Original Article

Determinants of Late-Stage HIV Disease at Diagnosis in Singapore, 1996 to 2009

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Abstract

Introduction: **The delay in HIV diagnosis has been identified as a significant reason for late presentation to medical care. This research aims to elucidate the significant determinants of late-stage HIV infection in Singapore between 1996 and 2009, after the advent of highly active anti-retroviral therapies.** Materials and Methods: **We included 3735 patients infected via sexual mode of transmission from the National HIV Registry diagnosed between 1996 and 2009. Late-stage HIV infection is defined as CD4 count less than 200 mm³ or AIDS-defining opportunistic infections at first diagnosis or within one year of HIV diagnosis. We determined independent epidemiological risk factors for late-stage HIV infection at first diagnosis using multivariate logistic regression.** Results: **Multivariate analysis showed that older age corresponded significantly with increasing odds of late-stage HIV infection. Compared to persons diagnosed at 15 to 24 years of age, those diagnosed at age 55 years and above were associated with 5-fold increased likelihood of late-stage infection (adjusted odds ratio (AOR): 5.17; 95% CI, 3.21 to 8.33). Chinese ethnicity, singlehood, and non-professional occupations were also significantly associated with late-stage HIV infection. Persons detected in the course of medical care had over 3.5 times the odds of late-stage infection (AOR: 3.55; 95% CI, 2.71 to 4.65). Heterosexual mode of transmission and having sex workers and social escorts as sexual partners, were the other epidemiological risk factors with significant associations.** Conclusion: **The findings of this study emphasises the need to increase HIV awareness and to encourage early and regular HIV testing among at-risk persons.**

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Key words: AIDS-defining illness, CD4 count, HAART

Introduction

The first case of HIV infection in Singapore was diagnosed in 1985,[1] and the first case of AIDS was diagnosed in September 1986.[2] Since then, the incidence of HIV infection has been on a rising trend (Fig. 1), and the proportion of late-stage HIV infection amongst newly diagnosed cases has also been noted to increase concomitantly (Fig. 2). The predominant mode of HIV transmission in Singapore since 1985 has been via the sexual route. Homosexual and bisexual modes of transmission were prevalent in the earlier period between 1985 and 1990. From 1991 onwards, heterosexual transmission became the dominant mode of HIV transmission in Singapore.[3,4] As of end 2009, a total of 4404 cases of HIV/AIDS had been diagnosed, out of which 3956 (89.8%) were males, and 448 (10.2%) were

females. This translates to a HIV notification rate of 12 per 100,000 persons in 2009.[5]

In a study to review AIDS-defining illnesses among patients diagnosed with HIV in Singapore between 1985 and 2001, opportunistic infections were found to be a common AIDS-defining illness despite the availability of highly active anti-retroviral therapies (HAART).[6] This was attributed by the researchers to the fact that most patients presented at the time of HIV diagnosis with advanced disease and with low levels of CD4 counts. In another study conducted to analyse the causes of death in the same cohort of HIV patients, it was found that the proportion of patients who died from AIDS-related infections remained high, unlike in the West, where the main causes of deaths were non-infectious and chronic conditions such as malignancies

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Address for Correspondence: Dr Tey Su Hui Jeannie, Epidemiology and Disease Control Division, Ministry of Health, Singapore. College of Medicine Building, 16 College Road, Singapore 169854.
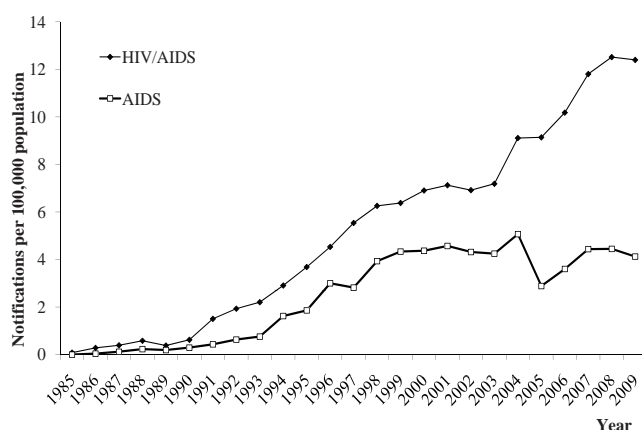Email: jeannie_tey@moh.gov.sg

