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Timmy J. Pierce II Date

Seafood Consumption, Glycemia, and Diabetes in Chennai, India: a Cross-Sectional Study

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Master of Public Health

Global Environmental Health

_____

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An abstract of
A thesis submitted to the faculty of the
Rollins School of Public Health of Emory University
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Abstract

Seafood Consumption, Glycemia, and Diabetes in Chennai, India: a Cross-Sectional Study

By Timmy J. Pierce II

Studies of the association between seafood consumption and diabetes risk generally focus on broad categories of fish and shellfish consumption. Seafoods are heterogeneous in nutrients and contaminants, so epidemiology considering specific seafoods is needed. Our objectives were to estimate the cross-sectional associations of seafood consumption with diabetes, glycated hemoglobin A1c, and fasting glucose and to evaluate if those associations differed across trophic level. A total of 6,979 adults participated in a diet and cardiometabolic disease survey in 2016, and a total of 24 types of seafood were considered in this analysis. More than monthly consumption of salmon and nagarai was associated with confounder-adjusted HbA1c distributions (Bonferroni-significant, with 3d F-test P-values of 4×10^{-4} and 1×10^{-6}); and confounder-adjusted fasting glucose was 5% lower among people eating salmon monthly, but this was not Bonferonni-significant. However, these fish were not commonly eaten by the Chennai population. More than monthly consumption of katla and koduva was associated with lower adjusted odds of diabetes, but reverse causality is possible, where diabetes diagnosis changed dietary patterns. In meta-regression, trophic levels of seafood items did not predict seafood-specific associations. Overall, these results suggest that seafood is not a major driver of diabetes in Chennai.

Keywords: One Health; marine biology; nutrition surveys; nutritional sciences; glycated hemoglobin A1c; diabetes mellitus

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Contents

Introduction

Twenty-five years ago, a diverse community of practice interested in characterizing the relationships between human activity, ecological change, and human health coalesced into the now defunct International Society for Ecosystem Health, and accelerated a paradigm shift in epidemiology to consider ecological function as a driver of human health (Rapport et al., 1999). The goal of the Ecosystem Approaches to Human Health (EcoHealth) intellectual movement has sought to understand and promote health and wellbeing in the contexts of social and ecological interactions (Alonso Aguirre et al., 2019). EcoHealth research began in earnest in 1997 with the start of the Ecosystem Approaches to Human Health (or EcoHealth) research program in Canada, which emphasized transdisciplinarity, multi-stakeholder participation, and gender and social analysis (Charron, 2014). Another trans-disciplinary examination of interconnected human and environmental wellbeing, which has gained wider interest in recent years, is One Health. The concept of One Health, which is the collaborative efforts of multiple disciplines working locally, nationally, and globally, to attain optimal health for people, animals, and our environment (King et al., 2008), has its origins in the 19th century discoveries of German physicist and pathologist Rudolf Virchow who thought there should be no division between human and animal health (Gyles, 2016). To facilitate sharing of information, a One Health Initiative was launched in 2018 to promote One Health across various platforms (One Health Initiative, 2018).

Studies of the associations between seafood consumption and diabetes risk have generally focused on very broad categories such as total fish consumed, dark meat fish, fried fish, dried fish, and shellfish (Djousse, Gaziano, Buring, & Lee, 2011; Kaushik et

al., 2009; Nanri et al., 2011; Patel et al., 2009). A 2009 population-based prospective cohort study focused on seafood consumption and incident considered fish exposures as lean or fatty (van Woudenbergh et al., 2009). A 2017 prospective cohort of Swedish men studying fish consumption in relation to diabetes looked at three more specific exposure groups of fish types: (herring/mackerel, salmon/whitefish/char, and cod/saithe/fish fingers) (Wallin et al., 2017). More detailed dietary assessment considering specific fish, in the context of their ecological niches, is needed, because nutrients and contaminants can vary dramatically with trophic position (Gribble et al., 2016).

In this study, we expanded on the seafood and diabetes epidemiological literature by considering specific types of seafood, in a large population-representative survey sample, and evaluating whether trophic position is salient for the direction and magnitude of association of fish consumption with diabetes.

The objectives of this study were to estimate the cross-sectional associations of specific seafoods with fasting glucose, glycated hemoglobin A1c (HbA1c), and diabetes status in Chennai, India, and evaluate whether those associations differed according to the ecological niches of the consumed marine life.

Methods

Study Population

The study sample consisted of 6,979 adults between 20 and 89 years old from Chennai, India participating in the Cardiometabolic Risk Reduction in South Asians (CARRS) study in 2016. The CARRS study is an ongoing population-based cohort study initiated from three cities in South Asia: Karachi, Delhi, Chennai (Nair et al., 2012).

