INCIDENCE AND RISK FACTORS OF CIGUATERA FISH POISONING IN THE CARIBBEAN AND FLORIDA

By

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Ciguatera fish poisoning is a type of food-borne illness caused by the consumption of coral reef fish containing toxins produced by dinoflagellates of the genus *Gambierdiscus* (microalgae). It is a significant health concern in tropical and sub-tropical areas, particularly the south Pacific and Caribbean, and causes illnesses in non-endemic areas due to fish importation. It is believed that the incidence of ciguatera and other illnesses caused by harmful algal blooms may increase with increasing seawater temperatures associated with global warming, but much is still unknown about the factors that influence ciguatera incidence. This dissertation describes three studies of ciguatera in St. Thomas, U.S. Virgin Islands and Florida performed to estimate incidence and improve our understanding of human influences on incidence. Study 1 is a cross-sectional telephone survey of residents of St. Thomas to estimate incidence and identify risk factors for illness. Results indicated that ciguatera incidence has decreased since a similar survey was performed in 1980, and that socioeconomic status, fish consumption, and history of previous ciguatera illness were associated with ciguatera. Study 2 is a case control study comparing cases enrolled at the emergency department on St. Thomas to population-based controls from the telephone survey performed for

Study 1. Factors associated with ciguatera illness were alcohol consumption, history of heart disease, fish consumption, socioeconomic status, and previous ciguatera illness. Study 3 combines public health reports of ciguatera illness to the Florida Department of Health and a survey of recreational saltwater fishing license holders in Florida to estimate underreporting of ciguatera and identify locations where illness-causing fish have been caught. The results suggested that incidence of ciguatera in Florida is higher than estimated based on public health reports alone. However, there was no evidence that incidence or geographic range has increased since earlier studies. Additionally, Hispanics were at higher risk of ciguatera in Florida than non-Hispanics. The findings from these three studies provide important information on risk factors of ciguatera in this region and suggest measures that could be taken to prevent illnesses, including targeted education and improved surveillance.

CHAPTER 1
LITERATURE REVIEW

Ciguatera fish poisoning is a type of food poisoning that results from the consumption of reef fish containing toxins produced by benthic dinoflagellates of the genus *Gambierdiscus*.[1, 2] The primary illness-producing toxins are called ciguatoxins, which are heat stable, lipid soluble polyether compounds. The toxic dose is quite low, with levels above 0.1 parts per billion (ppb) in the fish flesh consumed believed to present a health risk.[3] Other toxins have also been implicated that may account for the variable presentation of ciguatera illness.[4] Detailed ecology and toxicology of ciguatera has been reviewed elsewhere,[4, 5] and are not pertinent to this review.

Ciguatera is commonly found in tropical and subtropical countries and territories in the Pacific Ocean, the Caribbean, and the western Indian Ocean,[6] from latitudes of 35° N to 35° S,[5] where coral reefs are present. In rare cases, ciguatoxic fish have been caught as far north as South Carolina (approximate latitude of 32° N), though this was likely due to migration of the barracuda responsible for the illness.[7] A wide variety of fish species can contain ciguatoxins, with estimates up to 400 species.[4] Certain types of large carnivorous fish, including barracuda, jacks, and grouper are particularly high risk since the toxin bioaccumulates as it moves through the food chain to higher trophic levels.

In humans, there are an estimated 50-500 thousand cases of ciguatera each year worldwide,[8] with an estimate for Puerto Rico and the U.S. Virgin Islands alone reaching 20-40 thousand.[9] Because of the severe clinical presentation and potential for chronic illness, this represents a significant public health issue for affected areas. Cases can also occur in non-endemic areas through importation of toxic fish or consumption of fish

during tropical vacations.[10, 11] In addition to the health impacts, ciguatera is responsible for substantial economic loss as a result of lower fish product exports, liability concerns amongst the tourist industries in some islands, missed work, and medical costs.[12]

Chapter 1 will discuss both the human and environmental features of ciguatera fish poisoning with a particular focus on research from the Caribbean region. Human features include clinical presentation, incidence, and risk factors for ciguatera illness. Environmental factors include temperature/climate change and disturbances to coral reefs, which may lead to better understanding and prediction of changes in ciguatera incidence.

Clinical Presentation in Humans

There are a wide variety of signs and symptoms associated with ciguatera. Symptoms generally develop within 24 hours of contaminated reef fish ingestion,[13] and can occur in as quickly as two hours,[14] with shorter latency associated with increased severity of disease.[15] Attack rates can be as high as 90-100% among people eating affected fish,[16, 17] particularly when the fish is highly toxic. The symptoms, described below, are often severe enough to cause the affected individual to take to bed and miss work for multiple days.[13, 16] Ciguatera is rarely fatal. In one large study (N=3009) in the south Pacific, the case fatality rate was 0.1%.[13] Those who eat especially toxic portions of the fish such as viscera may be at increased risk of death.[18]

Based on several case series, there are demonstrable differences in the clinical presentation of ciguatera by geographic region. A summary of the frequency of symptoms reported in studies from the Caribbean are presented in Table 1-1 and the differences between Caribbean and Pacific ciguatera are discussed below. Generally in the Caribbean, illness initiates with gastrointestinal symptoms including abdominal pain,

diarrhea, and/or vomiting after a median of six hours following fish consumption.[14, 19, 20] These symptoms are typically short lived, resolving on their own in a median of 12 hours.[14, 15]

Onset of gastrointestinal symptoms is followed by development of a variety of neurologic and systemic symptoms. Circumoral and extremity paresthesia, temperature reversal, weakness in the extremities, headache, dizziness, myalgia, and arthralgia are commonly reported, with temperature reversal being a hallmark sign of ciguatera. These symptoms tend to last longer, with paresthesias and temperature reversal having a median duration of two weeks or more in St. Thomas, U.S. Virgin Islands.[20] Pruritis is often the final symptom to develop,[14, 15] and frequently lasts more than 10 days in those affected.[15]

In addition to the classic symptoms listed in Table 1-1, there are other signs sometimes reported with ciguatera illness. Patients sometimes report having a metallic taste, dental pain, tremors, dyspnea, and confusion. Two small case control studies (12 case-control pairs in each study) have suggested that ciguatera cases experience neuropsychological effects, including more depression, less vigor, higher anxiety, and higher neurotoxicity symptom severity scores than controls.[21, 22] Finally, cardiovascular symptoms are possible during acute illness in severe cases, with hypotension and bradycardia being the most common.[23]

The most complete accounting of clinical presentation of ciguatera from the south Pacific was reported by Bagnis, et al. in 1979. It included 3009 cases from French Polynesia and New Caledonia that presented between 1964 and 1977. Compared to the studies in the Caribbean reported in Table 1, the south Pacific cases were more

likely to experience paresthesia and headache, but less likely to experience diarrhea and vomiting.[13] Later studies in French Polynesia and Hong Kong had similar findings.[24, 25] The different clinical presentations are believed to be caused by different toxin structures between Pacific and Caribbean ciguatoxins.[6] Bagnis, et al. also found that several symptoms including paresthesia, burning or pain on contact with cold water, arthralgia, diarrhea, asthenia, headache, and chills were more likely to be present for the second or subsequent episode.[13]

While most persons affected by ciguatera recover fully from their symptoms within a few weeks to months, there is also risk of chronic illness lasting several months or years. In the south Pacific, one survey found that over 30% of individuals affected by ciguatera reported a time to recovery of greater than one year, but this survey took place in a clinic setting that may have oversampled those severely affected and with other health concerns.[26] A case control study in French Polynesia found that more than 50% of patients with ciguatera did not have normal values for neurologic testing two months post onset.[27] Overall, a review estimated that less than five percent of ciguatera cases in the Pacific experience symptoms lasting more than a year.[6] In the Caribbean, less is known about the rate of chronic illness, but one study found that 15 out of 23 cases (65%) experienced chronic symptoms for six months or longer.[10] Morris, et al. found that a number of cases experienced recurrent dysesthesias and pruritis after eating presumably non-toxic fish in the month after being poisoned,[20] while Lawrence, et al. reported several cases experienced paresthesia, myalgia, and pruritis for up to six months after the acute illness.[14]

The clinical picture described above represents our best understanding of ciguatera illness. However, in any study of ciguatera, there is an inherent bias in the symptoms reported. Because diagnosis of ciguatera is based on characteristic symptoms, generally including at least one neurologic symptom, and history of recent reef fish consumption rather than a conclusive diagnostic test, diagnosed and subsequently reported cases are highly likely to exhibit the characteristic symptoms. A few studies of common source outbreaks have suggested that there are cases who develop only gastrointestinal symptoms following ingestion of ciguatoxin contaminated fish.[15, 16, 28] Outside of an outbreak that includes someone with characteristic neurologic symptoms, cases with only gastrointestinal symptoms are unlikely to be diagnosed with ciguatera and thus would not be included in reports of symptom frequency. At least until a diagnostic test is developed, this will continue to limit our understanding of mild ciguatera illness.

Treatment for ciguatera is mainly supportive. Mannitol given intravenously has been reported to relieve neurologic symptoms associated with ciguatera when given quickly after symptom onset, but randomized trials have produced contradictory results.[29, 30] It is generally still recommended during acute illness. Other than mannitol, IV fluids to manage fluid and electrolyte balance are often indicated as are other symptomatic treatments. In endemic areas, many herbal and traditional remedies are used by residents, but their effectiveness has not been proven.[23]

Incidence

In order to understand ciguatera, we must also define its scope and magnitude by estimating incidence in different parts of the world. There are two general types of studies investigating ciguatera incidence. The first type uses data from public health

reporting or diagnosed cases at medical facilities. This study type tends to represent a small percentage of true ciguatera illnesses as it includes only those affected who had illness severe enough to seek medical care, and who were both diagnosed and reported to public health authorities.

With regards to illness severity, it is unclear what percentage of affected individuals seek medical attention. In the Virgin Islands, Brody, et al. reported that only 12% of ciguatera cases in St. Thomas reported visiting a physician and discussed anecdotal evidence from the British Virgin Islands suggesting that most residents had been poisoned but only rarely visited the physician.[31] Hanno, a physician in St. Thomas, also believed that residents were very familiar with the disease and were unlikely to seek medical attention for ciguatera.[32] However, two surveys performed in St. Thomas in 1978 and 1980 found that 45% and 71% of cases had sought medical care for their most recent ciguatera episode.[19, 33, 34] In a survey in Culebra, Puerto Rico, 75% of suspected ciguatera cases had sought medical attention, but this high percentage may be due to a strict case definition including multiple neurologic symptoms.[35]

In addition to the percentage not seeking medical care, cases without classic ciguatera symptoms are unlikely to be diagnosed if they seek medical care, as previously discussed. Beyond that, there is evidence that even with classic presentation, physicians have difficulty with diagnosis. McKee, et al. found that only 68% of physicians surveyed in Miami, Florida correctly diagnosed a case report with classic presentation and only 47% knew that ciguatera is a reportable disease.[36] In Puerto Rico, a highly endemic area, only one out of 15 presumed ciguatera cases who sought care were diagnosed with ciguatera.[35] Two cases in Cancun, Mexico were not

diagnosed for five weeks despite having classic symptoms including temperature reversal.[37]

The magnitude of this underreporting is still unclear. Lawrence, et al. hypothesized in 1980 that the true number of cases in Miami could range from 10 to 100 cases per reported case of ciguatera, with the upper range based on a community survey of a waterborne gastroenteritis.[14] Begier, et al. reported in 2006 that only 43% of ciguatera calls to the Florida Poison Information Center in Miami were reported to the Florida Department of Health.[38] Other studies in the south Pacific estimate that reported cases represent only 20% of true cases.[5, 39] Cases are more likely to be reported to public health authorities if they are associated with an outbreak rather than sporadic[14, 38] and if the symptoms are severe.[38]

A final issue in interpreting public health reports for incidence calculations occurs when comparing multiple geographic areas. There is very little consistency between countries and territories on their reporting rules and data quality. Therefore, observed differences in incidence may be due not to true differences, but rather to reporting variation.

The second type of ciguatera incidence study attempts to account for underreporting by performing population based surveys in order to identify ciguatera-like illnesses that were not diagnosed. This method suffers from some of the same issues already discussed, as respondents may not always be aware they had ciguatera without being diagnosed. Surveys also rely on self-report, which can be biased due to recall or misleading responses, and may suffer from selection bias as persons with an interest in ciguatera may be more likely to participate in the survey. Still, they currently represent

our best estimates for ciguatera incidence over short time periods. When available, we rely on a combination of survey data and public health data to approximate point incidence and understand trends over time.

In the Caribbean, incidence varies widely by region. Olsen, et al. suggested that the south coast of St. Thomas is considered high risk for ciguatera, while the north coast and nearby St. Croix are considered low risk.[12] In Cuba, there is evidence that different communities experience different ciguatera risk.[40] Therefore, we cannot draw conclusions about the Caribbean as a whole. There are two areas of the Caribbean where incidence has been investigated in some depth: St. Thomas in the U.S. Virgin Islands and Puerto Rico.

In St. Thomas, annual incidence among all ages was estimated as 7.3 per 1000 in 1980 based on an in person household survey.[19] A telephone survey in 1978 found that 22% of households had at least one ciguatera episode in the previous five years.[33] No incidence studies have been performed in St. Thomas recently until the current project. Public health reports from this island are not available.

In Puerto Rico, a recent household survey in Culebra that included 68% of households on the island found an annual incidence of approximately 11 per 1000 in 2005-06. However, this survey used a restrictive case definition that required multiple neurologic symptoms to be considered a probable case, suggesting that the true incidence is somewhat higher.[35] A telephone survey in San Juan in 1982 found that 7% of households had experienced ciguatera at some point.[41] Unfortunately, there is no way to compare these estimates to assess the trend over time given that one survey estimated incidence among individuals while the other estimated lifetime history among

households. The surveys also focused on different geographic areas. A small island like Culebra may be at higher risk than mainland Puerto Rico. In contrast to these fairly high estimates, public health reports from Puerto Rico for 1996 to 2006 indicated that the incidence was very low (0.003 per 1000),[42] which can be considered a dramatic underestimate. It is unclear whether this discrepancy between reported cases and survey estimates is strictly due to the underreporting issues already discussed or whether there are also regional differences within Puerto Rico.

