It is illegal to post this copyrighted PDF on any website. Observed Sex Differences in Cardiometabolic Indices in Patients on Antipsychotics: Secondary Analyses of a 12-Month Multicenter,

Randomized, Controlled Trial

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ABSTRACT

Objective: To define sex differences in cardiometabolic indices changes over 12 months in patients on antipsychotics and to describe treatment complexity, interventions, and patient satisfaction of pharmacist comprehensive medication management (CMM) services.

Methods: Secondary analyses of time effect–associated sex differences in cardiometabolic indices within and between study groups were done at baseline and 12 months. Each group consisted of 60 subjects who received full pharmacist CMM services (PCS) and 60 subjects who received either modified or no CMM services (NCS). Pharmacist CMM services are a team-based practice of providing direct patient care.

Results: Significant sex differences in mean change score were observed from baseline to 12 months in the combined PCS and NCS subjects. Compared to men, women had greater body weight (P = .003) and waist measurement (P = .02) reductions and increased serum level of highdensity lipoproteins (P<.001). In contrast, men had greater systolic (P < .001) and diastolic (P = .005) blood pressure levels, more hypertension diagnoses (P=.01), and less dyslipidemia diagnoses (P=.001) compared to women at 12 months. Significant sex differences were observed in combined PCS and NCS groups for glycated hemoglobin (HgbA_{1c}) (women: -0.33%, P=.02) and low-density lipoprotein (men: -21.63 mg/ dL, P = .04) at 12 months. In PCS women, a significant (P = .02) reduction in mean HgbA_{1c} percentages (-0.46%) compared to PCS men (0.28%) was observed at 12 months. A higher percentage (62%, n = 28/45) of PCS women compared to PCS men (38%, n = 17/45) at 12 months continued to receive CMM services. Satisfaction survey results positively favored CMM services; however, the response rate was only 25% (n = 18/72).

Conclusions: Women on antipsychotics appear more likely to keep follow-up visits, return satisfaction surveys, reduce abdominal weight, and improve HgbA_{1c} percentages and high-density lipid levels compared to men over 12 months. Women were satisfied overall with CMM services. Recognition of sex differences can promote a more personalized patient-centered care approach among patients prescribed antipsychotics.

Trial registration: ClinicalTrials.gov identifier: NCT02029989

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ntipsychotic medications for schizophrenia and bipolar disorder are associated with greater modifiable cardiometabolic risks including obesity, diabetes, dyslipidemia, and hypertension.¹⁻⁶ Sex differences are linked to higher associated risks for antipsychotic-associated hyperinsulinemia, abdominal obesity, and associated insulin resistance. Studies⁷⁻¹⁵ suggest that women have higher associated risks for abdominal obesity, metabolic syndrome, type 2 diabetes mellitus, and dyslipidemia compared to men. Genetic biomarkers for estrogen, testosterone, leptin, and methylenetetrahydrofolate reductase activity and other biomarkers, such as brain-derived neurotrophic factor (BDNF), may provide signals and etiologies for sex differences in hyperglycemia, dyslipidemia, and hypertension.^{7,16-19} Nonmodifiable risks such as sex differences may likely contribute to severity of cardiometabolic antipsychotic side effects and possibly predict treatment outcomes.

Even after almost 20 years of compelling evidence, patients on antipsychotics continue to have inadequate monitoring and difficulty attaining goals of treatment for metabolic-related conditions.^{20–28} Nonmodifiable risks such as sex differences may contribute to complexities and poorer prognoses of some cardiometabolic comorbidities.

To address the problem of inadequate monitoring among individuals on antipsychotics, pharmacists providing comprehensive medication management (CMM) can assist health care providers by increasing attention on patient-centered medication outcomes.^{22,23} Pharmacist CMM services are a team-based practice of providing direct patient care by resolving medicationrelated problems to optimize patient medication treatment outcomes.^{23,29–38}

In the original publication,²³ which the current study builds on, patients on antipsychotic medications receiving CMM services were found to have an increased likelihood of identifying dyslipidemia and hypertension monitored using point-of-care testing (POCT) compared to usual care. However, this study²³ did not fully describe the research protocol, pharmacist CMM intervention, and baseline to endpoint POCT and metabolic-related changes over



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Clinical Points

- Sex differences in women are linked to higher associated risks for antipsychotic-related side effects, metabolic syndrome, type 2 diabetes mellitus, and dyslipidemia compared to men.
- Female patients may be more likely to attend every 3-month metabolic monitoring visit with pharmacists, achieve gradual weight loss, and improve glucose control over 12 months compared to male patients.
- Recognition of sex differences can promote more personalized patient-centered care to ensure goals of therapy are being achieved among patients prescribed antipsychotics.

