BC CENTRE FOR EXCELLENCE IN HIV/AIDS
NON-OCCUPATIONAL POST-EXPOSURE PROPHYLAXIS PILOT PROJECT GUIDELINES

BACKGROUND

Produced under the leadership of the BC Centre for Excellence in HIV/AIDS (BC-CfE), these guidelines are intended to guide health care providers at the pilot sites caring for persons who have sustained exposure to blood and body fluids in the community setting. This guideline is designed to deal specifically with exposure to Human Immunodeficiency Virus (HIV) and is not applicable to other infections such as hepatitis. This guideline provides a framework for a program of expert advice and prompt antiretroviral prophylaxis for non-occupational exposures in the community. The guideline is based on scientific principles and with our extensive experience, in providing antiretroviral prophylaxis for occupational exposures (PEP) over the past fifteen years.

In British Columbia, post-exposure prophylaxis (PEP) is currently offered after accidental exposure to HIV in the occupational settings (e.g. healthcare, corrections personnel) and sexual assault settings, however not in non-occupational settings (consensual sexual exposure or injection drug use). Consensus guidelines from the US Department of Health and Human Services supporting PEP in the non-occupational setting (NPEP) were published in 2005 [1]. These guidelines acknowledge the scientific importance of NPEP in an HIV prevention portfolio.

The US Centers for Disease Control estimates the risk of acquiring HIV from a single infected needle stick exposure to be approximately 0.3%, whereas the risk after an episode of injection drug use needle sharing is higher at 0.67%. Higher still is the risk from unprotected receptive anal intercourse (0.1% - 3%) [1, 2].

A 28-day course of three-drug combination antiretroviral therapy is the current standard of care for PEP. Studies show that when antiretroviral therapy is offered in a timely

manner after exposure (within 72 hours), the risk of acquiring HIV decreases by approximately 80% [3, 4].

Most studies have found that NPEP is effective when offered after high-risk HIV exposure to body fluids [5, 6]. In addition, there has been no evidence that provision of NPEP has increased risk-taking behaviour.

The BC-CFE has therefore developed this pilot protocol and guidelines for the assessment and treatment of HIV exposure in the non-occupational setting, for a period of 18 months.

The Committee for Drug Evaluation and Therapy of the BC-CFE has unanimously recommended an 18-month pilot project of NPEP at six pilot sites in Vancouver, British Columbia, which was approved by Pharmacare, Ministry of Health.

1. GOAL OF THE PILOT PROJECT

To reduce the risk of transmission of HIV to persons exposed to blood or body fluids.

This will be accomplished by:

1. Dissemination of these guidelines to health care providers at the pilot sites who encounter persons exposed to blood and body fluids.
2. Assessment of the risk of HIV transmission in exposed persons.
3. Counselling of exposed persons to reduce anxiety, to ensure adequate management and follow-up and to reduce the risk of HIV transmission to others.
4. Appropriate use of antiretroviral therapy in exposed persons.
5. Avoiding antiretroviral prophylaxis (which is potentially toxic) in those persons who are not at significant risk of infection.
6. NPEP will be initiated only when the exposure is a single episode and when it can be given in a timely manner. It is not appropriate for cases of ongoing sexual exposures or injection drug use (IDU) exposures over time, or for exposures that occurred greater than 72 hours before presentation.

2. LOCATION

The BC-CfE NPEP Pilot sites are:

1. PHC - St. Paul's Hospital Emergency Department
2. PHC - St. Paul's Hospital Immunodeficiency Clinic
3. PHSA - BC Centre for Disease Control Sexually Transmitted Infections Clinics – Bute Street Clinic and
4. VCH - BC Centre for Disease Control Sexually Transmitted Infections Clinics –Health Initiative for Men (HiM)
5. VCH - Downtown Community Health Clinic (DCHC)
6. Spectrum Health Clinic

3. DEFINITIONS

3.1 HIV exposure

An event where blood or other potentially infectious body fluid comes into contact with mucus membranes or is introduced through percutaneous exposure.

