Trends in HIV prevalence, new diagnoses and mortality of persons with HIV who have entered care in Ontario, 1996 to 2009: a population-based study

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Text Count: 2412 **Abstract Word Count:** 246

Abstract

Background

Population-based estimates of HIV prevalence, rates of new HIV diagnoses and mortality rates among persons with HIV who have entered care are needed to optimize health service delivery and improve health outcomes of these individuals. However, these data are presently lacking for Ontario.

Methods

Using a validated case-finding algorithm, we conducted a population-based study using linked administrative healthcare databases to determine the prevalence of HIV and rates of new HIV diagnoses among adults aged 18 years and older in Ontario between 1996 and 2009, as well as all-cause mortality rates among persons with HIV over this same period.

Results

Between 1996 and 2009, the number of adults living with HIV increased by 98.6% and the age- and sex-standardized HIV prevalence increased by 52.8% ($p < 0.001$). Women and individuals 50 years and older accounted for an increasing proportion of persons with HIV, increasing from 12.8% to 19.7% ($p < 0.001$) and 10.4% to 29.9% ($p < 0.001$), respectively, between 1996 and 2009. Age and sex-standardized rates of new HIV diagnoses and mortality rates among persons with HIV decreased 32.5% ($p < 0.001$) and 71.9% ($p < 0.001$), respectively, during the study period.

Interpretation

The prevalence of HIV infection in Ontario has increased considerably between 1996 and 2009, with a greater relative burden being assumed by women and individuals aged 50 years and older. However, we estimate that only 55% of those infected have entered care. Interventions are required to link infected individuals to appropriate care.

Introduction

The natural history of human immunodeficiency virus (HIV) infection has been irrefutably altered by the introduction of combination antiretroviral therapy (cART) during the latter half of the 1990s.[1,2] Most notably, between 1995 and 2009, an estimated 14.4 million life-years have been gained globally among HIV-infected adults receiving cART.[3] In conjunction with this achievement, the epidemiology of HIV-infection has changed markedly since the earliest years of the epidemic, such that greater demographic diversity among persons being diagnosed and living with HIV has been described internationally.[4,5] In this context, accurate population-based estimates of the incidence and prevalence of persons with HIV who are entering care are needed to optimize health service delivery and improve health outcomes of these individual.

In Canada, surveillance of HIV infection is based on the analysis of HIV test reports provided to the Public Health Agency of Canada by provincial health authorities and public health laboratories.[6] However, these data do not provide insight into the characteristics of those individuals with HIV who have accessed the healthcare system. Consequently, existing methods of population-based HIV surveillance are not conducive to the study of longitudinal trends in rates of co-morbid illness, entry and retention in care, and demographic characteristics of persons with physician-diagnosed HIV. In contrast, administrative healthcare databases provide a means by which longitudinal population-based research of all persons living with HIV who have entered care can be conducted. Although these databases have been used for the surveillance of various chronic diseases, [7-11] there have been, to our knowledge, no studies describing the use of these databases to characterize trends in the epidemiology and outcomes of persons living with

HIV within a large geographic region. Accordingly, we used administrative healthcare databases to assemble a population-based cohort of all persons with HIV who have entered care, and used these data to quantify trends in rates of new HIV diagnoses, HIV prevalence, and mortality among persons with HIV in Ontario from 1996 to 2009.

Methods

Data Sources

We obtained data from Ontario's administrative health databases, which are available at the Institute for Clinical Evaluative Sciences (ICES) through a data sharing agreement with the Ontario Ministry of Health and Long-Term Care. Specifically, we used the Ontario Health Insurance Plan (OHIP) database to identify physician claims for HIV-related visits, and obtained sociodemographic and date of death information from the Registered Persons Database, a registry of all Ontario residents eligible for health insurance. We used validated disease registries maintained by ICES to identify co-morbid conditions in persons with HIV.[12-15] These databases were linked in an anonymous fashion using encrypted health card numbers, and are routinely used for population-based chronic disease surveillance.[7-11]

Study population

We generated a database of individuals in Ontario aged 18 years and older who were living with HIV between April 1, 1996 and March 31, 2010 using a previously validated case-finding algorithm, the development of which has been described in detail elsewhere.[16] Briefly, an

algorithm of three physician claims with an International Classification of Diseases, Ninth Revision code for HIV infection (042, 043, 044) within a three year period achieved a sensitivity and specificity of 96.2% [95% confidence intervals (CI) 95.2% to 97.9%) and 99.6% (95% CI 99.1% to 99.8%), respectively, for the identification of patients who were regular uses of primary care. We chose the end of the 2009 fiscal year for our analyses to meet the three-year 'look forward' criterion of the algorithm. Because HIV is incurable, individuals who met the case-definition for HIV infection remained part of the cohort throughout the study period unless they either died or moved out of the province of Ontario.

Outcomes

The primary outcomes of the study were age- and sex-standardized prevalence of HIV infection and rates of new HIV diagnoses per 100,000 population of Ontario between 1996 and 2009, and all-cause mortality rates per 1000 persons with HIV over this same period. We calculated these rates by direct standardization using the 1991 Ontario population as the reference population. We determined the annual prevalence of HIV infection by dividing the number of people with HIV who were alive at the end of each fiscal year by the census population of Ontario aged 18 years and older for the corresponding year. We classified patients as being newly diagnosed based on the date that they first met the algorithm definition for HIV infection, and calculated rates of new diagnoses by dividing the number of new diagnoses of HIV infection by the number of individuals aged 18 or older at risk for the disease that year (the total population minus the number of people with prevalent HIV in the previous year). To distinguish between a new diagnosis and a prevalent case, we required that individuals have no prior physician claims for

HIV-related visits in the five years preceding their diagnosis date. Individuals who had a claim during this window were counted as prevalent cases rather than new diagnoses. Because the OHIP database does not include claims prior to 1991, we chose to start reporting results in 1996 to allow for this five-year look back period. We estimated the annual rate of all-cause mortality among persons with HIV by dividing the annual number of deaths among these individuals by the number of people with HIV in each year. We reported annual rates of all-cause mortality because information on disease-specific mortality was unavailable in our databases.

