

Long-term prescribing patterns of hormone therapy and concomitant medications among women with menopausal disorders: a 20-year retrospective database study in Japan

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Abstract

Background

Hormone therapy is an effective treatment for menopausal symptoms, but its use has changed substantially since the Women's Health Initiative report. Long-term real-world data on hormone therapy and concomitant medication prescribing in Japan remain limited.

Methods

We conducted a 20-year retrospective database study using electronic prescription records from a tertiary university hospital in Japan. After describing overall prescription patterns among female patients, we focused on prescriptions issued to women aged 45–60 years with ICD-10-coded menopausal disorders. Annual trends in hormone therapy and six concomitant medication categories were examined using the Cochran–Armitage trend test. Patient-level logistic regression was used to explore factors associated with ever receiving hormone therapy.

Results

Among 132,523 prescriptions issued to 1,167 women with menopausal disorders, 268 women received hormone therapy. Hormone therapy prescribing declined significantly over time. Psychotropic medication prescribing did not show a corresponding increase in parallel with this decline. Kampo medicine showed a modest increase over time and was inversely associated with hormone therapy use in multivariable analysis.

Conclusions

In this single-centre Japanese university hospital database, hormone therapy prescribing among women with coded menopausal disorders declined over two decades. Concomitant medication patterns varied by drug category, and Kampo medicine showed only a modest increase. These findings describe real-world prescribing patterns and should be interpreted cautiously because treatment indications, symptom severity, and patient preferences were unavailable.

Introduction

Menopause is a natural stage in a woman's life that generally occurs between 45 and 55 years of age and is frequently accompanied by vasomotor symptoms, sleep disturbance, mood changes, and other physical and psychological complaints that may substantially impair quality of life [1, 2]. Menopausal hormone therapy (HT), including estrogen therapy and estrogen–progestogen therapy, remains the most effective treatment for vasomotor symptoms and is recommended for appropriately selected women by current international guidelines [3–6].

Prescribing practices for HT have changed considerably over the past two decades. Following publication of the Women's Health Initiative (WHI) trial in 2002, concerns regarding potential risks of HT resulted in a marked decline in its use in many countries [3, 4]. Subsequent reappraisal of the WHI findings and accumulating evidence have supported the favorable benefit–risk profile of HT for healthy women within 10 years of menopause or younger than 60 years [5, 6]. Nevertheless, real-world prescribing patterns may not necessarily reflect evolving clinical recommendations because treatment decisions are influenced by patient characteristics, physician preferences, comorbidities, and local healthcare systems.

In routine clinical practice, women with menopausal symptoms often receive medications other than HT. Depending on symptom profiles and clinical circumstances, antidepressants [7], anxiolytics [8], hypnotics [9], Kampo medicine [10, 11], cardiometabolic drugs [12–14], and osteoporosis medications [15–19] may also be prescribed. In Japan, Kampo medicine

has traditionally been incorporated into menopausal care and is widely used alongside Western medicine [11]. Although several studies have evaluated the effectiveness or safety of individual therapies, long-term real-world evidence describing overall prescribing patterns of HT and concomitant medications among women with menopausal disorders remains limited, particularly in Japan.

Therefore, the present study aimed to describe long-term prescription patterns of HT and major concomitant medication categories among women with menopausal disorders using a 20-year electronic prescription database from a Japanese university hospital. In addition to evaluating temporal prescribing trends, we explored patient characteristics associated with receiving HT using multivariable logistic regression analysis.

Methods

Study design and data source

This retrospective database study included all prescriptions issued between 1 April 2002 and 31 March 2022 (fiscal years 2002–2021) at a tertiary university hospital located in a metropolitan area of Japan. The hospital has 689 licensed beds and provides care to approximately 60,000–70,000 patients annually. All clinical activities, including prescribing, were managed through a hospital-wide computerized electronic medical record (EMR) system throughout the study period. Consequently, complete prescription data were available, and no missing prescription records were identified [20].