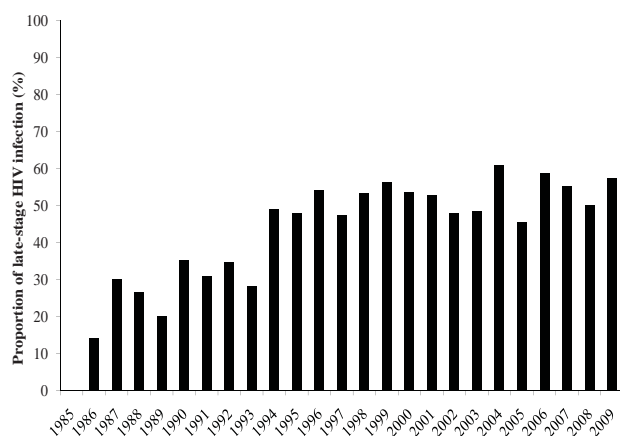Fig. 1. HIV/AIDS notification per 100,000 population in Singapore, 1985 to 2009.

Fig. 2. Proportion of late-stage HIV infection in Singapore, 1985 to 2009.

and cardiovascular diseases.[7] The study implied a need for the early detection of HIV amongst infected individuals so that they could benefit from early HARRT. In a separate local study, older age as well as lower baseline CD4 cell counts were identified to be significant predictors for rapid progression to AIDS at the time of diagnosis.[8]

In Singapore, a significant percentage of HIV infected persons present with late-stage HIV disease at first diagnosis.[9] As illustrated by past studies, this trend is not ideal as persons diagnosed with late-stage disease have lower CD4 counts, are more likely to develop opportunistic infections, progress rapidly to AIDS, and have a poorer clinical outcome. Even in the era where HAART is available, late HIV diagnosis remains a problem in developed countries like the United States (US)[10] and Australia.[11] To address this issue, routine, opt-out HIV testing in healthcare settings was recommended by the Centers for Disease Control and Prevention (CDC) in the US in 2006.[12]

This research aims to elucidate the significant determinants

of late HIV diagnosis in Singapore between 1996 and 2009, after the advent of HAART for the medical management of persons with HIV/AIDS infection. We confined the study to the post-HAART period as this would allow us to identify significant factors which determine late-stage HIV infection at diagnosis, independent of any barrier to early testing and diagnosis as a result of the lack of effective HIV treatment. The findings of this study would provide valuable information for review of the effectiveness of the current HIV prevention and control programme, and fine-tuning of the strategy by the Ministry of Health (MOH) to further reduce HIV transmission in Singapore.

Materials and Methods

In Singapore, notification of HIV/AIDS is a statutory requirement. Under the Infectious Diseases Act, all medical practitioners and laboratories are legally required to notify all cases of HIV/AIDS infection to the National HIV Registry using the MD131 form. Notifications can be carried out via the internet, fax or mail. The information obtained from the HIV/AIDS notification system is supplemented with additional information obtained through interview of the cases.[13]

In this retrospective study, epidemiological information on HIV infection and AIDS was obtained from the National HIV Registry at the National Public Health Unit (NPHU), which is under the purview of the Communicable Diseases Division (CDD), MOH. Demographic and relevant clinical information of these cases are maintained in the Registry for the purpose of surveillance, monitoring and contact tracing. As sexual transmission was the major mode of HIV infection accounting for 94% of the cases reported between 1996 and 2009, we only included cases who acquired the infection by the sexual route in our study. As HAART was only available from 1996 onwards, and the purpose of this study was to elucidate factors associated with late-stage HIV infection after the advent of HAART, cases diagnosed before 1996 were excluded. A person with late-stage HIV infection is defined as one with CD4 count of less than 200 mm³, or who developed AIDS-defining opportunistic infections at first diagnosis or within one year of HIV diagnosis. This is the same definition adopted by the US CDC.[14]

