Why treatment is good for you

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Neil McKellar-Stewart thought it was time we looked at all the health benefits to us of being on treatment. So, he tracked down the research and here it is.

1. IT EXTENDS LIFE

Multiple studies of large populations of people living with HIV (PLHIV [1]Person (or people) Living with HIV. This term is now preferred over the older PLWHA.) both on and off treatment have all conclusively demonstrated that antiretroviral therapy (ART) does indeed prolong life.

By studying the past health records of 4000 PLHIV in Denmark1, they estimate that prior to 1996 the probability of a newly diagnosed 25-year-old surviving for 15 years without effective ART was about 1 in 7; and that about two-thirds of PLHIV would die within 10 years of being diagnosed. The study was conducted in 2005 and estimated that of those who had been on the best treatments available up to that time, about 80% would survive 25 years or more and have a life expectancy only 10 years less than the general community.

Similar results came from a much larger study of nearly 45,000 PLHIV who were on treatment from 1996 through to 2005 in Canada, USA and Europe. This study2 estimated that a 20-year-old receiving effective ART from 2003 would have a life expectancy of 50 years and that 86% of all PLHIV on treatment would survive for at least 25 years. Significantly, this study also showed that these benefits were progressively lost as PLHIV started ART at lower CD4 counts.

Yet another large study3 of nearly 63,000 positive people in the USA and Europe compared those who commenced treatment when their CD4 counts were greater than 500 with those who didn't.

They estimated that the risk of death for those on treatment was 23% less than for those who were not. (Note that this is for people who started with counts above 500 CD4 cells which is currently the maximum recommended level for starting treatment in Australia.)

The study also showed that the lower your CD4 count at commencement of treatment the greater your probability of avoiding death compared to untreated PLHIV at the same CD4 count; and shows that treatment clearly gives benefit at every CD4 level.

A more recent study4 from the national HIV database in the Netherlands indicates that the life expectancy of PLHIV who receive timely and effective ART is now approaching that of the general community.

The message from all these studies is clear. HIV treatment reduces your risk of dying; and starting it earlier (at least when CD4 counts fall below 500) extends your longevity.

The International Antiviral [2]A medication or substance which is active against one or more viruses. May include anti-HIV drugs, but these are more accurately termed antiretrovirals. Society-USA Panel Antiretroviral treatment guidelines for adult HIV infection5, released in late July, recommends treatment for ALL adults with HIV, regardless of CD4 count. These are the second set of US guidelines to make this recommendation this year.

If you are currently not treating, this information should be good enough reason for you to start the conversation with your doctor. If you're still not convinced, then read on. There's a growing body of research evidence showing the other benefits as well.

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2. IT REDUCES INFLAMMATION

HIV is far more than a disease that slowly destroys the body's immune defences, ultimately resulting in AIDS and an untimely death. HIV is also a disease of chronic, ongoing inflammation that puts the immune system in a constant state of 'activation' 6.

This immune activation starts from the time when HIV first infects a person. At that time HIV attacks the body's lymphatic system, especially in the lower gastrointestinal tract or 'gut'. It destroys many of the CD4 cells located there and changes the structure of the lymphatic tissues.

The cells lining the gut are killed off and we are left with a less effective barrier to keep microbes or 'germs' out of the body's circulation system. The immune system is now stimulated and has to work harder to deal with germs that enter the body.

This inflammation and immune activation has serious consequences. We only need to look at what happened during the SMART study7 when they compared people who took treatment breaks with those who didn't. During the study, it became clear that those who stopped treatment had rapidly increased levels of inflammation and blood clotting or 'coagulation' — conditions which are both strongly related to death and to disease events in the heart, circulation, kidneys and liver [3]A large organ, located in the upper right abdomen, which assists in digestion by metabolising carbohydrates, fats and proteins, stores vitamins and minerals, produces amino acids, bile and cholesterol, and removes toxins from the blood..

Those who stayed on treatment had lower levels of this type of inflammation and less illness, whereas those who interrupted their treatments had 1.7 times more risk of developing one of these illnesses. Needless to say, the SMART study was terminated early.

One way to visualise all this is to imagine a skin injury. At the entrance of the wound, the body mounts an immune response.

The area becomes inflamed — red, hot and swollen — and may produce pus. This acute inflammation is a good thing. It shows that the immune system is dealing with an invasive microbe.

HIV causes a similar sort of inflammation which is longterm, low level and unseen or 'asymptomatic', but it results in a similar sort of immune activity.

When you have HIV, your body produces molecules or 'cytokines' which inflame blood vessels and disturb a range of metabolic processes8910. This may contribute to why we have an increased risk for diseases associated with inflammation such as cardiovascular disease, type 2-diabetes [4][Diabetes mellitus] A disorder in which sugars in the diet cannot be metabolised into energy due to a lack of the enzyme insulin. Late-onset diabetes mellitus may be a long-term side effect of some anti-HIV drugs., bone and kidney disease, neurological impairment, and psychological conditions such as depression and anxiety, and fatigue.

Treatment reduces inflammation and our risk of getting these diseases.

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3. IT IMPROVES QUALITY OF LIFE

Starting treatment improves your quality of life—both physically and mentally. Positive changes to people's physical health start as early as one month after commencing ART, and changes to mental health after about four months, according to data they collected from studying over 1000 PLHIV from across the USA11.

Those with the highest adherence levels showed the most striking progress in the study; with every quality of life measure showing an improvement — 23% in physical health, 17% in general health, 14% in energy, 14% in social functioning, 11% in emotional life, and 7% in mental health.

