Cascade of Care for People Living with HIV Infection in the Wellington Region

Nigel Raymond, Kelly Bargh, Kyi Lai Lai Aung, James Rice

ABSTRACT

AIM: Antiretroviral therapy (ART) is highly effective in providing better outcomes for people living with HIV infection (PLHIV) and reducing the risk of transmission to others. The ‘cascade of care’ describes steps in delivering care: diagnosis, linkage and retention in care, and the provision and success of ART.

METHODS: The cascade of care for PLHIV in the Wellington region was reviewed during 2015. An estimate of 20% undiagnosed HIV infection was used from past New Zealand research. ‘Suppression of HIV infection’ by ART was defined as a viral load less than 200 RNA copies/mL as commonly used in other cascade of care studies.

RESULTS: There were 307 people identified with HIV infection. The median age was 48 years, and 54 (18%) were women. At the time of the audit, each of the 307 PLHIV were accounted for and not lost to follow-up. ART was being taken by 272 (89%). Those with a CD4 count >500 x 10^6/L accounted for 26/35 not on ART. Of those on ART 254/272 (93.3%) had a suppressed viral load, including 252/259 (97.3%) of those established on treatment >6 months. Overall, 254/384 (66.1%) were estimated to have a suppressed viral load.

CONCLUSIONS: The study indicated a high level of retention in care, and of effective HIV suppression, with ART. The main gaps in the cascade of care were the people with undiagnosed HIV infection and those in whom treatment had not yet been initiated because their CD4 count was above 500 cells/10^6/L.

ARTICLE

Antiretroviral treatment (ART) provides considerable clinical benefit to people living with HIV infection. Since the availability of combination ART in the 1990s, there has been a fall in the mortality and number of those developing AIDS cancers and opportunistic infections. However, even with effective ART there is an observed increased occurrence of a variety of non-AIDS events, including cardiovascular, renal and liver disease and non-AIDS defining cancers, which could be best reduced by a combination of early and sustained control of the HIV infection together with other risk factor management and screening. The long-awaited START study, published in 2015, found that ART initiation at or soon after diagnosis leads to reductions in serious AIDS-related events, serious non-AIDS-related events, and death from any cause, although the absolute risk reduction may be small and treatment decisions will need to be individualised. This demonstrates that early diagnosis of HIV infection is of definite clinical benefit to the individual. Unfortunately, late diagnosis is still too common, as indicated by most of those diagnosed in New Zealand having a low CD4 count and some still presenting with AIDS.

Antiretroviral treatment is highly effective in reducing the risk of sexual transmission to others. In New Zealand, as in many other developed countries, the rates of new HIV diagnoses have risen over the last decade compared with prior to 2000. The improved clinical prognosis may have diminished perceptions of individual risk and reduced the public health imperative. The UNAIDS has set a goal of ‘90-90-90’: 90% of all people with HIV infection should have the infection diagnosed, 90% of all people with diagnosed HIV infection should be consistently receiving ART and 90% of all people receiving ART should have a fully suppressed viral load. Even if these targets are fulfilled more than 25% of all people with HIV infection would not have their HIV fully suppressed on ART.
During the period of this study, publicly funded antiretroviral therapy was available to New Zealand residents with a CD4 count less than $500 \times 10^6/L$ (normal $>600$) or who were symptomatic.\footnote{7}

International research has shown that there is often considerable loss of engagement at each step in the ‘cascade of care’ from HIV diagnosis to those whose infection is ‘suppressed’ with a low or undetectable viral load on antiretroviral medication. The practical challenges in achieving high levels of engagement in each step of the cascade of care were highlighted in a 2011 study of engagement in care in the US, which estimated only 19% of those living with HIV had their infection suppressed.\footnote{8} Reaching and engaging those with HIV infection in care is essential to the public health response and strategy to control HIV in the New Zealand community.

This audit aimed to describe the level of engagement in the cascade of care of people with HIV infection in the Wellington region.

