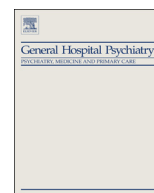




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Recent epidemiologic studies have found that most patients with mental illness are seen exclusively in primary care medicine. These patients often present with medically unexplained somatic symptoms and utilize at least twice as many health care visits as controls. There has been an exponential growth in studies in this interface between primary care and psychiatry in the last 10 years. This special section, edited by Jürgen Unutzer, M.D., will publish informative research articles that address primary care-psychiatric issues.

Population level effectiveness of implementing collaborative care management for depression ☆☆☆

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ABSTRACT

Objective: Care management is feasible to deploy in routine care, and the depression outcomes of patients reached by this evidence-based practice are similar to those observed in randomized controlled trials. However, no studies have estimated the population level effectiveness of care management when deployed in routine care. Population level effectiveness depends on both reach into the target population and the clinical effectiveness for those reached.

Method: This multisite hybrid Type 3 effectiveness-implementation study employed a pre-post, quasi-experimental design. The study was conducted at 22 Veterans Affairs community-based outpatient clinics. Evidence-based quality improvement was used as the facilitation strategy to promote adoption. Medication possession ratios (MPRs) were calculated for 1558 patients with an active antidepressant prescription. Differences in treatment response rates at implementation and control sites were estimated from observed differences in MPR.

Results: Reach into the target population at implementation sites was 10.3%. Patients at implementation sites had a significantly higher probability of having $MPR \geq 0.9$ than patients at control sites [odds ratio=1.38, confidence interval₉₅=(1.07, 1.78), $P=.01$]. This increase in MPR was estimated to yield a 1% point increase in response rates.

Conclusions: While depression care management improves outcomes for patients receiving services, low levels of reach can reduce overall population level effectiveness.

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1. Introduction

Collaborative care management (CCM) is an evidence-based practice that involves a multidisciplinary depression care team providing guideline-concordant depression treatment in the primary care setting. Mental health specialists (e.g., nurse care manager, psychiatrist) support primary care providers by helping patients overcome barriers to medication adherence, managing side-effects and identifying nonresponders. Numerous randomized controlled trials (RCTs) have demonstrated that CCM improves outcomes for primary care patients treated for depression [1–9]. The CCM model has been rolled out nationally in the United States by the Department of Veterans Affairs (VA) as part of the Primary Care/Mental Health Integration Initiative [10]. More recently, the VA has encouraged the

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implementation of CCM in its community-based outpatient clinics (CBOCs), where half of VA primary care patients receive care. However, there are numerous barriers to implementing a complex clinical program like CCM in CBOCs that lack on-site mental health specialists [11].

Two previous RCTs have documented that CCM can be successfully adapted for primary care clinics lacking on-site mental health specialists using telemedicine technologies [12,13]. While there is good evidence that telemedicine-based CCM improves outcomes in the context of an RCT, there is no evidence that it can improve outcomes when implemented in routine care. We used an implementation facilitation method known as evidence-based quality improvement (EBQI) to deploy telemedicine-based CCM in routine care at CBOCs. In EBQI, both researchers and local staff participate fully in the quality improvement process, with the researchers facilitating rather than dictating implementation efforts [14–16]. Clinicians and administrators contribute local knowledge needed to tailor the evidence-based practice for their own particular needs and organizational capabilities. Researchers contribute knowledge of the clinical evidence base, ensure fidelity to the evidence base and supply materials, procedures and tools needed for successful implementation.

Using the reach, efficacy, implementation, adoption and maintenance (RE-AIM) evaluation framework [17–20], we have previously reported that the EBQI process resulted in positive outcomes at implementation sites with regard to primary care provider adoption, patient reach, clinical effectiveness (for those patients reached), implementation fidelity and maintenance [11]. The purpose of this analysis is to estimate the “population impact” of the telemedicine-based CCM program by comparing outcomes at implementation sites to outcomes at control sites [21,22]. The population level effectiveness of a clinical program depends on the interaction between two of the RE-AIM implementation outcomes: reach and effectiveness. To have a meaningful impact on the population, the clinical program must reach a sufficient proportion of the target population, and the clinical program must be clinically effective for those patients reached.

