Delayed diagnosis of HIV infection in women in the Auckland and Northland regions

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ABSTRACT

aims: We aimed to describe the epidemiology of women with HIV infection in the Auckland and Northland regions, and to assess whether there were missed opportunities for an earlier diagnosis of HIV infection.

methods: We undertook a retrospective cohort analysis of women diagnosed with HIV infection between July 2011 and June 2021 under the care of the Infectious Disease Unit, Auckland City Hospital.

results: Fifty-six women (54 cis and 2 trans) were diagnosed during the period. Eleven (20%) were diagnosed following a presentation with one or more AIDS-defining illnesses. Three (6%) died within six months of diagnosis. Fifteen of 44 (34%) women residing in New Zealand prior to their diagnosis of HIV infection had identifiable healthcare interactions that could have resulted in an earlier diagnosis of this infection.

conclusions: Women account for one in eight of the total population of people diagnosed with HIV infection in the Auckland and Northland regions. There are currently inadequate levels of HIV testing for women in the Auckland and Northland regions. There is a need for targeted HIV screening efforts for women. HIV screening needs to be optimised to maximise coverage, normalise testing and reduce the stigmatisation associated with testing.

Anti-retroviral therapy (ART) has dramatically improved the life expectancy for people with HIV (PWH).[1] The early diagnosis of HIV infection and subsequent early initiation of ART is associated with significant health benefits and the prevention of HIV transmission.[2,3] Unfortunately, many PWH in New Zealand are diagnosed late, when their CD4 count has fallen to a level that places them at risk of, or when they present with, an AIDS-defining illness.[4] In the Auckland and Northland regions, we continue to see women whose HIV infection is diagnosed late.

The aims of this study were to describe the epidemiology of the cohort of women diagnosed with HIV infection in the Auckland and Northland regions during the 10-year period of 2011 to 2021 who received care from the Infectious Disease Unit at Auckland City Hospital; to compare these women to the cohort of men who were diagnosed during the same period and who received care from the same unit; and to assess whether there were missed opportunities where these women's HIV infection could have been diagnosed earlier.

Methods

This study was a retrospective cohort analysis.

The Infectious Disease Unit at Auckland City Hospital provides inpatient and outpatient care for adults with HIV infection residing in the Northland, Waitematā, Auckland and Counties Manukau district health board (DHB) regions.

Eligible patients were women aged 15 years and over, who were diagnosed with HIV infection during the 10-year period of July 2011 to June 2021, and who subsequently received care from the Infectious Disease Unit at Auckland City Hospital.

Demographic and clinical data were collected from each woman's medical record. These data were compared with those of the men who were diagnosed with HIV infection during the same period.

For the subset of women who resided in New Zealand prior to the diagnosis of their HIV infection, and who were not diagnosed with HIV infection at the time of the acute retroviral syndrome, we estimated the number of years since the acquisition of their HIV infection based on their CD4 count at diagnosis and data from the CASCADE study (Table 1).[5]

If a woman had a previous negative HIV test within the estimated period since her acquisition of HIV infection, then this period was reduced appropriately. We assessed whether there were potential missed opportunities for an earlier diagnosis of HIV infection for each woman during this period.

A woman met the definition of "certain or very

likely to have been infected outside of New Zealand" if she was diagnosed with HIV infection at the time of arrival to New Zealand; if she was diagnosed after arrival to New Zealand but had no sexual partners in New Zealand; or had sexual partners in New Zealand who were known to be HIV negative; or if she had an overseas sexual partner who was the definite or the very likely source of HIV infection. This decision was made by the HIV clinician and the woman at the time of the diagnosis of her HIV infection.

The Fisher's exact test, Chi-squared test and Mann–Whitney U-test were used to compare characteristics of the cohorts.

Ethical approval was granted by the Southern Health and Disability Committee (21/STH/180).

Results

During the 10-year study period, 451 adults in the Auckland and Northland regions were diagnosed with HIV infection, and subsequently received care from the Infectious Disease Unit at Auckland City Hospital; 56 (12%) women (54 cis and 2 trans women) and 395 (88%) men.