During the study period, 23 clinical departments were categorized into five groups: obstetrics and gynaecology, surgery, internal medicine, psychiatry, and others. The obstetrics and gynaecology group corresponded to the department of obstetrics and gynaecology. The surgery group included 12 departments of general surgery, neurosurgery, cardiac surgery, thyroid surgery, orthopaedics, plastic surgery, ophthalmology, otorhinolaryngology, dermatology, urology, oral surgery, and anaesthesia. The internal medicine group included six departments of general internal medicine, respiratory medicine, gastroenterology, cardiology, endocrinology, and palliative care. The psychiatry group corresponded to the department of psychiatry. The group of others included three departments of paediatrics, radiology, and emergency medicine.

This study was reported in accordance with the STROBE (strengthening the reporting of observational studies in Epidemiology) guidelines [21] for observational studies, and all data extractions and analyses were conducted in accordance with relevant guidelines and regulations.

Definition of medication use

HT was defined as prescriptions of estrogen and/or progestogen preparations. Three estrogen preparations (estriol [1960], conjugated estrogens [1964], and estradiol [1995]), four progesterone preparations (progesterone [1956], norethisterone [1957], medroxyprogesterone acetate [1963], and dydrogesterone [1965]), and four combination preparations (ethinylestradiol + norgestrel [1978], estradiol + norethisterone acetate [2009], ethinylestradiol + drospirenone [2010], ethinylestradiol + norethisterone [2016]) have been available for prescription at the study hospital (years in parentheses indicate approval in Japan) (Japan Pharmaceutical Information Centre 2026).

Concomitant medications were categorized into six groups: selective serotonin reuptake inhibitors (SSRIs)/serotonin-noradrenaline reuptake inhibitors (SNRIs), anxiolytic benzodiazepines, hypnotics, Kampo medicine, cardiometabolic drugs, and osteoporosis drugs. The SSRIs/SNRIs group included four SSRIs (escitalopram [2011], fluvoxamine [1999], paroxetine [2000], and sertraline [2006]); three SNRIs (duloxetine [2010], milnacipran [2000], and venlafaxine [2015]); and two related agents (mirtazapine [2009] and vortioxetine [2019]) in the study [22]. The anxiolytic benzodiazepines group included 14 drugs (alprazolam, bromazepam, chlordiazepoxide, clorazepate dipotassium, clonazepam, clobazepam, diazepam, ethyl loflazepate, etizolam, lorazepam, medazepam, mexazolam, oxazolam, and tofisopam) [22]. The hypnotics group included 10 hypnotic benzodiazepines (brotizolam, estazolam, flunitrazepam, flurazepam, haloxazolam, lormetazepam, nitrazepam,

quazepam, rilmazafone hydrochloride, and triazolam); three Z-drugs (eszopiclone [2012], zolpidem [2000], and zopiclone [1989]); and four newer non-benzodiazepine agents (lemborexant [2020], melatonin [2020], ramelteon [2010], and suvorexant [2014]) [23]. Although etizolam has been approved by the Japanese Ministry of Health, Labour, and Welfare for use as both an anxiolytic and a hypnotic benzodiazepine, it was classified as an anxiolytic benzodiazepine for the purposes of this analysis in this study. All benzodiazepines included in the analysis had been approved for prescription by 2000.

Concerning the Kampo medication group, three Kampo formulations: Kamishoyosan [1986], Keishibukuryogan [1986], and Tokishakuyakusan [1986] were selected for analyses, because they are frequently prescribed for relief of menopausal symptoms [10]. The cardiometabolic group included lipid-lowering agents (statin: atorvastatin [2000] and rosuvastatin [1998]), anti-hypertensives (amlodipine [1993]), antidiabetics (metformin [2010]), because previous studies have reported associations of menopausal symptoms with cardiovascular risks [12–14]. The osteoporosis group included bisphosphonate (alendronate [2001] and risedronate [2002]), selective estrogen receptor modulator (bazedoxifene [2010] and raloxifene [2004]), and vitamin D (alfacalcidol [1981] and eldecalcitol [2011]), because bone metabolism is one of the important factors affecting clinical course of menopausal disorders [15–19].