Statistical Analysis

We used negative binomial regression analysis to examine temporal trends in rates of new HIV diagnoses, prevalence of HIV and mortality rates, using the population denominators as the offset. All models included year as the main predictor, along with variables for age group (18 to 34 years, 36 to 49 years, and > 50 years) and sex. Because of statistically significant ($p < 0.001$) three-way interactions between age group, sex and year in all models, we stratified the regression analyses by age-group and sex. Therefore, for each age-sex stratum, the following model was fit:

$$log(outcome_{year}) = log(population_{year}) + \beta_0 + \beta_1 * year$$

where $\exp(\beta_0)$ is the outcome rate in the reference year (1996) and $100 \times [\exp(\beta_1) - 1]$ is the percent relative annual change in the outcome averaged over the fourteen-year study period.

All statistical analyses were conducted using SAS version 9.2 (SAS institute, Cary, North Carolina, USA).

Ethics approval

We obtained ethics approval for this study from the Research Ethics Board of Sunnybrook Health Sciences Centre.

Results

Between 1996 and 2009, the number of adults living with HIV infection increased by 98.6%, far outpacing the 23.3% relative increase in the adult population of Ontario during this period. Women accounted for an increasing proportion of all persons with HIV during the study period, increasing from 12.8% in 1996 to 19.7% in 2009 (Table 1) ($p < 0.001$). Similarly, the proportion of persons with HIV who were 50 years of age or older increased from 10.4% to 29.9% ($p < 0.001$) between 1996 and 2009 (Table 1). The majority (85.1%) of people with HIV aged 50 years or older in 2009 were men. Women and individuals over the age of 50 were also increasingly represented among new HIV diagnoses over the study period, increasing from 15.4% to 24.7% ($p < 0.001$) and 10.7% to 15.6% ($p = 0.002$), respectively, between 1996 and 2009. The prevalence of selected co-morbid conditions associated with aging increased over time (Table 1).

Prevalence

The age- and sex-standardized prevalence of HIV per 100,000 population increased from 92.8 (95% CI 90.7 to 94.9) in 1996 to 141.8 (95% CI 139.5 to 144.1) in 2009, representing a relative increase of 52.8% ($p < 0.001$) (Table 2). The age-standardized increase in HIV prevalence was

greater among women than men (Figure 1a), and the sex-standardized prevalence increased with age (Figure 1b). The prevalence of HIV increased in all age strata of women over the study period, ranging from an average increase of 3.2% (95% CI 2.5% to 3.9%) per year in women aged 18 to 35 years to 11.3% (95% CI 10.4% to 12.2%) per year in women aged 50 years and older (Table 3). In men aged 18 to 35 years, the prevalence of HIV decreased between 1996 and 2009, with a mean annual change of - 5.3% (95% CI - 4.7% to - 6.0%) observed for this group. In contrast, the prevalence of HIV increased in the other age strata of men, with the most notable change being observed in the 50 years and older age group [10.6% (95% CI 10.0% to 11.1%)] (Table 3).

New HIV diagnoses

The age- and sex-standardized rate of new HIV diagnoses per 100,000 population decreased from 12.3 (95% CI 11.5 to 13.1) in 1996 to 8.3 (95% CI 7.8 to 8.9) in 2009, representing a relative decrease of 32.5% ($p < 0.001$) (Table 2). However, despite this decrease, the annual number of new HIV diagnoses was relatively stable between 2002 and 2009, ranging from 802 to 863 cases per year during this period. The age-standardized rate of new diagnoses decreased among men (figure 2a), and overall sex-standardized rates declined in all age strata, most notably among individuals aged 18 to 35 (figure 2b). In contrast to men, the annual rate of new HIV diagnoses increased among women aged 36 to 49 years old [3.2%; 95% CI 1.0% to 5.2%)] and women over the age of 50 [5.0%; 95% CI 2.2% to 8.0%)] (Table 4).

All-cause mortality

The overall age- and sex-standardized all-cause mortality rate per 1000 individuals with HIV declined from 5.7 (95% CI 4.6 to 6.9) in 1996 to 1.6 (1.3 to 2.0) in 2009, representing a 71.9% relative decrease over this period ($p < 0.001$) (Table 2). All-cause mortality declined in all strata of men and women (Table 5, Figure 3a), although rates remained higher among individuals 50 years of age and older relative to younger patients (Table 5, Figure 3b).

Interpretation

In our population-based study, the number of adults with HIV increased by 98.6% between 1996 and 2009. This increase is most likely attributable to the striking reduction in all-cause mortality rates observed among these individuals during this period and the relatively stable number of new HIV diagnoses in the preceding decade. Importantly, however, women and adults aged 50 years and older accounted for an increasing proportion of new HIV diagnoses over the study period. Finally, we observed a steady increase in the prevalence of selected co-morbid conditions among persons with HIV who are in care, reflecting the transformation of HIV into a chronic complex disease characterized by an aging cohort of patients expected to be increasingly burdened by multiple co-existing illnesses.