3.2 Infectious body fluids (capable of transmitting HIV)

1. Blood
2. Any body fluid visibly contaminated with blood
3. Semen
4. Vaginal/rectal secretions

3.3 Non-infectious body fluids (unless bloody)

(Not implicated in the transmission of HIV unless visibly bloody)

Stool, urine, tears, saliva, nasal secretions, vomitus

3.4 Definition of persons at high risk for being HIV positive (if HIV status unknown)

1. Active injection drug users
2. Men who have sex with men
3. Sexual partners of persons known to be HIV-positive
4. Sex Trade Workers

4. PROCEDURES FOR ASSESSMENT OF HIV EXPOSURE RISK

Persons accidentally exposed to blood or body fluid should be assessed as soon as possible. If antiretrovirals are indicated, they are most effective if initiated **within two hours of exposure**. Antiretrovirals should not be offered if the exposure is >72hrs. If a high risk exposure occurred more than 72 hours prior to presentation, please contact the BC-CfE Pharmacy 1-888-511-6222 for further evaluation.

The health care provider (e.g. Physician or Nurse) should complete a risk assessment of the exposure as soon after arrival in the clinic/department as possible (See Algorithm Appendix 1).

4.1 Initial Assessment

Risk assessment of the exposure must occur. Risk of transmission will depend on the type of exposures and whether the Source is HIV positive or the probability the Source is at high risk for HIV.

4.1.1 The **exposed** person must undergo baseline HIV testing, preferably with Point of Care (POC) HIV rapid test following BCCDC guidelines [7]. Further workup and management of potential exposure to hepatitis B, C and other sexually transmitted infections is also required.

If the baseline HIV POC test is positive, confirmatory testing HIV serology should be ordered. NPEP should NOT be initiated. Post-test counselling for a preliminary positive result and referral for further workup and management of HIV infection is required [7].

If the baseline HIV POC testing is negative and risk assessment indicates a significant risk exposure, NPEP can be initiated. If the baseline HIV POC test is indeterminate, draw HIV serology (consisting of 4th generation assay – the antigen/antibody assay). If the baseline POC test is invalid, repeat the test with a new kit and if the result remains invalid, draw HIV serology as above. In these scenarios (indeterminate/invalid POC) consider HIV status to be unknown/negative and assess for NPEP until HIV serology results are known.

4.2 Risk Assessment

4.2.1 Table 1.

Risk of HIV Transmission by Exposure Type from **Known HIV Positive Source**

Exposure	Risk per 10,000 acts	Risk percent
Hollow Bore Needlestick injury	30	0.3%
Needle sharing – injection drug use	67	0.67%
Penile-vaginal intercourse (risk to male)	5	0.05%
Penile-vaginal intercourse (risk to female)	10	0.1%
Anal intercourse (risk to insertive partner)	6.5	0.06%
Anal intercourse (risk to receptive partner)	50	0.5% - 3%
Oral intercourse (risk to insertive partner)	0.5	0.005%
Oral intercourse (risk to receptive partner)	1	0.01%

Source: US Centers for Disease Control **MMWR January 21, 2005/Vol54/No.RR -2.**

4.2.2 Factors that can influence the risk of transmission

- Degree of Source HIV viremia. Higher viral loads increase the risk of transmission
- The presence of a sexually transmitted infection in either the Source or the exposed individual
- The presence of oral or mucosal disease of the mouth
- Degree of trauma associated with the sexual act

4.3 Source assessment

4.3.1 Source HIV status unknown, however considered to be high risk

- If the Source person is available for interview, additional information about risk history can be obtained and permission for an HIV POC test requested to assist in determining the likelihood of HIV exposure.
- If the Source POC test is positive, HIV serology should be drawn, and post-test counselling and referral for HIV management should occur. Risk assessment for known HIV positive source (Table1) can proceed.
- If the Source POC test is negative, but the risk history suggests additional exposures, draw HIV serology to rule out the window period. Risk assessment and initiation of NPEP should proceed under the assumption that the source is potentially HIV positive until serology results are available.
- RESULTS OF SOURCE RESULTS CANNOT BE DISCLOSED TO EXPOSED INDIVIDUAL. THEY CAN BE INFORMED ONLY OF THE RECOMMENDATIONS FOR NPEP OR NOT.
- When the Source is unknown/not available, the risk of HIV exposure can be determined using community prevalence estimates and the nature of the type of exposure that has occurred, **(see Appendix 2a).**

4.3.2 HIV positive source on antiretroviral therapy

- The risk of HIV transmission from an HIV positive Source who is receiving antiretroviral therapy is likely to be reduced.