Baseline assessment was conducted in 2010-2011, and annual follow-up visits were conducted thereafter. An ancillary study focused on diet, with emphasis on detailed seafood consumption history, was included in the Chennai survey component in 2016. The CARRS study was approved by the Institutional Ethics Committee of Public Health Foundation of India (TRC-IEC-34/09 (IRB no. IRB00006658), All India Institute of Medical Sciences (IEC/NP-17/07.09.09), Aga Khan University (1468-CHS-ERC-2010), and Madras Diabetes Research Foundation (IRB00002639), and the Institutional Review Board of Emory University (IRB00044159).

Sociodemographic, Anthropometric, and Behavioral Data

Sociodemographic information such as participant age, sex, educational attainment, and monthly household income, along with behavioral risk factors such as tobacco use and alcohol consumption, were assessed by questionnaire given by trained study staff. Questions were derived from the Chennai Urban Population Study (CUPS), Chennai Urban Rural Epidemiological Study (CURES), and the Sentinel Surveillance Study (Nair et al., 2012). Sedentary lifestyle was estimated using the short form of the International Physical Activity Questionnaire (Rosenberg, Bull, Marshall, Sallis, & Bauman, 2008).

Body mass index (BMI) was calculated as a weight (kg) divided by height-squared (m^2) based in the anthropometric measures collected by trained study personnel. Standardized procedures were used to measure weight to the nearest 0.1 kg (electronic body composition analyzer, Tanita BC-418, Tanita Co, Tokyo, Japan), height to the nearest 0.1 cm (portable stadiometer, SECA Model 213, SecaGmbh Co, Hamburg,

Germany), and waist and hip circumference to the nearest 0.1 cm (non-stretch measuring tape, Gulick II, Country Technology, Gay Mills, WI) based on the U.S. National Health and Nutrition Examination Survey (N-HANES-III) protocol (US Centers for Disease Control Prevention, 1988).

Dietary Data

Dietary data were obtained by a questionnaire administered in Tamil, Hindi, and English with illustrative pictures of the seafood items (e.g., fish or shellfish). The exposure variables were the specific types of seafood that participants reported to consume. The frequency of consumption for each seafood item was recorded as less than weekly, monthly but less than weekly, weekly, several times a week, or daily.

The unhealthy diet score variable was an index calculated from the consumption frequency of ten food groups: meats, organic meats, desserts, deep fried western-style foods, deep fried South Asian-style foods, Western-style desserts, South Asian-style desserts, refined cereals, pickles, and cold beverages. For each one of the ten food groups, participants were assigned scores of 0 (“never consume”), 1 (“consume monthly”), 2 (“consume weekly”), or 3 (“consume daily”). These scores were summed such that the maximum unhealthy diet score was 30 and the minimum was 0.

Ecological Data on Trophic Position of Fish

FishBase is a global species database that currently includes information on 34,200 species of fish (Froese & Pauly, 2019). The FishBase database was accessed on

April 17th, 2019 to retrieve information on the trophic level of 24 different species of fish whose consumption frequency had been assessed by questionnaire in the Chennai survey.

Glycemic Status of Participants

Diabetes status was defined by self-report of a physician's diagnosis, which would be based on fasting glucose ≥ 126 mg/dL (7.0 mmol/L), or HbA1c ≥ 6.5% (48mmol/mol) ("Classification and Diagnosis of Diabetes," 2017). Fasting glucose and HbA1c were used as outcome measures separately from the diabetes status. The hexokinase/kinetic method was used to measure fasting glucose while high performance liquid chromatography was used to measure HbA1c.

Statistical Analysis

All regression models used survey estimation methods for population inference accounting for the complex survey design. Missing data were handled using inverse-probability of observation weighs to re-weight the "observed" sample (i.e., the analytic sample with no missing data) to resemble the total sample (i.e., all participants at baseline) with respect to specified covariates. We created inverse-probability weights based on education, religion, employment, age, sex, and body mass index. The inverse-probability weights were multiplied by the survey design weight to generate a final analytic weight used in data analysis.

We modeled conditional HbA1c and fasting glucose distributions using generalized gamma regression models Generalized gamma regression models have position, scale, and shape parameters allowing for flexible modeling of continuous

variables (Cox, Chu, Schneider, & Munoz, 2007). In a simplified generalized gamma regression where the scale and shape parameters are held constant between exposed and unexposed groups, and only the position parameter is allowed to differ by group, then the generalized gamma regression model is a proportionate percentiles regression model. In a proportionate percentiles model, the same constant (the exponentiated regression coefficient) is multiplied by each quantile of the 'unexposed' outcome distribution to arrive at the estimated 'exposed' outcome distribution. This allows for a straightforward interpretation of the association as "levels of Y were X% higher in the exposed compared to the unexposed". In contrast, when the scale or shape parameters are significantly different by group, then there are different magnitude of differences between quantiles of the 'exposed' and 'unexposed' outcome distributions, rather than a constant proportional relationship. We first fit generalized gamma regression models allowing for three simultaneous regressions, one for the position parameter (multivariable-adjusted), one for the scale parameter (multivariable-adjusted), and one for the shape parameter (multivariable-adjusted). Then, in these flexible models, we tested for whether there were significant associations in scale and/or shape parameters; where these scale and shape parameter associations were not significant, we constrained the generalized gamma regression to be a proportionate percentiles model. Results from the models with significant scale or shape parameter associations are presented graphically; results from the proportionate percentile models are summarized in tables. We also estimated adjusted odds ratios for prevalent diabetes using logistic regressions models. Bonferroni correction was used to account for multiple comparisons and type 1 error. Our Bonferroni

significance threshold was 0.0007. This was calculated from seventy total tests that were being performed.

