

Compounded non-FDA–approved menopausal hormone therapy prescriptions have increased: results of a pharmacy survey

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Abstract

Objective: From a survey of compounding pharmacists, specific questions regarding compounded menopausal hormone therapy were used to estimate compounded hormone therapy (CHT) prescribing in the United States.

Methods: A national online survey was conducted by Rose Research—a market research company consisting of 12,250 US pharmacists from independent community pharmacies (ICPs) and compounding pharmacies (CPs). Pharmacists who completed the survey and met the prespecified criteria were eligible. Data from the survey were extrapolated to estimate overall CHT prescription volume and annual costs of CHT prescriptions for the United States based upon industry data from the National Community Pharmacists Association and IBISWorld.

Results: Surveys were completed by 483 pharmacies, including 365 ICPs and 118 CPs. On the basis of the survey responses and extrapolated industry data, an estimated 26 to 33 million CHT prescriptions were filled annually, with total sales estimated at \$1.3 to \$1.6 billion. CPs (vs ICPs) accounted for a higher proportion of CHT prescriptions. More than half of the ICPs (52%) and CPs (75%) expected continued compounding business growth, with most predicting 5% to 25% growth within 2 years, despite the potential effect of restrictive legislation regarding compounding.

Conclusions: On the basis of extrapolated data from numbers of prescriptions reported by pharmacists participating in the survey, the volume of CHT seems to approach that of Food and Drug Administration (FDA)-approved menopausal hormone therapy, and growth in the CHT market is expected. Thus, physicians should educate themselves and the women consulting them about the differences between the FDA-approved and the less-tested CHT formulations. More research on the efficacy, safety, and consistency of non-FDA–approved CHT is needed.

Key Words: Compounded hormone therapy – Compounding pharmacies – Estrogen therapy – Menopause – Progesterone.

Received May 14, 2015; revised and accepted September 22, 2015.

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Funding/support: TherapeuticsMD funded this study and medical writing assistance was provided by Laura Ninger, ELS and Jolene Mason, PhD (Precise Publications, LLC). Dr Pinkerton has received grants and research support (paid to the University of Virginia) from TherapeuticsMD Inc and EndoCeutics Inc, and has served as a consultant (fees paid to the University of Virginia) for Pfizer Inc, Noven Pharmaceuticals Inc, TherapeuticsMD Inc, and Shionogi Inc. Dr Constantine consults for pharmaceutical companies including but not limited to TherapeuticsMD. Financial disclosure/conflicts of interest: None reported.

Supplemental digital content is available for this article. Direct URL citations appear in the printed text and are provided in the HTML and PDF versions of this article on the journal's Website (www.menopause.org).

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Menopausal hormone therapy (MHT; see Table 1 for glossary of abbreviations), consisting of estrogen with or without a progestogen, is the most effective treatment for vasomotor symptoms (hot flashes and night sweats) and is often prescribed for other sequelae of menopause, such as sleep disturbances, mood, and quality of life; for osteoporosis prevention; and for relief of genitourinary syndrome of menopause (GSM, which encompasses vulvar and vaginal atrophy [VVA]).¹

Publications from the Women's Health Initiative (WHI), however, reported health risks associated with MHT. As a consequence, women and providers became apprehensive about MHT, and its usage declined dramatically after 2002.²⁻⁶ According to the National Health and Nutrition Examination Survey (NHANES), use of any oral MHT among women aged at least 40 years declined from 22.4% in 1999 to 2002, to 11.9% in 2003 to 2004, and reached a low of 4.7% in 2009 to 2010.³ Data from the past decade showed a 61% decrease in prescriptions for MHT, from 93 to 36 million.⁷ Pharmacy claims data also confirm a marked decline in

TABLE 1. Glossary of abbreviations

Abbreviation	Definition
AACE	American Association of Clinical Endocrinologists
ACCP	American College of Clinical Pharmacy
ACOG	American Congress of Obstetricians and Gynecologists
AMS	Australian Menopause Society
ASRM	American Society for Reproductive Medicine
BHRT	Bioidentical hormone replacement therapy
CHT	Compounded hormone therapy
CP	Compounding pharmacies
FDA	US Food and Drug Administration
GSM	Genitourinary syndrome of menopause
HT	Hormone therapy
ICP	Independent community pharmacies
MHT	Menopausal hormone therapy
NA	Not applicable
NAMS	North American Menopause Society
NCPA	National Community Pharmacists Association
NHANES	National Health and Nutrition Examination Survey
PCAB	Pharmacy Compounding Accreditation Board
Rx	Prescriptions
USP	United States Pharmacopoeia
VVA	Vulvar and vaginal atrophy
WHI	Women's Health Initiative

prescriptions written immediately after publication of the WHI findings,^{4,8,9} with one estimate indicating a 68% decline in overall MHT prescriptions between 2001 and 2008,⁵ and another citing up to an 85% decline for estrogen–progestins between 2001 and 2005.⁶ The decline of Food and Drug Administration (FDA)-approved MHT has slowly abated, with a very slight upturn between 2005 and 2010.⁶

