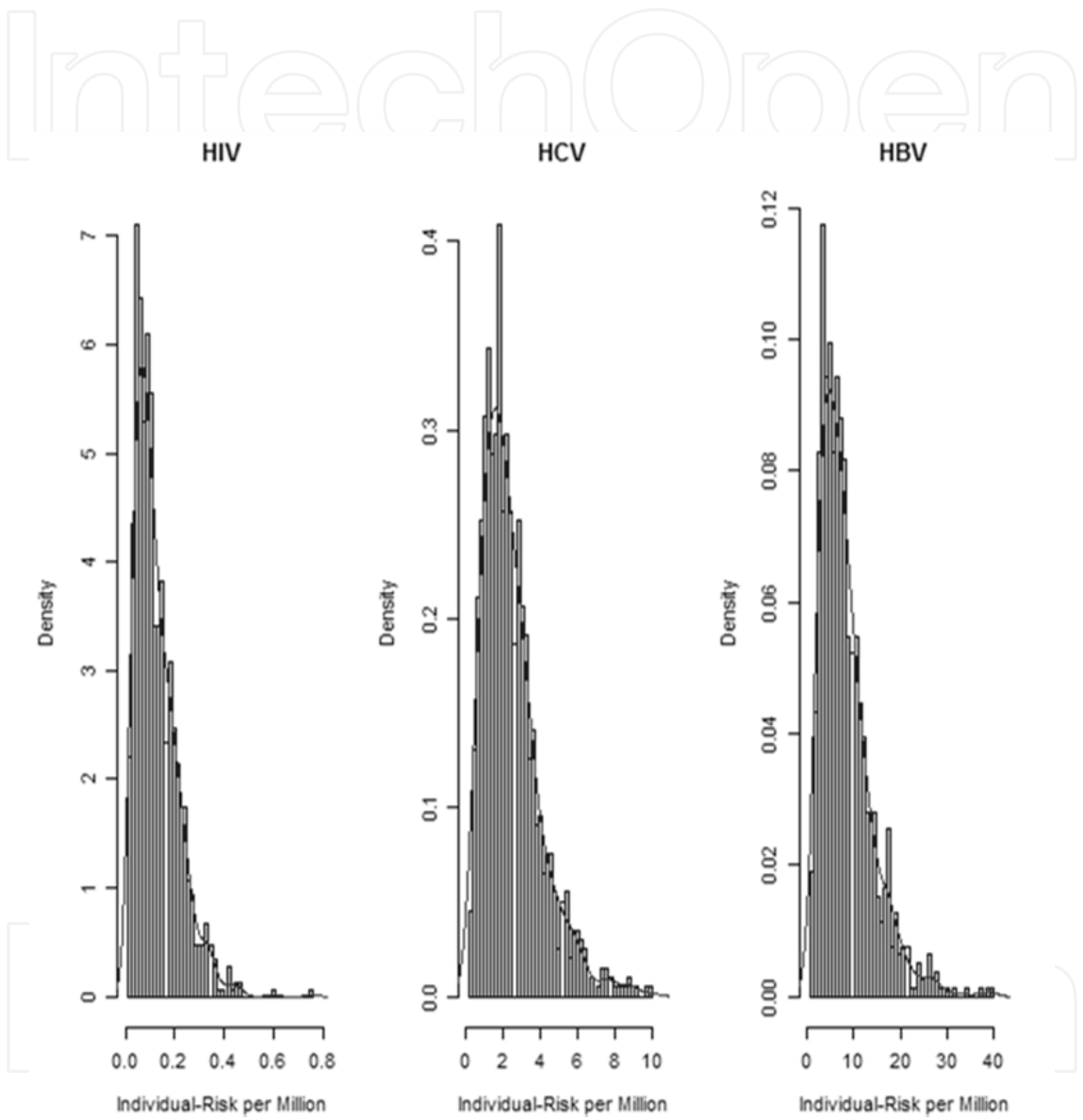


Fig. 1. Probability density function of individual risk of viral infection (y-axis) for HIV, HCV, and HBV per million person-procedures (x-axis) for the proximal setting scenario.