Data analysis

Statistical analyses were performed using SAS software version 9.4 (SAS Institute Inc., Cary, NC, USA) [24]. Two complementary analytical approaches were employed.

First, prescription-level analyses were conducted to describe annual prescribing patterns. The unit of analysis was the individual prescription. Annual prescribing prevalence of hormone therapy (HT) and six concomitant medication categories was calculated according to fiscal year. Temporal trends were evaluated using the Cochran–Armitage trend test.

Second, patient-level analyses were performed to identify characteristics associated with HT use. Women aged 45–60 years diagnosed with menopausal disorders (ICD-10: N95.1) were included in the patient-level analyses, which corresponds to the typical age range of menopausal transition reported in previous studies [1, 25]. Each woman contributed only one observation regardless of the number of prescriptions issued during the study period. Women were classified as HT users if they had received at least one HT prescription during the study period and as non-users otherwise. Simple and multiple logistic regression analyses were performed to evaluate associations between HT use and potential explanatory variables, including concomitant medication categories, department group, age group, inpatient or outpatient status at the first prescription, and 5-year calendar period. Adjusted odds ratios (ORs) and 95% confidence intervals (CIs) were calculated. All statistical tests were two-sided, and P values < 0.05 were considered statistically significant.

Overall, prescription-level trend analyses and patient-level regression analyses provided complementary information regarding long-term HT prescribing patterns.

This study was approved by the university ethics committee (approval no. 22-038-A) and was conducted in accordance with institutional guidelines.

Results

Overall characteristics of prescriptions

A total of 8,374,408 prescriptions for 180,226 female patients were identified during the study period, and overall prescription characteristics are shown in Table 1. The prescribing prevalence of HT as well as SSRIs/SNRIs, anxiolytic benzodiazepines, and hypnotics significantly decreased over the study period (all p for trend < 0.001). In contrast, the prescribing prevalence of Kampo medicine, cardiometabolic drugs, and osteoporosis drugs significantly increased over the study period (all p for trend < 0.001).

Table 1

Prescriptive analyses of hormone therapy (HT) drugs in relation to psychotropic, Kampo, osteoporosis, and cardiometabolic drugs in 180,226 female patients visiting a university hospital during 2002–2021.

Variables	Psychotropic drugs				Kampo medicine	Lifestyle-related drugs	
	HT drugs	SSRIs/SNRIs ^a	Anxiolytic BZPs ^b	Hypnotics ^c		Cardiometabolic drugs	Osteoporosis drugs
Department group							
Obstetrics and gynecology (n = 423,422)	11,993 (83.5%)	586 (0.4%)	2,473 (1.0%)	9,445 (2.9%)	4,646 (35.1%)	1,227 (0.6%)	517 (0.6%)
Surgery and related (n = 1,195,210)	153 (1.1%)	9,699 (5.2%)	21,327 (8.6%)	30,143 (9.2%)	676 (5.1%)	24,553 (11.6%)	58,945 (11.6%)
Internal medicine (n = 3,378,105)	348 (2.4%)	9,120 (6.2%)	50,026 (20.2%)	89,605 (27.2%)	2,044 (15.4%)	164,218 (77.3%)	21,991 (23.8%)
Psychiatry (n = 1,663,873)	379 (2.6%)	127,943 (86.7%)	161,947 (65.5%)	184,908 (56.2%)	2,913 (22.0%)	15,658 (7.4%)	3,852 (4.2%)
Others (n = 1,713,798)	1,497 (10.4%)	2,273 (1.5%)	11,418 (4.6%)	14,992 (4.6%)	2,982 (22.5%)	6,691 (3.2%)	7,259 (7.8%)
Age group, years old							
< 45 (n = 2,200,960)	6,121 (42.6%)	39,040 (26.5%)	77,385 (31.3%)	79,184 (24.1%)	5,430 (41.0%)	7,253 (3.4%)	7,994 (8.6%)
45–60 (n = 1,491,967)	4,364 (30.4%)	30,197 (20.5%)	59,803 (24.2%)	69,309 (21.1%)	5,278 (39.8%)	33,974 (16.0%)	7,740 (8.4%)
> 60 (n = 4,681,481)	3,885 (27.0%)	78,384 (53.1%)	110,003 (44.5%)	180,600 (54.9%)	2,553 (19.3%)	171,120 (80.6%)	76,830 (83.0%)
Hospitalization							
Outpatients (n = 5,608,261)	13,165 (91.6%)	113,207 (76.7%)	188,491 (76.3%)	219,440 (66.7%)	11,622 (87.6%)	144,450 (68.0%)	66,143 (71.5%)
Inpatients (n = 2,766,147)	1,205 (8.4%)	34,414 (23.3%)	58,700 (23.7%)	109,653 (33.3%)	1,639 (12.4%)	67,897 (32.0%)	26,421 (28.5%)
5-year course group							
2002–2006 (n = 1,991,498)	3,942 (27.4%)	36,076 (24.4%)	68,546 (27.7%)	90,061 (27.4%)	3,070 (23.2%)	35,234 (16.6%)	17,016 (18.4%)
2007–2011 (n = 2,186,435)	4,320 (30.1%)	40,193 (27.2%)	70,186 (28.4%)	88,517 (26.9%)	3,022 (22.8%)	52,962 (24.9%)	27,849 (30.1%)
^a SSRI = selective serotonin reuptake inhibitor, SNRI = serotonin noradrenaline reuptake inhibitor.							
^b BZP = benzodiazepine.							
^c Hypnotics included hypnotic benzodiazepines, Z-drugs, and related.							
^d Cochran–Armitage trend test, Statistics Z (P values)							