Compounded hormone therapy (CHT), also referred to as “bioidentical hormone replacement therapy” (BHRT), is a marketing term that is not recognized by the FDA.¹⁰ After the WHI reports in 2002, and the 2001 US Supreme Court ruling allowing pharmacies to market compounded products that were unregulated by the FDA,¹¹ the use of CHT became more prominent, whereas the use of FDA-approved MHT declined.^{2,12} Many women consider CHT options to be more “natural” and safer because of unsubstantiated safety and efficacy claims in the media, internet, and from celebrities promoting them as a superior alternative to approved MHT.^{2,12,13-15}

Prescription data for FDA-approved MHT are tracked and can be quantified, whereas compounded products are not FDA-approved and are thus not tracked. Therefore, surveys and market research studies have been performed in an attempt to understand the prescription numbers, use, and reasons for continued compounding. In a survey of 184 postmenopausal women presenting for consultation at the Mayo Clinic, Iftikhar et al¹³ found that 20% reported ever-use and 14% reported current use of CHT. Pinkerton and Santoro¹⁶ reported data from an online survey in 2013 and 2014 among more than 2,800 women aged 40 to 60 years, and extrapolating data from these surveys estimated that 1 to 2.5 million US women use CHT annually, with 21 to 39 million annual CHT prescriptions representing 28% to 68% of overall MHT prescribing, totaling \$1 to \$2 billion in spending.

Compounded hormone therapy formulations may have unique risks and may contain non-FDA–approved hormones (eg, estriol) or may have undesirable additives or preservatives. They are not monitored by the FDA for purity or dose standardization, and they are not required to carry a package insert (PI); thus they do not include potential warnings/contraindications as is required for FDA-approved MHT.^{1,12,15,17} The products have not undergone FDA-approved rigorous studies evaluating efficacy or potential risk,^{1,2} and no pharmacokinetic data are available for CHT formulations. Recent consumer online survey data indicate that 86% of consumers were unsure or unaware that these formulations are not FDA-approved,¹⁶ whereas many websites for CHT are claiming better safety than for FDA-approved products.¹⁸ Purported individualization of therapy frequently recommended by compounders via salivary estradiol and progesterone levels remains unproven.^{2,12,15} In 2008, the FDA censured seven pharmacies because of unsubstantiated product claims.^{2,14,19}

The majority of pharmacies and their professional organizations are dedicated to providing high-quality products.²⁰⁻²² Compounding pharmacies now have the option of being accredited by the Pharmacy Compounding Accreditation Board (PCAB).²² The US Pharmacopoeial Convention (USP) has developed standards for compounding to “help compounding practitioners adhere to widely acknowledged, scientifically sound procedures and practices, and facilitate the delivery of consistent and good-quality prepared medicines to people who are need of them.”²³

Given that the use and incidence of CHT prescribing seem to have increased,^{2,12} and that the population is aging,²⁴ more research on actual prescribing and use of compounded products is needed.¹³ To date, however, few reliable data are available on the extent of prescribing of CHT by US pharmacies and expected future trends.^{13,16} Previously published consumer surveys by Pinkerton and Santoro¹⁶ suggest high-volume use of CHT.

Using data from a large internet survey of US pharmacies conducted by Rose Research—a market research firm—and additional data from the National Community Pharmacists Association (NCPA)²⁵ and IBISWorld,²⁶ we have estimated the extent of CHT prescribing and overall annual costs.

METHODS

Survey design

Rose Research conducted a benchmarking Internet survey of pharmacists who provide compounding services in the United States. The survey was conducted on behalf of the *International Journal of Pharmaceutical Compounding* and *inThought Research, LLC*—a market research company, and was sponsored by TherapeuticsMD—a pharmaceutical company focused on research and development of products exclusively for women's health. Eligible participants were recruited from the healthcare populations of two online sample panel providers—Toluna and ResearchNow.

Sample and inclusion criteria

A representative sample of pharmacists ($n = 12,250$) was invited to participate in the survey between October and November 2014. This was out of a total estimated sample size for independent community pharmacies (ICPs) of approximately 3.1 pharmacists per each of the 23,000 ICPs, or 71,300 compounding pharmacists²⁵; similar total estimated sample size for community pharmacies (CPs) is not available. Large chain pharmacies were not included because they generally do not perform compounding of hormonal agents.

