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A. Inflammation and its discontents

When cells of the immune system encounter invading germs they can become activated and enter into a heightened state of alert. Such cells help to marshal the immune system against germs. Here is a greatly simplified response by the immune system to an infection:

- Chemical signals are released that attract other cells of the immune system with specialized functions to where the invading germs are concentrated.
- As the number of immune system cells increases at the site of infection, some of these cells try to contain the germs.
- Other cells take a molecular picture of the invading germ and then travel to lymph nodes and lymphatic tissues where they warn the immune system about the invader.
- As a result of these actions, the immune system becomes activated and lymph nodes and lymphatic tissues make many copies of CD8+ cells—the body's premier infection-fighting cells. These CD8+ cells are released into circulation to attack germs and kill infected cells.
- The body raises its temperature to try to kill germs.
- Usually all of these immune responses help to contain an infection, and as the number of germs decreases, the immune system releases anti-inflammatory signals and other cells that specialize in suppressing the immune system to dampen its responses.

However, when the immune system is not able to control and vanquish an infection, a state of activation persists. We discuss the consequences of this persistent activation later in this article.

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Where is the immune system?

The immune system is located in several organs and tissues such as the thymus gland, spleen and bone marrow. There are also many lymphatic tissues and lymph nodes scattered throughout the body between the neck and the knees, particularly around the intestines. Also, cells of the immune system are distributed throughout the body and found in other major organ-systems, including the brain, heart and blood vessels, kidneys, liver, lungs and so on. The emplacement of cells of the immune system in these different organ-systems serves to provide local protection for them.

In cases of chronic infection when the immune system remains activated, its inflamed cells release chemical signals that in turn cause inflammation in the organ-systems where they are resident. Thus, inflammation is transferred to other parts of the body. Temporary inflammation during short-lived infections is useful for marshalling the immune response and nutrients to feed the creation of millions (perhaps even billions in some cases) of new cells. However, chronic inflammation from ongoing infection—such as that arising from HIV—can injure organ-systems, causing them to slowly degrade.

Researchers are finding that in HIV-negative people excessive levels of inflammation appear to play a role in the injury associated with many health conditions, and perhaps even in the cause of some conditions, including the following:

- arthritis
- obesity
- psoriasis
- cardiovascular disease
- diabetes
- higher-than-normal blood pressure
- cancer
- thinning bones

It is possible that inflammation may also play a role in HIV-positive people when the above-listed conditions occur.

Reducing inflammation

Studies have found that taking combination anti-HIV therapy (commonly called ART or HAART) greatly reduces the level of HIV-related inflammation. However, because ART does not cure HIV infection, some degree of excess inflammation persists. Scientists are therefore

conducting studies to try to find ways to safely suppress the excess inflammation that occurs in HIV-positive people

In this issue, we review some studies that explore ways to help dampen HIV-related inflammation among ART users. Future issues of *TreatmentUpdate* will also report on HIV-related inflammation.

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B. Exercise—Potential impact on inflammation and mood

As mentioned previously in this issue of *TreatmentUpdate*, HIV infection is associated with activation of the immune system and inflammation. This inflammation is only partially suppressed with ART. Scientists are not sure why chronic inflammation occurs in HIV-positive people who use ART but suspect that it may be due to at least one of the following:

- continued production of low levels of HIV deep within the body, in places such as lymph nodes and lymphatic tissues
- changes to the immune system caused by HIV
- the presence of other germs or other unknown factors

Researchers at the University of Rome (Italy) and in Atlanta (U.S.) have proposed that one potential method for helping to reduce excess levels of inflammation and dampen immune activation in HIV-positive people is exercise.

Uncovered by fat

The impetus for exploring the effect of exercise comes from scientists at Harvard University who pointed out the following trends among HIV-negative people:

- more people are becoming obese
- obesity affects the immune system and likely promotes inflammation
- obesity and inflammation appear to increase the risk for developing unhealthy outcomes such as type 2 diabetes, stroke, heart attack, unfavourable levels of fatty substances in the blood (cholesterol and triglycerides), depression, dementia and cancers of the breast and colon

Even if a person is not obese, research on obesity-related inflammation underscores a previously underappreciated connection between the immune system and metabolism.

