Does Burden of Travel to Health Care Predict Survival among Chicagoans with Colorectal Cancer?

BY

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THESIS

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LIST OF ABBREVIATIONS

2SFCA	2-Step Floating Catchment Area
AHA	American Hospital Association
API	Application Program Interface
CI	Confidence Interval
CRC	Colorectal Cancer
СТА	Chicago Transit Authority
GIS	Geographic Information System
GTFS	General Transit Feed Specification
HR	Hazard Ratio
ISCR	Illinois State Cancer Registry
NAACR	North American Association of Central Cancer Registries
NDI	National Death Index
NHIA	NAACR Hispanic Identification Algorithm
NHTS	National Household Transportation Survey
OR	Odds Ratio
РСР	Primary Care Providers
PLCO	Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial
SES	Socioeconomic Status
TIGER	Topologically Integrated Geographic Encoding and Referencing
U1	Unstaged-1, unstaged due to missing information
U2	Unstaged-2, unstaged due to declining further work-up

SUMMARY

A study of the effect of travel burden on colorectal cancer prognosis was carried out in a retrospective cohort of Chicago residents diagnosed from 2006 to 2008. Potential travel between patients' homes and diagnosing facilities were modeled and scores were generated for use in logistic and proportional hazards models to assess whether potential difficulty of traveling to care is associated with colorectal cancer stage at diagnosis and survival in urban residents.

Burden of travel to cancer care is associated with colorectal cancer stage at diagnosis and colorectal cancer-specific survival. Increased travel burden score is associated with improved colorectal cancer-specific survival. Both transit and driving burden perform similarly in predicting stage at diagnosis. However, transit burden score is associated with colorectal cancer survival while driving burden score is not. Burden of travel to diagnosing facility is associated with increased odds of advanced stage at diagnosis in men, and decreased odds of advanced stage in women. Burden of travel to care does not interact with patient sex or race/ethnicity in predicting survival. Combining the components of travel burden into a single score improves model performance and coefficient interpretability.

Although travel burden is associated with stage at colorectal cancer diagnosis and transit burden is associated with survival, increased burden of travel to health care does not appear to account for racial/ethnic disparities in colorectal cancer prognosis among urban residents.

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I. INTRODUCTION

A. Background

1. Burden of Colorectal Cancer

Colorectal cancer (CRC) is the third most common incident cancer in men worldwide, and the second most common in women (1–3). In the US, CRC is the third most common incident cancer and the third most common cause of cancer death in both men and women (1). While this is also the case in Illinois, state cancer and mortality rates are higher than national rates in blacks, whites, and both sexes (1,4,5). In the US CRC incidence and mortality are highest among people 65 and older, men, and blacks (6,7). CRC incidence and mortality have been declining since the 1980s in all groups except people under 50. However, CRC remains rare in this age group (6,7).

CRC is largely preventable by modifying risk factors, especially dietary risk factors, and screening (1). Declines in incidence and mortality have been primarily attributed to screening, which can directly prevent CRC when it involves colonoscopy and removal of precancerous polyps (1,2). Screening for early stage cancers is also important in this site because early CRC is often asymptomatic or demonstrates symptoms that are non-specific (1). Population groups less likely to undergo colonoscopy, including people under 50 and blacks, are more likely to have later stage cancer at diagnosis (1,6).

Racial disparities characterize CRC burden. In the US and in Illinois, CRC incidence is higher in blacks than in whites (Table I). Black CRC patients are more likely than other racial or ethnic group to have late stage CRC at diagnosis, and have higher mortality rates than other groups (1). Although incidence and mortality rates are decreasing for all racial/ethnic groups, racial disparities have widened. For example, in Illinois in 1990 CRC incidence was 2.5 cases/100,000 greater in blacks than in whites. In 2011, the incidence difference was 14.6 cases/100,000 (4). Disparities have been attributed to differing prevalence of risk factors, use of recommended screening, and access to health care (1,8).

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Black Men	White Men	Black Women	White Women
63.8	50.9	47.6	38.6
75.7	58.3	53.2	42.8
29.4	19.2	19.4	13.6
32.5	21.3	22.2	14.8
	63.8 75.7 29.4	63.850.975.758.329.419.2	63.850.947.675.758.353.229.419.219.4

TABLE I. US AND ILLINOIS COLORECTAL CANCER INCIDENCE AND MORTALITY PER 100,000 POPULATION BY SEX AND RACE. 2006-2010 (9)

2. Spatial Access to Health Care

Spatial access to health care may predict CRC-specific survival and stage at diagnosis in CRC and other cancer sites. However, this research is in an early stage and has not been translated yet to urban areas.

For example, a state level analysis conducted by Wan, et al. found that lack of spatial access to oncology care predicts poorer CRC survival in Texas (10). However they found that the CRC survival of urban residents, while vulnerable to other forms of disadvantage, was not affected by disparities in spatial access to oncology services. The authors speculated that these services, which are concentrated in urban areas, may have reached a threshold of availability beyond which spatial access disparities do not have an important effect on survival because demand is still met.

However, there is evidence that spatial factors may harm urban residents in terms of cancer risk and stage at diagnosis. Research conducted in Illinois indicates that urban residents are at highest risk of common cancers including CRC (11). At the state level, Wang, et al. found that clusters of late stage breast cancer risk are found in areas with high social disadvantage and poorer access to health care (12). Among Illinois residents, primary care access, which related primary care physician supply to high health care-need population within a 30-minute travel time area, was a stronger predictor of stage at breast cancer diagnosis than travel time to the nearest mammography facility. However, social and demographic factors were more important within the city of Chicago. A common feature of research on spatial access and cancer prognosis to date is the assumption that patients will drive or be driven to their source of care. While this assumption may be valid for most patients, it may result in underestimation of the extent and effect of spatial access disparities within urban areas. This is particularly the case when the level of analysis is the state, because it will include many rural areas with a much larger scale of distance than urban areas. Although distances in urban areas may be shorter, they may also take longer to travel. For example, in an analysis of National Household Transportation Survey (NHTS) data by Probst, et al., trips to medical or dental care were more than twice as long among rural residents compared to urban residents. However, they took only 31% more time (13).

Such analyses also fail to take public transit into account as an important feature of urban transportation networks. Transit access to care should be of special interest in public health because it may be used more frequently by people with disabilities, urban residents, and groups that experience health disparities (14). Among people with disabilities whose households responded to the 2009 National Household Transportation Survey (NHTS), African Americans, people from low-income households, and people living in metro areas with available heavy rail are less likely than others to obtain car rides from household members (14). In the same survey, most car rides by household members were given to spouses (14). However, African Americans are less likely to be married than their white and Hispanic peers, and this relationship holds among cancer patients (15,16). African Americans with cancer are also more likely than whites to refuse recommended treatment (17–19). Differences in insurance coverage and attitudes towards cancer are established reasons for refusal; difficulty in complying with the demands of treatment when it cannot be accessed regularly may be another reason (19–21).

Because urban residents and racial/ethnic groups that experience cancer disparities have different transportation opportunities and constraints that have seldom been modeled, spatial access to health care has not been excluded as a prognostic factor in cancer in urban areas; nor has it been excluded as a potential cause of racial disparities in cancer treatment and CRC-specific survival.

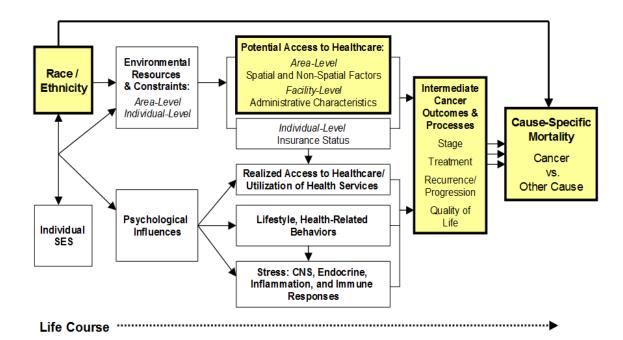
3. The Chicago Prostate and Colorectal Cancer Survival Study

The Chicago Prostate and Colorectal Cancer Survival Study is a population-based retrospective cohort study conducted to determine the causes of racial disparities in cancer survival in the Chicago area. The study brings together individual and area level data on case characteristics, health care facilities and availability, and area level sociodemographic factors in database of more than 86,000 incident cancers in Cook County, IL between 1995 and 2008.

