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Original Article

Prevalence and related drug cost of comorbidities in HIV-infected patients receiving highly active antiretroviral therapy in Taiwan: A cross-sectional study

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KEYWORDS
Cost-burden;
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Abstract *Background:* To determine the prevalence of chronic comorbidities and associated medication costs in Taiwanese HIV patients in order to increase awareness of the disease burden among healthcare providers and patients.
Methods: HIV-diagnosed patients receiving highly active antiretroviral therapy (HAART; 2010–2013) were identified from the Taiwan National Health Insurance Research Database with the corresponding International Classification of Diseases, ninth revision (ICD-9) code. Comorbidities (type II diabetes mellitus, hypertension, dyslipidemia, major depressive disorder, acute coronary syndrome, and cholelithiasis/nephrolithiasis) were identified according to ICD-9 or relevant medication use. Comorbidity medication and associated costs were identified using the drug classification code from the Anatomical Therapeutic Chemical classification system code series and series outpatient prescriptions.
Results: Of 20,726 HIV-diagnosed Taiwanese patients (2010–2013), 13,142 receiving HAART were analyzed. Prevalence of all chronic comorbidities was significantly greater ($p < 0.0001$) in patients aged ≥40 years versus <40 years (diabetes mellitus, 14.95% vs. 3.30%; hypertension, 46.73% vs. 26.83%; dyslipidemia, 34.93% vs. 18.37%; depression, 23.75% vs. 19.88%; acute coronary syndrome, 1.16% vs. 0.21%; nephrolithiasis/cholelithiasis, 7.26% vs. 4.56%; >2 comorbidities, 24.80% vs. 7.21%). An increase in comorbidity medication spending (2010 vs. 2013 medication costs) was observed (antidyslipidemia, $88,878 vs.

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$168,180; antihyperglycemia, $32,372 vs. $73,518; antidepressants, $78,220 vs. $125,971; sedatives, $60,009 vs. $85,055; antihypertension, $47,115 vs. $95,134), contributing to overall treatment costs increasing almost two-fold from 2010 to 2013.
Conclusions: Among HIV-infected Taiwanese patients receiving HAART, significant increases in comorbidity prevalence with age, along with rising comorbidity medication costs, suggest the need for preventative as well as chronic care.

Introduction

Since the year 2000, the occurrence of new human immunodeficiency virus (HIV) infections has declined by 35% worldwide.[1] In 2015, 15.8 million people living with HIV had access to antiretroviral therapy, an increase of 84% since 2010.[1] The year 2015 also saw the highest number of people living with acquired immunodeficiency syndrome (AIDS; approximately 37 million).[1] Clearly, advances in the treatment and prevention of HIV and AIDS, such as the introduction of highly active antiretroviral therapy (HAART), have led to increased life expectancy in patients globally. Further, cohort studies and modeling data suggest that the life expectancy of a patient living with HIV and maintaining viral suppression with HAART approaches that of HIV-negative individuals.[2]

In Taiwan, the HIV/AIDS epidemic began in 1986, and largely comprised injection drug users (IDUs) between 2004 and 2007; after 2007, the epidemic mainly comprised men who have sex with men.[3] With the introduction of HIV testing and education and government-initiated programs aimed at harm reduction, HIV outbreaks among IDUs have been brought under control.[4,5] Currently, however, men having sex with men have replaced IDUs as the group most at-risk of HIV infection in the country.[6] To counteract the HIV/AIDS epidemic, the government also introduced universal free HAART in 1997. A 2004 report estimated that this led to a 53% drop in the HIV transmission rate.[7] Consequently, Taiwan has seen an increase in the number of patients living with HIV/AIDS. As of 2016, the total number of reported cases of HIV, which includes patients living with HIV, stands at 32,241 or 0.14% of the population.[6]

However, while AIDS-related deaths and the incidence of opportunistic infections may have decreased, non—AIDS-related chronic diseases have gradually increased among HIV patients in Taiwan as well as globally.[8,9] Reports indicate that compared with non—HIV-infected subjects, HIV patients have a greater prevalence of comorbidities such as diabetes mellitus (DM), hypertension, dyslipidemia, cardiovascular disease (CVD), and chronic kidney disease.[10—13] This can be attributed to not just an aging HIV patient population as a result of increased life expectancy but also the premature aging characteristic of HIV-infected patients as well as drug toxicity due to sustained exposure to antiretroviral therapy.[14—16] Studies show that HIV infections are particularly associated with an increased risk of CVD surrogate markers such as carotid intima-media thickness (IMT), arterial stiffness, and endothelial dysfunction.[17] HAART use is also linked with insulin resistance and an increased risk of DM.[18,19] Thus, both the HIV infection itself and long-term exposure to HAART may increase the risk of comorbidities.