**Methods**

**Setting**

Wellington regional HIV specialist services were provided by the Infectious Diseases Department, CCDHB based at Wellington Hospital, in conjunction with a smaller number of PLHIV cared for by the Immunology Department CCDHB, and since January 2015, by an Infectious Diseases Physician serving the Hutt Valley & Wairarapa DHBs. Some PLHIV not yet on antiretroviral medication were cared for by the Wellington Sexual Health Service. Most people with HIV infection were also under the care of a GP. Occasional patients have been cared for by their GP alone, although at the time of the audit none were. The audit was conducted in April 2015.

**Information sources**

**Regional HIV clinical service**

PLHIV under the care of the regional HIV service were recorded in a secure database (Excel file) maintained manually by the HIV clinical nurse specialist. The CCDHB hospital laboratory is the only laboratory providing HIV viral load testing in the region. The hospital laboratory system was queried for all HIV viral load tests, to ensure our HIV database was complete. An HIV care summary form on the main hospital clinical record system (Concerto) for each patient with HIV under care was used to identify the cohort of people with known HIV infection, and to record relevant clinical information (eg, antiretroviral treatment). This allowed reports to be generated for the cohort by the Information Services Department, including other electronically recorded information (eg, clinic attendance) or demographic information. Clinical information at Hutt Valley and Wairarapa DHBs was accessible to clinical staff using an ‘e-tree’ link. Laboratory results from the regional community provider (Aotea Pathology Ltd) for patients under specialist care were periodically copied to the CCDHB electronic clinical records. Selected GP care information, including diagnoses and results, were accessible from the hospital electronic clinical records.

**Information from other providers and sources**

In order for as complete inclusion as possible of those with diagnosed HIV infection, we sought further information from laboratory sources and other HIV care providers in the region.

The serology sections of the regional community (Aotea Pathology Ltd) and hospital laboratories had clinical oversight by senior medical staff who were also members of the regional HIV clinical service. New laboratory HIV diagnoses were individually followed up with the referring doctor and assistance was provided for referral to the regional HIV service.

Regional HIV care providers assisting with the study included the Wellington Sexual Health Clinic, HIV NGO Wellington offices (NZAF, Body Positive), and high case-load GPs.

**Ethics**

The study was undertaken as a registered audit by the Infectious Diseases Department compliant with institutional quality assurance policies at Capital and Coast DHB.

**Definitions**

**Wellington region**

The Wellington region was regarded as the area served by the Capital & Coast
Hutt Valley DHBs. People with HIV infection who reside primarily in the Wellington region comprised the cohort which was the focus of the study.

Some people from the neighbouring Wairarapa DHB who historically received their HIV specialist care in Wellington, and a very few other PLHIV who had continued care from Wellington, were included. We included all those PLHIV who were diagnosed and initially treated outside the Wellington region and who transferred into the Wellington region following receipt of written communication from those services. We wrote to HIV services in other regions to transfer care when PLHIV under the care of our HIV service moved to reside out of the Wellington region.

We planned to exclude any occasional PLHIV temporarily residing in Wellington while receiving on-going specialist care from another region and communicated to us, although there were none at the time of the audit.

Cascade of Care

Estimated total of HIV infected

The total number of people with HIV infection is the sum of those with diagnosed and undiagnosed infection. An estimate of 20% undiagnosed was used in this study (based on past New Zealand research) to calculate the “Estimated Total HIV Infected” (estimated total HIV infected = 100/80 x observed number diagnosed).

Diagnosed with HIV infection

Those diagnosed with HIV infection were defined as having positive serological or viral load tests regarded as true positives on further laboratory and clinical assessment. A positive card test result performed by a trained health provider (eg, Āwhina Centre, New Zealand AIDS Foundation) was also included as a serological test. PLHIV transferred to Wellington HIV services by specialist HIV services from another region with written correspondence confirming HIV infection were included.

Linked to care

Those diagnosed with HIV infection were defined as linked to care if they had been seen at least once by a medical practitioner (GP, sexual health physician, specialist HIV physician) for assessment and planning of ongoing management of the HIV infection following completion of an initial positive HIV test, in practice almost always with 3 months of diagnosis. We included GPs in the definition of linked to care, anticipating that some people with early HIV infection might initially remain under their GPs care alone, although there were none at the time of the audit.