The study included a range of PLHIV including women, injecting drug users, and people of lower socioeconomic status. All had advanced HIV infections with quite impaired immune systems — average CD4 counts of 230 and mean viral loads of around 90,000 copies. At the start, they had quality of life scores similar to those seen in other studies of PLHIV whose disease was established, so these are significant improvements and cannot be put down simply to chance.

In another study12, 500 positive Brazilians were surveyed four months after they had commenced treatment. Those who rated their quality of life as good or very good after starting reported improvement in the following areas: energy levels, physical mobility, ability to work, memory/ability to concentrate, physical appearance, self-esteem, personal relationships, and their sex life.

The SMART study also included a sub-study on quality of life13 and found that every measure was better for those who remained on treatment compared to those who took breaks from it.

The greatest improvements were seen in those who started treatment for the first time and stayed on it for the three years covered by the study. They saw improvements in their general health—both physically and mentally—including their physical functioning, emotional health, energy and social functioning.

The STACCATO trial also examined the effect of treatment interruptions on the quality of life14 of around 250 Thai participants who all showed significant levels of anxiety, depression and stress. Many of them received HIV antiretrovirals [5]A medication or other substance which is active against retroviruses such as HIV. which have now largely been discontinued because of their less-favourable side effects. Yet, despite this, those who stayed on treatment reported significant improvements in their mental health.

Similar results were reported in the AIDS Clinical Trial [6]A clinical trial is a research study to answer specific questions about vaccines or new therapies or new ways of using known treatments. Clinical trials are used to determine whether new drugs or treatments are both safe and effective. Carefully conducted clinical trials are the fastest and safest way to find treatments that work in people. Trials are in four phases: Phase I tests a new drug or treatment in a small group; Phase II expands the study to a larger group of people; Phase III expands the study to an even larger group of people; and Phase IV takes place after the drug or treatment has been licensed and marketed. Group (ACTG) 5170 trial15 which included 167 PLHIV who had all been on stable ART for an average of 4.5 years. The group had good immune status — their median CD4 count was 833 and 82% of them had viral loads of less than 400. Over two-thirds were on older protease inhibitor-based treatments combined with older nucleoside reverse transcriptase inhibitors (NRTIs) (including AZT and stavudine).

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Some of the drugs given to these PLHIV have significant side effects and are now rarely used in Australia. All these participants interrupted their treatment and were followed for two years.

Quality of life deteriorated for about one-third of the participants and they resumed treatment.

Research has demonstrated that such treatment interruptions are not safe or desirable, and in all the studies indicated above led to reduced quality of life for some, if not all the participants.

These findings confirm that starting and staying on treatment is the best strategy to improve your quality of life both in the short term and into the future. As we develop better tolerated drugs with fewer side effects and simpler dosing regimens these improvements seem destined to improve.

4. IT REDUCES DEPRESSION AND FATIGUE

There is some good evidence to suggest that treatment reduces depression and fatigue — which makes sense as depression is increasingly recognised as a disease associated with inflammation.[16][17][18]

Several trials[19][20] have shown that treating HIV reduces depressive symptoms in some people.

One looked at the effects of efavirenz (one of the drugs in Atripla) on key neurological markers in around 300 PLHIV who had never treated previously. The trial also included PLHIV who received treatments other than efavirenz. It showed that depression decreased regardless of what drugs were taken and that participants showed improvements in key neuropsychological measures, including motor skills, sustained attention, response speed, and conceptual thinking.

There is good evidence to suggest that when PLHIV get their HIV under control their mental health improves. This was demonstrated in 2003 with a large US study[21] of nearly 2500 people. Those who started treatment showed significant improvements in their mental health despite them being on older drugs with considerably more side effects than the ones we use today.

A more recent study in the Netherlands[22] found that levels of depression are directly related to viral load, which explains why depression is lower for those on effective treatments.

This was demonstrated over a decade ago in large groups of PLHIV in Australia[23], USA[24] and Canada[25]. Similar effects are reported from focus groups of PLHIV starting treatment and from community surveys of PLHIV in Australia.

Depression is still an issue for PLHIV as community surveys and research studies indicate (including a recent national survey from Spain[26]), but treatment can and does seem to improve the degree of depression people experience.

The effect of treatment on levels of fatigue has not been as well studied. However, there is a growing body of evidence from focus groups[27] and workshop for PLHIV that treatment improves energy levels and reduces fatigue.

It is thought that inflammation contributes to fatigue in a range of chronic medical conditions, including cancer,

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multiple sclerosis, type 2-diabetes and chronic fatigue syndrome itself28. A recent US study29 of more than 400 people with fatigue (some of it classified as 'chronic fatigue syndrome') found that there was a consistent association between level of inflammation and fatigue symptoms even after taking into account whether people were depressed. It seems that the relationship between these three: depression, fatigue and chronic inflammation is complex; however, it would be reasonable to expect that reducing inflammation by effective treatment of HIV would improve energy levels, and at the same time reduce depression.

There is much more to be said on the benefits of treatment for improving your cardiovascular, brain, kidney and bone health, and for reducing your risk of cancer. We'll discuss these in upcoming issues of Positive Living.

If you are on treatment, then congratulate yourself. You're doing the best thing you can for your health right now and into the future. If you're not currently treating or you're unhappy with the combination you are on, now is the time to start a conversation with your doctor about which treatment combination might be right for you.

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- Understanding HIV treatments
- Treating HIV

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