Frequency of fish consumption was recoded into a binary variable for statistical anlaysis, distinguishing at least monthly consumption from less than monthly consumption. Other variables that were controlled for in the multivariable generalized gamma and logistic regression models included both continuous variables: participant age (linear and quadratic terms), and BMI; and categorical variables: sex, tertile of unhealthy diet score, educational attainment (3 categories: up to primary school, high school/secondary, or college graduate), tobacco use (3 categories: current, ever, or never), monthly household income (Indian Rupees [INR] ≤ 10,000 [equivalent to US $200], INR 10,001-20,000 [US $200-$400], INR ≥ 20,001 [US $400], or income not declared), sedentary lifestyle (indicator for sitting or reclining but not sleeping ≥ 5 hours/day), self-reported physician diagnosis of high blood pressure (yes or no), and self-reported diagnosis of high cholesterol (yes or no).

To assess whether the specific seafood consumption-glycemia associations differed according to the trophic level of the seafood, we performed a second-stage inverse-variance-weighted random-effects meta-regression (Thompson & Higgins, 2002). Separate meta-regression models were fit for fasting glucose, HbA1c, and diabetes status. The outcome of the meta-regression were the regression coefficient from the earlier models (i.e., differences in log-medians from the glycemic biomarker proportionate percentiles models; differences in log odds from the logistic regressions). The predictor variable of the meta-regression was trophic position of the seafood.

All analyses were conducted using Stata SE 15.1 (StataCorp LLC, College Station, TX).

Results

Seafood Consumption, HbA1c, Fasting Glucose, and Diabetes

Table 1 presents the total consumption frequencies and the estimated percentage of the population that consumed the seafood items analyzed in the study. **Table 2** presents baseline characteristics of the study participants. There were 3,755 (53.8%) women and 3,224 (46.2%) men participating in this study. Their mean age was 41.37 years old. Almost a quarter (n=1,453; 24.1%) of the participants reported a physician's diagnosis of having diabetes.

There were 5 seafood items whose generalized gamma regression models had significant "scale" or "shape" parameters, indicating that the extent of difference in HbA1c distributions of persons consuming seafood more vs. less than monthly was heterogenous across the quantiles of the HbA1c distribution.: salmon, karapodi, nagarai, sheela, and vanjaram. The distributions of HbA1c were different according to frequency of salmon and nagarai consumption, based on a Bonferroni-significant P-value from the 3d F-test for the generalized gamma model's beta, sigma, and kappa parameter regression coefficients. The comparison of HbA1c distributions by salmon consumption had a 3d F-test P-value of 4×10^{-4}, while the comparison by nagarai consumption had a 3d F-test P-value of 1×10^{-6}. Modeled HbA1c distributions, adjusted for confounders, are shown in **Figure 1**.

The associations between seafood consumption frequency and HbA1c for the remaining 17 seafood items could be described adequately using proportionate percentile models. Results from the survey estimation multivariable-adjusted proportionate percentile generalized gamma regressions models for HbA1c are shown in **Table 3**. We did not see any significant associations of seafood item consumption with HbA1c. The point estimates for these 17 seafood-HbA1c associations were approximately null except for surameen, which had an estimated ~4% lower HbA1c among persons eating more than monthly compared to persons eating less than monthly (percentile ratio: 0.96, 95% Confidence Interval: 0.88, 1.03).

The extent of difference between fasting glucose distributions according seafood consumption frequency was different across the quantiles of the fasting glucose distribution (i.e., significant "scale" or "shape" parameters in the generalized gamma regression) for 8 seafood items: karapodi, kezhanga, navara, nethili, suthumbu, valai, vavval, and kola. The fasting glucose distributions between monthly vs. less than monthly consumers of navara and valai were distinct at a level that was Bonferroni-significant: for each fish, there was a P-value of 5×10^{-7} for the 3d F-test of the generalized gamma model's position, scale, and shape parameters' regression coefficients. Modeled fasting glucose distributions, adjusted for confounders, are shown in **Figure 2**.