Our findings have important implications for HIV prevention and public health. The data suggest that the increased relative burden of HIV among women and older individuals may be mostly due to the decreased rate of new diagnoses among younger men, perhaps reflecting the differential emphasis or success of HIV prevention efforts. Older adults, in particular, have not been routinely targeted by public health HIV prevention interventions despite a general lack of

knowledge about the disease and evidence of HIV risk behavior among these individuals.[17-19] In addition, the absolute number of new HIV diagnoses has remained relatively stable in Ontario over the last decade. Because rates of new HIV infections in British Columbia, Ontario and Quebec have been shown to decline 8% for each 10% increment in antiretroviral treatment coverage, universal coverage of these drugs in Ontario might augment existing prevention programs.[20] Finally, the Ontario HIV Epidemiology Monitoring Unit estimates that 27,420 Ontarians have had a positive test for HIV and were alive as of 2009.[21] Because we identified 15,107 individuals in Ontario's administrative healthcare databases who met our case-finding definition for HIV infection and were alive as of 2009, our results suggest that almost one-half of persons with HIV are either unaware of their infection or are not retained in care once diagnosed. Because these individuals may unknowingly contribute to the annual incidence of new infections and are unable to benefit from HIV-specific care, innovative interventions are required to increase the proportion of persons infected with HIV who are diagnosed and receiving appropriate care.[22]

Several limitations of our work merit emphasis. First, administrative healthcare databases can only identify individuals with physician-diagnosed HIV who are in care, and will not capture people with HIV who are unaware of their diagnosis. Furthermore, we could not identify individuals who obtain their care from physicians who do not bill OHIP and/or are not eligible for provincial public health insurance (i.e. refugee claimants). Our findings therefore underestimate the true incidence and prevalence of HIV in Ontario. In addition, we had no access to clinical data and information regarding method of HIV acquisition, rendering it impossible to examine epidemiologic trends in relation to risk factors for HIV-infection, stage of

illness at the time of diagnosis or country of birth. However, these limitations are common to all studies which use administrative data for chronic disease surveillance, and must be balanced against the strengths of using these data for this purpose, including the identification of all patients who are in care within a geographically large jurisdiction, complete follow-up of these patients over time and the potential for linkage with other health care datasets.[12-15] Finally, the potential for misclassification is always a consideration when using administrative data for health services research. To address this concern, we used a validated algorithm with excellent test characteristics for discriminating between HIV-infected and non-infected individuals to assemble our cohort.[16] To our knowledge, this is the first population-based study using a validated case-finding algorithm and administrative data to examine trends in the epidemiology of persons with HIV who have entered care.

In summary, we have assembled a population-based cohort of persons with HIV who have entered care and examined trends in new HIV diagnoses, prevalence and mortality over a 14-year period. Our findings suggest that if current trends continue, HIV-related health and support services will be required to adapt to the needs of an aging cohort of patients with multiple morbidities who may inevitably require the expertise of sectors of the healthcare system which have not been traditionally involved in the provision of HIV-related care, such as gerontology and long-term care. In addition, a large proportion of HIV-infected persons in Ontario are not receiving HIV-related care. Future research examining patterns of and disparities in health services utilization, entry and retention in care and trends in the prevalence of co-morbid conditions will be required to ensure that HIV-related services continue to evolve in a manner that anticipates the needs of the growing population of persons with HIV.

Competing interests: During the past three years, Tony Antoniou has received unrestricted research grants from Merck for different studies and Mona Loutfy from Abbott Laboratories, Merck Frosst Canada Ltd, Pfizer, and ViiV Healthcare. All other authors declare (1) no support from any company for the submitted work; (2) no relationships with any companies that might have an interest in the submitted work in the previous 3 years; (3) their spouses, partners, or children have no financial relationships that may be relevant to the submitted work; and (4) no non-financial interests that may be relevant to the submitted work.

Funding: This project was supported by the Institute for Clinical Evaluative Sciences (ICES), which is funded by an annual grant from the Ontario Ministry of Health and Long-Term Care (MOHLTC). The sponsors had no role in the design or conduct of the study; in the collection, analysis or interpretation of the data; or in the preparation, review or approval of the manuscript. The opinions, results and conclusions reported in this paper are those of the authors and are independent from the funding source. No endorsement by ICES or the Ontario MOHLTC is intended or should be inferred.

Tony Antoniou is supported by a post-doctoral fellowship from the Ontario HIV Treatment Network. Mona Loutfy is the recipient of salary support from the Canadian Institutes for Health Research. Ahmed M. Bayoumi is supported by a Canadian Institutes for Health Research / Ontario Ministry of Health and Long-Term Care Applied Chair in Health Services and Policy Research. Janet Raboud is supported by an Ontario HIV Treatment Network Career Scientist Award and the Skate the Dream Fund, Toronto and Western Hospital Foundation.

Contributors: All authors contributed to the concept and design of the study. Tony Antoniou and Brandon Zagorski acquired the data, and all authors were involved in the analysis and interpretation of the data. Tony Antoniou drafted the manuscript, and all authors were involved in critical revision of the manuscript. All authors approved the manuscript submitted for publication. Tony Antoniou and Brandon Zagorski provided administrative, technical or material support. Tony Antoniou is the guarantor for the manuscript.