One approach to measuring the population level effectiveness of a clinical program is to extrapolate the results of RCTs by specifying algorithms that make assumptions about how trial inclusion/exclusion criteria would affect reach into the target population if the intervention was deployed in routine care. A good example of this approach is presented by Zatzick et al. [21]. Another approach is to directly compare clinical outcomes in the target population at implementation sites with the clinical outcomes in an equivalent population at control sites. While it is relatively straightforward to measure the clinical outcomes of patients reached by the program, it is much more difficult to measure clinical outcomes for those patients targeted, but not reached, at implementation sites and for equivalent patients not targeted at control sites. More specifically, it is highly resource intensive to collect primary data from all (or a sample of) patients in the target population at both implementation and control sites, especially if informed consent must be obtained. A good example of this resource intensive approach is the well being among veteran enhancement study (WAVES) evaluation of the translating initiatives for depression into effective solutions (TIDES) CCM implementation initiative [23].

An alternative approach, used in this analysis, is to compare implementation sites and control sites with respect to process of care measures derived from routinely collected data stored in administrative datasets. This is only feasible if there is a process of care measure available in the administrative data that is known to be correlated with clinical outcomes. For example, Dijkstra et al. used HbA1c levels (which are available in laboratory records) to estimate diabetic outcomes in their implementation study [24]. For the case of telemedicine-based CCM, previous research conducted in a population of veterans treated for depression in CBOCs has documented that,

controlling for casemix, patients with medication possession ratios (MPR) ≥ 0.9 were significantly more likely to respond to treatment by 6 months (defined as a 50% reduction in depression severity) compared to those with $MPR < 0.9$. The response rate among patients with antidepressant MPR ≥ 0.9 was 28.9% compared to 15.9% among those with $MPR < 0.9$ [odds ratio (OR)=2.43, confidence interval (CI)₉₅=1.29–4.57, $P=.006$] [25]. The objective of this research was to estimate the population level effectiveness of telemedicine-based CCM using this significant correlation between antidepressant MPRs derived from administrative pharmacy data and treatment response rates. We hypothesized that, compared to the population of patients at control CBOCs, the population of patients at implementation CBOCs would have significantly higher antidepressant MPRs and, by assumption, higher treatment response rates.

2. Methods

2.1. Overview

This multisite pragmatic hybrid Type 3 effectiveness–implementation study employed a pre-post, quasi-experimental design with a nonequivalent control group. The primary aim of a hybrid Type 3 effectiveness–implementation study design was to test an implementation strategy, while the secondary aim was to assess the effectiveness of the clinical intervention in routine care [26]. The results of the primary aim have been published previously [11]. This analysis focuses on the secondary aim of assessing the clinical effectiveness of telemedicine-based CCM. VA Medical Centers (VAMCs) from two Veterans Integrated Service Networks (VISNs) were chosen as implementation sites based on their number of affiliated contract CBOCs, their willingness to participate and their potential for success as perceived by VISN leadership. The implementation sites included 11 small (<1500 patients), medium (1500–5000 patients) or large (5000–10,000 patients) contract CBOCs associated with three parent VAMCs. None of the implementation CBOCs were staffed by an on-site psychiatrist. Using site-level matching, the control group was chosen from a set of 15 small and medium contract CBOCs lacking an on-site psychiatrist associated with the other seven VAMCs located in the same two VISNs.