Associations between seafood consumption frequency and fasting glucose distributions for the remaining 16 seafood items are shown in **Table 4.** Fasting glucose was approximately 5% lower (95% Confidence Interval: 1% lower, 10% lower) among persons eating salmon at least monthly vs. less than monthly. However, with a p-value of

0.042, this finding was not Bonferroni-significant. The other estimated associations were all approximately null.

The odds ratios for prevalent diabetes according to seafood consumption are shown in **Table 5**. Frequent consumption of katla and koduva was associated with lower odds of diabetes. The odds ratio for physician-diagnosed diabetes among frequent consumers of these two types of seafood were 0.30 (95% CI: 0.11, 0.84) for katla and 0.42 (95% CI: 0.26, 0.67) for koduva. Neither of these were observed to have Bonferroni-significance.

The meta-regression findings are shown in **Figure 3-5.** We observed null associations for fasting glucose, HbA1c, and diabetes status across the different trophic levels of the seafood.

Discussion

In summary, there was little evidence supporting a relationship between monthly seafood consumption and diabetes status. We observed Bonferroni- significant cross-sectional joint associations in the beta, sigma, and kappa regression coefficients between consuming salmon and nagarai with HbA1c; and navara and valai with fasting glucose. However, it is possible that these associations are nonetheless spurious given the small number of participants who consumed these specific fish more than monthly. Meta-regression analysis did not support trophic levels of fish as a strong predictor of the associations between seafood consumption frequency and diabetes, fasting glucose, or HbA1c. Based on these results, we conclude that biomagnifying seafood contaminants are unlikely to be major contributors to the diabetes epidemic in Chennai, India. However, two types of seafood, katla and koduva were associated with lower odds of

prevalent physician-diagnosed diabetes; this may be consistent with changes in dietary behaviors after diabetes has been diagnosed, or possibly some nutritional idiosyncrasies of those specific seafood items.

Our study has several strengths, but limitations as well. A strength of our study is that it is a complex survey sample and our data was collected using standardized procedures. The complex survey sample helps us ensure reasonable inference without selection bias for the population of Chennai. Our study is a cross-sectional observational study, and no temporal relationship between exposure and outcome can be assessed. Another limitation of this study is that we are lacking data on the way the seafood was prepared. Fish in India is either eaten dried, fried, or fried and then cooked with vegetables, gravy, or lots of spices, condiments, and cooking oil (Agrawal, Millett, Subramanian, & Ebrahim, 2014), which may alter the health consequences of fish consumption. A study in Alaska in 2009 found that seafood preparation methods could significantly affect contaminant concentrations (Moses, Whiting, Muir, Wang, & O'Hara, 2009). A prospective cohort study in the UK did not find fried fish significantly associated with diabetes risk (Patel et al., 2009), but a study involving Dutch participants observed a relative risk decrease after an additional adjustment for fried fish intake (van Woudenbergh et al., 2009).

Another limitation of the study is that we did not have trophic level data for kadamba, nagarai, kezhanga, kilachi, and kola. These species of seafood were excluded from the meta-regression analysis.

In conclusion, our data indicates that no particular species of seafood that is consumed in Chennai is associated with diabetes. Additional research is needed to understand the contaminants and concentrations in the seafood.

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Tables and Figures

Table 1

Consumption Frequency of Specific Seafood Items	
Seafood	N (% of population)
Eral	**1,532 (21.54%)**
Kadamba	**236 (3.44%)**
Kanankelithi	**595 (8.11%)**
Karapodi	**269 (3.80%)**
Katla	**85 (1.23%)**
Kezhanga	**642 (9.71%)**
Kilachi	**209 (2.87%)**
Koduva	**97 (1.42%)**
Kola	**39 (0.75%)**
Mathi	**669 (10.44%)**
Naakumeen	**32 (0.39%)**
Nagarai	**81 (1.17%)**
Nandu	**708 (9.93%)**
Navara	**321 (4.58%)**
Nethili	**351 (4.63%)**
Paarai	**143 (1.74%)**
Salmon	**22 (0.22%)**
Sankara	**2,089 (29.26%)**
Sheela	**444 (6.01%)**
Surameen	**55 (1.00%)**
Suthumbu	**77 (1.28%)**
Valai	**143 (1.95%)**
Vanjaram	**645 (8.83%)**
Vavval	**172 (2.14%)**