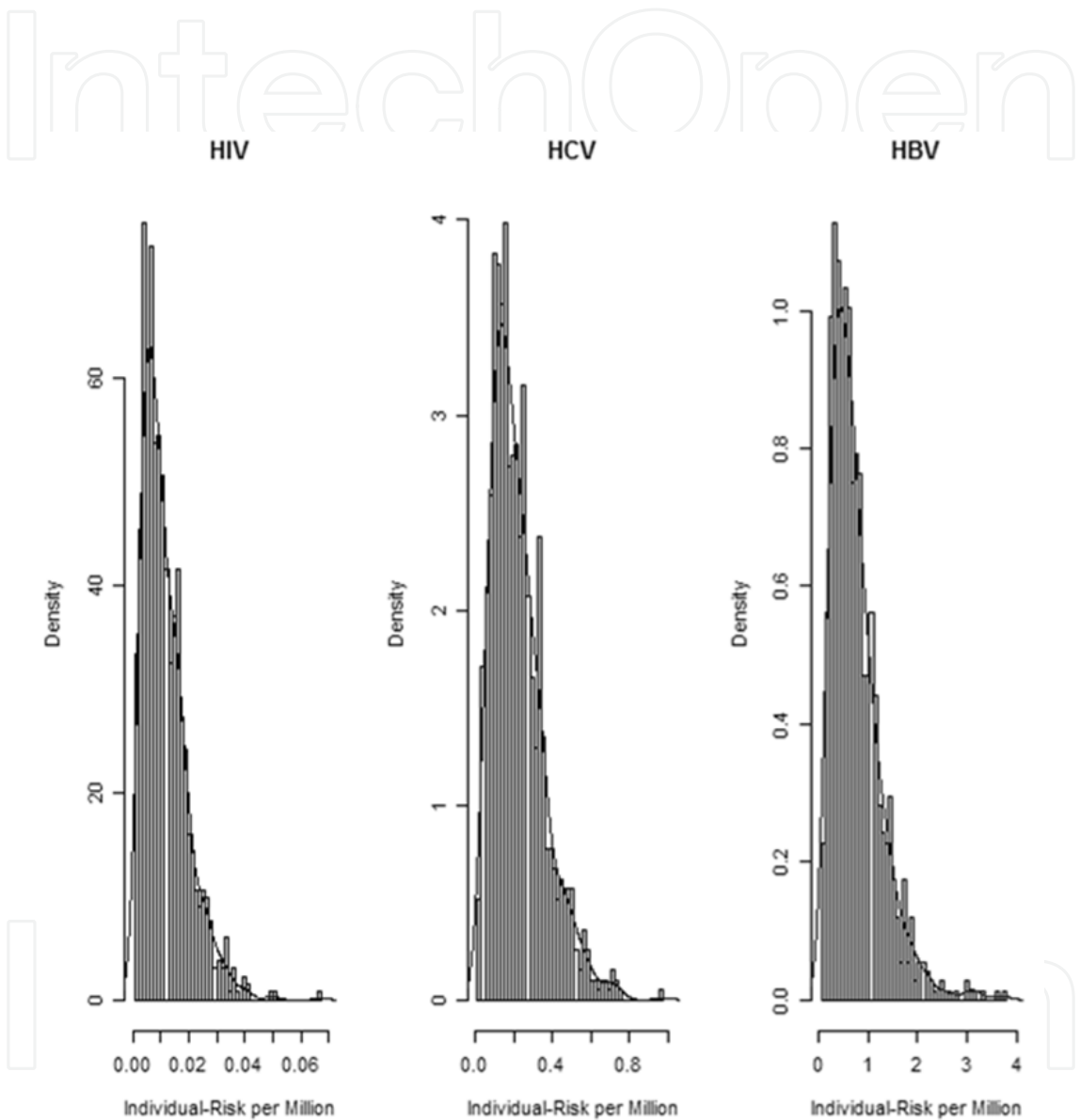


Fig. 2. Probability density function of individual risk of viral infection (y-axis) for HIV, HCV, and HBV per million person-procedures (x-axis) for the distal setting scenario.

Analysis of the resultant probability density functions (refer to Figures 1 and 2) of the individual risk per million person-procedure indicates that the distribution is right-skewed for the three infections for both proximal and distal injection into IV lines. The dispersion is relatively close in both settings for each viral infection. However, the median risk (used for skewness concerns) in the distal setting is about 10% of that resulted for the proximal setting similar to what was found in a study by Perceval (1980). This indicates that individual risk of viral contamination is highly dependent on whether injection takes place at a site proximal or distal to the IV set.

Table 3 and Table 4 present the individual risk per million people for proximal and distal medication injection sites. It is clear that the risk of HBV is highest in both settings due the higher efficacy of transmission inherent in the nature of the virus.

Virus	95% CI	Mean	Median	Coefficient of Variation
HIV	[0.0205, 0.3361]	0.1248927	0.1030704	0.6939076
HCV	[0.4584, 6.2700]	2.430697	2.090218	0.6436132
HBV	[1.7917, 21.8748]	8.292251	7.016490	0.6660043

Table 3. Output of the uncertainty analysis- the mean, median and coefficient of variation for the individual risk per million person procedure for a medication injection site that is *proximal* to the patient’s IV set

Virus	95% CI	Mean	Median	Coefficient of Variation
HIV	[0.0017, 0.0313]	0.01138309	0.009550734	0.6966828
HCV	[0.0407,0.5597]	0.2197540	0.1911161	0.6202549
HBV	[0.1487, 2.0497]	0.7553183	0.6323613	0.6755055

Table 4. Output of the uncertainty analysis- the mean, median and coefficient of variation for the individual risk per million person procedure for a medication injection site that is *distal* to the patient’s IV set

A Monte Carlo Bayesian sensitivity analysis was performed, using the “tgp” package (Gramacy & Taddy, 2009) on the R statistical software (R Development Core Team, 2010). From a series of box plots (attached in Appendix 2) it is clear that prevalence, especially of HIV and HBV, should be considered in future analyses to identify the risk of patient infection with viral pathogens following syringe re-use. In the case of HIV, resolving the uncertainty surrounding prevalence alone would reduce the total variance by 45%, while it takes all other factors combined to contribute the same magnitude of effect.

Additionally, it appears the main effect due to changes in the prevalence is linear (results not shown here but available upon request). The probability of (re-use) practice and the efficacies of transmission and contamination follow the prevalence in their influence and linear effect on the output. The remaining factors can be fixed to any value within their range without significantly impacting the output.

4. Discussion

The model estimated a broad range of infection risk for HIV, HCV, and HBV transmission through syringe re-use in the health care setting, as of the year 2008. The model estimated

the risk of contracting infection after syringe re-use to range from .02 - .34 in a million person-procedure for HIV; from .5 - 6.3 in a million person-procedure for HCV; and from 1.8 - 21.8 in a million person-procedure for HBV. Moreover, vulnerable groups with reduced seroprotection and reduced immunity may experience more severe outcomes if exposed to blood-borne viruses by this route.

In a similar study it was concluded that the risk of HBV on the Canadian population is highest in the proximal setting with risk of infection 12 - 53 per million followed by HCV (1 - 4.3 per million) and HIV (.03 - .15 per million) (Sikora et al., 2010). The last two ranges are subsets of the ranges we give above while the probability of practice used in Sikora et al. (2010) is 20% - 80% which is higher than the range we used 2.2% - 60%. The risk of HBV is smaller in our results may be because the Population Health Branch-Saskatchewan Health study focused on the Albertan population when the authors estimated probability of susceptibility for HBV (Population Health Branch-Saskatchewan Health, 2009).

