THE HUMAN HEALTH EFFECTS OF FLORIDA RED TIDE (FRT) BLOOMS: AN EXPANDED ANALYSIS

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Acknowledgements

This research was sponsored by the National Science Foundation under NSF/CNH Grant No. 1009106. For help with compiling data, we thank Adrienne Henderson and Gloria Barker of the Florida Agency for Health Care Administration, Steve Hood of the Smith Travel Research, Inc. SHARE Center, Chris Knight of the Florida Department of Agriculture and Consumer Services, and students Stephanie Lavey (Duke University) and Amored Amaya (University of Miami). We also thank Brooke Wikgren (New England Aquarium) for help with ArcGIS. We benefitted from discussions with Bruce Garrison, Gary Hitchcock, Kate Kohler, Becky Lazensky, Cathy Li, Vince Lovko, Katrin Rudge, Rick Stumpf, and Sharon Watkins. L.E. Fleming acknowledges support from the European Regional Development Fund and the European Social Fund Convergence Programme for Cornwall and the Isles of Scilly. Use of the Florida Agency for Health Care Administration data on human health outcomes was determined to meet IRB exempt criteria by the Human Subjects Research Office at the University of Miami.

Abstract:

Human respiratory and digestive illnesses can be caused by exposures to brevetoxins from blooms of the marine alga *Karenia brevis*, also known as Florida red tide (FRT). *K. brevis* requires macro-nutrients to grow; although the sources of these nutrients have not been resolved completely, they are thought to originate both naturally and anthropogenically. The latter sources comprise atmospheric depositions, industrial effluents, land runoffs, or submerged groundwater discharges. To date, there has been only limited research on the extent of human health risks and economic impacts due to FRT. We hypothesized that FRT blooms were associated with increases in the numbers of emergency room visits and hospital inpatient admissions for both respiratory and digestive illnesses. We sought to estimate these relationships and to calculate the costs of associated adverse health impacts. We developed environmental exposure-response models to test the effects of FRT blooms on human health, using data from diverse sources. We estimated the FRT bloom-associated illness costs, using extant data and parameters from the literature. When controlling for resident population, a proxy for tourism, and seasonal and annual effects, we found that increases in respiratory and digestive illnesses can be explained by FRT blooms. Specifically, FRT blooms were associated with human health and economic effects in older cohorts (≥ 55 years of age) in six southwest Florida counties. Annual costs of illness ranged from \$60,000 to \$700,000 annually, but these costs could exceed \$1.0 million per year for severe, long-lasting FRT blooms, such as the one that occurred during 2005. Assuming that the average annual illness costs of FRT blooms persist into the future, using a discount rate of 3%, the capitalized costs of future illnesses would range between \$2-24 million.

1 Introduction

Sporadic blooms of the marine alga *Karenia brevis* take place from Texas to Florida along the Gulf of Mexico coastline (Kusek et al. 1999, Magaña et al. 2003, Vargo 2008).[1] The southwest Florida Gulf coast has experienced red tides more frequently than other areas of the Gulf. The blooms typically originate offshore on the shallow west Florida shelf, but the science of bloom formation, transport, and dispersion is still incipient (Vargo 2008). Through its Harmful Algal BloomS Observing System (HABSOS) program, the US National Oceanic and Atmospheric Administration (NOAA) tracks research studies and monitoring efforts that measure the spatial, temporal, and cell-density dimensions of *K. brevis* blooms (NCDDC 2014).

Like other marine algae, *K. brevis* requires macro-nutrients to grow. The sources of these nutrients have not been resolved completely, but they are thought to originate both naturally and anthropogenically. The latter sources comprise atmospheric depositions, industrial effluents, land runoffs, or submerged groundwater discharges (Lapointe and Bedford 2007; Vargo 2008; Charette et al. 2013). After decades of excessive nutrient releases by agriculture, heavy industry, residential septic systems, and both treated and untreated wastewaters, nutrient stocks are now present in coastal waters that may be helping to cause or sustain FRT blooms (Brand and Compton 2007).

The physical manifestations of FRT blooms, including dead manatees, fishkills, shellfish closures, noxious odors, changes in water color, and human respiratory impairments, are concerning to affected communities in Florida that rely heavily upon coastal tourism. At local levels, several studies have estimated economic losses to tourism businesses from FRT blooms

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[1] The molecular structure of K. brevis can be found in the US Food and Drug Administration's "Bad Bug Book" (FDA 2012).

(Habas and Gilbert 1975; Adams et al. 2002; Larkin and Adams 2007; Morgan et al. 2009, 2010). Natural hazards comprise a process of joint production involving nature and humans (Russell 1970). Unless humans are literally "in harm's way," FRT blooms cannot impose measurable environmental, public health, or socio-economic impacts. Humans sometimes contribute to the occurrence of a natural hazard, but establishing that contribution for the FRT case has been problematic (Vargo 2008). Humans still must bear the adverse effects of FRT blooms, however, even if they have not taken actions to cause them.

The population dynamics for the 23 counties along the Florida Gulf coast can be characterized as growing rapidly from very small populations nearly a century ago (Hoagland 2013). Intra-annual fluctuations of visitors, beginning in October and lasting through April, overlay secular residential growth. These visitors comprise short-term tourists and longer-term "snow-birds," the latter mainly seniors who reside in Florida for extended periods during the winter months (Smith and House 2006). Because of this growth, humans living in and visiting these counties now are more exposed to red tides, even if bloom frequencies may have been unchanged.

Human respiratory and digestive illnesses are known to have been caused by exposures to brevetoxins associated with FRT blooms (Kirkpatrick et al. 2004, 2006, 2008, 2010; Fleming et al. 2005, 2007, 2009, 2011; Backer 2009; Hoagland et al. 2009). These illnesses may exhibit varying severities, leading to increases in costs associated with purchases of over-the-counter medications; self-treatment by asthmatics utilizing prescription pharmaceuticals; visits to outpatient clinics, doctors, and emergency departments; or hospital inpatient admissions. In theory, even human mortalities could result from neurotoxic shellfish poisoning (NSP), although no mortalities have yet been linked conclusively to this source (Fleming et al. 2011). FRT-associated mortalities have been observed in marine mammals, however, including manatees and oceanic dolphins, and also in sea turtles, seabirds, and finfish (Flewelling et al. 2005, Landsberg et al. 2009, Fire and Van Dolah 2012, Capper et al. 2013).