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Table 1: Characteristics of persons living with HIV in Ontario

Variables (%)	1996 (n = 7,608)	2002 n = 10,850)	2009 (n = 15,107)	p-value
Age (years)				< 0.01
18 to 35	3,713 (48.8%)	2,973 (27.4%)	2,695 (17.8%)	
36 to 49	3,101 (40.8%)	5,902 (54.4%)	7,892 (52.2%)	
> 50	794 (10.4%)	1,975 (18.2%)	4,520 (29.9%)	
Sex				< 0.01
Female	971 (12.8%)	1,781 (16.4%)	2,974 (19.7%)	
Male	6,637 (87.2%)	9,069 (83.6%)	12,133 (80.3%)	
Urban residence	7,353 (96.6%)	10,401 (95.9%)	14,500 (96.0%)	0.02
Co-morbidity				
Diabetes	213 (2.8%)	563 (5.2%)	1,313 (8.7%)	< 0.001
COPD	293 (3.9%)	588 (5.4%)	1,171 (7.8%)	< 0.001
Congestive Heart Failure	53 (0.7%)	133 (1.2%)	284 (1.9%)	< 0.001
Hypertension	456 (6.0%)	1,142 (10.5%)	2,398 (15.9%)	< 0.001
Myocardial infarction	28 (0.4%)	96 (0.9%)	200 (1.3%)	< 0.001

Table 2: Age- and sex-standardized HIV prevalence, incidence rate and all-cause mortality rate in adults 18 years and older in Ontario (1996 to 2009)

ar	Number of adults (> 18 years) living with HIV in Ontario	Age/sex – standardized prevalence of HIV per 100,000 population (95% CI)	Number of adults (> 18 years) with new HIV diagnosis in Ontario	Age/sex – standardized rate of new diagnoses per 100,000 population (95% CI)	Number of deaths among adults (> 18 years) living with HIV in Ontario	Age stand mortali 1000 per with HIV
	7,608	92.8 (90.7 to 94.9)	994	12.3 (11.5 to 13.1)	447	5.7 (4
	8,079	97.1 (94.9 to 99.2)	926	11.3 (10.6 to 12.1)	244	4.4 (3
	8,622	101.9 (99.8 to 104.1)	803	9.7 (9.1 to 10.4)	194	3.2 (2

ar	Number of adults (> 18 years) living with HIV in Ontario	Age/sex – standardized prevalence of HIV per 100,000 population (95% CI)	Number of adults (> 18 years) with new HIV diagnosis in Ontario	Age/sex – standardized rate of new diagnoses per 100,000 population (95% CI)	Number of deaths among adults (> 18 years) living with HIV in Ontario	Age stand mortali 1000 per with HI
	9,193	106.4 (104.2 to 108.6)	762	9.0 (8.4 to 9.7)	224	2.8 (2
	9,712	109.1 (106.9 to 111.3)	781	9.1 (8.5 to 9.8)	212	3.0 (2
	10,228	111.2 (109.1 to 113.4)	744	8.6 (7.9 to 9.2)	189	2.6 (1
	10,850	114.6 (112.5 to 116.8)	836	9.4 (8.8 to 10.1)	209	2.7 (2
	11,439	118.1 (115.9 to 120.3)	812	9.0 (8.3 to 9.6)	182	2.5 (1
	12,072	122.2 (120.0 to 124.40	848	9.3 (8.7 to 10.0)	196	2.0 (1
	12,702	126.3 (124.1 to 128.6)	863	9.4 (8.8 to 10.0)	209	1.9 (1
	13,319	130.5 (128.3 to 132.8)	838	9.1 (8.5 to 9.7)	199	1.7 (1
	13,893	134.0 (131.7 to 136.2)	820	8.6 (8.0 to 9.2)	210	1.9 (1
	14,516	138.0 (135.8 to 140.3)	835	8.7 (8.1 to 9.3)	214	2.1 (1

ar	Number of adults (> 18 years) living with HIV in Ontario	Age/sex – standardized prevalence of HIV per 100,000 population (95% CI)	Number of adults (> 18 years) with new HIV diagnosis in Ontario	Age/sex – standardized rate of new diagnoses per 100,000 population (95% CI)	Number of deaths among adults (> 18 years) living with HIV in Ontario	Age stand mortali 1000 per with HI
	15,107	141.8 (139.5 to 144.1)	802	8.3 (7.8 to 8.9)	228	1.6 (1

Table 3: Age- and sex-specific prevalence of HIV in Ontario

Group	Crude prevalence per 100,000 population			Percent relative annual change (95% CI)
	1996	2002	2009	
Female				
18 to 35 years	37.37	51.48	55.47	3.2% (2.5% to 4.0%)
36 to 49 years	23.69	52.65	99.53	11.0% (10.2% to 11.8%)
> 50 years	7.29	14.88	29.63	11.3% (10.4% to 12.2%)
Male				
18 to 35 years	205.09	144.12	112.38	- 5.3% (- 4.7% to - 6.0%)

Group	Crude prevalence per 100,000 population			Percent relative annual change (95% CI)
36 to 49 years	234.60	369.97	455.75	5.2% (4.4% to 6.0%)
> 50 years	50.40	105.04	191.10	10.6% (10.0% to 11.1%)

Table 4: Age-and sex specific rate of new HIV diagnoses in Ontario

Group	Crude rate per 100,000 population			Percent relative annual change (95% CI)
	1996	2002	2009	
Female				
18 to 35 years	6.47	6.95	5.48	- 0.3% (- 2.0% to +1.5%)
36 to 49 years	2.78	3.43	5.22	3.2% (1.0% to 5.4%)
> 50 years	1.33	1.35	1.58	5.0% (2.2% to 8.0%)
Male				
18 to 35 years	30.17	18.32	14.44	-4.3% (-2.8% to -5.8%)
36 to 49 years	24.45	22.63	19.90	-1.1% (-0.2% to -2.0%)
> 50 years	6.31	3.89	4.42	-0.3% (-2.4% to +1.7%)