12 months. The purpose, therefore, is to expand on the previously published study to explore if sex differences may be associated with changes in cardiometabolic indices (eg, diabetes, hypertension, and dyslipidemia) over 12 months. A secondary objective is to describe CMM services in terms of medical complexity and pharmacist interventions including patient satisfaction among subjects prescribed antipsychotics. (See the original study²³ for research design, flow diagram of study subjects, baseline subject demographics, and baseline/12-month POCT results of metabolic syndrome risk criteria.)

METHODS

Secondary statistical analyses were conducted on data from a previously published 12-month prospective, multisite, randomized, controlled research design comprised of subjects recruited from 3 community mental health clinics.²³ All subjects taking antipsychotic agents received anthropometrics, glycated hemoglobin (HgbA_{1c}) results, sphygmometer measurements, and lipid results provided by the pharmacist investigators at each study visit.²³ Baseline and 12-month diagnoses used in the sex comparison analyses included diabetes, dyslipidemia, hypertension, schizophrenia, bipolar disorder, anxiety disorder, and major depressive disorder. Medication-related metabolic risk scores were assigned to antipsychotic agents and other medications (see original study²³).

The study was approved by the institutional review board (study no. 0900M72212; ClinicalTrials.gov identifier: NCT02029989). The duration of the study by the dates of first and last subject visits was from January 20, 2010, to January 13, 2012. Subjects (females: 59.2%, n = 71/120 and males: 40.8%, n = 49/120) were randomized to receive either full pharmacist CMM services (PCS) (total: n = 60, females: n = 36, males: n = 24) or modified or no CMM services (NCS) (control subjects total: n = 60, females n = 25). Modified CMM services were provided to almost half of the control subjects identified with abnormal POCT findings. At the end of the 12-month period, the number of subjects completing the study was PCS: n = 45 and NCS: n = 49. Table 1 describes the research protocol.

Table 1. Research Protocol

Subject recruitment: subjects were approached by care providers to consider study participation

- Informed consent: assessment of ability to consent and informed consent were obtained for all subjects
- (2) Randomization: consented subjects were randomized to receive either pharmacist comprehensive medication management (CMM) services (PCS intervention group) or no CMM services (NCS control group)

Baseline/follow-up screening checklist for all subjects

- Demographic information (age, sex, race, pregnancy, employment, marital status, mental illness diagnoses, primary care provider, date of last primary care visit)
- (2) Metabolic screening results: glucose, lipid panel, glycosylated hemoglobin A_{1c}, blood pressure, pulse, body weight, body mass index, waist/hip circumference and ratio, time since last food intake (post-prandial time)
- (3) Social information (substance use, stages/readiness to change for tobacco, activity levels)
- (4) Subject (self) and family history (dyslipidemia, hypertension, diabetes)
- (5) Medication information
- (6) Follow-up visits: PCS every 3 months or more frequently and NCS every 6 months

All subjects were provided with the following:

- (1) Point-of-care testing and metabolic screening results
- (2) Appointment reminder postcard for the next study visit (mailed at least 2 weeks prior to study visit)

Subjects^a receiving CMM services intervention (PCS study group, n = 58) included the following:

- (1) Recorded medication lists and medical condition (diagnoses) reviews
- (2) Identification of medical/psychiatric conditions (diagnoses) and listing of related drug therapy problems
- (3) Formulation of drug therapy care plan recommendations
- (4) Written drug therapy care plan recommendations and copy faxed to the subject's primary care provider
 (5) Rescheduling PCS subjects (eg, 2- to 12-week follow-up intervals)
- ^aChange in protocol: some NCS subjects (n = 28) were provided "modified" CMM services interventions and instructed to seek medical attention due to significant medical problems identified at point-of-care testing screenings.