Public health specialists and managers of clinical care would like to assess the nature of human health risks due to blooms of FRT, but there has been only limited research on this topic. Fleming et al. (2011) found that brevetoxin aerosols during active FRT blooms could exacerbate asthma and other respiratory conditions with subchronic sequelae. Kirkpatrick et al. (2006, 2008) found that visits to a hospital Emergency Department (ED) in Sarasota, Florida for respiratory and digestive illnesses were associated with FRT blooms. Hoagland et al. (2009) used an exposure-response framework to estimate the potential effects of FRT blooms on ED visits to the same hospital for respiratory illnesses during 2001-06. These authors found that a local measure of *K. brevis* cell counts, lagged by one week, could explain ED visits when controlling for local air temperatures, regional influenza outbreaks, regional pollen counts, and a local measure of tourist visits. The one-week lag was explained by a delay between observances of live *K. brevis* cells, releases of the toxin as the algal cells lysed after death, movements of the toxin from the water column to the atmosphere through physical aerosolization, and eventual human inhalations of and reactions to the toxin.

Consumption of brevetoxin-contaminated shellfish, and possibly finfish, during active FRT blooms are associated with NSP (Watkins et al. 2008). Kirkpatrick et al. (2010) found ED visits for digestive illnesses at the Sarasota Memorial Hospital increased by 40% during an FRT bloom event in 2001 (0.07 ± 0.01 per 100,000 cases) relative to 2002 (0.05 ± 0.01 per 100,000 cases) when there was no FRT bloom. Although shellfish harvest areas (SHAs) typically were closed during FRT blooms to mitigate the risks of NSP from the consumption of molluscan bivalves, these authors argued that humans could be contracting digestive illnesses through other pathways, including the consumption of illegally harvested shellfish, whole finfish (especially the entrails, where brevetoxins may be concentrated), the breathing of aerosols contaminated with brevetoxins, or the inadvertent swallowing of contaminated seawater (Flewelling et al. 2005).

Using a broader set of data on both FRT bloom occurrences and health outcomes, we present here the results of a study of human respiratory and digestive FRT-related health risks over a longer period of time and across a substantially wider geographic range than previous studies, and stratified by age. We compiled panel data on two distinct measures of FRT blooms: (i) counts of *K. brevi*s cells (*Kb* cell counts) obtained through opportunistic water sampling efforts and (ii) the number of FRT-related closures of coastal shellfish harvesting areas (SHA closures) in counties along the Florida Gulf coast.

2 Materials and Methods

2.1 Study area. Fig. 1 depicts the static spatial heterogeneities comprising human populations in coastal counties and the dynamic heterogeneities comprising FRT bloom events, as represented by shellfish closures (Hoagland 2013). The figure shows how the chief FRT "hazard" (defined as jointly distributed humans and blooms) is located from the Tampa-St. Petersburg region (Pinellas and Hillsborough counties) southward through Lee County (Hoagland 2013).

2.2 Model. To develop an analysis of the effects of FRT occurrence on human health, we constructed time-series, cross-section regression models using monthly data at the county level. Let V be the response (*e.g.*, the number of visits or admissions to hospital facilities per month in a county). We modeled V as follows:

$$V_{it} = \alpha_0 + \alpha_1 FRT_{it} + \alpha_2 POP_{it} + \alpha_3 TOUR_{it} + \sum_{j=1}^{11} \beta_j M_j + \sum_{k=1}^{K} \gamma_k Y_k + a_i + b_t + \varepsilon_{it} \qquad (1)$$

where i is the index for individual county (1, 2, …, 6); t is the index for time (month); α_0 is the intercept; FRT_{it} is a measure of FRT bloom events, measured by *Kb* cell counts or SHA closures, in county i at t; POP_{it} is the population in county i at t; $TOUR_{it}$ is a measure of tourist visits (*i.e.*, number of hotel and motel rooms rented) in county i at t; M_j is a (0,1) dummy for month j; Y_k is a (0,1) dummy for year k; a_i is a time-invariant, cross-sectional unit effect; b_t is a cross-sectional unit-invariant time effect; and ε_{it} is a residual effect unaccounted for by the other predictors and the specific time and cross-sectional unit effects. The vectors α, β, and γ comprise coefficients to be estimated.

2.3 ED visit and hospital inpatient data. Data on ED visits and hospital admissions were obtained from the Florida Agency for Health Care Administration (AHCA). The AHCA data consisted of two sets of annual files containing emergency department (ED) data (2005-10) and hospital inpatient (INPT) data (1988-2010). Each annual data file contained 0.5-1.5 million patient records (representing individual visits to a hospital facility) and 65-195 variables (due to changing data formats over time). Five variables were compiled from the AHCA data: patient admission date; county location of a medical facility; patient age at admission; principal diagnosis code; and patient permanent residence zipcode. The principal diagnosis (ICD-9) code for each patient was used to identify relevant categories of two general types of illnesses: diseases of the respiratory system (ICD-9 codes 460.0–519.2) and diseases of the digestive system (520.0–579.9).

The patient's permanent residence zipcode was used to distinguish coastal from inland residents. We defined coastal residents as those who resided within 8.1 km (5 mi) of the coast. Patients at hospitals within each county with non-Florida zip codes (i.e., outside the range of zipcodes 32000-35000) were assumed to be coastal tourists (i.e., we assumed they were visiting within 8.1

km of the coast in each relevant county).

2.4 Measures of FRT bloom events. We compiled data on two different measures of FRT bloom events as environmental exposures: (1) opportunistic water sampling of the number of *K. brevis* cells per liter of seawater within 15.0 km of the coast (*Kb* Cell Counts); and (2) the closures of shellfish harvesting areas (SHA Closures) to mitigate NSP illnesses resulting from the consumption of contaminated shellfish. Both measures exhibited limitations, but we judged that these limitations were minor, manifesting themselves in unique ways for each measure. Importantly, we ran four separate models with each measure in order to determine whether human health responses (by type and severity) were robust to the choice of environmental exposure measure; if so, this would strengthen our confidence in the existence of adverse health effects.