Studies including other areas around the Caribbean have been based on public health reports and may also suffer from underreporting. In Miami, Florida, case reports from 1974 to 1976 suggested that the annual incidence was approximately 0.05 per 1000 per year, but the authors hypothesized that it could be as high as 5 per 1000 after accounting for underreporting.[14] Tester, et al. obtained data on ciguatera cases from public health officials in several countries and territories in and bordering the Caribbean for 1996 to 2006. A few areas had high annual incidence even limited to only reported cases, including Montserrat (6 per 1000), Antigua and Barbuda (3 per 1000), and the British Virgin Islands (2 per 1000). The Bahamas (0.6 per 1000), Cayman Islands (0.3 per 1000), St. Croix (0.2 per 1000), and Aruba (0.2 per 1000) had fairly low reported incidence. Several areas, including Grenada, Guadeloupe, Martinique, Dominican Republic, Jamaica, and Colombia had very low levels of ciguatera (<0.1 per 1000).[42] In all cases, we would expect the true incidence to be at least 5-10 times higher.

In the Pacific, there is some limited information on the trend over time. The South Pacific Epidemiological and Health Information Service (SPEHIS) compiles ciguatera reports from across the region, an advantage over the Caribbean where there is no

centralized reporting system. From 1973-1983, average annual incidence from SPEHIS was approximately 1 per 1000, ranging from less than 0.001 on some islands up to 7 per 1000 in Tokelau and 5 per 1000 in French Polynesia.[393] As in the Caribbean, the wide range could be attributed partly to reporting differences and these numbers do not account for underreporting. SPEHIS data from 1998 to 2008 indicated that overall incidence had risen to 2 per 1000, with a true incidence of 10 per 1000, assuming only 20% of true cases were reported. Many of the individual countries studied had also experienced increases in incidence, but there were some that experienced decreases.[43] French Polynesia was among the latter group, with incidence of 4 per 1000 from 1992 to 2001,[24] 3 per 1000 from 1998 to 2008,[43] and 2 per 1000 from 2000-2008.[44] The changes in incidence have not been fully explained, but some possible reasons include changes in diet, toxin variability, and environmental changes.

Overall, it is clear that regional differences in incidence exist but the true magnitude of the problem has not been enumerated in most countries and territories. Some areas may have incidence of at least 10 per 1000 per year, making it a significant public health concern, particularly given the risk for chronic symptoms discussed earlier. Other countries within the geographic range report essentially no ciguatera cases. It is still not known what factors are responsible for regional differences or changes over time. In the sections on risk factors and environmental influences we will explore proposed explanations for the differences, but many of these topics require further research.

Risk factors

In order to decrease risk of ciguatera in the Caribbean and elsewhere, it is helpful to identify factors that increase individual risk. By doing this, we can target high risk

populations for education and develop other interventions to lower risk. Thus far, only a few factors have been identified that are associated with an individual's risk for developing ciguatera, or for having more severe illness. Socioeconomic status is one, with lower income individuals more likely to be affected because they have few affordable alternatives to locally caught fish for their dietary protein[45]. Similarly, less developed islands typically report more cases of ciguatera than more developed islands. [39] These findings are based on the Pacific, but are believed to be applicable to the Caribbean as well.

A few studies have also examined the relationship between demographic factors and ciguatera illness. Age is commonly discussed as a potential risk factor for illness, but there is some variation in study findings. Children are believed to be at low risk for ciguatera, but cases do occur at all ages, including those less than one year old.[20] Age specific attack rates in a common source outbreak in St. Croix, U.S. Virgin Islands were similar across age categories.[15] However, Glaziou, et al. found that age specific attack rates in 551 cases from French Polynesia were highest in those aged 30-49 and 49 or older.[46] Two studies, a case series of 2647 cases from French Polynesia and a common source outbreak in Hawaii also found illness severity[17, 24] and duration[17] were associated with increased age, while a second case series in French Polynesia did not.[47] It is not clear whether increased age is itself a risk factor for illness based on immunologic or other changes, or whether sensitization to the toxin can occur after eating toxic fish for many years. In some areas, the rate may be highest among those between 30 and 49 years of age[48] because older individuals avoid eating high risk fish.[40]

Regarding gender, in two large case series (N=3009 and 551) of reported ciguatera cases, men are overrepresented in the case numbers, with a ratio of around 1.5:1,[13, 46] perhaps because the fishing occupation is predominated by men. However, in two common source outbreaks and one convenience sample, attack rates did not vary by sex.[15, 17, 26] This may indicate that men are more likely to be diagnosed and reported but are not actually at increased risk. There are also some reports of men eating part of a fish before bringing it home to their families, which may account for higher sporadic, non-outbreak associated case numbers.[48] Illness severity was not associated with gender in French Polynesia.[24, 47]

History of ciguatera illness is often considered an important predictor of future illness. Among 3009 cases of ciguatera in the South Pacific from 1965 to 1977, those on their second or subsequent episodes were more likely to have severe disease.[13] This was also observed among cases in French Polynesia in 1991[46] and the relationship trended towards significance in another French Polynesia case series.[47] In the St. Croix outbreak, history of ciguatera was not associated with illness severity or duration,[15] nor was it associated with severity in a third case series in French Polynesia, however the former sample size was much smaller than the others (N=47) and the latter measured only variability of symptoms and not strictly severity, so this may explain the lack of an observed relationship.[24, 47] This relationship may also help explain the relationship between age and ciguatera, as older individuals will have had more opportunities to have experienced ciguatera, and if affected, may be at increased risk of a future episode.

In terms of behaviors, portion size of toxic fish appears to be an important factor. Patients in St. Croix were more likely to have diarrhea and dysesthesia if they had eaten a full portion of fish, but other hypothesized risk factors such as eating the head of fish and drinking alcohol did not predict illness severity.[15] Amount of fish consumed was also found to be associated with disease severity in Hawaii, while part of fish consumed was not.[17] On the other hand, eating organs versus the whole fish was associated with disease severity in French Polynesia.[47] This disparity in findings may be due to the small sample sizes of the the St. Croix and Hawaii studies (N=50 and 15, respectively), but further evidence is needed to conclusively implicate fish viscera as higher risk than other portions.

Type of fish consumed is also an important risk factor for development of ciguatera. In French Polynesia, severe disease was associated with ingestion of carnivorous fish in two studies.[46, 47] The household survey in Culebra, Puerto Rico suggested that households that regularly ate barracuda were more likely to report ciguatera cases.[35] The previous three studies, as well as many anecdotal reports, suggest that type of fish consumed is an important risk factor for ciguatera. Fish type has also been reported to affect the clinical presentation and severity of illness.[49]

Modification of fish consumption behaviors is one way that ciguatera incidence could change over time. Unfortunately, there is no effective method to detect ciguatoxic fish, as they appear, taste, and smell normal. Based on the research already discussed, current prevention messaging recommends avoiding fish that are likely to be toxic. This includes large carnivorous reef fish such as barracuda, jacks, groupers, and some snappers. Public health officials also recommend avoiding the viscera of reef fish and

eating small portions.[23] If fishermen and consumers are better educated about the risk of ciguatera and these ways to prevent it, there is the possibility of ciguatera cases declining. This could also occur if overall fish consumption declined in a region.

Environmental Influences

In addition to attempting to control ciguatera risk by managing individual and behavioral risk factors, researchers have also striven to understand the environmental dynamics that influence ciguatera. The hope is that by characterizing these environmental factors and the specific impacts they have on *Gambierdiscus* and ciguatera, we will be able to accurately predict when increases in ciguatera are likely to occur. Seawater temperature and coral reef health are the most thoroughly researched and are discussed below. Other factors that have been found to influence *Gambierdiscus* growth include salinity, light, waves, and nutrient levels.[50] To understand ciguatera fully, we will need to assess these factors in greater detail.

Seawater Temperature

With seawater temperatures rising as a result of climate change, speculation has arisen about whether ciguatera will be affected. Studies going back to the 1980s have shown that *G.toxicus* growth rates are highest with warm temperatures, with the maximum around 29 or 30°C, above which growth rates drop off dramatically.[51, 52] Similar results have been obtained more recently among five *Gambierdiscus* species (*G. belizeanus*, *G. caribaeus*, *G. ruetzleri*, *G. carolinianus*, and *G.* Ribotype 2) from the Caribbean and one from the Pacific (*G. Pacificus*), with all but *G. carolinianus* having positive or maximum growth rates at or above 29°C.[42]

A few studies have attempted to determine whether the association of *Gambierdiscus* growth rates with temperature will translate into an observable increase

in ciguatera under climate change scenarios. Hales et al. used ciguatera incidence data from SPEHIS, which received reports from 22 Pacific islands during 1973 to 1994. The authors found a correlation between sea surface temperature, the Southern Oscillation Index, and incidence of fish poisoning. On islands that experienced warming during El Nino events, there was an increase in ciguatera during the events. However, there were also increases in ciguatera on islands that experience water cooling during El Nino events, but this negative association was weaker.[53] Also using SPEHIS but for 1973 to 1996, Llewelyn found that ciguatera is most common in areas of the South Pacific that do not experience sea surface temperatures far below 24°C and is highest where average sea surface temperatures are at least 28-29°C. He also observed that there may be a threshold temperature at which it is too warm for ciguatera to thrive and estimated this threshold as above 30°C.[54] This has important implications for predicting the effect of climate change on ciguatera incidence and distribution, as it suggests that there may be areas where ciguatera incidence declines as a result of climate change.

Also in the South Pacific, Chateau-Degat, et al. found a significant association between seawater temperature and abundance of *Gambierdiscus* in French Polynesia from 1993 to 2001 using time series analysis. Specifically, there was a 13 month and 17 month lag in *Gambierdiscus* abundance following a change in temperature. They also found that an increase in *Gambierdiscus* abundance was followed by an increase in recorded cases of ciguatera, with a three month lag. The authors concluded that temperature is an important predictor of ciguatera incidence.[55]

Less study on the association with temperature has been focused on the Caribbean region. In ciguatera data from 32 island and mainland countries around the

Caribbean from 1996 to 2006, Tester et al. found that ciguatera incidence was highest in areas with warmer seawater temperatures and ciguatera was not present in areas where annual average seawater temperature was below 25°C. Because the researchers relied on individual countries to supply reported case numbers, a significant limitation of these results is that data quality may be inconsistent across different countries which may bias the incidence estimates.[42] More geographically focused studies have not been performed in the Caribbean.

Taken together, these studies are supportive of the idea that ciguatera incidence is positively associated with seawater temperature, at least up to a maximum temperature threshold. If more areas begin to experience warm temperatures in the optimum growth range, we can probably expect to see an expansion in the range of ciguatera. Areas that are currently at the upper end of the growth range may experience a lessening of ciguatera incidence if it becomes too warm for *Gambierdiscus* to thrive.

In addition to the direct impact of temperature on *Gambierdiscus* growth rates, there are other possible links between ciguatera and climate change. Increased temperature could affect the production of ciguatoxin by *Gambierdiscus*. Temperature also impacts coral reef health through bleaching, which will be discussed in the following section. Finally, climate change may cause more intense hurricane activity, which produces water movement that may affect algal growth. Further study is needed to explore these possibilities.

Disturbance to Coral Reefs

In addition to seawater temperature, coral reef health is considered one of the most important factors potentially influencing ciguatera incidence. Reef disturbances have been reported to be temporally associated with increases in ciguatera incidence.

It is hypothesized that this association could be explained by the colonization of the newly bare sections of reef by *Gambierdiscus*. Types of disturbances include both natural, such as large storms, and man-made, such as dredging channels and anchoring ships.[56] There are several examples of increased incidence or outbreaks following nuclear test explosions,[57] blasting of channels in the reef,[58] and ship anchorages[59] in the south Pacific. In Cuba, outbreaks of ciguatera were anecdotally linked to degraded coral reef ecosystems, and out of three fishing communities, poor coral reef health appeared to be associated with higher ciguatera risk.[40] Outside of coral reefs, petroleum production platforms have been found to act as fresh substrates facilitating *Gambierdiscus* growth,[60] providing support for the bare substrate hypothesis.

On the other hand, three studies have examined coral reef disturbances and have not found an association with ciguatera. Gillespie monitored changes in dinoflagellate populations resulting from dredging of a boat channel in Hayman Island over 12 months and found that *Gambierdiscus* populations were lower following the dredging. However, he did suggest that colonization may take longer than the observation period of 12 months allowed for.[56] Kaly and Jones measured *Gambierdiscus* abundance and ciguatoxicity of fish in Tuvalu, and found that blasting for boat channels did not increase the ciguatera risk, but they believed that some disturbances could still have an impact.[61] Lastly, Skinner, et al. examined data from eleven countries in the south Pacific to investigate the association between environmental disturbance and coral bleaching with ciguatera and found no significant relationship,[43] though this may be due to the small number of countries included.

Overall, it appears likely that disturbances to coral reef health can impact the growth of *Gambierdiscus* dinoflagellates, which can in turn influence ciguatera incidence. More research needs to be done to determine the level of disturbance that is necessary to cause these changes. As mentioned previously, coral bleaching is a consequence of climate change, which complicates the interpretation of temperature data given that the two effects could work synergistically, at least until the hypothesized upper temperature threshold is reached.

Conclusions

Research on ciguatera fish poisoning has made significant progress in the last forty years, but there are still many areas that are lacking including: trends in incidence over time and explanations for the changes, prediction of ciguatera outbreaks with environmental data, individual risk factors, and improved testing for the toxin (for diagnostic testing in humans and rapid quality assurance checks for fish products). Chapter 2 will describe the efforts this project has undertaken to make progress on the first three of these areas.

