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British Columbia researchers examine past and future directions in the HIV epidemic

25 February 2015

Researchers at the British Columbia Centre for Excellence in HIV/AIDS (CfE) in Vancouver have amassed extensive health-related data collected from HIV-positive people. These data have been stripped of information that could be used to identify individual patients. From time to time this data is analysed to produce reports. Recently, researchers at the CfE sought to examine trends in AIDS-related illnesses (infections, cancers and complications) between 1981 and 2013. They found that rates of AIDS-related illnesses and deaths fell once potent combination anti-HIV therapy (commonly called ART or HAART) became available in the mid-to-late 1990s. Data from the CfE has also contributed to many reports, including one that predicts near-normal life span for some HIV-positive people.

In its latest report, published in the journal *Lancet HIV*, the CfE team underscores the importance of comprehensive barrier-free access to the offer of HIV testing, counselling, and swift referral to care (in cases where test results are positive), followed by the offer of treatment as well as ongoing care and monitoring. The B.C. team states that such comprehensive services have helped to make massive progress against AIDS. However, they note that further investment in such services is needed to sustain progress and to further reduce the spread of HIV.

**Study details**

Researchers restricted their analyses to people aged 19 years or older at the time they entered the study and analysed health-related information from January 1981 to December 2013, or until participants died.

Researchers divided their data into the following periods:

- 1981 to 1996 – before the rollout of ART
- 1996 to 1999 – the initial rollout of ART
- 2000 to 2003 – stable increase in initiation of ART
- 2004 to 2012 – the second rollout of ART

The research team reviewed data from at least 3,097 men and 453 women with AIDS.

**Results—Age and infections**

The average age at the time of participants’ first AIDS-related illness was 41 years. In the CfE study, each person had an average of two AIDS-related illnesses, though some people had as many as seven.

**Peak of AIDS**

The peak of cases of AIDS occurred in 1994. In that year there were about 42 cases of AIDS per 100 participants. By 1997, with the initial rollout of ART underway, there were seven cases of AIDS per 100 participants. By 2013 there was only one case of AIDS per 100 participants. This is tremendous progress.

**Gender**

Throughout the study, researchers found that more men than women had HIV and, not surprisingly, more men had AIDS-related infections. In 1991 the ratio of men to women who had AIDS was nearly 50:1. By 1996 the ratio had
fallen to 10:1 and by 2013 the ratio was 3:1. This massive decrease was driven by fewer men experiencing AIDS because more were taking ART.

**Revisiting age**

The CfE researchers noticed that beginning in 2004, AIDS-related illnesses were most common in people between the ages of 40 and 49. They added that “more recently” AIDS is now most concentrated in people aged 50 years and older.

**AIDS in 2013**

Among people who were aged 50 years and older and who developed AIDS in 2013, here are some common AIDS-related illnesses that occurred:

- severe unintentional weight loss (HIV wasting syndrome)
- non-Hodgkin lymphoma
- tuberculosis
- severe yeast infection (caused by *Candida*) of the throat and airways of the lungs
- dementia

**Compare and contrast**

In the pre-ART era, common AIDS-related illnesses included the following:

- Pneumocystis pneumonia (PCP) – a disease caused by *Pneumocystis jirovecii*, formerly called *Pneumocystis carinii*
- Kaposi’s sarcoma (KS)
- MAC (*Mycobacterium avium* complex)
- *Candida* infection of the throat, airways of the lungs and in some cases, all of the lungs
- HIV wasting syndrome

After ART became available, common AIDS-related illnesses were as follows:

- PCP
- HIV wasting syndrome
- lymphomas (including non-Hodgkin, Burkitt’s, immunoblastic and others)
- KS
- *Candida* of the throat and lungs
- recurring bacterial infections

**Trends in deaths**

Deaths from AIDS-related causes have been falling since 1994 in B.C. In that year the rate of such deaths was 19 per 100 people. By 2013 the rate had fallen to three per 100 people. The CfE researchers noted that there were two periods when deaths due to AIDS-related complications were relatively high:

- between 1994 and 1997
- between 2000 and 2003

The researchers explained that during the first period, deaths likely peaked because people did not have access to ART or were taking weak regimens.