We compiled a data set that included *K. brevis* cell counts ("*Kb* Cell Counts") measured greater than 10^3/L within 15.0 km of waters along the six Florida counties on the Gulf coast (from north to south): Pinellas, Hillsborough, Manatee, Sarasota, Charlotte, and Lee (FWRI 2013). The data characterized blooms from 1999-2009 once they were known to occur (Brand and Compton 2007). We assumed that all FRT blooms were identified and sampled during the period of study, and we assigned zeros (i.e., no blooms) to those months when no samples were taken. We used the square of the maximum *Kb* Cell Count in a month and county as a proxy for bloom severity. The water monitoring data represented opportunistic sampling, but modern sampling efforts, particularly those occurring near the coast, rely upon satellite measurements of bloom formation (NCDDC 2014) as well as the samples and reports of marine scientists, environmental and public health agencies, fishermen, lifeguards, beachgoers, and others who have become practiced at identifying and reporting Florida red tides, especially those occurring near the coast.

Consequently, we believe that the assumption that all major FRT blooms were identified and sampled during the period of study is not unrealistic.

The occurrence of FRT blooms resulted also in closures of shellfish harvest areas ("SHA Closures"), another measure of FRT events. Florida SHAs are not distributed uniformly along the coast, but each county is associated with one or more SHAs (Fig. 1). We compiled data on the dates of individual SHA closures due to FRT blooms during January 2000 to December 2009 through a review of electronic copies of original SHA closure memoranda published by the Florida Department of Agriculture and Consumer Services (FDACS). We calculated the number of closures by month, year, and county.

2.5 Population and tourism data. Annual population data by county were compiled for 1999-2009 from the US Census Bureau (BoC 2013). Monthly data on the number of hotel and motel rooms rented by county were compiled for 1999-2009 (STR 2013), and we assumed these data were a proxy for tourist fluxes, including snowbirds. Note that the total numbers of tourists would be underestimated with the hotel and motel room rental data, because condominium rentals and time-shares have become a significant component of the Florida coastal housing market. We assumed that monthly variations in condominium use matched monthly variations in hotel and motel room rentals, and we used the latter as a proxy for the monthly variability (but not actual numbers) of each county's tourist visits.

2.6 Descriptive statistics. The ranges of variables used in the regression analyses are summarized in Table 1. Descriptive statistics for patients aged 55 and above are summarized in Tables 2 and 3. Regressions involving younger age groups did not result in significant associations. The two measures of FRT blooms were generally consistent across the six counties in the study area. One noticeable inconsistency occurred in Charlotte County where the number of SHA closures was relatively high, while the FRT cell counts were relatively low. Note that the threshold *K. brevis* cell count in water samples leading to an SHA closure is 5,000 cells/L, well below the mean monthly maximum cell counts for Charlotte County in Tables 2 and 3.

3 Results

3.1 Exposure-Response. We estimated equation (1) separately for respiratory and digestive illnesses, using the two FRT bloom measures and monthly emergency department (ED) data from 2005-09 and monthly hospital inpatient (INPT) data from 1999-2009. For each regression, the baseline was December 2009.[2] The results of all eight model runs are presented in Table 4, labeled with Roman numerals. Models I-IV comprised estimates of the effects of FRT blooms on ED visits; models V-VIII comprised estimates of the effects on INPT admissions. The odd-numbered models examined respiratory illnesses, and the even-numbered models examined digestive illnesses. Models I, II, V, and VI examined the effects of *Kb* Cell Counts, and models III, IV, VII, and VIII examined the effects of SHA Closures. Because SHA Closures were obtained only from 2000-09, 1999 is not included in models VII and VIII.

Models I and II present the results of regressions on the number of ED visits using the *Kb* Cell Counts as a measure of the occurrence of FRT blooms in coastal waters. The data incorporated 360 observations. The dependent variables in both models were the number of ED visits by month and by county. The independent variable, "*Kb* Cell Counts," was the square of the maximum cell count observed in each month and county. The respiratory illness model indicated that ED visits were significantly affected by FRT bloom events. The coefficient for the *Kb* Cell

[2] In estimating these models, we explored a number of alternative specifications and variable transformations. Further, we explored the effects of the FRT bloom exposure variables on different age cohorts, finding that only individuals with ages ≥ 55 years showed significant ED visit or INPT admission responses. Summaries of the alternative models are available upon request from the authors.

Counts variable suggested that a one unit increase (10^7 cells/L) would lead to five additional ED visits per month in a county. Both the Population and Tourism variables were positively related to ED respiratory visits. Most coefficients for the monthly dummies were statistically significant, and the magnitudes suggested a strong seasonal fluctuation within a year, with more ED visits in the winter and fewer in the summer. For the digestive illnesses, the FRT bloom effect was smaller than that for respiratory illnesses; a one unit increase (10^7 cells/L) was associated with 2.4 more visits per month and county. ED visits for digestive illnesses were inversely related to Population but positively related to the Tourism measure. The magnitudes of the monthly dummies also reflected a similar seasonal fluctuation within a year, albeit weaker than that for respiratory visits.

We developed similar regressions for the numbers of hospital inpatient admissions (INPT) in models V and VI. In these models, the data ranged from 1999-2009, comprising 792 observations. Hospital admissions for both respiratory and digestive illnesses were significantly affected by FRT bloom events, and both types of illnesses exhibit approximately the same marginal effects. The magnitudes of the effects on hospital admissions were much smaller than those predicted for ED visits from models I and II. The coefficient for *Kb* Cell Counts suggests that a one unit increase (10^7 cells/L) would lead to 0.4 additional hospital admissions per month in a county for each illness type. Population and tourism measures both were positively related to hospital admissions for both types of illnesses. The magnitudes of the monthly dummy coefficients suggested a strong seasonal fluctuation within a year, with more visits in the winter and fewer in the summer.