The worst-case scenario risk assessment detailed here focuses on this event of syringe re-use as a way to quantify levels of risk for blood-borne viruses, to provide risk assessment information for better decision making, and to identify public health risk management lessons. Calculations were performed using the best available data at the time of this incident; the data used here are for the years 2008-2009. The authors acknowledge the fact that more and better data have become and will continue to become available. This risk assessment model allows for adaptation, further refinements, and future re-assessments based on improved input data.

One of the more interesting and important outcomes of the modeling, is the identification of information gaps and sources of uncertainty in this kind of analysis. We identified a number of information gap areas that are amenable for improvement. First, there was substantial uncertainty surrounding the time period of events in this model. For example, the publication of guidelines in 1995 and 1996 must have had a time dependent effect on the practice of syringe re-use. Changes in syringe re-use practice over time were incorporated by using a wide range of probability, from a 2.2% chance of re-use to a 60% chance. As it is assumed that syringe re-use practice is decreasing, then the model may well have overestimated the probability of acquiring infection.

Second, substantial uncertainty exists around the nature of the viruses targeted in this model context. Several aspects of the dose-response relationship and infectivity of the three viruses have been treated in a simplified manner to account for uncertainty around the potential concentration of the HBV/HCV/HIV within one exposure unit, the volumetric quantity to be considered a single exposure, and the values for viral survival. In addition, the simplification of the presence of virus to a binary (yes/no), does not take into account viral load which is an important factor. Regardless, these assumptions are necessary for generating a conservative risk estimate because all assumptions made will lead to an overestimated probability of acquiring infection.

Third, estimates of the population level effect of infection acquisition were compromised by lack of data on the number of exposures. Infection control breaches may go unnoticed or unreported. In addition, estimates of the average number of exposures at the patient level are not available.

Fourth, reasons for syringe re-use by a HCW are seldom known - for example cost, time constraints, knowledge on the status of the patient (e.g., if the patient is known to be HIV or HCV positive, the HCW may avoid re-using the needle), and training may be contributing factors. Additionally, uncertainty surrounds the technique that the HCW uses to deliver the syringe content to the IV tubing; i.e., what factors determine a proximal vs. distal injection site, and does the HCW always verify line placement via blood return prior to administering the medication?

In conclusion, syringes are not meant to be re-used in health care settings in order to protect patient safety and guidelines were established in both Canada (1997) and the US (1995) to prevent this type of exposure. It is important to stress this message, especially when guidelines are not followed. Using a systematic tool to facilitate assessment of risk is very helpful in this regard. Thus, when there is a breach in practice guidelines or an outbreak of disease due to syringe re-use, quantitative risk assessments can provide estimates to help guide the response of regulators, public health officials and clinicians.

5. Acknowledgement

The authors thank Caroline Desjardins and Angela Catford for their assistance in preparing this manuscript. The authors also thank the referee for the invaluable comments and suggestions.

6. Appendix 1: Proofs of equations 1, 2 and 3

Proof of Equation 1

Let us suppress the dependence on year t for brevity in the following argument. Let k be the order of the patient among the s patients on which one syringe was used. If $k = 1$ then there is null risk on him/her. For each $k = 2, \dots, s$, if the patient is not susceptible, there is also null risk on him/her. This patient will not contract the viral infection from any of the previous $k - 1$ patients if for each previous patient j , neither of the following happens:

1. carrying the virus,
2. transfer the virus to the syringe,
3. transmission happens to a patient after $k-j$ re-uses

which has probability $(1 - Prev \times P^{(cont)} \times P_{k-j}^{(trans)})$. Thus given that patient k is susceptible, by independence between the $k - 1$ patients the probability that the patient will not contract the viral infection from any of the previous $k - 1$ patients is $\prod_{j=1}^{k-1} (1 - Prev \times P^{(cont)} \times P_{k-j}^{(trans)})$. Therefore, the probability of contracting the disease is

$$R_k = P^{(sus)} \times \left[1 - \prod_{j=1}^{k-1} (1 - Prev \times P^{(cont)} \times P_{k-j}^{(trans)}) \right].$$

Proof of Equation 2

Let us suppress the dependence on year t for brevity in the following argument. An individual chooses a national health care provider (HCP) that is practicing syringe re-use

(SR) with a probability $P(\text{practice})$. If the selected HCP is practicing SR, then that individual can be uniformly any one of the group of S patients (S here is random since there is no guarantee of a specific system of SR) on which one syringe was re-used. So his/her probability of being any one of the group is $\frac{1}{S}$. Therefore, given that k is his/her order in the group, the probability of contracting a viral infection from any one of the previous $k - 1$ patients in the group is R_k .

Using the **Total Probability Rule**, the probability of acquiring the viral infection is given by

$$\begin{aligned} & P(\text{acquiring viral infection} | \text{practice done on } S \text{ patients}) \\ &= \sum_{k=1}^S P(\text{acquiring viral infection} | \text{the patient's order among the } S \text{ patients is } k) \\ &\quad \times P(\text{the patient's order among the } S \text{ patients is } k) = \sum_{k=1}^S R_k \times \frac{1}{S}. \end{aligned}$$

Let $P(S = s)$ be the discrete probability distribution of the number of patients in one group. Using the **Total Probability Rule** one more time, the individual risk is given by

$$\begin{aligned} \text{Risk} &= P(\text{acquiring viral infection} | \text{practice}) \times P(\text{practice}) \\ &\quad + P(\text{acquiring viral infection} | \text{no practice}) \times (1 - P(\text{practice})). \end{aligned}$$

But $P(\text{acquiring viral infection} | \text{no practice}) = 0$. Hence,

$$\text{Risk} = P(\text{acquiring viral infection} | \text{practice}) \times P(\text{practice})$$

and

$$P(\text{acquiring viral infection} | \text{practice}) = \sum_{s=2}^{\infty} P(\text{acquiring viral infection} | \text{practice done on } S = s) \times P(S = s) =$$

$$\sum_{s=2}^{\infty} \frac{1}{s} \sum_{k=1}^s R_k \times P(S = s).$$

Therefore,

$$\text{Risk} = P(\text{practice}) \times \sum_{s=2}^{\infty} \frac{1}{s} \sum_{k=1}^s R_k \times P(S = s).$$

Note that s starts from 2 since to have an SR practice it should be done on at least 2 patients in the one group and theoretically it can be on infinite number of patients but practically the sum will be truncated due to numerical negligence of the terms added.