2.2. Clinical program

During the EBQI process, all three implementation VAMCs chose to include one telephone depression nurse care manager and one supervising telepsychiatrist on the CCM team. All three VAMCs chose to exclude patients with serious mental illnesses, as well as patients already receiving specialty mental health. All three VAMCs chose to use the VA's Depression Case Finder tool to identify patients with a new antidepressant prescription and to request consults (i.e., provider referrals) for these patients. In addition, primary care providers were encouraged to refer other patients to the care managers who they thought would benefit from the CCM program. The vast majority of patients referred to the CCM program were prescribed antidepressant medications [11]. Care management activities at all three VAMCs included education/activation, barrier assessment/resolution, symptom monitoring, medication adherence monitoring, side-effects monitoring and self-management. Care manager telephone encounters were scheduled every 2 weeks for patients in the acute phase of treatment.

2.3. Target population

To estimate population impact, it is necessary to identify the target population [22]. Because of the emphasis on antidepressant treatment in the CCM program, we chose to define candidates as all patients diagnosed with depression and prescribed an antidepressant

medication. This choice was supported by the fact that 94.3% (116/123) of the patients at implementation sites with an encounter with a depression care manager were prescribed an antidepressant medication. Nevertheless, this definition is likely to be an overly broad approximation of the target population because many patients prescribed with antidepressants are stable (i.e., asymptomatic) and would not have been good candidates for referral to the CCM program. However, symptom severity was not available in VA administrative data and, thus, could not be used to further narrow the definition of the target population for the analysis.

2.4. Data sources

We extracted data from the Medical SAS Datasets at the Austin Information Technology Center for fiscal years 2005–2009. Pharmacy data were extracted from the Decision Support System National Data Extracts [27] and patient characteristics were extracted from the National Patient Care Database (NPCD) Outpatient Care Encounters Clinic Stops Events [28]. Characteristics of veterans were extracted from the NPCD datasets and included age, gender, marital status, percentage service connection (the proportion of disability attributable to military service) and ZIP code. The per capita income of each patient's ZIP code was determined from the US Census. In addition, ZIP code was used to categorize patients as rural or urban based on the rural–urban commuting area codes categorization Scheme A.

2.5. Analytical sample

The start date for each implementation site was the date the first patient was enrolled in the CCM program and ranged from April 2006 to February 2008. The start date for control sites was the average of the implementation site start dates in that VISN. Because of the lack of site-level randomization, implementation sites may have been systematically different from control sites in terms of structure, process and outcomes. Therefore, it was necessary to use a pre-post Quasi-experimental study design (see Fig. 1). The *enrollment postperiod* was defined as the 6 months after the implementation start date at each site, and the *follow-up postperiod* was defined as months 6 to 12 after the implementation start date. The *enrollment preperiod* was defined as months 6 to 12 prior to the implementation start date, and the *follow-up preperiod* was defined as the 6 months prior to the implementation start date. Index visits during the 6-month pre- and postenrollment periods were defined as the first primary care encounter (clinic stop code 323) with a primary or secondary depression diagnosis (i.e., *International Classification of Diseases-9* code of 296.2×, 296.3×, 298.0, 300.4, 309.1 or 311). Patients were excluded from the analytical sample if they had a specialty mental health encounter (primary clinic stop code: 500–599) or a diagnosis of serious mental illness (schizophrenia, bipolar disorder or substance dependence) at their index visit or during the 6 months prior to the index visit.

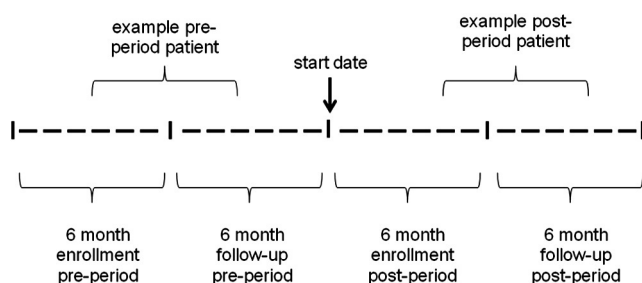


Fig. 1. Pre-post quasi-experimental study design.