Models III and IV consider the effects of SHA Closures as the measure of exposure on ED visits for respiratory and digestive illnesses. The two models were estimated using data from only four counties in the study region (Hillsborough, Lee, Pinellas, and Sarasota), comprising 240 observations. Charlotte and Manatee counties, which had much smaller population and patient numbers, were excluded. The ED visits for both respiratory and digestive illnesses were significantly influenced by the number of FRT-related SHA closures and larger than those associated with the FRT cell counts. The marginal effects of a single SHA closure were roughly 17 visits for respiratory illnesses and three visits for digestive illnesses per month per county. With SHA closures as an FRT measure, the tourism and seasonal effects were qualitatively similar to the results using the *Kb* Cell Closures as an exposure. In contrast, population was inversely related to ED visits.

Models VII and VIII consider the effects of SHA Closures as the measure of exposure on INPT admissions for respiratory and digestive illnesses. Two models were estimated using data from 2000-09 for only three counties with large patient numbers (Hillsborough, Pinellas and Sarasota, see Table 2), comprising 360 observations. With SHA Closures as an FRT measure, the overall results were consistent with the results of the models using the *Kb* Cell Count exposure. There was a statistically significant relationship between INPT for both respiratory and digestive illnesses and FRT blooms. One FRT-related SHA closure is expected to cause three patient admissions per month per county due to respiratory illness and six for digestive illness. Both types of hospital illnesses were positively related to the population and tourism measures.
Using all eight models, comprising both FRT bloom measures, we predicted the number of FRT-related respiratory and digestive illnesses (means and 95% confidence intervals) for each of the relevant counties. For each model, we averaged these county-specific predictions over the relevant years of analysis, and we summed the averages across the counties to yield regional estimates of the average number of illnesses of each type. Because the different models predicted

differing numbers of respiratory and digestive illnesses, we characterized these model results as low and high predictions for each type of illness. As described in the next section, we also developed low and high estimates for the costs of each type of illness. We matched these cost ranges to the ranges for illness predictions to yield low and high estimates of the annual and capitalized costs of illness resulting from blooms of Florida red tides.

3.2 Costs of illness**.** Our estimates of the numbers of respiratory and digestive illnesses allowed us to develop estimates of the costs of illness. We modified an approach outlined by Hoagland et al. (2009). Our estimated illness costs focused on treatment costs and lost incomes during both treatment and recuperation. Leisure time or sick leave was valued at the margin as lost income. Daily income of $120/d was calculated using Florida annual personal income per capita (BEA 2013). As such, these costs were conservative, because they did not incorporate the non-market costs associated with pain and suffering. Further, it may be assumed that the value of lost incomes would be higher among coastal- and tourist/snowbird-attracting geographic areas as compared to inland and northern counties with lower-than-average income levels. Because our models estimated only a small number of FRT-related respiratory and digestive illnesses, and because we expected that the costs of treating these illnesses in emergency or hospital settings are not extraordinary or long-lasting, we assumed that marginal costs were the most appropriate measure of illness costs.

We identified average charges for the treatment of respiratory and digestive illnesses across the relevant counties in the AHCA data. We took the lowest and highest average charges to construct a full range of plausible average charges. Average *charges* are an overestimate of the average *costs* of treatment, because hospitals often subsidize the costs of patients who are unable or unwilling to pay for treatments by charging other patients more. Hospitals also may crosssubsidize certain procedures with the proceeds from other procedures. Further, hospitals may have different negotiated charges with different private insurance or managed care companies as well as with state (for Medicaid) and federal (for Medicare) governments.

Studies of hospital cost functions provided estimates of the marginal costs of certain treatments or of the ratio of marginal costs to average charges (e.g., Williams 1996, Sutherland 2006). Following the method employed by Hoagland et al. (2009), we used the ratio of marginal ED costs to average ED charges of 0.23 to adjust the ranges of average ED charges from the AHCA data. Based upon a study of emergency treatments in California, Bamezai and Melnick (2006) argued that this ratio may have significantly undervalued the marginal costs of emergency treatment, suggesting that our approach to estimating ED visit costs was conservative.

To estimate the marginal costs of hospital inpatient (INPT) admissions, we first compiled data on both average charges and average costs from a statewide survey of Florida health care costs for respiratory and digestive illnesses (AHRQ 2013). We used the statewide ratio of average costs to average charges to convert the average charges from the county AHCA data to average costs. In order to estimate the marginal costs of INPT admissions, we relied upon the results of Sutherland (2012), who analyzed costs of hospitalizations in British Columbia. Following a similar approach to that used for adjusting ED costs, we used a ratio of marginal INPT costs to average INPT costs of 0.67 to adjust the ranges of calculated average INPT costs from the AHCA data.

We assumed that the total marginal costs of ED visits comprised the costs of medical treatment and three days of lost income (one for the ED visit and two for recuperation). For the INPT admissions, we used the minimum and maximum number of days hospitalized for respiratory or digestive illnesses from the Florida statewide survey of hospital costs (AHRQ 2013). We assumed that the total marginal costs of INPT care comprised the costs of medical treatments and lost incomes during recuperation. We assumed that the number of days of recuperation upon release from the hospital were three times the number of days hospitalized (this assumption is identical to that used for ED visits). We multiplied the marginal costs associated with each illness severity (ED or INPT) and each illness type (respiratory or digestive) times the predicted range of the number of illnesses to calculate a range of illness costs for each severity and type (Table 5).

As described in Section 3.1, the eight models yielded low and high predictions with 95% confidence intervals for each type of illness. In Table 6, we matched these low and high illness predictions to the low and high cost ranges to yield low and high estimates of the annual and capitalized costs of illness resulting from blooms of Florida red tides. We summed the total illness costs across severity and type to result in ranges of the annual cumulative costs of illness. These costs were adjusted to 2013 dollars using the US consumer price index (BLS 2013). The annual total marginal costs of illness ranged from $0.01-0.17 million for ED visits and from $0.01-0.42 million for INPT admissions. Taken together, the total illness costs across both illness types and severities ranged from $0.06-0.73 million. Assuming that the average annual illness costs of FRT blooms persist into the future, and employing a constant discount rate of 3%, with the effect of the discount rate being that the present value of the future costs of the red tide asymptotically approach zero as one goes out further into the future, the capitalized costs of predicted future illnesses would range between $2-24 million.[3]

We also estimated the annual costs of illnesses by severity and type for predictions of the numbers of illnesses resulting from the severe FRT bloom event of 2005. These estimates were representative of the extreme effect of a severe, long-lasting FRT bloom event. Predicted

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[3] We calculate this capitalized estimate in the conventional manner by dividing the average annual costs of illness by the discount rate.

respiratory and digestive illnesses ranged from 257-350 for ED visits and from 26-50 for hospital admissions. The annual total marginal costs of illness were predicted to range from $0.1-0.7 million for ED visits and $0.1-0.7 million for INPT admissions. Total annual illness costs for such an extreme event were estimated to range between $0.2-1.4 million.