Proof of Equation 3

Assuming that the nurse makes the decision of disposing the syringe randomly and independently of previous re-uses, the probabilistic experiment underlying the process is a geometric experiment. Let us also assume that the probability of syringe disposal (p) is independent of the number of elapsed re-uses and $M \geq 2$ be the average number of re-uses done in a HCP which need not to be an integer. Therefore, conditional that the number of re-uses of one syringe (or number patients in one group) S is at least 2, since we assume a SR practice; the mean would be given as

$$M = \sum_{s=2}^{\infty} s P(S = s) = \sum_{s=2}^{\infty} s \times p \times (1 - p)^{s-2}$$

which implies that $p = \frac{1}{M-1}$.

Thus, the discrete probability distribution of the number of patients in one group is given by

$$P(S = s) = \frac{1}{M-1} \times \left(1 - \frac{1}{M-1}\right)^{s-2}$$

and equation (3) follows.

7. Appendix 2: Sensitivity analysis

The results of sensitivity analyses of the model output of the risk of HIV infection for several input variables for the proximal setting are shown in figure SI-1. This figure indicates that the model was most sensitive to uncertainty in the prevalence, followed by syringe re-use practice.

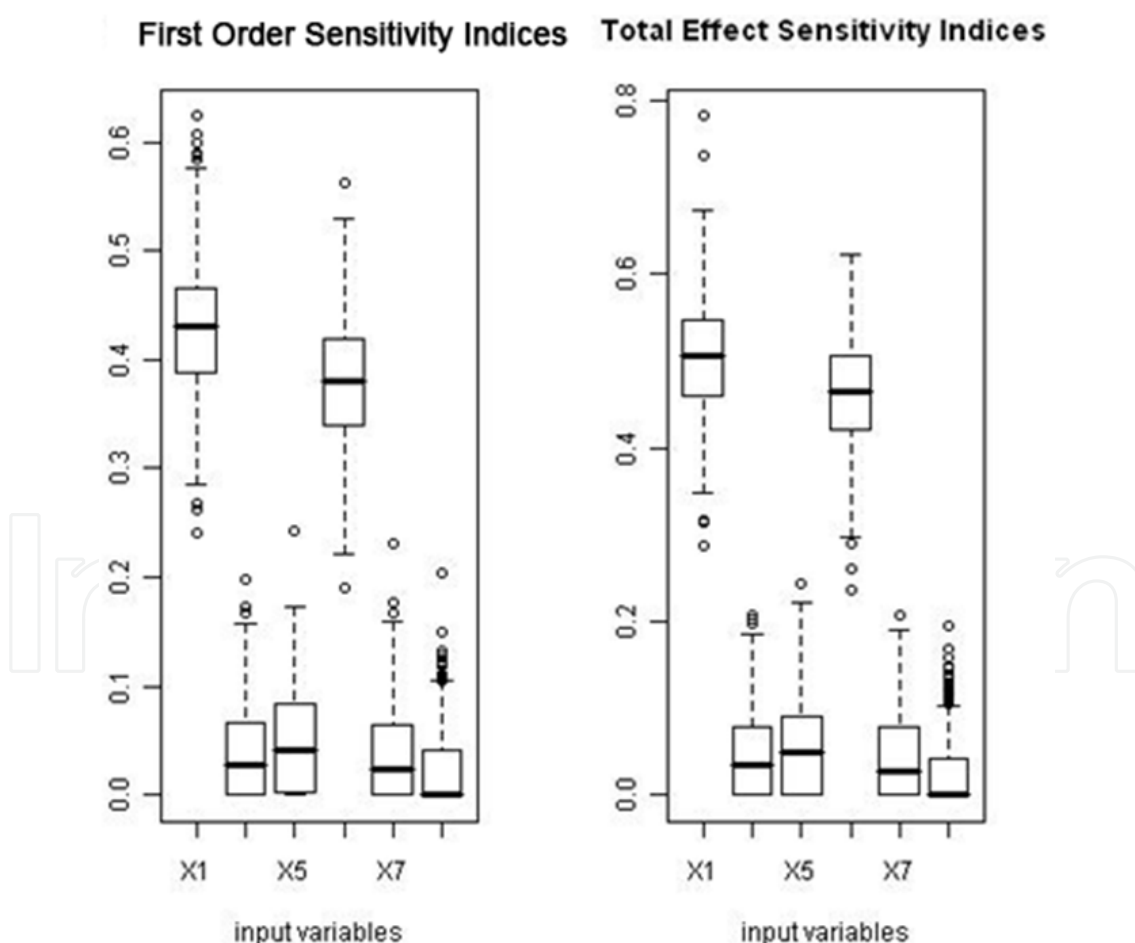


Fig. SI-1. First order sensitivity indices and total effects sensitivity indices for HIV infection risk in proximal setting scenario. *Legend:* X1 prevalence, X4 transmission, X5 contamination, X6 syringe re-use practice, and X7 the mean number of syringe re-use, and X8 log reduction.

Figure SI-2 shows the results of sensitivity analyses of the model output of the risk of HCV infection for several input variables for the proximal setting scenario. The figure shows the model was most sensitive to risk of transmission (X4), followed by the practice of syringe re-use (X6).