Table 2

Demographics			
	Diabetes Status	**Fasting Glucose ≥ 126 mg/dL**	**HbA1c ≥ 6.5%**
Gender			
Male	**660**	**947**	**1,161**
Female	**793**	**867**	**1,123**
Age			
20-29	**51**	**29**	**54**
30-49	**720**	**454**	**659**
50-64	**527**	**297**	**478**
65+	**155**	**83**	**142**
Body Mass Index (kg/m^2)			
<23	**210**	**138**	**201**
≥23 and <25	**730**	**103**	**138**
≥25 and <30	**1,674**	**268**	**422**
≥30	**2,252**	**354**	**572**
Sedentary Lifestyle			
No	**341**	**511**	**630**
Yes	**1,112**	**1,303**	**1,654**
Educational Attainment			
No Education	**399**	**187**	**253**
Up to Primary	**299**	**159**	**212**
High School/Secondary	**3,278**	**1,257**	**1,570**
College Graduate	**599**	**211**	**249**
Tobacco Use			
Never	**1,800**	**1,332**	**1,695**
Ever	**69**	**49**	**68**
Current	**535**	**433**	**521**
Monthly Household Income (Indian Rupees)			
≤10,000	**1,169**	**1,472**	**1,844**
>10,000	**279**	**333**	**428**
Self-Reported High Blood Pressure			
No	**1,056**	**1,490**	**1,841**
Yes	**397**	**324**	**443**
Self-Reported High Cholesterol			
No	**1,371**	**1,744**	**2,193**
Yes	**82**	**70**	**91**
Unhealthy Diet Score			
0-6	**509**	**539**	**716**
7-12	**746**	**952**	**1,178**
13-18	**182**	**291**	**352**

19-24	**16**	**32**	**38**
25-30	**0**	**0**	**0**

Table 3

Multi-Variable Proportion-Percentile Generalized Gamma Regression Results for HbA1c		
Seafood	Relative Median	Confidence Interval
Eral	**0.99**	**0.97, 1.00**
Kadamba	**1.00**	**0.98, 1.03**
Kanankelithi	**1.00**	**0.99, 1.02**
Katla	**0.98**	**0.94, 1.02**
Kezhanga	**1.00**	**0.98, 1.02**
Kilachi	**1.00**	**0.98, 1.03**
Koduva	**0.98**	**0.95, 1.02**
Mathi	**1.00**	**0.98, 1.02**
Naakumeen	**0.98**	**0.96, 1.00**
Nandu	**0.99**	**0.97, 1.01**
Navara	**1.00**	**0.98, 1.02**
Nethili	**0.99**	**0.97, 1.02**
Paarai	**0.98**	**0.94, 1.01**
Sankara	**0.99**	**0.98, 1.01**
Surameen	**0.96**	**0.88, 1.03**
Valai	**0.99**	**0.96, 1.02**
Vavval	**1.00**	**0.98, 1.03**

Table 4

Multi-Variable Proportion-Percentile Generalized Gamma Regression Results for Fasting Glucose		
Seafood	Relative Median	Confidence Interval
Eral	**0.99**	**0.97, 1.01**
Kadamba	**0.97**	**0.89, 1.05**
Kanankelithi	**0.98**	**0.95, 1.02**
Katla	**1.02**	**0.99, 1.06**
Kilachi		
Koduva	**1.02**	**0.99, 1.06**
Mathi	**1.00**	**0.97, 1.03**
Naakumeen	**1.00**	**0.96, 1.05**
Nandu	**1.01**	**1.00, 1.03**
Nagarai	**1.01**	**0.97, 1.05**
Paarai	**0.98**	**0.94, 1.02**
Salmon	**0.95**	**0.91, 1.00**
Sankara	**1.00**	**0.98, 1.02**
Sheela	**1.00**	**0.98, 1.02**
Surameen	**1.00**	**0.95, 1.06**
Vanjaram	**1.00**	**0.97, 1.01**

Table 5

Seafood	Odds Ratio	Confidence Interval
Eral	**0.88**	**0.65, 1.19**
Kadamba	**1.14**	**0.70, 1.85**
Kanankelithi	**0.99**	**0.69, 1.42**
Karapodi	**1.28**	**0.65, 2.52**
Katla	**0.29**	**0.11, 0.79**
Kezhanga	**1.36**	**1.03, 1.79**
Kilachi	**1.13**	**0.73, 1.74**
Koduva	**0.46**	**0.28, 0.76**
Kola	**1.28**	**0.77, 2.13**
Mathi	**0.98**	**0.64, 1.50**
Naakumeen	**0.81**	**0.29, 2.24**
Nagarai	**0.78**	**0.16, 3.75**
Nandu	**0.84**	**0.61, 1.16**
Navara	**0.76**	**0.54, 1.05**
Nethili	**0.71**	**0.43, 1.18**
Paarai	**1.17**	**0.70, 1.93**
Salmon	**0.78**	**0.39, 1.55**
Sankara	**0.94**	**0.69, 1.27**
Sheela	**1.00**	**0.69, 1.45**
Surameen	**0.70**	**0.14, 3.45**
Suthumbu	**2.27**	**0.98, 5.23**
Valai	**1.06**	**0.44, 2.54**
Vanjaram	**0.91**	**0.63, 1.31**
Vavval	**1.69**	**0.96, 2.97**