Associations between patients with late-stage HIV infection and various demographic factors, the mode of HIV diagnosis as well as exposure factors including the mode of sexual transmission and the type of sexual partners, were assessed among the HIV/AIDS cases included in the study. Bivariate analysis was first carried out using chi-square test. Multivariate logistic regression was used to determine independent epidemiological risk factors for late-stage HIV infection at first diagnosis, using forward stepwise selection

based on maximum partial likelihood estimates. All *P* values reported were 2-sided and statistical significance was defined as *P* <0.05. All statistical analyses were performed using the Statistical Package for Social Science (SPSS), version 17.0 (SPSS Inc., Chicago, Illinois, USA).

Results

A total of 3735 persons diagnosed with HIV infection during the period between 1996 and 2009 were included in the study. Of these, 53.9% had late-stage HIV infection at first diagnosis (Table 1). Compared to persons without late-stage HIV infection at diagnosis, a greater percentage of persons with late-stage HIV infection at diagnosis were aged 55 years old and above (21.7% vs 10.0%). A higher percentage of persons with late-stage HIV infection were male (92.8% vs 86.4%), Chinese (86.3% vs 79.9%), divorced, separated or widowed (14.7% vs 11.3%), blue-collar workers (31.9% vs 20.0%) and unemployed (17.4% vs 7.7%). A much higher proportion of the persons with late-stage HIV infection were diagnosed in the course of medical care (91.6% vs 54.6%), infected via heterosexual mode of transmission (79.5% vs 60.4%), and had sex workers and social escorts as sexual partners (69.4% vs 44.1%).

Bivariate analyses showed that the risk of late-stage HIV infection at diagnosis was associated with age, gender, ethnic group, marital status, occupation, mode of detection, mode of sexual transmission and type of sexual partners (Table 2). In the multivariate logistic regression, older age at HIV diagnosis corresponded with increasing odds of late-stage HIV infection at diagnosis, with persons diagnosed at age 55 years and above having the highest risk of late-stage infection. Compared to persons diagnosed at 15 to 24 years of age, those who were diagnosed at age 55 years and above were significantly more likely to have late-stage HIV infection (adjusted odds ratio (AOR): 5.17; 95% CI, 3.21 to 8.33). Compared to the Chinese, Indians were significantly less likely to be diagnosed with late-stage HIV infection (AOR: 0.58; 95% CI, 0.38 to 0.87). Persons who were married, or divorced, separated or widowed were at decreased odds of late-stage HIV infection compared to those who were single.

Compared to persons with professional and executive occupations, persons with administrative or service-oriented occupations, blue-collar workers, as well as unemployed persons, were at increasingly higher risk of late-stage HIV infection at diagnosis. Persons detected in the course of medical care had over 3 times the odds of late-stage HIV infection (AOR: 3.55; 95% CI, 2.71 to 4.65) than those detected through voluntary screening. Persons infected via heterosexual mode of transmission were also significantly more likely to be diagnosed with late-stage HIV infection

Table 1. Characteristics (%) of Patients who Acquired HIV Infection via Sexual Route, Singapore, 1996 to 2009

Characteristic	With late-stage HIV infection (n = 2012)	Without late-stage HIV infection (n = 1723)	Total (n = 3735)
Age at diagnosis (years)			
15 to 24	1.6	10.5	5.7
25 to 34	16.5	32.1	23.7
35 to 44	32.9	30.9	32.0
45 to 54	27.3	16.5	22.3
55+	21.7	10.0	16.3
Gender			
Male	92.8	86.4	89.9
Female	7.2	13.6	10.1
Ethnic group			
Chinese	86.3	79.9	83.4
Malay	9.1	11.2	10.0
Indian	2.4	5.4	3.8
Others	2.2	3.5	2.8
Marital status			
Single	50.6	58.4	54.2
Married	34.7	30.3	32.7
Divorced/separated/widowed	14.7	11.3	13.1
Occupation			
Professional/executive	12.8	20.7	16.4
Administrative/service-oriented	29.5	33.9	31.5
Blue-collar worker	31.9	20.0	26.4
Unemployed	17.4	7.7	13.0
Others	8.4	17.7	12.7
Mode of detection			
Own request	4.4	15.7	9.6
Medical care*	91.6	54.6	74.5
Contact tracing	1.6	11.0	5.9
Others	2.4	18.7	10.0
Mode of sexual transmission			
Homosexual/bisexual	20.5	39.6	29.3
Heterosexual	79.5	60.4	70.7
Type of sexual partners			
Regular only	10.9	18.4	14.4
Regular and casual only	19.7	37.5	27.9
Sex workers and social escorts	69.4	44.1	57.7