The increased prevalence of chronic comorbidities among HIV patients and the advancing age of patients living with HIV have also led to an escalation of the total healthcare costs of HIV-infected patients.[20,21] While the total medical costs associated with an HIV patient will depend on the stage of the disease at which the HIV infection is diagnosed, choice of therapeutic approach, and utilization measures, it is worthwhile to investigate the impact that chronic comorbidities in HIV patients may have on the public health system.

Though a few recent studies have examined the prevalence of comorbidities that co-occur with HIV/AIDS in patients in Taiwan,[22—24] more extensive studies, especially those assessing the related cost expenditure burden, are lacking. The objective of this study was to understand the prevalence and economic burden of chronic comorbidities in Taiwanese patients with HIV in order to increase awareness of comorbidities and the associated burden among healthcare providers and patients.

Methods

Study population

This cross-sectional study, conducted with the approval of the Joint Institutional Review Board (14-S-023) of all institutions involved, analyzed a dataset obtained from the Taiwan National Health Insurance Research Database (NHIRD).[25] The NHIRD, covering 99.9% of Taiwan's population as of 2014,[26] contains comprehensive reimbursement claim records of outpatient and inpatient care from the National Health Insurance in Taiwan. Records of HIV-infected patients (International Classification of Diseases, ninth revision [ICD-9] diagnostic codes 042, 043, and 044) enrolled in the NHIRD between 2010 and 2013 and receiving HAART were analyzed (Fig. 1). Foreigners, defined as non-Taiwan citizens, were excluded. To maintain patient privacy, data could not be extracted and included in the analysis if the number of patients was less than five after using a combination of geographic location and birth date.

HAART use was defined as the prescription of any of the following typical combinations: two nucleotide/nucleoside reverse transcriptase inhibitors (N(t)RTIs) + one or two

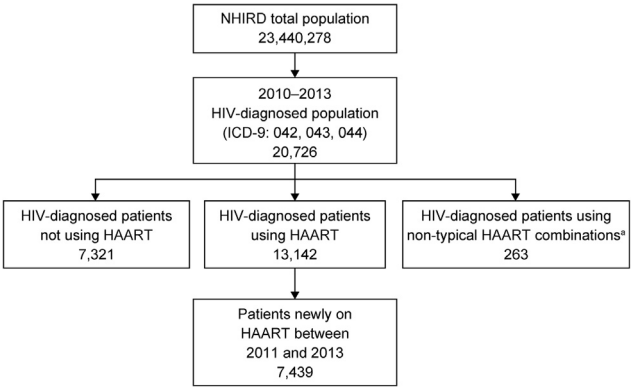

Figure 1. Data extraction profile. [a]Non-typical HAART combination was defined as use of non-nucleoside reverse transcriptase inhibitors + protease inhibitors. HAART, highly active antiretroviral therapy; HIV, human immunodeficiency virus; ICD-9, International Classification of Diseases, ninth revision; NHIRD, National Health Insurance Research Database of Taiwan.

protease inhibitors (PIs); two N(t)RTIs + one non-nucleoside reverse transcriptase inhibitor (NNRTI); or two N(t)RTIs + one integrase strand transfer inhibitor (InsTI) or one fusion inhibitor or one chemokine receptor type 5 inhibitor (CCR5).

Definitions

HIV patients were regarded as having comorbidities if, as per the NHIRD, they were coded with the specified ICD-9 code or had relevant medication use as determined by series outpatient prescriptions. Comorbidities of type II DM (ICD-9 codes 250.x, 790.2, 791.5, and 791.6), hypertension (ICD-9 codes 401.x, 402, 403, 404, 405, and 437.2), dyslipidemia (ICD-9 code 272), major depressive disorder (ICD-9 codes 296.20—296.26 and 296.30—296.36), acute coronary syndrome (ACS) or acute myocardial injury (AMI; ICD-9 codes 410, 411.81, and 412), nephrolithiasis (ICD-9 codes 592, 592.0, 592.1, and 592.9), and cholelithiasis (ICD-9 code 574) were identified from the sampled database, while the use of sedative agents was defined as the use of barbiturates (plain and combination), aldehydes and derivatives, benzodiazepine derivatives, melatonin receptor agonists, or combinations of these drugs.