Table 1-1. Symptoms of ciguatera fish poisoning reported in all clinical studies in the Caribbean

	Barkin, 1974	Lawrence, et al. 1980	Morris, et al. 1982	Engleberg, et al. 1983	Holt, et al. 1984	deMotta, et al. 1986	deMotta, et al. 1986	Frenette, et al. 1988	Arena, et al. 2004
Setting (where fish acquired)	Cargo ship, Brazil to Key West	Miami	St. Thomas, USVI	St. Croix, USVI	Puerto Rico	Puerto Rico	Puerto Rico	Cuba	Miami
Data source	Common source outbreak	Dade County Health Dept.	ER	Common source outbreak	PCC	ER, PCC; Probable cases	ER, PCC; Suspect cases	Common source outbreak	Case control study
Years studied	1972	1974-76	1980	1981	1982	1980-82	1980-82	1987	*
Sample size	24	129	53	47	45	80	132	57	12
Diarrhea	100%	76%	91%	81%	67%	83%	77%	77%	75%
Vomiting	100%	68%	70%	40%	71%	69%	42%	37%	42%
Myalgia	75%	86%	30%	34%[a]	*	56%	6%	70%	75%
Arthralgia	88%	*	52%	*	36%	60%	9%	37%	83%
Extremity paresthesia	*	71%	33%	40%	*	36%	13%	77%	100%
Circumoral paresthesia	46%	54%	36%	38%	*	38%	3%	46%	*
Unspecified paresthesia	100%	*	*	*	11%	*	*	*	*
Pruritis	50%	48%	58%	66%	5%	45%	5%	68%	67%
Headache	15%	47%[b]	33%	45%	24%	39%	11%	56%	*
Dizziness	58%	*	21%	*	*	33%	32%	*	58%
Weakness	*	30%	58%	81%	*	*	*	84%	100%
Sweating	17%	24%	18%	36%	*	*	*	*	*
Temperature reversal	*	*	36%	23%	30%	48%	2%	*	92%

[a]Myalgia or arthralgia; [b]Headache or dizziness
*=Not reported; ER=Emergency Room; PCC=Poison Control Center

CHAPTER 2
SPECIFIC AIMS AND RATIONALE

This project consists of three studies (presented in Chapters 3-5) addressing the incidence of ciguatera in the Caribbean and Florida and the risk factors for illness. There are four specific aims described below, some of which are addressed in more than one of the studies.

Aim 1 – Estimate Incidence

The first aim of this project was to estimate the incidence of ciguatera fish poisoning in St. Thomas, U.S. Virgin Islands (USVI) and Florida. Prior estimates of incidence in these two areas date to approximately 1980, even though the disease is highly endemic to the U.S. Virgin Islands and Florida is the U.S. state with the largest number of reported cases each year. To understand the factors that influence the occurrence of ciguatera fish poisoning and develop and monitor prevention methods, it is critical to have up to date incidence estimates. Study 1 includes a telephone survey and medical record review used to estimate incidence in St. Thomas, and Study 3 includes an estimate of incidence in Florida based on public health reports and underreporting.

Aim 2 – Identify Risk Factors

The second aim was to identify risk factors for ciguatera illness in St. Thomas and Florida. An understanding of the demographic, health-related, and behavioral factors that increase risk of illness is necessary for the development of prevention strategies and targeting of high risk individuals. Studies 1 and 2 address risk factors in St. Thomas, with Study 1 limited to demographic factors and fish consumption in a cross-sectional survey and Study 2 focused on factors associated with severe illness,

including medical history, health behaviors, and demographics using a case control design. Study 3 includes an analysis of demographic and fish-related risk factors in Florida.

Aim 3 – Assess Population-level Changes in Risk Factors

The third aim was to assess whether population-level changes in identified risk factors could influence ciguatera incidence in the U.S. Virgin Islands. In Study 1, a decrease in ciguatera incidence was observed, which was contrary to the study hypothesis. Study 1 was subsequently expanded to determine whether population-level changes in the observed risk factors (socioeconomic status, age, fish consumption) could theoretically explain the unexpected decrease in incidence.

Aim 4 – Describe Illness Causing Fish

The final aim was to describe the types and geographic distribution of fish that have caused ciguatera illnesses in Florida. These data were obtained for Study 3 from ciguatera illnesses reported to the Florida Department of Health and from an email survey of recreational saltwater fishing license holders. It is important to determine whether ciguatoxic fish are being caught outside areas traditionally believed to be endemic for ciguatera as this could indicate a shift in ciguatera risk due to climate change or other factors, or a bias in illness reporting.

CHAPTER 3
CIGUATERA INCIDENCE IN THE U.S. VIRGIN ISLANDS HAS NOT INCREASED OVER A 30 YEAR TIME PERIOD, DESPITE RISING SEAWATER TEMPERATURES[a]

Introduction

Ciguatera fish poisoning is the most frequently reported illness associated with harmful algal blooms (HABs) and the most common marine food poisoning worldwide. There are an estimated 50 to 500 thousand cases per year worldwide,[8] making it an important public health concern. It has a global distribution and is endemic in regions where consumption of reef fish is common, particularly in the south Pacific and Caribbean. Affected individuals are classically described as presenting with initial gastrointestinal symptoms, followed by neurologic symptoms and (in severe cases) cardiac manifestations. Chronic neurologic symptoms are often reported and may be ongoing or reappear after a period of presumed recovery.[4] In order to prevent cases of ciguatera, it is critical to understand the environmental influences on ciguatera incidence, as well as demographic and behavioral risk factors.

Ciguatera is caused by the ingestion of tropical reef fish that have accumulated potent neurotoxins (ciguatoxins) in their flesh and viscera. Ciguatoxins have their origins in precursor compounds called gambiertoxins produced by *Gambierdiscus* genus dinoflagellates, a type of microalgae. Gambiertoxins undergo biotransformation to ciguatoxins as they move through coral reef trophic levels from herbivorous to large carnivorous fish, where they are eventually consumed by humans.[5] Because temperature directly impacts algae growth rates, it is commonly hypothesized that the

[a] Reprinted with permission from Radke EG, Grattan LM, Cook RL, Smith TB, Anderson DM, Morris JG, 2013. Ciguatera incidence in the U.S. Virgin Islands has not increased over a 30 year time period despite rising seawater temperatures. Am J Trop Med Hyg 88: 908-913.

incidence and geographical range of ciguatera and other HABs will be affected by climate change. In keeping with this hypothesis, positive associations have been found between seawater temperature and ciguatera incidence.[42, 53-55] One study also suggested that there is an upper temperature threshold that would limit *Gambierdiscus* growth and ciguatera incidence.[54] However, studies have been concentrated in the South Pacific, and have been largely dependent on public health reporting systems for estimates of incidence.

Members of our group were responsible for an island-wide incidence survey in St. Thomas, U.S. Virgin Islands, in 1980, with survey data correlated with reported cases from the Emergency Department of the St. Thomas hospital (the only hospital on the island).[19] In the intervening 30 years, seawater temperatures at St. Thomas have shown a steady increase. In this setting, we hypothesized that ciguatera incidence would show a similar increase across this 30 year period. To test this hypothesis, we undertook island population surveys and reviews of Emergency Department records to assess incidence, and to explore possible changes in risk factors for illness.

Methods

Telephone Survey

We performed two telephone surveys in St. Thomas in November 2010 and October 2011. We used random digit dialing to select a sample of listed and unlisted residential landline and cellular telephone numbers on the island. The sampling design was single stage with each telephone number within the sample frame having an equal probability of selection. The household member aged 18 years or older with the next birthday was selected for interview. Households were screened to ensure they were

located on St. Thomas. Phone calls with no response were re-contacted at least five times over the duration of the survey.

The survey was designed to take approximately 10 minutes to complete. We developed the questionnaire (Appendix A) based on prior research in St. Thomas.[19, 34] It included questions on demographic characteristics, recent fish consumption (frequency, type of fish, how obtained), and history of ciguatera episodes in the participant and their household members and ciguatera awareness. History of ciguatera was assessed with the questions: “Have you ever been poisoned by fish? If yes, how many times have you had fish poisoning in your lifetime?” In St. Thomas, the term fish poisoning is considered synonymous with ciguatera. The questionnaire was modified in 2011 to include the number of times the participant had experienced fish poisoning in the past five years, which was the primary measure of incidence as described below.

Emergency Department Visits

We also performed a medical record review to determine the number of patients diagnosed with ciguatera in the emergency department at Roy Schneider Hospital, the sole hospital on St. Thomas. All available records with a discharge diagnosis of ciguatera were identified from a database of emergency visits and were reviewed by the study coordinator. Data on emergency department visits for pre-1980 were obtained from past research on the island.[19, 34, 62] We were able to obtain annual counts of visits for 1971-1979, and 1995-2011, with gaps from 2000-01 and 2006 due to unavailable records.

Incidence Calculations

Descriptive statistics were examined for all variables obtained in the telephone survey. We used two approaches to calculate incidence on St. Thomas.

Incidence from telephone survey

We calculated the annual incidence rate among adults using the average number of episodes per year over the previous five years as obtained from the 2011 survey. The estimate was weighted for the age, education, and sex distributions in the 2000 Census,[63] the most recent year for which data was available in USVI.

Incidence from emergency department visits

We also indirectly calculated the annual incidence using the counts of emergency department visits for ciguatera obtained from the medical record review divided by the proportion of telephone survey participants who visited the emergency department for their most recent ciguatera episode. 2000 Census data was used as the denominator of this incidence estimate. The same calculation was used for 1971-79, using a weighted average of 1970 and 1980 Census data as the denominator.

Risk Factor Analysis

To identify demographic and behavioral risk factors associated with increased odds of ciguatera illness in the telephone survey, we used univariable and multivariable logistic regression with lifetime history of at least one ciguatera episode as the outcome. Variables significant at the $p \leq 0.05$ level were retained in the final model and participants with missing values for these variables were excluded from the logistic analysis. We created a second logistic model for any ciguatera illness in the previous five years to assess age and history of past ciguatera illness as risk factors because these variables could not be assessed in a lifetime model. Older individuals have a longer period of risk and therefore would be more likely to experience ciguatera in their lifetime, regardless of whether age is a risk factor. Odds ratios and 95% confidence intervals were obtained for both models. Among those with ciguatera in the telephone survey, we also used

McNemar's test to assess differences between their most recent fish meal and the fish that was associated with their most recent ciguatera episode.

Behavioral and Demographic Changes from 1980 to 2010

Finally, to determine whether the identified risk factors could be associated with the change in incidence over time, we compared the 1980 and 2010-11 populations based on demographic information from the U.S. Census and behavioral data from this survey and surveys performed in 1980.[19, 33] Separately for age, education, and fish consumption, we calculated strata specific rates from the 2011 survey and applied them to the U.S. Virgin Islands population in 1980 and 2000 to obtain a hypothetical total incidence for each time period. We then subtracted the estimate for 1980 from 2000 to estimate the hypothetical risk difference based on the observed changes in the population for the variables of interest. The purpose of this analysis was to preliminarily assess whether, if strata specific rates remained the same, changes in the population demographics (age, education) and behavior (fish consumption) could explain the change in incidence over time. All analyses were performed with SAS version 9.2. Human subjects research for the telephone survey and medical record review was approved by the University of Florida and University of Maryland School of Medicine Institutional Review Boards.

Seawater Temperature

Sea surface temperature (SST) data were obtained from the Extended Reconstructed Sea Surface Temperature V3b dataset maintained by the National Ocean & Atmospheric Administration's Earth System Research Laboratory in the Physical Sciences Division.[64] This dataset was chosen as it provides continuous measurement back to the 1971, however the data source nearest the U.S. Virgin

Islands is located at the southeast coast of Puerto Rico. The temperature curve followed a similar pattern to temperature readings from 1990 to 2011 taken in the U.S. Virgin Islands.

Results

Telephone Survey

Eight hundred and seven individuals participated in the telephone surveys (407 in 2010 and 400 in 2011). The combined response rate was 25% according to guidelines from the American Association for Public Opinion Research, version 3.1[65] and was consistent over the two years. Characteristics of the survey population are presented in Table 3-1. Of the participants, 186 (23%) reported that they had ever had ciguatera. Among these affected individuals, there were 339 total episodes. The majority (59%) reported only one episode in their lifetime, with 19% and 12% reporting two and three episodes, respectively. Ten percent reported four or more episodes, with a maximum of ten. Including illness in household members, 43 households (11%, 95% confidence interval (CI)=8-14%) reported an episode of ciguatera in the past five years.

When asked about their most recent illness, 56 (30%, 95% CI =21-39%) reported visiting the emergency department and 24 (13%, 95% CI=8-18%) reported seeing another physician. The symptoms caused the affected participants to “take to bed” for a mean of 2.0 days (95% CI=1.6-2.4, range 0-14) and miss work for a mean of 2.4 days (95% CI=1.7-3.0, range 0-21).

Emergency Department Visits

A total of 1829 cases of ciguatera at Roy Schneider Hospital were recorded from 1971-79 (annual mean=203) and 1385 cases were recorded from 1995-2011 (with gaps from 2000-01 and 2005-06, annual mean=106 for 1995-2011 and 63 for 2007-2011).

Incidence

The annual incidence of ciguatera weighted to the 2000 Census was 12 per 1000 (95% CI=10-21) based on the 2011 telephone survey. The trend in indirect incidence estimates from the emergency department visits is shown in Figure 3-1. The average for 2007-11 was 6 per 1000 in adults (95% CI=5-8), down from 18 per 1000 in the 1970s, as collected in 1980.

Risk Factors

Participants with less education were more likely to report a history of ciguatera illness (Table 3-2). Those born in the Caribbean, but outside the U.S. Virgin Islands had the highest odds of illness, while location of birth outside the Caribbean was associated with lower odds of illness, but the difference between these groups was not significant after adjusting for other factors. After excluding participants who reported never eating fish because it is a prerequisite for illness, those who ate fish at least three times per week had 2.2 times higher odds than those who ate fish less than three times a week (95% CI=1.4-3.5). Among participants reporting a ciguatera illness, the fish meal that caused their ciguatera episode was more likely to have been self-caught (vs. purchased) than the fish meal they ate most recently (17% vs. 6% of fish meals, p=0.02).

From the 2011 survey, having at least one previous episode of ciguatera more than five years ago increased the odds of an episode in the five years preceding the interview after controlling for age, frequency of fish consumption, education, and location of birth (OR=3.4, 95% CI=1.4-8.5). Age was not significant in this model, particularly after adjusting for previous episodes (Table 3-2).