Retained in care

Those diagnosed with HIV infection were defined as retained in care if they had been seen in a clinic within the last 1 year, or otherwise were continuing on current ART and in communication with the regional HIV service. For PLHIV who moved to another region, we noted details of care transfer correspondence to other HIV services or other patient assistance. PLHIV were defined as lost to follow-up when attempts to contact them by various means repeatedly failed. Measures of clinic attendance were derived from the hospital electronic Patient Administration System. Details of circumstances affecting suboptimal retention in care for individual people were described by the treating clinical team.

Current antiretroviral therapy (ART)

PLHIV were defined as currently receiving ART based on verbal history at their most recent HIV clinic visit and supplemented by ID clinical nurse specialist communication with the patient, even if adherence was known to be suboptimal. PLHIV who had previously taken ART, but ceased over recent months were defined as not on current ART. PLHIV receiving antiretroviral therapy were further categorised as either recently ‘starting’ or ‘established’ on ART, based on whether they had been on treatment for less or more than 6 months. For people not on current ART we noted the most recent CD4 count and other known reasons.

Suppression of HIV infection

PLHIV were defined as having “suppression of HIV infection” or a “suppressed viral load (VL)” if they were in receipt of current ART and their most recent HIV VL test result was <200 RNA copies/mL for a test completed within the last 12 months. This is consistent with the epidemiologic definitions used in other literature reports of the HIV cascade of care,
which have used a threshold of 200–400 RNA copies/mL. The laboratory testing platforms available at the time of the study quantitated VLs down to 20 RNA copies/mL, below which they are reported as either <20 RNA copies/mL (if detectable) or “not detectable”. Therefore the term “suppressed VL” in the study refers to a higher threshold than similar common terms used clinically. For those PLHIV receiving ART we also categorised and tabulated the most recent VL test results.

Clinic attendance
Clinic attendance was obtained from electronic records from the hospital Patient Administration System. Clinic attendance for each patient over the last 2 years was assessed comparing the number of clinic appointments attended with the total number of clinics booked. We defined poor clinic attendance when people missed at least 4 or half their booked appointments.

General Practice
The GP or GP practice for those with HIV infection was that registered in the electronic patient administration system as most recently notified by the patient. A high case-load GP was defined as caring for 10 or more people with HIV infection.

Results
People diagnosed with HIV infection
There were 307 people identified with HIV infection. The median age was 48 years, with an age range of 16 to 80 years.

Ethnicity & gender
The ethnicity of those with HIV infection was New Zealand European 200 (65.1%), Māori 22 (7.2%), Asian 22 (7.2%), Pacific Island 12 (3.7%), African 37 (12.1%), and other 14 (4.6%). Women made up 54 (17.6%) overall with a disproportionately larger number of women (54%) in those of African ethnicity (Table 1).

Linkage to care
There were no people with HIV infection identified who were never linked to care after laboratory diagnosis. Members of the HIV service had overseen HIV testing in the local laboratories, and generally knew of positive test results before the referrer. Positive card test results following testing by NGOs were promptly referred to the HIV service usually with telephone contact.

Retention in care
Lost to follow-up (LTFU)
There were no people with HIV infection identified who were lost to follow-up at the time of the audit. It was observed that about 10 PLHIV per year moved out of the Wellington region, with handover of care to a receiving service, and a similar number moved into the Wellington region.

Current Antiretroviral Therapy (ART)
Of those with HIV infection, 272 (89%) were currently receiving antiretroviral therapy (ART). Characteristics of the remaining 35 people (21%) not receiving ART were: CD4 count >500 (26) (public funding criteria for ART were a CD4 count <500 or symptomatic), only recently diagnosed, re-referred or meeting criteria yet to start (4), and patient choice to decline or discontinue (5).