CMM services treatment interventions and point-of-care results in both PCS and NCS subject groups were documented by the CMM research pharmacists using a proprietary electronic medical record (EMR) currently known as Genoa Medication Management Solution.³⁰ Pharmacist researchers did not have collaborative prescribing authority to make medication changes during the study. At study completion, a practice management report by the EMR software (created on April, 5, 2013) summarized the CMM services including clinical complexity and interventions. The CMM services clinical complexity summaries include number of medical/ psychiatric conditions, number of medications, number of identified medication therapy problems, and how these problems were addressed. The clinical outcome measure of the CMM services interventions was defined as the percentage change in medical/psychiatric conditions status and summarized as "improved," "unchanged," or "worsened." Change in clinical status of conditions was measured in subjects (PCS: n = 54, NCS: n = 10) who had at least 2 study follow-up visits.

Statistical Analyses

Standard descriptive statistics included mean and standard deviation change score differences for continuous

Table 2. Cardiometabolic Sex Differences From Baseline to 12-Month Follow-Up

	All (combined female and male)			Female			Male			Change Scores (0–12 months) for Females vs
Variable	Baseline (n=120)	12 Months (n=94)	<i>P</i> Value	Baseline (n=71)	12 Months (n=59)	P Value	Baseline (n=49)	12 Months (n=35)	P Value	Males, P Value
Waist, mean \pm SD, cm	44.5±7.3	43.8±7.2	.547	43.4±7.3	42.9±7.7	.727	45.9±7.0	45.1±6.3	.591	.022*
Hip, mean±SD, cm	46.3 ± 7.0	45.6 ± 76.5	.451	47.1±7.4	46.1±6.6	.475	45.1 ± 6.3	44.7 ± 6.2	.772	.071
Weight, mean \pm SD, kg	99.4±26.1	97.6±25.2	.676	95.7 ± 25.0	92.9±23.7	.523	104.8 ± -26.9	105.4 ± 26.1	.919	.003*
BMI, mean \pm SD (kg/m ²) ³⁷	34.3 ± 8.7	33.7 ± 8.7	.572	35.0 ± 9.3	34.2±9.2	.623	33.2 ± 7.8	32.8 ± 7.8	.782	.180
Diabetes, n (%) ^a	25 (20.1)	20 (21.3)	.954	15 (21.1)	14 (23.7)	.726	10 (20.4)	6 (17.1)	.713	.573
HgbA _{1c} , mean±SD, % ⁴⁰	5.7 ± 1.1	5.7 ± 1.1	.464	5.7 ± 1.0	5.5 ± 0.9	.316	5.7 ± 1.1	5.7 ± 1.3	.948	.445
Hypertension, n (%) ^a	45 (37.5)	34 (36.2)	.916	2 (31.0)	17 (28.8)	.790	23 (46.9)	17 (48.6)	.885	.010*
SBP, mean \pm SD, mm Hg ³⁸	118.0±18.8	117.2±18.1	.888	113.0±17.2	110.8±17.3	.353	124.3 ± 19.5	127.9±14.0	.353	<.001*
DBP, mean ± SD, mm Hg ³⁸	81.9±12.7	80.1±13.2	.343	80.1±12.1	77.8±14.3	.329	84.5±13.1	83.8±10.3	.791	.005*
Dyslipidemia, n (%)ª	69 (57.5)	56 (59.6)	.662	34 (47.9)	30 (50.9)	.739	35 (71.4)	26 (74.3)	.777	.001*
TChol, mean \pm SD, mg/dL ³⁹	191.7±42.5	179.6±38.2	.033*	193.7±42.4	180.0 ± 36.2	.054	188.6±42.9	178.9±41.9	.316	.562
LDL, mean ± SD, mg/dL ³⁹	105.5 ± 35.3	94.2±31.4	.031*	100.8 ± 33.0	93.9±29	.252	112.1±37.7	94.6±35.9	.058	.194
HDL, mean \pm SD, mg/dL ³⁹	40.8±13.0	43.0±16.0	.371	44.6±12.7	46.3±16.2	.526	34.8±11.3	36.8 ± 14.0	.513	<.001*
Triglycerides, mean±SD, mg/dL ³⁹	239.6±154.4	233.5±147.0	.767	249.6±168.6	226.0±141.2	.397	224.3±130.2	246.1±157.6	.500	.809
Framingham score, mean ± SD	9.0 ± 5.9	8.5 ± 5.8	.637	8.6±5.7	8.2 ± 5.5	.746	9.5±6.3	9.0±6.3	.732	.309
Schizophrenia, n (%)	61 (50.8)	50 (53.2)	.649	30 (42.3)	27 (45.7)	.692	31 (63.3)	23 (65.7)	.820	.004*
Anxiety, n (%)	83 (69.2)	68 (72.3)	.692	55 (77.5)	47 (79.7)	.765	28 (57.1)	21 (60.0)	.797	.002*
Bipolar, n (%)	55 (45.8)	43 (45.7)	.953	36 (50.7)	28 (47.5)	.716	19 (38.8)	15 (42.9)	.713	.213
Depression, n (%)	79 (65.8)	58 (61.7)	.523	47 (66.2)	38 (64.4)	.833	32 (65.3)	20 (57.1)	.455	.591