Exercise or no exercise

Much research has been done with HIV-negative people and exercise, and scientists have found that exercise can have many beneficial effects, including reducing the risk for type 2 diabetes and cardiovascular disease.

Studies with HIV-negative people who do *not* exercise have found that they are at increased risk for developing chronic low-grade inflammation. The problem of inflammation arises because many people who do not exercise tend to build up fat deep within their belly. This fat, called visceral fat, wraps itself around vital organs and produces hormones and chemical signals that favour inflammation. These hormones and signals produced by visceral fat also affect the immune system.

Exercise in HIV-positive people

Scientists at several centres around the world have recently studied the impact of exercise with HIV-positive people and we now summarize such studies.

Brazil

Researchers at the University of Bahia in Brazil conducted a six-month randomized, controlled study with 63 HIV-positive participants.

They assigned participants to one of the following interventions:

- one hour of supervised gym activity (stretching, weight training and aerobics) three times weekly and monthly nutritional counselling
- once-monthly workshops to discuss the importance of physical activity and to receive nutritional counselling

At the end of the study, participants who engaged in regular exercise had decreases in the following assessments:

- body fat
- waist size
- blood sugar levels

They also had increases in the following assessments:

- muscle size
- CD4+ cell counts (very modest)
- improvements in mood

Australia

Scientists at the Alfred Hospital in Melbourne conducted a randomized, controlled study with 35 HIV-positive men for six months that involved the following interventions:

- two one-hour supervised fitness classes (including both aerobic and weight training) per week
- unsupervised walking twice per week and attending a monthly group meeting

As with some other studies, participants who received supervised fitness training had improved cardiovascular health, quality of life and cognitive function.

Italy—Even brisk walking is good

Some HIV-positive people experience a lack of energy and/or become tired very easily. Perhaps, for such people, a program of brisk walking may be more suitable. Researchers in Milan, Italy, enrolled 59 HIV-positive people and assigned them to one of the following interventions for 12 weeks:

- three one-hour sessions per week of brisk walking outdoors
- three one-hour sessions per week of brisk walking and three 30-minute sessions per week of weight training

At the end of this study, all participants had statistically significant decreases in their total cholesterol and bad-cholesterol (LDL-C) and in their waist size.

There were also significant decreases in levels of proteins in the blood associated with immune activation, including the following:

- interleukin-6 (IL-6)
- D-dimer
- high-sensitivity C-reactive protein (hsCRP)
- activated CD8+ cells

Thus, even modest levels of exercise can have a beneficial effect on inflammation.

Pleasure

People who engage in regular exercise report feeling good or even high afterward. The Italian researchers suggest that this is likely for at least the following reasons:

- Exercise can cause cells to produce chemical signals called endorphins. These have a similar effect to the pain reliever morphine. People who exercise regularly can also experience greater tolerance of pain because of the release of endorphins. These chemical signals are also used by cells of the immune system to communicate.
- Exercise causes the brain and other parts of the body to produce and release another group of chemical signals called neurotransmitters. Initially, scientists thought that these chemical signals were used only by brain cells to communicate; however, other cells are sensitive to neurotransmitters. For instance, upon initiating exercise, the body produces neurotransmitters to help the heart cope with exertion from exercise. Also, together with endorphins, neurotransmitters can help people better deal with anxiety and stress. Exercise has an added benefit—it helps the brain to transition to a more relaxed state that makes falling asleep easier.
- Experiments with HIV-negative people suggest that regular exercise can improve cognitive functioning. The precise way that exercise does this is not clear. Some scientists think that exercise can increase the size of certain parts of the brain. Other scientists have found that exercise can increase the production of chemical signals such as BDNF (bone-derived neurotropic factor). These

signals are associated with the development of new brain cells and memory formation.