Figure 1

HbA1c Generalized Gamma Regression Results

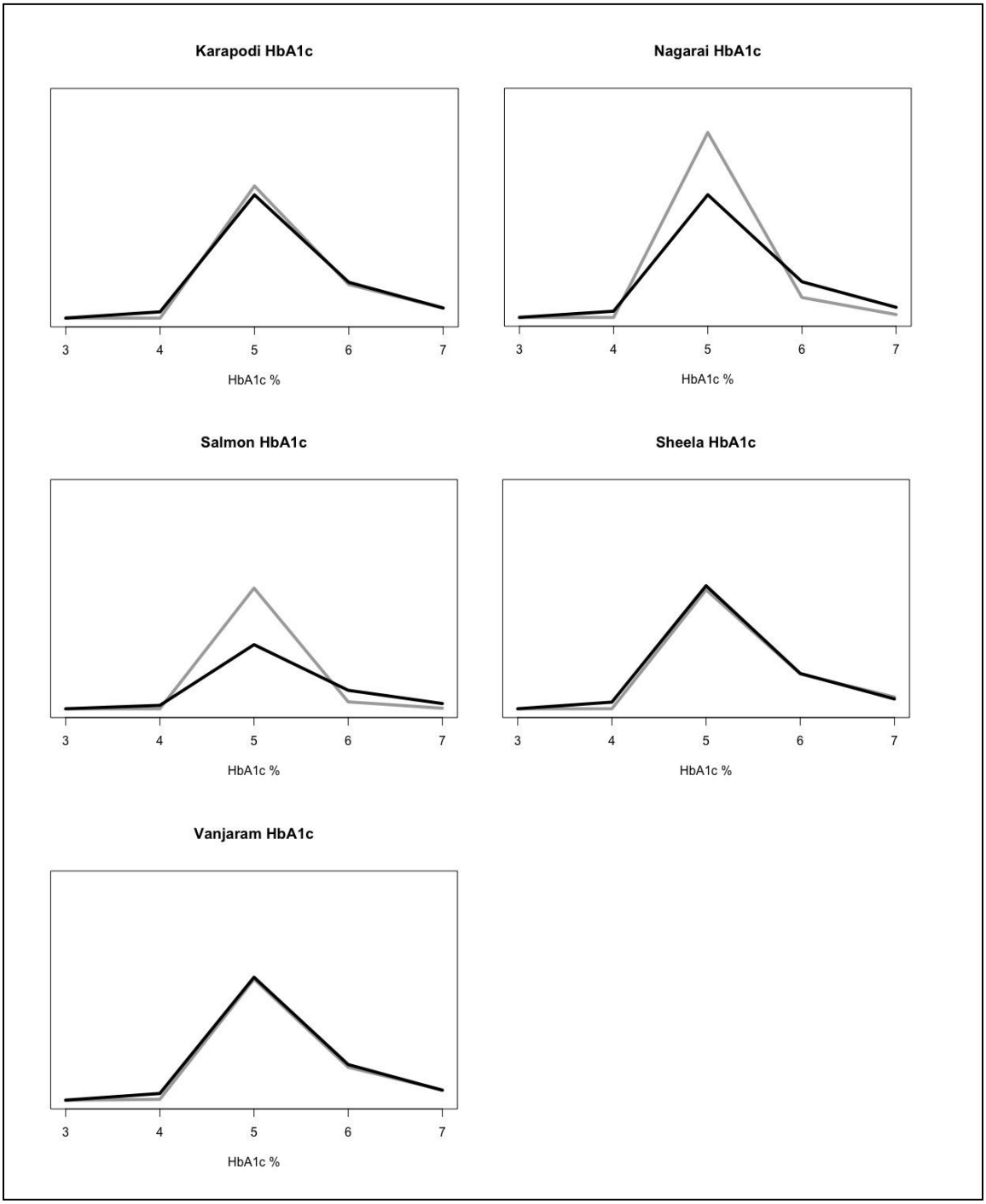

Figure 2

