Direct and Indirect Costs of Women Diagnosed With Menopause Symptoms

Nathan L. Kleinman, PhD, Nicholas J. Rohrbacker, PhD, Andrew G. Bushmakin, MS, Jennifer Whiteley, EdD, MSc, MA, Wendy D. Lynch, PhD, and Sonali N. Shah, RPh, MPH, MBA

Objective: To quantify employee burden of those diagnosed with menopause symptoms. Methods: This regression-based study analyzed 2001-to-2010 medical, pharmacy, sick leave, disability, workers' compensation, and productivity data of large US employers. A cohort of employed women with diagnosed menopause symptoms (DMS), aged more than 40 years, were identified using medical claims International Classification of Diseases, Ninth Revision, Clinical Modification codes 627.xx. Control employees were propensity matched on age, employer, plan enrollment length, and enrollment end date. Results: The study included 17,322 in each cohort. Employees with DMS had significantly higher medical (\$4315 vs \$2972, P < 0.001), pharmacy (\$1366 vs \$908, P < 0.001), sick leave costs (\$647 vs \$599, P < 0.001), and sick leave days (3.57 vs 3.30, P < 0.001). Employees with DMS had 12.2% (P = 0.007) lower hourly productivity and 10.9% (P = 0.014) lower annual productivity than controls. Conclusions: Although all women experience menopause, women with DMS have significantly higher utilization and productivity burdens.

ecause menopause is considered a normal aspect of ag-B ing, menopausal and perimenopausal symptoms are underrecognized as a disruptive health condition. Nevertheless, its impact includes many uncomfortable and difficult challenges, including sleep problems, depression, night sweats, and hot flashes. These symptoms can be frequent, consistent and endure for many years. Approximately two million US women will reach the age of menopause onset each year for the next decade.1

The time frame leading up to menopause, during which ovarian hormone production and menstruation decline, is termed perimenopause and begins at a median age of 47.5 years. Menopause is defined as the absence of menstrual flow, amenorrhea, for 12 consecutive months, ending at a median age of 52.4 years.² Many women experience significant adverse health symptoms during perimenopause, menopause and into postmenopause. These can include hot flashes and night sweats (vasomotor symptoms),^{3–5} low self-rated health,³ sexual difficulties,⁴ insomnia,^{3–5} anxiety,⁶ and depression.^{6–8} It is estimated that half to three fourths (or more) of perimenopausal and postmenopausal women experience menopause symptoms.^{4,9-11} Increased prevalence of these symptoms can last 6 to 10 years or more after menopause.^{3,10} In one study, 40% of women had hot flashes for more than 7 years, and 15% had them for more than 15 years.¹²

For some women, the symptoms are severe. A 2009 study by Reed et al⁶ indicates that 42% of perimenopausal or menopausal

Medicine

DOI: 10.1097/JOM.0b013e3182820515

women not using hormone therapy had moderate to severe vasomotor symptoms in the 4 weeks prior to the survey, and 25% had moderate to severe vaginal dryness and/or pain within the prior 4 weeks. Among women experiencing hot flashes, Kronenberg¹² reported that 48% to 63% had predominantly moderate to severe hot flashes. In a 2007 study, Williams et al⁹ report that 47% of perimenopausal women and 62% of postmenopausal women have sought care from a health care professional for their menopause symptoms.

After the 2002 Women's Health Initiative (WHI) study¹³⁻¹⁵ was released, many women were confused regarding who should take hormone therapy. Many women depended on their doctor for guidance, whereas others explored the use of alternative therapies for menopause symptoms, such as massage therapy, herbal supplements, and acupuncture,9 which are often managed in chiropractic care offices. These alternative therapies have been found in 22% to 53% of menopausal women and have had mixed results.5,16-18 Many women have tried both hormone therapies and alternative treatments without complete relief of symptoms.⁹

Given that more than 26.5 million employed women in the United States are 45 to 64 years old,¹ an estimated 15 to 20 million employees in the United States currently experience menopause symptoms, which suggests that the potential burden of menopause symptoms on employers may be significant. Botteman et al¹⁹ found that the drug cost, therapy initiation, and care for bleeding/spotting to be \$681 to \$848 per year for hormone management, and Kjerulff et al²⁰ estimated \$483 in incremental total health expenditures per woman with diagnosed menopause symptoms. Using self-report questionnaires, several studies found negative impacts of menopause symptoms on quality of life, including greater impairment while working.^{21–23} Currently, no studies were identified that quantified the direct and indirect costs of menopause symptoms from a societal or an employer perspective.