The cohort study is based on the pathway linking SES and health in the MacArthur Model, adapted for cancer outcomes (22). The model for the cohort study is depicted in Figure 1.

Case and facility data from this study were used in the present research to model individual trips from case residential addresses to diagnosing facilities in Chicago. This research also uses area level measures of socioeconomic status and supply of primary care that were created by the parent study. These measures are described in the Methods section below.

Conceptual Framework



The MacArthur model for pathway from SES to health modified for cancer outcomes

Figure 1. The conceptual model for the Chicago Prostate and Colorectal Cancer Survival Study

B. Study Purpose

1. Travel Burden

Travel burden is an individual level spatial barrier to health care within the context of a local transportation network. Travel burden is a measure of the difficulty of traveling from an individual's home or neighborhood to their actual source of health care for a given condition. Travel burden does not yet have an operational definition. This research proposes three components: time, cost, and complexity.

The purpose of this research is to build a measure of travel burden that takes into account features of an urban public transit network, and determine the relationship or travel burden to CRC prognosis.

2. <u>Questions</u>

Is travel burden a prognostic factor in CRC? Specifically, does it associate with stage and presentation and CRC-specific survival?

If travel burden is a prognostic factor, does it partially account for racial disparities in CRCspecific survival? If travel burden is not a prognostic factor, why not?

3. <u>Aims</u>

<u>Aim 1</u>

Construct individual measures of potential travel burden by public transit and driving based on the results of systematic literature review on methods of spatial access measurement.

<u>Aim 2</u>

Determine whether travel burden is independently associated with CRC prognosis.

Primary Hypothesis: Individual burden of travel to care is associated with cancer-specific survival and stage at diagnosis in people with colorectal cancer.

<u>Aim 3</u>

Explore the nature of the association between travel burden and colorectal cancer prognosis.

Secondary Hypothesis A: If travel burden is associated with colorectal cancer survival, this association is driven primarily by travel time and prediction is improved by adding variables related to travel cost and complexity.

Secondary Hypothesis B: If travel burden is associated with colorectal cancer prognosis, it interacts with patient race/ethnicity and contributes to racial disparities in both stage at diagnosis and cancer-specific survival.

Secondary Hypothesis C: If travel burden is not associated with colorectal cancer survival, this is because its effect is already captured by socioeconomic status or neighborhood disadvantage.

4. <u>Conceptual Model</u>

The conceptual model for this research is adapted from the model of the parent study (Figure 2).

Travel burden is conceptualized as a consequence of area- and individual level environmental resources and constraints. Time needed for a care trip may be a consequence of availability of area-level health care resources; this is seen in lack of spatial access among rural residents whose nearest facility may be miles away. Individual resources, such as health insurance and income, may also influence travel burden when patients choose health care facilities based on insurance coverage instead of or in addition to location. A combination of personal and area level resources could also allow some patients to choose a preferred or perceived highest quality facility outside their neighborhood, increasing their apparent travel burden.

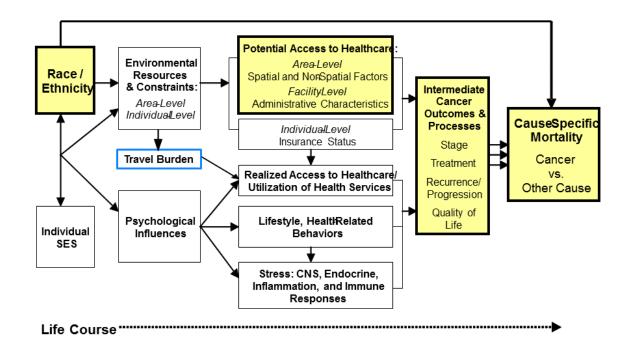


Figure 2. Conceptual model of SES and cancer outcomes modified to include travel burden

Realized access to health care may be partially influenced by burden of travel to care. Travel burden estimates individual level difficulty of accessing health care using patient residential addresses and the locations of the health care facilities where they were diagnosed. Travel burden is hypothesized to influence stage at diagnosis and CRC-specific survival through its effect on the difficulty of routinely accessing care. High travel burden could influence patients to delay screening or care, refuse further treatment if they know they will have difficulty accessing the health care facility, or unintentionally miss appointments because their transportation is burdensome or unreliable.

II. LITERATURE REVIEW

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A. Colorectal Cancer Treatment and Survival

Disparities in overall mortality between black and white CRC patients are large, have been increasing since at least the 1980s, and are partially attributable to later stage at diagnosis among black patients (7,23). However, stage-specific mortality disparities have grown as well (23).

Racial disparities in CRC stage at diagnosis and mortality are unlikely to be caused by biological differences. In the past 30 years CRC incidence and mortality have declined in all US population groups except people under 50 (6,7). The proximate cause of the increasing disparity is greater decline of mortality rates among whites compared to blacks. Prior to the 1980s, white patients experienced the highest CRC mortality rate (7,23).

In CRC as in other cancer sites, racial survival disparities are minimal or absent among black and white patients treated in equal access health care systems (24–27). Black patients may be less likely than whites to receive standard treatment, and adjustment for treatment reduces the apparent effect of race or ethnicity, suggesting that differences in referral or actual treatment may contribute to survival disparities (28–30). Greater frequency of advanced stage at CRC diagnosis among black patients may also be related to health care use or access. Among people 50 or older, receipt of recommended screening is more common among whites than among blacks (1). Among participants in the Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial (PLCO), black patients were less likely than whites to have diagnostic colonoscopy when study-sponsored flexible sigmoidoscopy was abnormal. However, actual frequency of CRC was similar between white and black participants (8).

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B. Spatial Access to Health Care

1. <u>Measurement</u>

General Measurement Issues

A paramount issue in modeling spatial access to care is the validity of the estimates. This has been examined in both driving and public transit.

In a 2008 study, Cinnamon, et al. surveyed patients undergoing treatment for CRC or other common cancers at several hospitals in northern England (31). Patients' recalled travel times to the hospital were compared to modeled travel times over road networks. The researchers used both a straight-line and a typical network analysis approach that assigned average road segment speeds based on road type and urban/rural location. They found that the GIS estimates of travel time were reasonably close to time reported by patients (r = 0.856), although modeled times tended to be overestimates with increasing distance between the hospital and individual's home. However, based on the survey responses they concluded that GIS modeled trips may be superior for outcome modeling purposes because they are closely related to actual travel times, eliminate rounding errors made by patients, and represent average conditions.

In an urban accessibility analysis, Salonen and Toivonen compared public transit and driving access to central Helsinki in sets of increasingly complex spatial models (32). Modeling both time and distance, they demonstrated that correlations were generally strongest across transit modes when the network models had comparable levels of complexity. Intermediate driving models included speed limits and congestion estimates, while advanced models added parking and a "door-to-door approach". Intermediate transit models included simplified vehicle speeds and transfer times; schedules and arrival/departure times were considered advanced. Model details tended to be sources of delay such as parking, congestion, and transfers, and estimates of travel time increased with model complexity. Therefore mismatched models still correlated well—sometimes better than matched models—when they were advanced and intermediate.

A common format for transit schedule data, General Transit Feed Specification (GTFS), is used by many transit agencies in the US including CTA (33). This format was developed to incorporate transit data into web maps, and some researchers have suggested using web maps directly or through application program interfaces (APIs) to generate travel measures for batches of trips (34,35). This method has the advantage that it can be carried out in SAS, sample code is freely available, and the program can write the results of the analysis directly to a SAS dataset. Transit and driving analyses can also be carried out at the same time using this method. Most web map hosts place limits on repeated queries, however additional access can be purchased. A disadvantage of this method is that the data sources and analytic methods of the underlying maps may not be transparent to the researcher.

Several authors have proposed methods, especially kernel density and 2-step floating catchment area (2SFCA), to measure area level access to resources (36–38). Lian, et al. reported that distance-based measures such as average time to nearest facility have poor agreement with other area level measures and perform poorly in predicting mammography stage at diagnosis compared to 2SFCA (37). However, these area level measures cannot necessarily be imputed to individual patients and do not make use of patients' actual choice of facility if this is known.