Behavioral and Demographic Changes from 1980 to 2010

As frequent fish consumption was identified as the risk factor with the highest odds of illness, we compared fish consumption patterns between the time periods (Table 3-3). The percentage of participants who said they did not eat fish increased from 8% in 1980[33] to 17% in 2010/2011. In parallel, the percentage of participants who ate fish at least three times per week decreased from approximately 33%[34] to 12% over the same period. The difference in incidence rates from 1980 to 2010 if frequent fish consumption in the population did change by 21% was estimated as -3.1 per 1000.

The types of fish consumed that were not associated with poisoning displayed considerable overlap between the two time periods. In 1980, olewife/triggerfish (46%), king mackerel (31%), grouper (28%), doctorfish (26%), red hind (24%), yellowtail snapper (19%), parrotfish (19%), and grunt (13%) made up the most commonly eaten fish consumed in the past month.[34] In 2010/2011, yellowtail snapper (15%), other or unspecified snapper (14%), olewife/triggerfish (12%), grouper (10%), hardnose (9%), red hind (7%), and king mackerel (6%) were the most commonly eaten for the most recent meal.

Table 3-4 presents age, income, and education information for the U.S. Virgin Islands in 1980 and 2000. The risk difference in incidence rates based on the changes in the population demographics from 1980 to 2000 for age was +1.7 per 1000 and for education was -1.3 per 1000. Age was used despite not being significant in the logistic model because older individuals were more likely to report previous illnesses. These factors combined with fish consumption have a crude estimated risk difference of -2.7 per 1000 from 1980 to 2010/2011.

Discussion

Ciguatera remains a major public health problem in the U.S. Virgin Islands, affecting approximately 1% of the population each year. Although comparable studies are yet to be conducted in other regions, these data suggest that the current rate of ciguatera in the Virgin Islands is among the highest in the world. The findings are consistent with a recent estimate of 11 per 1000 for Culebra, Puerto Rico[35] and higher than an estimated average for the South Pacific of 2-10 per 1000.[43]Given the potential for chronic, debilitating symptoms, there is a need to understand risk factors for ciguatera. Climate change (i.e., global warming) has been recently introduced as a potential contributor to increased disease rates in some areas.[42, 53-55] Therefore in this study, it was hypothesized that increases in sea surface temperature from 1980 to the present would be accompanied by an increase in disease rates over the same time period.

Contrary to the original hypothesis however, our study results indicated a possible decline in ciguatera incidence in St. Thomas from 1980 to 2010/2011. The annual incidence in 1980, based on a household survey, was estimated as 7 per 1000, but after adjusting to include only adults as in this study, it was 14 per 1000. In contrast, the rate in adults in the current survey was 12 per 1000. We found that 11% of households had at least one person with a ciguatera episode, as compared with 22% in a survey by McMillan et al. in 1980.[33] Where numbers were most striking was the drop in calculated incidence based on number of emergency room cases, from an estimated 18 per 1000 in the 1970's to 6 per 1000 in 2007-2011, which was statistically significant. Taken together, these studies suggest that rates have declined or at least remained stable.

One plausible explanation for these results is that St. Thomas could have reached an upper temperature threshold that is limiting *Gambierdiscus* growth. Multiple studies have shown that *Gambierdiscus* growth rates are highest at warm temperatures, with the maximum around 30°C, above which growth rates drop off dramatically.[42, 51, 52, 66] A threshold was also suggested by Llewellyn based on data in the South Pacific.[54] However, the threshold suggested in the past is approximately 30°C, which St. Thomas does not typically exceed; the average temperature in the warmest month was 29.3°C from 2007-2010. Alternatively, a positive association between seawater temperature and ciguatera incidence may exist in St. Thomas, but is obscured by other environmental or human factors, some of which would act to decrease incidence. The complexity of this relationship is also highlighted in other regions. For instance, while most studies in the Pacific Islands suggest an increase in ciguatera incidence from 1973-83 to 1998-2008 while seawater warmed; some countries and territories reported declines over that period without explanation.[39, 43]

Our findings support the idea that other factors, including demographic and behavioral, are associated with changes in ciguatera incidence over time, with lower socioeconomic status (particularly education), fish consumption three times a week or more, being born in the Caribbean (outside the USVI), and previous ciguatera episodes were associated with illness.[13, 45, 46] Lower socioeconomic status presumably increases risk of ciguatera because lower income individuals may have few affordable protein alternatives to locally caught fish.[45] Persons born on another Caribbean Island may not have had as much experience with ciguatera (and fish at high risk of being toxic, such as barracuda) as persons born in the Virgin Islands; this may also serve as a proxy for

differences in socioeconomic status. Lastly, a change in incidence may be driven further by the corresponding change in the number of people at higher risk due to previous ciguatera episodes.

Aside from seawater temperature and the factors explored in this study, several factors that we did not asses may also influence ciguatera incidence and should be considered in future studies. Coral reef health may impact *Gambierdiscus* growth, as disturbances to coral reef, whether through bleaching, hurricanes, or other physical injury open surfaces for *Gambierdiscus* to colonize.[56-58] These factors are episodic, and may not follow a consistent trend over the past decades. Another factor could be a change in the toxins produced by the dominant *Gambierdiscus* species present in the U.S. Virgin Islands. Richlen et al. (unpublished data) have identified at least four *Gambierdiscus* species in the region, which differ in toxicity. Changes in the *Gambierdiscus* species composition through time, in response to differential environmental tolerances, could then alter the types and amount of toxins produced and vectored into the food chain.

This study has a few important limitations. We relied on self-report in the telephone survey for both case ascertainment and risk factor history. As with most telephone surveys performed in recent years, our response rate was low, primarily due to non-answers. Despite this, studies have indicated that increasing the response rate of surveys does not drastically change the study findings.[67, 68] The telephone survey format is known to preferentially sample households with higher income and education levels as some lower income households may not have a telephone. By weighting the survey sample by education, gender, and age, we attempted to reduce this bias.

Selection bias may also have been an issue, with persons interested in ciguatera more likely to participate. Finally, we used 2000 Census data for our weighted estimate. Annual updates are not available for the U.S. Virgin Islands and 2010 demographic data are not yet available. However, the total population of St. Thomas changed very little from 2000 to 2010 (51181 to 51634).[63]

While the above limitations are important to consider when interpreting our results, it is also noteworthy that very few studies on ciguatera have been performed with as detailed data. Most studies thus far have relied on public health reports of illness, which vary in quality by location and are biased by underreporting. We have not been able to identify any other studies that included primary data collection from different time periods. To best manage the potential biases described above, we examined both survey data, which is sensitive but not necessarily specific, and emergency department visits, which are specific but not sensitive to mild cases, and found the same trend in both.

In summary, our findings provide important insight into the occurrence of ciguatera fish poisoning in the Caribbean. Despite existing predictions based on increasing seawater temperatures, incidence has not increased since 1980. This may be partly due to changes in the population makeup, with fewer people in the lowest socioeconomic category, and changes in ciguatera related behaviors, with less fish consumption overall and lower risk fish types making up a larger proportion of fish consumed. The influence of environmental factors, including seawater temperature and coral reef health is still not clear. Further research is needed to identify and characterize the factors associated with ciguatera in this region in order to improve our understanding of how the human

effects of HABs such as ciguatera can be prevented. This information could also inform climate change policy that impacts seawater temperature and coral reef health.

Table 3-1. Characteristics of telephone survey participants in St. Thomas, USVI, 2010 and 2011

Variable	Total (N=807)	
	n	%
Age		
18-44	248	31%
45-64	338	42%
65+	154	19%
Not provided	67	8%
Gender (Female)	498	62%
Education		
Some high school or less	114	14%
High school graduate	240	30%
Some college or more	420	52%
Not provided	33	4%

Table 3-2. Crude and adjusted logistic regression models for ciguatera illness in telephone survey participants in St. Thomas, USVI

Variable	Crude		Adjusted[a]	
	OR	95% CI	OR	95% CI
Model 1 – Lifetime history of ciguatera illness (n=720)				
Gender (Female vs. Male)	0.7	0.5-1.1	-	-
Location of birth				
U.S. Virgin Islands	ref		ref	
Caribbean, outside USVI	2.0	1.3-2.9	1.5	1.0-2.2
Outside Caribbean	0.7	0.4-1.1	0.6	0.4-1.1
Education				
Some high school or less	ref		ref	
High school graduate	0.5	0.3-0.8	0.7	0.4-1.2
Some college or more	0.3	0.2-0.5	0.6	0.3-0.9
Model 2 – Ciguatera episode in the past five years (n=369)				
Previous ciguatera episode	4.2	1.9-9.5	3.4	1.4-8.5
Age				
18-44	ref		ref	
45-64	2.2	0.7-7.0	1.6	0.5-5.3
65 or older	3.1	0.9-10.4	1.5	0.4-5.6

[a]Adjusted for location of birth, education, and fish consumption, and age. Model 2 is also adjusted for previous ciguatera episode; OR = Odds ratio, CI = Confidence Interval

Table 3-3. Ciguatera related behaviors in 2010/2011 telephone survey and 1980 in St. Thomas, U.S.V.I.

Variable	2010/2011 survey (N=807)		1980 surveys		
	n	%	n	%	Data Source
Household had at least one episode in past five years[a]	43/400	11%	22/100	22%	McMillan[33]
Visited emergency room for most recent episode	56	30%	5/22, 5/7	23%, 71%	McMillan[33], Morris[19]
Fish consumption					
Do not eat fish	138	17%	8/100	8%	McMillan[33]
3 or more times per week	99	12%	~22/67	~33%[b]	Morris[34]
Believe certain types of fish are poisonous	502	62%	39/54	72%	Morris[34]
Avoid certain types of fish	407	50%			
Believe can tell if a fish might be poisonous	324	40%	14/54	26%	Morris[34]

[a]For current survey, collected only in 2011, [b]Published for ED cases only for 1980 data, survey controls not significantly different

Table 3-4. Demographics of U.S. Virgin Islands, 1980 and 2000

	U.S. Virgin Islands 1980 [a]	U.S. Virgin Islands 2000 [a]	St. Thomas 2000 [a]	Observed strata-specific rate per 1000 in 2011 survey
Total population	96569	108612	51181	12
Age				
Under 18	40924 (42%)[b]	34289 (32%)	15077 (29%)	-
18-44	38022 (39%)[b]	38171 (35%)	18884 (37%)	7
45-64	13148 (14%)	27035 (25%)	12900 (25%)	15
65 and above	4475 (5%)	9117 (8%)	4320 (8%)	24
Education				
Some high school or less	22472 (50%)	25876 (39%)	11915 (37%)	25
High school graduate	11543 (26%)	17044 (26%)	8483 (27%)	9
Some college or more	10971 (24%)	22683 (35%)	11511 (36%)	13

[a]Data obtained from U.S. Census Bureau, [b]Values are approximate as 1980 Census data is recorded as 15-19, proportional distribution assumed.

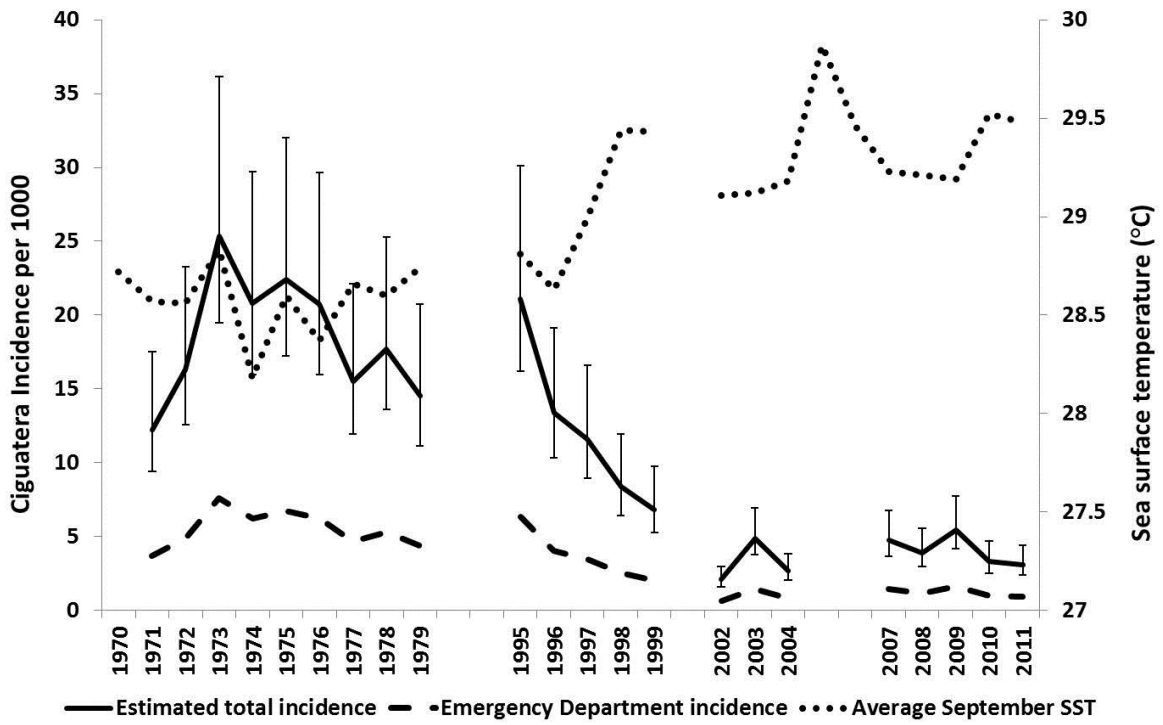

Figure 3-1. Time series of ciguatera incidence in adult residents of St. Thomas based on emergency department (ED) visits* and sea surface temperature.

*Total incidence estimates were calculated by dividing the ED incidence by the proportion of persons with ciguatera who visit the ED (30%). Error bars indicate 95% confidence intervals for incidence.

CHAPTER 4
INFLUENCE OF CARDIAC DISEASE AND ALCOHOL USE ON THE DEVELOPMENT OF SEVERE CIGUATERA ILLNESS[b]

Introduction

Ciguatera is a food-borne illness endemic to many tropical and subtropical areas that results from the consumption of reef fish containing toxins produced by *Gambierdiscus* dinoflagellates (microalgae).[1] Illness is characterized by gastrointestinal followed by neurologic symptoms (paresthesias, pruritis, temperature perception alteration, weakness, and others), and in severe cases, cardiac signs. Currently, our understanding of risk factors for illness is limited, with socioeconomic status,[45, 69] previous ciguatera illness,[13, 46, 69] and the size, amount, and type of fish consumed[17, 47] being the only well-established individual factors. Better characterization of risk factors will allow for targeting of prevention messaging to high-risk populations, including those from non-endemic areas traveling to the Caribbean or south Pacific.

