

Notice of submission: This protocol was finalized and uploaded to GitHub on November 15, 2019 and modified on November 15, 2019.

Driving Times to Opioid Treatment Programs and Pharmacies

Study Protocol

Methods and Statistical Analysis Plan

Summary:

Purpose: The purpose of this study is to estimate the mean driving time, in the United States (US), to the closest opioid treatment program (OTP) and pharmacy, for individuals from their places of residence.

Primary outcome: The mean driving time for individuals from their residence to the nearest OTP and pharmacy is the primary outcome and will be estimated by a two-step process. First, the driving time from the ‘mean center of population’ (MCOP) of each US Census tract (within the 50 states and District of Columbia) to the closest OTP and pharmacy will be calculated. Second, a weighted mean of these driving times will be calculated, with the population of each census tract as weightings.

The “closest” OTP and pharmacy to a MCOP will be defined as the OTP and pharmacy with the shortest driving time from that location (see further details below).

Data sources:

Census tracts: A public data file containing the population of and geographic coordinates of the mean population center of each census tract from the 2010 US Census was downloaded from : <https://www.census.gov/geographies/reference-files/2010/geo/2010-centers-population.html>. Also included in the file was Federal Information Processing System (FIPS) code for the census tract and corresponding county/county-equivalent entity and state. Census tracts and accompanying information from United States territories were removed.

Opioid treatment programs: A list of currently certified and provisionally certified OTPs was downloaded from Substance Abuse and Mental Health Services Administration (SAMSHA) (<https://dpt2.samhsa.gov/treatment/directory.aspx>). OTPs located in territories of the United States were removed. Addresses with a “P.O. Box” were manually confirmed by visiting the treatment center website or calling the treatment center.

Pharmacies: A list of pharmacies in the U.S. ~~registered with the Drug Enforcement Agency (DEA) will be downloaded. Included pharmacies will be limited to pharmacies with active DEA registrations. If technically feasible with the dataset, included pharmacies will be further limited to pharmacies that are permitted to dispense Schedule II narcotics. enrolled in RxOpen (by~~

Healthcare Ready) was downloaded as the intended product for purchase (single issue for single user list of DEA registrants) was discontinued by the NTIS. Pharmacies with a status of “open” on November 15, 2019 were included in the analysis.

Geocoding:

Addresses will be batch geocoded using ArcGIS with StreetMaps Premium Locators. OTP addresses that are not matched on batch geocoding will be hand-reviewed. OTP addresses will be clarified as necessary for geocoding, potentially including using treatment facility websites and/or calling clinics to confirm addresses. Given the large number of pharmacies, pharmacy addresses that are not matched during batch geocoding will be excluded.

Determination of closest OTP and Pharmacy:

For the geographic coordinates of the mean center of population of each census tract, the “point-to-point” distances to all OTPs and pharmacies in the United States will be calculated using the Haversine formula. The Haversine formula determines the great-circle distance between two points, assuming a spherical globe. The list of ten nearest OTPs and pharmacies, for each mean center of population, as measured by great-circle distance will be created.

For each of the ten nearest OTPs and pharmacy, the driving time and driving distances will be calculated using the ArcGIS Network Analyst (OD Distance Matrix) with StreetMaps Premium using historical average driving speeds. The OTP and pharmacy with the lowest drive time from each MCOP will be used as the “closest” OTP/pharmacy for each census tract. The maximum (one-way) driving time that will be allowed is 12 hours, given that longer driving times are unrealistic for patients who often have to obtain methadone on a near-daily basis and to reduce computational times.

Statistical plan

Analyses will be conducted in R or another accepted statistical program. Descriptive statistics will be generated to help readers understand census tracts. An example of further descriptive statistics to be presented is included in Table 1.

Table 1:

	Number of census tracts	Mean population (+/-) std of census tracts	Total population	Percentage of census tracts with driving option to OTP	Population with driving option to OTP	Percentage of census with driving option to pharmacy	Population with driving option to OTP
United States							
NCHS Large							

central metro							
Large Fringe Metro							
Medium Metro							
Small Metro							
Micropolitan							
Non-core							

Primary outcome:

The primary outcome of this study is to estimate the mean driving time to the closest OTP and pharmacy from the places of residence of all people residing in the United States. This will be estimated by calculating the driving time from the MCOP of each census tract within the 50 states and District of Columbia (obtained from the US Census Bureau) to the closest OTP and pharmacy. A weighted mean of the MCOP to OTP and MCOP to pharmacy driving times will be calculated, using the population of the census tract as the weight. (An MCOP to OTP and MCOP to pharmacy driving time will only be included in the calculation of weighted mean and statistical testing if both an MCOP – OTP and MCOP – pharmacy driving route is identified for that MCOP, with times are under 12 hours).

The “closest” OTP and pharmacy to an MCOP will be based on the OTP and pharmacy with the shortest driving time from that location. This will be calculated by the ArcGIS OD Distance Matrix using the StreetMaps Premium Extension (see details of algorithm in “Determination of closest OTP and Pharmacy:” above).

The hypothesis is that the weighted mean of driving times to OTPs will be longer than the weighted mean driving time to pharmacies. The null hypothesis is that the weighted mean driving times to OTPs and pharmacies will be equal. A weighted one-sample t-test on the differences between OTP and pharmacy driving times will be conducted to determine the likelihood that the results occur if the null hypothesis were true.

Secondary outcomes:

For each of the classifiers in the 2013 NCHS Urban-Rural County Classification Scheme (“Large Central Metro”; “Large Fringe Metro”; “Medium Metro”; “Small Metro”; “Micropolitan”; and “Non-Core”), the mean driving time to the closest OTP and pharmacy from places of residence will be calculated and will represent a secondary outcome.