<u> Public Transit</u>

Although it has not yet been applied to disparities in cancer outcomes, a body of research addresses transit equity and issues in modeling public transit trips and access to area resources.

Martin, et al. describe how the availability of digitized transit schedules and standard formats have made programmatic analyses of transit access practical (39). The authors point out that although the goal of modeling transportation access to resources may be to characterize the network or region, it requires the modeling of individual trips with specific destinations and origins. Modeling transit trips requires additional assumptions not only about origin, destination, and time of day traveled, but wait time as well. However, the authors implemented their transit database in Visual Basic. Network analytic methods available in GIS software are better able to multiple origins and destinations efficiently and are more widely used. Peipins, et al. demonstrate a similar approach that incorporates the transit database and assumed mean travel speeds into a network dataset (40).

Detailed manual modeling of the components of a transit network in ArcGIS has been described in an urban planning context (41,42). A key issue in appropriate modeling of public transit trips is control of users' entry into the network, which must be at designated stops and may have other restrictions, such as wait time or direction of travel. While a raster-based approach to control network entry has been proposed by Fuglsang, et al., modeling of lines is more common unless the researcher has raster data that must be incorporated into the analysis (36).

Tribby and Zandbergen recommend creation of separate network feature classes for roads and bus lines, with linkage of these networks by chains of boarding points – lines – stops. Time needed to travel along bus lines was modeled based on scheduled bus headway. Automated approaches to building network models with this structure and incorporating transit schedules have since been described and implemented by Esri, the owner of ArcGIS (43). In a 2012 paper describing the method, the authors demonstrated that even modeling of typical (as opposed to scheduled) bus wait times can provide high enough resolution to compare the effects of changes to transit service at the household level (42).

2. <u>Travel as a Prognostic Factor In Cancer</u>

In Illinois, cancer risk and odds of later stage at diagnosis are highest in Chicago. Social and demographic factors are important but not exhaustive prognostic factors in cancer throughout the state (11). According to an analysis conducted by Wang, et al., better spatial access to PCP is also associated with reduced risk of late stage breast cancer among Illinois residents. However, spatial access to care predicted breast cancer stage at diagnosis only when the state was considered as a

whole. Within the city of Chicago, area SES and health care needs predicted stage but spatial access did not (12).

Other state level analyses have also found that SES is a particularly important prognostic factor among urban residents. In a population-based study in California, Parikh-Patel, et al. reported that SES predicted stage at CRC diagnosis among urban residents and not rural residents. Although urban residents generally have better spatial access to health care, this study found that urban residents experienced no overall survival benefit compared to rural residents. (44).

At the county or metropolitan level, ecologic factors related to ease of transportation (vehicle access and average commute time) were not associated with disparities in breast and cervical cancer screening (45). However, urban racial segregation is prevalent throughout the US and may contribute to disparate spatial access to care within metropolitan areas (46,47). In hypersegregated cities such as Chicago, not only is the population segregated by race and ethnicity, but black neighborhoods are concentrated on the city's periphery (46,47). Comparisons at the state or county level risk averaging away sharp racial disparities in access through comparison to majority-white rural residents using very different transportation networks, or inappropriate aggregation of segregated racial groups within urban areas.

3. <u>Survival</u>

Spatial access to oncologists, race and ethnicity, and socioeconomic status predict CRC survival (10). A state level analysis conducted by Wan, et al. in Texas found that Hispanics, non-Hispanic blacks, and people in geographic areas with high SES disadvantage were more likely than others to die from CRC. Urban residents had the greatest spatial access to oncology care, and survival disparities within these areas were due to other social and demographic factors.

III. METHODS

A. Data Sources

1. <u>Overview</u>

The data sources for this research include: 1) clinical and demographic characteristics of individual cancer cases in Chicago as well as their residential address at the time of their cancer diagnosis as abstracted from the Illinois State Cancer Registry (ISCR); 2) the address and administrative characteristics of Chicago cancer registry hospitals; 3) publicly available GIS and other data files that describe the transportation systems of Cook County, IL; 4) information about CTA fare policies and typical costs of vehicle ownership during the study period; 5) census tract-level social and demographic characteristics; and 6) census tract level primary care physician access scores (48).

Availability and characteristics of spatial data CTA schedules, routes, and service levels may change over time; however, detailed information about changes to CTA service was not available throughout the parent study period of 1995-2008. The CTA pink line opened in 2006, the last major expansion in CTA service, and information about this change is easily available (49). This line connects the Chicago Loop and West Side to the Illinois Medical District, where several major hospitals are located, this change potentially affects access to health care for patients throughout Chicago. Therefore this study uses 2015 CTA schedules and includes patients diagnosed in 2006, 2007, and 2008. Because no major expansion or reduction in CTA service was made after 2006, current service levels may be a reasonable approximation of the transit options available to patients diagnosed in this period.

CTA is part of the Regional Transit Authority (RTA) and serves the city of Chicago and multiple suburbs (50). However, this analysis is restricted to patients who were Chicago residents at diagnosis, and who were diagnosed at hospitals located in Chicago. There are two reasons for this restriction: 1) the purpose of this research is to evaluate the prognostic effect of travel burden

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within an urban area, and restriction eliminates the need to adjudicate which areas are urban or dense enough for inclusion; 2) the method of modeling patients' travel times to their actual treatment facility is new, and this approach avoids a priori assumptions about what is a reasonable transit time or distance.

The public transit model is between intermediate and advanced according to the categories proposed by Salonen and Toivonen. The driving model is also between intermediate and advanced; it includes congestion and attempts to take a door-to-door approach. However, realistic parking information was not available for all Chicago hospitals, many of which operate their own lots in addition to street and private parking garages nearby.

2. <u>Cases</u>

Clinical and demographic characteristics of cases diagnosed in Chicago, IL between 2006 and 2008 were abstracted by the Illinois State Cancer Registry. Case characteristics included the patient residential address at the time of diagnosis; diagnosing facility codes; sex, race/ethnicity, and age at diagnosis; and tumor location, grade, and SEER stage.

Sex, tumor location, and age at diagnosis were used as reported by ISCR. For analysis age was centered at age 65 and scaled to 15 years.

SEER stage includes four stages: in situ, local disease, regional disease, and distant/metastatic disease. Subjects with unstaged disease were included in the analysis. They were divided into unstaged due to missing staging data (unstaged-1 or U1) and unstaged due to the cases declining further work-up (unstaged-2 or U2) during survival analyses performed for the Chicago Prostate and Colorectal Cancer Survival Study based on other disease characteristics and CRC-specific survival. In that analysis, people with unstaged-1 cancer had CRC-specific survival curves that behaved like regional stage disease. People with unstaged-2 cancer had CRC-specific survival curves that behaved like distant stage disease.

A single race/ethnicity variable was constructed using race and Hispanic ethnicity as reported by ISCR. Patients identified as Hispanic by the North American Association of Central Cancer Registries (NAACCR) Hispanic Identification Algorithm (NHIA) were categorized as Hispanic. Patients identified as non-Hispanic were categorized according to reported race: white (as reported), black (as reported), Asian (combined Asian/Pacific Islander groups), Other (American Indian/Alaska Native and Other combined).

Cases were geocoded as part of the parent study. Case location was based on residential address at the time of diagnosis and geocoded to a 2012 Census TIGER/Line (Topologically Integrated Geographic Encoding and Referencing) file of Cook County streets using the ArcGIS geocoding tools and standard address locator for North America. Of cases included in geocoding, 98% were able to be located automatically using a threshold of 73% match between recorded address and street file location. The small remaining number of unmatched addresses were reviewed by study investigators and matched if a reasonable correction could be made to an error in the recorded address. Remaining unmatched addresses and post office box addresses were excluded.

3. Vital Status and Cause of Death

Cases were linked to NDI (National Death Index) Plus to ascertain time and cause of death. Search information was submitted to NDI by ISCR. Vital status and underlying cause of death were linked to subject records by the parent study team using ISCR-assigned case study IDs.

Deaths were attributed to CRC or other cause based on ICD-10 codes. Underlying causes of death that were attributed to CRC were coded C61 or C18-21.