Cost expenditure analysis

Medication involved in the treatment of comorbidities was identified according to the drug classification code from the Anatomical Therapeutic Chemical classification system code series and using series outpatient prescriptions. In those patients prescribed comorbidity medication, cost of medication was calculated in New Taiwan dollars (NTDs), converted to US dollars (conversion ratio, 1 NTD = 0.031 US$), and compared to the total medication costs (HAART therapy + all other medications, including comorbidity medication) to determine the contribution of comorbidity medication expenditure.

Statistical analysis

Descriptive analyses were applied for patient characteristics, prevalence of comorbidities, and cost expenditure of comorbidity medication. Differences between categorical variables were analyzed using the chi-square test. A p-value of <0.05 was considered statistically significant. All analyses were performed using SAS® version 9.4 (SAS Institute Inc., Cary, NC, USA).

Results

Baseline characteristics of the population

Of the 23,440,278 patients included in the NHIRD, 20,726 were diagnosed as having HIV between 2010 and 2013. Of these, 13,142 receiving HAART were included in the analysis (Fig. 1). Most patients were male (93.56%), and the mean age of the entire population was 36.63 ± 10.60 years, with 34.1% of patients aged ≥40 years (Table 1). The majority of HIV patients (60.1%) were prescribed a combination of two N(t)RTIs and an NNRTI, and prescription of an InsTI or fusion inhibitor or CCR5 inhibitor containing HAART increased from 0.02% in 2010 to 3.01% in 2013. The annual number of patients newly receiving HAART increased from 2011 to 2013 and ranged from approximately 1800 to 3400. The age and gender distributions of patients newly receiving HAART were similar to those of the total HIV patient population on HAART.

Comorbidity prevalence

Among the metabolic comorbidities examined in the total patient population, hypertension affected the highest number of HIV patients (33.60%), followed by dyslipidemia (24.01%) and type II DM (7.27%; Table 2). The overall prevalence of cholelithiasis or nephrolithiasis was 5.48%, and 13.20% of patients had more than two concomitant metabolic comorbidities. Mental health disorders constituted a considerable proportion of the comorbidities in HIV patients, with 21.20% of the patient population diagnosed as having a major depressive disorder and 39.54% of patients prescribed sedative agents.

Among patients newly receiving HAART, the occurrence of all comorbidities remained steady from 2011 to 2013 (Fig. 2). However, comorbidity prevalence in all HIV patients (2010—2013) increased significantly after the age of 40 years, especially for metabolic comorbidities (≥40 vs. <40 years: type II DM, 14.95% vs. 3.30%; hypertension, 46.73% vs. 26.83%; dyslipidemia, 34.93% vs. 18.37%; ACS and AMI, 1.16% vs. 0.21%; and cholelithiasis or nephrolithiasis, 7.26% vs. 4.56%, respectively). In patients aged ≥40 years, the prevalence of more than two concomitant metabolic comorbidities also showed a sharp increase (≥40 vs. <40 years, 24.80% vs. 7.21%, respectively; Fig. 3).

Comorbidity medication costs

The total number of comorbidity medication prescriptions in HIV patients almost doubled between 2010 and 2013 (Table 3); consequently, there was a steady increase in the

Table 1 Baseline characteristics of the study population.

