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Will de-simplification of HIV treatment become common in high-income countries?

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- **As more people start HIV treatment, researchers are exploring ways to cut costs**
- **Single tablets can be replaced by a few pills comprising cheaper generic drugs**
- **Alberta clinic projects $4.3 million saved by "de-simplifying" one treatment regimen**

Initiating and staying on HIV treatment (ART) results in most people having very low levels of HIV in their blood. Such low levels are commonly called undetectable and result in improved measures of health and projections of near-normal life expectancy for many HIV-positive people in Canada and other high-income countries. Also, studies have found that people who achieve and maintain an undetectable viral load do not pass on HIV to their sexual partners.

These twin benefits of ART are so transformative that major HIV treatment guidelines encourage doctors and nurses to make an offer of ART immediately after HIV infection has been diagnosed.

Keeping the cost of treatment sustainable

As more HIV-positive people use ART (which has to be taken for life), the cost of providing treatment increases, both for public and private insurance plans.

Several research teams in high-income countries have been concerned about the current and long-term cost of HIV treatment in the face of largely stagnant healthcare budgets. Researchers at the Southern Alberta Clinic in Calgary have been exploring ways to save money. In a paper in the journal *HIV Medicine* they wrote that some of the long-term cost benefits of ART are "deferred and future saved costs are not visible in any budget line. The increase in immediate costs raises the question of the financial sustainability, using current care models, of maintaining lifelong HIV suppression for large HIV-infected populations living in high-income countries. Healthcare systems, especially single-payer systems, are under increasing scrutiny to mitigate rising costs. Three-quarters of the immediate and long-term direct medical costs of HIV infection are incurred via the cost of ART."

As a result, the researchers argue that one area for which cost savings could occur is to explore the use of some generic medicines. They note, "with recent or imminent patent expiry of many core agents used in ART, the greater use of generic [anti-HIV drugs] has become of immediate relevance to policy makers, plan holders, prescribing physicians and patients; some [high-income] countries have begun incorporating generics into their HIV health policies in order to reduce costs."

De-simplification

For about the past 12 years, pharmaceutical companies have introduced single tablet formulations (STFs)—an entire HIV regimen in a pill. These are widely used because of their convenience. However, the researchers argue that "one immediate and logical move is to 'de-simplify' branded STFs to multi-tablet generic and patented components, thereby generating substantial savings." For instance, if the Southern Alberta Clinic switched all 600 patients who were taking a particular STF to generic treatment, the researchers estimate that the clinic could save approximately CAN $4.3 million.

Rather than immediately impose the change to multi-tablet regimens, the researchers developed and validated

surveys and then had a pharmacist encourage people (doctors and patients) to complete online surveys about switching from STFs to multi-tablet components. All the physicians surveyed felt that de-simplification could occur safely, with no impact on patient health. A total of 48% of patients were agreeable to switching to save costs, 27% did not want to switch and 25% were unsure about switching. Thus, de-simplification may not be acceptable for every patient. The Southern Alberta team plans further research to monitor "the medical and cost impacts of de-simplification strategies."

Study details

Researchers used publicly available costs of anti-HIV drugs available from the clinic's pharmacy, which dispenses ART to patients. The clinic has about 1,800 patients, of whom 1,673 were on ART. About 62% of ART users were taking an STF, 607 of whom were taking the STF Triumeq in 2016. Triumeq contains the following three medicines:

- dolutegravir
- abacavir
- 3TC

Dolutegravir enjoys patent protection but the patent for co-formulated abacavir + 3TC has expired and this co-formulation is also made generically. Thus, a patient whose regimen is de-simplified would move from taking one Triumeq pill to taking two pills (one dolutegravir pill and one pill containing abacavir-3TC) once daily. The researchers picked Triumeq because other STFs "did not have as clear de-simplification options."

Results—Cost savings

Researchers calculated that their clinic spent CAN $26.2 million on ART in 2016. Triumeq accounted for almost 32% of this budget. The researchers then calculated the savings that would ensue if different proportions of current Triumeq users switched to a combination of dolutegravir + generic abacavir-3TC. Here are three scenarios:

- 100% of patients switched: $ 4.3 million in savings
- 80% of patients switched: $3.5 million in savings
- 60% of patients switched: $2.6 million in savings

Physician responses

A total of 13 physicians (a mix of infectious disease, internal medicine and family medicine specialists) prescribed ART for patients at the clinic, all of whom responded to the survey. Researchers said that all of the doctors "felt comfortable, in principle, discussing and offering, for cost reasons, the switch from one Triumeq pill to two pills (one dolutegravir and one abacavir-3TC)." The physicians estimated that between 25% and 99% of their patients would be willing to make the switch.