4. Facilities

Location and Administrative Characteristics: Diagnosing facilities are identified in subject records by ISCR hospital code. These codes were matched by name to hospitals from the AHA hospital list from 2006. Hospitals were geocoded using the address of the main facility from the AHA list. Due to the small number of facilities included in the study, unlocated hospitals were placed manually after consulting web maps and local news sources (in the case of hospitals that have since closed).

5. Transportation Networks & Other Geography

Public Transportation

The GIS files representing streets come from the National Transportation Dataset for Illinois, distributed by the US Geological Survey (51). For this analysis the feature set was limited to include all streets in Cook County to allow for routes that might briefly pass through neighboring suburbs. The shapefiles representing CTA train and bus routes were built from General Transit Feet Specification (GTFS) data distributed by CTA. GTFS is a standard text file format used by many transit agencies to share transit service data with mappers and developers (33). Shapefiles were built within ArcMap using an add-on tool called Add GTFS to a Network Dataset (43). The tool generates shapefiles of stops, transit routes, and connectors between stops and streets. It includes an evaluator that uses scheduled stop times to estimate time needed to travel through the network. After a literature search pedestrian speed was modeled based on average walking speed of older adults as reported by Knoblauch, et al. (52)

Costs of travel were estimated based on information published by CTA and the US Department of Transportation. Fare amounts and policies were collected from archived pages of the CTA website (53,54).

<u>Driving</u>

Driving analyses were conducted in ArcGIS using the ArcGIS Online Network Dataset. This service allows access to ArcGIS traffic and map data through web platforms or the ArcGIS for Desktop programs. The Online Network Dataset includes historical and live traffic for all US roads and was used to model the fastest driving trip under typical traffic conditions of the study period (55). Traffic data accessed through the Online Network Dataset is provided by HERE, a cloud map and traffic service. HERE collects data from GPS devices, smart phones, and traditional sources of traffic information to provide real-time and historical traffic data (55,56).

Costs of vehicle ownership and travel for the year of diagnosis were collected from Table 3-17 of National Transportation Statistics (57). This analysis was based on cost of ownership per 15,000 miles in order to include some fixed costs of vehicle ownership.

<u>Area Concentrated Disadvantage</u>

Census data were used to calculate a concentrated disadvantage score for each patient's census tract of residence in the year before diagnosis. The formula for concentrated disadvantage is:

0.85(% in poverty + % unemployed + % female-headed households) + 0.85(1 - % collegeeducated)

This formula is an adaptation of a measure proposed by Browning and Cagney to predict asthma severity and self-rated health among Chicago residents (58,59). The original measure also included the percent of tract population that was African American; this was left out of the formula because the purpose of the main study is to identify determinants of racial disparities in cancer mortality.

Access to Primary Care Providers

Census tract level spatial access to health care providers was calculated for all subjects as part of the parent study. For this analysis the 2-step floating catchment area method (2SFCA) method was used. 2SFCA, developed by Luo and Wang, relates physician supply to the local area level population (60,61). The 2SFCA measure used for this analysis represents number of primary care providers per 1000 census tract residents in the year of diagnosis. The measurement used for this analysis includes all PCP locations, both office based and non-office based.

Locations of primary care providers (PCP) are from area physicians' addresses listed in the AMA Physician Masterfile (48). Census tract population and characteristics are from the 2000 Decennial Census.

B. <u>Spatial Model</u>

1. Public Transit

The USGS street file and CTA GTFS files were used to create a network model of the Chicago public transit system in ArcMap 10.3 for Desktop. GTFS files are text files that describe the service of a given transit agency. The tool Add GTFS to a Network Dataset, distributed by Esri, was used to create a GIS representation of CTA lines that incorporates the service schedule (43).

The workflow for adding GTFS to a network dataset is described in the user guide for the tool set (62). The first tool generates two feature classes representing the locations of transit stops and the lines that connect them. Line length and shape are arbitrary in a network dataset created with the tool; they only represent straight lines between served stops rather than the shape of the rail or street network.

In the next step, a feature class is created that copies transit stops and snaps them to the street network. This allows movement through the network even when a stop is located in a driveway or back from the street. A final feature class of connectors links the original and snapped stops (62).

The structure of the transit network dataset is shown in Figure 3 and Figure 4. Figure 3 shows part of downtown Chicago. Blue lines represent the street network, which is only traversed on foot in this model. Red lines represent the transit network, both bus and rail, and demonstrate that these lines represent the shortest distance between two stops. Black and yellow dots show the original stops and the copies snapped to streets.

Figure 4 illustrates the relationship of stops and snapped stops. Figure 4 is a close-up of the center top of Figure 3, representing the area between LaSalle St. and Dearborn St., and south of Wacker Dr. In the transit network dataset, the transit and street networks are only connected through the stop-connector-snapped stop sequence. Connectors are shown in green. All stops have a snapped copy and a connector, even if the distance from the stop to the street is very small, as in the center bottom of Figure 4. The structure of this network dataset is extremely similar to that

developed by Tribby and Zandbergen, except that it evaluates travel time through the network based on the transit schedule rather than average headway (42).

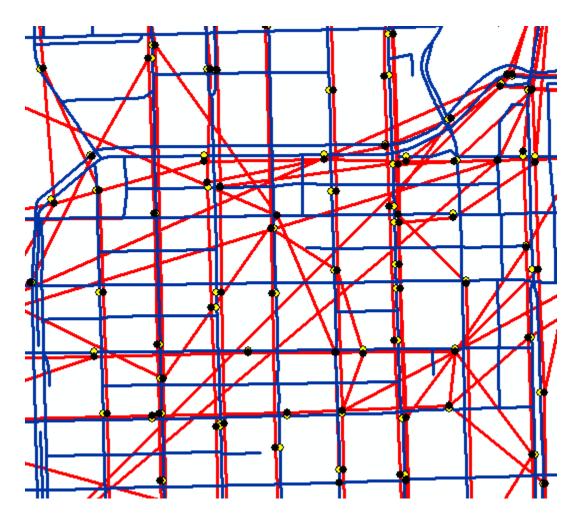


Figure 3. The general structure of the transit network dataset as shown in downtown Chicago.

Once the feature classes are created, the next step is to create a network dataset that relates them. The network dataset also incorporates rules about travel through the network and how costs such as time and distance will be evaluated. In the transit network dataset, the Add GTFS to a Network Dataset tools create a cost evaluator that uses the transit service schedule to calculate time in minutes. A separate cost evaluator was created for pedestrian travel over streets using a speed of 1.25 m/s observed by Knoblauch, et al. (52) A cost evaluator was created to count transfers by assigning a value of 1 to connectors in the from-to direction only.

The Origin-Destination (OD) Cost Matrix tool was used to estimate the fastest public transit route from each patient's residential address to their individual treatment facility. An OD cost matrix solves the least-cost route between multiple destinations and origins and outputs the solutions as lines (63). OD cost matrix was chosen because it can solve batches of routes in a single analysis, reducing processing time and potential for errors. An OD cost matrix also outputs simple lines rather than images of routes which are not needed for this analysis. The attribute table for the lines contains the name of the origin, destination, and value of any costs (e.g. time, distance) specified by the analyst.

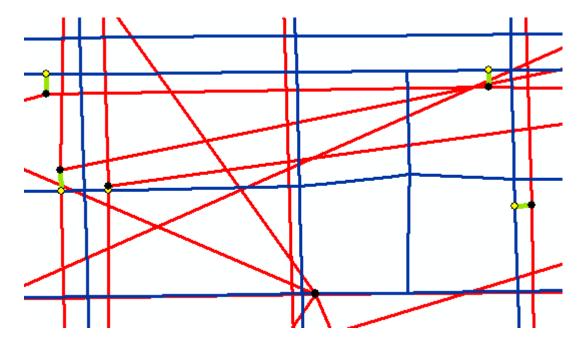


Figure 4. The street and transit networks are linked by stops, connectors, and stops snapped to streets.