- HIV transmission is related to degree of HIV viremia. The results of recent observational studies and a randomized clinical trial demonstrate that full suppression of the HIV viral load in the Source partner in a stable heterosexual serodiscordant relationship can reduce transmission by 92-96%.
- If the Source is available for interview, the history of antiretroviral medication use and most recent viral load measurement should be considered when selecting antiretroviral medications for NPEP.
- If the Source is willing to do so, blood work can be obtained in order to confirm viral load suppression.
- For low-risk exposures from a Source with demonstrated long-term (>6 months) HIV suppression on antiretroviral therapy (undetectable viral load within the last four weeks), NPEP may not be required.

4.4 Specimens drawn from the Source should be clearly identified as coming from an accidental exposure episode and they will be dealt with promptly by the laboratory. The specimens can be sent to the UBC Virology Laboratory at St. Paul's Hospital (604 806-8420).

- Ensure appropriate follow-up for the Source to obtain their test results through their family physician or other identified follow-up physician.

When in doubt, the initial starter kit can be supplied, and further review by the BC-CfE will determine if further prophylaxis is required, by contacting 1-888-511-6222.

5. RECOMMENDATION FOR PROPHYLAXIS

A 28-day course of combination antiretroviral therapy is recommended for non-occupational exposure to blood, or other potentially infectious body fluids of a person known to be HIV positive, or at high risk for HIV, when that exposure represents a substantial risk for transmission, and when the person seeks care within 72 hours of exposure.

Type of Exposure	Source	Action
Substantial Risk for HIV Exposure EXPOSURE OF vagina, rectum, mouth, or other mucous membrane, or percutaneous contact WITH blood, semen, vaginal secretions, rectal secretions, or any body fluid that is visibly contaminated with blood	Known HIV infection OR Unknown HIV status and considered high risk for HIV	Initiate NPEP starter kit: Tenofovir 300mg once a day + Lamivudine (3TC) 150 mg bid + Kaletra 2 tablets bid Arrange for follow-up consultation for consideration of continuing 28 day NPEP
Negligible Risk for HIV Exposure EXPOSURE OF vagina, rectum, eye, mouth, or other mucous membrane, or percutaneous contact WITH urine, nasal secretions, saliva, sweat, or tears if not visibly contaminated with blood	Known HIV infection OR Unknown HIV status and considered high risk for HIV	NPEP **not** recommended Consult with the BC-CfE if unusual exposure has occurred

Expert advice can be obtained from the BC-CfE by contacting 1-888-511-6222

6. NPEP ANTIRETROVIRAL THERAPY

6.1 The NPEP starter kit consists of a 7 day supply of:

- Tenofovir: one tablet (300 mg) once a day
- Lamivudine (3TC): one tablet (150 mg) twice a day
- Kaletra: two tablets twice a day

NOTE: Taking all three drugs with food may reduce stomach upset.

6.2 Contraindications to Antiretroviral Therapy

There are many drug interactions with antiretroviral medication, particularly with protease inhibitors such as Kaletra. A careful medication history and use of all alternative therapy should be reviewed. Non-essential medications and all alternative therapy should be discontinued during antiretroviral therapy. Questions regarding drug interactions should be directed to the BC-CfE Pharmacy (1-888-511-6222).

- Avoid or use with extreme caution in persons with chronic renal insufficiency (creatinine more than three times normal), hepatic insufficiency, or bone marrow dyscrasia. Specific cases should be discussed with a BC-CfE physician or pharmacist.
- Avoid or use with extreme caution in persons treated with myelosuppressive, nephrotoxic or hepatotoxic drugs in the two weeks prior to starting antiretroviral therapy.