Pharmacists qualified for participation if they met the following criteria: pharmacy is in the United States; pharmacy is either an independent community pharmacy (ICP—defined as a small chain with <50 stores) or an independent compounding pharmacy (CP—defined as a retail pharmacy not directly affiliated with any chain of pharmacies or not owned or operated by a publicly traded company); pharmacist has knowledge of the pharmacy's annual revenue and prescription volume composition for both compounded and noncompounded prescriptions for all pharmacy locations; and the prescription volume from nonsterile-compounded prescriptions represents at least 1% of the total prescription revenue and volume. Participants were advised of the goals of the survey and that the composite results would be published. Individual participants were not identified; therefore they were not asked to provide written informed consent. Multiple pharmacists per pharmacy could potentially have responded to the survey, but due to the confidential nature of the survey, the number of pharmacists who responded per pharmacy was not quantified. Participation was voluntary and participants were assured that their answers and identifying information would remain confidential. Respondents received an equivalent of up to approximately \$17 to \$35 in cash or merchandise for their time utilized to complete the survey.

Survey instrument

The survey was intended to gather data on compounding practices and expected future trends in various classes of pharmaceuticals, including analgesic, adult antibiotic, MHT/CHT, pediatric, veterinary, and others, and also details about business practices (eg, consumer categories, services other than prescribing, and other aspects of the business model).

The overall survey goals were to provide insight into the role that compounding plays in the marketplace for both ICPs and CPs; quantify the nature of business for sterile compounded medications and nonsterile compounded medications for pharmacies in the United States; analyze the types of medicines compounded for what purposes; analyze the importance of compounding and other services in the business model; and identify past trends and future expectations for ICPs and CPs with regard to how growth, acquisitions, and regulation affect their business model.

Thirty-one questions about sterile and nonsterile compounding were included in the survey. Specific questions were included in the survey to ask about the number, volume, and overall costs of prescriptions for CHT sold by US

pharmacies; specific quantities and types of CHT provided; and reported past trends and estimated future growth of the CHT industry. Six questions specific to compounded menopausal hormone therapies (Appendix A, Supplemental Digital Content 1, <http://links.lww.com/MENO/A141>), including CHT prescription numbers and percentage of total volume, percentages of various types of CHT, and the likelihood of change in CHT prescribing over the next 2 years, formed the basis of our analysis. Questions about testosterone alone were not included in this study as testosterone alone is not used for treatment of vasomotor symptoms.

Data analyses

Nationwide volume and sales of CHT were estimated utilizing two different methods to assure consistency of results. In the first method, pharmacists were asked to quantify and report the number of "compounded menopausal hormone therapies" that they dispensed per month. These data were then paired with data from the NCPA (2013)²⁵ and IBISWorld (Industry Data, 2014)²⁶ that estimate overall numbers. The number of CHT prescriptions written annually was calculated based upon the estimate of CHT dispensed by the individual compounding pharmacists who participated in the survey and multiplied by the total number of ICPs and CPs. The average out-of-pocket monthly cost to the consumer of \$49 per prescription previously reported by completers of the Rose consumer survey¹⁶ was used to estimate the annual nationwide CHT spent. The second method asked the pharmacists to indicate the volume of each individual type of CHT dispensed per month (eg, estradiol, progesterone). The individual compounded hormones were used in conjunction with the industry data (NCPA, 2013²⁵ and IBISWorld [Industry Data, 2014]) to reach an estimate of nationwide CHT volume. The \$49 per month cost per prescription was applied as in the first method.

RESULTS

Response rates and pharmacy characteristics

Of the 12,250 candidate pharmacists, 2,902 (24%) answered the online survey screening questions, and 904 of these were eligible for the survey based on meeting inclusion criteria. Although we have no way of confirming number of respondents per pharmacy, our responses indicated that 685 pharmacies from this sample performed compounding services (76%). Surveys were completed by 483 of these pharmacies (71%), including 365 ICPs and 118 CPs (Fig. 1). Characteristics of the respondents are listed in Appendix B (Supplemental Digital Content 2, <http://links.lww.com/MENO/A142>). No statistical comparisons were made between the ICP and CP groups as demographic data were not requested of the survey participants. Also, given the confidential nature of the survey, we do not know if more than one pharmacist from each pharmacy participated. Geographic distribution of the pharmacies (Appendix C, Supplemental Digital Content 3, <http://links.lww.com/MENO/A143>) shows widespread representation across the country.