Based on these and other studies, more scientists are in favour of exercise programs for HIV-positive people so that fitness, quality of life, overall sense of well-being and reduction of inflammation can occur.

Long-term clinical trials are needed to assess the effects of exercise and other interventions on the overall health of HIV-positive people as well as measures of inflammation.

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C. Statins—Overall many benefits and a few risks

Statins are a group of medicines that work in a particular way to reduce the body’s production of cholesterol. Examples of potent statins in common use include atorvastatin (Lipitor) and rosuvastatin (Crestor). As a result of their inhibition of cholesterol manufactured within a cell, and possibly other actions at the molecular level, statins have been found to reduce the risk for heart attacks and other cardiovascular complications in several clinical trials in HIV-negative people.

Analyses of data from clinical trials suggest that a minority of participants that take statins is at increased risk for the following side effects:

- muscle pain and weakness
- very rare cases of liver injury
- rising levels of blood sugar that approach the high end of the normal range—a prelude to developing pre-diabetes and diabetes

However, the risk for developing diabetes among statin users is not evenly distributed. In a recent analysis of data from a very large clinical trial called Jupiter, in which participants received either rosuvastatin or fake rosuvastatin (placebo), researchers found that only participants who had “one or more major diabetes risk factors were at highest risk of developing diabetes than those without a major risk factor.”

Furthermore, researchers found that the many benefits of taking a statin such as rosuvastatin outweighed the smaller risk of developing diabetes.

A note on side effects

Researchers at Harvard University conducted a review of hospital records from nearly 108,000 patients, focusing on their interruption of statin therapy. The researchers found that in about 18% of cases, patients likely discontinued statins because of side effects. This figure of 18% is not vastly different from the figures reported for side effects from rosuvastatin or placebo in the Jupiter study (between 15% and 16% of participants in Jupiter reported side effects, as mentioned in the report on that study that follows). What was interesting about the Harvard study is the following statement made by the researchers:

“We found that the majority—over 90%—of patients who were rechallenged with a statin after a statin-related event were ultimately able to tolerate one. Few of the rechallenged patients had another statin-related event, and serious reactions, such as rhabdomyolysis [the breakdown of muscle, causing the release of the protein myoglobin into the blood; myoglobin is broken down into substances that can injure the kidneys] were quite rare....” Indeed, the researchers also stated that “overt rhabdomyolysis was found in only 0.006% of the study patients.”

These findings are important and worth considering when trying to get a picture of statin safety in the everyday world of hospital clinics.

Statins also have anti-inflammatory activity, and clinical trials are planned or underway with HIV-

positive people to explore their possible beneficial effect. It is therefore possible that statins may become more widely prescribed by doctors who care for HIV-positive people either as part of a plan to help protect them from complications of cardiovascular disease or to help reduce excess inflammation.

Caution with drug interactions

Care must be taken when selecting a statin because of the potential for drug interactions. A consultation with a doctor and pharmacist can be useful for uncovering potential interactions between statins and HIV medicines and other prescription and over-the-counter medicines.

Flying by Jupiter

As a service to our readers, we explore an in-depth analysis of the clinical trial Jupiter, which studied the use of a modern and potent statin—rosuvastatin—and its possible relationship to diabetes and other side effects and what these might mean for people who take the drug. The advantage of examining trial data from Jupiter is that it was a very well-designed study with HIV-negative people. We also explore the interim results of another study called Saturn—a placebo-controlled study of rosuvastatin with HIV-positive people.

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D. Exploring Jupiter—An important clinical trial

In a landmark clinical trial called Jupiter, scientists sought to assess the impact of 20 mg/day of rosuvastatin vs. placebo in more than 17,000 HIV-negative participants whom they described as “apparently healthy.” In other words, these participants were seemingly at low risk for a heart attack or other major cardiovascular event.