6.3 Pregnancy

If the exposed person is pregnant, contact the BC-CfE pharmacy (1-888-511-6222) as soon as possible. Tenofovir has not been used extensively in pregnancy and we will substitute with zidovudine. However, in a significant exposure, the existing kit should be given as soon as possible. Tenofovir is a Pregnancy Category B medication.

6.4 Pre-treatment and Follow-up Laboratory Evaluation of the Exposed Person

- No laboratory evaluation except HIV testing is required prior to initiation of the antiretroviral therapy starter kit, unless the exposed person is suspected of having significant haematologic or hepatic or renal disease.
- Additional testing for hepatitis B/C and syphilis may be indicated.

- Laboratory assessment will occur at weeks two and four to monitor for adverse effects.

6.5 Potential Adverse Effects of One Month of Antiretroviral Therapy

Tenofovir: Tenofovir is well tolerated and side effects are mild. They may include: nausea, diarrhea and gas.

Lamivudine (3TC): Lamivudine is usually well tolerated in short-term therapy and side effects are rare. Reversible decreased white blood cell count is the commonest side effect. Tingling of the hands and feet (peripheral neuropathy) is very unlikely to occur with one month of treatment.

Kaletra: Side effects include: diarrhea, nausea, vomiting and abdominal pain. Occasionally, there will be changes in liver function tests. Kaletra may interact with a wide number of medications including: inhaled/nasal corticosteroids, neuroleptic medications, Sildenafil, Midazolam, Triazolam, Fentanyl, and Rifampin.

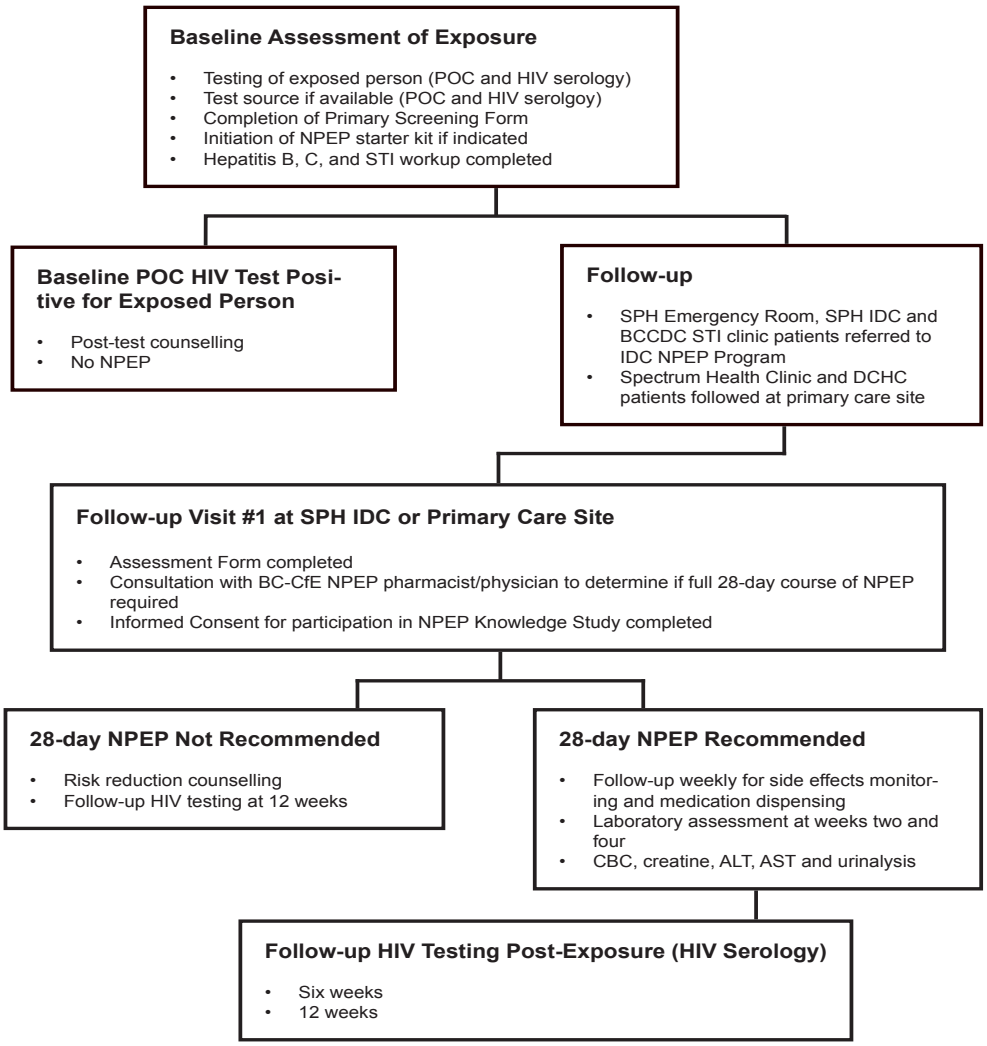
Estimates of the incidence of side effects are based on published data from the use of this regimen in the Post Exposure Prophylaxis (PEP) setting:

- Overall side effects were experienced by 42% [8] and included: diarrhea (78%), fatigue (78%), nausea and/or vomiting (59%).

Estimates of the incidence of more serious side effects are based on the experience of the BC-CfE in the use of HIV PEP and in the treatment of HIV infection:

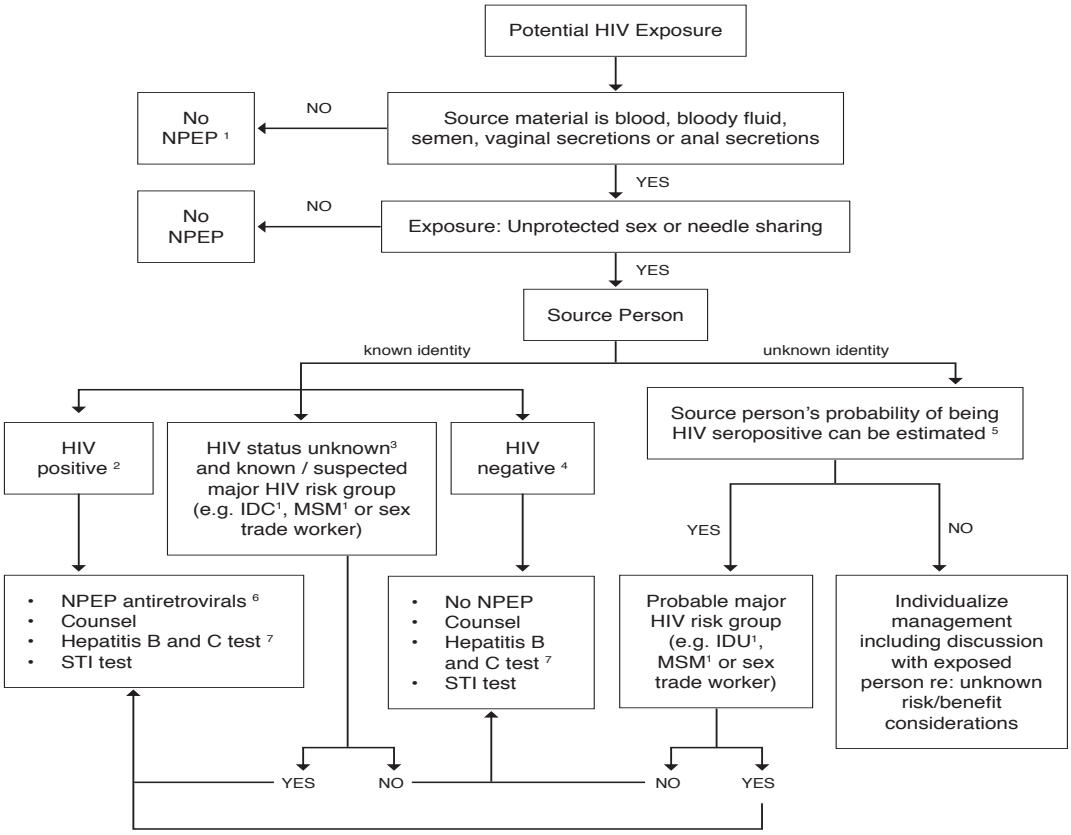
- Long term adverse effects of kidney or liver function 1:5,000
- Risk of death is unknown, however, we would estimate that the risk of dying due to an adverse event is 1:15,000 to 1:150,000. Using three drugs without appropriate follow-up, it may actually be much higher.