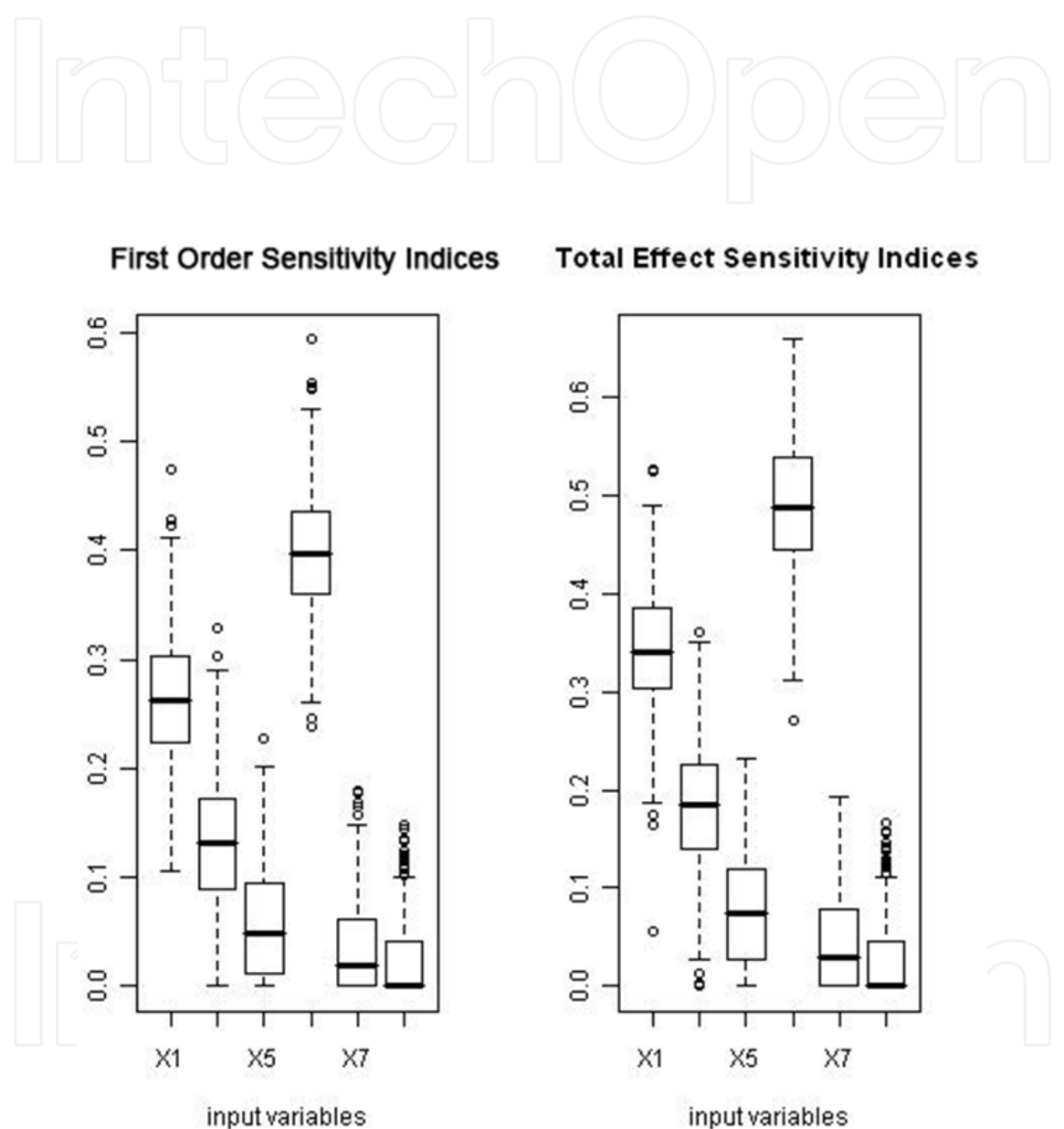


Fig. SI-2. First order sensitivity indices and total effects sensitivity indices for HCV infection risk in the proximal setting scenario. *Legend:* X1 prevalence, X4 transmission, X5 contamination, X6 syringe re-use practice, and X7 the mean number of syringe re-use, and X8 log reduction.

Figure SI-3 shows the first order sensitivity indices and total effects sensitivity indices for HBV infection risk in the proximal setting scenario. The individual risk was sensitive to prevalence (X1), transmission (X4), and practice of syringe re-use (X6).