^aBaseline demographics prior to point-of-care testing.

*P values were considered significant at the .05 level.

Abbreviations: BMI = body mass index, DBP = diastolic blood pressure, HDL = high-density lipoprotein, HgbA_{1c} = glycosylated hemoglobin, LDL = low-density lipoprotein, SBP = systolic blood pressure, TChol = total cholesterol.

Figure 1. Mean Glycosylated Hemoglobin (HgbA_{1c}) Percent Differences (\pm SEM) From Baseline to 12 Months by Sex in PCS and NCS Subjects^a



^aAll subjects with identified conditions received pharmacist comprehensive medication management services (PCS) or modified or no comprehensive medication management services (NCS).

variables of cardiometabolic indices based on the National Cholesterol Education Program's Adult Treatment Panel III^{39,40} including waist and hip circumference (cm), weight (kg), body mass index,⁴¹ systolic and diastolic blood pressure (mm Hg),⁴² total cholesterol (mg/dL), low-density lipoprotein (LDL, mg/dL), high-density lipoprotein (HDL, mg/dL), triglycerides (mg/dL),⁴³

and HgbA_{1c}(%)⁴⁴ at baseline and 12 months. Categorical variables included frequency and percentages of diabetes, dyslipidemia, hypertension, Framingham scores,45 psychiatric diagnoses, and patient care survey items. Comparisons of sex differences were completed using independent t tests for continuous variables and χ^2 association test for categorical variables. To adjust for time effect from baseline to 12 months, mean score change differences (12 months subtracted from baseline) were calculated and t tests (mixed model) were performed using difference as dependent variable and sex as independent variable. Two-sided P values were calculated and reported to indicate the significance (ie, P < .05). Baseline to 12 months 95% confidence interval mean and standard error of mean (\pm SEM) change score differences were calculated in groups stratified by sex randomized to PCS and NCS subject groups for HgbA_{1c} and LDL values. The Department of Mathematics and Statistics at the University of Minnesota, Duluth provided statistical consultation support. SAS version 9.4 (SAS Institute Inc, Cary, North Carolina) was used for all statistical analyses including descriptive statistics, *t* tests, and χ^2 tests.

RESULTS

Cardiometabolic Analyses

A total of 120 subjects including 71 female (PCS: n = 36, 51%; NCS: n = 35, 49%) and 49 male (PCS: n = 24, 49%; NCS: n = 25, 51%) subjects participated at baseline. The baseline mean age of the subjects was 42.9 ± 11.3

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Figure 2. Mean Low-Density Lipoprotein (LDL) Differences (± SEM) From Baseline to 12 Months by Sex in PCS and NCS Subjects^a



^aAll subjects with identified conditions received pharmacist comprehensive medication management services (PCS) or modified or no comprehensive medication management services (NCS).

years. There were no significant mean age differences between women 42.4±11.5 (n=71) and men 43.7±11.1 (n=49). At the end of the 12-month period, the remaining proportion of subjects completing the study was 62% PCS females (n=28/45) and 63% NCS females (n=31/49) compared to 38% PCS males (n=17/45) and 37% NCS males (n=18/49). No statistical differences in cardiometabolic indices were observed when comparing PCS and NCS groups over 12 months. At baseline, PCS (80%, 48/60) and NCS (76.7%, 46/60) subjects were sedentary with no significant differences observed between the groups at baseline or 12 months. For antipsychotic risk scores, there were no statistical differences observed between/within the PCS and NCS groups at baseline or at 12 months. All of the subjects had relatively high mean total metabolic side effect risk scores approaching a score of 3 at baseline and at 12 months (see original study²³).