Variables	Psychotropic drugs				Kampo medicine	Lifestyle-related drugs	
	HT drugs	SSRIs/SNRIs ^a	Anxiolytic BZPs ^b	Hypnotics ^c		Cardiometabolic drugs	Osteoporosis drugs
2012–2016 (n = 2,147,590)	3,293 (22.9%)	33,578 (22.8%)	60,755 (24.6%)	81,131 (24.7%)	3,196 (24.1%)	59,793 (28.2%)	27,653 (29.9%)
2017–2021 (n = 2,048,885)	2,815 (19.6%)	37,774 (25.6%)	47,704 (19.3%)	69,384 (21.1%)	3,973 (30.0%)	64,358 (30.3%)	20,046 (21.7%)
Trend, statistics Z (P values) ^d	-17.56 (< 0.001)	-4.61 (< 0.001)	-70.29 (< 0.001)	-60.23 (< 0.001)	10.5 (< 0.001)	90.6 (< 0.001)	11.1 (< 0.001)
Total (n = 8,374,408)	14,370 (100%)	147,621 (100%)	247,191 (100%)	329,093 (100%)	13,261 (100%)	212,347 (100%)	92,564 (100%)
^a SSRI = selective serotonin reuptake inhibitor, SNRI = serotonin noradrenaline reuptake inhibitor.							
^b BZP = benzodiazepine.							
^c Hypnotics included hypnotic benzodiazepines, Z-drugs, and related.							
^d Cochran–Armitage trend test, Statistics Z (P values)							

Trends in HT and concomitant medications for menopausal disorders

Prescription-level analyses included 132,523 prescriptions issued to 1,167 women aged 45–60 years with menopausal disorders. Prescription-level findings are summarized in Table 2. When stratified by age group (< 50, 50–55, and > 55 years), HT prescribing prevalence was highest in the age group of 50–55 years.

Table 2

Prescription-based analyses among 132,523 prescriptions issued to 1,167 women aged 45–60 years with menopausal disorders.