In the second period, they argue that the reason for the increase in deaths may have been due to the following two factors:

- In the late 1990s and for several years after, standard therapy was more complex than it is now. Back then it was routine for HIV-positive people to take many pills, two or even three times daily, with certain food and water restrictions. Furthermore, regimens in common use in that era tended to have unpleasant side effects. As a result, there was interest in interrupting treatment. Preliminary results from small studies as early as 1999
suggested that short-term interruption of ART might not lead to the appearance of life-threatening infections in some people. However, results from a very large, sophisticated and well-designed clinical trial called SMART became available several years later and showed that interrupting ART carried a high risk of harm. In particular, researchers found that such treatment interruptions increased the risk not only for AIDS-related infections but also inflammatory-related complications including heart attack, stroke and serious kidney and liver injury. Furthermore, interrupting ART was linked to a significantly increased risk of dying. Therefore, such interruptions largely came to an end.

- In those days, available therapies, although powerful, were not well tolerated and in weighing the risks and benefits, initiating treatment was discouraged unless the need for it was relatively urgent by the standards of the day. Therefore, HIV treatment guidelines at that time encouraged doctors and patients to defer initiating ART until serious immunological dysfunction had appeared.

**Envisioning the end of AIDS**

The BC researchers made the following statement:

“Our results strengthen the evidence that programmes that aggressively distribute free ART to infected individuals have great potential to decrease [illness and death] caused by AIDS.”

Furthermore, they added:

“Our data support the proposition that expanded access to ART, in the presence of evidence-based guidelines and systems to ensure early HIV diagnosis, timely ART initiation and sustained virological response, can transform AIDS from an epidemic to an endemic disease, and eventually might lead to the elimination of AIDS. However, as no curative therapy exists and lifelong suppressive ART needs high adherence for this effect to be sustained, treatment programmes and related support must be strengthened on a long-term basis.”

**Mind the gap**

The continuum between the offer of an HIV test to a person receiving care and treatment and having a continuously low viral load thanks to ART is a long one. This continuum is called the “cascade of care” by researchers. Here are some of the steps in a simplified version of the cascade:

- diagnosed with HIV
- linked to care
- retained in care
- in care and counselled about starting ART
- initiated ART
- taking ART and has an undetectable viral load

The CfE team, in a separate study, has explored the cascade of HIV care in its province and found that gaps exist. We should point out to readers that, to some degree, such gaps likely exist in other parts of Canada and in other high-income countries. Indeed, the U.S. Centers for Disease Control and Prevention (CDC) has found gaps in the U.S. cascade of HIV care.

**Back to the present study**

The study by the CfE shows that tremendous progress against AIDS has been made but there is still room for improvement. As the researchers stated: “...the number of [new] AIDS cases is still not zero.”

**Understanding the phrase “end of AIDS”**

The CfE researchers note that there is increasing optimism by policy planners that it may be possible to bring about the “end of AIDS”—a phrase that has been heard at AIDS conferences in recent years. The researchers made an important statement that clarifies what is possible at least over the next several years:

“Ending AIDS and ending HIV are two different issues, with substantially different levels of complexity. Our report specifically analysed [new cases of AIDS] rather than HIV. Ending AIDS could be achieved with the identification of all HIV-infected individuals in a given jurisdiction before they develop AIDS and intervening with effective treatment on a
sustained basis. Ending HIV would imply stopping HIV transmission, which in all likelihood would not be feasible without a cure, a vaccine, or both.”

A global view

In a commentary to accompany the report from the CfE in the *Lancet HIV*, former International AIDS Society president Professor Stefano Vella, MD, acknowledges the tremendous progress made against AIDS. He notes that gaining a similar magnitude of progress against the global spread of HIV will be challenging but outlines how such progress against HIV might be achieved. Importantly, he ends his call with these words: “…the HIV epidemic is definitely not over. Let’s not leave the job half-done.”

Resources

Interactive graphics from B.C. Centre for Excellence in HIV/AIDS (scroll down page to view)

Changing the Narrative: Why HIV prevention work in Canada needs to embrace HIV treatment – *Prevention in Focus*

Gaps in British Columbia’s HIV treatment cascade – *CATIE News*

—Sean R. Hosein

REFERENCES:

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Production of this content has been made possible through a financial contribution from the Public Health Agency of Canada.

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