For this analysis cases and hospitals were split into 31 datasets by treatment facility. Each group of patients was solved in a separate OD cost matrix to force the patient's actual treatment facility as the solution regardless of whether other hospitals were closer to the patient's home. Modeled travel times represent the fastest public transit trip from the patient's home to their diagnosing facility at 10 a.m. on a generic Monday in 2015. Transit time, stops/transfers, walking distance, and walking time were output. To reduce the potential for error in running 31 separate analyses, a workflow model was built in ArcMap that saved the OD cost matrix settings and automated the process except for selection input datasets. Pairs of patient groups and hospitals were then input in batches.

Attribute tables containing model output were exported and joined to patient records in SAS.

2. Driving

In order to use historical traffic data and street network status, the driving analysis used the ArcGIS Online Network Dataset rather than creating a new network model.

The ArcGIS Online Network Dataset includes a street map of North America and historical and live traffic data. The traffic data is a proprietary service provided by HERE, a map service that collects data from GPS probes and other sources of traffic information. The Online Network Dataset can be accessed through ArcMap.

Location allocation was used to solve the driving analyses because OD cost matrix is not supported on the Online Network Dataset. However, the settings of location allocation can be manipulated to give an equivalent result. Similar to OD cost matrix, location allocation is a network analysis method that involves solving batches of routes for multiple destinations and origins. While OD cost matrix can output multiple destinations for each origin, ranking them by impedance, location allocation assigns each origin to a single destination based on both impedance and other weights set by the user (64). However the underlying method of solving multiple routes optimized on impedance is the same. The 31 subject and 31 hospital datasets were reused for this analysis to force each subject's actual hospital as the solution to each location allocation. A workflow model was built in ArcMap to save the analysis settings. Solved routes had the shortest driving time in minutes from each subject's home to their diagnosing facility. Routes were solved for 10 a.m., Monday, July 9th, 2007.

Location allocation output includes a feature set of lines between origins and destinations that includes point names, value of the impedance measure used to solve, and values of any additional impedance measures selected by the user—in this case, distance in miles. Each attribute table was exported and joined back to patient records in SAS.

C. <u>Travel Burden Measures</u>

1. <u>Calculation of Costs</u>

<u>Public Transit</u>

On CTA fares are paid to board and transfer. Discounts are available for riders 65 and older or who have disabilities. Fares were consistent throughout the study period except for the introduction of the Seniors Ride Free program in March 2008 (65).

Cost of a trip was calculated under the assumption that riders before March 2008 could have qualified for discounted fares, and that eligible riders used Seniors Ride Free if they were diagnosed in or after March 2008. The standard base CTA fare during the study period was more expensive for rail than for bus; however, the network model does not differentiate between rail and bus lines (53,54). The discounted base fare was the same for bus and rail. Therefore the discounted trip cost is the only one that can be calculated precisely from the model. It may also be reasonable to assume that many subjects in this sample qualified based on either pre-existing illnesses, their diagnosis of CRC, or their age.

Some subjects lived close enough to their diagnosing facility that their optimal trip involved walking only; their number of stops and cost were zero. Among subjects who were 65 or older and

diagnosed in or after March 2008, cost was zero. Among all other subjects, transit cost in dollars was: 0.85 + 0.15(stops – 1).

<u>Driving</u>

Cost of a driving trip is commonly calculated as a function of miles. Miles traveled were output by the location allocation analysis for use in calculating cost. Average cost by year of owning and operating a vehicle according to the Bureau of Transportation Statistics were used (57). The average cost per 15,000 miles was used because it incorporates fixed costs such as license, taxes, and insurance. The average total costs including fixed costs by year of diagnosis are shown in Table II. Cost per mile was multiplied by trip distance to find trip cost.

TABLE II. FIXED AND VARIABLE COSTS PER MILE OF OWNING AND OPERATING A VEHICLE BY		
YEAR OF SUBJECT DIAGNOSIS		
Year	Cost per mile (¢)	
2006	52.15	
2007	53.97	
2008	54.14	

No conceptual equivalent of stops/transfers could be output from the driving model.

2. <u>Calculation of Scores</u>

Each score represents the mean of the standardized components for that individual and method of travel. Components of transit burden (cost, time, and stops) and driving burden (cost and time) were z-standardized to have mean 0 and standard deviation 1. The mean standardized value of the components within each individual was assigned as that subject's score for the method of travel.

D. Statistical Methods

All statistical analyses were carried out in SAS 9.4.

Area level concentrated disadvantage and PCP availability were categorized in quintiles. Age was centered at 65 years and scaled so that 1 unit of change in age represents 15 years.

Means and other descriptive statistics were calculated for analysis variables and differences across categories were compared using type III tests from linear regression.

Logistic models were used to predict odds of favorable stage (in situ, local) vs. unfavorable (regional, distant, unstaged). One-way interactions with the travel burden scores or components were eliminated using backward selection at p = 0.06 and critical evaluation of the meaning of any differential effects.

Cox proportional hazards models were used to predict relative CRC-specific survival. The proportional hazards assumption was evaluated using both statistical (extended Cox model) and graphical methods. In the full follow-up period the proportional hazards assumption was violated. In the entire sample CRC-specific survival was markedly worse after three years of follow-up and overwhelmed the predictive power of any explanatory variable. Selection bias may have contributed to this effect because this dataset included follow-up through 2011 only. Therefore the Cox proportional hazards model for this analysis includes the full sample but is censored at the first three years of follow-up.

Survival model selection followed the same backward selection procedure as the logistic model. Race/ethnicity and sex were retained in the final survival models regardless of significance because of their relevance to the research questions.

IV. RESULTS – AIM 1

A. Transit and Driving Burden Scores

Both the transit and driving burden scores had a mean of 0 and standard deviation near 1, reflecting their structure as means of the standardized underlying variables ($s_t = 0.84$, $s_d = 0.98$).

Driving score was right-skewed but with a median of -0.21. Transit score was minimally skewed and with a median of 0.03.

B. Spatial and Demographic Distribution of Scores

Included cases were diagnosed with CRC from 2006 to 2008, lived in Chicago at the time of diagnosis, and were initially reported to ISCR by a non-VA hospital located in Chicago. There were 27,174 records in the original analytic dataset of CRC cases in Cook County, 2000-2008. 18,471 were excluded because they were diagnosed before 2006. An additional 5,843 cases were diagnosed outside Chicago or living outside Chicago at the time of diagnosis. Cases with unknown race were excluded leaving 2,678 cases used for analysis.

Table III shows the characteristics of the subjects included in the analysis. Subjects were predominantly either non-Hispanic black (45%) or non-Hispanic white (35%), and most were between 50 and 79 years old (mean = 66.5) at diagnosis, and women slightly out-number men (51.3% vs. 48.7%). The most common stage at diagnosis was local (36%), followed by regional (31%), and distant (21%). Subjects with unstaged disease were included in the analysis and together made up 5% of cases (n = 143). 71 patients were recorded as unstaged due to missing data (U1). 72 patients were recorded as unstaged due to declining further work-up (U2).

Both drive score and transit score vary by individual and neighborhood characteristics (Table III). Black and Hispanic Chicagoans diagnosed with CRC have the highest burden of travel to care as measured by transit score or drive score; whites and Asians have the lowest. Mean travel burden decreases with age. Travel burden does not vary meaningfully by sex. Mean travel burden decreases as area level access to primary care increases. However, mean travel burden scores are

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similar among people whose neighborhoods are in the top 3 quintiles of primary care availability; the greatest difference in travel burden is between people in the 2nd quintile (less primary care) and 3rd quintile. Mean travel burden scores are highest in the middle quintile of neighborhood concentrated disadvantage, although mean scores are still higher in the most disadvantaged areas compared to the least.