The baseline characteristics of the newly diagnosed women are shown in Table 2. Their median age at diagnosis was 37.5 (interquartile range (IQR) 29.5–45.5) years. Their DHB of domicile was Counties Manukau (n=25), Auckland (n=16), Waitematā (n=12) or Northland (n=3). The baseline characteristics of the women compared with the men who were diagnosed during the same period are shown in Table 2. There was a difference in the proportion of diagnoses made over time, with women continuing to be diagnosed in similar numbers during the study period compared with men whose diagnoses peaked in the middle years of the study period. There was a difference in the self-reported ethnicity of the women compared with the men (Table 2) or with the Auckland Region population obtained from the 2018 New Zealand Census (Table 3).[6] This showed that women more likely to be of sub-Saharan African and Pacific ethnicity, and less likely to be of NZ European/Other European/Other ethnicity; and more likely to be of sub-Saharan African and Pacific ethnicity and less likely to be of European and Asian ethnicity, respectively. Twenty-four women were certain (n=18) or very likely (n=6) to have been infected with HIV outside of New Zealand. The self-reported ethnicity of the women who were certain or very likely to have been infected within New Zealand compared with those certain or very likely to have been infected outside of New Zealand is shown in Table 4. The women who were certain or very likely to have been infected within New Zealand were more likely to self-report their ethnicity as Māori, Pacific or NZ European, and less likely to self-report this as Asian.

At the time of diagnosis, 27 (49%) women had a CD4 count less than 350 cells/mm^3 and 15 (27%) women had a CD4 count less than 200 cells/mm^3. There was no difference in the CD4 count at diagnosis of the newly diagnosed women compared with the newly diagnosed men (Table 2) or with a New Zealand wide study looking at the CD4 count at diagnosis in the cohort of people diagnosed with HIV infection from 2005 to 2010.[4]

The possible risk factors for acquisition of the 56 women were sexual transmission (n=49), sexual transmission and injecting drug use (IDU) (n=6), and perinatal transmission that occurred outside of New Zealand (n=1).

The reason for performing the HIV test that resulted in the women's diagnosis was presentation with one or more AIDS-defining illnesses (n=11), presentation with the acute retroviral syndrome (n=3), presentation with symptoms or an illness that highlighted the need for HIV testing (n=4), patient request (n=5), testing once the woman's partner or child was diagnosed with HIV infection (n=10) or HIV screening (n=23) (antenatal screening (n=8), Immigration Service screening (n=7), Community Alcohol and Drug Service screening (n=2), Prison Service screening (n=2), Refugee Service screening (n=2), Hospital screening (n=1) or Psychiatry Service screening (n=1)).

Eleven of the 56 (20%) women were initially diagnosed with one or more AIDS-defining illnesses that resulted in their HIV infection being diagnosed; *Pneumocystis jirovecii* pneumonia (n=3); *Pneumocystis jirovecii* pneumonia, disseminated *Mycobacterium avium-intracellulare* complex infection and oesophageal candidiasis (n=1); *Pneumocystis jirovecii* pneumonia and oesophageal candidiasis (n=1); lymphoma (n=2); tuberculosis (n=2); cerebral toxoplasmosis (n=1); or oesophageal candidiasis (n=1). During the same period, 34 of the 395 (9%) men were diagnosed with one or more AIDS-defining illnesses that resulted in their HIV infection being diagnosed (p=0.02).

Three of the 56 (6%) women died within six months of their diagnosis of HIV infection. All deaths were due to the AIDS-defining illness they presented with. An additional woman, who presented with cerebral toxoplasmosis, remained severely incapacitated 12 months after her presentation. During the same period, three of the 395 (1%) men died within six months of their diagnosis of HIV infection due to the AIDS-defining illness they presented with (p=0.03).