The primary objective of the current study was to evaluate the incremental economic burden of employees who sought care and were diagnosed with menopause symptoms (DMS) when compared with matched female employees who were not diagnosed with menopause symptoms and who may or may not have sought care. The employee burden includes direct costs (medical, pharmacy), indirect costs (sick leave, short- and long-term disability, and workers' compensation), work absence days, productivity output loss, and turnover. A secondary objective was to compare the difference in prevalence of selected comorbidities (including depression, anxiety, insomnia, and osteoporosis), prescription medications, and procedures between a cohort of employed women with DMS and a matched cohort of employed women without DMS.

METHODS

Research Population and Cohort Definitions

Patients were selected from the Human Capital Management Services Research Reference Database (RRDb), which included nearly 750,000 employees, dispersed across the United States, whose medical, drug, work absence claims, salary, job, and demographic data are maintained in the Research Reference Database at an employee level. These data also contain electronically measured objective productivity data for a subpopulation. This study includes data

From the HCMS Group LLC (Dr Kleinman, Dr Rohrbacker, Ms Lynch), Cheyenne, Wis; WellPoint, Inc (Dr Rohrbacker), Indianapolis, Ind; and Pfizer Inc (Mr Bushmakin, Dr Whiteley, Ms Shah), New York, NY.

This study was sponsored by Pfizer Inc. Nathan Kleinman, Nicholas Rohrbacker, and Wendy Lynch were employees of HCMS Group LLC, an affiliate of the Research and Education on Health as Human Capital Foundation, who were paid consultants to Pfizer in connection with the study and the development of this manuscript. Andrew Bushmakin, Jennifer Whiteley, and Sonali Shah are employees of Pfizer Inc.

Address correspondence to: Nathan L. Kleinman, PhD, 415 W 17th Street, Suite 250, Cheyenne, WY 82001 (nathan_kleinman@hcmsgroup.com). Copyright © 2013 by American College of Occupational and Environmental

from 2001 to 2010 that were de-identified to comply with Health Insurance Portability and Accountability Act requirements.

Female employees with diagnoses for menopausal and postmenopausal disorders (primary, secondary, or tertiary ICD-9-CM [International Classification of Diseases, Ninth Revision, Clinical Modification] codes of 627.xx) in their health insurance claims data were defined to be the DMS cohort. The control cohort comprised female employees without menopause symptom diagnoses that were propensity-score matched one-to-one to the DMS cohort on birth year, employer, length of health plan enrollment period, and the year enrollment ended.

Index dates for the DMS cohort were defined as the date of the first menopause symptom *ICD-9* diagnosis. Each employee in the control cohort was assigned the same index date as the corresponding matched employee from the DMS cohort.

To be included in the study, employees were required to have at least 90 days of health plan enrollment after the index date and be at least 40 years old on the index date. Also, employees with any malignant nonmelanoma neoplasm diagnoses (*ICD-9* codes 140.xx-172.xx or 174.xx-209.39) were excluded because they may have hot flashes as a side effect of treatment management. Employees were also excluded if their index dates were less than 6 months before the last date their employer supplied data to Human Capital Management Services (to ensure sufficient claims run-out).

Definition of Outcomes

Descriptive characteristics compared between the DMS and control cohorts included age, marital status, race, annual salary, tenure (years with employer), exempt status (exempt employees are not eligible for overtime pay), full-time/part-time status, region (based on the first digit of the employee's Zip code), Charlson Co-morbidity Index²⁴ (calculated during the 3 months prior to the index date), and number of quarters of health plan enrollment (length of the employee's measurement period).