Table 5: Age- and sex-specific all-cause mortality rate among persons living with HIV in Ontario

Group	Crude rate per 100,000 population			Percent relative annual change (95% CI)
	1996	2002	2009	
emale				
18 to 35 years	3.18	0.65	0.22	-14.2% (-9.5% to -18.6%)
36 to 49 years	3.79	1.63	1.42	-7.7% (-4.3% to -10.9%)

Group	Crude rate per 100,000 population			Percent relative annual change (95% CI)
> 50 years	6.09	4.35	2.53	-4.7% (-0.8% to -8.4%)
Male				
18 to 35 years	4.26	1.36	0.44	-13.8% (-10.6% to -17.0%
36 to 49 years	7.40	1.74	1.19	-10.6% (-7.8% to -13.4%)
> 50 years	10.16	3.55	2.70	-7.9% (-5.5% to -10.2%)

Figure Legends

Figure 1a: Age-standardized trends in HIV prevalence, by sex

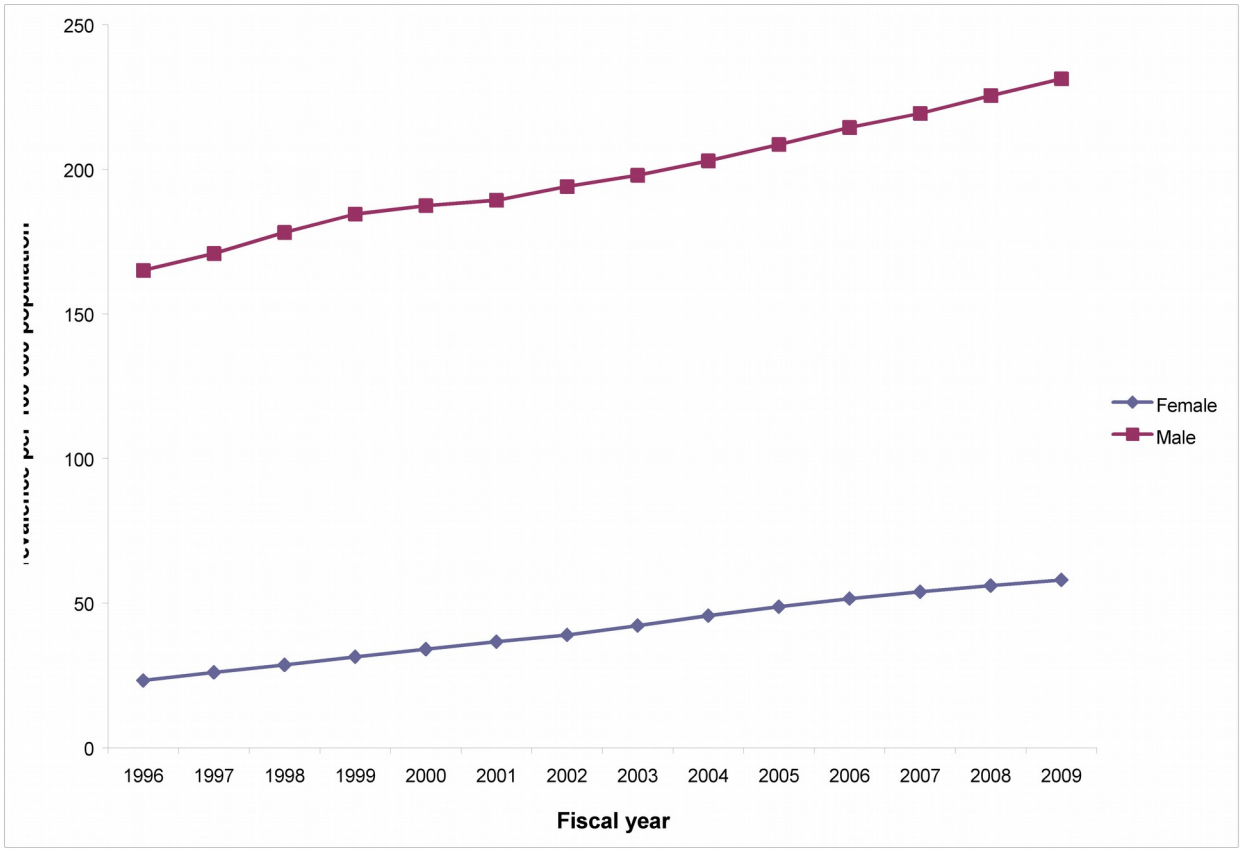
Figure 1b: Sex-standardized trends in HIV prevalence, by age-group