Pharmacy data were extracted for all eligible patients. Prescriptions for antidepressants below the therapeutic dose were dropped (e.g., trazodone <300 mg for sleep). The days supply of nonconcurrent antidepressant prescription fills was summed to calculate the total cumulative days supply during the 6 months after the index visit. The days supply for antidepressant prescriptions written before the index visit was prorated in the calculation of days supply if the days supply carried over into the beginning of the 6-month enrollment postperiod. Likewise, the days supply for antidepressant prescriptions written near the end of the 6-month enrollment postperiod was prorated in the calculation of days supply. For multiple concurrent prescriptions of the same antidepressant, the days supply of each prescription fill was summed to calculate cumulative days supply. For multiple concurrent prescriptions of different antidepressants, the days supply of the earlier prescription was truncated (to account for possible switching). MPR during the 6 months after the index visit was calculated by dividing the cumulative days supply by 180 days. Patients with an MPR=0 were excluded from the analytical sample. Patients were classified as having adequate antidepressant adherence if their MPR is ≥ 0.9 . Based on a previous analysis of patients from the same population/setting, this cutoff was found to be the most predictive of treatment response compared to other cutoff points, including the more traditionally used cutoff point of 0.8.

2.6. Site matching

There were 15 other contract CBOCs located in the same two VISNs that also lacked on-site psychiatrists. To minimize differences between sites, we used the nearest neighbor method to match control CBOCs to implementation CBOCs with respect to MPR in the preperiod. Specifically, we calculated the proportion of patients with $\text{MPR} \geq 0.9$ during the preperiod separately for each site and matched one control site to each implementation site for a total sample of 22 sites. This process resulted in dropping the four nonimplementation CBOCs with the lowest rates of $\text{MPR} \geq 0.9$ in the preperiod.

2.7. Statistical analysis

Because there were statistically significant differences across implementation sites and control sites with respect to the proportion of patients with $\text{MPR} \geq 0.9$ in the preperiod (despite site-level matching), it was necessary to adjust statistically for preperiod differences in the multivariate analysis. Therefore, we created a variable representing the overall proportion of patients at each CBOC with $\text{MPR} \geq 0.9$ in the preperiod and used it as a covariate in the multivariate analyses. Other covariates included the patient's age, gender, marital status, service connection, per capita income and rurality.

To test the hypothesis, we used PROC GENMOD (SAS Enterprise Guide 4.1) to conduct a logistic regression analysis that controlled for the clustering of patients within sites. The clustering of patients within sites can cause significant intraclass correlation that violates the independence assumption of standard regression models and may lead to incorrect inferences concerning the rejection of the null hypotheses. We hypothesized that patients prescribed antidepressants at implementation sites would be more likely to have $\text{MPR} \geq 0.9$ than patients at control sites.

2.8. Marginal effects and incremental effectiveness

We used the results of the logistic regression analysis to generate the marginal effect associated with implementation and used it in a formula to convert adjusted differences in the probability of having $\text{MPR} \geq 0.9$ to expected differences in treatment response rates. To generate the marginal effect of being treated at an implementation site, we used the parameter estimates from the logistic regression to calculate two predictions for each patient. The first prediction was

