Letters

RESEARCH LETTER

Drive Times to Opioid Treatment Programs in Urban and Rural Counties in 5 US States

Methadone for opioid use disorder can be dispensed only from US Substance Abuse and Mental Health Services Administration (SAMHSA)-certified opioid treatment programs (OTPs), creating access barriers in rural counties with a shortage of facilities. Canada and Australia allow primary care prescribing and pharmacy dispensing of methadone to expand access.[1] Therefore, we examined drive times to the nearest OTP in urban and rural counties in 5 US states with the highest county rates of opioid-related overdose mortality.[2] In addition, we compared drive times to federally qualified health centers (FQHCs) as potential primary care methadone-prescribing locations and to dialysis centers as treatment locations for a different chronic disease requiring frequent engagement.

Methods | The outcome was the minimum drive time in minutes from the county mean center of population to the nearest OTP, FQHC, and dialysis center using the Esri ArcGIS rural drive-time tool (September 2017 version), which simulates automobile movement between 2 points along a national street network based on historical average speeds.[3] From the 2010 US Census, we obtained the coordinates of the county mean center of population for all counties in Indiana, Kentucky, Ohio, Virginia, and West Virginia, excluding counties with geographic changes after the census. We geocoded 2017 OTP, FQHC, and dialysis center street addresses from the SAMHSA OTP Directory and the Health Resources and Services Administration data warehouse. Addresses not matched during batch geocoding were hand reviewed. We excluded school-based FQHCs and facilities remaining unmatched after hand review.

We stratified counties by the 2013 National Center for Health Statistics urban-rural county classification scheme, dividing counties into urban (large central metros, large fringe metros, medium metros, and small metros) and rural (micropolitan and noncore) levels (**Table**). We assessed the association across urban-rural classification using Welch analysis of variance. We used a paired *t* test to compare drive times to the nearest OTP with drive times to the nearest FQHC or dialysis center, using a Bonferroni correction for multiple comparisons. Hypothesis tests were 2-sided with α=.05. We completed our analyses in Stata 15 (StataCorp).

Results | Of the 487 of 489 counties included, 270 (55.3%) were rural. Within the 5 states, 109 OTPs, 952 FQHCs, and 837 dialysis centers were included. Among all counties, the mean drive time to the nearest OTP was 37.3 (95% CI, 35.5-39.1) minutes and the mean drive time to the nearest OTP increased from 7.8 (95% CI, 5.7-9.9) minutes in the urban classification to 49.1 (95% CI, 46.3-51.8) minutes in the noncore rural classification ($P < .001$; Table). The mean drive time to the nearest FQHC was 15.8 (95% CI, 14.8-16.9) minutes (difference with OTP, 21.5 [95% CI, 19.5-23.4] minutes) and to the nearest dialysis center was 15.1 (95% CI, 14.1-16.2) minutes (difference with OTP, 22.1 [95% CI, 20.5-23.8] minutes). Longer drive times for OTPs vs FQHCs and dialysis centers were found for all urban-rural classifications (**Figure**) except large central metros, with the greatest difference in rural counties.

Table. Drive Time From County Mean Center of Population to the Nearest Treatment Centers by Urban-Rural Classification, 2017

	Drive Time, Mean (95% CI), min					Difference in Drive Time, Mean (95% CI), min	
Classification[a]	To OTP	To FQHC	*P* Value[b]	To Dialysis Center	*P* Value[c]	To OTP vs FQHC	To OTP vs Dialysis Center
All counties	37.3 (35.5 to 39.1)	15.8 (14.8 to 16.9)	<.001	15.1 (14.1 to 16.2)	<.001	21.5 (19.5 to 23.4)	22.1 (20.5 to 23.8)
Noncore	49.1 (46.3 to 51.8)	17.3 (15.4 to 19.2)	<.001	22.6 (20.5 to 24.6)	<.001	31.7 (28.3 to 35.2)	26.5 (23.8 to 29.2)
Micropolitan	41.1 (37.7 to 44.6)	15.7 (13.2 to 18.2)	<.001	10.1 (8.6 to 11.6)	<.001	25.4 (21.6 to 29.2)	31.0 (27.2 to 34.9)
Small metro	35.0 (29.4 to 40.6)	14.7 (11.8 to 17.6)	<.001	14.9 (11.9 to 17.9)	<.001	20.3 (14.3 to 26.3)	20.1 (14.7 to 25.6)
Medium metro	21.1 (17.7 to 24.5)	13.4 (11.0 to 15.7)	<.001	9.6 (7.1 to 12.2)	<.001	7.8 (4.8 to 10.7)	11.5 (8.4 to 14.6)
Large fringe metro	25.2 (22.5 to 27.9)	16.2 (13.8 to 18.6)	<.001	11.3 (9.7 to 12.9)	<.001	9.0 (6.1 to 12.0)	13.9 (11.5 to 16.4)
Large central metro	7.8 (5.7 to 9.9)	6.3 (3.4 to 9.2)	.32	5.4 (4.0 to 6.8)	.06	1.4 (−1.7 to 4.5)	2.4 (−0.1 to 4.8)