*HIV infection was detected in persons who sought medical care when they presented with medical complaints/symptoms

Table 2. Proportion, Crude Odds Ratios (OR) and Adjusted Odds Ratios (AOR) of Late-Stage HIV Infection in Patients who Acquired HIV Infection via the Sexual Route, Singapore, 1996 to 2009

	% with late-stage HIV infection	Bivariate model		Multivariate model	
		OR (95% CI)	*P* value	AOR (95% CI)	*P* value
Age at diagnosis (years)			<0.0005		<0.0005
15 to 24	15.4	1.00 (referent)		1.00 (referent)	
25 to 34	37.6	3.30 (2.22, 4.90)	<0.0005	2.21 (1.43, 3.43)	<0.0005
35 to 44	55.4	6.81 (4.62, 10.04)	<0.0005	4.07 (2.63, 6.29)	<0.0005
45 to 54	65.8	10.57 (7.10, 15.73)	<0.0005	4.84 (3.08, 7.62)	<0.0005
55+	71.7	13.90 (9.22, 20.97)	<0.0005	5.17 (3.21, 8.33)	<0.0005
Gender					
Male	55.6	1.00 (referent)			
Female	38.3	0.49 (0.40, 0.62)	<0.0005		
Ethnic group			<0.0005		0.029
Chinese	55.8	1.00 (referent)		1.00 (referent)	
Malay	48.7	0.75 (0.61, 0.93)	0.009	1.16 (0.90, 1.50)	0.250
Indian	34.0	0.41 (0.29, 0.58)	<0.0005	0.58 (0.38, 0.87)	0.008
Others	42.3	0.58 (0.39, 0.86)	0.007	1.11 (0.69, 1.77)	0.672
Marital status			<0.0005		0.035
Single	50.3	1.00 (referent)			
Married	57.2	1.33 (1.15, 1.53)	<0.0005	0.82 (0.67, 0.99)	0.046
Divorced/separated/widowed	60.3	1.50 (1.23, 1.84)	<0.0005	0.74 (0.57, 0.95)	0.018
Occupation			<0.0005		0.001
Professional/executive	41.9	1.00 (referent)		1.00 (referent)	
Administrative/service-oriented	50.4	1.41 (1.16, 1.71)	0.001	1.41 (1.13, 1.76)	0.003
Blue-collar worker	65.1	2.58 (2.10, 3.18)	<0.0005	1.52 (1.19, 1.94)	0.001
Unemployed	72.5	3.66 (2.83, 4.72)	<0.0005	1.82 (1.35, 2.45)	<0.0005
Others	35.7	0.77 (0.60, 0.99)	0.037	1.32 (0.97, 1.78)	0.076
Mode of detection			<0.0005		<0.0005
Own request	24.5	1.00 (referent)		1.00 (referent)	
Medical care	66.2	6.04 (4.69, 7.77)	<0.0005	3.55 (2.71, 4.65)	<0.0005
Contact tracing	14.9	0.54 (0.35, 0.84)	0.006	0.39 (0.25, 0.62)	<0.0005
Others	13.2	0.47 (0.32, 0.69)	<0.0005	0.37 (0.25, 0.26)	<0.0005
Mode of sexual transmission					
Homosexual/bisexual	37.7	1.00 (referent)		1.00 (referent)	
Heterosexual	60.6	2.54 (2.19, 2.93)	<0.0005	1.64 (1.29, 2.07)	<0.0005
Type of sexual partners			<0.0005		0.005
Regular only	40.8	1.00 (referent)		1.00 (referent)	
Regular and casual only	38.1	0.89 (0.72, 1.10)	0.294	1.07 (0.8, 1.41)	0.657
Sex workers and social escorts	64.8	2.67 (2.20, 3.24)	<0.0005	1.41 (1.11, 1.78)	0.005