Table 1
Characteristics of patients at study sites

Postperiod					
Independent variables	Full samplen=1588Mean (S.D.)/%	Implementation CBOCs _n =1132Mean (S.D.)/%	Control CBOCs _n =456Mean (S.D.)/%	χ^2/t	P
Patient characteristics					
Age	62.3 (14.5)	62.8 (14.7)	61.1 (13.9)	$t=-2.09$.04
Male	92.0%	92.5%	90.8%	$\chi^2=1.28$.26
Married	59.5%	58.8%	61.2%	$\chi^2=0.75$	<.39
Rural	30.7%	27.8%	37.7%	$\chi^2=15.0$	<.01
Per capita income	20,683 (9809)	20,812 (9754)	20,362 (9948)	$t=0.83$.41
Service connection 10–40%	15.2%	14.8%	16.2%	$\chi^2=0.55$.46
Service connection >50%	21.0%	19.8%	23.9%	$\chi^2=3.32$.07
Preperiod					
Independent variables	Full samplen=1488 Mean (S.D.)/%	Implementation CBOCs _n =1057 Mean (S.D.)/%	Control CBOCs _n =431Mean (S.D.)/%	χ^2/t	P
Utilization					
Primary care visits	2.36 (1.74)	2.04 (1.21)	3.17 (2.32)	$t=11.87$	<.01
Depression primary care visits	1.44 (0.75)	1.36 (0.63)	1.63 (0.96)	$t=6.36$	<.01
Mental health visits	1.29 (6.46)	1.38 (7.47)	1.08 (2.69)	$t=-81$.42
MPR	0.70 (0.29)	0.71 (0.28)	0.66 (0.29)	$t=-3.19$	<.01
MPR>.9	36.6%	39.2%	30.2%	$\chi^2=10.70$	<.01

based on the assumption that the patient was treated at an implementation site, and the second prediction was based on the assumption that the patient was treated at a control site. The difference between these two predictions represents the marginal effect of being at an implementation site for that particular patient. We then averaged the difference between the two predicted values for each patient across all patients to generate an overall marginal effect. A previous RCT conducted in the same patient population reported that CBOC patients diagnosed with depression with MPR ≥ 0.9 have significantly higher odds [OR=2.4, 95% CI=(1.29–4.57), $P=.006$] of responding to treatment by 6 months compared to CBOC patients diagnosed with depression with MPR<0.9 [25]. Based on this finding, it was determined that a 10% point increase (from 25% to 35%) in the percentage of patients with MPR ≥ 0.9 would translate into an expected 1.3% point increase in response rates. Using the CI for the MPR OR [95% CI=(1.29–4.57)], the 95% CI for this 10% increase would be 0.3%–2.5%. Applying that formula to the estimated marginal effect yields the expected difference in postperiod response rates between patients treated at implementation and control sites. This expected difference represents the population level incremental effectiveness, which we then converted into the number-needed-to-treat (NNT) statistic and corresponding 95% CI.

3. Results

The average number of patients treated was 3848 (range: 1325 to 7411) at the 11 implementation sites and 2394 (range: 712 to 4991) at the 11 control sites. There were 1558 patients ($n=1132$ at implementation sites and $n=456$ at control sites) who had an index visit during the 6-month enrollment postperiod with a depression diagnosis and an active antidepressant prescription sometime during the 6-month follow-up period. There were few significant differences between patients at implementation and control sites (see Table 1). Patients at implementation sites were statistically, but not substantially, older than patients at control sites ($t=-2.09$, $P=.04$). Likewise, patients at implementation sites were significantly less rural than patients at control sites ($\chi^2=15.0$, $P<.01$).

Of the 1132 patients prescribed an antidepressant at implementation sites, 10.3% ($n=116$) had an encounter with a depression care manager documented in the administrative data in the 6 months after their index visit. Thus, the telemedicine-based CCM program only reached about 1 in 10 of the targeted patients. In the preperiod, implementation sites had a significantly ($\chi^2=10.70$, $P<.01$) higher percentage of patients (39.2%) with MPR ≥ 0.9 than control sites (30.2%). The proportion of patients with MPR ≥ 0.9 increased between the pre-

and postperiods at implementation sites but remained essentially unchanged at control sites. Thus, in the postperiod, implementation sites also had a significantly ($\chi^2=18.3$, $P<.01$) higher percentage of patients with MPR ≥ 0.9 (42.5%) than control sites (30.9%).