	Total	2010	2011	2012	2013
Number of samples	13,142	5703	1819	2202	3418
Age, years, (median)	35	37	34.45	36.09	36.97
Age, years, (mean ± SD)	36.63 ± 10.6	37.33 ± 8.77	34.45 ± 8.75	36.09 ± 11.22	36.97 ± 13.34
Age group					
<20 years	63 (0.48)	11 (0.19)	7 (0.38)	7 (0.32)	38 (1.11)
20–29 years	3575 (27.20)	1113 (19.52)	596 (32.77)	688 (31.24)	1178 (34.46)
30–39 years	5029 (38.27)	2436 (42.71)	741 (40.74)	821 (37.28)	1031 (30.16)
40–49 years	3012 (22.92)	1626 (28.51)	367 (20.18)	427 (19.39)	592 (17.32)
≥50 years	1463 (11.13)	517 (9.07)	108 (5.94)	259 (11.76)	579 (16.94)
Gender					
Female	840 (6.39)	351 (6.15)	117 (6.43)	146 (6.63)	226 (6.61)
Male	12,296 (93.56)	5348 (93.78)	1702 (93.57)	2054 (93.28)	3192 (93.39)
Not known	6 (0.05)	4 (0.07)	0 (0)	2 (0.09)	0 (0)
HAART combination					
Two N(t)RTIs + one NNRTI	7904 (60.14)	2577 (45.19)	1135 (62.40)	1599 (72.62)	2593 (75.86)
Two N(t)RTIs + one or two PIs	5122 (38.97)	3125 (54.80)	683 (37.55)	592 (26.88)	722 (21.13)
Two N(t)RTIs + (one InsTI or one fusion inhibitor or one CCR5 inhibitor)	116 (0.88)	1 (0.02)	1 (0.05)	11 (0.50)	103 (3.01)

Data are presented as *n* (%) unless otherwise stated. Data for years 2011, 2012, and 2013 include only those HIV patients newly receiving HAART.
CCR5, chemokine receptor 5; HAART, highly active antiretroviral therapy; HIV, human immunodeficiency virus; InsTI, integrase strand transfer inhibitor; NNRTI, non-nucleoside reverse transcriptase inhibitor; N(t)RTI, nucleoside/nucleotide reverse transcriptase inhibitor; PI, protease inhibitor; SD, standard deviation.

Table 2 Age group-wise distribution of comorbidities in HIV patients using HAART (n = 13,142).

Comorbidities, *n* (%)	Total	<30 years	30–39 years	40–49 years	≥50 years
Type II DM	955 (7.27)	65 (1.79)	221 (4.39)	326 (10.82)	343 (23.44)
Hypertension	4416 (33.60)	791 (21.74)	1534 (30.50)	1257 (41.73)	834 (57.01)
Dyslipidemia	3155 (24.01)	419 (11.52)	1173 (23.32)	989 (32.84)	574 (39.23)
Major depressive disorder	2786 (21.20)	552 (15.17)	1171 (23.28)	750 (24.90)	313 (21.39)
Use of sedative agent	5196 (39.54)	1009 (27.74)	2174 (43.23)	1419 (47.11)	594 (40.60)
ACS and AMI	70 (0.53)	4 (0.11)	14 (0.28)	23 (0.76)	29 (1.98)
>2 metabolic comorbidities	1735 (13.20)	137 (3.77)	488 (9.70)	594 (19.72)	516 (35.27)
Nephrolithiasis/cholelithiasis	720 (5.48)	88 (2.42)	307 (6.10)	232 (7.70)	93 (6.36)

ACS, acute coronary syndrome; AMI, acute myocardial injury; DM, diabetes mellitus; HAART, highly active antiretroviral therapy; HIV, human immunodeficiency virus.

annual spending on comorbidity medication (2010 vs. 2013 medication costs; antidyslipidemia agents, $88,878 vs. $168,180; antihyperglycemia agents, $32,372 vs. $73,518; antidepressive agents, $78,220 vs. $125,971; sedatives, $60,009 vs. $85,055; and antihypertensive agents, $47,115 vs. $95,134). This contributed to the total cost of treating HIV patients (including costs of HAART and comorbidity medication) increasing almost two-fold from 2010 to 2013. The average cost of antihyperglycemic medication ($142.20) was the highest among the comorbidity medications examined and consequently contributed to approximately 2% of the total annual medication costs for HIV patients on HAART in 2013.

Discussion

While HIV-associated morbidity and mortality have declined significantly since the introduction of HAART, the prevalence of comorbidities has increased in persons living with HIV. The results of our cross-sectional study demonstrate that comorbidities including cardiovascular risk factors such as hypertension, dyslipidemia, and type II DM were highly prevalent in HIV patients using HAART in Taiwan. These results were more pronounced in patients aged ≥40 years, where over 20% were affected by more than two metabolic comorbidities. The findings of this study are in line with other epidemiological studies showing an increased prevalence of chronic comorbidities in HIV patients.[12,13,24,27,28]

The pathophysiologic mechanisms associated with HIV comorbidities cannot be fully elucidated due to the difficulty of separating the effects of HIV infection from those of HAART use, comorbidities, or interindividual variability.[27] It is likely that a combination of factors may be responsible for the occurrence of comorbidities. For instance, HIV infection is independently associated with

