Thank you for inviting me to speak today. And thank you to the person who is taking my place. There's lots I wanted to share with you today, but not my sinuses in their current state.

I was tasked with identifying three important developments in the medical treatment of HIV or in the care of people living with HIV. As you can imagine, these parameters cast a wide net of possibilities. And each person here might pick a different set of three. But I also imagine if we compiled everyone's list we would see a lot of similarities, a lot of overlap. So let's take a minute and think of what you would identify as the top 3, or even 2, medical advances of the last 40 years and then if we have time at the end we can compare lists and see which ones I've missed.

The first major advance I will share with you today only recently came to my attention, while reading the book "How to Survive a Plague" by David France. I learned a lot about HIV history from the stories in there; the book tells the tale of AIDS activism, mostly in New York City, during the 1980s and 90s. It's a powerful story, and I definitely recommend adding it to your reading list.

That's where I read about the first of my three medical advances that I'll talk about today: how Septra came to be standard of care to prevent PCP pneumonia. PCP, which has since been renamed PJP, was one of the more devastating opportunistic infections (or "aids-defining illnesses"). It was responsible for numerous deaths in the early days of the epidemic. Some stats say up to 75% of people with HIV would develop this infection at that time. Now, PCP can affect all sorts of people with significant immunosuppression (so not just people with HIV, think also people with leukemia or on immune suppressant medications for organ transplants). And, we now know, Septra, a combination medication of two antibiotics: trimethoprim and sulfamethoxazole, can prevent this pneumonia if people take the medication before they get sick.

Now, most of the PCP history that I know about comes from the writings of a New York physician, Joseph Sonnabend. I'm sorry that I couldn't find Canadian information about PCP, but I think the information will still resonate even if it is American. According to Sonnabend, Septra became standard of care to prevent pneumonia in children with leukemia in 1977. It wasn't until 1989 that the CDC issued guidelines on the use of Septra for PCP prophylaxis in HIV and not until 1994 did the FDA approve Septra for this indication. So what happened between 1977 and 1989? Why the 12 year delay between PCP guidelines for leukemia and PCP guidelines for HIV? Sonnabend, and other advocates, like Michael Callen, pressured the CDC for years to issue these guidelines, but the CDC was resistant due to lack of data or lack of research backing up such recommendations; data that

was finally published in 1988.

What stands out for me about this history is less about the regulatory processes and politics that drive them (including ideas about what research priorities are important, or what funding decisions are made and the like), but more about how members of the HIV community (in this case physicians and PHAs) respond to health needs with a mix of creativity, independence and critical thought. Sonnabend and many other physicians were using Septra off-label for years before the guidelines were released. PHAs and their networks spread the word about this intervention to get more people to ask their doctors for it and more doctors to offer it to their patients. And they put pressure on the CDC to do more. Not only did the medical advancement of PCP prevention guidelines help save lives, it showed me there are years of work behind the scenes that go into many of the interventions that we take for granted today.

Which leads us to the next major medical advancement, the development of highly active antiretroviral therapy, aka HAART, combination therapy, or triple therapy. In 1996, combination therapy was announced at two conferences (CROI in Washington and IAS in Vancouver) as effective in controlling HIV and allowing people's immune systems to recover. I think this is a date basically everyone working in HIV is aware of. 1996: the year the epidemic changed forever, the great turning point; 1996: the year HIV went from a fatal disease to a chronic manageable condition, as if someone had flipped a switch and the lights went on and things were right again in the world. That's how it feels sometimes when we talk about that year. But we know there was a lot more to it. Even to get to three drugs used in triple therapy, we had to figure out what those three drugs could be, that they could impact HIV and that they would work in combination. And those discoveries takes us back to 1987, the year AZT was approved for use in US and Canada. AZT was the first ARV approved to treat HIV (one that we still use for HIV+ people during pregnancy and childbirth today). We also needed people with HIV to volunteer to take these experimental drugs in research trials and then continue taking them after they were approved, keeping in mind that some medications worked, some didn't and almost all had major side effects. And even after 1996, it took a while for the new treatment protocols to be available. Irene Goldstone, a nurse in BC, said “there were still those patients that were too ill to benefit from the drugs and so the dying...carried on right through 1997 and it only started to feel better in about 1998.” It took time for this new medical advancement to feel real, for the drugs to get to the people who needed them, for the drugs to do their work and for people to recover and their immune systems to reconstitute.

And it feels like it's still taking time to take effect today. Because we still have work to do. We have the medical know-how to treat HIV, but we're still working on

getting the medications to the people who need them. We need creativity and critical thinking to work on the problems that HIV still poses for us.

And so, on to the third and final medical advancement on my short-list today: HPV vaccines. In 2006, the HPV vaccine that covers 4 strains of HPV, was first approved in Canada for use in “females age 9-26”, and over the next ten years, the age and genders that were approved for use expanded. Today, the vaccine now covers 9 strains of HPV and is recommended for use in “females age 9-45” and “males age 9-26”. The vaccine is even covered by some provincial immunization programs for some members of those groups.

HPV is important because it is responsible for basically all cervical cancers and almost 90% of all anal cancers. We also know that anal and cervical cancer rates are higher in people with HIV than the general public and, according to a conference presentation I attended a few years ago, the rates of anal cancer in HIV+ men is higher than the rate of cervical cancer in HIV-negative women. Keep in mind we have robust screening programs for cervical cancer (that's what those uncomfortable PAP tests are for), but we still lack consensus guidelines on anal cancer screening for people with HIV (for all genders).

What interests me most about HPV prevention and screening, when considering the topic of medical advances, is not that we have all the answers. In fact we still have a lot to learn: is HPV-vaccination effective in older adults? Does it provide any cancer-preventing benefit to people with HIV? What followup is needed when we find pre-cancerous anal cells on an “anal pap test”? And many more.

No, what interests me is knowing what we're going to do to find these answers. Some clinicians are using HPV vaccines off-label, advocating for coverage for their use in people with HIV, regardless of gender and regardless of age. Some scientists are trying to find answers to these questions through research and mathematical modelling. And some clinicians are starting screening programs for anal cancer for their clients, hoping for reassuring results and knowing that they might have to work hard to find options for follow up if results are abnormal.

Perhaps one day we will look back on HPV prevention the way we look back on PCP prophylaxis or HIV combination therapy. And when we do, I hope we remember how much work went into finding these answers, how much uncertainty we had to face before we figured it out and got it right, and how we had to work together as patients, clinicians, and others. That way, we won't lose hope when faced with uncertainty in the future from new challenges that come our way and we'll remember how much work is needed to develop the next major medical advances in HIV treatment and care. Thank you.