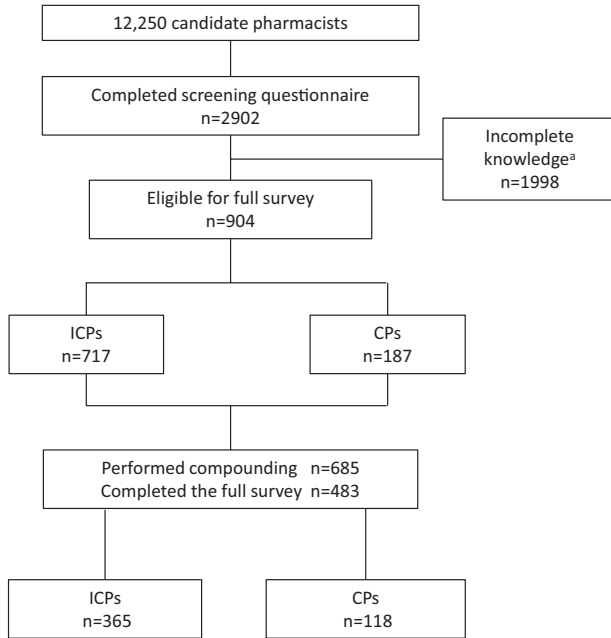


FIG. 1. Flow of participants into the study. CPs, compounding pharmacies; ICPs, independent community pharmacies. ^aIncomplete knowledge about their pharmacies compounding volume and revenue.

CHT prescribing volume and costs estimated using overall prescription volume

Survey responses for mean and median number of prescriptions filled per week are indicated in Table 2. Median values for total annual prescriptions were extrapolated from weekly data, amounting to 65,520 for ICPs and 61,100 for CPs (Table 2, Fig. 2A), and served as the basis of all subsequent calculations. ICPs reported that 8.6% of overall prescriptions (mean) were for nonsterile compounded products, and out of this number, 16.1% (mean) were CHT; respective values for CPs were 36.0% (mean) and 25.7% (mean; Fig. 2A). Data from NCPA estimate that there are at least 23,000 ICPs in the United States and 63% of these offer compounding services,²⁵ which amounts to approximately 14,490 compounding ICPs (Fig. 2A). Data from IBISWorld cite 3,556 CPs in the United States in 2013,²⁶ so a conservative estimate of 3,500 was used

in calculations to estimate total number of CHT prescriptions per year and the total cost of those prescriptions (Fig. 2A). Therefore, based on survey responses and extrapolated industry data, an estimated 33 million CHT prescriptions are filled annually by both ICPs and CPs combined (Fig. 2A).

Calculations of total costs used the estimate of \$49 out-of-pocket per prescription.¹⁶ Multiplying the total volume per year by this price yields an estimated \$1.61 billion in spending for CHT each year (Fig. 2A).

CHT prescribing volume and costs estimated using volume of individual types of prescriptions

Estimates of the number of CHT prescriptions per year and the costs of those prescriptions were also extrapolated from the volumes of individual types of CHT provided (Table 2, Fig. 2B). In the survey, ICPs and CPs reported the number of prescriptions filled per month for each type of CHT they provide (Table 2). Most common was progesterone/progestin only, followed by estrogen and progesterone/progestin combinations, and 17β-estradiol/estrogen combinations. The predominant route of administration was transdermal gel or lotion (reported by 46% of ICPs and 37% of CPs), followed by oral (24% and 27%) and vaginal (22% and 17%).

The sum of all prescriptions reported per CHT type per pharmacy in Table 2 is an estimated 76.3 total CHT prescriptions filled per month per pharmacy for ICPs and 296.3 prescriptions per month per pharmacy for CPs. When annual volume was estimated using these numbers and the same industry data as in Figure 2A,^{25,26} the calculations showed total combined CHT prescriptions of 26 million per year (Fig. 2B). Cost calculation based on the unit cost of \$49 yields an estimated total cost of \$1.26 billion in spending (Fig. 2B).

Comparison of ICPs and CPs

Surveyed CPs (vs ICPs) accounted for a numerically higher proportion of CHT prescriptions, whether expressed in relation to overall annual prescribing (26% vs 16%; Fig. 2A) or sum of annual prescriptions for all individual CHT products (3,555 vs 915; Fig. 2B). CPs (vs ICPs) also

TABLE 2. Total prescriptions filled per week (extrapolated per year) per pharmacy and number of monthly prescriptions by specific CHT type from the pharmacy survey

	Independent community pharmacy (n = 365)		Compounding pharmacy (n = 118)	
	Weekly	Yearly ^{a,b}	Weekly	Yearly ^{b,c}
Total prescriptions				
Mean	2,081	108,212	1,510	78,520
Median	1,260	65,520	1,175	61,100
Monthly prescriptions, mean (±SE)				
17β-estradiol/estrogen only	11.44 (±2.19)		50.44 (±16.61)	
Progesterone/progestin only	21.28 (±3.78)		80.34 (±14.81)	
Estrogen and progesterone/progestin combination	19.45 (±3.59)		76.59 (±21.35)	
Estrogen and testosterone combination	12.2 (±2.45)		45.28 (±9.63)	
Testosterone, estrogen, and progesterone/progestin combination	11.89 (±2.42)		43.5 (±10.62)	

CHT, compounded hormone therapy; SE, standard error.