The current study compared the post-index prevalence of selected comorbidities, procedures, and medications between the two employee cohorts by age band. Comorbidities studied were identified in medical claims data using primary ICD-9 codes for major depression (296.2x-296.3x, or 311.xx), other depression (298.0x, 300.4x, or 309.0x-309.1x), anxiety (293.84, 300.0x-300.3x, or 309.21), insomnia (307.41, 307.42, 307.49, 327.0x, or 780.52), osteoporosis (733.0x), vertebral column fracture (805.xx), and hip fracture (820.xx). Medication classes examined were hypnotics, selective serotonin reuptake inhibitors (SSRIs), serotonin-norepinephrine reuptake inhibitors (SNRIs), and bisphosphonates. The percent of employees receiving certain procedures during the post-index period was calculated using current procedural terminology codes. These procedures included chiropractic care (98940-98943), acupuncture (97780, 97781, or 97810-97814), and hysterectomies (58150-58294, 58541-58544, 58550, or 58552-58554).

The following employee-related outcomes were also compared between cohorts (annualized over each employee's post-index enrollment period): medical and drug costs (employer-paid amounts for all medical and prescription pharmacy claims), sick leave costs and absence days (actual payments made to employees and number of days absent as detailed in payroll data), short-term disability (STD) and long-term disability (LTD) costs and absence days (actual payments made to employees and number of days absent during STD and LTD leaves as detailed in disability insurance carrier data), workers' compensation costs and absence days (actual payments for workrelated injury medical and pharmacy claims and payments made to employees as salary replacement while absent due to a work-related injury, and number of days absent during a workers' compensation leave from workers' compensation claims data), turnover measured as the percent of employees in the study (with available termination information from human resource data) who terminated during

the 3- to 15-month period after the index date, and work output employee productivity data (electronically measured work output data for a subset of employees in the form of number of units of work performed per person each day and number of hours worked each day). Productivity data were converted to hourly productivity (number of units of work performed per hour worked—productivity while at work) and annual productivity (number of units of work performed per year—includes the effect of absence on productivity). Cost values were adjusted for inflation to 2010 US dollar values using medical services, prescription drug, and all consumer goods' consumer price indices.²⁵

Statistical Analysis

Comparisons of descriptive characteristics were made using t tests for continuous variables and chi-square tests for discrete variables. Prevalence values were compared using chi-square tests.

Each type of cost and work absence was compared between cohorts using two-part repeated-measures regression modeling with first-order autoregressive covariance structures. In the first part, logistic regression was used to model the likelihood of having any costs or absence days during each quarter after the index date. The second part employed generalized linear regression modeling with gamma distribution and log link function to model the amount of cost or absence days in the quarter for those employees with any costs or days in the quarter. The estimates from the two parts were then multiplied to obtain estimated quarterly costs or days for all employees. Quarterly values were then annualized. The regression models controlled for any remaining differences between the matched DMS and control cohorts using the patient characteristic variables.

Turnover was compared using logistic regression modeling, and productivity output was compared using repeated-measures generalized linear regression modeling as in the second-part models described earlier. These models controlled for the same variables as in the cost and absence models.

RESULTS

Employee Selection and Descriptive Statistics

Of the 293,763 female employees in the database, there were 31,514 with menopause symptom diagnoses (*ICD-9* codes of 627.xx) in medical claims data, and of that group, 21,593 were from plans providing enrollment information and had at least 90 days of health plan enrollment following the index date of the diagnosis. Of this group, 20,075 did not have malignant cancer diagnoses in the claims data, and of these, 18,246 were at least at the age of 40. Finally, 17,322 had index dates that were at least 6 months before the end of data availability.

The demographic characteristics of the two cohorts were similar due to the propensity matching (Table 1). Employees were 51 years old on average, 42% to 44% were married, and the majority were white. The employees had been with their employer for approximately 12 years on average and had an average of more than 2 years (8 quarters) of employment and health plan enrollment after the index date over which outcomes were measured. Also, the CCI was similar between the cohorts. Finally, the groups were not significantly different in geographical location or ethnicity.