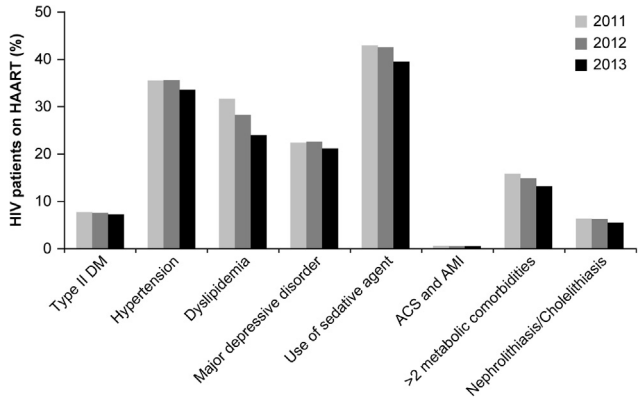

Figure 2. Prevalence of comorbidities among HIV patients newly on HAART (2011–2013). ACS, acute coronary syndrome; AMI, acute myocardial injury; DM, diabetes mellitus; HAART, highly active antiretroviral therapy; HIV, human immunodeficiency virus.

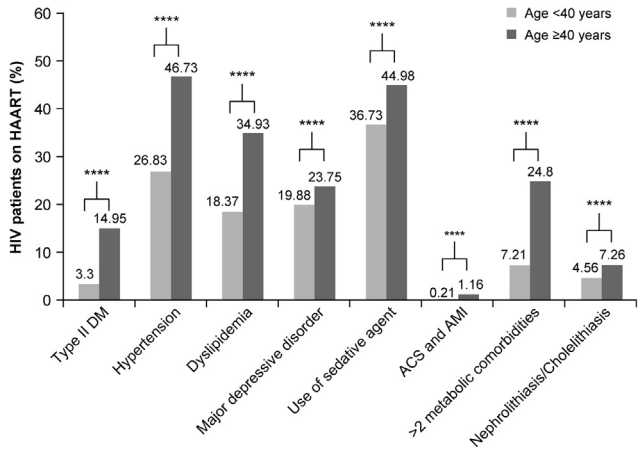

Figure 3. Prevalence of comorbidities among HIV patients according to age group. ****$p < 0.0001$. ACS, acute coronary syndrome; AMI, acute myocardial injury; DM, diabetes mellitus; HAART, highly active antiretroviral therapy; HIV, human immunodeficiency virus.

carotid IMT and increased arterial stiffness, while HAART use is linked to increased stiffness of the femoral artery.[17] Furthermore, although the use of HAART is associated with a decreased incidence of conditions associated with advanced immune deficiency, a significant number of successfully treated individuals remain in a proinflammatory state, which in turn has been associated with non–AIDS-related conditions, particularly CVD.[29] Exposure to a certain class of HAART drugs (N(t)RTIs and NNRTIs) and a cumulative dose effect may also contribute to the increased prevalence of DM in HIV patients.[18,28] More extensive studies are necessary to demonstrate the possible association of specific HAART combinations with comorbidity prevalence.

In an 11-year study of the risk factors of cholelithiasis and nephrolithiasis in HIV patients in Taiwan, it was found that 4.3% and 3.7% of patients, respectively, were affected.[23] In the current study, a 5.48% overall incidence of cholelithiasis and/or nephrolithiasis was observed. Differences in the results between the two studies may be attributed to differences in the patient population; the study by Lin et al. specifically assessed the medical records of HIV-infected patients who had undergone abdominal sonography. Their study also found that exposure to the HAART drug ritonavir-boosted atazanavir for over 2 years was associated with incident cholelithiasis.[23] Multiple studies associate the high prevalence of cholelithiasis and nephrolithiasis in Asian countries with the use of antiretrovirals, necessitating measures to balance risk factors with desired treatment outcomes.[30,31]