4 Discussion

Our research comprised significant spatial and temporal extensions of earlier work that demonstrated the relationships between FRT bloom events and human respiratory and digestive illnesses in Sarasota County, Florida (Kirkpatrick et al. 2004; Backer 2009; Fleming et al. 2011). We found that adverse respiratory and digestive health effects were associated with increases in two measures of Florida red tides, agreeing with the results of these earlier studies. Our study examined these health effects over a broader geography, constituting as many as six counties along the southwest coast of Florida, finding that they were expressed in the responses of patients aged 55 and older. FRT bloom occurrences were associated with increases in ED visits and hospital inpatient admissions for residents and coastal tourists, and the numbers of illnesses varied with the severity of FRT blooms. These results are critical for public health, because the southwest coast of Florida is an important location for retirees and snowbirds, and both groups make up a significant part of the resident and transient populations.

With respect to ED visits, the marginal effects of FRT bloom events were larger for respiratory illnesses than for digestive illnesses. Unlike previous work, we did not distinguish among specific types of respiratory illnesses. Hoagland et al. (2009) failed to find that FRT blooms could explain variation in ED visits due to asthma, contrasting with other studies that focused specifically on the effects of aerosolized brevetoxins on asthmatics (Fleming et al. 2005, 2007, 2009; Kirkpatrick et al. 2009). The incidence of respiratory illnesses, including and perhaps being driven by asthma cases, has been climbing over the last two decades in Florida, and the potential role that aerosolized brevetoxins play in this growth for populations in coastal locations along the Gulf of Mexico may be important to scrutinize further.

We examined the broader regional health effects of Florida red tides, using measures that exhibited limitations, in contrast to the systematic (hourly) sampling that occurs at the Mote Marine Laboratory for the city of Sarasota. The regional approach required a broader temporal (monthly) focus, unlike earlier efforts that focused on weekly data on exposures and responses (Hoagland et al. 2009). Consequently, we were unable to look for lags associated with human health responses to bloom events. Moreover, the possibility exists that some FRT blooms occurring near the end of one month could result in illnesses at the beginning of the following month, leading potentially to larger standard errors around the exposure coefficients. The ability to characterize response lags suggests that, with prior warning, humans might be able to react to the FRT hazard, and health care providers may be better prepared to provide medical care and treatments to those in need. Thus, testing for human health response lags remains a priority for future research.

Although some authors have pointed to FRT blooms as a source of digestive illnesses (Kirkpatrick et al. 2006, 2010; Backer 2009; Fleming et al. 2011), this effect has been discounted largely because of an effective program to monitor and manage SHAs to mitigate the harvesting of shellfish potentially contaminated with brevetoxins. Because the pathway that brevetoxins take from *K. brevis* to humans is uncertain, our result that digestive illnesses are related to FRT bloom events was surprising. Given that our results agreed with earlier conjectures and results of human digestive illnesses arising from FRT bloom events, this area is a clear priority for future public health research.

We controlled for county resident populations, hotel and motel room rentals as a measure of tourist fluxes, and seasonal and annual effects. As expected, illnesses of both types increased with the tourism measure, implying larger numbers of older cohorts were at risk, and hospital inpatient admissions increased with county resident populations. We also found strong seasonal fluctuations for respiratory visits, with more visits in winter and fewer in summer, which was likely due both to cold and flu effects and increases in local snowbird populations in the winter. A similar seasonal pattern existed for digestive illnesses, although the effect was not as pronounced. Contrary to expectations, ED visits tended to decline with or be unrelated to increased county resident populations. While an explanation was not immediately apparent from the models, this effect could have resulted from the resident population's higher level of familiarity with FRT bloom events or from individual preferences for either self-treatment or visits to the resident's primary care physicians in lieu of ED visits.

Using the SHA Closure variable, we were not as successful in assessing the exposure-response relationship for all six counties taken together. The SHA Closure variable is a coarser measure of Florida red tides than the *Kb* Cell Count. The SHA Closure variable is binary, and the threshold for a closure is very low (~5,000 cells/L). With the SHA Closure measure, health effects were detected only in those counties with high population exposures to Florida red tides. For two of the counties, Charlotte and Manatee, other effects (e.g., the flu season and colder temperatures, as captured by the monthly dummies) appear to be more dominant. In the case of Lee County, the SHA Closures (the two four-digit sub-areas comprising the two-digit SHA #62 and one comprising SHA #58) are located in Pine Island Sound, Matlacha Pass, and Gasparilla Sound. (Detailed maps of the geographic locations of Florida SHAs have been published online by FDACS and are updated on a regular basis (FDACS 2014).) While Matlacha Pass is adjacent to the municipality of Cape Coral, the Pine Island Sound and Gasparilla Sound SHAs are positioned at some distance from the Lee County human population centers in both Cape Coral and Ft. Myers. The SHAs in both Sounds exhibited several closures when Matlacha Pass remained open, especially in 2002, late 2005, 2006, and 2009, suggesting that a significant number of humans may not have been exposed when SHAs for Lee County were closed. Taken together, these two explanations imply that the SHA Closure data may be not as useful as water sampling as a measure of the FRT bloom hazard. Nevertheless, the SHA closure data does serve an important purpose here of validating the human health response seen with the opportunistic water sampling data.

5 Conclusions

The southwest Florida coast is the locus of the highest public health risks associated with FRT blooms, although other coastal locations, including the Florida panhandle and Texas, may bear their own public health risks. Using two different measures, we found that FRT bloom events were significant predictors of emergency department visits and hospital inpatient admissions for both respiratory and digestive illnesses. Estimates of illnesses were comparable to those of an earlier study by the authors that was more narrowly focused across both time and geography. Annual costs of illness ranged from $60,000 to $700,000 annually, but these costs could exceed $1.0 million per year for severe, long-lasting FRT blooms, such as the one that occurred during 2005. Assuming that the average annual illness costs of FRT blooms persist into the future, using discount rate of 3%, the capitalized costs of future illnesses would range between $2-24 million.