Figure 2a: Age-standardized trends in rates of new diagnosis, by sex

Figure 2b: Sex-standardized trends in rates of new diagnosis, by age-group

Figure 3a: Age-standardized trends in deaths of persons with HIV, by sex

Figure 3b: Sex-standardized trends in deaths of persons with HIV, by age-group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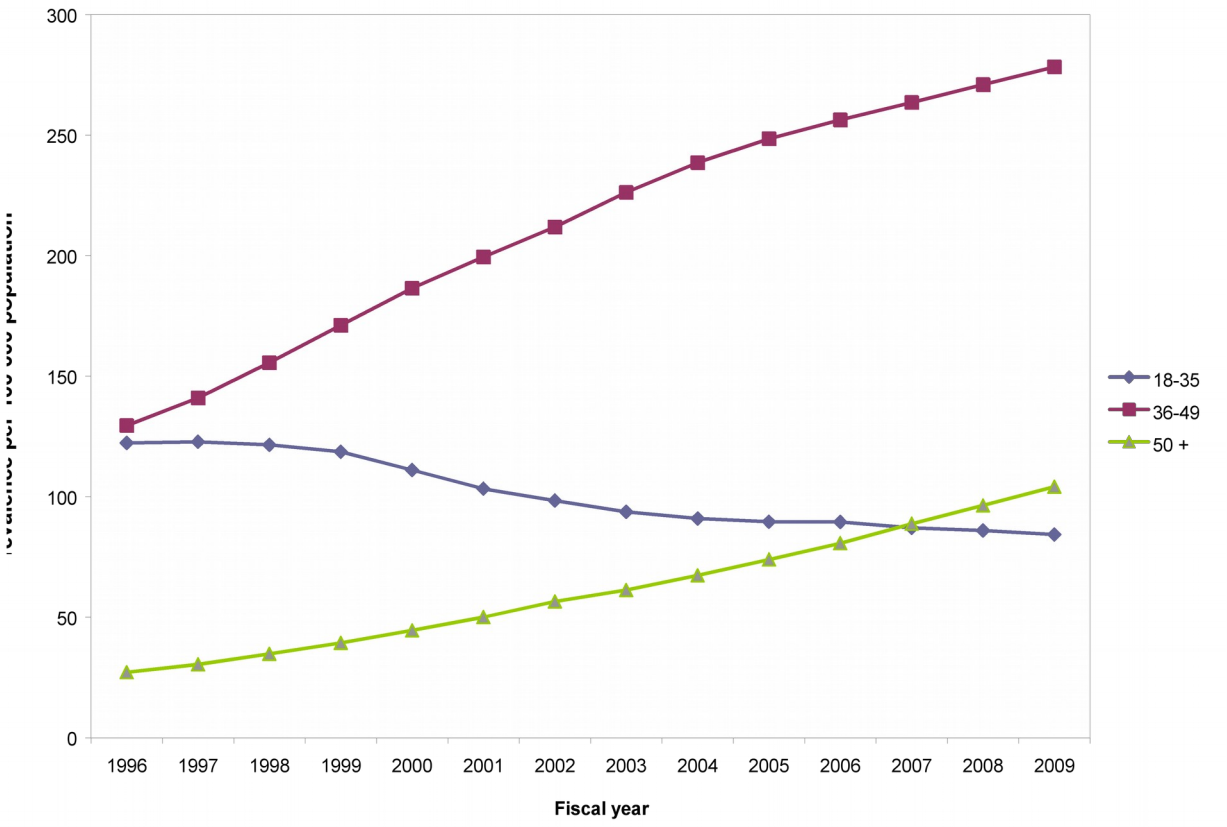
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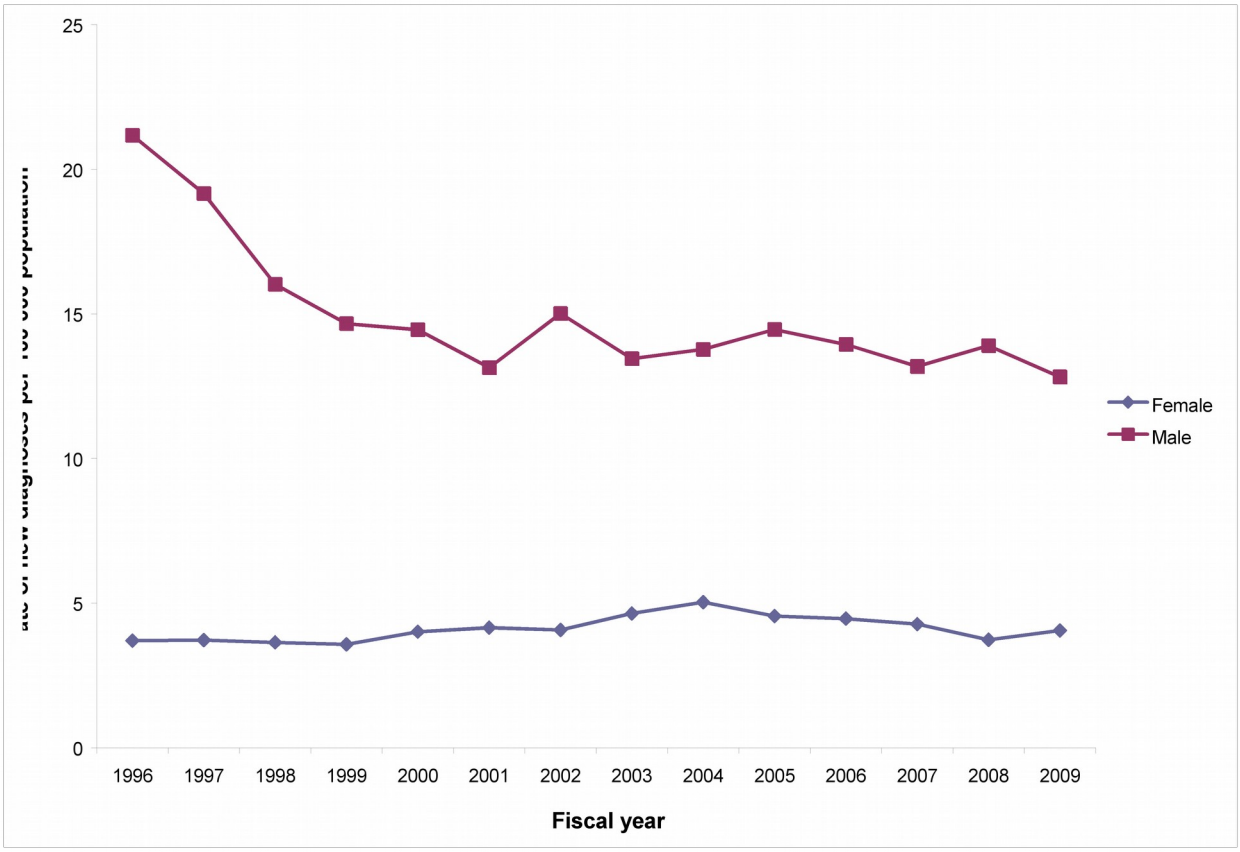
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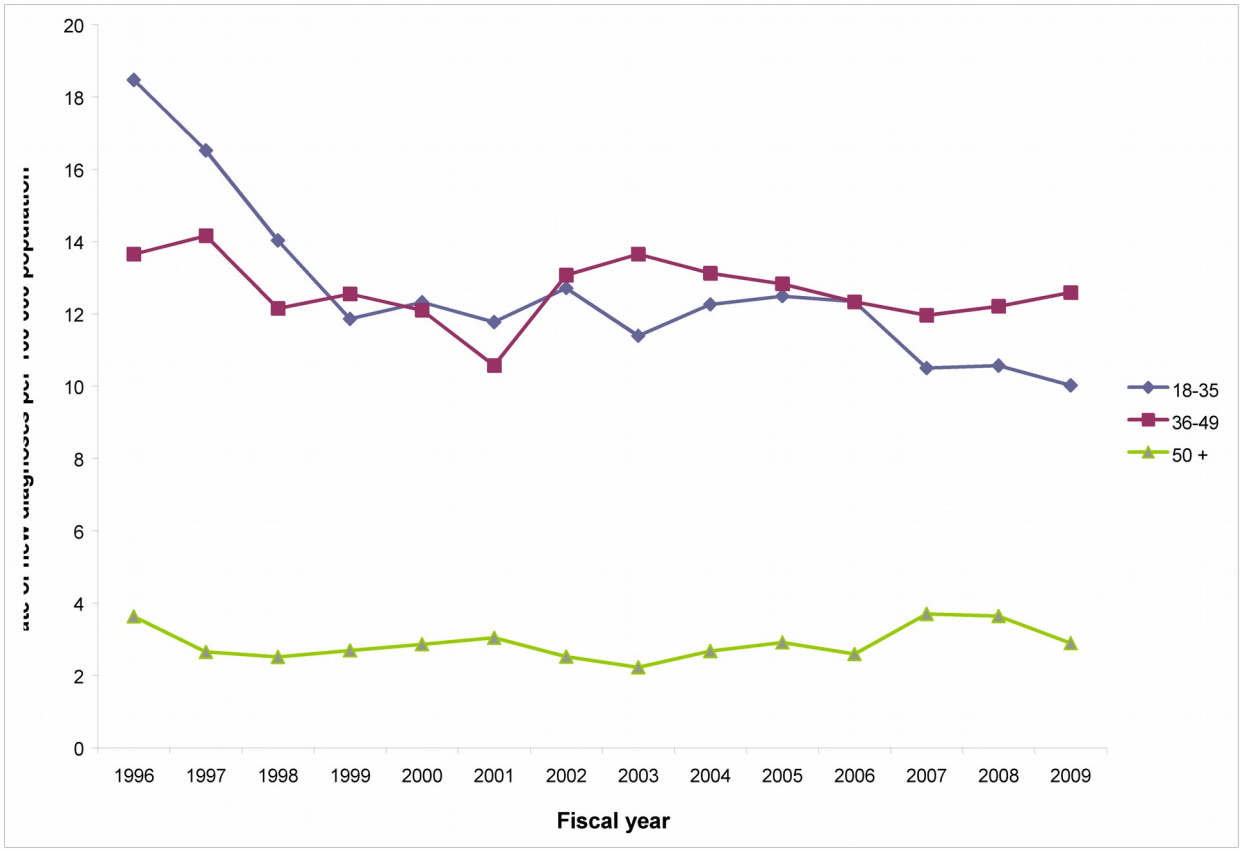