It is unclear whether the increased prevalence of comorbidities in patients aged ≥40 years observed in this study may be attributed to faster aging of the HIV-infected population alone. However, it has been reported that with increasing age, compared with HIV-uninfected patients, HIV patients have lower HIV viral loads but are prescribed multiple medications and have a higher prevalence of comorbidities, including hypertension and hypercholesterolemia.[32,33] In the recent Taiwan Health Promotion Administration report, the prevalence of hypertension, diabetes, and hyperlipidemia was 29.7%, 12.4%, and 28.7%, respectively, in the age group of 40–64 years, and 5.7%, 2.3%, and 11.4%, respectively, in the age group of 20–39 years.[34] The comorbidity prevalence rate in our study was higher in patients with HIV infection as compared with the general population in both age groups of ≥40 years and <40 years (hypertension, diabetes, and hyperlipidemia: 46.73%, 14.95%, and 34.93% and 26.83%, 3.30%, and 18.37%, respectively). The results of this indirect comparison support our hypothesis that HIV-infected patients have a higher comorbidity burden and a faster aging process than the general population. As their life expectancy increases and they live longer, patients with HIV also become susceptible to metabolic syndrome. In Brazil, metabolic syndrome is increasingly common in HIV-infected individuals and may play an important role in the higher risk of metabolic comorbidities such as DM and CVD in these patients compared with the general population.[35] Further, a survey of 803 HIV-infected patients in Taiwan found that receipt of HAART and prolonged exposure to PIs and N(t)RTIs were associated with the prevalence of metabolic syndrome in one-fourth of the infected patients.[36]

The findings of a study examining prevalence of comorbidities in HIV patients aged ≥40 years in Taiwan are also consistent with those of the current study.[24] It was found that patients aged ≥50 years were more likely to have been receiving two or more concurrent medications than those aged <50 years (22.9% vs. 6.4%, respectively). This is in line with our results, which showed that a greater number of patients aged ≥50 years had more than two comorbidities than patients aged between 40 and 49 years.

Results of the current study also indicate that a significant number of patients were affected by depression, suggesting the need to address mental health needs of HIV patients. A recent study showed that quality of life in social and psychological domains is significantly affected in HIV patients compared with the general population in Taiwan.[37] Other reports have noted the positive correlation between quality of life and HAART initiation,[38] indicating the continuing need for mental health support in HIV patients.

Table 3 Cost (US$) expenditure burden of comorbidity medication.

	2010	2011	2012	2013
Antidyslipidemia medication				
Total patients[a]	734	831	964	1248
Total prescriptions[b]	6268	7574	8652	11,741
Total medication cost[c]	6,378,720	7,080,971	7,608,989	9,417,147
Antidyslipidemia agent cost[d]	88,878	110,234	113,520	168,180
Cost proportion[e]	1.39%	1.56%	1.49%	1.79%
Mean cost[f]	121.09	132.65	117.76	134.76
SD	138.81	136.34	119.36	124.15
Antihyperglycemic agent				
Total patients[a]	269	306	370	517
Total prescriptions[b]	3723	4511	4977	8334
Total medication cost[c]	2,053,784	2,330,211	2,837,975	3,820,873
Antihyperglycemic agent cost[d]	32,372	39,652	42,001	73,518
Cost proportion[e]	1.58%	1.70%	1.48%	1.92%
Mean cost[f]	120.34	129.58	113.52	142.20
SD	203.84	199.14	165.73	214.06
Antidepressive agent				
Total patients[a]	956	1056	1124	1625
Total prescriptions[b]	6777	7723	8759	12,865
Total medication cost[c]	4,23,608	5,679,458	6,991,381	9,781,961
Antidepressive agent cost[d]	78,220	94,775	92,356	125,971
Cost proportion[e]	1.81%	1.67%	1.32%	1.29%
Mean cost[f]	81.82	89.75	82.17	77.52
SD	156.72	171.33	153.10	150.62
Sedative agent				
Total patients[a]	2215	2550	2758	3517
Total prescriptions[b]	19,590	23,450	27,109	35,419
Total medication cost[c]	11,152,353	14,525,188	16,938,27	22,271,499
Sedative-hypnotic agent cost[d]	60,009	72,445	70,278	85,055
Cost proportion[e]	0.54%	0.50%	0.41%	0.38%
Mean cost[f]	27.09	28.41	25.48	24.18
SD	42.15	49.83	44.14	35.93
Antihypertensive medication				
Total patients[a]	1290	1387	1519	2079
Total prescriptions[b]	8400	10,318	11,208	17,699
Total medication cost[c]	6,716,659	8,354,452	10,027,177	14,090,508
Antihypertensive agent cost[d]	47,115	57,686	55,314	95,134
Cost proportion[e]	0.70%	0.69%	0.55%	0.68%
Mean cost[f]	36.52	41.59	36.41	45.76
SD	90.40	100.35	73.00	82.73

HIV, human immunodeficiency virus; SD, standard deviation.
[a] Total patients: patients who met the loose definition of comorbidities.
[b] Total medications: per outpatient department records, if each prescription/visit contained a comorbidity medication, it was counted as a single medication.
[c] Total medication cost: annual medication cost of the enrolled patients (including HIV medications and all other medication costs).
[d] Annual cost of specific medication for the enrolled patients.
[e] Cost proportion: individual comorbidity cost to the total annual medication cost.
[f] Mean cost: individual comorbidity mean cost.