Using the same method as described in “Primary Outcome”, the mean driving time to the closest OTP and pharmacy from the places of residence of all people residing in each of the NCHS county classifications across the United States. This will be estimated by calculating the driving time from the MCOP of each census tract within the 50 states and District of Columbia (obtained from the US Census Bureau) to the closest OTP and pharmacy. A weighted mean of the MCOP to OTP and MCOP to pharmacy driving times will be calculated for each Urban-Rural county classifier, using the population of the census tract as the weight. (An MCOP to OTP and MCOP to pharmacy driving time will only be included in the calculation of weighted mean and statistical testing if both an MCOP – OTP and MCOP – pharmacy driving route is identified for that MCOP, with times are under 12 hours).

The “closest” OTP and pharmacy to an MCOP will be based on the OTP and pharmacy with the shortest driving time from that location. This will be calculated by the ArcGIS OD Distance Matrix using the StreetMaps Premium Extension (see details of algorithm in “Determination of closest OTP and Pharmacy:” above).

The hypothesis is that the weighted mean of driving times to OTPs will be longer than the weighted mean driving time to pharmacies within each county classifier. The null hypothesis is that the weighted mean driving times to OTPs and pharmacies will be equal for each county classifier. A weighted one-sample t-test on the differences between OTP and pharmacy driving times for each county classifiers. The t-tests will be conducted using the “weights” package in R or another implementation if an alternative statistics software is used.³ A Bonferroni correction for 7 statistical tests (6 secondary outcomes plus primary outcome) will be applied to all secondary outcome assessments.

The Welch ANOVA will be used to determine whether driving time to OTP and driving time to pharmacy vary by NCHS county classification. The hypothesis is that county classes that are more urban will have shorter drive times to OTP and shorter drive times to pharmacies.

Pre-planned descriptive analysis: The proportion of individuals living in census tracts which have an MCOP that is a greater than or equal to 30-minute drive to the closest OTP and closest pharmacy will be estimated for the United States, by state, geographic census division, and by NCHS county classification. This will similarly be estimated for the proportion of individuals a greater or equal to 60-minute drive to the closest OTP and pharmacy. This will be reported by state in either the main text, a table/figure, or supplementary appendices. The number of people living in census tracts which have a drive time to a pharmacy that is lower than the drive time to an OTP will be estimated.

Mean weighted driving times and driving distances will also be reported by state in either the main text, a table/figure, or supplementary appendices.

A note on changes:

Changes have been made between the initial request to the Stanford Institutional Review Board for a Human Subjects Research determination and the final request for determination of Human

Subjects Research (all submissions uploaded). The finalization of this protocol reflects the information contained in the final Human Subjects Research Determination.

Changes include:

- 1) ~~Using a different pharmacy address data source. The previously identified database was inconsistently displayed on the website, included only pharmacies in US areas affected by disasters, and did not allow for determination of which pharmacies were permitted to dispense narcotics. The originally identified data source, a list of pharmacies enrolled in RxOpen by Healthcare Ready was re-downloaded on 11/15/2019, as the intended product for purchase (single issue for single user list of DEA registrants) was discontinued by the National Technical Information Service.~~
- 2) Using ArcGIS software for driving time estimation to use industry-standard software with increased control of parameters instead of the Google Maps/Bing Maps APIs identified.
- 3) Using ArcGIS software for geocoding instead of the Google Maps/US Census Bureau geocoders originally identified. The US Census Bureau geocoder was not used due to too many unmatched results and closer reading of the Google Maps Terms of use precluded the storage of geocodes longer than 30 days.
- 4) Refinement of the algorithm for finding closest OTP and pharmacy. To provide a better estimate of the “closest” OTP/pharmacy to each MCOP, the “closest” OTP or pharmacy was re-defined as the OTP and pharmacy with the smallest driving time rather than based on the smallest great-circle distance. This better reflects functional access for patients, based on road network characteristics, than great-circle distance. To reduce computational times, and to reflect real-world driving options, one-way drive times over 12 hours will be excluded.

All the changes were made before calculating any distances between census tract MCOPs and pharmacies/OTPs, or any determination of the closest OTPs and pharmacies to census tract MCOPs.

Declaration at the time of upload of the protocol:

At the time of uploading the protocol, the following have been conducted:

- This project has been determined not to be human subjects research by the Stanford Institutional Review Board. The further changes/refinements have been confirmed with the IRB to not change the previous determinations.
- Python code (for determining the ten closest OTPs/pharmacies to each MCOP and interfacing with ArcGIS) has been developed and tested with independent data from Data.gov.
- Data files for OTPs and Census Tracts have been downloaded. Data files containing lists of pharmacies have been downloaded (“Healthcare Facilities”, <https://www.usda.gov/reconnect/eligible-area-map-datasets>) and

https://fusiontables.google.com/DataSource?docid=1iomOmbp8LWCNcFUXgSAHeKZCWKzohFMf7g_Rv6U#rows:id=1. The data file of DEA registrants has not yet been purchased.

- The testing spreadsheet has been created. The algorithm has been tested using sample data files from Data.gov.
- Geocoding has been partially performed using US Census Bureau and Google Maps Geocoders. The BingMaps Geocoder has also been tested.

At the time of the re-submission of this protocol, the following have not been completed:

~~— Purchasing of the DEA registrant data file~~

- Geocoding with ArcGIS software
- Any calculation of distances or drive times between census tract MCOPs and pharmacies/OTPs using any software
- Determination of the closest OTPs and pharmacies by distance or driving times to census tract mean centers of population
- Any statistical analysis

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November 15, 2019