These cost estimates are conservative, because they represent only the marginal costs of emergency or hospital treatments. Importantly, these estimates do not include the costs of self-treatments, outpatient physician visits, or the costs of pharmaceuticals utilized outside the emergency department or the hospital inpatient environments. Further, these cost estimates did not incorporate the non-market costs of pain and suffering, and they did not include potential—but unknown—morbidities and possibly mortalities from brevetoxin exposures. Public health impacts add to other sources of potential economic loss due to FRT blooms, including losses to local service businesses, such as restaurants and hotels, increased costs of beach cleanups, lost recreational opportunities, reduced fishery yields, and mortalities of passively valued protected species. Placing public health effects in context among these broader impacts could help public officials, stakeholders, and citizens focus on appropriate mitigation approaches.

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Table 1: Descriptive Statistics
(Monthly Data across Counties[a])

		Emergency Department Visits (2005-09)				Hospital Inpatient Admissions (1999-2009)			
Variable	Units	mean	s.d.	min	max	mean	s.d.	min	max
Total respiratory illness	illnesses	134.31	103.29	9.00	701.00	199.97	146.91	28.00	842.00
Total digestive illness	illnesses	136.51	70.69	22.00	358.00	256.61	172.41	42.00	893.00
Population	10^5 people	5.96	3.59	1.54	12.01	5.61	3.48	1.37	12.01
Tourist Visits	10^4 rooms	17.71	14.17	1.04	52.89	18.03	14.19	1.04	52.89
Kb Cell Counts	10^7 cells per L	0.31	1.68	0.00	16.22	0.19	1.22	0.00	16.22
SHA Closures	closures	0.13	0.47	0.00	3.00	0.15	0.50	0.00	3.00

[a]The number and identity of the counties vary by model, depending on the relevant exposure variable. See the text for a full description.

Table 2. Descriptive Statistics by County of Emergency Department (ED) Visits and Other Predictors
(Monthly Averages, 2005-09)

	HILLSBOROUGH	PINELLAS	MANATEE	SARASOTA	CHARLOTTE	LEE
Resident respiratory illness	140.38	207.65	53.83	143.73	33.17	103.98
Resident digestive illness	133.93	230.08	72.22	141.77	37.98	125.02
Visitor respiratory illness	14.27	32.07	11.50	30.90	6.80	27.55
Visitor digestive illness	8.73	20.05	9.20	18.05	3.42	18.60
Total respiratory illness	154.65	239.72	65.33	174.63	39.97	131.53
Total digestive illness	142.67	250.13	81.42	159.82	41.40	143.62
Population (10^5)	11.77	9.42	3.13	3.84	1.62	5.98
Tourism (10^4 rooms)	38.22	32.81	6.28	8.88	1.55	18.52
Kb Cell Counts ($10^7 L^{-1}$)	0.06	0.06	0.16	1.26	0.05	0.30
SHA Closures (number)	0.08	0.08	0.03	0.10	0.17	0.33

Table 3. Descriptive Statistics by County of Hospital Inpatient (INPT) Admissions and Other Predictors
(Monthly Averages, 1999-2009)

	HILLSBOROUGH	PINELLAS	MANATEE	SARASOTA	CHARLOTTE	LEE
Resident respiratory illness	211.03	433.88	91.82	146.14	73.88	185.91
Resident digestive illness	247.22	531.80	132.02	221.83	85.73	237.79
Visitor respiratory illness	8.55	16.39	5.66	7.87	4.04	14.68
Visitor digestive illness	10.05	23.30	8.86	13.56	5.61	21.89
Total respiratory illness	219.58	450.27	97.48	154.01	77.92	200.59
Total digestive illness	257.27	555.10	140.87	235.39	91.34	259.67
Population (10^5)	11.02	9.34	2.92	3.59	1.54	5.27
Tourism (10^4 rooms)	37.20	34.85	6.66	9.05	1.84	18.58
Kb Cell Counts ($10^7 L^{-1}$)	0.04	0.04	0.09	0.74	0.08	0.16
SHA Closures (number)[a]	0.10	0.10	0.04	0.14	0.21	0.33

[a]SHA Closures data range only from 2000-2009.

Table 4: Exposure-Response Models Testing for Relationships between Measures of Florida Red Tides and Human Respiratory and Digestive Illnesses[a]