7. FOLLOW-UP


Baseline Assessment of Exposure
• Testing of exposed person (POC and HIV serology)
• Test source if available (POC and HIV serolgoy)
• Completion of Primary Screening Form
• Initiation of NPEP starter kit if indicated
• Hepatitis B, C, and STI workup completed
Baseline POC HIV Test Positive for Exposed Person
• Post-test counselling
• No NPEP
Follow-up
• SPH Emergency Room, SPH IDC and BCCDC STI clinic patients referred to IDC NPEP Program
• Spectrum Health Clinic and DCHC patients followed at primary care site
Follow-up Visit #1 at SPH IDC or Primary Care Site
• Assessment Form completed
• Consultation with BC-CfE NPEP pharmacist/physician to determine if full 28-day course of NPEP required
• Informed Consent for participation in NPEP Knowledge Study completed
28-day NPEP Not Recommended
• Risk reduction counselling
• Follow-up HIV testing at 12 weeks
28-day NPEP Recommended
• Follow-up weekly for side effects monitoring and medication dispensing
• Laboratory assessment at weeks two and four
• CBC, creatine, ALT, AST and urinalysis
Follow-up HIV Testing Post-Exposure (HIV Serology)
• Six weeks
• 12 weeks

APPENDIX 1

HIV EXPOSURE ALGORITHM



Note: It is not the intent of this pilot project to prophylax all sexual events where no risk exists

HIV EXPOSURE ALGORITHM FOOTNOTES

1. NPEP = non-occupational post exposure prophylaxis. IDU = injection drug user. MSM = men who have sex with men.
2. Source person is considered HIV positive if there is a positive test for HIV antibody, HIV PCR, or physician diagnosed AIDS. A low or undetectable viral load greatly diminishes the risk however does not eliminate the risk.
3. If HIV status unknown and source person consents, then test for HIV using POC and HIV serology, draw hepatitis serology: anti-HCV Ab, HBsAg.
4. Source person is considered HIV negative if POC test and HIV serology are negative.
5. Source person's probability of being HIV seropositive can be estimated; it may be possible to estimate the risk (see Appendix 2a) of potential HIV prevalence within certain risk groups, and thus the risk of seroconversion. In low seroprevalence exposures the risk of a serious drug related adverse reaction of PEP (estimated to be 1:5000) may exceed that of HIV seroconversion.
6. NPEP: Three drugs are recommended for significant risk exposures involving confirmed HIV sources. Prophylaxis is recommended for significant risk exposures involving sources whose HIV status is unknown, if the source is known/strongly suspected to have a major HIV risk factor.
7. Counsel regarding precautions for minimizing risk of exposure to HIV/ hepatitis B/C and other sexually transmitted pathogens, obtain baseline bloodwork (outlined below) and advise patient regarding timing of follow-up testing;

NPEP toxicity monitoring should include CBC, creatinine, ALT, AST, and urinalysis.

For individuals who may be susceptible to hepatitis B and C, collect exposed person's blood samples for anti-HBs, HBsAg, and anti-HCV.