Prevalence of Conditions, Medication Use, and Procedures

Overall, four of the common menopause-related comorbidities (major depression, other depression, anxiety, and insomnia) began with high prevalence rates between ages 40 and 44 and then decreased as the age category reached 65+ (Fig. 1). The DMS cohort had significantly higher prevalence rates of major depression, insomnia, and osteoporosis in the younger age groups (between ages 40 and 59) compared with the control cohort (each P < 0.05), which

© 2013 American College of Occupational and Environmental Medicine

Variable	Employees With Diagnosed Menopause Symptoms (N = 17,322)	Control Cohort (N = 17,322)		
Mean age (SE), y	51.0 (0.0)	51.2 (0.0)		
Age, %				
40–44	14.1	15.2		
45–49	30.9	30.0		
50-54	33.4	30.9		
55–59	15.0	15.1		
60–64	5.5	6.9		
65+	1.1	1.9		
Married, %	44.2	41.8		
Not married, %	36.8	37.5		
Missing marital status, %	19.0	20.7		
Annual salary ^a (SE), US \$	53,350 (252)	51,998 (720)		
Tenure (SE), y	12.3 (0.1)	11.5 (0.1)		
Exempt ^b , %	31.6	28.4		
Part-time ^c , %	6.3	7.0		
Charlson index (SE)	0.1 (0.0)	0.1 (0.0)		
Number of quarters in eligibility period (SE)	8.4 (0.1)	8.3 (0.1)		

TABLE 1. Descriptive Statistics for Employees With and

 Without Menopause Symptom Diagnoses

N indicates number of employees; SE, standard error.

^a N = 17,238 for employees with menopause symptom diagnoses, and N = 17,133 for employees without diagnosis.

^b Exempt employees are salaried (not hourly) and are not eligible for overtime pay. ^c N = 17,297 for employees with menopause symptom diagnoses, and N = 17,203 for employees without diagnosis. is in the range of the peri- and postmenopausal cycle. The other depression and anxiety prevalence rates were significantly higher in the DMS cohort up to the age group of 50 to 54 years (each P < 0.05). This figure shows that both groups had symptoms during this time period; however, those diagnosed with menopause symptoms had more comorbidities during the menopausal phase. The prevalence of osteoporosis had the opposite trend compared with the other comorbidities; as age increased, so did the prevalence, up to the 60- to 64-year age category.

Prevalence values for vertebral fractures and hip fractures were quite small (between 0% and 1%). The only significant difference in fracture prevalence between the DMS and control cohorts was for vertebral fractures (0.21% and 0.06%, respectively, P < 0.05) in the 50- to 54-year age range.

Figure 2 shows that the prevalence trends of medications were similar to those of the comorbidities. There was a higher prevalence rate of use of the SSRIs, SNRIs, and selected non-benzodiazepine hypnotics (SNHs) in the younger age categories, and as age increased the usage decreased. For the bisphosphonates, as the age increased, the medication use also increased up to the 60- to 64-year age category. The DMS cohort had significantly higher medication use than controls for SSRIs, SNRIs, SNHs, and bisphosphonates between the ages of 40 and 59 years (P < 0.05), and for SSRIs, SNHs, and bisphosphonates between the ages of 60 and 64 years (P < 0.05). There was no significant difference between the two cohorts for use of these medications in the 65^+ age category.

In Figure 3, both groups had greater rates of chiropractic services (4% to 14%) than acupuncture (1% to 2%) or hysterectomies (0% to 6%). Women with DMS were significantly more likely to have chiropractic and acupuncture procedures in the younger age categories of menopause than the control cohort (for chiropractic procedures, P < 0.05 between DMS and control for all age groups of people younger than 60 years; for acupuncture procedures, P < 0.05 between DMS and control for all age groups rates of hysterectomies than the control group in all age categories except 65⁺.



* Indicates a significant difference between the DMS and Control cohorts

FIGURE 1. Post-index prevalence of comorbid conditions for women with and without diagnosed menopause symptoms.

© 2013 American College of Occupational and Environmental Medicine



* Indicates a significant difference between the DMS and Control cohorts





* Indicates a significant difference between the DMS and Control cohorts

FIGURE 3. Post-index prevalence of procedure types for women with and without menopause symptom diagnoses.