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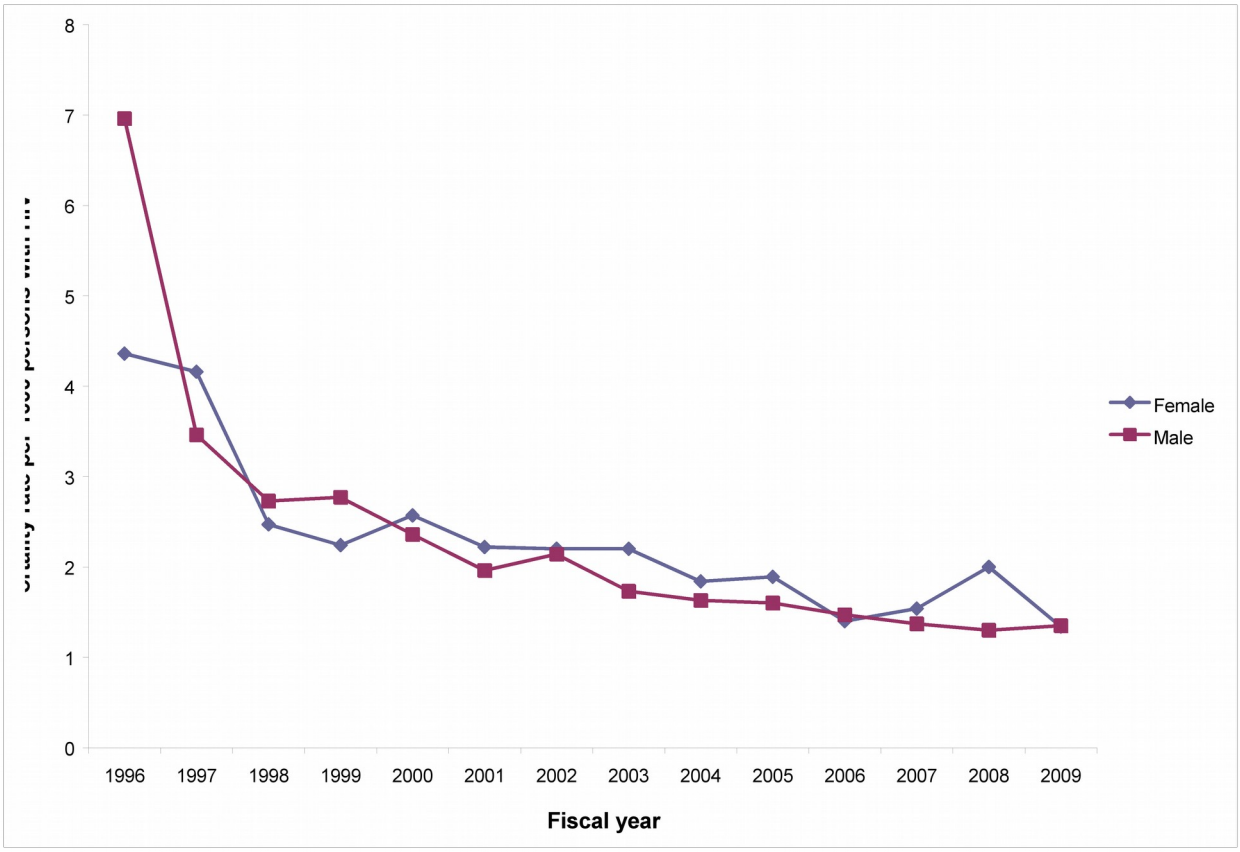
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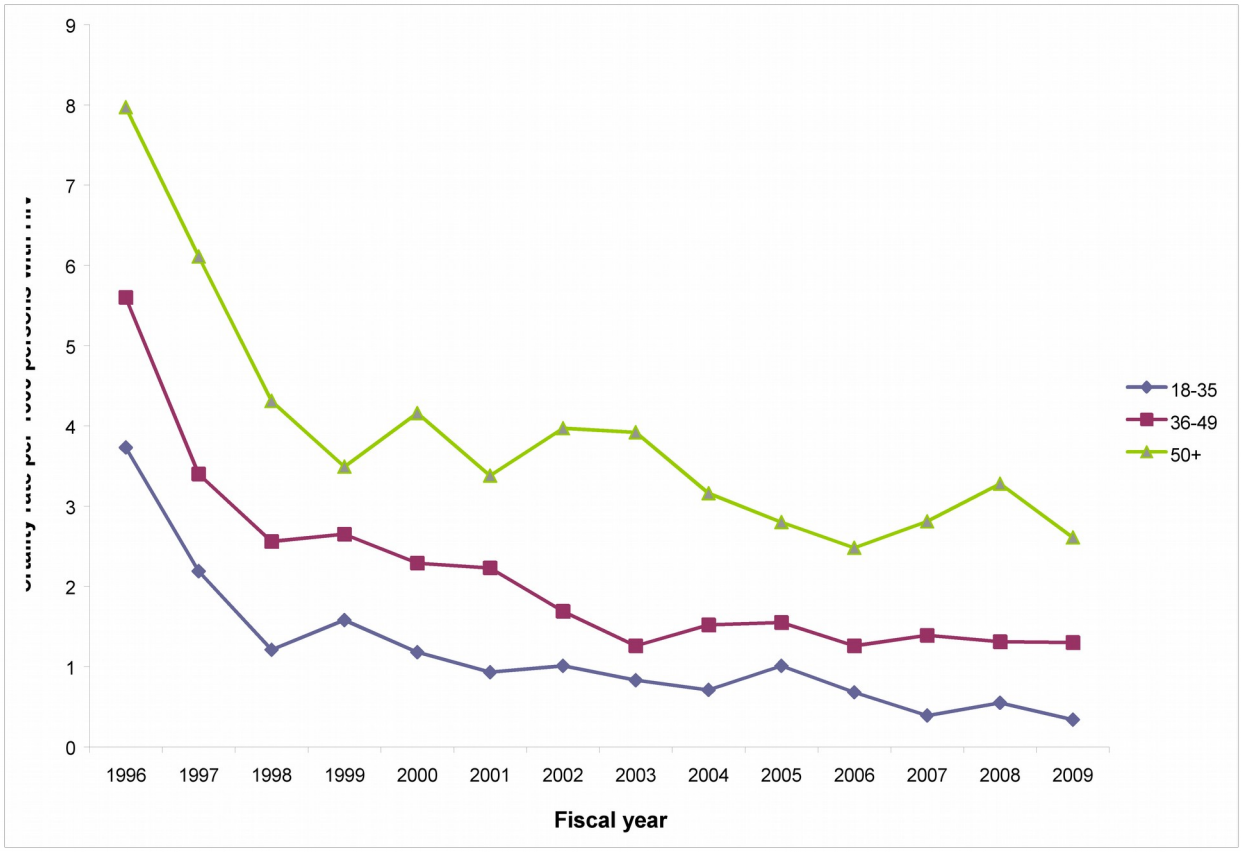
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