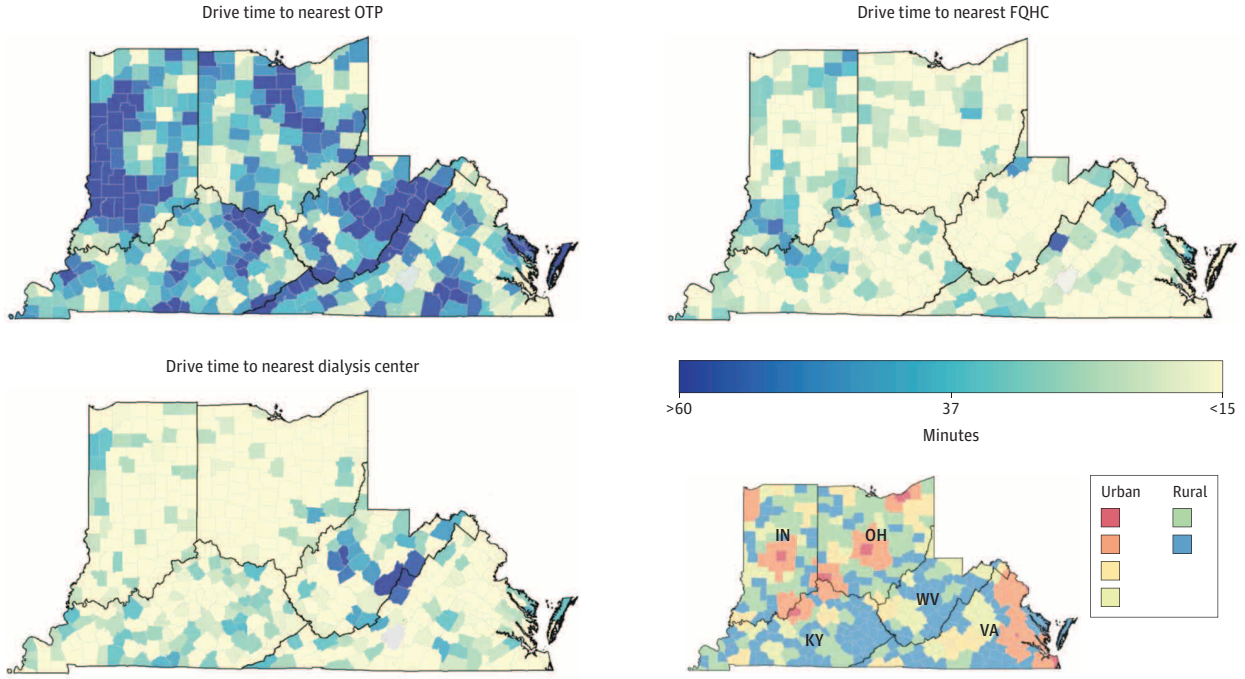
Abbreviations: FQHC, Federally Qualified Health Center; OTP, opioid treatment program.

[a] 2013 National Center for Health Statistics urban-rural county classification scheme divides counties into urban (large central metros, large fringe metros, medium metros, and small metros) and rural (micropolitan and noncore) levels.

[b] Paired *t* test for drive time to OTP vs drive time to FQHC.

[c] Paired *t* test for drive time to OTP vs drive time to dialysis center.