HIV viral load
Of those 272 people receiving antiretroviral therapy, 13 (4.8%) had recently started and 259 (95.2%) were established on ART (Table 2). Overall, 254/272 (93.4%) met the study definition of a suppressed VL below 200 copies/mL. Of those established on ART,

<table>
<thead>
<tr>
<th>Ethnicity</th>
<th>Female N</th>
<th>Male N</th>
<th>Total N</th>
</tr>
</thead>
<tbody>
<tr>
<td>NZ European</td>
<td>17</td>
<td>183</td>
<td>200</td>
</tr>
<tr>
<td>NZ Māori</td>
<td>3</td>
<td>19</td>
<td>22</td>
</tr>
<tr>
<td>Asian</td>
<td>7</td>
<td>15</td>
<td>22</td>
</tr>
<tr>
<td>Pacific Island</td>
<td>4</td>
<td>8</td>
<td>12</td>
</tr>
<tr>
<td>African</td>
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</tr>
<tr>
<td>Other</td>
<td>3</td>
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<td>14</td>
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<tr>
<td><strong>Total</strong></td>
<td><strong>54</strong></td>
<td><strong>253</strong></td>
<td><strong>307</strong></td>
</tr>
</tbody>
</table>
Table 2: Relationship of viral level to antiretroviral treatment (ART) duration.

<table>
<thead>
<tr>
<th>HIV Viral Load (copies/mL)</th>
<th>Duration of ART</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Starting (&lt;6 months)</td>
<td>Established (&gt;6 months)</td>
<td>Total</td>
<td></td>
</tr>
<tr>
<td>&gt;100,000</td>
<td>4</td>
<td>0</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>10,00–100,000</td>
<td>3</td>
<td>2</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>1,000–9,999</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>200–9,999</td>
<td>3</td>
<td>4</td>
<td>7</td>
<td></td>
</tr>
<tr>
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<td>9</td>
<td>11</td>
<td></td>
</tr>
<tr>
<td>20–49</td>
<td>0</td>
<td>21</td>
<td>21</td>
<td></td>
</tr>
<tr>
<td>&lt;20 or ‘not detectable’</td>
<td>0</td>
<td>222</td>
<td>222</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>13</td>
<td>259</td>
<td>272</td>
<td></td>
</tr>
</tbody>
</table>

*Suppression of HIV infection was defined as <200 copies/mL (grey area)

Figure 1: Cascade of HIV care in the Wellington region—Proportion of People with HIV Infection Meeting Sequential Criteria.

*The estimated 20% of PLHIV undiagnosed is based on reported data elsewhere (see Methods)
252/259 (97.3%) met the study definition of achieving a “suppressed VL” below 200 copies/mL, whereas only 2/13 (15%) of those starting ART within 6 months of the VL test had yet to achieve a suppressed VL. The VL was below 50 in 243 (93.8%) and below 20 in 222 (85.7%) of those established on ART.

Cascade of HIV care in the Wellington region

The overall cascade of HIV care in the region is illustrated in Figure 1. Including the estimate of 20% undiagnosed together with the audit results for the other measures indicates an overall 66% of people in the region having a suppressed viral load (<200 copies/mL). The main contributors to the 34% who did not have an undetectable viral load were those PLHIV undiagnosed (estimated 61/307, 20%), those with a CD4 count above 500 x 10^6/L (26/307, 8.4%), and those who had recently started ART within 6 months and were yet to achieve a suppressed VL (11/307, 3.6%).

Clinic attendance

Overall, there was an 18% clinic appointment non-attendance rate. For individual PLHIV during the 2-year period there was a median of 5 clinic appointments scheduled (range 0–19) and 4 clinic appointments attended (range 0–14). With the definition used 11.8% of PLHIV were poor clinic attenders.

PLHIV per GP

The median number of PLHIV per GP or GP practice was one (range 1–41), with 142/150 (95%) GPs caring for 3 or less people with HIV infection. High case load GPs (10 or more PLHIV) cared for 22% of the PLHIV, while 5% of PLHIV had no regular GP.

Discussion

Early HIV diagnosis and antiretroviral treatment provides advantages for personal health, and protection of others. Antiretroviral therapy is highly effective in reducing the risk of sexual transmission to others for both heterosexual partners and men who have sex with men (MSM), and for mother-to-child transmission during delivery, when the viral load is consistently suppressed to undetectable or very low levels. ART is also protective, although evidence for the degree of protection varies in other settings, including breast feeding, occupational exposure and intravenous drug use. ART is therefore a key public health intervention, together with sustaining high rates of condom use in at-risk groups.