Variables	Psychotropic drugs				Lifestyle-related drugs		
	HT drugs	SSRIs/SNRIs ^a	Anxiolytic BZPs ^b	Hypnotics ^c	Kampo medicine	Cardiometabolic drugs	Osteoporosis drugs
Department group							
Obstetrics and gynecology (n = 11,918)	2,280 (85.6%)	38 (1.0%)	337 (4.3%)	577 (6.4%)	1,575 (48.0%)	25 (1.0%)	57 (7.4%)
Surgery and related (n = 17,283)	48 (1.8%)	186 (4.7%)	974 (12.3%)	626 (6.9%)	279 (8.5%)	208 (8.2%)	369 (48.1%)
Internal medicine (n = 44,904)	85 (3.2%)	102 (2.6%)	1,154 (14.6%)	1,940 (21.5%)	429 (13.1%)	2,070 (81.2%)	277 (36.1%)
Psychiatry (n = 399,900)	100 (3.8%)	3,544 (90.2%)	5,055 (64.1%)	5,573 (61.7%)	600 (18.3%)	216 (8.5%)	46 (6.0%)
Others (n = 18,518)	151 (5.7%)	58 (1.5%)	372 (4.7%)	322 (3.6%)	400 (12.2%)	30 (1.2%)	19 (2.5%)
Age group (45–60 years old)							
<50 (n = 44,192)	674 (25.3%)	1,405 (35.8%)	2,957 (37.5%)	3,088 (34.2%)	1,185 (36.1%)	622 (24.4%)	290 (37.8%)
50–55 (n = 49,672)	1,111 (41.7%)	1,509 (38.4%)	2,675 (33.9%)	3,492 (38.6%)	1,413 (43.0%)	955 (37.5%)	271 (35.3%)
>55 (n = 38,658)	879 (33.0%)	1,014 (25.8%)	2,260 (28.6%)	2,458 (27.2%)	685 (20.9%)	972 (38.1%)	207 (27.0%)
Hospitalization							
Outpatients (n = 106,740)	2,479 (93.1%)	3,416 (87.0%)	6,831 (86.6%)	7,258 (80.3%)	3,032 (92.4%)	2,140 (84.0%)	646 (84.1%)
Inpatients (n = 25,783)	185 (6.9%)	512 (13.0%)	1,061 (13.4%)	1,780 (19.7%)	251 (7.7%)	409 (16.1%)	122 (15.9%)
5-year course group							
2002–2006 (n = 31,317)	1,171 (44.0%)	1,182 (30.1%)	2,329 (29.5%)	2,165 (24.0%)	737 (22.5%)	425 (16.7%)	101 (13.2%)
2007–2011 (n = 29,682)	372 (14.0%)	811 (20.7%)	1,978 (25.1%)	1,666 (18.4%)	765 (23.3%)	652 (25.6%)	206 (26.8%)
^a SSRI = selective serotonin reuptake inhibitor, SNRI = serotonin noradrenaline reuptake inhibitor.							
^b BZP = benzodiazepine.							
^c Hypnotics included hypnotic benzodiazepines, Z-drugs, and related.							
^d Cochran–Armitage trend test, Statistics Z (P values)							

Variables	Psychotropic drugs				Lifestyle-related drugs		
	HT drugs	SSRIs/SNRIs ^a	Anxiolytic BZPs ^b	Hypnotics ^c	Kampo medicine	Cardiometabolic drugs	Osteoporosis drugs
2012–2016 (n = 34,259)	585 (22.0%)	898 (22.9%)	2,102 (26.6%)	2,336 (25.9%)	787 (24.0%)	755 (29.6%)	263 (34.2%)
2017–2021 (n = 37,265)	536 (20.1%)	1,037 (26.4%)	1,483 (18.8%)	2,871 (31.8%)	994 (30.3%)	717 (28.1%)	198 (25.8%)
Trend test, statistics Z (P values) ^d	-18.55 (< 0.001)	-7.25 (< 0.001)	-19.25 (< 0.001)	6.07 (< 0.001)	1.86 (0.032)	4.85 (< 0.001)	3.49 (< 0.001)
Total (n = 132,523)	2,664 (100%)	3,928 (100%)	7,892 (100%)	9,038 (100%)	3,283 (100%)	2,549 (100%)	768 (100%)
^a SSRI = selective serotonin reuptake inhibitor, SNRI = serotonin noradrenaline reuptake inhibitor.							
^b BZP = benzodiazepine.							
^c Hypnotics included hypnotic benzodiazepines, Z-drugs, and related.							
^d Cochran–Armitage trend test, Statistics Z (P values)							

The annual prevalence of HT use significantly decreased over the study period (p for trend < 0.001). In contrast, the use of Kampo medicine showed a modest increasing trend, whereas the use of psychotropic medications, including SSRIs/SNRIs, anxiolytic benzodiazepines, and hypnotics, did not increase in parallel with the decline in HT (Table 2). Prescription-level annual trends of HT, psychotropic drugs (e.g., SSRIs/SNRIs), Kampo medicine, and lifestyle-related drugs (e.g., cardiometabolic drugs) are presented in Fig. 1.