We conducted a case-control study to identify health-related risk factors for severe ciguatera illness in St. Thomas, U.S. Virgin Islands (USVI). No prior study has investigated whether the presence of co-morbidities and health behaviors such as frequent alcohol consumption and tobacco use are associated with ciguatera illness.

Methods

Case and Control Selection

Cases (N=47) were residents of St. Thomas who had a diagnosed episode of ciguatera illness from June 2010-August 2012. They were primarily recruited at Roy Schneider Hospital emergency department (ED), the only hospital on the island and the

[b] Co-authors: LM Grattan, JG Morris

primary source of urgent care. Ciguatera illness was the presenting issue in all cases. After diagnosing a case, with patient consent, the attending physician contacted the study coordinator who subsequently contacted the patient. All residents diagnosed with ciguatera during the study period were asked to participate. A small number of cases (n=6, 13%) were identified through community flyers requesting those with symptoms of ciguatera to contact the study coordinator. By focusing primarily on ED cases, we expected the sample to be weighted towards those with illness severe enough to seek urgent medical attention.

The case definition for inclusion in the study was based on characteristic symptoms of ciguatera, specifically presentation with gastrointestinal symptoms followed by neurologic, cardiovascular, or dermatologic symptoms.[23] Cases were also required to have a history of reef fish consumption within 24 hours of illness and lack an alternative diagnosis.

We randomly identified three population-based controls for each case (N=141), matched for age (±5 years) and gender, from a telephone survey of St. Thomas residents.[69] Age has been associated with ciguatera illness previously, possibly due to toxin sensitization from previous exposures,[45] while gender was considered important due to its association with several of the risk factors of interest including cardiovascular disease and alcohol consumption. Cases and controls were limited to those at least 18 years of age with no ciguatera illness in the previous five years, and who had complete responses to the matching variables.

Data Collection

Cases were interviewed in person during their acute illness by a registered nurse and controls were interviewed by telephone during a single survey period in October

2011 by trained personnel. Personal information included age, sex, education level (less than high school graduate/high school graduate/some college), and frequency of fish consumption. Health information collected included medical history (history of diabetes, cancer, heart disease, high blood pressure, kidney disease, hepatitis, and others), and health behaviors (frequency of alcohol consumption and smoking status) (Appendix A). Race and ethnicity were collected for cases only. Lastly, data on cardiac symptoms for cases enrolled at the ED were collected from medical records, including blood pressure, heart rate, and receipt of atropine. Approval for human subjects research was provided by the University of Florida's Institutional Review Board. Written informed consent was obtained from all case subjects, and oral consent was obtained from controls.

Analysis

We used univariable and multivariable conditional logistic regression to estimate odds ratios and the associated 95% confidence intervals (CIs) for hypothesized risk factors. All variables that were statistically significant in univariable analyses were included in the multivariable model. We also performed a sensitivity analysis using only cases enrolled at the emergency department and their matched controls to determine whether the results were affected by the differing illness severity. As an exploratory analysis, we compared frequency of cardiac symptoms in cases with prior history of heart disease to cases without history of heart disease using Fishers exact tests. All statistical analyses were carried out using SAS v9.2.

Results

Participant characteristics and the results of the logistic regression models are shown in Table 4-1. The mean age of both groups was 54 (standard deviation ±13), and 45% were female. The participation rate for cases was 45%, and those who participated

were similar to non-participants with regard to gender, history of ciguatera, and illness severity, but were more likely to be older and non-Hispanic. (p=0.006).

The final multivariable logistic regression model identified several risk factors that were significantly associated with ciguatera illness. Cases were more likely than controls to report alcohol consumption at least weekly (OR=5.7, 95% CI=2.7-24.8), and in the adjusted estimates, the odds were higher with increasing alcohol consumption. Cases also more frequently had a history of heart disease (OR=6.3, 95% CI=1.2-32.7). Reporting previous ciguatera episodes, lower levels of education, and frequent fish consumption were also associated with illness. Interpretation of results and statistical significance did not differ after excluding cases not identified through the ED. Eight out of 41 cases (20%) enrolled through the ED had a history of heart disease, and six (15%) took medication for heart disease. Cases with heart disease were not significantly more likely than those without to experience cardiac symptoms during their illness (bradycardia: 75 vs. 61%, p=0.7; hypotension: 50 vs. 39%, p=0.7).

Discussion

This epidemiologic study provides preliminary evidence that pre-existing health status influences an individual's risk of developing severe ciguatera illness. We observed a strong relationship between increased alcohol consumption and ciguatera, as well as a history of heart disease and ciguatera. These findings may help explain why certain people suffer from ciguatera after exposure to toxic fish, while others remain asymptomatic.[15] It is not yet clear whether these factors are associated with experiencing any ciguatera illness, or only severe illness. The other identified factors (socioeconomic status, previous episodes, fish consumption) are likely not limited to severe cases, as they have been observed in past research.[13, 45, 46]

In interpreting these results, it is important to note an important limitation in the study. Selection bias is a concern due to the identification of the majority of cases at the emergency room, in that cases selected at a hospital may be more likely to suffer from comorbidities. It is possible that the observed associations are due to those with heart disease or frequent alcohol consumption being more likely to go to the emergency room for their acute ciguatera illness. However, if this were the case, one might expect the other comorbidities to also be associated, which was not the case. In addition, while heart disease and alcohol consumption have not been studied as risk factors previously, these relationships are consistent with past knowledge. Alcohol has previously been implicated in the recurrence of ciguatera symptoms,[70-72] while the cardiac symptoms of ciguatera could explain an association with heart disease, though this was not significant in our fairly small sample. Still, more research is needed to confirm these relationships and understand their mechanisms.

Despite this limitation, as well as other possible sources of bias, the novel findings of this study offer insights into the development of ciguatera illness. Physicians should keep in mind that ciguatera is a potential cause of severe gastrointestinal and neurologic illness that can require emergent treatment for bradycardia. Persons without travel to endemic areas may experience ciguatera poisoning due to fish importation. It may be worth considering whether persons with heart disease, frequent alcohol consumption, or previous ciguatera illness should be counseled on avoidance of high risk fish species (barracuda, jacks, grouper, snapper, etc.) when living in or traveling to ciguatera endemic areas. Education on recognizing the symptoms of ciguatera and the need to seek care could also be beneficial if further studies confirm that illness is more

severe in these groups. In areas like St. Thomas where approximately one percent of the population is affected each year,[69] this targeting of high risk groups may be particularly useful, though the risk attributable to these factors is still uncertain.

Table 4-1. Case and control characteristics and matched logistic regression models for ciguatera illness in St. Thomas, USVI

Variable	Cases N=47 n (%)	Controls N=141 n (%)	Crude OR (95% CI)	Adjusted OR (95% CI)
Education				
Some high school or less	23 (49)	21 (15)	1.0	1.0
High school graduate	9 (19)	43 (30)	0.2 (0.1-0.5) ‡	0.1 (0.02-0.4)†
Some college or more	15 (32)	77 (55)	0.1 (0.1-0.4) ‡	0.1 (0.01-0.3)‡
Alcohol consumption				
Never	14 (30)	78 (55)	1.0	1.0
Less than weekly	20 (43)	37 (26)	3.5 (1.5-8.1) †	2.5 (0.8-7.9)
At least weekly	13 (28)	26 (18)	3.5 (1.3-9.4) †	5.7 (1.3-26.1)*
Fish consumption				
Less than weekly	13 (28)	83 (59)	1.0	1.0
1 or 2 times per week	15 (32)	45 (32)	2.2 (0.9-5.4)	2.2 (0.6-7.3)
3 or more times per week	19 (40)	13 (9)	7.7 (3.1-19.1)‡	8.3 (2.8-25)‡
Tobacco use	6 (13)	8 (6)	2.6 (0.8-8.3)	
Diabetes	10 (21)	23 (16)	1.4 (0.6-3.4)	
Cancer	1 (2)	5 (4)	0.6 (0.1-5.1)	
Heart disease	9 (19)	9 (6)	4.1 (1.3-13) †	6.3 (1.2-33)*
High blood pressure	19 (40)	54 (38)	1.1 (0.5-2.2)	
Previous ciguatera episode	21 (45)	27 (19)	3.4 (1.6-7.2) †	5.0 (1.8-14)†

*p<0.05; †p<0.01; ‡p<0.001

CHAPTER 5
EPIDEMIOLOGY OF CIGUATERA IN FLORIDA[c]

Introduction

Ciguatera fish poisoning is a marine food-borne illness that causes severe gastrointestinal and neurologic symptoms. It is endemic in many tropical and subtropical areas worldwide, including south Florida. Annual incidence in Miami, Florida in 1980 was estimated as 5-500 per 100,000,[14] but a more recent and precise estimate is not available. From 1954 to 1991, the vast majority of ciguatera cases in Florida were caused by fish either imported from the Bahamas or caught in Monroe or Miami-Dade counties in Florida.[73] A few sporadic ciguatoxic fish were caught in counties further north, but all were in migratory species such as barracuda.[73] Because of hypotheses that increasing seawater temperatures associated with global warming may increase ciguatera incidence and range worldwide, it is important to update our estimates of disease incidence and the geographic range of ciguatoxic fish, especially in areas on the border of the current ciguatera range.

Obtaining complete epidemiologic information on ciguatera is difficult. Ciguatera is reportable in Florida and other states, but it is likely that case reports do not represent all true cases. Underreporting occurs at multiple levels: (1) affected individuals who do not seek medical attention for their illness; (2) individuals who seek medical attention but are not appropriately diagnosed; and (3) individuals who are diagnosed but are not reported. Experts estimate that only 20% of ciguatera cases are reported,[5] but a data driven estimate of underreporting is needed to more accurately determine the burden of disease and improve surveillance.

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[c] Co-authors: A Reich, JG Morris

We performed a survey of recreational fishermen and an analysis of public health reports of ciguatera in order to estimate incidence by adjusting for underreporting, identify high risk demographic groups, and identify high risk fish types and catch locations that cause ciguatera illness in Florida.

Methods

Data

Public health reports

The Florida Department of Health (FDOH) maintains records of cases of ciguatera fish poisoning reported through the statewide notifiable disease surveillance system. These cases are classified as confirmed based on the FDOH case definition (Appendix B), which likely has higher specificity than the survey described below. We obtained de-identified data from FDOH on all cases of ciguatera with onset from 2000-2011. The following information was collected regarding the affected individuals: county of residence, age, gender, race and ethnicity, origin of fish, and case notes on fish meal. In analyzing fish types and catch locations, outbreaks were used instead of individuals to avoid over-weighting fish involved in large outbreaks where a single fish poisoned multiple people. An outbreak was defined as one or multiple reported cases of ciguatera linked by a common fish meal.

Survey of recreational fishermen

We also performed an email survey of recreational saltwater fishing license holders to identify cases of ciguatera not reported to FDOH. Fishermen were selected rather than a sample of the general population because we believed they may be at higher risk due to fish consumption, which increased the likelihood of identifying cases. We also hypothesized they would be more aware of where the fish was caught and of

ciguatera. Contact information for all recreational saltwater fishing licenses in 2011 was obtained from the Florida Fish and Wildlife Conservation Commission (FWC). Approximately 41% of the license holders provided an email address and the survey was emailed to all 311,799 of these individuals, of which 10% were undeliverable. The survey was sent to each email address two times approximately one week apart. A Spanish language version was available.

The survey (Appendix C) was focused on those with a history of ciguatera illness, which was assessed using two questions. Participants were classified as probable cases of ciguatera if they responded affirmatively to the question: *Have you ever been diagnosed with ciguatera fish poisoning after eating saltwater fish?* They were classified as suspect cases if they answered “No” to ciguatera diagnosis and “Yes” to: *Have you ever experienced vomiting and/or diarrhea combined with numbness around the mouth or hands, or weakness in the legs, or reversal of hot and cold sensations after eating saltwater fish?* Cases who reported that their symptoms were caused by eating shellfish were excluded from the case analyses as these illnesses are unlikely to be ciguatera.

Probable and suspect cases were then asked whether they or someone they knew had caught the fish that caused their illness, where it was obtained, the type of fish, when their illness occurred (within the past year, more than one year ago, more than five years ago), whether they sought medical attention (emergency room, private physician, called poison control, other), whether they were a Florida resident when the illness occurred, whether the medical attention was obtained in Florida, ethnicity, and zip code of current residence. Cases were also asked to provide name and date of birth for linking to the FDOH public health reports, but this request for information was noted

as optional. A subsample of 75,000 emails received a shorter survey that was limited to only ciguatera illnesses caused by fish caught by the participant or someone they knew and did not include collection of identifiers or ethnicity.

Analysis

Incidence and demographic risk factors

We calculated crude average annual incidence rates of ciguatera for each county in Florida based on case residence and the state overall using FDOH data for 2007-2011. Since these values account for only reported cases, we also estimated underreporting based on the email survey in order to approximate the true incidence. We calculated the percent of probable and suspect cases that did not seek medical attention and the percent of cases that sought medical attention who were not diagnosed (i.e. suspect cases that sought medical attention). To adjust for non-reporting after diagnosis, we assumed that only 47% of physicians reported diagnosed cases based on a survey by Begier et al.[38] The overall incidence for Florida and high incidence counties was then adjusted for all three levels of underreporting.

We also estimated the risk associated with each demographic group (age, gender, race/ethnicity) by calculating group-specific incidence rates and relative risks for 2007-2011 using FDOH data. We repeated this analysis on Miami-Dade County alone as it is the county with the highest total case count and has a different demographic makeup than much of the state, with a high proportion of Hispanics, a group hypothesized to be high risk.