The cascade of HIV care is a simple way to visualise an overview of the challenges, for both affected individuals and health services, of putting treatment as prevention into consistent practice. Interpretation of cascade of care estimates depends on the means of data collection and definitions used. These vary in other national and regional reports. There is considerable variation in the sampling approach used to estimate those undiagnosed. Most used mandatory notification of diagnosis. ART use has commonly been based on prescribing, and sometimes dispensing, data. Some jurisdictions have mandatory CD4 and VL reporting to health departments. Linkage to care is commonly defined as being within 3 months, and retention in care when seen during the last 1 year. Distinguishing migrations in and out of the region/country from lost to follow-up is important, but not always easy. In clinical practice this is reliant on good communication between regional services, the PLHIV providing new contact details, and maintaining service database records. When initiating ART it can normally take several months for the VL to become suppressed. In the cascade of care this could appear to be a treatment failure, while clinically it is not. We observed that PLHIV during the first 6 months of starting ART comprised an important subset of those on ART whose VL was not suppressed.

Overall, women comprised 54/307 (18%) of the cohort, of whom more were African and less were of New Zealand European descent. This in part reflects patterns of immigration from countries were heterosexual transmission is more common.

The estimated proportion of 66% having viral suppression of all those with HIV compares favourably to reported estimates from Australia (59%), the UK (62%) and the US (19%), noting some differences in methodology. In Australia, the Kirby Institute has estimated 59% of those infected to have a suppressed viral load <400 copies/mL, with an estimated 88% of those with HIV infection diagnosed. Public Health
England estimated that for HIV in the UK, 76% are diagnosed, 90% on treatment, and 90% undetectable. Lower rates of engagement in care and viral suppression have been observed in cascade studies for young adults, immigrants, intravenous drug users and females, whereas higher rates were observed for MSM, heterosexuals, and those in a universal healthcare system. This is consistent with the needs and challenges facing specific key groups with HIV as described in the 2013 UNAIDS Gap Report. Research studies have recently been reviewed on the cost-effectiveness of interventions to improve each step in the cascade.

For ART to have more impact on New Zealand’s increased rate of new diagnoses since 2000 would require us to do better for the remaining third we observed their unsuppressed HIV infection. The main gaps in the cascade of care identified in this study were for the estimated proportion of people not yet diagnosed with HIV infection and treatment initiation for those diagnosed with a CD4 count above 500 cells/\(10^6\)/L.

There is clearly a need to reach and test those who do not yet know they have HIV infection, and to engage those at high risk of HIV in care and prevention. The estimate of 80% of those with HIV knowing their diagnosis was based on an Auckland survey of MSM. This estimate is below the 90% UN goal. The high rate of HIV suppression on ART observed in this study implies that the undiagnosed group is a key driver of new cases in New Zealand and that an ambitious target is needed to reach people unaware of their HIV infection. The likely risk factors and other characteristics of people with undiagnosed HIV infection are estimated by national notifications of those recently diagnosed. HIV is diagnosed in a variety of primary and secondary care settings. If HIV is included in the differential diagnosis it should be tested for, with significant benefits of diagnosing even an occasional person. Diagnosis of acute seroconversion syndrome, which commonly presents with rash and flu-like symptoms, is of particular advantage due to the associated higher level of viraemia and transmission risk. The New Zealand AIDS Foundation, and other NGOs, have already done much work on optimising the national strategy for increasing and targeting HIV testing, and Ministry of Health support of these efforts and for earlier diagnosis in primary and secondary care is important.

In general, ART should be recommended soon after diagnosis of HIV infection, with the HIV infected person having an opportunity for open discussion and establishing a relationship with the treating service. While the majority of people are likely to choose to start ART early, it will still be a person’s informed choice. For those with a CD4 count in the normal range, the slow decline in the CD4 count will usually mean there is time for people to make a considered decision. A few ‘elite controllers’ with a very low viral load off-treatment may not warrant immediate ART. Removal of the PHARMAC CD4 count funding eligibility threshold is a priority.