APPENDIX 2A - RISK ASSESSMENT : ESTIMATED PROBABILITY OF HIV FOLLOWING A SINGLE EXPOSURE IN BRITISH COLUMBIA

Exposure Type	Source Person Category (estimated seropositive probability[1])							
	Major Risk Group			Risk Factors Unknown			Not in Major Risk Group	
	Known HIV+	IDU	Gay Men	Men	Women	Gender?	Men	Women
Estimated Seroconversion probability[2]	(p=1)	(p=.2)	(p=.2)	(p=.005)	(p=.0005)	(p=.0025)	(p=.0005)	(p=.00005)
Non-Occupational								
Penile-vaginal intercourse (risk to male) (p=.0005)	0.0005	0.0001	0.0001	0.0000025	0.00000025	0.0000012	0.00000025	0.000000025
Penile-vaginal intercourse (risk to female) (p=.001)	0.001	0.0002	0.0002	0.000005	0.0000005	0.0000025	0.0000005	0.00000005
Insertive anal intercourse (p=.0006)	0.0006	0.00012	0.00012	0.000003	0.0000003	0.0000015	0.0000003	0.00000003
Receptive anal intercourse (p=.03)	0.03	0.006	0.006	0.00015	0.000015	0.000075	0.000015	0.0000015
Receptive oral intercourse (p=.0001)	0.0001	0.00002	0.00002	0.0000005	0.00000005	0.00000025	0.00000005	0.000000005
Occupational								
Percutaneous needle (p=.003)	0.003	0.0012	0.0006	0.000015	0.0000015	0.0000075	0.0000015	0.00000015
Mucocutaenous (p=.001)	0.001	0.0004	0.0002	0.000005	0.0000005	0.0000025	0.0000005	0.00000005

1. Based on Provincial STD Control data 1997 and VIDUS Study

2. Based on published estimates for each exposure type (Katz et al NEJM 1997; 336:1097; Royce et al NEJM 1997; 336:1072)

These figures represented only an average risk; the risk to an individual may be higher depending on the presence of other factors.

REFERENCES:

1. Smith DK, Grohskopf LA, Black RJ, et al. Antiretroviral postexposure prophylaxis after sexual, injection-drug use, or other nonoccupational exposure to HIV in the United States: recommendations from the U.S. Department of Health and Human Services. MMWR Recomm Rep 2005; 54:1-20.
2. Panlilio AL, Cardo DM, Grohskopf LA, Heneine W, Ross CS. Updated U.S. Public Health Service guidelines for the management of occupational exposures to HIV and recommendations for postexposure prophylaxis. MMWR Recomm Rep 2005; 54:1-17.
3. Cardo DM, Culver DH, Ciesielski CA, et al. A case-control study of HIV seroconversion in health care workers after percutaneous exposure. Centers for Disease Control and Prevention Needlestick Surveillance Group. The New England journal of medicine 1997; 337:1485-90.
4. Young TN, Arens FJ, Kennedy GE, Laurie JW, Rutherford G. Antiretroviral post-exposure prophylaxis (PEP) for occupational HIV exposure. Cochrane database of systematic reviews (Online) 2007:CD002835.
5. Kahn JO, Martin JN, Roland ME, et al. Feasibility of postexposure prophylaxis (PEP) against human immunodeficiency virus infection after sexual or injection drug use exposure: the San Francisco PEP Study. The Journal of infectious diseases 2001; 183:707-14.
6. Mayer KH, Mimiaga MJ, Cohen D, et al. Tenofovir DF plus lamivudine or emtricitabine for nonoccupational postexposure prophylaxis (NPEP) in a Boston Community Health Center. Journal of acquired immune deficiency syndromes (1999) 2008; 47:494-9.
7. BC Centre for Disease Control. Communicable Disease ControlPoint of Care HIV Test Guidelines for Health Care Settings May 2011. Available at http://www.bccdc.ca/NR/rdonlyres/9C1C7D54-AA3946BB8ED37DDF6C23931A/0/POCHIVTestGuidelines_May2011.pdf. Accessed February 24,2012.
8. Tosini W, Muller P, Prazuck T, et al. Tolerability of HIV postexposure prophylaxis with tenofovir/emtricitabine and lopinavir/ritonavir tablet formulation. AIDS (London, England) 2010; 24:2375-80.