Types and catch locations of illness causing fish

We summarized the type of fish that caused illness for the confirmed outbreaks and probable and suspect individual cases. To adjust for overall consumption, we

calculated the ratio between the percentage of ciguatera cases caused by a fish type to the percentage of combined commercial and recreational fish landings for that fish type, which were obtained from the National Oceanic and Atmospheric Administration's Office of Science and Technology, National Marine Fisheries Service.[75] We also analyzed fish types by ethnicity using chi squared tests to determine whether there are ethnic variations in fish consumption. Confirmed outbreaks were analyzed as one observation per outbreak and included only if all individuals were of the same ethnicity.

We created separate maps of fish catch locations for confirmed, probable, and suspect cases, with probable and suspect further divided into more than five years and five years or less prior to survey. We also mapped data from a study by deSylva[73] that included ciguatoxic fish catch locations for outbreaks reported to a hotline maintained by the University of Miami from 1954-1992. The maps of different time periods were used to qualitatively assess whether ciguatoxic fish have been more frequently caught outside south Florida in recent years.

Analyses were performed using SAS 9.2. This study was approved by the Institutional Review Board at the University of Florida.

Results

There were 291 cases of ciguatera reported to FDOH from 2000-2011. Of these, 245 provided some information about the fish that caused their illness, and these were divided into 97 distinct outbreaks. A total of 5352 individuals responded to the fishermen survey (response rate=5352/(0.9*311,799)=1.9%), of which 245 were classified as probable cases and 74 were classified as suspect cases. Twenty responders and five cases used the Spanish language version of the survey.

Incidence and Demographic Risk Factors

The crude annual incidence rate of ciguatera in Florida based on FDOH reports was 0.2 per 100,000 (Table 5-1). Crude estimates by county are displayed in Figure 5-1. In estimating underreporting, 183 (57%, 95% CI=52-63) cases in the email survey sought medical attention for their illness, with different rates among probable (66%, 95% CI=60-72) and suspect (30%, 95% CI=19-40) cases. Most cases in the survey (88%, 95% CI=83-93) who sought medical attention were diagnosed with ciguatera. The combination of all three levels of underreporting increases the incidence by a factor of 4 to 0.8 per 100,000 for Florida. Normalized cases per county among fishermen are shown in Figure 5-2. The crude incidence among fishermen was approximately 400 per 100,000 (106 cases in previous five years/(5352*5)), or 2,000 times higher than the estimate based on FDOH reports, likely due at least in part to nonresponse bias in the survey.

In the demographic risk factor analysis, Hispanics were the group with the highest incidence rate and their relative risk was 3.4 compared to non-Hispanics (Table 5-2). Blacks and other races had lower risk that Whites, and those less than 20 and over 64 had lower risk than those from 20-34 and 35-64.

Types and Catch Locations of Illness Causing Fish

Among confirmed outbreaks, barracuda were the most commonly reported fish (37%), followed by grouper (33%) and amberjack (8%) (Table 5-3). There was more variation in the fishermen cases, with barracuda representing only 13% of probable and 9% of suspect cases. Looking at fish from all three case classifications combined, grouper was the most commonly reported (31%), followed by barracuda (18%), amberjack (8%), and hogfish (7%). All four of these fish types were overrepresented in

ciguatera cases compared to fish landings, with hogfish and barracuda having the highest ratios (32 and 23, respectively, Table 5-3). In looking at fish types by ethnicity, Hispanic individuals were more likely to eat barracuda than non-Hispanics, while amberjack were more frequently eaten by non-Hispanics in both FDOH reports and the fishermen survey (Table 5-4).

The most common fish catch locations in all three case classifications combined were the Bahamas (107, 34%) and the Florida Keys in Monroe County (63, 20%). Cuba and Palm Beach County were the next most common, each with 5%, followed by Miami-Dade County with 4%. Figure 5-3 shows the catch locations by case classification and time period. Among confirmed outbreaks with catch location in Florida, 7 (17%) were caught outside Monroe or Miami-Dade County, while for probable cases, this value was 19 (29%) and for suspect, it was 16 (62%). Overall, cases in northern Florida were sporadic and infrequent in all time periods and case classifications, and were caused by relatively migratory fish species.

Discussion

The results of this study suggest that incidence of ciguatera fish poisoning is likely significantly higher than estimated based on public health reports alone. However, there is little evidence that incidence or geographic range has increased due to climate change since earlier studies. Cases are caused by fish caught in parts of Florida north of Miami-Dade County, but only sporadically and in migratory fish species. This is consistent with cases from 1954-1992.[73] Compared to a 1980 estimate for Miami of 5 per 100,000 before adjusting for reporting, we estimated Miami's incidence as 1 per 100,000 based on FDOH reports, indicating that incidence has, if anything, decreased over the last three decades. This may be due to changes in fish consumption behavior

as hypothesized in the U.S. Virgin Islands[69] and/or changes in the fisheries or other environmental factors. However, there is strong evidence of a relationship between seawater temperature and growth of the *Gambierdiscus* dinoflagellates that produce the toxin,[51, 53, 54] so incidence and range in Florida should be monitored further in the future.

In evaluating the magnitude of underreporting using survey data, we estimated that true cases were higher than FDOH reports by at least a factor of 4. However, because of the low response rate and the fact that ciguatera is a very distinctive and memorable illness for those who have suffered from it, it is extremely likely that this survey suffers from significant nonresponse bias. In other words, persons who had sought medical attention for their illness and were diagnosed would be much more likely to participate in a survey about ciguatera than those who were unaffected or who had experienced illness, but were unaware of the cause. This is supported by the high incidence among fishermen in the survey and the generally higher response rates in south Florida. This bias would tend to overestimate the percentage of probable cases compared to suspect cases in the survey and underestimate the first two levels of underreporting. If we theoretically increase the number of suspect cases by 5 or 10 times[74] to account for this bias (Table 5-5), the updated underreporting estimates would increase incidence by a factor of 8-13, to 1.5-2.6 per 100,000 for Florida, and 8-13 and 23-39 per 100,000 for Miami-Dade and Monroe counties, respectively. These estimates should be interpreted with caution, as the adjustment is fairly arbitrary, but we believe they more closely represent the true magnitude of underreporting.

We also found that Hispanics experience the highest rate of ciguatera illness, possibly due to more frequent consumption of barracuda than non-Hispanics. This may

represent an opportunity for targeted, culturally relevant educational messaging after more narrowly identifying high risk cultural groups. The disparity may also be due to socioeconomic factors, as illness in non-Hispanics was more commonly caused by amberjacks which are generally caught offshore in deep water. Clarifying the reasons for differences in consumption would require further qualitative research, which could be partially done by adding questions to FDOH ciguatera case investigations about country of origin, reason for eating barracuda, etc. In addition, given this risk factor, it is important to note that illegal immigrants may as a group be particularly prone to underreporting, and this was not accounted for in this study's underreporting estimates.

With regards to fish type, barracuda were extremely overrepresented in ciguatera cases compared to fish landings in Florida. Despite past public health education efforts on avoidance of high risk fish like barracuda, commercial and recreational fishermen combined produced an average of 90 thousand pounds of barracuda per year over the last decade, and fishers should be further encouraged to avoid this species. However, barracuda were more common among FDOH reports than probable and suspect cases. This may suggest a bias where cases involving barracuda are more likely to be diagnosed and reported due to public health awareness of the risk associated with barracuda. Since outbreaks are more likely to be reported than sporadic cases,[38] this bias could also be due to the fact that a single large barracuda can feed many people. Besides barracuda, hogfish were a high risk fish species in this study, which may be less commonly known.

Our results also clearly show that the majority of ciguatera cases in Florida are caused by fish caught in the Bahamas and the Florida Keys. There is risk of catching

ciguatoxic fish throughout the Caribbean, and a small risk throughout the state of Florida, likely due to fish migration. FDOH reports included the smallest percent of fish caught in northern Florida, and also had fewer case residences in northern Florida than fishermen. This may suggest another diagnosis and reporting bias, as physicians in this area may be less familiar with the disease than in south Florida.

In addition to the nonresponse bias already discussed, there are a few limitations that should be considered when interpreting our results. First, we relied on self-report, so the information provided may not be completely accurate. In particular, there may be false positives in the sample, including those from outside the typical ciguatera range, and incorrectly identified fish types due to restaurants mislabeling the fish being served. At the same time, the sample of cases may be biased towards the traditional ciguatera range due to selection bias. Lastly, the survey sampled only fishermen with current saltwater fishing licenses. Fishers who fish only from land based structures are not required to have a license in Florida, so these individuals, as well as those who ignore the licensing laws, would not have been captured.

Despite these limitations, we were able to identify over 300 cases of ciguatera, the majority of which were not reported to FDOH. This increased our sample of fish types and catch locations and gave us valuable information on potential biases in the current surveillance system. Moving forward, FDOH may be able to improve reporting by educating physicians on the possibility of acquiring ciguatera from fish caught outside typical areas, and emphasizing the unique clinical presentation of ciguatera illness. There is a continuing need to monitor ciguatera in Florida.

Table 5-1. Ciguatera average annual incidence estimates for the state of Florida and Miami-Dade and Monroe counties, 2007-2011, per 100,000.

	Florida	Miami-Dade County	Monroe County
Crude incidence from FDOH reports	0.2	1	3
Adjusted for underreporting	0.8	4	12

Table 5-2. Average annual incidence of reported ciguatera by demographic group in Florida and Miami-Dade County, cases reported to FDOH 2007-2011

Variable	Florida N=206 n (%)	Florida Incidence (per 100,000)	Florida Relative risk	Miami-Dade County N=94 n (%)	Miami-Dade County Incidence (per 100,000)	Miami-Dade County Relative risk
Age						
<20	20 (10%)	0.1	0.3	8 (9%)	0.3	0.3
20-34	45 (22%)	0.3	Ref	26 (28%)	1.0	Ref
35-64	134 (65%)	0.4	1.4	54 (57%)	1.1	1.1
65+	7 (3%)	0.04	0.2	6 (6%)	0.3	0.3
Gender						
Female	92 (45%)	0.2	Ref	39 (41%)	0.6	Ref
Male	114 (55%)	0.2	1.3	55 (59%)	0.9	1.5
Race						
White	167 (81%)	0.2	Ref	84 (89%)	0.9	Ref
Black	4 (2%)	0.03	0.1	2 (2%)	0.1	0.1
Other	7 (3%)	0.1	0.3	0		
Unknown	28 (14%)	0.1	0.3	8 (9%)		
Ethnicity						
Non-Hispanic	93 (45%)	0.1	Ref	16 (17%)	0.4	Ref
Hispanic	92 (45%)	0.4	3.4	78 (83%)	1.0	2.6
Unknown	21 (10%)			0		

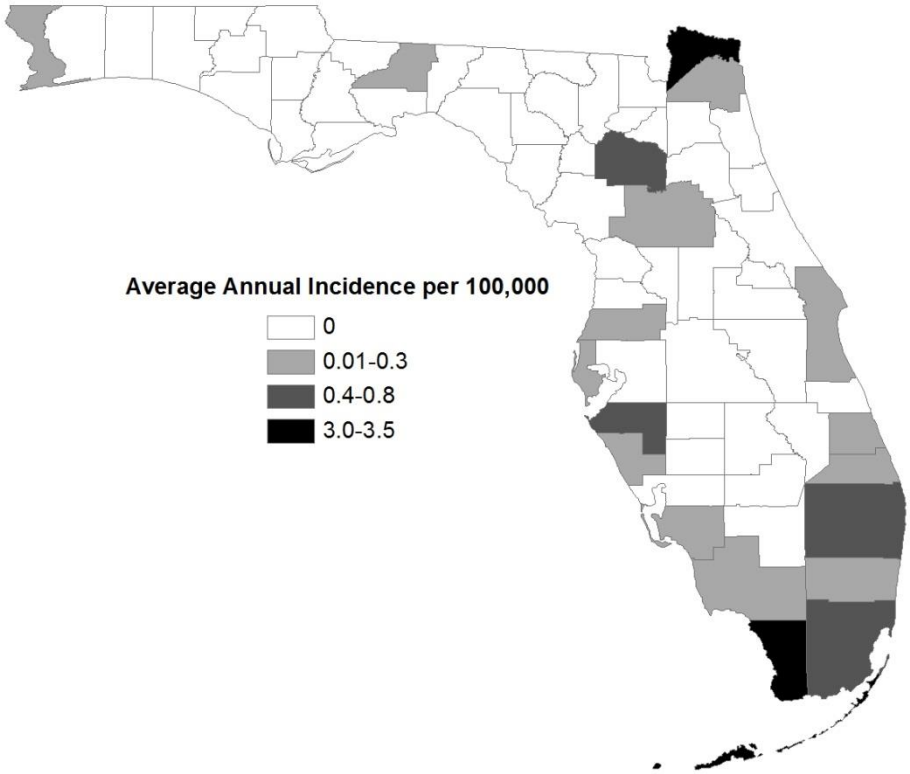

Figure 5-1. Incidence of reported ciguatera fish poisoning in Florida by county of residence, 2007-2011.

Incidence rates were calculated using the number of cases of ciguatera were reported to the Florida Department of Health and population data from the 2010 U.S. Census.