Fasting Glucose Generalized Gamma Regression Results

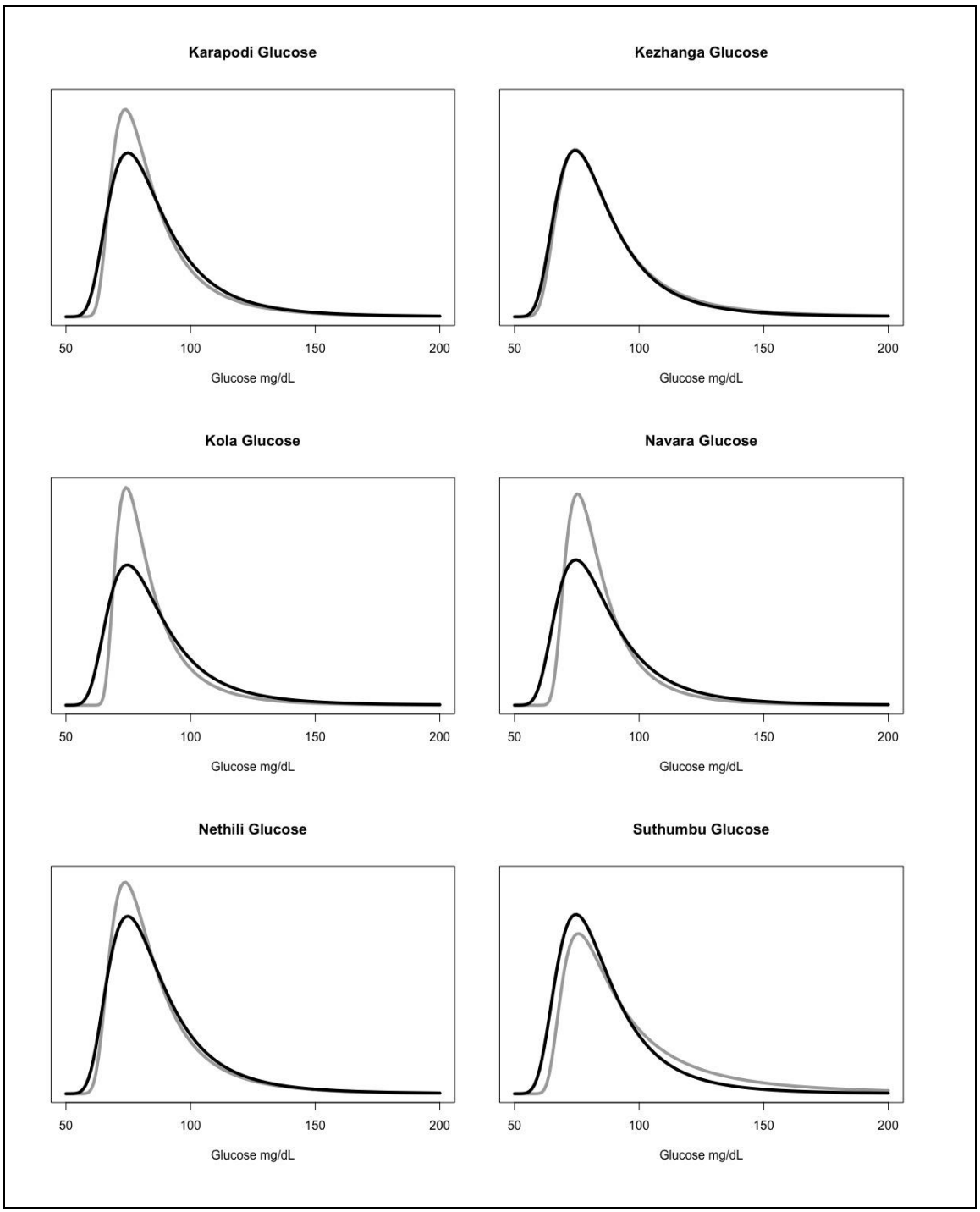

Figure 2 cont.