Twelve women were either not residing in New Zealand prior to their diagnosis of HIV infection

Table 1: Estimated years since acquisition of HIV infection based on the CD4 count at diagnosis.[5]

CD4 count range at diagnosis (cells/mm³)	Estimated years since acquisition of HIV infection
≤ 199	7
200–349	5
350–499	3
≥ 500	1

Table 2: Baseline characteristics of the women and men diagnosed with HIV infection in the Auckland and Northland regions July 2011 to June 2021.

Baseline characteristic		Women, n=56 (%)	Men, n=395 (%)	p value
Date of diagnosis	July 2011–June 2013	9 (16)	77 (19)	0.049*
	July 2013–June 2015	15 (27)	100 (25)	
	July 2015–June 2017	9 (16)	106 (27)	
	July 2017–June 2019	9 (16)	67 (17)	
	July 2019–June 2021	14 (25)	45 (12)	
Age at diagnosis, n (IQR) (years)		37.5 (29.5–45.5)	38 (30–49)	0.48†
Self-reported ethnicity	Māori	5 (9)	28 (7)	<0.001*
	Asian	13 (23)	76 (19)	
	sub-Saharan African	13 (23)	7 (2)	
	Pacific peoples	12 (21)	33 (8)	
	NZ European	11 (20)	172 (44)	
	Other European/Other/NA	2 (4)	79 (20)	
CD4 count at diagnosis (cells/mm³)#	<200	15 (27)	99 (25)	0.71*
	200–349	12 (22)	66 (17)	
	350–499	12 (22)	89 (23)	
	≥500	16 (29)	140 (35)	

Note. NA: not available.
*Chi-squared test, †Mann–Whitney U-test (two tailed), # CD4 count result not available for one woman and one man.

Table 3: Self-reported ethnicity of women diagnosed with HIV infection in the Auckland and Northland regions July 2011 to June 2021 compared with the Auckland population self-reported ethnicity.

Self-reported ethnicity	Women n=56 (%)	Auckland population (%)*†	p value
Māori	5 (9)	11.5	<0.001#
European	13 (23)	53.5	
Asian	13 (23)	28.2	
Middle Eastern/Latin American/African	13 (23) ‡	2.3	
Pacific peoples	12 (22)	15.5	
Other	0 (0)	1.1	

*From 2018 NZ Census data (all ages and genders).[6]
†Where a person reported more than one ethnic group, they were counted in each applicable group.
#Chi-squared test.
‡All 13 women self-reported their ethnicity as sub-Saharan African.

Table 4: Self-reported ethnicity of women diagnosed with HIV infection in the Auckland and Northland regions July 2011 to June 2021 who were certain or very likely to have been infected within New Zealand, compared with those who were certain or very likely to have been infected outside of New Zealand.

Self-reported ethnicity	Women certain or very likely to be infected within New Zealand (n=32) (%)	Women certain or very likely to be infected outside of New Zealand (n=24) (%)	p value
Māori	5 (16)	0 (0)	<0.001#
NZ European	10 (31)	1 (4)	
Pacific peoples	9 (28)	3 (13)	
sub-Saharan African	5 (16)	8 (33)	
Asian	2 (6)	11 (46)	
Other European/Other	1 (3)	1 (4)	

#Chi-squared test.

(n=8), or presented with the acute retroviral syndrome (n=4). There were therefore 44 women whose HIV infection could have potentially been diagnosed earlier if they had received HIV testing during the period that they were estimated to have had HIV infection. The median estimated duration of infection prior to HIV diagnosis for these 44 women was three (IQR 1–7) years. Fifteen of the 44 (34%) women had identifiable healthcare interactions that could have resulted in HIV testing being performed prior to their diagnosis of HIV infection (Table 5). If these 15 women had been offered an HIV test at the earliest of these interactions, it is very likely that their HIV infection would have been diagnosed a median of 14 (IQR 6.5 to 33) months earlier. Assuming that this earlier diagnosis was made, it is almost certain that three episodes of *Pneumocystis jirovecii* pneumonia, one of which resulted in a woman's death, would have been prevented as the diagnosis of HIV infection for these three women would have been made 27, 38 and 74 months prior to their presentation with this AIDS-defining illness.