In the multivariate logistic analysis that controlled for patient characteristics and preperiod site differences in MPR ≥ 0.9 (Table 2), patients at implementation sites had a significantly higher probability of having MPR ≥ 0.9 than patients at control sites [OR=1.38, 95% CI=(1.07–1.78), $P=.01$]. Of the covariates, the variable representing the proportion of CBOC patients in the preperiod with MPR ≥ 0.9 was the biggest predictor [OR=8.48, 95% CI=(1.43–50.22), $P=.02$] of a patient having MPR ≥ 0.9 in the postperiod. Age was also a significant and positive predictor of having MPR ≥ 0.9 .

Using the parameter estimates from the logistic regression, the MPR marginal effect of being treated at implementation sites compared to control sites is 7.35%. Applying the MPR to treatment response conversion formula indicates that a 7.35% point increase in the proportion of patients with MPR ≥ 0.9 translates into an expected 1% point increase in treatment response rate [95% CI=(0.2%–1.8%)]. In other words, for every 100 veterans prescribed an antidepressant at sites with telemedicine-based CCM, there would be one additional treatment responder compared to those sites without telemedicine-based CCM. The NNT is 100 [95% CI=(500–56)].

Table 2
Multivariate logistic regression results for MPR ≥ 0.9

Variable	OR	Parameter estimate95% CI	P value
Site			
Control site [ref]	–	–	–
Implementation site	1.38	[1.07, 1.78]	.01
Preperiod MPR at site	8.48	[1.43, 50.2]	.02
Age	1.01	[1.00, 1.02]	<.01
Gender			
Female [ref]	–	–	–
Male	0.77	[0.58, 1.02]	.07
Marital status			
Not married [ref]	–	–	–
Married	1.22	[0.98, 1.52]	.07
Rural	1.03	[0.85, 1.24]	.79
Per capita income ^a	1.00	[0.99, 1.01]	.69
Service connection			
<10% [ref]	–	–	–
10%–50%	0.96	[0.71, 1.31]	.81
>50%	1.31	[0.86, 2.00]	.20

^a Measured in thousands of dollars.

4. Discussion

Few studies have statistically estimated the overall effectiveness of implementing a clinical intervention on the mental health symptoms of a population of patients. The population impact of a clinical intervention depends on both its reach into the targeted population and its effectiveness for those reached [21]. It can be extremely difficult to measure population impact because both reach and effectiveness are difficult to measure at the population level. To estimate population level effectiveness, previous studies have either collected primary symptom data from implementation and control sites at great expense [23] or used differences in symptoms between intervention and control groups observed in RCTs along with assumptions about how trial inclusion/exclusion criteria would impact reach into the target population if the intervention were deployed in routine care [21]. In contrast, this study measured MPRs (derived from administrative data) at implementation and control sites and used a previous estimate of the correlation between MPR and treatment response to calculate population level effectiveness. Each of these three approaches has its strengths and limitations. The first approach is likely to have the best internal and external validity, but it is expensive to compile the large sample sizes needed to detect statistically the small differences in clinical outcomes that are likely to be observed at the population level. The second approach uses an internally valid estimate of clinical effectiveness for those patients reached but relies on making accurate assumptions about how trial inclusion/exclusion criteria would impact reach during subsequent implementation in routine care. The third approach (used in this analysis) uses an accurate estimate of reach into the target population during implementation but relies on having a valid estimate of how a process of care measure derived from administrative data contributes to clinical outcomes. In this study, the accuracy of this estimate is enhanced by the fact that the correlation between process and outcome was estimated using data from a study that was conducted in the same population and clinical setting.