Model:	I		II		III		IV		V		VI		VII		VIII	
	ED/Respiratory		ED/Digestive		ED/Respiratory		ED/Digestive		INPT/Respiratory		INPT/Digestive		INPT/Respiratory		INPT/Digestive	
	Coefficient	t-value	Coefficient	t-value	Coefficient	t-value	Coefficient	t-value	Coefficient	t-value	Coefficient	t-value	Coefficient	t-value	Coefficient	t-value
Intercept	123.70***	2.64	262.24***	10.03	1943.99***	43.96	1241.48***	35.56	-125.15***	-3.38	87.89*	1.79	82.18	0.72	334.42**	2.36
***Kb* CELL COUNTS**	**0.25****	**2.30**	**0.12*****	**54.83**					**0.02*****	**5.56**	**0.02*****	**3.54**				
SHA CLOSURES					**16.84*****	**110.78**	**3.47*****	**35.17**					**2.78*****	**9.17**	**6.23*****	**27.68**
Population	0.06	0.01	-20.06***	-10.82	-233.80***	-85.71	-131.39***	-64.47	59.26***	38.48	43.01***	26.43	25.87***	9.95	16.67***	8.27
Tourism	2.22**	2.23	0.92***	25.27	4.60***	47.84	0.26***	4.87	2.71***	50.61	6.93***	116.13	3.14***	26.14	5.66***	78.75
January	33.02*	1.70	3.51	0.86	19.90	0.85	4.35	0.80	32.50***	5.36	5.46	0.83	42.04***	4.68	10.45	1.27
February	66.20***	3.34	-4.48	-0.73	69.15***	2.72	-2.09	-0.26	8.17	0.88	-28.07***	-2.76	7.52	0.57	-45.68***	-3.63
March	58.07***	2.76	7.50	1.20	43.12*	1.66	17.34**	2.07	3.57	0.37	-31.23***	-2.92	-5.10	-0.38	-37.51***	-2.87
April	-15.71	-0.80	-8.14	-1.32	-33.63	-1.31	-5.47	-0.66	-44.62***	-4.75	-27.70***	-2.66	-56.82***	-4.33	-34.62***	-2.71
May	-51.98***	-2.70	-12.99**	-2.09	-74.95***	-2.91	-14.80*	-1.78	-71.31***	-7.52	-29.71***	-2.83	-89.70***	-6.79	-30.81**	-2.39
June	-80.91***	-4.22	-33.63***	-5.45	-110.49***	-4.27	-39.33***	-4.76	-94.27***	-9.97	-45.69***	-4.34	-119.27***	-9.10	-51.68***	-4.01
July	-82.99***	-4.32	-28.61***	-4.60	-113.85***	-4.42	-30.51***	-3.66	-104.15***	-10.99	-52.69***	-5.02	-131.80***	-9.97	-63.26***	-4.91
August	-80.08***	-4.20	-29.32***	-4.77	-109.83***	-4.27	-37.12***	-4.51	-94.86***	-10.10	-37.49***	-3.60	-122.05***	-9.32	-43.02***	-3.37
September	-69.21***	-3.62	-34.61***	-5.54	-80.89***	-3.11	-42.88***	-5.12	-87.45***	-9.12	-31.06***	-2.91	-106.59***	-8.07	-36.63***	-2.81
October	-65.89***	-3.45	-27.95***	-4.56	-90.62***	-3.56	-34.96***	-4.27	-80.16***	-8.66	-27.36***	-2.69	-103.25***	-7.88	-37.85***	-3.01
November	-44.51**	-2.33	-18.71***	-4.59	-61.06***	-2.62	-22.37***	-4.12	-61.40***	-10.12	-18.43***	-2.81	-78.29***	-8.74	-23.17***	-2.82
1999									-10.86***	-5.32	-188.84***	-88.11				
2000									-7.55***	-3.58	-215.51***	-93.22	-50.87***	-16.14	-271.82***	111.78
2001									10.08***	4.49	-223.37***	-91.93	-8.80***	-2.45	-304.92***	116.59
2002									81.90***	36.26	-230.13***	-92.33	84.56***	21.04	-333.66***	-121.84
2003									14.66***	6.50	-230.85***	-93.06	9.53**	2.22	-306.14***	-109.09
2004									-58.37***	-26.65	-245.24***	-101.64	-124.28***	-28.38	-339.32***	-124.03
2005	39.95***	3.05	-35.01***	-42.95	-43.81**	-2.29	-112.85***	-112.05	-56.62***	-27.36	-280.33***	-121.84	-117.58***	-28.20	-400.38***	-153.33
2006	-9.63	-0.76	-10.11***	-12.72	-52.39***	-2.71	-48.11***	-52.89	-29.32***	-15.28	-146.82***	-70.10	-59.45***	-16.29	-219.89***	-89.63
2007	-27.59**	-2.22	2.97***	3.84	-35.99*	-1.86	-19.28***	-21.77	-19.09***	-11.66	-73.48***	-40.12	-47.71***	-15.53	-87.24***	-41.20
2008	-12.64	-1.03	6.33***	9.90	-2.62	-0.14	-12.32***	-15.37	-0.81	-0.63	-43.28***	-32.26	-39.72***	-17.85	-61.76***	-37.30
n	360		360		240		240		792		792		360		360	
R^2	0.44		0.45		0.24		0.56		0.51		0.54		0.55		0.68	
Hillsborough	●		●		●		●		●		●		●		●	
Pinellas	●		●		●		●		●		●		●		●	
Manatee	●		●						●		●					
Sarasota	●		●		●		●		●		●		●		●	
Charlotte	●		●						●		●					
Lee	●		●		●		●		●		●					

[a]The results of time-series, cross-section multiple regression models, estimated using equation (1), as discussed in the text. The table compiles the results of models run with patients aged ≥55 years and older. Response variables: **ED** = Emergency Department visits; **INPT** = Hospital Inpatient admissions. (See the text for a description of the specific types of respiratory and digestive illnesses for each illness severity.). Exposure variables: ***Kb* CELL COUNTS** = *Karenia brevis* cell counts in opportunistic water samples taken within 15km of the coast of each county; **SHA CLOSURES** = closures of Florida coastal shellfish harvesting areas. Tourism is a measure of the occupation of hotel and motel rooms in each county. The baseline for the (0,1) dummy variables is December 2009 for all models. The filled circles [●] indicate the Florida counties for which a model was run. The symbols *, **, and *** denote statistical significance at p-values of 0.10, 0.05, and 0.01, respectively.

Table 5: Ranges of Illness Costs and Lost Incomes[a]
(2013 $)

		A	B	C	D	E	F	G
	Illness Type	Days Hospitalized	Days to Recuperate	Treatment Average Charge (ACh)	Treatment Marginal Cost (MC)	Total MC Treatment (A x D)	Lost Income (B x $120)	Total (E + F)
Emergency Department Visits (ED)	R (low cost)	1.0	3.0	$2,766	$636	$636	$359	$995
	R (high cost)	1.0	3.0	$4,491	$1,033	$1,033	$359	$1,391
	D (low cost)	1.0	3.0	$4,366	$1,004	$1,004	$359	$1,363
	D (high cost)	1.0	3.0	$7,570	$1,741	$1,741	$359	$2,100
Hospital Admissions (INPT)	R (low cost)	3.2	9.6	$6,670	$939	$3,004	$1,530	$4,534
	R (high cost)	3.8	11.4	$8,955	$1,215	$4,618	$1,816	$6,435
	D (low cost)	4.9	14.7	$7,397	$1,053	$5,162	$2,342	$7,504
	D (high cost)	6.7	20.1	$12,731	$1,785	$11,961	$3,203	$15,164

[a]Calculations of ranges were based upon estimates of low and high average charges (ACh) for treatments of illness types in 2010 (AHRQ 2013). The marginal costs (MC) of treatment for Emergency Department (ED) visits was 23% of ACh; the MC of treatment for INPT admissions was 14% of ACh. Lost income is estimated at $120/d. Days Hospitalized have been included in the Days to Recuperate for the purposes of the Lost Income calculation (column F). **Key:** ACh = average charge; AC = average cost; D = digestive; ED = Emergency Department; INPT = Hospital Inpatient; MC = marginal cost; R = respiratory.