Adjusted Cost, Absence, Productivity, and Turnover Outcomes

On the basis of regression analysis, Table 2 contains the annual estimates of adjusted health benefit cost, work absence, work output, and turnover rates for the DMS and control cohorts. The DMS cohort had significantly higher medical costs (\$4315 vs \$2972, P < 0.0001), prescription drug costs (\$1366 vs \$908, P < 0.0001), and sick leave

costs (\$647 vs \$599, P < 0.0001) than the control cohort. The DMS cohort also had significantly more sick leave days per year (3.57 vs 3.30 days, P < 0.0001) than the control cohort. Turnover rates were nearly significantly lower in the DMS cohort (P = 0.0573). Both hourly (14.1 vs 16.1 units of work, P = 0.0072) and annual (21,176 vs 23,775 units of work, P = 0.0135) productivity rates were significantly lower in the DMS cohort. The significant differences

© 2013 American College of Occupational and Environmental Medicine

Category	Employees With Diagnosed Menopause Symptoms		Control Cohort		Comparisons		
	N	Adjusted Mean	N	Adjusted Mean (A)	Difference (B)	Р	Percent Difference (100 × B/A)
Medical	17,322	\$4,315	17,322	\$2,972	\$1,343	< 0.0001	45.2%
Drug	17,322	\$1,366	17,322	\$908	\$457	< 0.0001	50.3%
Sick leave	6,558	\$647	6,410	\$599	\$48	< 0.0001	8.0%
Short-term disability	9,755	\$479	9,715	\$353	\$126	0.1510	35.7%
Long-term disability	14,112	\$73	14,079	\$46	\$26	0.9082	56.5%
Workers' compensation	16,098	\$175	16,118	\$134	\$42	0.7740	31.3%
Total costs (sum of above)		\$7,055		\$5,012	\$2,042		40.7%
Sick leave days	6,558	3.57	6,410	3.30	0.27	< 0.0001	8.2%
Short-term disability days	9,755	3.42	9,715	2.57	0.85	0.1750	33.1%
Long-term disability days	14,112	1.26	14,079	0.94	0.33	0.9393	35.1%
Workers' compensation days	16,098	0.27	16,118	0.21	0.06	0.9294	28.6%
Total days (sum of above)		8.53		7.03	1.50		21.3%
Annual turnover	7,048	10.9%	6,978	11.4%	-0.5%	0.0573	-4.4%
Units of work performed per hour worked	318	14.1	286	16.1	-2.0	0.0072	- 12.4%
Units of work performed per year	318	21,176	286	23,775	-2,600	0.0135	-10.9%

TABLE 2. Adjusted Annual Health Benefit Cost, Work Absence, Work Output, and Turnover Rates

between cohorts ranged from 8% to 50% of the control cohort's outcomes.

DISCUSSION

Summary

All women will go through the menopause cycle and have some level of symptoms. The severity and the length of menopause symptoms vary, but many women will experience moderate to severe symptoms for which they will seek medical or alternative treatments. The consistency of comorbidity, medication, and procedure trends in both the DMS and control cohorts suggests that women do have symptoms but they may vary in severity and in their decision to seek care.

Because documentation of symptoms, diagnoses, and treatments is not consistently applied in health care claims, there is inherent ambiguity in classifying those actively managing problems associated with menopause. Under the assumption that all women experience the phenomenon of menopause, the distinction here is between those who actively sought treatment and were classified as such versus those who did and did not seek care and were not classified with a menopause symptom diagnosis. The control group may have sought care but not enough for the physician to warrant a diagnosis in his or her view.

Although the distinction relies on coding, it is of note that most (83%) of the women in the DMS cohort did not receive their initial menopause symptom diagnosis at the same time as an annual well-woman examination. This means the majority of the women had a separate physician visit request beyond the annual visit to discuss their postmenopausal symptoms, an indication that symptom severity could have lead most DMS women to seek care. Furthermore, because the methodology likely under-indentifies cases of menopause symptoms (meaning some of those in the control group are being treated), the results found herein are a conservative estimate of the difference between more and less severe menopause symptoms. A modest percentage of the control group (23.8%) received prescriptions for menopause-related hormone therapy at some point in time (before or after the index date). A sensitivity analysis was performed by excluding employees with menopause-related prescriptions from consideration in the control cohort and then recreating and rematching the control cohort. Subsequent regression comparisons found that cost and absence day results for the new control cohort were very similar to those in the original study. Productivity results were qualitatively similar, but no longer statistically significant, and turnover rates in the new control group were significantly greater.