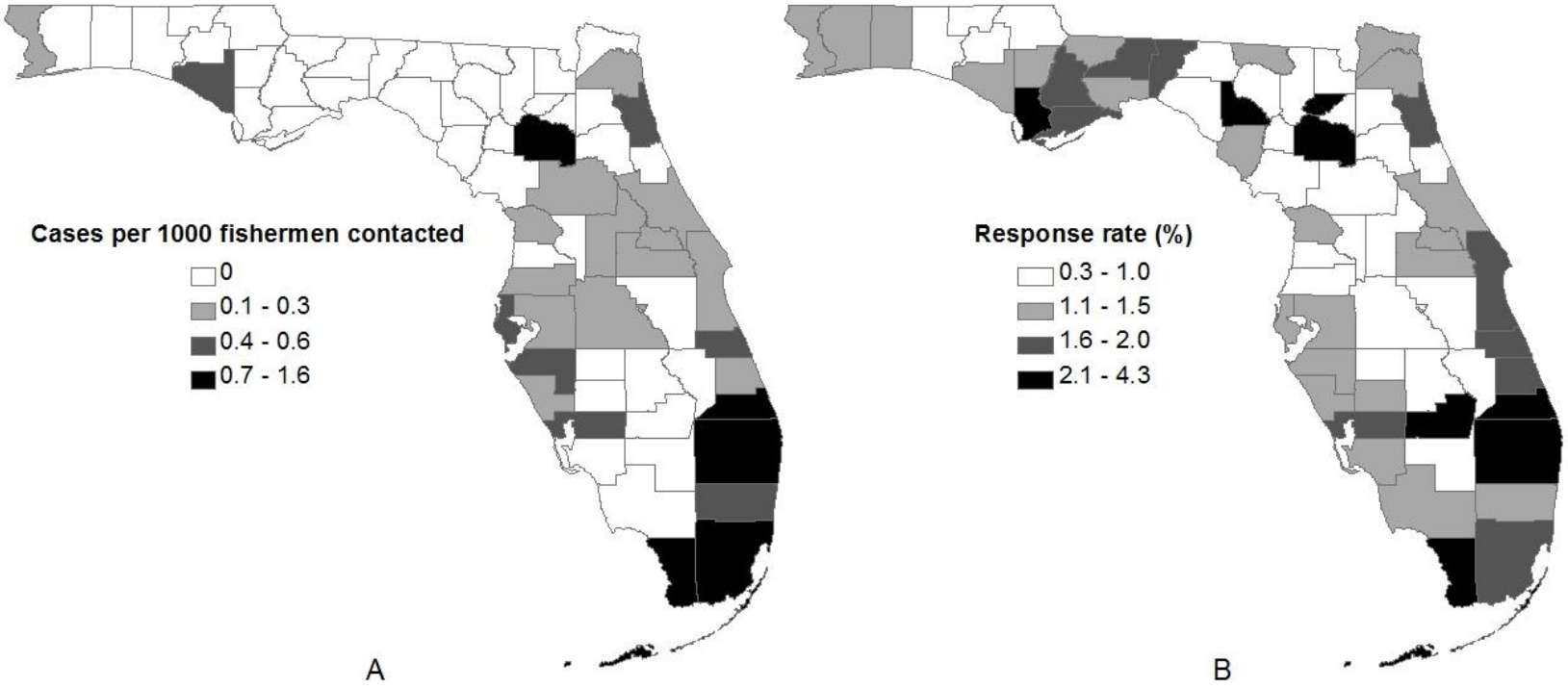

Figure 5-2. Ciguatera cases and response rate of recreational fishing license holders by county of residence in email survey. A) Number of cases of ciguatera per 1000 fishermen contacted by email; B) Percentage of emailed fishermen that responded to the survey.

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Table 5-3. Fish types associated with ciguatera cases in Florida, 2000-2011

Type of fish	Confirmed Outbreaks N=97 n (%)	Probable Cases N=245 n (%)	Suspect Cases N=74 n (%)	Combined N=416 n (%)	Average Commercial and Recreational Landings in Florida, 2000-10 Lbs (% total)	Ratio of % Combined Ciguatera Cases to % Landings by fish type
Hogfish	1 (1%)	28 (11%)	1 (1%)	34 (7%)	296,154 (0.3%)	32
Barracuda	36 (37%)	32 (13%)	7 (9%)	75 (18%)	897,461 (0.8%)	23
Amberjack	8 (8%)	23 (9%)	1 (1%)	32 (8%)	2,638,570 (2%)	4
Grouper	32 (33%)	83 (34%)	14 (19%)	129 (31%)	8,942,747 (8%)	3
Snapper	4 (4%)	16 (7%)	14 (19%)	26 (8%)	8,200,017 (7%)	1
Other jack	0	10 (4%)	1 (1%)	11 (3%)	4,717,613 (4%)	0.6
Mackerel/Kingfish	3 (3%)	15 (6%)	4 (5%)	22 (5%)	16,825,185 (15%)	0.4
Mahi mahi	2 (2%)	4 (2%)	2 (3%)	8 (2%)	6,731,426 (6%)	0.3
Other	8 (8%)	17 (7%)	19 (26%)	51 (12%)		
Multiple fish	1 (1%)	7 (3%)	6 (8%)	14 (3%)		
Unknown	2 (2%)	10 (4%)	5 (7%)	17 (4%)		

Landings data are published by the National Oceanic and Atmospheric Administration's Office of Science and Technology[75] and may not be final.

Table 5-4. Top three fish types consumed in ciguatera outbreaks reported to Florida Department of Health by ethnicity

	Confirmed Outbreaks* (FDOH reports)		Probable and Suspect Cases (Fishermen survey)	
Type of Fish	Hispanic n (%)	Non-Hispanic n (%)	Hispanic n (%)	Non-Hispanic n (%)
Barracuda	29 (76%)	3 (7%)	10 (24%)	19 (9%)
Grouper	4 (11%)	26 (58%)	6 (14%)	70 (34%)
Amberjack	0	7 (16%)	4 (10%)	12 (6%)
Other	5 (13%)	9 (20%)	22 (52%)	102 (50%)
p value	<0.0001		0.007	

*Ethnicity of all individuals affected by the outbreak

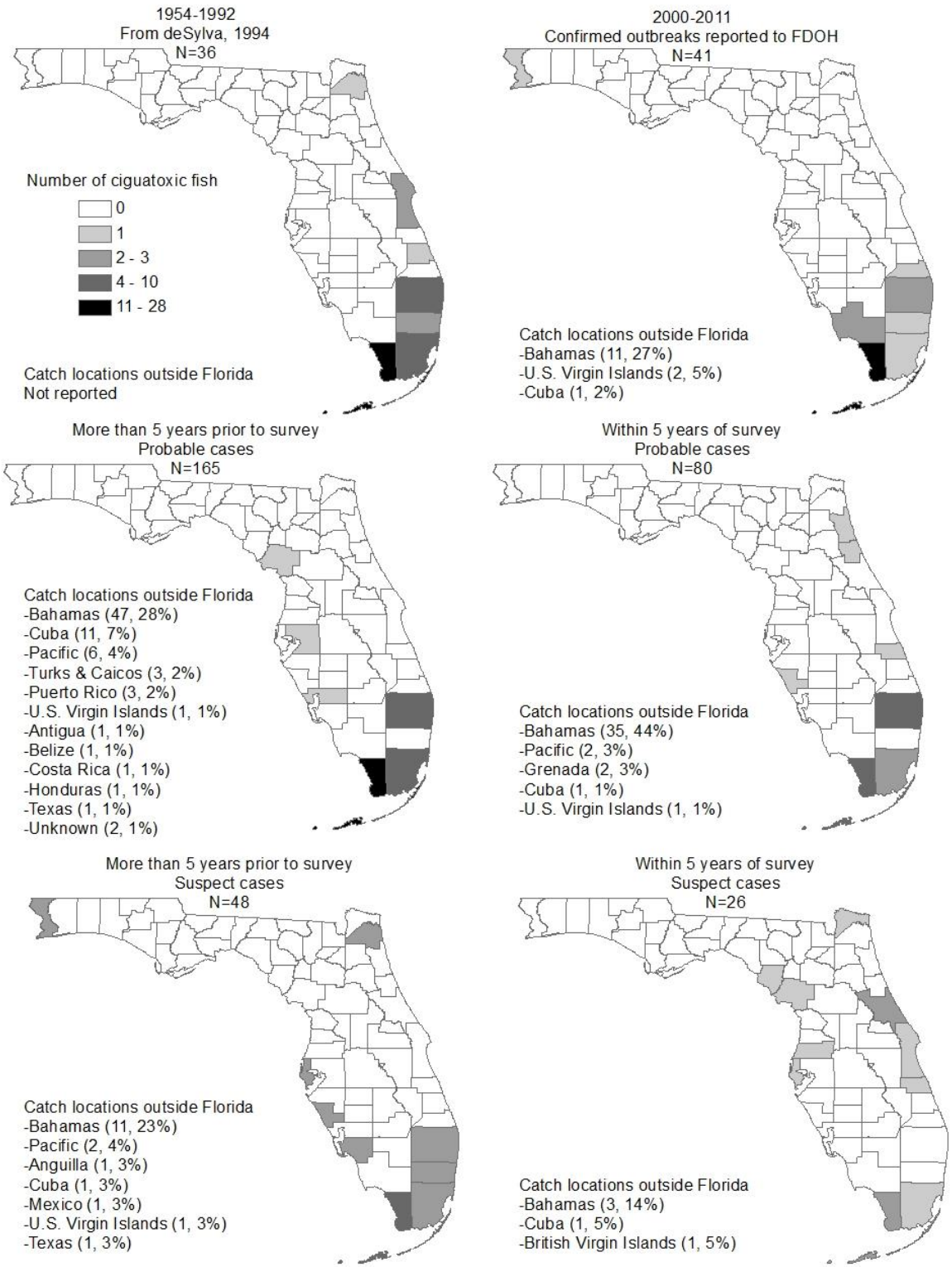

Figure 5-3. Catch locations of ciguatoxic fish in Florida cases.

Table 5-5. Adjusting annual incidence of ciguatera in Florida from FDOH reports for underreporting and nonresponse bias using data from survey of recreational fishermen

	Probable cases	Suspect cases	Overall
Crude incidence from FDOH reports per 100,000			0.2
No nonresponse bias	245	74	319
Seek medical attention	161 (66%)	22 (30%)	183 (57%)
Diagnosed if sought medical attention			161/183 (88%)
Reported if diagnosed			47%[b]
Underreporting factor			0.57*0.88*0.47=4
Incidence per 100,000			0.8
Adjusted for nonresponse bias (x5[a])	245	370	615
Seek medical attention	161 (66%)	110 (30%)	271 (44%)
Sought medical attention, diagnosed			161/271 (59%)
Underreporting factor			0.44*0.59*0.47=8
Incidence per 100,000			1.5
Adjusted for nonresponse bias (x10[a])	245	740	985
Seek medical attention	161 (66%)	220 (30%)	381 (39%)
Sought medical attention, diagnosed			161/381 (42%)
Underreporting factor			0.39*0.42*0.47=13
Incidence per 100,000			2.6

[a]Factor by which suspect cases were multiplied to account for nonresponse bias, in which individuals who are aware of their diagnosis (probable cases) are more likely to participate than others (suspect cases and non-cases).[b]The same rate of reported if diagnosed was used for all three estimates.

CHAPTER 6
CONCLUSIONS

Summary of Findings

Aim 1 – Estimate Incidence

The overarching goal of this project was to improve our understanding of the factors that impact the occurrence of ciguatera fish poisoning, particularly in the Caribbean and Florida. As has been discussed in earlier chapters, there are a wide range of probable environmental influences, including seawater temperature, health of coral reefs, salinity, nutrient levels, water movement, and others. In addition, there are human factors that likely influence ciguatera, but which have not received the same amount of research attention and are the focus of this project. In order to better understand and characterize both the environmental and human factors, it was critical to first update our estimates of ciguatera incidence. Incidence estimates prior to this project were obtained around 1980 in both St. Thomas, USVI and Miami, Florida. These earlier estimates give us the opportunity to assess the change in incidence over time.

As part of Studies 1 and 3, incidence of ciguatera was estimated in St. Thomas and Florida. In St. Thomas, incidence was approximately 12 per 1000 in an island-wide telephone survey. A second estimate based on emergency department visits was 6 per 1000. Both of these estimates were lower than estimates of 14 per 1000 from a household survey on the island in 1980[19] and 18 per 100,000 in the 1970s based on emergency department visits.[33] Additionally, 11% of households had at least one person with a recent ciguatera episode, compared to 22% in a 1980 telephone survey.[33] Observing the same relationship in multiple data sources improved confidence that incidence has not increased, and may have decreased, over the past 30 years.

The observed decrease in incidence was counter to a priori expectations, as seawater temperature has increased over the same time period, which was hypothesized to increase ciguatera incidence and incidence of other harmful algal blooms. There are a few possible explanations for the lack of increase in St. Thomas. First, it is possible that St. Thomas has reached an upper temperature threshold as described by Llewellyn,[54] and water temperatures are beyond the optimal range for *Gambierdiscus* growth. Additional data will be needed to assess this possibility, but based on preliminary environmental data in St. Thomas, this does not appear to be the case (Don Anderson, personal communication, September 2012). It is also possible that there is a positive association between seawater temperature and ciguatera in St. Thomas, but other environmental or human behavioral factors are driving incidence lower. This is supported by the work discussed in Aim 3.

While the trend in incidence is consistent in both St. Thomas data sources, there is some disparity between the rates estimated from emergency department visits and those from the survey, with the latter being larger (12 vs. 6 per 1000). This could be explained in part by some cases of ciguatera who visit the emergency department not being diagnosed as ciguatera because of its complicated diagnosis. In cases where symptoms resolve on their own in a matter of days, there is little incentive to reach a conclusive diagnosis. A study in Puerto Rico, another endemic area, found that only one out of 15 presumed ciguatera cases were diagnosed with ciguatera.[35] Since there have not been any dramatic shifts in diagnostic capabilities for ciguatera, the diagnosed emergency room visits are the best way to assess the trend in ciguatera over time. However, it is important to note that they represent a fairly small proportion of true

ciguatera cases. Alternatively, or in addition, it is possible that there is some selection bias in the telephone survey wherein individuals who had experienced ciguatera were more likely to participate, which would make the survey estimates artificially high.

In Florida, incidence was estimated based on cases reported to FDOH, which was not possible in St. Thomas due to reporting practices. Statewide, incidence was 0.2 per 100,000 without adjusting for underreporting, and1.5-2 per 100,000 after accounting for underreporting and survey bias. Incidence was higher in the southernmost counties: 6-10 per 100,000 in Miami-Dade and 23-36 per 100,000 in Monroe County (Florida Keys) after adjusting for underreporting and survey bias, which is consistent with past research in Florida[73] and because of the ecology of these areas (warmer seawater temperatures and presence of coral reefs). As in St. Thomas, there was evidence of a decrease in incidence, or at least not an increase, since 1980. The earlier estimate in Miami was 5 per 100,000 or 50-500 per 100,000 after roughly adjusting for underreporting. The reasons for the decrease in Florida may be similar to St. Thomas with regards to changes in fish consumption, but data on frequency of fish consumption and type of fish most commonly eaten was not available in Florida. In addition, there may be changes in the fisheries over time, but this was not quantified in this project.