compared to those infected via homosexual mode (AOR: 1.64; 95% CI, 1.29 to 2.07). Persons whose sexual partners involved sex workers and social escorts had about 1.4 times the odds of late-stage HIV infection (AOR: 1.41; 95% CI, 1.11 to 1.78) than those who had regular sex partners only. Gender was not identified to be significantly associated with late-stage HIV infection in the multivariate model.

Discussion

The findings of this study are similar to those carried out in several developed countries. Studies on the determinants of late-stage HIV disease at first diagnosis carried out in France,[15] United Kingdom[16] and Australia[11] identified factors such as increasing age, heterosexual mode of transmission, as well as large number of sexual partners to be significant determinants. A similar study carried out in Italy[17] revealed

older age and male gender to be significant determinants. In the United States,[14] factors including younger age, ethnic minorities, heterosexual mode of HIV transmission, lower educational level, having previously tested negative for HIV, and HIV testing because of illness, were found to be associated with late-stage HIV disease at first diagnosis.

The delay in HIV diagnosis has been identified as a significant reason for late presentation to care.[18] In Singapore, the proportion of late-stage HIV infection among newly diagnosed HIV-positive persons has been greater than 50% since 1994, and is 57% in 2009. Studies have revealed that persons who are aware of their HIV-positive status are less likely to transmit the disease because early presentation to healthcare and treatment results in lower viral load levels and safe sexual practices as well as appropriate antenatal therapy to prevent vertical transmission.[19-21] In a meta-analysis of 11 independent studies carried out by Marks et al,[22] it was estimated that persons who are unaware of their HIV infection (about 25% of the HIV infected individuals in the United States) are responsible for more than 50% of the new HIV infections occurring in the population, mainly through engaging in high-risk sexual behaviours. The importance of the diagnosis of HIV infection at its early stages is underscored by the fact that persons with late HIV diagnosis have poorer survival,[23] and HIV-infected persons who receive HAART as well as prophylactic treatment against opportunistic infections have better outcomes in terms of slowing down disease progression as well as reducing morbidity and mortality secondary to opportunistic infections.[24] A local study revealed that the median survival of patients with late-stage HIV infection was 5 years, while the cumulative proportion of patients without late-stage HIV infection surviving till the 5th year since diagnosis was 80%.[25]

Our study identified factors such as heterosexual mode of transmission, older age groups, singlehood, and lower socioeconomic status to be significant factors associated with late-stage HIV infection at first diagnosis. HIV infected individuals with these factors may be less likely to utilise HIV voluntary counselling and testing (VCT) services.[15,26,27] To encourage voluntary testing, MOH has allowed medical clinics to offer HIV screening using oral-fluid or blood-based rapid HIV test kits since August 2007.[28] These tests allow patients to learn their HIV status in the same clinic visit. In August 2008, hospitals/healthcare institutions were also given the option of using HIV rapid tests for screening in point-of-care settings. Recognising that the fear of HIV-related stigma and discrimination can be a significant barrier to voluntary HIV testing, MOH increased the number of anonymous HIV test sites from 3 to 7 in November 2008.[29] The implementation of these measures to increase HIV testing in the healthcare setting is aimed at facilitating early diagnosis of HIV infection, and incorporating HIV prevention with clinical management. These efforts could be further strengthened by targeting the high risk groups that have been identified in this study for more focused HIV prevention and testing programmes.