Researchers involved with the Jupiter study have reanalyzed the data to assess the impact of rosuvastatin on the development of diabetes.

Study details

Enrolled participants did not have any history of diabetes. However, upon entering the study, many participants had what researchers called “major risk factors for diabetes,” such as the following:

- metabolic syndrome – this term refers to a cluster of risk factors such as excess waist size, elevated levels of fatty substances in the blood (triglycerides), less-than-ideal levels of good cholesterol (HDL-C) in the blood, higher-than-normal blood pressure, elevated levels of fasting blood sugar (more than 5.5 mmol/L but less than 6.99 mmol/L)
- high fasting blood sugar
- abnormal average blood sugar in red blood cells (this is called hemoglobin A one C, written as HbA_{1C})
- being overweight or obese

Researchers analysed data collected from 17,603 participants. Participants were monitored for up to five years.

Results

In analysing the data, here are some of the findings at the start of the study:

- 6,095 participants had no major diabetes risk factors
- 11,508 participants had one or more major diabetes risk factors
- participants with no major diabetes risk factors were more likely to smoke tobacco

According to researchers, participants who had one or more major diabetes risk factors at the start of the study were “more likely to be female” and have higher-than-normal levels of the following:

- blood pressure
- HbA_{1C}
- fasting blood sugar
- triglycerides

Results—diabetes

Overall, participants who had one or more major diabetes risk factors when they entered the study

had about an 11-fold increased risk for developing this complication while in the study.

Who was at risk?

When researchers analysed which of the participants who developed diabetes were taking rosuvastatin or placebo, they found that, overall, cases of diabetes were somewhat more common among participants who received rosuvastatin (270 cases) than among those who received placebo (216 cases).

This amounted to a 25% overall increased risk for developing diabetes among rosuvastatin users. However, this is not the final word on this risk, as researchers made the following statement:

“Almost all the excess risk of diabetes associated with rosuvastatin occurred in participants with [evidence of abnormal blood sugar levels when they entered the study].”

Another way to look at the study’s findings is as follows:

- About 2% of people with major diabetes risk factors and who took rosuvastatin developed diabetes.

Other side effects

The rate of other side effects seen in Jupiter was similar (about 15%) whether participants were taking rosuvastatin or placebo. This points to the relative safety and tolerability of statins.

Historically, statins have been found to sometimes cause the following side effects:

- muscular issues – stiffness, weakness or pain (usually not severe)
- rhabdomyolysis – the breakdown of muscle, causing the release of the protein myoglobin into the blood; myoglobin is broken down into substances that can injure the kidneys (extremely rare side effect)

In Jupiter, the proportions of participants who reported muscle stiffness, weakness or pain were very similar in participants who received either placebo or rosuvastatin (15% and 16%, respectively). This difference was *not* statistically significant. It shows that, on average, low-dose rosuvastatin is generally well tolerated and has similar side effects to a placebo.

One case of rhabdomyolysis occurred (representing 0.1% of participants) in a person taking rosuvastatin and no cases occurred in participants taking placebo.

Rosuvastatin—preventing serious problems

Among participants who had at least one major diabetes risk factor when they entered the study, rosuvastatin reduced their risk of the following by 39% when compared to placebo:

- heart attack
- sudden and temporary chest pain or discomfort while resting (unstable angina); such pain was linked to circulatory problems
- having major cardiac surgery such as implanting a stent or transplanting blood vessels to help improve the heart’s ability to move blood to the rest of the body (coronary bypass)
- death from cardiovascular complications

This difference in risk reduction caused by rosuvastatin compared to placebo was statistically significant; that is, not likely due to chance alone.