^aICPs: 8.6% (mean) of overall prescriptions are for non-sterile compounded products; 16.1% of this number was CHT.

^bCalculated per year based on weekly report of CHT.

^cCPs: 36.0% (mean) of overall prescriptions are for non-sterile compounded products; 25.7% of this number was CHT.

COMPOUNDED HORMONE PRESCRIPTION PHARMACY SURVEY

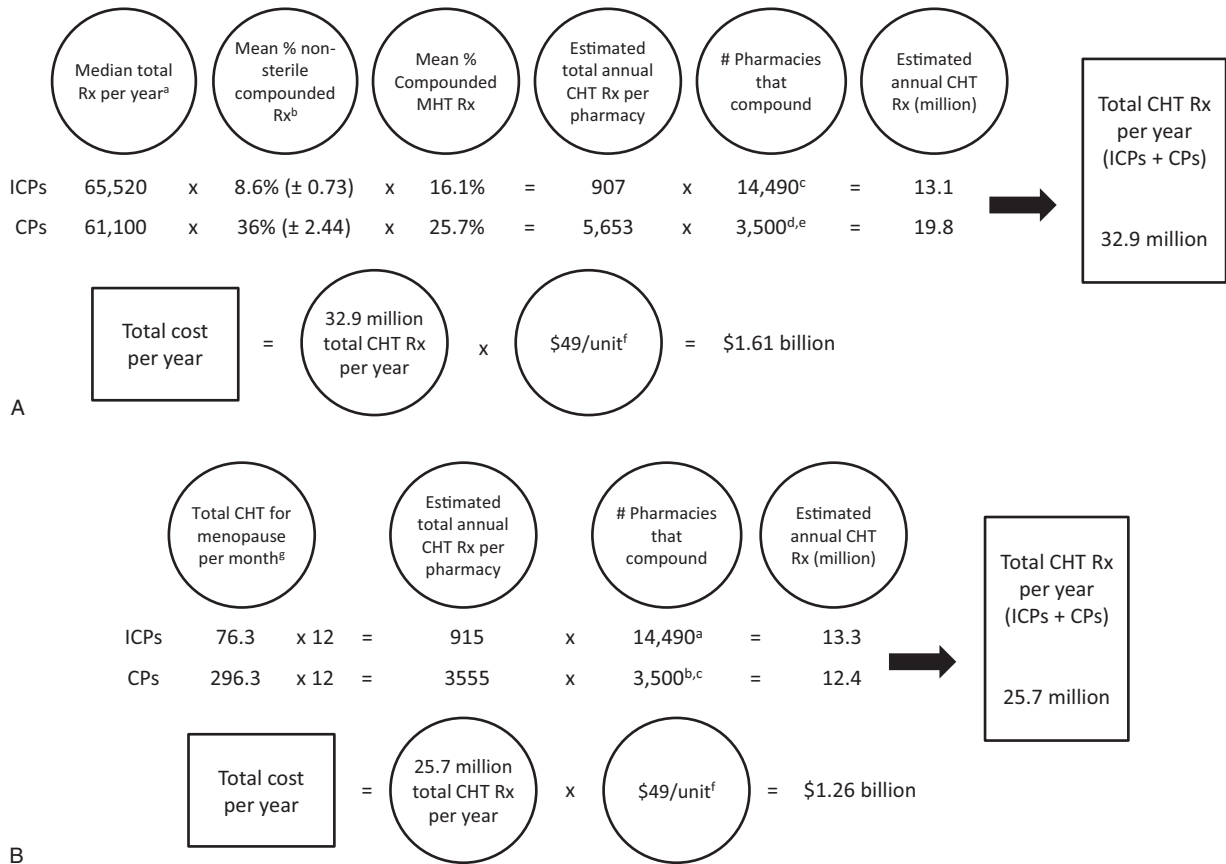


FIG. 2. Two different estimates of volume and sales of compounded hormone therapy at ICPs and CPs based on (A) overall annual prescribing from the survey of compounding pharmacists and (B) annual prescriptions for individual products from the same survey. CHT, compounded hormone therapy; CPs, compounding pharmacies; ICPs, independent community pharmacies; MHT, menopausal hormone therapy; Rx, prescriptions. ^aExtrapolated from reported weekly prescriptions per pharmacy (Table 2). ^bMean percentage of prescriptions that are nonsterile compounded prescriptions (± standard error). ^cFrom National Community Pharmacists Association data. ^dFrom IBISWorld Industry data. ^eRounded number based on estimated 2013 value. ^fFrom consumer survey data. ^gBased on reported numbers of CHT prescriptions per type shown in Table 2.

accounted for numerically more prescriptions of all specific CHT types (Table 2).