TABLE III. CHARACTERISTICS OF COLORECTAL CANCER PATIENTS INCLUDED IN TRAVEL BURDEN ANALYSIS										
Driving Transit										
Variable	N	%	Mean	р	Mean	р	Mean	р	Mean	р
			Time		Score		Time		Score	
Race/Ethnicity				< 0.0001		< 0.0001		< 0.0001		< 0.0001
White, non-Hispanic	947	35.36	13.52		-0.21		38.36		-0.20	
Black, non-Hispanic	1228	45.86	16.02		0.16		45.01		0.15	
Hispanic	334	12.47	17.10		0.09		42.80		0.10	
Asian	127	4.74	14.01		-0.17		37.86		-0.21	
Other	42	1.57	14.68		-0.03		40.56		-0.10	
Age at diagnosis				< 0.0001		< 0.0001		< 0.0001		< 0.0001
<50	288	10.75	17.51		0.25		46.18		0.26	
50-64	865	32.30	16.42		0.16		44.18		0.19	
65-79	1032	38.54	14.84		-0.04		41.66		-0.07	
≥80	493	18.41	12.21		-0.33		36.30		-0.33	
Sex				0.86		0.97		0.71		0.13
Female	1375	51.34	15.13		0.00		41.83		-0.02	
Male	1303	48.66	15.18		0.00		42.11		0.02	
Stage at Diagnosis				0.01		0.003		0.0008		0.01
In situ	175	6.53	16.00		0.09		43.61		0.05	
Local	963	35.96	14.79		-0.05		40.64		-0.03	
Regional	828	30.92	14.68		-0.05		41.00		-0.05	
Distant	569	21.25	15.98		0.10		44.19		0.09	
Unstaged 1	71	2.65	17.04		0.28		47.30		0.14	
Unstaged 2	72	2.69	15.15		0.00		44.19		0.02	
Hospital				< 0.0001		< 0.0001		< 0.0001		< 0.0001
Public/Safety-Net	1214	45.33	16.82		0.20		45.63		0.16	
Private	1464	54.67	13.77		-0.17		38.94		-0.13	
Concentrated				< 0.0001		< 0.0001		< 0.0001		< 0.0001
Disadvantage										
Q1 (least	536	20.01	12.76		-0.28		35.42		-0.32	
disadvantage)										
Q2	538	20.09	15.11		-0.03		42.95		-0.01	
Q3	530	19.79	17.64		0.28		47.44		0.19	
Q4	541	20.20	16.94		0.21		45.70		0.19	

TABLE III. CHARACTERISTICS OF COLORECTAL CANCER PATIENTS INCLUDED IN TRAVEL BURDEN ANALYSIS (CONTINUED))				
			Driving	Transit				Driving	Transit	
Variable	Ν	%	Mean	р	Variable	Ν	%	Mean	р	Variable
			Time					Time		
Q5 (most	533	19.90	13.33		-0.17		38.34		-0.06	
disadvantage)										
PCP Offices per				< 0.0001		< 0.0001		< 0.0001		< 0.0001
1000										
Q1	536	20.01	20.14		0.64		55.81		0.47	
Q2	537	20.05	17.22		0.27		47.32		0.25	
Q3	537	20.05	13.57		-0.23		36.51		-0.19	
Q4	537	20.05	13.43		-0.24		37.63		-0.16	
Q5 (most offices)	531	19.83	11.39		-0.44		32.53		-0.37	

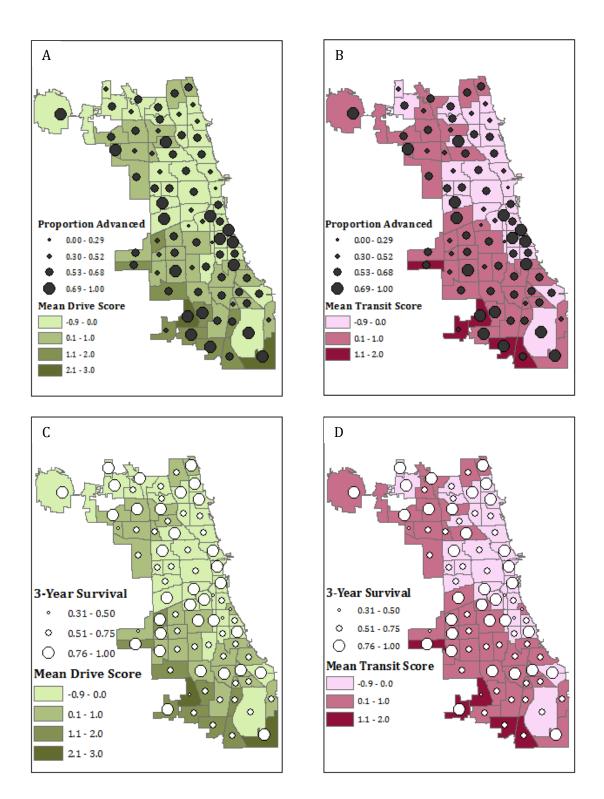


Figure 5. Relationship of travel scores to stage at diagnosis and survival. A. Mean drive score and proportion of CRC cases advanced at diagnosis by community area. B. Mean transit score and proportion of cases advanced at diagnosis by community area. C. Mean drive score and three-year CRC survival by community area. D. Mean transit score and three-year CRC survival by community area.

V. RESULTS – AIM 2

Primary Hypothesis: Individual burden of travel to care is associated with cancer-specific survival and stage at diagnosis in people with colorectal cancer.

Burden of travel to cancer care is associated with CRC stage at diagnosis and CRC-specific survival. Both transit and driving burden perform similarly in predicting stage at diagnosis. However, transit burden score is associated with CRC survival while driving burden score is not.

Estimates of stage at diagnosis and survival were adjusted for race/ethnicity and age at diagnosis. Stage models included an interaction with sex. Survival models were adjusted for sex and stage at diagnosis. PCP access and concentrated neighborhood disadvantage were dropped from final models due to non-significance.

A. <u>Stage at Diagnosis</u>

Travel burden had a small but highly significant differential effect on odds of favorable CRC stage at diagnosis between males and females. Among males, a one standard deviation increase in transit score was associated with 13% decreased odds of having favorable stage at diagnosis (OR 0.87, 95% CI 0.76, 1.00). (See Figure 5). Among females, increased transit score improved the odds of favorable stage at diagnosis (OR 1.18, 95% CI 1.03, 1.35). Among men a one standard deviation increase in drive score carried 12% decreased odds of favorable stage at diagnosis (OR 0.88, 95% CI 0.78, 1.00). (See Figure 6). The same increase in drive score improved odds of favorable diagnosis in women (OR 1.12, 95% CI 1.00, 1.25).

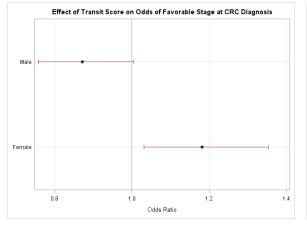


Figure 6. Effect of transit burden on odds of favorable stage at CRC diagnosis

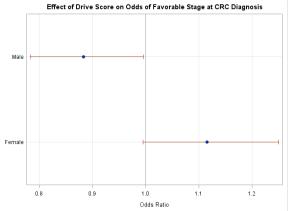


Figure 7. Effect of driving burden on odds of favorable stage at CRC diagnosis

B. Cancer-Specific Survival

1. Transit Score

Burden of travel to care by public transit is a significant prognostic factor in the first three years after CRC diagnosis, however, its effect is protective (HR 0.87, 95% CI 0.80, 0.94). After adjustment for transit burden score, age, and stage at diagnosis, no other case or area level variables were significant predictors of relative CRC-specific survival (See Table IV). Race/ethnicity was retained in the final model for its relevance to the research question; sex was retained for comparison to the stage models. Unlike in the stage model, there was no evidence of meaningful effect modification across case or area level variables.

Although the adjusted joint effect of race/ethnicity is not a significant predictor of CRC survival, the independent effect of black race/ethnicity remains significant at Wald p = 0.05. There was no effect of sex on CRC-specific survival, either as a main effect or as part of an interaction with transit burden score. Adjusted relative hazard increases 12% for each 15-year increase in age at diagnosis, centered at 65 years.

2. Drive Score

Drive score is neither a significant nor a meaningful predictor of CRC survival in the first three years after diagnosis (HR 0.94, 95% CI 0.88, 1.01). As in the transit models, after adjustment for travel burden, stage, and age at diagnosis, no other individual or area level factors were significant in the model. Again race/ethnicity and sex are retained for comparison to the hypotheses and stage models.

Estimates of the effect of individual level factors were very similar between the driving and transit models.