A significant reduction in total cholesterol (P=.03) and LDL (P=.03) values was observed in combined subjects across groups and sex at 12 months (Table 2). Significant sex differences in mean change score were observed from baseline to 12 months in the combined PCS and NCS subject groups (Table 2). Compared to men, women had greater mean body weight (P=.003) and waist measurement (P=.02) reductions and increased mean serum level of HDLs (P<.001). Compared to women, men had greater mean systolic (P<.001) and diastolic (P=.005) blood pressures, more hypertension diagnoses (P=.01), and less dyslipidemia diagnoses (P=.001). Mean diagnostic differences across sex were also observed after 12 months including anxiety (female > male) and schizophrenia (male > female) (Table 2).

A significant mean change score difference (P = .02) was observed over 12 months for HgbA_{1c} in combined female groups (n = 53; -0.33%; 95% CI, -0.55% to -0.12%) versus combined male groups (n = 33; 0.07%; 95% CI, -0.22% to 0.36%) (Figure

1). Also, a significant mean change score difference (P = .02) was observed for HgbA_{1c} percentages in PCS females (n = 27; -0.46%; CI, -0.84% to -0.08%)

compared to PCS males (n = 16; 0.28%; 95% CI, -0.2% to 0.8%) over 12 months (see Figure 1). There was no significant change score mean difference found between NCS female (n = 26) and NCS male (n = 17) subjects for HgbA_{1c} indices at 12 months.

A significant mean change score difference (P=.04) was observed for LDL in all male subjects (n=27; -21.63 mg/dL; 95% CI, -37.7 mg/dL to -5.6 mg/dL) versus female (n=46; -3.65 mg/dL; 95% CI, -10.8 mg/dL to 3.5 mg/dL) subjects over 12 months (Figure 2).

Practice Management Report: Treatment Complexity

CMM services were provided to a total of 86 subjects, including 97% (PCS: n = 58/60) who received extensive CMM services and 47% (NCS: n = 28/60) who received modified CMM services over 12 months. Dyslipidemia (73%, n = 63/86) was the top condition identified in the combined study groups receiving CMM services (Table 3). Hypertension (39.5%, n = 34/86) and diabetes (22%, 19/86) were also among the top 12 medical conditions identified in the combined study groups (see Table 3). A majority of the subjects were prescribed more than 5 medications. Pharmacist investigators resolved 712 medication therapy problems in 72% (n = 86/120) of combined subjects by often recommending the need for changing or starting new medications to medical providers, subjects themselves, subjects' caregivers, or all parties.

In the PCS group, pharmacists evaluated 453 (mean: 11.9; range, 4–28 per PCS subject) medical/psychiatric conditions and reviewed an average of 13 (range, 1–38) medications per subject over 236 documented study visits. A total of 691 medication therapy problems were identified and resolved with a majority (93%; n = 54/58) of PCS subjects having \geq 5. The top 3 medication therapy problems were "needs additional drug therapy" (50%, 346/691), "dose too low" (15.5%, 107/691), and "nonadherence" (11.5%, 79/691). Medical/psychiatric conditions associated with common medical therapy problems included diabetes mellitus: "dose too low"; dyslipidemia: "needs additional drug therapy" and "dose too low"; and hypertension: "adherence," "needs additional drug therapy," and "dose too low."

Among NCS subjects (n = 28) receiving modified CMM services, 32 (mean: 5; range, 1–11 per NCS subject) medical/psychiatric conditions were identified. Pharmacists reviewed an average of 9 (range, 3–20) medications per subject. A total of 21 medication therapy problems were identified and resolved over 40 documented study visits. Common drug therapy problems associated with diabetes mellitus type 2 included "nonadherence," medication "dose too low," and "needs additional drug therapy."



^cTop 12 conditions represent 55% of all indications for drug therapy.

^dTop 12 conditions represent 73% of all indications for drug therapy.