Past trends and expected future growth

Most pharmacies reported, in the survey, that their compounding business had stayed the same or had grown during the past 2 years, with 40% of ICPs and 58% of CPs citing 5% to 25% growth (Fig. 3A). More than half of the ICPs (52%) and CPs (75%) expect continued growth of their compounding business over the next 2 years, with most predicting 5% to 25% growth (Fig. 3B). Although a sizeable proportion of respondents, especially ICPs, believed that legislation may have a detrimental effect on the overall compounding market during the next 2 years (Fig. 3C), both groups seemed confident that the CHT market will remain the same or continue to grow (Fig. 3D).

DISCUSSION

A larger than expected proportion of US women are prescribed compounded, non-FDA-approved HT based upon extrapolations of this online market research survey of US pharmacists and data from NCPA²⁵ and IBISWorld.²⁶ On the

basis of survey responses and industry data,^{25,26} an estimated 26 to 33 million CHT prescriptions are filled or dispensed annually at community and compounding pharmacies. This large number approaches that written for FDA-approved MHT,¹⁶ and is consistent with the revenue findings of \$1 to \$2 billion spent by consumers as previously found by Pinkerton and Santoro.¹⁶ We believe that this is the first report in the literature to estimate total annual CHT prescribing and revenue for US-independent community and compounding pharmacies.

The assumptions used in our cost calculations are supported by data in the literature. The total numbers of US compounding pharmacies were derived from recent industry data (NCPA²⁵ and IBISWorld).²⁶ The percentage of respondents that reported that they performed compounding in this survey was 76% (685/904; Fig. 1), which is similar to an estimate from the NCPA of 63%.²⁵ The assumption of \$49 per unit per month is in line with the previous reports citing \$42 for compounded vaginal estrogen²⁷ and \$45 to \$55 as an average cost for CHT.²⁸ Our estimate of \$1.3 to \$1.6 billion in annual CHT spending is within the range reported in the consumer surveys cited earlier (ie, \$1-\$2 billion),¹⁶ and is supported by