SURVIVAL				
	Trans	sit	Drivi	ng
Variable	HR (95% CI)	Wald p	HR (95% CI)	Wald p
Score	0.87 (0.80, 0.94)	0.0007	0.94 (0.88, 1.01)	0.11
Race/Ethnicity		0.086		0.14
Asian	0.97 (0.71, 1.34)	0.86	0.99 (0.72, 1.36)	0.94
Black	1.16 (1.00, 1.36)	0.05	1.14 (0.98, 1.34)	0.09
Hispanic	1.17 (0.93, 1.45)	0.18	1.15 (0.92, 1.43)	0.22
Other	0.59 (0.31, 1.56)	0.12	0.59 (0.30, 1.15)	0.12
Age (15-year	1.11 (1.08, 1.14)	< 0.0001	1.12 (1.09, 1.15)	< 0.0001
change from age				
65)				
Female Sex	0.97 (0.85, 1.10)	0.60	0.98 (0.85, 1.11)	0.71
Stage		< 0.0001		< 0.0001
In situ	0.64 (0.41, 1.01)	0.05	0.64 (0.41, 1.00)	0.05
Local	ref		ref	
Regional	1.63 (1.34, 1.99)	< 0.0001	1.63 (1.34, 1.99)	< 0.0001
Distant	9.48 (7.89,	< 0.0001	9.33 (7.77,	< 0.0001
	11.39)		11.21)	
Unstaged-1	2.64 (1.76, 3.96)	< 0.0001	2.66 (1.77, 3.99)	< 0.0001
Unstaged-2	5.86 (4.05, 8.46)	< 0.0001	5.71 (3.95, 824)	< 0.0001

TABLE IV. FINAL MODELS OF EFFECT OF TRANSIT AND DRIVE SCORE ON CRC- SPECIFIC SURVIVAL

VI. RESULTS – AIM 3

A. Secondary Hypothesis A

Secondary Hypothesis A: If travel burden is associated with colorectal cancer survival, this association is driven primarily by travel time and prediction is improved by adding variables related to travel cost and complexity.

In order to evaluate this hypothesis, separate stage and survival models were run using the untransformed independent components of each score. Although complexity was retained as a component of overall transit score, it was dropped from the independent component models because it is highly correlated with, and directly precedes, transit cost. Therefore the independent component models of transit and driving burden each included time and cost.

1. <u>Stage at Diagnosis</u>

Transit Components

Contrary to the hypothesis, transit time is not a meaningful independent predictor of favorable stage at CRC diagnosis (Table V).

Transit cost drives the observed interaction between transit burden and sex. Compared to the score model, the apparent effect on stage at diagnosis is strengthened by modeling transit cost as an independent predictor. Neighborhood concentrated disadvantage and availability of primary care were non-significant regardless of how transit burden was specified, and were dropped from both models.

Driving Components

In contrast to the transit models, driving time is the strongest component of the drive scorestage relationship and the source of the interaction with sex.

However, including additional components does not necessarily strengthen the predictive power of the score. A comparison of the two models (Table VI) shows that modeling the score shifts the estimates of the sex-specific effects downward rather than uniformly strengthening them. While

manobib				
Components			Score	
OR (95% CI)	Wald p	Variable	OR (95% CI)	Wald p
	0.0028	Score		0.0019
0.76 (0.56, 1.03)		in Males	0.87 (0.76, 1.00)	
1.32 (1.00, 1.75)		in Females	1.18 (1.03, 1.35)	
0.93 (0.86, 1.01)	0.10			
	< 0.0001	Race/Ethnicity		< 0.0001
ref		White	ref	
0.98 (0.67, 1.43)	0.73	Asian	1.00 (0.68, 1.47)	0.80
0.68 (0.57, 0.82)	< 0.0001	Black	0.69 (0.57, 0.82)	< 0.0001
0.99 (0.76, 1.28)	0.68	Hispanic	0.99 (0.76, 1.28)	0.65
1.81 (0.94, 3.48)	0.03	Other	1.83 (0.95, 3.50)	0.03
1.03 (1.00, 1.07)	0.06	Age (15-year	1.03 (1.00, 1.07)	0.04
		change from		
		age 65)		
	Components OR (95% CI) 0.76 (0.56, 1.03) 1.32 (1.00, 1.75) 0.93 (0.86, 1.01) 0.93 (0.86, 1.01) 	Components Wald p OR (95% CI) Wald p 0.0028 0.0028 0.76 (0.56, 1.03)	Components Image: Components OR (95% CI) Wald p Variable 0.0028 Score 0.76 (0.56, 1.03) in Males 1.32 (1.00, 1.75) in Females 0.93 (0.86, 1.01) 0.10 0.93 (0.86, 1.01) 0.10 0.93 (0.86, 1.01) 0.10	Components Score OR (95% CI) Wald p Variable OR (95% CI) 0.0028 Score in Males 0.87 (0.76, 1.00) 1.32 (1.00, 1.75) in Females 1.18 (1.03, 1.35) 0.93 (0.86, 1.01) 0.10 Image: Component State Kace/Ethnicity Variable Variable Variable Kace/Ethnicity Variable Variable Variable Variable Variable Variable Variable 0.10 Infernales 1.18 (1.03, 1.35) 0.93 (0.86, 1.01) 0.10 Variable Variable Variable Variable Variable Variable Variable Variable Variable Variable Variable <td< td=""></td<>

TABLE V. EFFECT OF TRANSIT BURDEN SCORE AND COMPONENTS ON ODDS OF FAVORABLE STAGE AT CRC DIAGNOSIS

TABLE VI. EFFECT OF DRIVING BURDEN SCORE AND COMPONENTS ON ODDS OF FAVORABLE STAGE AT CRC DIAGNOSIS

	Components			Score	
Variable	OR (95% CI)	Wald p	Variable	OR (95% CI)	Wald p
Time (15-		0.004	Score		0.005
minute					
scale)					
in Males	0.94 (0.62, 1.41)		in Males	0.88 (0.78, 1.00)	
in Females	1.41 (0.94, 2.12)		in Females	1.12 (1.00, 1.25)	
Cost	0.96 (0.88, 1.06)	0.43			
Race/Ethnicity		0.0002	Race/Ethnicity		0.14
White	ref		White	ref	
Asian	1.01 (0.69, 1.47)	0.80	Asian	1.01 (0.69, 1.48)	0.82
Black	0.70 (0.58, 0.84)	< 0.0001	Black	0.69 (0.58, 0.83)	< 0.0001
Hispanic	0.97 (0.74, 1.26)	0.50	Hispanic	0.99 (0.76, 1.28)	0.59
Other	1.86 (0.97, 3.57)	0.03	Other	1.85 (0.96, 3.55)	0.03
Age (15-year	1.03 (1.00, 1.06)	0.05	Age (15-year	1.03 (1.00, 1.06)	0.05
change from	-		change from	-	
age 65)			age 65)		

the estimate of the protective effect in women is attenuated, the estimate of the harmful effect in men is strengthened.

2. <u>Survival</u>

Contrary to the hypothesis, the relationship between transit burden and CRC-specific survival is driven by transit cost. Transit time has no meaningful effect on CRC-specific survival in the first three years after CRC diagnosis. While transit cost is significantly associated with CRC survival, in a backward selected model it was also implicated in multiple statistical interactions that impeded analysis and interpretation. Therefore a benefit of using the score to predict CRC-specific survival was the avoidance of fitting (or overfitting) a model that could not be interpreted.

Neither driving time nor driving cost was a significant independent predictor of CRC survival. The lack of predictive value of the driving score with respect to survival reflects the lack of effect of both underlying components.

B. Secondary Hypothesis B

Secondary Hypothesis B: If travel burden is associated with colorectal cancer prognosis, it interacts with patient race/ethnicity and contributes to racial disparities in both stage at diagnosis and cancer-specific survival.

Neither transit score nor driving score interacts meaningfully with race/ethnicity. They also do not account for racial disparities in disease-specific survival or stage at diagnosis among Chicagoans with CRC.

Table VII compares the estimates of the association between race/ethnicity and odds of favorable stage at CRC diagnosis. The estimates are nearly identical before and after adjustment for travel burden, indicating that neither measure mediates the relationship between race/ethnicity and disease stage. Apparent statistical interactions between travel burden scores and race/ethnicity on stage at diagnosis were eliminated after it became clear they were being driven by differences in the 'Other' and 'Unstaged due to missing information' categories, respectively. While the relative hazard associated for black patients is reduced in the survival models, this

reduction is due to adjustment for stage at diagnosis.