Points of interest

1. Jupiter was a very large placebo-controlled study with monitoring lasting for up to five years (though participants were in the double-blind phase for about two years). Its findings are therefore powerful.
2. At the start of the study, all participants had elevated levels of inflammation, as measured with high-sensitivity C-reactive protein (hsCRP) testing of the blood.
3. The risk of developing diabetes among participants taking rosuvastatin was limited to people who were already at high risk for diabetes. Such people had lab tests suggestive of abnormal blood sugar or elevated HbA_{1c}, or obesity, or a collection of risk factors called the metabolic syndrome.
4. The study researchers noted that the cardiovascular and survival benefits of rosuvastatin “exceeded the diabetes hazard in the trial population as a whole as well as in participants at increased risk of developing diabetes.”
5. The cardiovascular benefits of rosuvastatin were accompanied by an earlier onset of diabetes (by about six weeks). The researchers

noted that “whether this finding has clinical relevance is uncertain because [in the community] most patients with diabetes are treated with statin therapy.” There was no difference in the risk of developing diabetes by age. That is, older and younger participants had similar risks when given rosuvastatin.

Just one piece of the puzzle

The study researchers noted that statins are meant to be used as part of a plan that has at least the following elements:

- healthier dietary habits
- increased levels of exercise
- quitting smoking

Advice from researchers

In an editorial to accompany this analysis of Jupiter, cardiovascular researchers encouraged doctors who treat patients who have major diabetes risk factors to do the following:

- inform patients about the potential risk of statins
- monitor their blood sugar regularly
- advise them to lose weight
- encourage them to engage in regular exercise

A super study and weight

A different study has performed a re-analysis of 20 randomized clinical trials of statins and confirms that these drugs can increase the risk for developing diabetes. Researchers with this massive re-analysis suggest that the increased risk for developing diabetes is linked to increased weight. This supports the previously mentioned advice from Jupiter researchers that people with major risk factors for diabetes need to lose weight.

For the future

As mentioned earlier in this issue of *TreatmentUpdate*, studies with statins are likely to be undertaken with HIV-positive people in order to assess the ability of such medicines to reduce the risk for cardiovascular disease and inflammation. Although the Jupiter trial enrolled HIV-negative people, one study with HIV-positive people has released preliminary results. That study, called Saturn, is discussed in the next article.

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E. A trip through Saturn with low-dose rosuvastatin among HIV-positive people

HIV infection is associated with an increased risk for cardiovascular disease, including heart attack and stroke. This risk is likely driven by several factors, including HIV infection, changes to the immune system, and inflammation. Taking potent combination anti-HIV therapy (commonly called ART or HAART) can greatly reduce HIV-related inflammation and improve overall health, but additional steps are needed to reduce the risk for cardiovascular disease. For more information about how to reduce this risk, see the CATIE fact sheet HIV and cardiovascular disease.

Past studies with thousands of participants have found that elevated levels of certain proteins in the blood are associated with an increased risk of serious complications and death among HIV-positive people. Examples of these proteins include the following:

- high-sensitivity C-reactive protein (hsCRP)
- interleukin-6 (IL-6)
- D-dimer

Many research teams are studying ways to help reduce excess inflammation in ART users.

Among HIV-negative people, the use of certain cholesterol-lowering medicines called statins,

such as atorvastatin (Lipitor) and rosuvastatin (Crestor), has been found to reduce the level of proteins associated with inflammation and immune activation in the blood.

Researchers in Cleveland in the U.S. are conducting a study called Saturn designed to assess the impact of low-dose rosuvastatin (10 mg/day) vs. placebo among HIV-positive people with normal levels of cholesterol but elevated levels of inflammation or immune activation.

Interim results from Saturn have not found any signals of harm from exposure to low-dose rosuvastatin. This should not be surprising, as low-dose rosuvastatin is generally well tolerated. Furthermore, participants who took rosuvastatin had significantly decreased levels of bad cholesterol (LDL-C). However, most proteins or markers associated with immune activation and inflammation did not change appreciably. Saturn is an ongoing study so further results are expected in the years ahead.