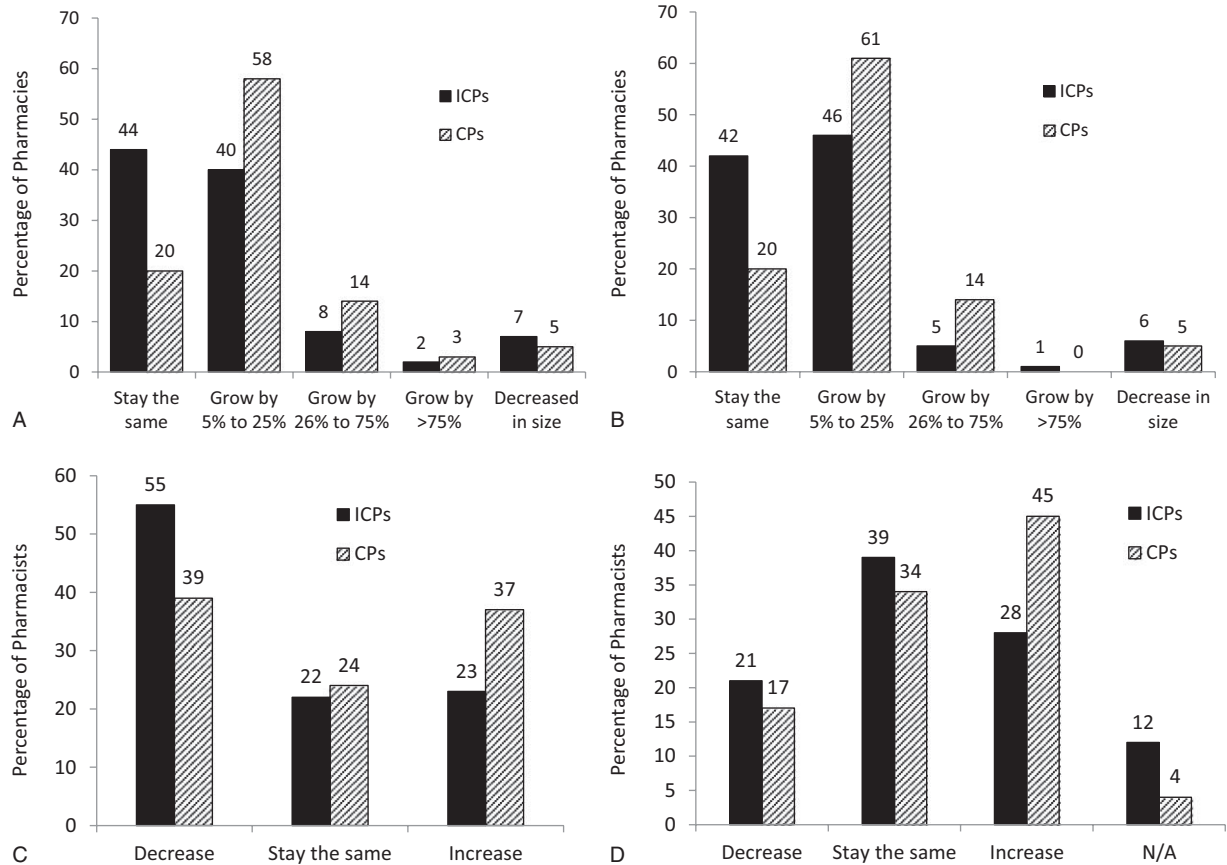


FIG. 3. Survey respondents' outlook on growth of the compounding industry, including (A) reported past growth, (B) expected future growth; and the expected impact of legislation on (C) the overall US compounding industry, considering "recent legislation (national and state)" and (D) the compounded hormone therapy market over the next 2 years, considering changes "specifically because of the law as opposed to general economic conditions." CPs, compounding pharmacies; ICPs, independent community pharmacies; NA, not applicable. Responses to C and D were on a scale of 1 to 7 (from "significant decrease" to "significant increase").

an *inThought* analysis by Symphony Health Solutions that estimated current spending on CHT is at \$1.8 billion.⁷ The ranges of our two estimates of 26 to 33 million CHT prescriptions per year and \$1.3 to \$1.6 billion in annual CHT spending reflect the two separate methods of the pharmacists estimating dispensed menopausal hormones (combined estimate of CHT vs summing of individual hormonal products). The two estimates were within 20% of one another, which was not unexpected, given that the average standard error for the survey questions that were used in the estimates was approximately 20%. Both estimates show the large volume of CHT use.

The population of women who could benefit from FDA-approved MHT shows no sign of declining, and according to population data, may even grow.²⁴ Ages 65 and older will be the fastest growing population segment in the United States in the next 25 years,²⁴ and studies have shown that many women in this age group continue to experience menopausal symptoms.²⁹⁻³¹ A study, published in 2003, of 377 women aged 50 to 69 years, reported that 26% who had attempted to stop hormone therapy (HT) chose to resume because of troublesome postmenopausal symptoms.³² An analysis by *in Thought* of the current US market for MHT projected

growth of revenue to \$4.6 billion within the next decade, but acknowledged that the market may be affected by recent legislation that has prohibited the compounding of already available FDA-approved drugs.⁷ The efficacy of MHT for vasomotor symptoms is undisputed.¹ For some women, CHT may be recommended over MHT because of dosing or formulation flexibility or lack of allergens (peanut oil).^{12,33} Some authorities suggest possible savings with CHT versus FDA-approved MHT,^{12,27} although others cite higher costs and lack of insurance reimbursement.¹⁷

Pharmacists from both ICPs and CPs indicated that CHT represented an important percentage of their compounding business volume (16% and 26%, respectively), despite recent legislation about compounding. More than two-thirds of pharmacists from ICPs and more than three-quarters of pharmacists from CPs reported that they expected the same or greater volume of business in CHT over the next 2 years.

Many women and some healthcare providers may be unaware of the lack of FDA oversight of CHT. In the survey reported by Iftikhar et al,¹³ more than two-thirds of 184 women (67%) believed that CHT was safer than FDA-approved MHT. Similarly, in the consumer surveys by Pinkerton and Santoro¹⁶ cited earlier, only 14% of respondents

reported that they knew that CHT was not FDA-approved, with 76% saying “not sure” and 10% saying they believed that CHT was FDA-approved. Twenty-seven percent of women did not know whether their MHT formulation had been compounded.¹⁶ Sixty-seven percent of women who responded to a “10-minute” paper survey offered at compounding pharmacies agreed that “natural” hormones are safer and cause fewer side effects than “synthetic” hormones,³⁴ and in a questionnaire given online or on paper to women with nonmetastatic breast cancer, 79% admitted a lack of knowledge about risk-benefit considerations of bio-identical and nonhormonal treatments for symptoms of menopause.³⁵ Certain types of CHT have been touted to have the ability to prevent chronic diseases such as breast cancer and cardiovascular disease, achieve weight loss, or slow the aging process³⁶ without robust clinical studies to back up these assertions. It is of concern that women may assume CHT products to be safe because no warnings are provided about their risks, and the FDA does not require CHT product regulation. Additionally, CHT products do not come with a package insert of indications and potential risks,^{1,37} whereas all FDA-approved estrogen products include this along with the boxed warning based on the findings from the WHI.