TABLE VII. COMPARISON OF ASSOCATION BETWEEN RACE/ETHNICITY AND ODDS OF FAVORABLE STAGE AT CRC DIAGNOSIS BEFORE AND AFTER ADJUSTMENT FOR TRAVEL BURDEN

	Unadju	sted	Transit	Model	Driving Model	
	OR (95%	Wald p	OR (95%	Wald p		Wald p
	CI)		CI)		OR (95%	
					CI)	
Race/Ethnicity		< 0.0001		< 0.0001		0.14
White	ref		ref		ref	
Asian	0.99 (0.68,	0.79	1.00 (0.68,	0.80	1.01 (0.69,	0.82
	1.45)		1.47)		1.48)	
Black	0.69 (0.58,	< 0.0001	0.69 (0.57,	< 0.0001	0.69 (0.58,	< 0.0001
	0.82)		0.82)		0.83)	
Hispanic	0.96 (0.74,	0.53	0.99 (0.76,	0.65	0.99 (0.76,	0.59
	1.24)		1.28)		1.28)	
Other	1.80 (0.94,	0.03	1.83 (0.95,	0.03	1.85 (0.96,	0.03
	3.45)		3.50)		3.55)	

C. Secondary Hypothesis C

Secondary Hypothesis C: If travel burden is not associated with colorectal cancer survival, this is because its effect is already captured by socioeconomic status or neighborhood disadvantage.

This hypothesis was not directly evaluated because according to this analysis, travel burden does associate with CRC stage at diagnosis and cancer-specific survival. However, there is indirect evidence that the effect of travel burden on CRC prognosis is not captured by neighborhood disadvantage. Quintile of neighborhood disadvantage was highly non-significant in the models built to evaluate the primary hypothesis, and was dropped from the models presented here. This resulted in no change in magnitude of travel burden effect on either stage at diagnosis or survival.

VII. DISCUSSION

The results of Aim 1 of this research demonstrate the feasibility of modeling burden of travel to facilities where individuals with CRC realized access to relevant health care, and some possible relationships between travel burden and other patient characteristics. Using GIS software such as ArcGIS, individual trips to health care facilities are readily modeled for use in public health analyses. The network analysis conducted in this study was made possible by geographic data that have become increasingly detailed and available from both commercial and public entities such as HERE and government open data portals, respectively. Prominent uses of these data involve route planning, logistics, and web development. However, growing interest in the effects and proper measurement of spatial access to health care indicate that these data have important public health uses as well.

This network analysis was able to be conducted with a high level of detail and specificity due to the underlying patient level detail provided to the parent project by ISCR. Travel between residential addresses and clinic choices of individual cancer patients has been modeled in health system-based studies such as that conducted by Smith, et al. (9). However, these analyses are restricted to individual hospitals or health systems and cannot capture the travel burden of nonpatients who deliberately choose one facility over another. Significant differences in mean potential trip time and score by hospital type suggest that these decisions may be important contributors to overall burden. There are legitimate confidentiality concerns to sharing individual residential addresses with researchers. However, to the extent that individual patient locations and facility choices predict cancer outcomes, sharing of these data may be justified.

The results of Aim 2 indicate that travel burden is associated with CRC prognosis in Chicago residents. Its precise relationship with CRC-specific survival is unexpected.

The presence of effect modification between travel burden and sex on stage at diagnosis suggests that travel burden is related to decisions about health care utilization made before

patients know they are ill. After diagnosis there is no difference between men and women in either the effect of travel burden or overall CRC-specific survival. Because mean travel times and burdens were equivalent between men and women, the differential effect may reflect different attitudes toward screening or preventive care when the care is perceived as inconvenient and not needed. The fact that this effect disappeared in the survival models may indicate that travel burden is perceived and affects patients differently depending on whether they are seeking preventive care or managing a known illness.

Although driving is the default measure of travel time or distance in most analyses, in this study driving burden was not a significant predictor of CRC survival and performed no better than transit at predicting stage at diagnosis. One possible explanation is that, despite urban density and congestion, few subjects' initial hospitals are so difficult to reach by car that they interfere with care. This is a reasonable interpretation if, as seems likely, most patients had access to a car to get to the hospital most of the time and selected facilities they found reasonably easy to reach. Another possibility is that the spatial model used to estimate driving times did not include enough detail to identify the most difficult trips. There was no clear analogue to transfers in the driving model, and time or cost needed to park was not modeled.

The protective effect of transit burden in predicting relative CRC survival is counterintuitive. More difficult transit trips may indicate that patients left their own neighborhoods, possibly to seek a higher level of care than was available nearby. Neighborhood concentrated disadvantage, which includes percentage of the population living in poverty and percentage unemployed, was not predictive of CRC-specific survival in this analysis. However, income or SES of individual patients is unknown. Although patients of public and safety-net hospitals had longer mean potential travel times, this analysis cannot rule out the possibility that longer and more expensive trips were undertaken by those most able to afford them. Several of Chicago's major hospitals are located near downtown or the Illinois Medical District, not in residential neighborhoods, so even patients who lived near these facilities may have had longer and more expensive average trips than patients who chose to use a neighborhood hospital. Future analyses that are able to take into account patients' actual choice of facility should include measures of local and destination facility quality to determine whether and how patients benefit from travel to health care.

Aim 3 explored the nature of travel burden as it relates to CRC prognosis and racial/ethnic disparities. The results of the analysis of components support the use of driving time as a measure of spatial access to health care and prognostic factor in CRC among Chicago residents. Modeling the effect of transit components on survival did not yield meaningful results in this analysis. Although the model still could be used to perform a standardization, the meaning of multiple component interactions in this exploratory research, and without the sample size to support them, is questionable. The interpretability of the score, which incorporates all the components, supports its use for modeling travel burden by public transit.

Multiple other studies have found that racial disparities in CRC include disparities in treatment referral, acceptance, and receipt (66). However, in this analysis race/ethnicity was a significant predictor of stage at diagnosis only. In the survival models, the effect of race/ethnicity was completely accounted for by stage at diagnosis. Furthermore, travel burden did not account for racial/ethnic disparities in stage at diagnosis and therefore does not explain racial/ethnic CRCspecific survival disparities even indirectly.

This research has several limitations that may provide opportunities for future research. The actual mode of transportation used by patients in this study is not known. This necessitated the use and informal comparison of parallel models of transit and driving burden. Although driving times modeled by GIS compare favorably with travel times reported by patients, no similar analysis was found for public transit in this review. This analysis also does not use information about subsequent facilities reported to ISCR. Of the patients included in this analysis, 432 (16%) had at least one

other facility in their record. High burden of travel could be one reason that some patients changed hospitals.

While patients' actual origins and destinations within Chicago were modeled without respect to neighborhood boundaries, this study was restricted to residents of Chicago who were also treated in the city. This was done to restrict analyses and conclusions to the public transit network's central service area and avoid imposing assumptions of a reasonable transit trip on exploratory research. However, future studies should attempt to delineate the catchment areas of public transit networks so that the full scope of their services and effects on health care utilization can be understood.

The strengths of this study include its population-based cohort design, modeling of both driving and transit, and evaluation of both stage at diagnosis and survival. All Chicagoans diagnosed with CRC at non-VA Chicago hospitals during the study period were eligible for inclusion. Although travel burden does not account for racial disparities in stage at diagnosis, the distribution of computed scores reflects racial and socioeconomic disparities in the spatial distribution of CRC cases in Chicago. This analysis found an association between travel burden and both stage at CRC diagnosis and CRC-specific survival; the latter which would not have been apparent if only driving burden had been modeled.

VIII. CONCLUSION

Burden of travel to health care is a prognostic factor among urban residents diagnosed with colorectal cancer. More-burdensome trips increase the odds of unfavorable diagnosis in males, and favorable diagnosis in females. More burdensome modeled trips to the hospital predict CRC-specific survival; however, only over public transit networks and the effect is protective. Increased burden of travel to health care may reflect the decision to leave one's neighborhood to seek out a higher level of care.

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