No prior studies were found in the literature that quantified absence costs, lost time from work, or productivity loss associated with menopause symptoms from a societal or an employer perspective. Two studies were found that quantified aspects of medical and pharmaceutical costs. Botteman et al¹⁹ quantified costs of hormone treatment (cost of drug acquisition, therapy initiation, and care for bleeding/spotting) at \$681 to \$848 per year, and Kjerulff et al²⁰ estimated \$483 in incremental total health expenditures per woman with diagnosed menopause symptoms.

The current research encompasses a more comprehensive picture of the economic and work-related burden of these symptoms than has been described before and demonstrates the need for both physicians and employers to manage and support women reaching this phase of life. Even though all women do not seek care, the majority will need support in managing their symptoms. Productivity was significantly (11% to 12%) lower in the DMS group than in the control group, demonstrating the direct impact on work output.

Despite the significant burden of menopause symptoms and the very large number of women affected by these symptoms, the optimal course to follow for treatment is not clear. Given the initial WHI study¹³ and other studies,^{26,27} the subsequent WHI reanalysis²⁸ indicating some hormone therapy safety for certain women, various studies showing hormone therapy efficacy,^{29,30} and the mixed results found for alternative treatments,¹⁸ many women and physicians are unsure about therapy and management of symptoms.⁹ Further study of treatment options is needed.

This uncertainty surrounding treatment of symptoms and the fact that all women go through menopause highlight the need for increased communication between women and their physicians. This dialog could be more systematically recommended during a woman's annual examination, for all women nearing the median age of symptom onset.

LIMITATIONS

This analysis has limitations that are common to retrospective database studies, including limited pre-index information. Some women in the study may have reached the age of 40 before their employer began providing data to the Research Reference database or before beginning employment with that employer (although average tenure was 12 years as of the index date). This leaves the possibility that, for some women in the DMS cohort, the index date was not their initial diagnosis of menopause symptoms, and that some women in the control cohort may have had a diagnosis prior to data becoming available. Also, employees with serious but undiagnosed menopause symptoms may be in the control cohort, making the estimates of the incremental costs and other outcomes measured herein more conservative. The level of menopause symptom severity is unknown as well.

This is a cross-sectional analysis comparing two groups with missing information. Therefore, we cannot infer any causal relationships, and unmeasured confounding variables may explain some of the observed differences in outcomes between cohorts.

CONCLUSIONS

Women with diagnosed menopause have higher costs than matched undiagnosed women (approximately 40% higher overall) stemming not only from medical and pharmacy utilization but also from work absence. In addition, work productivity output was 11% to 12% lower for diagnosed women. Given the high prevalence of menopause symptoms in employed populations and the significant impact of these symptoms, this study emphasizes the need for employers to ensure appropriate care is available. Also, the additional comorbidity of women with diagnosed symptoms adds complexity to the clinical management of the symptoms themselves. Both the additional cost and complexity highlight the need for better management of menopause symptoms to reduce the associated burden.

REFERENCES

- United States Department of Labor. Bureau of Labor Statistics Current Population Survey. Available at: http://data.bls.gov/pdq/querytool.jsp?survey=ln. Accessed May 9, 2011.
- Umland EM. Treatment strategies for reducing the burden of menopauseassociated vasomotor symptoms. J Manag Care Pharm. 2008;14:S14–S19.
- Berecki-Gisolf J, Begum N, Dobson AJ. Symptoms reported by women in midlife: menopausal transition or aging? *Menopause*. 2009;16:1021–1029.
- NIH State-of-the-Science Conference Statement on management of menopause-related symptoms. NIH Consensus State-of-the-Science Statements. 2005. 21-23;22:1–38.
- Keenan NL, Mark S, Fugh-Berman A, et al. Severity of menopausal symptoms and use of both conventional and complementary/alternative therapies. *Menopause*. 2003;10:507–515.
- Reed SD, Ludman EJ, Newton KM, et al. Depressive symptoms and menopausal burden in the midlife. *Maturitas*. 2009;62:306–310.
- Freeman EW, Sammel MD, Lin H, Nelson DB. Associations of hormones and menopausal status with depressed mood in women with no history of depression. *Arch Gen Psychiatry*. 2006;63:375–382.