Comparison between HT (+) and HT (-) groups

Among the 1,167 women, 268 (23.0%) received at least one HT prescription during the study period. Patient-level comparisons between women who had ever received HT and those who had never received HT are presented in Table 3. Significant differences were observed in concomitant medication use (i.e., “anxiolytic benzodiazepines, hypnotics, Kampo medicine, cardiometabolic drugs, and osteoporosis drugs” vs “others”) and clinical characteristics (i.e., department group: “obstetrics and gynecology, surgery and related, internal medicine, and psychiatry” vs “others”; age group: “<50 and 50–55 years” vs “>55 years”; patient group: “outpatients” vs “inpatients”; and 5-year course group: “2002–2006, 2007–2011, and 2012–2016” vs “2017–2021”) between the two groups in univariable analysis. Patient-level multivariable logistic regression identified several characteristics independently associated with ever receiving HT. Kampo medication was significantly more likely to be prescribed in the HT (-) group than in the HT (+) group, after adjusting for age group, department group, inpatient/outpatient status, and 5-year course group, (Table 3).

Table 3

Comparisons of prescription patterns according to HT exposure status among 1,167 women with menopausal disorders.

	Group comparison ^a		Odds ratio [95% C.I.] of logistic regression analysis ^b	
	HT (+) groups	HT (-) groups	Univariate	Multivariate
Prescriptions except HT drugs, n (%)				
Psychotropic drugs:				
SSRIs, SNRIs, and related	847 (3.0%)	3,081 (3.0%)	1.005 [0.930, 1.086]	0.829 [0.765, 0.899]
Anxiolytic BZPs	1,780 (6.3%)	6,112 (6.0%)	1.064 [1.007, 1.124]	0.967 [0.914, 1.024]
Hypnotics	2,383 (8.4%)	6,655 (6.6%)	1.309 [1.246, 1.374]	1.131 [1.074, 1.190]
Kampo medicine	738 (2.6%)	2,545 (2.5%)	1.060 [1.246, 1.374]	0.838 [0.768, 0.915]
Lifestyle-related drugs:				
Cardiometabolic drugs	363 (1.3%)	2,186 (2.2%)	0.607 [0.542, 0.679]	0.619 [0.552, 0.693]
Osteoporosis drugs	191 (0.7%)	577 (0.6%)	1.210 [1.026, 1.426]	1.539 [1.298, 1.825]
Others	22,001 (77.7%)	80,400 (79.2%)	Reference	Reference
Department group				
Obstetrics and gynecology	3,153 (11.1%)	6,485 (6.4%)	2.429 [2.293, 2.573]	2.210 [2.081, 2.346]
Surgery and related	2,079 (7.4%)	15,156 (14.9%)	0.685 [0.645, 0.728]	0.653 [0.615, 0.694]
Internal medicine	9,949 (35.2%)	34,870 (34.3%)	1.426 [1.363, 1.491]	1.464 [1.399, 1.533]
Psychiatry	10,059 (35.5%)	29,741 (29.3%)	1.690 [1.616, 1.767]	1.677 [1.599, 1.758]
Others	3,063 (10.8%)	15,304 (15.1%)	Reference	Reference
Age group (45–60 years old)				
<50	10,099 (35.7%)	33,420 (32.9%)	1.694 [1.634, 1.756]	1.587 [1.530, 1.646]
50–55	12,484 (44.1%)	36,077 (35.5%)	1.939 [1.873, 2.008]	1.883 [1.818, 1.951]
>55	5,720 (20.2%)	32,059 (31.6%)	Reference	Reference
^a Prescriptions in 268 patients receiving any HT were categorized as HT (+), and those in the remaining 899 patients receiving no HT were categorized as the HT (-) group.				
^b Dependent variable: HT (+) = 1; HT (-) = 0.				