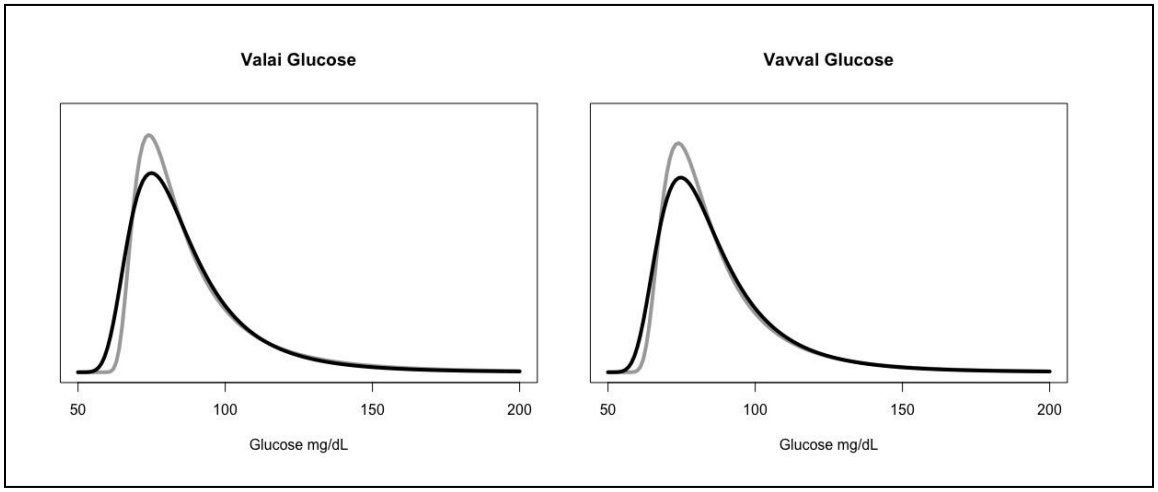

Figure 3

Diabetes Meta-Regression Results

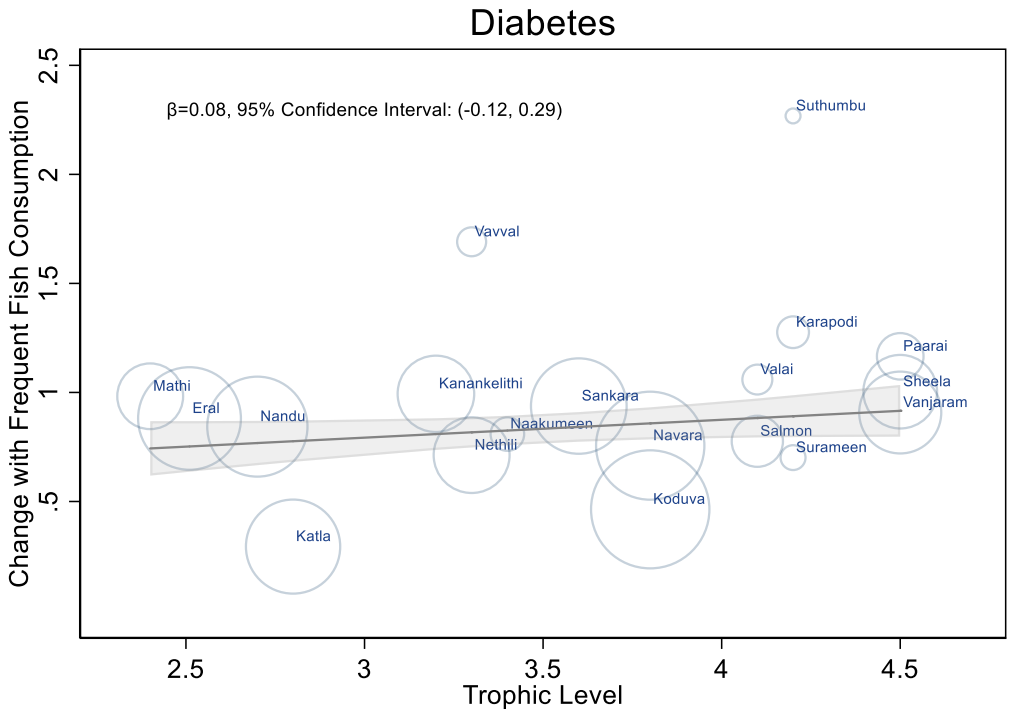

Figure 4

Fasting Glucose Meta-Regression Results

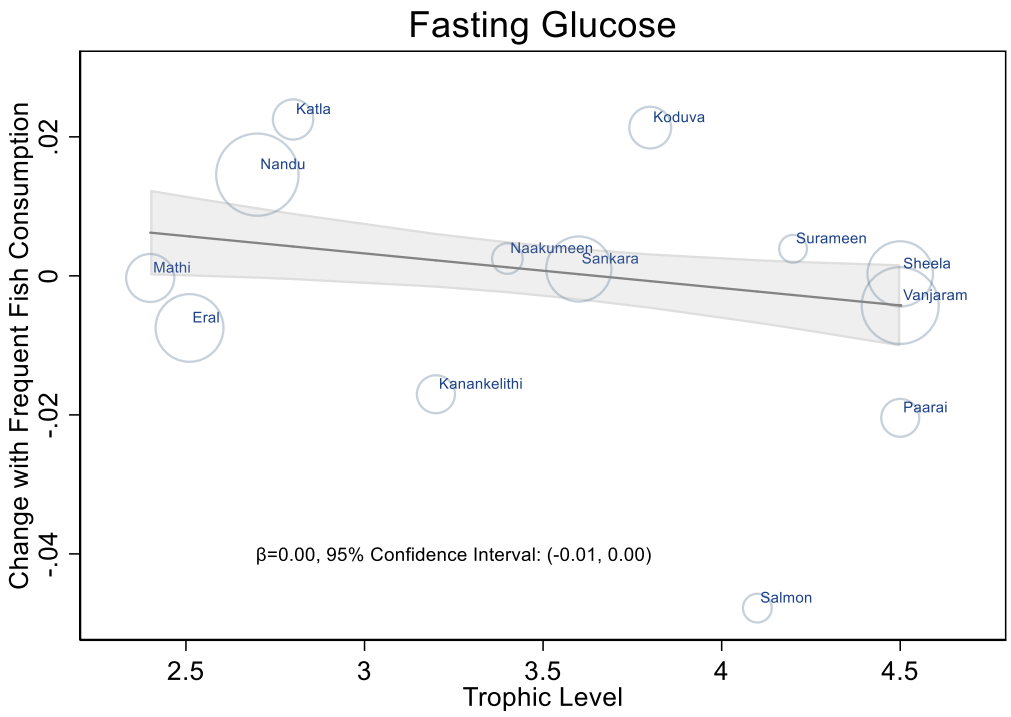

Figure 5

HbA1c Meta-Regression Results