According to the researchers, the main issues that the physicians were generally concerned about involving de-simplification were as follows:

- "diminished adherence"
- "perceived patient preference"
- "increasing pill burden on vulnerable patients"

The researchers noted that none of the physicians were concerned about the possibility of "diminished potency or tolerability" because of de-simplification.

When researchers asked the physicians if patients would switch "if the cost savings were explained," the physicians predicted that their patients' responses would be as follows:

- yes – 31%
- no – 8%
- maybe – 54%

(Figures do not total 100% because not all of the physicians answered this question.)

Patient responses

A total of 221 (36%) patients taking Triumeq completed the survey and 85% felt that the clinic should routinely offer de-simplification. Fourteen percent were against the idea and a couple of participants declined to answer.

When researchers asked patients if "they would personally switch" to de-simplified regimens, the responses were distributed as follows:

- yes – 48%
- no – 27%
- maybe – 26%

(Figures do not total 100% due to rounding.)

In general, patients who said "yes" were somewhat older, living with HIV for longer and took a greater number of pills (for other health conditions) than patients who said "no."

Bear in mind

The researchers in Southern Alberta provided calculations that showed they would save about 18% of their HIV program's ART budget, or about $4 million per year. They noted that as more generic anti-HIV drugs became available, "the question of de-simplification may become even more relevant."

Researchers in the Netherlands have also been considering the issue of de-simplification. Several years ago, they surveyed 322 patients about it and found that 47% were willing to switch from an STF to taking three pills simultaneously as a replacement. A total of 26% said "maybe" and 27% said "no." Researchers found that immigrants to the Netherlands were more likely to say "no" to switching. The researchers suggested that this population likely had concerns about disclosure of their HIV status and "the perceived difficulties of hiding multiple medication bottles." The Dutch researchers suggested that before implementing de-simplification on a large scale, it would be useful to assess the effectiveness of generic vs. brand-name drugs, cost savings and patient preferences.

Counting pills

In the first decade after the release of ART, the number of pills that people had to take on a daily basis could be substantial. Moreover, some formulations of anti-HIV drugs in that era had to be taken twice or even three times daily. However, the Southern Alberta researchers noted that as HIV-positive people are becoming older, they are taking more non-HIV drugs for aging-related conditions.

De-simplification is not for everyone

Breaking up STFs will not be for everyone.

It is likely that certain populations, at least for a time, may not be best served by de-simplification, such as the following (there may be more):

Vulnerable populations

According to the researchers, "vulnerable populations living in unsafe environments for medication storage" would likely be a group that would benefit from an STF.

Travellers

People who travel may prefer the simplicity of STFs if only because of fewer pill bottles to transport.

The elderly

The data on elderly people and de-simplification are not as straightforward to interpret. For instance, in elderly people with declining neurocognitive abilities, having to deal with more pills might cause confusion. However, STFs are usually bigger than pills of their individual component drugs and swallowing smaller pills may be helpful for some older people. The researchers said that "swallowing, a complex process of coordination between nerves and

muscles, is affected as a function of age." Furthermore, prior to the present study, the pharmacist at the clinic had received requests for de-simplification from some patients to switch to multi-tablet regimens, as the smaller pills were easier to swallow.

Adherence

People who have difficulties with adherence will probably continue to benefit from using STFs.

Four futures

The Calgary researchers said that the availability of "core" anti-HIV agents gives public and private insurance companies at least the following four options:

1. "The system can continue to pay for ART at the current pace and at current market values. ART and STF use would be at the discretion of physicians, often based on guidelines (which seldom provide guidance on costs or formulation use)."

2. "Mandatory de-simplification of STFs when generics are available. This may result in less adherence and resentment [from some patients], potentially leading to worse [health] outcomes."

3. "Continue to prescribe STFs to [patients who have adherence difficulties] and those at risk for non-adherence, and use multi-tablet formulations with generic options in other [patients]."

4. "Initiate patients who are starting regimens with generic options on a multi-pill regimen and encourage those on STFs to consider de-simplification."

Not just in Alberta

Almost simultaneous with the publication of the report from the Southern Alberta Clinic, researchers in the U.S. published their perspective on the issue of de-simplification in the *New England Journal of Medicine* , saying the following:

"Greater use of generic ART in the U.S. could provide some relief to government programs that already face severe budgetary pressures and serve the majority of people with HIV and those at highest risk for infection." The American researchers also mentioned de-simplification of Triumeq to branded dolutegravir + generic abacavir-3TC as one option. They found that such a switch would result in about a 25% reduction in costs.

Austerity and its discontents

As long as austerity holds sway over health budgets in high-income countries, the pressure to reduce prescription drug costs will continue. As a result, de-simplification and other measures may become of interest to more stakeholders who pay for the treatment of HIV and other conditions.

—Sean R. Hosein

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