	Group comparison ^a		Odds ratio [95% C.I.] of logistic regression analysis ^b	
	HT (+) groups	HT (-) groups	Univariate	Multivariate
Hospitalization				
Outpatients	21,648 (76.5%)	82,613 (81.4%)	0.746 [0.723, 0.770]	0.749 [0.725, 0.774]
Inpatients	6,655 (23.5%)	18,943 (18.7%)	Reference	Reference
5-year course group				
2002–2006	7,139 (25.2%)	23,007 (22.7%)	1.101 [1.062, 1.142]	1.270 [1.223, 1.318]
2007–2011	6,308 (22.3%)	23,002 (22.7%)	0.973 [0.938, 1.010]	1.102 [1.060, 1.145]
2012–2016	6,783 (24.0%)	26,891 (26.5%)	0.895 [0.863, 0.928]	0.933 [0.899, 0.968]
2017–2021	8,073 (28.5%)	28,656 (28.2%)	Reference	Reference
Total	28,303 (100%)	101,556 (100%)		
^a Prescriptions in 268 patients receiving any HT were categorized as HT (+), and those in the remaining 899 patients receiving no HT were categorized as the HT (-) group.				
^b Dependent variable: HT (+) = 1; HT (-) = 0.				

Discussion

This retrospective database study described long-term prescribing patterns of HT and major concomitant medication categories among women with menopausal disorders in a Japanese university hospital over a 20-year period. Consistent with international reports following publication of the Women's Health Initiative (WHI) trial, HT prescribing declined significantly during the study period [3–6, 26]. Our findings extend previous reports [27] by providing long-term real-world prescribing data from routine clinical practice in Japan while simultaneously describing trends in several clinically relevant medication categories.

An important observation was that psychotropic medication prescribing did not increase in parallel with declining HT use. This finding suggests that changes in HT prescribing were not accompanied by comparable changes in prescriptions for antidepressants, anxiolytics, or hypnotics within this hospital population. However, because prescription indications and symptom severity were unavailable, these findings should not be interpreted as evidence that psychotropic medications were or were not used as substitutes for HT.

We also observed a modest increase in prescriptions for Kampo medicine during the study period. Kampo formulations are widely incorporated into menopausal care in Japan and are recommended in several domestic clinical settings [10, 11]. Although the temporal increase in Kampo prescribing was observed alongside declining HT use, the present observational study cannot determine whether Kampo medicine replaced HT or was prescribed for different clinical indications. Future multicentre studies incorporating symptom severity and treatment indications will be necessary to clarify these relationships.

Patient-level multivariable analysis identified several characteristics associated with ever receiving HT. For example, cardiometabolic drug use was independently associated with a lower likelihood of receiving HT. These associations should be interpreted as descriptive rather than causal because treatment selection is influenced by multiple clinical factors that were not available in the present database, including symptom severity, contraindications, and patient preferences [28, 29].

The present study has several strengths. First, the database included more than 8.3 million prescriptions collected over two decades using a comprehensive electronic medical record system. Second, complete prescription records minimized the possibility of missing prescribing information. Third, prescription trends were evaluated together with patient-level analyses, providing complementary information on long-term prescribing practices.

Several limitations should be acknowledged before stating conclusions. First, this was a single-centre study conducted at a tertiary university hospital, and prescribing patterns may differ from those in primary care or community hospitals. Second, only women with ICD-10-coded menopausal disorders were included in the primary analyses; therefore, women receiving HT for other indications may not have been captured. Third, the database contained prescription records but did not include symptom severity, treatment indications, adherence, or patient preferences. Finally, because of the observational study design, causal relationships between HT and concomitant medication use cannot be inferred.

Conclusions

This study provides long-term real-world evidence describing prescribing patterns of hormone therapy and concomitant medications among women with menopausal disorders in Japan. HT prescribing declined over the study period, whereas prescribing patterns of concomitant medications varied according to medication category. These findings contribute to understanding routine clinical practice and may inform future multicentre and population-based studies evaluating pharmacological management of menopausal symptoms.