Practice Management Report: Interventions

The CMM pharmacist provided clinical recommendations based on the medical conditions and medical therapy problems identified and resolved at follow-up visits over 12 months. For PCS subjects, 51% had letters or facsimiles sent directly to their care provider; 42.5% of subjects and 6.5% caregivers were provided verbal recommendations to subjects by the CMM pharmacist. Likewise, 87% of NCS subjects had letters or facsimiles sent to their provider; 10% of subjects and 3% caregivers were provided verbal recommendations to subjects by the CMM pharmacist.

For medical/psychiatric conditions identified in the study groups, types of medication therapy problems most commonly resolved for both PCS (n = 58) and NCS (n = 28) subjects were initiating new medications, changing medication therapy, and obtaining laboratory monitoring (Table 4). Changes in medical conditions or clinical status were documented by the CMM pharmacists as "improved," "unchanged," or "worsened" in combined PCS (n = 54) and NCS (n = 10) subjects. For medical conditions not at goal at study baseline, 53% (144/272) of conditions improved, 9.2% (25/272) had no change, and 37.9% (103/272) of conditions worsened in the combined PCS (n = 54) and NCS (n = 10) subjects (see Table 4).

CMM Services Satisfaction Survey

After completion of the study, approximately 72 surveys were mailed to a sample group of study subjects. Survey participants consisted of 14 (78%) women and 4 (22%) men. Of the 18 surveys returned (25% response rate), 2 of the surveys had no responses and 1 survey was incomplete. Of the subjects who participated (n = 15), 40% were in the PCS group, 33% were in the modified NCS group, and 22% were not sure which group they were randomized to. The findings indicated that 50% of subjects (n = 17) felt their health improved and 44% (n = 17) indicated no change in physical health while in the study. A majority of the subjects (89%, n = 18) were satisfied or very satisfied with the counseling

and care provided by the pharmacist and 83% (n = 18) would recommend these services to a friend. Seventy-eight percent (78%, n = 15) of subjects reported that they were more aware and more concerned (79%, n = 16) about their health problems (eg, weight, blood pressure, sugar, and cholesterol). A majority (83.3%, n = 16) of subjects indicated that they trusted the advice of the pharmacist; only 1 subject indicated not trusting the advice of the pharmacist and 2 subjects did not respond. Although 50% (n = 15) of the subjects indicated improved medication adherence after talking to the pharmacist, 33.4% were not being more medication adherent. Sixty-one percent of subjects (n = 15) indicated that either the nurse practitioner or the doctor accepted the pharmacist's medication recommendations, and 22.2% of the subjects indicated that the recommendations were not accepted.

DISCUSSION

The primary key findings were significant reduction of body weight and waist circumference indices observed in combined female subject groups and significant HgbA_{1c} % reductions observed in the PCS female subgroup. For combined male subject groups, significant mean worsening of cardiometabolic indices were observed including weight gain, abdominal obesity, higher associated diagnosed hypertension, and worsening HDL levels compared to female subjects over 12 months.

The significant reductions in mean HgbA_{1c} percentages (0.27%–0.75%) observed in this study are comparable to pharmacist intervention groups in other reported studies.^{33,36,46–48} The beneficial impact of frequent direct patient care contacts is also supported by evidence of moderate reductions in HgbA_{1c} in patients receiving approximately 6–15 hours of self-management education over a 1-year duration.⁴⁹

The secondary key findings were descriptions of subjects' clinical complexity, pharmacist interventions,

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It is illegal to post this converighted PDE on any Table 4. Comprehensive Medication Management (CMM) Intervention Data: Resolution of Medication Therapy Problems With Prescribers^a

Recommended Intervention	PCS (n = 58) Recommended Interventions, % ^b	NCS (n=28) Recommended Interventions, % ^b			
Initiate new medication	43	39			
Change medication	27	12			
Initiate monitoring (eg, laboratories, etc)	18	15			
Discontinue medication	8	12			
Change medication dosage	0	8			
Other	4	14			
Change in Clinical Status of Medical/Psychiatric Conditions ^c	PCS (n = 54) Clinical Status (CS) Change in 251 Conditions Not at Goal at Baseline, %, n/n (total % CS change in conditions, %, n/n)	NCS (n = 10) CS Change in 21 Conditions Not at Goal at Baseline, %, n/n (total % CS change in conditions, %, n/n)			
Improved	50, 126/251 (28, 127/453)	86. 18/21 (56. 18/32)			
Unchanged	10, 25/251 (50, 227/453)	0, 0/21 (35, 11/32)			
Worsened	40, 100/251 (22, 99/453)	14, 3/21 (9, 3/32)			

^aThe data were generated by Genoa Medication Management Solution Practice Management Report.