A limitation of this study is its cross-sectional design which limited the analysis of the various factors associated with late-stage HIV disease to a particular point in time. The various associations that have been identified could have been caused by secular trends unique to the HIV epidemic in Singapore, which would need to be elucidated by further studies. For example, the association of older age groups with late-stage HIV disease at diagnosis could have been a result of being infected at an earlier age without being diagnosed earlier. Alternatively, this association could have been due to a lower perceived HIV risk by older persons, resulting in a lower likelihood to go for HIV testing during the early stage of the disease. Similarly, the association of unemployment with late-stage HIV disease could have been due to the fact that being ill had affected the ability of patients to work. On the other hand, being of lower socioeconomic status could be an independent risk factor for a higher risk of late-stage HIV disease at diagnosis.

While our study showed that the detection of HIV during the course of medical care was significantly associated with late-stage HIV infection at diagnosis, information was limited as to whether the reasons for medical care were related to the presentation of HIV symptoms or non-related symptoms. Hence, patients who were diagnosed through medical care might not necessarily present with symptoms of opportunistic infection characteristic of late-stage HIV infection, as assumed in our study. Nevertheless, as voluntary HIV screening is not widespread,[28] we believe that HIV testing during the course of medical care would have been mainly carried out when there was clinical suspicion of HIV infection based on disease presentations or risk profiles.

This research provides a baseline reference for monitoring further evolution of the local HIV epidemic and future trends of cases with late-stage disease at diagnosis. The study also emphasises the need to increase HIV awareness and to encourage early and regular HIV testing among at-risk persons. Moving forward, regular assessments of the effectiveness and efficacy of local public health initiatives in reducing the number of cases who present with late-stage infection at diagnosis would be necessary.

REFERENCES

1. Ministry of Health, Singapore. Update on AIDS/HIV infection In Singapore (1). Press release 02 Sep 1997. Available at: http://www.moh.gov.sg/mohcorp/pressreleases.aspx?id=658 Accessed 9 April 2009.

2. Chew SK, Monteiro EH. The acquired immunodeficiency syndrome in Singapore-epidemiological perspectives. Singapore Med J 1989;30:28-31.

3. Sen P, Chio MT, Tan HH, Chan RK. Rising trends of STIs and HIV infection in Singapore - a review of epidemiology over the last 10 years (1994 to 2003). Ann Acad Med Singapore 2006;35:229-35.

4. Chew SK. Trends in human immunodeficiency virus infection: epidemiology in Singapore. Ann Acad Med Singapore 1993;22:142-5.

5. Ministry of Health, Singapore. Update on AIDS/HIV infection In Singapore 2009. Press release 13 May 2010. Available at: http://www.moh.gov.sg/mohcorp/pressreleases.aspx?id=24284. Accessed 22 May 2010.

6. Bellamy R, Sangeetha S, Paton NI. AIDS-defining illnesses among patients with HIV in Singapore, 1985 to 2001: results from the Singapore HIV observational cohort study (SHOCS). BMC Infect Dis 2004;4:47.

7. Bellamy R, Sangeetha S, Paton NI. Causes of death among patients with HIV in Singapore from 1985 to 2001: results from the Singapore HIV observational cohort study (SHOCS). HIV Med 2004;5:289-95.

8. Chow KY, Ang LW, Verghesse I, Chew SK, Leo YS. Measurable predictive factors for progression to AIDS among HIV-infected patients in Singapore. Ann Acad Med Singapore 2005;34:84-9.

9. Ministry of Health, Singapore. News. Press Release. Date of issue: 13 May 2010. Update on the HIV/AIDS Situation in Singapore 2009. Available at: http://www.moh.gov.sg/mohcorp/pressreleases.aspx?id=24284.Accessed 20 May 2010.

10. Ronald O. Valdiserri. Late HIV diagnosis: bad medicine and worse public health. PLoS Med 2007;4:e200.

11. McDonald AM, Li Y, Dore GJ, Ree H, Kaldor JM. Late HIV presentation among AIDS cases in Australia, 1992-2001. Aust N Z J Public Health 2003;27:608-13.

12. Branson BM, Handsfield HH, Lampe MA, Janssen RS, Taylor AW, Lyss SB, et al; Centers for Disease Control and Prevention (CDC). Revised recommendations for HIV testing of adults, adolescents, and pregnant women in health-care settings. MMWR Recomm Rep 2006;55:1-17.