Declarations

CRedit authorship contribution statement

Mutsuhiro Nakao: Conceptualization, Data curation, Funding acquisition, Methodology, Project administration, Resources, Writing—original draft, Writing—review & editing. **Hokuto Morohoshi:** Data curation, Methodology, Project administration, Resources, Writing—original draft. **Yumiko Kurata:** Conceptualization, Writing—original draft, Writing—review & editing. **Akiou Nakamura:** Conceptualization, Data curation, Funding acquisition, Methodology, Writing—review & editing.

Ethics approval and consent to participate

This study was approved by the Ethics Committee of Showa Medical University (approval No. 22-038-A) and was conducted in accordance with the Declaration of Helsinki and relevant institutional guidelines. Because this was a retrospective observational study using anonymized electronic medical records, the requirement for individual written informed consent was waived by the Ethics Committee. Information regarding the study was disclosed through an institutional opt-out procedure.

Financial Disclosures

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Declaration of Competing Interest

The authors report no conflicts of interest in this work.

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Data availability

The datasets generated and analyzed during the current study are not publicly available because they contain potentially identifiable patient information but are available from the corresponding author upon reasonable request.

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Figures

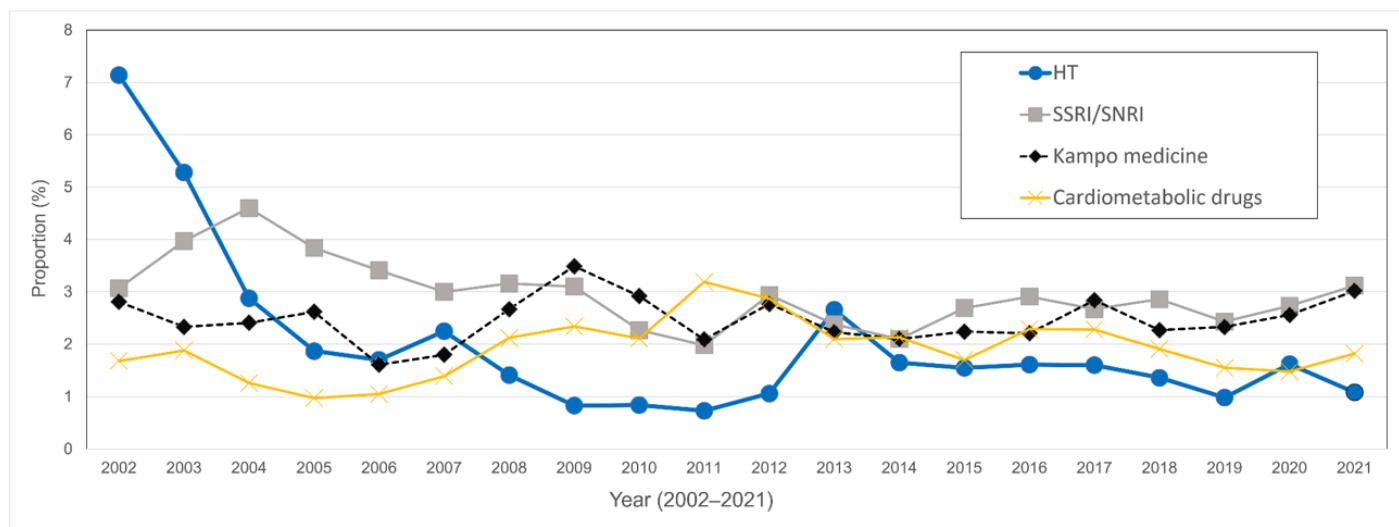


Figure 1

Long-term trends in hormone therapy (HT) and selected concomitant medications from 2002 to 2021.

Annual proportions of prescriptions are shown for HT and representative concomitant medication categories among women aged 45–60 years with menopausal disorders. HT use declined significantly over the study period, whereas Kampo medicine showed a modest increase. SSRIs/SNRIs use did not increase in parallel with the decline in HT.