The medication cost burden associated with HIV comorbidities increased from the year 2010–2013, contributing to a steady increase in overall costs of medical treatment for HIV patients. Although the emergence of comorbidities in HIV patients newly on HAART remained fairly steady from 2011 to 2013, the overall number of chronic HIV comorbidities in the total population has continued to increase, further burdening the healthcare system. While HAART accounted for the majority of the total cost, comorbidity expenditure contributed to almost 2% of the cost in the case of antihyperglycemic medication. It is likely that if age-wise cost-expenditure data were available, this proportion would be even higher for those aged $\geq$40 years. Research indicates that the lower medical costs associated with higher CD4+ counts are offset by increases in the healthcare costs associated with the occurrence of comorbidities in older patients.[20] Taken together with our results, which show a sharp increase in

comorbidities in HIV patients aged ≥40 years, it is worthwhile to closely monitor the impact of medication costs associated with comorbidities on overall healthcare costs. The high costs of treating mental health in HIV patients also necessitate a comprehensive plan for multidisciplinary collaboration with psychiatry to improve clinical outcomes for these patients who may be particularly vulnerable to depression, insomnia, and other affective disorders.

One of the limitations of this study is the lack of a control population to evaluate whether the prevalence of comorbidities was different from the general population and/or HIV-infected patients not on HAART. However, the National Health Survey conducted over 5 years (2002—2007), covering 6600 subjects from the general population in Taiwan, reported the incidence of hypertension and hyperglycemia at 24.2% and 7.3%, respectively.[39] In the current study, the overall 3-year incidence of hypertension was greater (33.60%) and that of hyperglycemia was similar (7.27%) to the National Health Survey results, indicating, at least in the case of hypertension, a possible exclusive HIV-related effect. However, a propensity scores matching comparison study with the general population to evaluate the impact of comorbidities is still warranted for further clarification. Another possible limitation is that the diagnoses of HIV and comorbidities were based on ICD-9 and related medications coded in the database and not on clinical laboratory data. To offset this, a loose definition of comorbidities was chosen, to include all possible events and overestimate rather than underestimate the results. Further, the low representation of women in the study, although a reflection of the HIV patient profile in Taiwan,[6] may result in a gender bias in the results, especially since gender is known to play a role in the prevalence of HIV comorbidities.[40]

As of 2014, the National Health Insurance of Taiwan covers 99.9% of Taiwan's 23.5 million population and, therefore, the NHIRD represents a fairly complete record of HIV-infected patients across the country. We analyzed data over a 3-year span, providing an extensive, representative database to study comorbidity prevalence in the country and the associated costs involved. This is also one of the few comprehensive studies to show the prevalence of a wide range of comorbidities associated with HIV patients in Taiwan. The results of this study can help inform physicians and patients regarding the treatment and care involved in improving long-term clinical outcomes. In addition, our results can provide information to government officials for HIV care and prevention.

In conclusion, according to a nationwide surveillance between 2010 and 2013 in Taiwan, the prevalence of comorbidities such as hypertension, dyslipidemia, and DM was significantly higher in HIV patients on HAART aged ≥40 years compared with those <40 years. The cost of medication for treating comorbidities in HIV patients receiving HAART also showed a steady rise, suggesting the need to address the risk of comorbidities and the necessity for a comprehensive chronic care program.

Conflicts of interest statement

H-Y W is a former employee of Janssen Pharmaceuticals, Taiwan. All other authors have no conflicts to declare.

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This work was sponsored by Janssen Pharmaceuticals, Taiwan.

Author contributions

All authors substantially contributed to conception, design, and planning of the study and in critically revising the manuscript for important intellectual content. T-C C was involved in the acquisition and analysis of the data. C-J Y, H-Y W, and C-J C were involved in interpretation of the results. All authors have read and approved the final manuscript.

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