13. Cutter JL, Lim WY, Ang LW, Tun Y, James L, Chew SK. HIV in Singapore - past, present, and future. AIDS Educ Prev 2004;16:110-8.

14. Centers for Disease Control and Prevention (CDC). Late versus early testing of HIV—16 sites, United States, 2000-2003. Morb Mortal Wkly Rep 2003;52:581-6.

15. Delpierre C, Dray-Spira R, Cuzin L, Marchou B, Massip P, Lang T, et al. VESPA Study Group. Correlates of late HIV diagnosis: implications for testing policy. Int J STD AIDS 2007;18:312-7.

16. Porter K, Wall PG, Evans BG. Factors associated with lack of awareness of HIV infection before diagnosis of AIDS. BMJ 1993;307:20-3.

17. Borghi V, Girardi E, Bellelli S, Angeletti C, Mussini C, Porter K, et al. Late presenters in an HIV surveillance system in Italy during the period 1992-2006. J Acquir Immune Defic Syndr 2008;49:282-6.

18. Girardi E, Aloisis M, Arici C, Pezzotti P, Serraino D, Balzano R, et al. Delayed presentation and late testing for HIV: demographic and behavioral risk factors in a multicenter study in Italy. J Acquir Immune Defic Syndr 2004;36:951-9.

19. Centers for Disease Control and Prevention (CDC). Adoption of protective behaviors among persons with recent HIV infection and diagnosis—Alabama, New Jersey, and Tennessee, 1997-1998. Morb Mortal Wkly Rep 2000;49:512-5.

20. Gray RH, Wawer MJ, Brookmeyer R, Sewankambo NK, Serwadda D, Wabwire-Mangen F, et al. Probability of HIV-1 transmission per coital act in monogamous, heterosexual, HIV-1-discordant couples in Rakai, Uganda. Lancet 2001;357:1149-53.

21. Quinn TC, Wawer MJ, Sewankambo N, Serwadda D, Li C, Wabwire-Mangen F et al. Viral load and heterosexual transmission of human immunodeficiency virus type 1. Rakai Project Study Group. N Engl J Med 2000;342:921-9.

22. Marks G, Crepaz N, Janssen RS. Estimating sexual transmission of HIV from persons aware and unaware that they are infected with the virus in the USA. AIDS 2006;20:1447-50.

23. Chadborn TR, Delpech VC, Sabin CA, Sinka K, Evans BG. The late diagnosis and consequent short-term mortality of HIV-infected heterosexuals (England and Wales, 2000-2004). AIDS 2006;20:2371-9.

24. Hogg RS, Yip B, Chan KJ, Wood E, Craib KJ, O'Shaughnessy MV, et al. Rates of disease progression by baseline CD4 cell count and viral load after initiating triple-drug therapy. JAMA 2001;286:2568-77.

25. Ang LW, Tey SH and James L. Determinants of late-stage human immunodeficiency virus infection at first diagnosis. Epidemiological News Bulletin 2008;34:47-50.

26. Mugavero MJ, Castellano C, Edelman D, Hicks C. Late diagnosis of HIV infection: the role of age and sex. Am J Med 2007;120:370-3.

27. Ang LW, Tey SH, James L. HIV-positive cases detected during medical care versus voluntary HIV screening in Singapore – how are they different? Epidemiol News Bulletin 2009;35:52-6.

28. Ministry of Health, Singapore. Press release. Date of issue: 30 November 2007. HIV cases on the rise in 2007 - MOH urges at-risk groups to go for voluntary testing. Available at: http://www.moh.gov.sg/mohcorp/pressreleases.aspx?id=17838. Accessed 7 April 2009.

29. Ministry of Health, Singapore. Press release. Date of issue: 30 Oct 2008. Expansion of anonymous HIV testing programme in Singapore. Available at: http://www.moh.gov.sg/mohcorp/pressreleases.aspx?id=20158. Accessed 20 October 2009.