Partly due to the broad definition concerning which patients would have been good candidates for telemedicine-based CCM, the reach into the target population was relatively low (10%). Primary care providers only referred patients to the program who they thought would benefit from the telemedicine-based CCM program. Presumably, many of the patients treated with antidepressants who were not referred to the program were stable on medications during the time period and would not have benefitted clinically from the program. In terms of the population impact (reach*effectiveness), we estimate that 33.85% of patients prescribed an antidepressant at sites without telemedicine-based CCM programs would have $MPR \geq 0.9$ while 41.20% would have $MPR \geq 0.9$ at sites with telemedicine-based CCM programs (a difference of 7.4% points). These relatively low levels of medication possession are similar to those observed in other depression CCM studies conducted in the VA setting [29,23]. In addition, the 7.4% point difference in rates of $MPR \geq 0.9$ between implementation and control sites observed in this study is similar to the 5.2% point difference in rates of $MPR \geq 0.8$ observed in the WAVES implementation study of depression CCM [23]. Given that only 10.3% of patients prescribed antidepressants at implementation sites had a documented encounter with a care manager, the finding that the rate of $MPR \geq 0.9$ was 7.4% points higher at implementation sites compared to control sites could be interpreted a number of different ways. First, it is possible that primary care providers referred patients to the care managers who were very likely to experience medication adherence problems and the care managers were able to help most of these patients remain adherent (i.e., $71.8\% = 7.4\%/10.3\%$). This explanation is supported by the fact that the telemedicine-based CCM program was specifically designed to promote antidepressant adherence. However, it is also possible that there was a spillover effect such that patients not

referred to care managers also benefited from the telemedicine-based CCM program (e.g., raised awareness in the clinic about antidepressant adherence). However, given the short time frame (6 months), this explanation is unlikely. Third, it is possible that the care managers had encounters with patients that were not documented in the electronic health record (i.e., coding errors) and, thus, that the reach of the program was actually larger than the observed 10.3%.

The higher probability of patients having $MPR \geq 0.9$ translated into a population level effectiveness of telemedicine-based CCM implementation of 0.01, or equivalently an $NNT = 100$. This is a very small effect size, and its magnitude primarily reflects the low reach into the target population rather than the ineffectiveness of the CCM program (which had good outcomes for those patients reached) [11]. Nevertheless, this effect size, when applied to the very large population of CBOC patients prescribed with antidepressants, suggests that implementing telemedicine-based CCM could have a clinically meaningful impact at a larger scale. Considering that about 2.5 million primary care patients are treated at CBOCs annually, that 6.9% of CBOC patients screen positive for depression annually [12] and that 70% of these fill an antidepressant prescription [25], this level of population effectiveness would result in an estimated additional 1208 veterans responding to treatment each year compared to usual care. This effect could be improved if implementation strategies were developed that increased the reach of telemedicine-based CCM.

For policy makers to interpret the population level effectiveness, it will also be necessary to consider the costs of implementation. Population level cost-effectiveness analyses will need to compare the cost and benefits of implementing a clinical intervention across the entire target population and not just those reached. While the estimated effectiveness of the telemedicine-based CCM program was small when measured at the population level, we can also expect that the costs (when distributed across the entire target population) will also be relatively small. Thus, the cost-effectiveness of the telemedicine-based CCM program could fall well below standard thresholds for deployment when measured at the population level.

An important limitation of this study is that the population level impact of telemedicine-based CCM was estimated using data collected during the early phase of implementation. Thus, these findings do not reflect the steady state of the implementation initiative, which may have become more or less successful over time. Another limitation is that the formula used to convert differences in MPR into differences in treatment response rates was based on observational data, which could have been subject to selection bias. Similarly, if depression CCM has other mechanisms of action besides antidepressant adherence (e.g., self-management, social support), we may have underestimated population level effectiveness [13,30]. In addition, the accuracy of our estimate of the marginal effect of CCM on MPR relied on the internal validity of our quasi-experimental study design. Internal validity may have been compromised by the fact that VAMCs were chosen based on their willingness to participate and their potential for success as perceived by VISN leadership. Despite these limitations, this study makes an important contribution to the growing field of comparative effectiveness research, as it is one of only a handful of studies that have measured the population level effectiveness of a clinical intervention deployed in routine care.

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