Discussion

During the 10-year study period, one in eight (12%) adults newly diagnosed with HIV infection who received care from the Infectious Disease Unit at Auckland City Hospital were women. This demonstrates that women make up a significant minority of the total population of people diagnosed with HIV infection in the Auckland and Northland regions. This proportion of 12% is similar to, or somewhat lower than, recently reported proportions of 12, 19, 24 and 26% from Australia, the United States of America, Europe and the United Kingdom respectively.[7–10]

Women resided in all four DHBs in our region at the time of diagnosis of their HIV infection. There was no difference in age or CD4 count at diagnosis comparing the newly diagnosed women with the newly diagnosed men. This would suggest that as a cohort, these women were infected with HIV at a similar age and were diagnosed with this infection after a similar duration of infection when compared with the newly diagnosed men. There was a difference in the proportion of diagnoses made over time with women continuing to be diagnosed in similar numbers during the study period compared with men whose diagnoses peaked in the middle years of the study period. The causes of this difference are uncertain but include the possibility that recent HIV prevention strategies in New Zealand, such as pre-exposure prophylaxis, are more targeted at men who have sex with men, or men in general. There were differences in self-reported ethnicity when comparing the newly diagnosed women, with the newly diagnosed men or with the total Auckland population, with sub-Saharan African and Pacific women being over-represented and NZ European/European and Asian women being under-represented. These differences may have been the result of a higher rate of undiagnosed and/or untreated HIV infection in the men that some of the sub-Saharan African and Pacific women had as sexual partners. Some of the women contracted HIV infection before arriving in New Zealand, complicating any further analysis of the self-reported ethnicity differences.

Half of the women in this cohort had a CD4 count at diagnosis that met the definition of a "late presentation" (<350 cells/mm^3); this reflects current inadequate levels of HIV testing for women in the Auckland and Northland regions. This proportion is the same as that found in an earlier New Zealand wide study from 2005 to 2010.[4]

One fifth of the women in this cohort were diagnosed with HIV infection after they presented with one or more AIDS-defining illnesses. These AIDS-defining illnesses had an associated six-month mortality of 6%. These presentations illustrate an absence of HIV testing in this subset of the cohort; the higher proportion of presentations with AIDS-defining illnesses, and the higher associated six-month mortality when compared with the newly diagnosed men, demonstrates that at least a subset of the newly diagnosed women were diagnosed later than the newly diagnosed men.

The Ministry of Health recommends HIV testing for the following groups: persons with a history of unprotected sexual exposure that could result in HIV transmission; persons with a history of injecting drug use that involves the sharing of drug injecting equipment; persons seeking assessment for sexually transmitted infections; pregnant women; persons with recently diagnosed tuberculosis infection; persons with sexual contacts from countries where transmission of HIV infection is common; prospective partners in a new sexual relationship and any person whose blood or body fluids is the source of an occupational exposure for a healthcare provider.[11] Some of these groups are not clearly defined and for some of them, the healthcare provider is required to perform a relatively detailed risk-based assessment. Previous antenatal HIV testing in New Zealand following a risk-based assessment has been shown to result in the missed diagnosis of maternal HIV infection resulting in the subsequent transmission of HIV infection to the woman's new-born child.[12] The Ministry of Health's recommendations include only two indicator

Table 5: Identifiable healthcare interactions during the estimated period of HIV infection that could have resulted in HIV testing being performed.