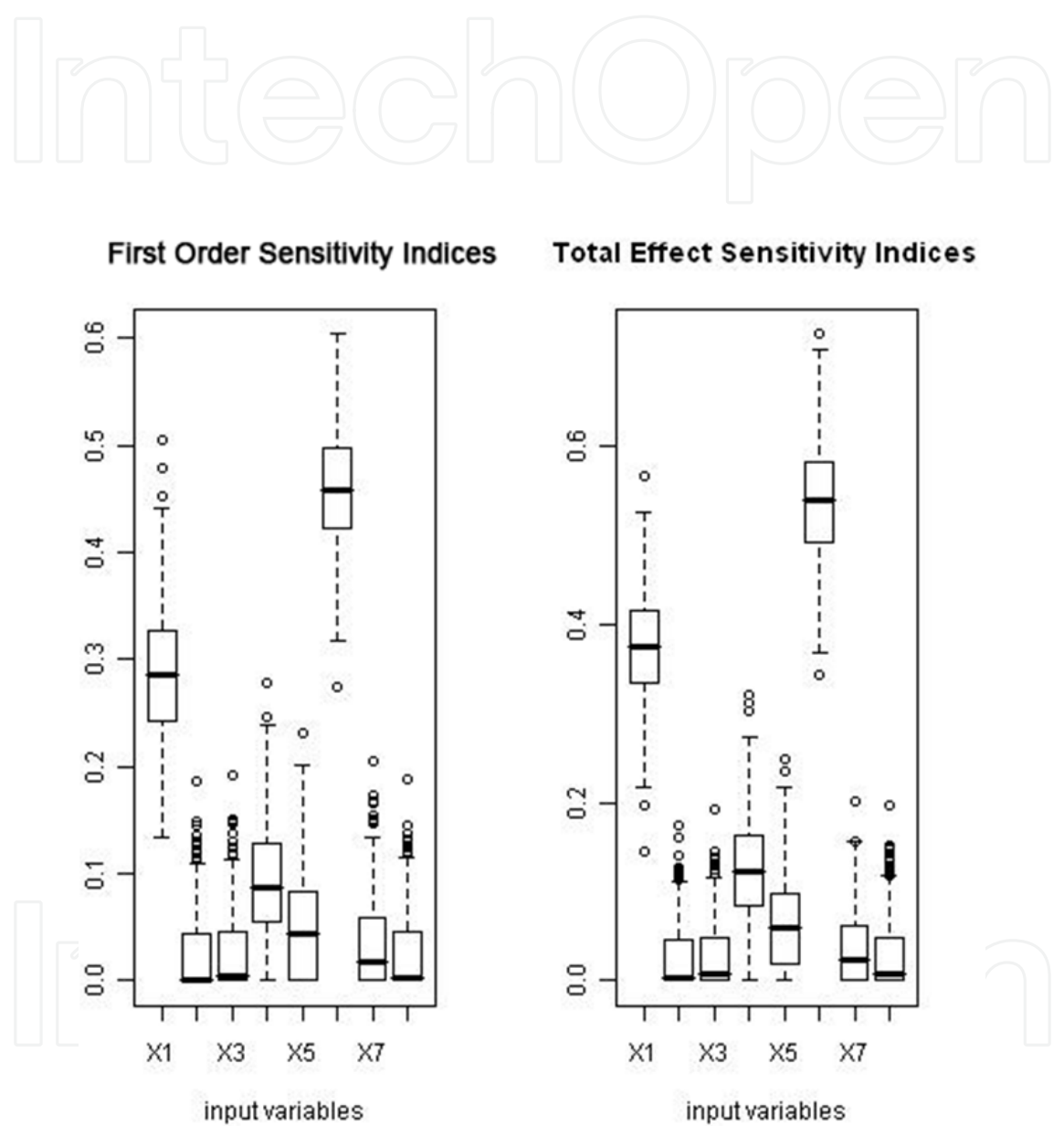


Fig. SI-3. First order sensitivity indices and total effects sensitivity indices for HBV infection risk in the proximal setting scenario. *Legend:* X1 prevalence, X2 immunized, X3 immunized but infected, X4 transmission, X5 contamination, X6 practice, X7 mean number of re-use, X8 log reduction.

Figure SI-4 shows the results of sensitivity analyses of the model output of the risk of HIV infection for several input variables for the distal setting (a scenario in which the syringe is re-used to inject drug in a site distal to the patient’s IV set). As for the proximal setting, the model was sensitive for the prevalence (X1) and the practice of syringe re-use (X6).