The American Congress of Obstetricians and Gynecologists (ACOG), the American Association of Clinical Endocrinologists (AACE), the American College of Clinical Pharmacy (ACCP), the Australian Menopause Society (AMS), the Endocrine Society, The North American Menopause Society (NAMS), the American Society for Reproductive Medicine (ASRM), and the US Preventive Services Task Force have released statements on their concerns about the lack of rigorous randomized trials on CHT,^{1,12,17,38-41} and the AACE also emphasized the potential for exaggerated claims of safety and efficacy.¹⁷ These professional organizations state that women should be advised to use FDA-approved products whenever possible instead of CHT regimens, given the wide range of FDA-approved combinations, dosages, and dosage forms of bio-identical HT options.^{1,12,17,39}

Shared decision-making about MHT should include discussion of FDA-approved therapies. Concern exists about the potential of liability if women are not educated about unique risks possible with CHT, and thus documentation should include why CHT is being recommended over FDA-approved therapies.⁴² Before considering or prescribing CHT, women should be counseled about the potential risks and unknowns possible with compounded products and lack of FDA approval and monitoring.⁴¹ Women should understand that compounding pharmacies can be licensed through PCAB, which allows identification of pharmacies that have passed a national certification process. Ideally, pharmacists would thoroughly document origin, purity, dose, and sterility of compounded product(s).⁴²

Limitations of this study include the self-selected participation by pharmacists in this survey; thus the findings may be limited by sampling bias due to the survey design⁴³ and participants' self-report.⁴⁴ Consequently, the participants

may not be representative of all ICPs and CPs in the United States. Demographic data on the pharmacists were not collected and thus no comments can be made about the age, race, sex, and so on of the participants. However, the geographical distribution of the pharmacists surveyed (Appendix C, Supplemental Digital Content 3, <http://links.lww.com/MENO/A143>) shows that pharmacists across the nation responded and a wide geographic range was achieved. Another limitation was that we could not correct for the number of pharmacists who responded per pharmacy due to the confidential nature of the survey. Thus, although multiple pharmacists from a single pharmacy could have responded to the survey, reassurance is provided that the results were not affected, given the large number of pharmacists participating (see Fig. 1), their widespread geographic distribution (see Appendix C, Supplemental Digital Content 3, <http://links.lww.com/MENO/A143>), and the small average number of pharmacists per pharmacy (see Appendix B, Supplemental Digital Content 2, <http://links.lww.com/MENO/A142>). Despite the limitations associated with response rates in surveys, conducting a survey was the only current option available to estimate the size of the compounding market, given that compounding prescriptions and revenue are not tracked in a systematic manner. The response rate in this study was relatively robust at 24% of the eligible 12,250 pharmacists, compared with the 9% to 10% figure cited recently for online and telephone surveys.⁴⁵⁻⁴⁷

Estimated calculations using national data have inherent risks of over or underestimation. However, the most recent, relevant published industry data available (NCPA²⁵ and IBIS-World)²⁶ were used to perform the reported extrapolations. In addition, the pharmacists were asked questions about compounding MHT in two different ways (see Appendix A, Supplemental Digital Content 1, <http://links.lww.com/MENO/A141>) to provide internal consistency for the numbers found in the survey.

CONCLUSIONS

This analysis and extrapolation of survey data provide new and potentially valuable information on the extent of compounding of postmenopausal hormone preparations obtained from online survey data among US ICPs and CPs. On the basis of extrapolations of the survey data using national published data (see Fig. 2), CHT accounts for an estimated 26 to 33 million prescriptions annually, reaching potentially \$1.3 to \$1.6 billion in revenues, and pharmacists expect continued growth in the CHT market over the next 2 years. Our results are consistent with those of a survey of consumers recently published by Pinkerton and Santoro,¹⁶ with 21 to 39 million CHT prescriptions and a revenue of \$1 to \$2 billion annually reported. Large numbers of women are exposed to CHT with prescription volume approaching that of FDA-approved MHT; growth is expected in the CHT market by compounding and independent pharmacists; and CHT carries unique risks due to lack of FDA approval or monitoring of compounded therapies. Thus, providers should educate themselves and the

women who visit them about the differences between FDA-approved and less regulated CHT formulations, and the availability of FDA-approved and monitored therapies. This study also demonstrates the need for more research on the efficacy, safety, and consistency of non-FDA-approved CHT to better understand benefits and risks for our patients and the need for tracking non-FDA-approved menopausal hormone therapies to better understand how and why it is being used.

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