Our audit indicates a high level of linkage and retention in care and of effective viral suppression with established antiretroviral treatment. It is acknowledged that the cascade of care aims to represent retention in care and the other steps in the cascade over time. The cross-sectional study design of this audit is a snapshot to estimate the continuum of care. Although at the time of the audit all of the known people with HIV infection had been linked to care and were at the time engaged in care, we are not claiming to demonstrate 100% linkage or retention over time. However, the results of the audit are consistent with our clinical observations over recent years of a very high level of linkage to care and of a high level of retention in care. There has been a very close link between HIV laboratory diagnosis in the region and linkage to the HIV specialist services, which were provided by a single regional hospital-based HIV service principally within the Infectious Diseases Department. For some years, specialists in the HIV service have had concurrent positions with each of the regional laboratories providing HIV testing, and have coordinated linkage to care for each person newly diagnosed with HIV infection with the HIV. More recently, with people diagnosed using rapid HIV card testing, there was a routine prompt link between the NGO staff performing the testing and the clinical nurse specialist with the HIV service. Each person had been
subsequently seen either in HIV service clinics or for a small number of people in the Sexual Health Clinic. Additionally, as part of the audit, we had widely enquired about any person with HIV infection not linked to care with healthcare staff providing HIV care in the region.

Retention in care will always be a challenge, as it involves sustaining treatment relationships over a prolonged time, with HIV infected people who have varied and sometimes complex needs. A variety of strategies were used to facilitate clinic attendance. Most people are being reviewed once or twice annually, attending clinics reliably over the longer term. Reasons for clinic non-attendance are multifactorial, including communication issues, practical patient issues with attending, and common factors affecting engagement in care. There were no PLHIV lost to follow-up at the time of the study, although this has occasionally occurred at other times. Active case management approaches were taken for clinic non-attenders, often by the clinical nurse specialist in discussion with the treating physician. This included lists and individual plans for at-risk people with assistance from the HIV social worker and ID pharmacist, not discharging people from clinic in the event of missed appointments, and continued antiretroviral prescription despite missed appointments. As the primary benefit of ART derives from viral suppression, we have prioritised supporting uninterrupted ART ahead of clinic attendance per se. The study was conducted in association with efforts to improve and update service database records, and we noted that transfers in and out of the region were not uncommon.

Coordination between community and hospital HIV services has been crucial for people with HIV infection to remain engaged in care and to keep their HIV infection under control. Community services include primary care general practitioners (GP), HIV NGOs, community pharmacies and the Sexual Health Service. Most of those with HIV had a GP, although most were not high HIV case-load GPs. HIV NGOs play a number of central roles. Community pharmacies play a key role in maintaining uninterrupted ART treatment and liaising with the HIV service about suspected adherence difficulties. We liaise with multiple pharmacies, as any retail pharmacy can now dispense antiretrovirals, although several pharmacies in the region dispense for the majority of PLHIV.

Ongoing challenges for engagement in care include understanding and responding to the broader social and health needs of different groups with HIV infection, including MSM, women, young adults, immigrants, and those aging with HIV. Substance abuse and mental health problems are particularly important. The increasing number of people living with HIV may pose challenges for small services to maintain the quality of care. While antiretroviral medications are much improved from the early combination regimens, there is still a need for safer medications for very long term use. Strengthening relationships with primary care will be needed with mainstreaming of preventative and general healthcare.

A key limitation of the study is that we have no specific estimates of the undiagnosed proportion of those with HIV infection in the Wellington region. The audit was a snapshot of care, whereas engagement in care often changes over time and HIV care is now a continuum over the longer term. It is possible that occasionally, PLHIV moved into the Wellington region unknown to us, having been diagnosed or under the care of HIV services in another region. This could have occurred if they remained under the care of the service in the other region and this was not communicated to us, or if they were lost to follow-up by the other service. We would expect our findings to be similar to those in other larger New Zealand cities.

In conclusion, the audit indicated a high level of continuing engagement of care and of effective viral suppression with established antiretroviral treatment. The main gaps in the cascade of care were for the estimated proportion of people with undiagnosed HIV infection and for treatment initiation of those diagnosed with a CD4 count above the 500 cells/10^6/L threshold for publicly funded antiretrovirals.
Competing interests:
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