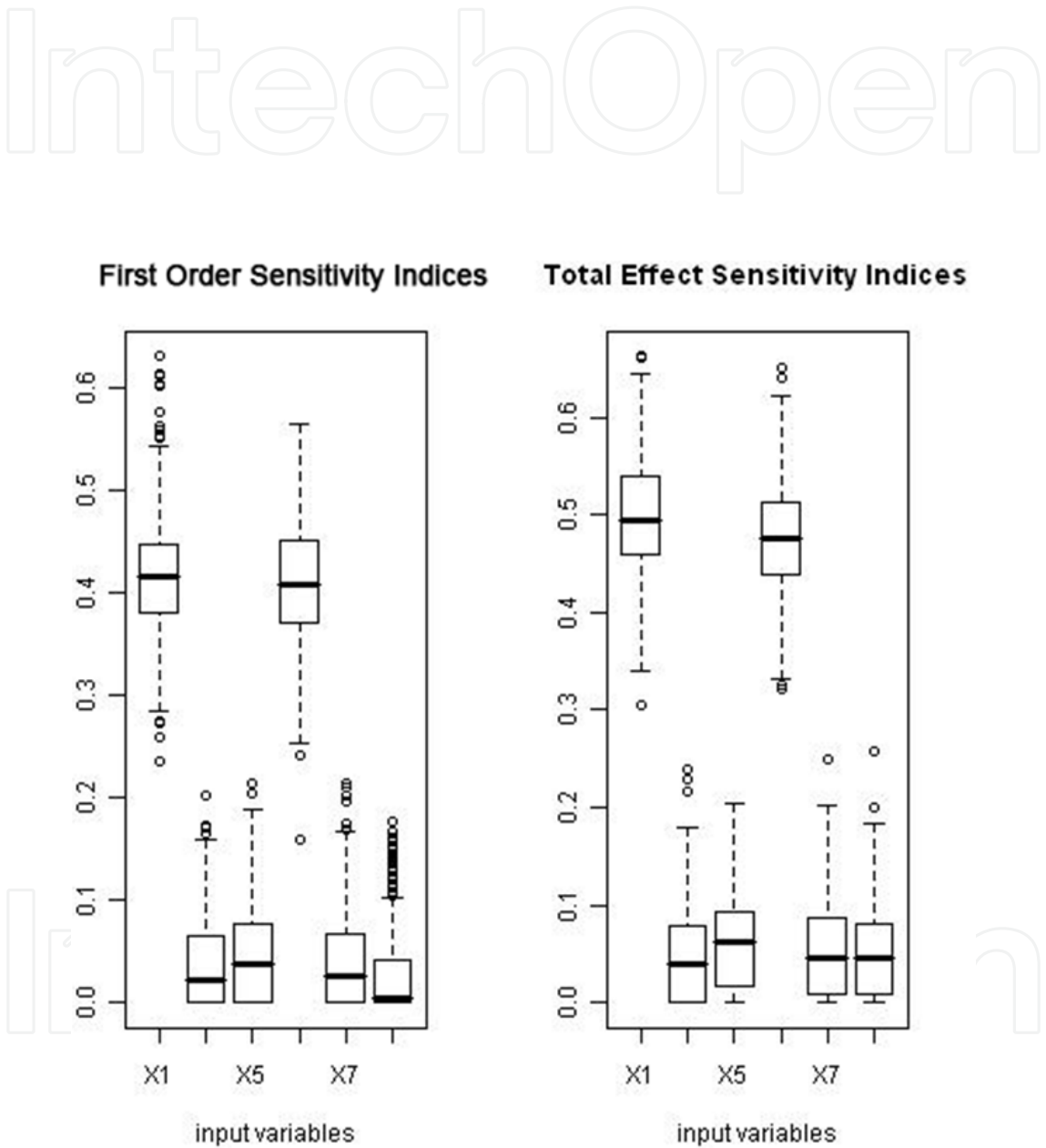


Fig. SI-4. First order sensitivity indices and total effects sensitivity indices for HIV infection risk in the distal setting scenario. *Legend:* X1 prevalence, X4 transmission, X5 contamination, X6 syringe re-use practice, and X7 the mean number of syringe re-use, and X8 log reduction.

Figure SI-5 shows the results of sensitivity analysis of the model output of the risk of HCV infection for several input variables for distal settings. The figure shows the model was most sensitive to uncertainty in the transmission (X4), followed the practice of syringe re-use (X6).

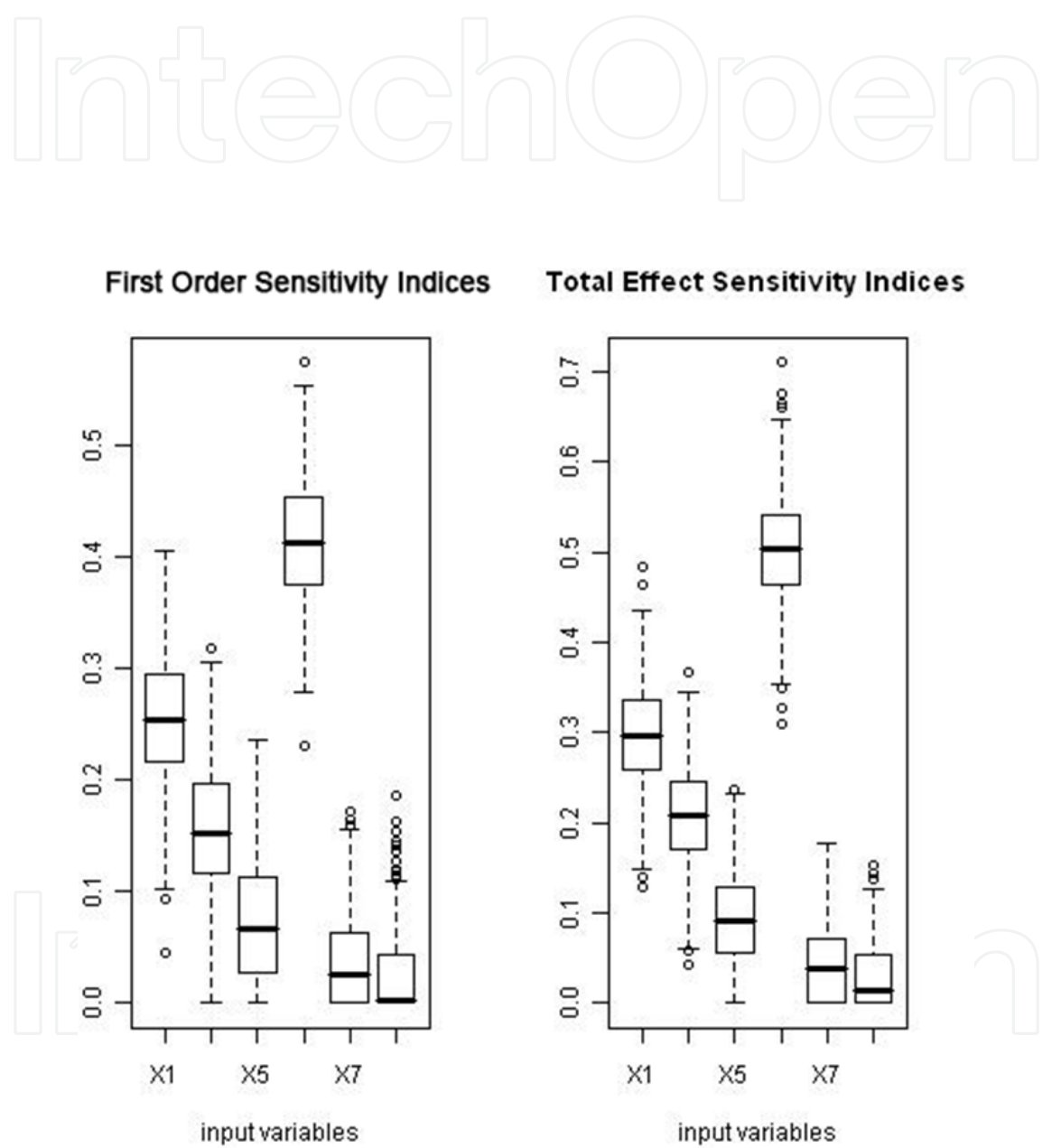


Fig. SI-5. First order sensitivity indices and total effects sensitivity indices for HCV infection risk in the distal setting scenario. *Legend:* X1 prevalence, X4 transmission, X5 contamination, X6 syringe re-use practice, and X7 the mean number of syringe re-use, and X8 log reduction.