Study details

Researchers enrolled adult HIV-positive participants who had normal LDL-C but elevated levels of inflammation or T-cell activation as assessed by blood tests. All participants were using ART and were randomly assigned to receive one of the following:

- 72 people – rosuvastatin 10 mg (one pill daily)
- 75 people – fake rosuvastatin (placebo, one pill daily)

The average profile of participants at the start of the study was as follows:

- age – 47 years
- 78% men, 22% women
- CD4+ cell count – 613 cells/mm³
- HIV viral load less than 50 copies/ml – 76%
- duration of HIV infection – 12 years

Results

By the 24th week of the study, levels of LDL-C decreased by 28% among rosuvastatin users compared to an increase of 4% in people on placebo.

No significant differences between participants who used rosuvastatin or placebo were found

when researchers reviewed levels of commonly assessed fatty substances in the blood such as good cholesterol (HDL-C) and triglycerides.

Researchers found that rosuvastatin helped to greatly slow the decline of the kidneys' ability to filter the blood when compared to placebo. This finding of preservation of kidney function is important. Over a decade ago, when rosuvastatin first became available, it was taken at much higher doses and it adversely affected kidney health. However, the present and other recent studies reinforce the overall safety of low-dose rosuvastatin.

Inflammation

Researchers conducted extensive analyses of blood proteins or markers associated with inflammation and immune activation. Surprisingly, there were no significant differences in changes of such markers between users of rosuvastatin or placebo. Past smaller studies in HIV-positive people had found minor changes in such markers.

An unusual marker

Failing to find changes in the usual assessments of inflammation and immune activation, the researchers focused on an uncommonly used protein called lipoprotein-associated phospholipase A₂ (Lp-PLA₂). Levels of this protein fell by 10% among rosuvastatin users compared to a 2% decrease among placebo-users; this difference was statistically significant. However, other researchers have questioned whether this difference made any difference to the health of users. In other words, did this change have any clinical significance? Lp-PLA₂ levels are not routinely assessed as part of the care and treatment of HIV-positive people, nor are levels of this protein routinely assessed in HIV clinical trials.

Furthermore, it is noteworthy that the experimental drug darapladib was being tested in a placebo-controlled trial called Stability with HIV-negative people. The drug lowers Lp-PLA₂ levels and was hoped to have an impact on cardiovascular events such as heart attack, stroke and so on. Unfortunately, this drug did *not* have a significant effect on these events in the Stability study. Thus caution is needed when assessing changes in Lp-PLA₂ levels and trying to make projections about the future health of patients based on those changes.

Looking at the future

As mentioned earlier, the Saturn study is ongoing and researchers plan additional analyses, such as ultrasound scans of the arteries in the neck. Such assessments that measure the narrowing of arteries due to cardiovascular disease are a well-validated method for predicting the risk of future events such as a stroke.

Even if Saturn and other studies ultimately show that statins fail to significantly suppress HIV-related inflammation, they will have yielded valuable information. Such information may cause scientists to question the source of the excess inflammation in HIV-positive people and attempt further experiments to address the following issues:

- Is the excess inflammation linked to T-cells or other cells of the immune system such as monocytes and/or macrophages?
- Is the excess inflammation caused directly by HIV or its proteins and their impact on the immune system?
- Do other germs, particularly herpes viruses, play a role in excess inflammation seen in HIV-positive people?

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F. Can statins help to reduce the risk of cancer?

In 2012 a massive observational study in Denmark compared nearly 19,000 people who had used statins to 277,000 people who had not used these drugs. Participants were HIV negative. Scientists found that participants who used statins were at a reduced risk for dying from complications caused by a range of cancers. Due to the study's observational design, researchers cannot prove that taking statins was linked to a reduced risk for cancer. It is possible that there were factors—smoking tobacco, the size of tumours, the response to anti-cancer therapy—that researchers did not take into account when analysing the data. Such factors could have inadvertently biased their conclusions.

Still, the Danish findings are interesting but at a minimum require confirmation from other large databases in other countries.

Previous studies suggest that HIV-positive people who use statins may be at reduced risk for HIV-related cancers, including non-Hodgkin's lymphoma.