- Joffe H, Hall JE, Soares CN, et al. Vasomotor symptoms are associated with depression in perimenopausal women seeking primary care. *Menopause*. 2002;9:392–398.
- Williams RE, Kalilani L, DiBenedetti DB, et al. Healthcare seeking and treatment for menopausal symptoms in the United States. *Maturitas*. 2007;58:348– 358.
- Utian WH. Psychosocial and socioeconomic burden of vasomotor symptoms in menopause: a comprehensive review. *Health Qual Life Outcomes*. 2005;3:47.
- Feldman BM, Voda A, Gronseth E. The prevalence of hot flash and associated variables among perimenopausal women. *Res Nurs Health*. 1985;8:261–268.
- Kronenberg F. Hot flashes: epidemiology and physiology. Ann N Y Acad Sci. 1990;592:52–86.
- Rossouw JE, Anderson GL, Prentice RL, et al. Risks and benefits of estrogen plus progestin in healthy postmenopausal women: principal results from the Women's Health Initiative randomized controlled trial. *JAMA*. 2002;288:321– 333.
- Buist DSM, Newton KM, Miglioretti DL, et al. Hormone therapy prescribing patterns in the United States. *Obstet Gynecol*. 2004;104:1042–1050.
- Hersh AL, Stefanick ML, Stafford RS. National use of postmenopausal hormone therapy: annual trends and response to recent evidence. *JAMA*. 2004;291:47–53.
- Newton KM, Buist DSM, Keenan NL, et al. Use of alternative therapies for menopause symptoms: results of a population-based survey. *Obstet Gynecol.* 2002;100:18–25.
- Gold EB, Bair Y, Zhang G, et al. Cross-sectional analysis of specific complementary and alternative medicine (CAM) use by racial/ethnic group and menopausal status: the Study of Women's Health Across the Nation (SWAN). *Menopause*. 2007;14:612–623.
- Pinkerton JV, Stovall DW, Kightlinger RS. Advances in the treatment of menopausal symptoms. *Women's Health*. 2009;5:361–384.
- Botteman MF, Shah NP, Lian J, et al. A cost-effectiveness evaluation of two continuous-combined hormone therapies for the management of moderate-to-severe vasomotor symptoms. *Menopause*. 2004;11: 343–355.
- Kjerulff KH, Frick KD, Rhoades JA, Hollenbeak CS. The cost of being a woman: a national study of health care utilization and expenditures for female-specific conditions. *Womens Health Issues*. 2007;17:13–21.
- Williams RE, Levine KB, Kalilani L, et al. Menopause-specific questionnaire assessment in US population-based study shows negative impact on healthrelated quality of life. *Maturitas*. 2009;62:153–159.
- Bolge SC, Balkrishnan R, Kannan H, et al. Burden associated with chronic sleep maintenance insomnia characterized by nighttime awakenings among women with menopausal symptoms. *Menopause*. 2010;17:80–86.
- Chedraui P, San Miguel G, Avila C. Quality of life impairment during the female menopausal transition is related to personal and partner factors. *Gynecol Endocrinol*. 2009;25:130–135.
- Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis. 1987;40:373–383.
- United States Department of Labor. Consumer price indices for medical services, prescription drugs, and all consumer goods. Available at: http://data.bls.gov/PDQ/outside.jsp?survey=cu. Accessed April 1, 2011.
- Hulley S, Grady D, Bush T, et al. Randomized trial of estrogen plus progestin for secondary prevention of coronary heart disease in postmenopausal women. *JAMA*. 1998;280:605–613.
- Beral V. Breast cancer and hormone-replacement therapy in the Million Women Study. *Lancet*. 2003;362:419–427.
- Rossouw JE, Prentice RL, Manson JE, et al. Postmenopausal hormone therapy and risk of cardiovascular disease by age and years since menopause. *JAMA*. 2007;297:1465–1477.
- AACE Menopause Guidelines Revision Task Force. American Association of Clinical Endocrinologists medical guidelines for clinical practice for the diagnosis and treatment of menopause. *Endocr Pract.* 2006;12: 315–337.
- The North American Menopause Society. Treatment of menopause-associated vasomotor symptoms: position statement of The North American Menopause Society. *Menopause*. 2004;11:11–33.