^bAll subjects with identified conditions received pharmacist CMM services (PCS) or modified CMM services (NCS). ^cRepresents percentage of change in status of medical conditions, within each group, evaluated at least at 2 CMM followup study visits.

and satisfaction surveys of CMM services. Our findings are similar to a retrospective study by Cobb,³¹ utilizing the same EMR software, which also showed improved clinical status in over 50% of subjects for medical conditions not at goal at baseline. The level of clinical complexity in our study is also comparable to larger CMM studies based on the number of medical and psychiatric comorbidities, number of prescribed medications, and types of medical therapy problems (ie, needs additional medication, dose too low, and adherence).^{38,47}

The satisfaction survey, mostly completed by female subjects, indicated participants were satisfied overall with the pharmacists' care, more aware and concerned with their health-related problems, and trusted recommendations provided by the pharmacists. Similar to satisfaction survey key findings, Cobb^{31} reported a 30% satisfaction survey response. Patients surveyed (n = 154) in a mental health setting were very satisfied with pharmacist CMM services.³¹

Other sex differences in the current study were consistent with other study findings regarding psychiatric diagnoses and health care utilization. For example, female subjects in this study were more likely to have an anxiety diagnosis and less likely to be diagnosed with schizophrenia compared to males at 12 months.⁵⁰ Anxiety and depression can significantly increase diabetes risk severity in both females and males.^{50–52}

A higher percentage of female subjects completed this 12-month study, which is consistent with the literature findings of higher rates of health care utilization among women compared to men.^{53,54} Women may respond better to social aspects of care and elicit more patient-centered communication compared to men, especially if psychosis is present.⁵⁵

In summary, sex differences affecting multiple factors such as diabetes, anxiety symptoms, and the doctor-patient relationship may help explain this increase in health care utilization and help-seeking behaviors in women compared to men.^{52,56} Sex differences impacting the doctor-patient relationship may be affected by factors such as engagement in patient-centered communication,⁵⁵ influences of psychosis risk predictive symptoms,⁵⁷ and preferred provider-patient gender dyads⁵⁸ in patients taking antipsychotics. Strategies to improve a patient's utilization of health services may include providing frequent telephone/mailed reminders, flexible rescheduling to facilitate the initial clinical encounter, immediate outpatient follow-up after hospital discharge, scheduled visits with an established provider, and referral to case management.⁵⁹

website.

Limitations

Specific to this secondary analysis, a major limitation in the practice management report outlining the CMM services interventions was the inability to stratify results by sex, which obscured the impact of the CMM services for female and male subjects. The low subject participation and higher female representation in the satisfaction survey is also a limitation. For additional limitations see the original study.²³

For POCT lipid indices, several missing data points were the result of the POCT device limitation in calculating an LDL value. The POCT device limitation occurred when triglycerides were \geq 650 mg/dL (severe hypertriglyceridemia fasting \geq 500 mg/dL⁴³). As a result, 10 subjects (female: n = 6, male: n = 4) were excluded from the statistical analysis of lipid indices. However consistent with the results, among the 6 excluded female subjects, TRGs improved to near-moderate hypertriglyceridemia in 50% of female subjects (NCS: n = 2, PCS: n = 1) compared with worsening or no improvement seen in male subjects (PCS: n = 2, NCS: n = 2) over 12 months.

Strengths

The results of this study support the emerging evidence supporting sex differences affecting cardiometabolic indices. This study also contributes to the literature in the areas including observing sex differences in cardiometabolic indices over 12 months, impact of sex differences on rates of appointment no shows, response to disease state

Observed Sex Differences in Cardiometabolic Indices

It is illegal to post this con management, and patient satisfaction of pharmacist CMM practices in mental health settings. This study provides a signal to support future research to determine if sex differences affect treatment outcome of metabolic indices with regular follow-up visits among subjects treated with antipsychotics.

CONCLUSION

There is increasing evidence that sex-based dimorphic neurologic and physiologic mechanisms can

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