Now researchers in Milan, Italy, have scoured the medical records of HIV-positive ART users to investigate the potential anti-cancer effect of statins. The researchers found that among about 5,357 participants, 740 people (14%) had a history of using statins. Among these statin users, 12 cases of cancers (2%) occurred vs. 363 cases of cancer (8%) among participants who did not use statins. Researchers estimated that statins helped to reduce the risk of cancer by about 55%. The cancers were those known to occur among some HIV-positive people, including lymphoma, Kaposi's sarcoma (KS) and cervical cancer.

Study details

Researchers at the San Raffaele Scientific Institute and associated hospital reviewed data collected from participants between January 1991 and October 2012. Cancer diagnoses were confirmed by a report from a pathologist who examined tumours.

Results

Over the study period, researchers found 375 participants who developed cancer. The cancer cases were distributed as follows:

- 194 HIV-related cancers
- 191 cancers unrelated to HIV

Twelve cancers (2%) occurred among statin users. All 12 cancers were unrelated to HIV.

A total of 363 cancers (8%) occurred among non-statin users, distributed as follows:

- 194 HIV-related cancers
- 169 cancers unrelated to HIV

This difference in the number of cases between statin and non-statin users was statistically significant; that is, not likely due to chance alone.

The most commonly used statin was rosuvastatin (Crestor) 10 mg/day, followed by pravastatin 20 mg/day.

Overall, most participants began using statins about 11 years after their HIV diagnosis.

Researchers stated that statin users were “older, more frequently smokers [were overweight and entered the study with higher-than-normal blood pressure, cholesterol, triglyceride and blood sugar levels].” Thus, initially statin users had many risk factors for cardiovascular disease.

They also found that statin users tended to have higher pre-ART CD4+ cell counts and were less likely to be co-infected with hepatitis C virus than non-statin users.

Bear in mind

This Italian study is also observational in design. Drawing robust conclusions from such studies is fraught with risk because of a problem called confounding. That is, researchers can never entirely

rule out the presence of unmeasured factors that could potentially bias their results. Indeed the research team made the following statement:

“It is possible...that statin users had a more favourable HIV status [such as higher pre-ART CD4+ counts] and different health behaviours that could lead to differences in cancer risk over time than [participants] who were not prescribed statins.”

What do the findings mean?

Researchers in the U.S. and France have commented on the Italian research in an editorial in the journal *AIDS*:

“It is possible (likely even) that statin users were more frequent visitors to [the study] clinic and therefore more likely to have controlled and suppressed [HIV viral load] and higher CD4+ cell counts over time. These factors would have decreased statin users’ risk for [cancer].”

In an era of austerity

Analyses of observational studies are relatively easier, faster and cheaper than prospective, large randomized clinical trials. These days there are many demands for research dollars. However, due to low or stagnant economic growth and austerity policies in high-income countries, funds for scientific research are not increasing on a grand scale, and in some countries are even decreasing. Unless massive amounts of money are made available for scientific research, cheaper methods of attempting to answer research questions will become more common, even if such methods may not yield firm answers. As a result, some research and clinical issues may be plagued by lingering uncertainty.

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Disclaimer

Decisions about particular medical treatments should always be made in consultation with a qualified medical practitioner knowledgeable about HIV- and hepatitis C-related illness and the treatments in question.

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CATIE is Canada's source for up-to-date, unbiased information about HIV and hepatitis C. We connect people living with HIV or hepatitis C, at-risk communities, healthcare providers and community organizations with the knowledge, resources and expertise to reduce transmission and improve quality of life.

For more than 20 years, CATIE has been there to provide information that enables people to make informed choices about their health and enhances the ability of healthcare providers and other frontline organizations to respond to their clients' needs.

CATIE provides such information through a comprehensive website (www.catie.ca), electronic and print resources, webinars and other online learning, a national reference library, regional conferences, subscriptions to e-newsletters and a confidential phone inquiry service.

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