Figure. Drive Time From County Mean Center of Population to Nearest Opioid Treatment Program (OTP), Federally Qualified Health Center (FQHC), and Dialysis Center, 2017



Discussion | Rural county classification was associated with longer drive times to the nearest OTP compared with urban counties. Drive times to OTPs were longer than to FQHCs or dialysis centers. The greater geographic availability of hemodialysis, which requires engagement 3 times a week, contrasts with methadone treatment availability, for which federal law requires engagement 6 times a week for medication dispensing. Enabling FQHC methadone provision in the United States, mirroring practices in Canada and Australia, would expand geographic access without construction of additional facilities and may further integrate opioid use disorder treatment into primary care. An alternative path to improving access would be constructing new OTPs, as was done previously with dialysis centers whose access was expanded by the 1972 extension of Medicare disability coverage,[4] although this would require significantly more investment in rural health care infrastructure. Limitations include that drive times were county-level population estimates, individual drive times within counties vary, and smaller geographic units would improve drive time estimation. County estimates are presented given the importance of local government approval of OTPs. The urban geographic availability of methadone was likely overestimated because of public transportation.

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COMMENT & RESPONSE

Metformin for Type 2 Diabetes

To the Editor Drs Flory and Lipska[1] reviewed the literature on metformin, analyzing several aspects such as its mechanism of action, clinical use, and safety.

The efficacy of metformin has also been investigated in other studies, comparing it with other drugs already in use. In the short and medium term, metformin has shown an efficacy comparable with sulfonylureas, without exposing the patient to hypoglycemic risk, and to acarbose and pioglitazone, and with efficacy higher than dipeptidyl peptidase 4 (DPP-4) inhibitors but lower than glucagon-like peptide 1 (GLP-1) receptor agonists. In long-term monotherapy, metformin shows an increased efficacy compared with sulfonylureas.[2]

In addition, in patients with type 2 diabetes aged 10 to 16 years, several randomized studies have shown an efficacy and tolerability of metformin similar to that in adults.[3] In elderly individuals, because of renal function impairment, patients may become ineligible for metformin.[2] In these patients, the risk of developing metformin-induced lactic acidosis increases. However, the incidence of this adverse event has decreased over time, thanks to an education campaign by specialists on the proper use of metformin in patients at risk, with a decrease in incidence from 76.8 cases per 100 000 in 2010 to 32.9 cases per 100 000 in 2014.[4] The use of metformin in elderly men with type 2 diabetes showed a reduced risk of all-cause mortality and age-related comorbidities such as cardiovascular diseases, neoplasms, dementia, depression, and frailty.[5]

In patients who do not tolerate metformin, sulfonylureas represent a good option; however, insufficient data are available to assess differences in outcomes (hospitalization, complications, all-cause death) or cost-effectiveness, or compared with long-term use of new brand-name drugs.

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To the Editor In their Clinical Update on metformin, Drs Flory and Lipska succinctly highlighted metformin's robust safety data and low cost, rendering it a good first-line pharmacologic treatment for type 2 diabetes in most patients.[1] We agree with their conclusion but wish to mention metformin-induced vitamin B_{12} deficiency, an elusive yet common and potentially reversible adverse effect of long-term metformin use that may have implications for patients' quality of life.

Symmetrical polyneuropathy is the most common form of neuropathy associated with diabetes and vitamin B_{12} deficiency. A symmetrical lower extremity sensorimotor polyneuropathy in patients with diabetes on metformin may masquerade as diabetic neuropathy, prompting clinicians to add superfluous pharmacologic therapies such as gabapentin or pregabalin.

Instead, many cases of diabetic neuropathy may represent vitamin B_{12} deficiency. Observational studies suggest that as much as 30% of patients with diabetes taking metformin develop clinically significant vitamin B_{12} deficiency.[2] Vitamin B_{12} deficiency has been associated with larger doses and long-term use (>6 months) of metformin. In a recent meta-analysis of 31 studies, patients with diabetes taking metformin had a significantly higher risk of developing vitamin B_{12} deficiency compared with patients not taking metformin (relative risk, 2.09 [95% CI, 1.49-2.93]; $P = .0001$).[3] Metformin alters ileal enterocyte calcium-dependent membranes, which impairs vitamin B_{12}-intrinsic factor absorption and can be partially reversed by calcium intake.[4]

Treating vitamin B_{12} deficiency is straightforward and risk free and may have profound implications for a patient's quality of life, with symptoms related to peripheral neuropathy improving in as little as 3 months.[5] Hence, we suggest that patients with diabetes taking long-term metformin therapy undergo annual screening for vitamin B_{12} deficiency using a serum vitamin B_{12} measurement. In patients with a normal-range serum vitamin B_{12} level who have an unexplained macrocytosis, peripheral neuropathy despite glycemic control, or other risk factors for vitamin B_{12} deficiency (eg, concomitant proton pump inhibitor use, vegan diet), we recommend obtaining a serum methylmalonic acid measurement.

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