Figure SI-6 shows the first order sensitivity indices and total effects sensitivity indices for HBV infection risk in the distal setting scenario. As for the proximal setting, the total effect was sensitive for prevalence (X1), transmission (X4), and practice of syringe re-use (X6).

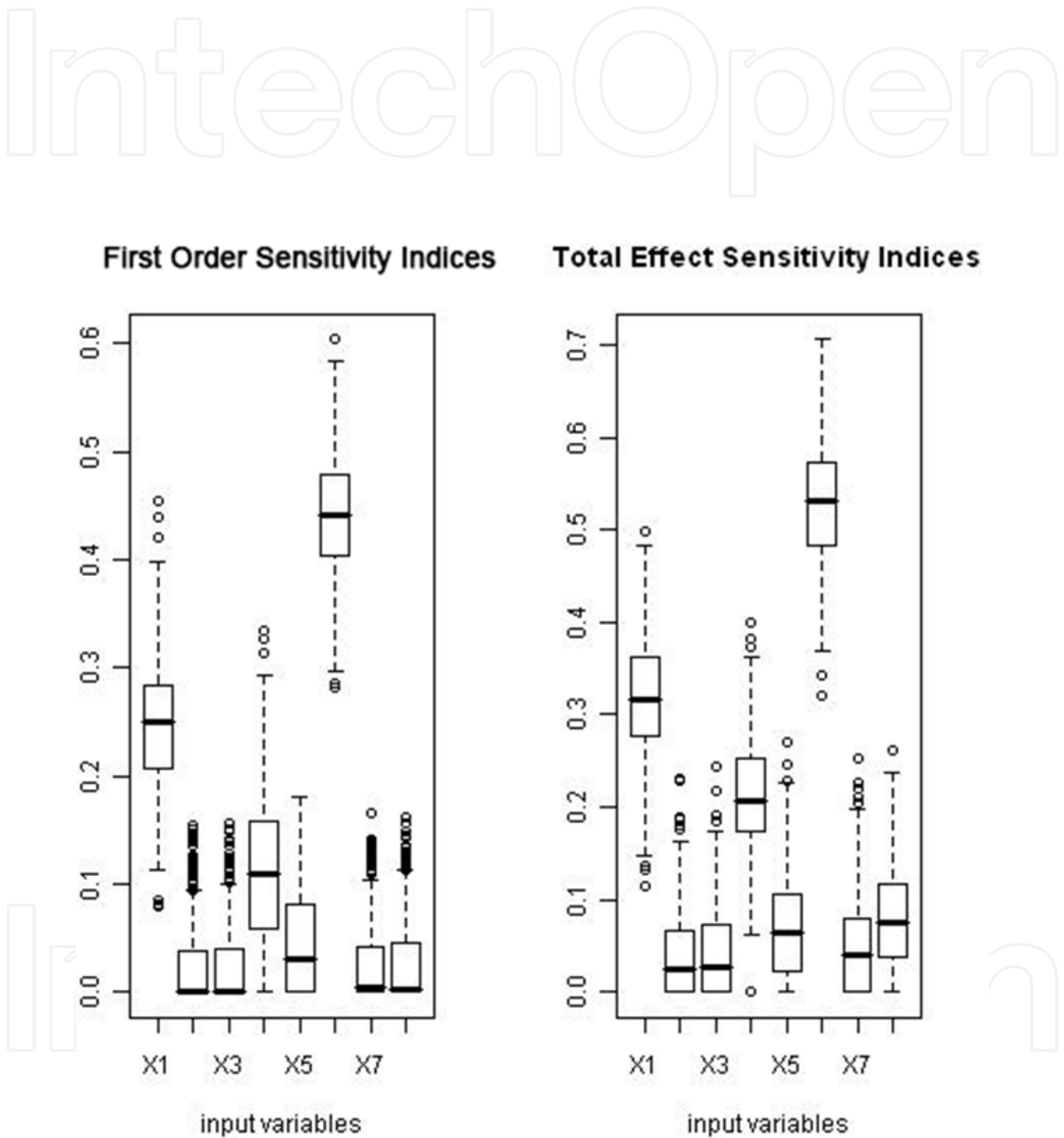
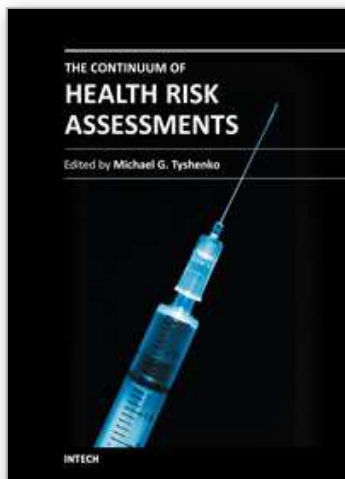


Fig. SI-6. The first order sensitivity indices and total effects sensitivity indices for HBV infection risk in the distal setting scenario. *Legend:* X1 prevalence, X2 immunized, X3 immunized but infected, X4 transmission, X5 contamination, X6 practice, X7 mean number of re-use, X8 log reduction.

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This book presents a collection of health risk assessments for known and emerging hazards that span a continuum. Case studies for existing health risks include psychoactive drug usage in delivery truck drivers and using look-back risk assessment for accidental syringe re-use in healthcare settings. Case studies for emerging risks include precautionary actions to safeguard blood supplies; nanoparticle deposition in the lung; and the epistemic issues surrounding genetically modified organism risk assessments. The final section of the book deals with advancing health risk assessment analyses through a post-genomics lens and provides case studies on personalized genomics, new data analyses and improving in silico models for risk assessment. These case studies provide much insight into the ongoing evolution of health risk assessments.

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