Patient	Age at diagnosis (years)	CD4 count at diagnosis (cells/mm3)	Potential undiagnosed period (years)	Sexual health screen (n)	Earliest interaction (months prior to diagnosis)	Chlamydia or gonorrhoea from sexual health screen	Earliest interaction (months prior to diagnosis)	Abnormal cervical smear (n, grade)	Earliest interaction (months prior to diagnosis)	Colposcopy (n, grade)	Earliest interaction (months prior to diagnosis)	Other	Earliest interaction (months prior to diagnosis)	Cumulative earliest interaction (months prior to diagnosis)
1	40	4	7	8	74	C	54	1, LG	22	1, CIN1/HPV	21	ED review: viral illness, thrombocytopenia & lymphopenia	55	74
2	39	18	7	4	27									27
3	31	20	7	1	10	C	10							10
4	48	29	7					6, LG	79	2, CIN1/HPV 1, LSIL/HPV	51			79
5	29	60	7					2, LG	6					6
6	48	106	7	1	38							ORL review: asymmetric tonsils, biopsy showed reactive hyperplasia	6	38
7	30	131	7			G	12							12
8	53	156	7									SHS review: perineal discomfort	36	36
9	16	187	7									ED review: pneumonia, thrombocytopenia, lymphopenia & variant lymphocytes	3	3
10	37	319	5	1	14									14
11	26	395	3	6	29									29

Table 5 (continued): Identifiable healthcare interactions during the estimated period of HIV infection that could have resulted in HIV testing being performed.

Patient	Age at diagnosis (years)	CD4 count at diagnosis (cells/mm3)	Potential undiagnosed period (years)	Sexual health screen (n)	Earliest interaction (months prior to diagnosis)	Chlamydia or gonorrhoea from sexual health screen	Earliest interaction (months prior to diagnosis)	Abnormal cervical smear (n, grade)	Earliest interaction (months prior to diagnosis)	Colposcopy (n, grade)	Earliest interaction (months prior to diagnosis)	Other	Earliest interaction (months prior to diagnosis)	Cumulative earliest interaction (months prior to diagnosis)
12	41	453	3	5	30	C	30					Pregnancy, no HIV testing with standard antenatal screen	24	30
13	42	638	1					1, LG	1					1
14	18	650	1	1	7									7
15	38	931	1	1	1									1

Note. C: *Chlamydia trachomatis*, G: *Neisseria gonorrhoeae,* LG: low grade cervical smear change, CIN1: cervical intraepithelial neoplasia grade 1, LSIL: low-grade squamous intraepithelial lesion, HPV: human papillomavirus, ED: Emergency Department, ORL: Otorhinolaryngology, SHS: Sexual Health Service.

conditions that can be used to highlight where HIV testing should be performed. The British HIV Association's (BHIVA) recent Adult HIV Testing Guidelines recommend among their HIV testing groups, all people presenting with symptoms and/or signs consistent with an HIV indicator condition.[13] Their list of indicator conditions includes, in addition to the standard AIDS-defining illnesses, sexually transmitted infections, cervical dysplasia, herpes zoster, acute or chronic hepatitis B or C, unexplained lymphadenopathy, a mononucleosis-like illness, unexplained thrombocytopenia or leukopenia lasting greater than four weeks, unexplained weight loss, unexplained oral candidiasis and unexplained fever. The Australasian Society for HIV Medicine (ASHM) includes a very similar list of indicator conditions in their Indications for HIV testing document.[14] Using a combination of the Ministry of Health and the BHIVA/ASHM guidelines, a third of women in this cohort who were residing in New Zealand prior to their diagnosis of HIV infection had healthcare interactions where there were one or more missed opportunities for an earlier diagnosis of this infection. If HIV testing had been performed at the earliest of these interactions, these women's HIV infection would very likely have been diagnosed a median of 14 months earlier with the associated prevention of three episodes of *Pneumocystis jirovecii* pneumonia and one death. These missed opportunities demonstrate an area where a significant improvement in HIV testing needs to occur.

Almost half the women in this cohort had their HIV infection diagnosed following testing from an established screening programme. These screening programmes need to ensure that the approach they take to HIV testing results in the maximum coverage and the normalisation of this testing. Regular audits of these programmes should be undertaken to highlight areas where improvements can be made. For most screening settings, universal offer opt-out HIV testing, where people are informed that they will automatically receive an HIV test unless they actively decline, is felt to be the most effective method to increase testing coverage, normalise testing and reduce the stigmatisation associated with testing.[13,15] The different ways in which various HIV screening programmes in New Zealand offer HIV testing may result in a higher or lower proportion of women receiving an HIV test.