Table 6: Predicted Ranges for Annual Average and Capitalized Costs of Illness[a]

(2013 $ or $m)

	Illness Type	Total Illness Costs ($) [Table S4; Col. G]	Predicted Average Annual ED/INPT Illnesses	Low Average Annual Costs ($m)	Mean Average Annual Costs ($m)	High Average Annual Costs ($m)	Annual Average Illness Cost Ranges ($m)	Capitalized Ranges ($m @3%)
Emergency Department Visits (ED)	R (low cost)	$995	52 ± 45 §	$0.01	$0.05	$0.10	$0.01 - $0.17	$0.22 - $5.72
	R (high cost)	$1,391	121 ± 2 ω	$0.17	$0.17	$0.17		
	D (low cost)	$1,363	25 ± 1 ω	$0.03	$0.03	$0.04	$0.03 - $0.05	$1.09 - $1.82
	D (high cost)	$2,100	25 ± 1 §	$0.05	$0.05	$0.05		
Hospital Admissions (INPT)	R (low cost)	$4,534	2 ± 1 ω	$0.01	$0.01	$0.02	$0.01 - $0.09	$0.24 - $2.98
	R (high cost)	$6,435	11 ± 2 §	$0.06	$0.07	$0.09		
	D (low cost)	$7,504	2 ± 1 ω	$0.01	$0.01	$0.02	$0.01 - $0.42	$0.18 - $13.83
	D (high cost)	$15,164	26 ± 2 §	$0.36	$0.39	$0.42		
TOTALS							$0.06 - $0.73	$1.73 - $24.36

[a]Total illness costs are calculated in Table S4 and presented here in 2013 dollars. Predictions were made from the models in Table 4 of low and high illnesses across the two alternative FRT measures. These predictions were averaged for each county over the periods of analysis to obtain annual estimates per county and then summed over the counties. See the text for more detail on the method. Predicted average annual ED/INPT illnesses are taken from models with both exposures to yield low and high estimates of illnesses of both types and severities (§ represents predictions from the models using SHA Closures as the measure of exposure, averaging over 2005-09; ω represents predictions from the models using *Kb* Cell Counts as the measure of exposure, averaging over 2000-09). Prediction intervals are based on predictions ± 2 s.e.'s around the exposure coefficient from the relevant model. Capitalized ranges are constructed by dividing the range extremes by a discount rate (0.03).

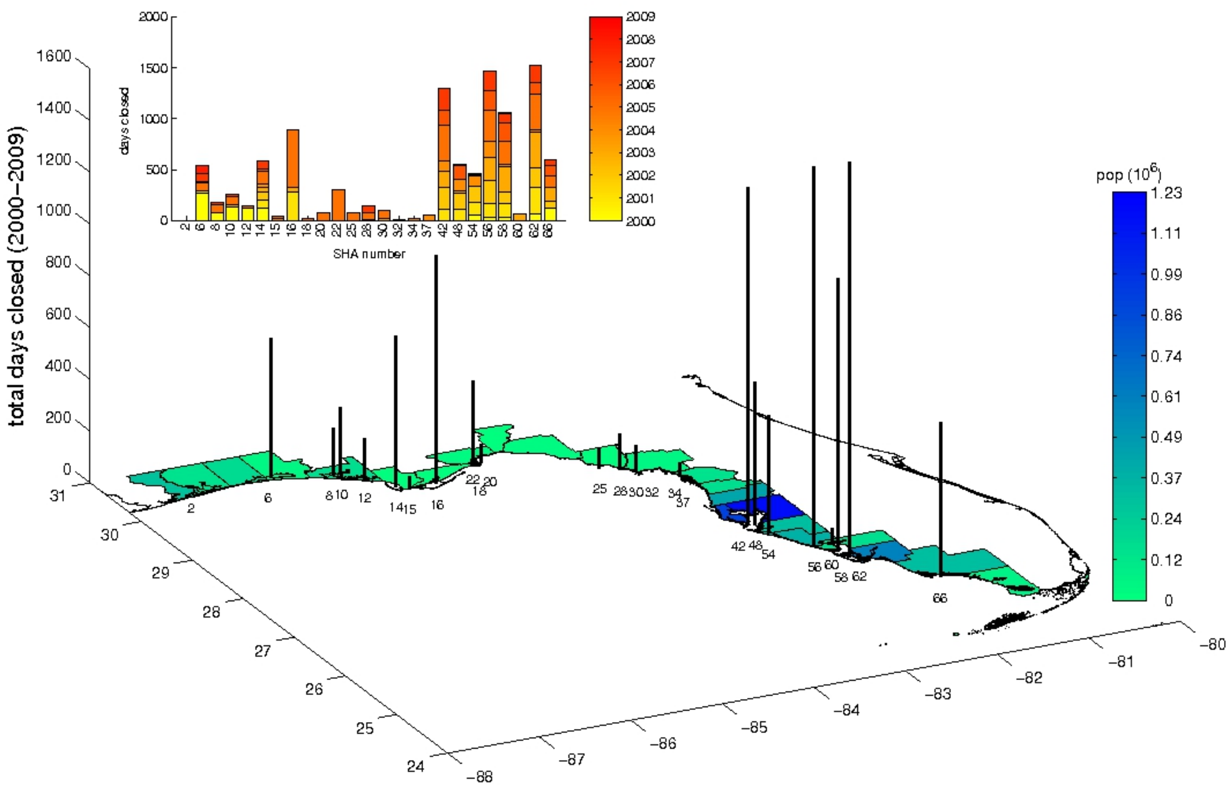

Fig. 1: Map showing the 2010 distribution of county resident populations along the Gulf Coast of Florida and the total number of days closed of closures occurring during 2000-2009 within two-digit shellfish harvest areas (SHAs) due to Florida red tides (Hoagland 2013; data from FDACS and US Census Bureau).