Current antenatal HIV screening in New Zealand illustrates how an HIV screening programme may miss some women with undiagnosed HIV infection. It was removed from the National Screening Unit's oversight in 2015, resulting in less available data demonstrating the proportion of pregnant woman who have HIV testing performed. The Ministry of Health's 'Pregnancy and Breastfeeding with HIV' website[16] states that antenatal HIV screening is a universal offer opt-in process which is likely to be less effective when compared with universal offer opt-out screening. The New Zealand College of Midwives Consensus Statement[17] takes a risk-based approach which is less effective when compared with universal offer opt-out screening: "the pregnant woman determines her risk factors following this discussion and decides whether to undertake HIV screening". There is a further hurdle to antenatal HIV screening with the Auckland and Northland community laboratory testing form including two separate tick boxes in the antenatal section; one for "1st Antenatal screen & HIV" and the other for "1st Antenatal screen no HIV"; this approach is very likely to result in a lower proportion of pregnant women receiving HIV testing and does not contribute to normalising testing or reducing stigma. In order to maximise and normalise antenatal HIV screening, we believe this test should be reinstated to the National Screening Unit's oversight, that it should be a universal offer opt-out process and that an HIV test should be included as one of the standard tests in the initial antenatal screen on the community laboratory testing form.

Consideration should also be given as to whether there are other areas where HIV screening for women would be beneficial. In this cohort, women were not diagnosed following routine General Practitioner (GP) screening which would provide a significant opportunity to diagnose women with HIV infection earlier; an HIV test should be considered as part of a GPs standard well women's check.

Healthcare providers should be aware that almost all women in New Zealand contract HIV infection from sexual transmission, with only one in eight women in this cohort having a further possible risk factor for the acquisition of HIV infection. Basing HIV testing decisions for women on the requirement of further risk factors, in addition to sexual transmission, will result in missed diagnoses.

Trans women have a higher prevalence of HIV infection when compared with other adults with HIV.[18] This higher prevalence is contributed to by a number of factors including challenges in accessing HIV prevention interventions, and high rates of sex work, substance misuse and mental health disorders.[19] There is also evidence from the UK that trans adults with HIV are diagnosed later than other adults with HIV.[19] Trans women attending sexual health clinics in Australia were more likely to be diagnosed with a sexually transmissible infection

(STI) when compared with cis women,[20] and cisgenderism and transphobia were found to be associated with a lower likelihood of recent HIV/STI testing.[21] These factors highlight that trans women in the Auckland and Northland regions need access to supportive environments where they can obtain regular HIV/STI testing.

Although the number of women in this cohort is relatively small, the Infectious Disease Unit at Auckland City Hospital is very likely to provide care for more women with HIV than any other Infectious Disease or Sexual Health Unit in New Zealand. It is possible that women who may have a higher risk of HIV infection, such as trans women and sex workers, may be more likely to receive their care from a Sexual Health Unit and so may be under-represented in this study. This study is limited by its retrospective design; there will have been other healthcare interactions that we are unaware of that should have highlighted the need for HIV testing during the period that women in this cohort were estimated to have had undiagnosed HIV infection. It is possible that some women may have been offered HIV testing during the time that they were estimated to have had undiagnosed HIV infection but declined this offer.

Women make up a significant minority of the total population of people recently diagnosed with HIV infection in the Auckland and Northland regions. This study shows that there are currently inadequate levels of HIV testing for women in the Auckland and Northland regions. This finding is further supported by the higher proportion of women who presented with one or more AIDS-defining illnesses and the higher six-month mortality when compared with newly diagnosed men. There is a need for targeted HIV screening efforts for women in the Auckland and Northland regions. The Ministry of Health's HIV testing guideline needs updating and HIV screening in New Zealand needs to be optimised to maximise coverage, normalise testing and reduce the stigmatisation associated with testing. We expect the Ministry of Health's HIV testing guideline will be updated as part of the upcoming Ministry of Health's HIV Elimination Action Plan.

COMPETING INTERESTS
Nil.

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