Also in Florida, it was clear that public health reports likely do not represent all true cases of ciguatera. Based on the email survey of recreational saltwater fishermen described in Study 3, not all affected individuals seek medical attention, and of those that do, not all are diagnosed and/or reported. Adjusting for these levels of underreporting results in at least a factor of 4 increase in incidence, and perhaps much higher. This is consistent with past research indicating that 12-70% of ciguatera cases

seek medical attention[31-35] and that ciguatera is often misdiagnosed. In Miami, Florida, only 68% of physicians correctly diagnosed a classically presented ciguatera case report.[36] There are many reasons for these levels of underreporting. Individuals with mild illness, particularly those with low socioeconomic status, may assume, often correctly, that their symptoms will go away without medical attention. Physicians in non-endemic areas may be very unfamiliar with ciguatera and will not arrive at the diagnosis until chronic symptoms develop and all other explanations have been exhausted. Lastly, physicians may be accustomed to relying on infection control departments and laboratories to report cases to the health department, which would not occur for ciguatera. For all of these reasons, and others, is important to account for underreporting to accurately estimate incidence.

Aim 2 – Identify Risk Factors

Identifying individual level risk factors for ciguatera illness was the next step to understanding the influences on incidence. Risk factors were explored in Studies 1, 2, and 3. In both Studies 1 and 2 in St. Thomas, we found that socioeconomic status (as measured by education), fish consumption, and a previous ciguatera illness were associated with ciguatera illness. Socioeconomic status has been identified as a risk factor previously, likely because lower income individuals have fewer low cost protein alternatives other than local fish.[45] Previous ciguatera episodes have also been noted in past research, particularly as a risk factor for more severe disease.[13,46] Frequency of fish consumption has not been studied previously, but others have found that amount,[15,17] and type of fish[35,46,47] consumed do impact risk.

It was useful to explore these risk factors in two different studies, as the first used self-reported ciguatera illnesses in a telephone survey, while the second used ciguatera

cases diagnosed by a physician. Cases identified in the telephone survey likely included less severe cases than those enrolled through the emergency department, since it was not necessary to have sought medical attention to be classified as a case. Thus, the telephone survey had higher sensitivity. On the other hand, it is possible that cases identified through the telephone survey did not actually have ciguatera illness and were misclassified in the analysis. The case control study (Study 2), therefore, had higher specificity and was less susceptible to false positives because the illnesses were confirmed by a physician. Since the same risk factors were found in using both case definitions, we can be fairly confident in the results.

Also in Study 1, location of birth was associated with illness in St. Thomas, with the highest odds of illness among those born in the Caribbean, but outside USVI, and the lowest odds in those born outside the Caribbean. This has not been observed previously, but may be due to different cultural practices, with those born outside the Caribbean being less likely to eat local fish. Those born in the Caribbean but outside USVI may be at higher risk if they relocated from islands where ciguatera was not a major concern, and consequently are not familiar with preventive measures.

Age was not associated with illness in Study 1 after adjusting for other risk factors, but there was a crude relationship, with higher odds of illness with increasing age. Existing studies on age and ciguatera are similarly mixed. Some have found that illness severity is associated with increasing age,[17,24,46], while others have found no relationship.[15,47] This may be due to the increased risk from previous episodes, which is likely more common in older individuals. Others have hypothesized that there is

sensitization to the toxin that can occur after eating toxic fish for many years. It was not possible to assess age as a risk factor in Study 2 as it was used as a matching variable.

Study 2 looked at some additional risk factors not assessed in Study 1 using a case control design. History of heart disease and frequent alcohol consumption were associated with ciguatera illness. These factors have not been examined for development of illness previously, but are consistent with existing knowledge about ciguatera. Cardiac symptoms are present in severe ciguatera illnesses,[23] so it makes sense that those with pre-existing heart disease may be more likely to have severe illness. Alcohol has been associated with recurrence of neurologic symptoms among individuals recovered from ciguatera.[70-72]

In Study 3, which focused on Florida, most of the risk factors examined were demographic characteristics. The highest risk group was Hispanics, which has not been observed previously other than in anecdotal evidence. This risk may be attributed, at least in part, to more frequent consumption of barracuda as observed in this study. There may be cultural reasons for this behavior that need to be explored, and, similar to St. Thomas, some groups may have originated from areas where ciguatera was not a concern and eating barracuda was comparably safe.

In addition to ethnicity, blacks and other races had lower risk than whites, and those less than 20 and over 64 had lower risk than those from 20-34 and 35-64. Males and Females had roughly similar risk, which is consistent with St. Thomas. Besides the risk factors discussed here, the types of fish consumed clearly have an impact on the level of ciguatera risk an individual has, which is discussed in Aim 4.

Aim 3 – Assess Population-level Changes in Risk Factors

Given the observation that incidence of ciguatera has not increased in St. Thomas despite rising seawater temperatures, it was important to explore other possible drivers of incidence. There are many possible factors that were not assessed as part of this project, but the risk factors identified in Aim 2 provided one possible explanation. Since 1980, there have been changes in the population of St. Thomas. According to Census data, the population in St. Thomas is made up of a greater proportion of older individuals, and income and education levels are higher.[63] At the same time, survey data indicates that fish consumption has decreased, with the percentage eating fish three or more times a week decreasing from one-third in 1980[34] to 12% in 2010/2011. Given the association of these factors with ciguatera, it is reasonable that these population-level changes could explain a change in incidence. The findings of Study 1 support this idea. Increasing age would be expected to cause an increase in ciguatera incidence, but increasing socioeconomic status and decreasing fish consumption could account for the overall decrease in incidence. Additionally, this decrease may feed on itself, as a decrease in incidence would lead to a smaller number of people being at increased risk due to prior ciguatera episodes. Some or all of these factors may also help explain the lack of increase in incidence in Florida.

Aim 4 – Describe Illness Causing Fish

Lastly, in Study 3, the fish types and catch locations of ciguatoxic fish that caused illness in Florida were examined. It was particularly important to update the catch locations, as Florida is on the border of the geographic range for ciguatera, and so is an excellent setting to assess changes in range due to increasing seawater temperature. The vast majority of fish were caught in the Bahamas and Florida Keys, though fish

were caught in many locations throughout the Caribbean. There were sporadic fish catches in northern Florida, but all were in migratory fish species such as barracuda, and this phenomenon does not seem to have increased in frequency since an earlier study in Florida.[73] Thus, as with incidence in Studies 1 and 3, increasing seawater temperature does not yet seem to have increased the geographic range of ciguatera. However, it is possible that there has been an increase in range that was not observed in FDOH reports or the survey due to bias. Fishermen and physicians in areas that are traditionally ciguatera-endemic may have been more likely to participate in the survey or diagnose and report illnesses. There was some evidence that this was true for physicians at least, as the proportion of cases in residents of northern Florida was far smaller among FDOH cases than fishermen.

The fish types identified as highest risk in this study were barracuda, grouper, amberjack, and hogfish. All of these types have been identified as high risk previously,[23] and with the exception of hogfish, were identified in St. Thomas as well. There was more variation in fish types identified by recreational fishermen than in cases reported to the FDOH, which suggests there may be a bias in diagnosis or reporting towards stereotypical fish species. Barracuda are the fish most commonly linked to ciguatera by public health educational materials, so it is reasonable to think that mention of barracuda consumption would increase the likelihood of a correct diagnosis. Other reporting biases that have been documented are towards severe and outbreak-associated cases,[38] which could similarly be easier to diagnose.

Strengths and Limitations

The results of these three studies are bolstered by the use of high quality data that is uncommon in ciguatera research. The majority of studies on ciguatera rely on public

health reports alone to quantify cases, which is prone to the underreporting issues already discussed. Data quality of these reports also varies by location. In contrast, these studies included primary data collection of ciguatera cases, and compared these data to other existing data sources in both St. Thomas and Florida. Observing the same trends in multiple datasets provides a great deal of confidence in the results.

At the same time, there are some important limitations that are common in all three studies. First, case classification of ciguatera is a challenge, whether relying on self-report or physician diagnosis. Diagnosis is difficult as it is based on characteristic symptoms and history of reef fish consumption rather than a confirmatory test. This may have led to misclassification of cases in all of the studies.

In addition, the telephone survey in St. Thomas and the email survey in Florida had low response rates. This is an increasing problem in survey research, and the samples may suffer from selection bias. With the email survey in particular, contacted individuals who had been diagnosed with ciguatera may have been more likely to participate. This may have been less of an issue in St. Thomas as the population is much more familiar with ciguatera due to the high incidence. To reduce this problem in Florida, one approach could have been to promote the survey as a more general survey on fishing. This could have reduced the bias, but would have likely reduced the number of ciguatera cases identified, which would have had a negative impact on the analysis of catch locations. Other strengths and limitations of the individual studies are described in their respective chapters.

Despite these limitations, the results of the three studies in this project provide some interesting insights into ciguatera and the factors that influence its incidence.

There are several implications to public health practice regarding the management of ciguatera surveillance and prevention.

Public Health Implications and Suggestions for Future Research

Ciguatera is an important global health problem that causes severe and often chronic symptoms. In endemic areas such as St. Thomas, approximately 1% of the population may be affected each year (Chapter 3), which leads to significant economic impacts as well as personal health problems. The findings described above answer important public health questions and identify and reinforce others that should be answered. The recognition that ciguatera incidence has likely not increased in either St. Thomas or Florida over the last 30 years supports the possibility that factors other than seawater temperature may have a strong influence on ciguatera incidence. This suggests there may be public health adaptations to climate change that could mitigate the influence of climate change with regards to ciguatera. There is still much to understand about the range of human and environmental factors influencing ciguatera incidence, as described in Chapter 1. Future work will improve our response to the risk of increased harmful algal blooms caused by climate change by identifying mitigation techniques, and ideally prevention measures to protect coral reefs and avoid higher seawater temperatures as much as possible.

Most of the risk factors identified in this project relate to the consumption of high risk fish species. The association between ciguatera and socio-economic status, location of birth, and frequency of fish consumption in St. Thomas, and Hispanic ethnicity in Florida are connected to the availability of other protein sources and the cultural acceptability of consuming high risk fish. Public health workers can use this information to identify high risk groups for targeted education about high risk fish

species. History of heart disease and frequent alcohol consumption are risk factors less related to fish consumption, and may provide an opportunity for prevention of ciguatera illness by physicians, who can educate their patients with these characteristics on ciguatera risk if they live in or travel to endemic areas. More research is needed to confirm and understand the mechanisms behind these risk factors and identify additional individual-level factors that will allow for identification of high risk individuals for directed messaging.

Lastly, these findings provide support for improved surveillance of ciguatera, as it is clear that diagnosed and reported cases do not represent the entire burden of disease. There is a need to educate clinicians, including those outside the traditional ciguatera endemic regions, about the clinical presentation of ciguatera and its status as a notifiable disease in order to reduce underreporting. This may also help address some of the reporting bias observed in this project, where cases outside the typical ciguatera geographic range and those who ate fish other than barracuda or grouper seemed less likely to be reported. This bias is a problem that public health workers should monitor in the future, as having more complete surveillance data will enable us to recognize future shifts in ciguatera incidence or range.

APPENDIX A
ST. THOMAS TELEPHONE SURVEY QUESTIONNAIRE

Questions indicated with an asterisk (*) were also collected from cases in the case control study described in Chapter 4. These cases also completed additional information about their current illness, received a physical examination, and completed the Boston Occupational and Environmental Neurology Questionnaire, the Brief Michigan Alcohol Screening Test, and neurocognitive testing as part of a cohort of ciguatera cases in St. Thomas.

Telephone script: Hello, my name is %name and I am calling from the Florida Survey Research Center at the University of Florida. University researchers are conducting a survey of citizens in the Virgin Islands about their experiences with the illness ciguatera, sometimes called "fish poisoning."

This is not a sales call and your answers will be completely confidential. You may stop the interview at any time. The survey should only take about 15 minutes to complete. May I please speak with the person in the household who is age 18 or older and has the next birthday?

First, we'd like to know about your experiences with eating fish.

1. *How often do you eat locally caught fish? Would you say you eat locally caught fish more than 3 times a week; 1 or 2 times a week; less than once a week but more than once a month; less than once a month; or never? [More than 3 times a week; 1 or 2 times a week; Less than once a week but more than once a month; Less than once a month; Never; Don't know; Refuse]

   IF "Less than once a month" or "Never"
   1A. Is concern about "fish poisoning" one of the reasons why you rarely or never eat fish? [YNDR]

   GO TO Q5

IF Q1 "More than 3 times a week"; "1 or 2 times a week"; or, "Less than once a week but more than once a month":

Next, please think about the last time you ate locally caught fish.

2. What kind of fish was the last locally caught fish you ate? [INT: Do not read. Mark ONE.] [checkbox
   Barracuda
   Carang
   Grouper
   INT: If "Grouper," prompt for specific type & mark. If specific type not known, just mark "Grouper."
   Black grouper
   Gag
   Red hind
   Red grouper
   Roch hind
   Scamp
   Yellowfin grouper

Hardnose (Blue Runner)
Hogfish
Jack
INT: If "Jack," prompt for specific type & mark. If specific type not known, just mark "Jack."
Amber jack
Bar jack
Black jack
Blue runner
Horse-eye jack
Yellow Jack
Olewife ('Old Wife') / Triggerfish
Mackerel
INT: If "Mackerel," prompt for specific type & mark. If specific type not known, just mark "Mackerel."
Cero mackerel
King mackerel / Kingfish
'Pot fish' (Small fish caught in fish traps)
Snapper
INT: If "Snapper," prompt for specific type & mark. If specific type not known, just mark "Snapper."
Blackfin snapper
Cubera snapper
Dog snapper
Gray snapper
Yellowtail snapper
Other
Don't know
Refuse]

IF "Other"
2A. Specify 'other' type of fish [text]

3. Did you eat that fish at home, at a restaurant, or somewhere else? [Home, Restaurant, Other, Don't know, Refuse]
IF Q3 NOT RESTAURANT:
3A. Did you buy the fish or did someone in your household catch the fish? [Buy, Catch, Other (describe), Don't know, Refuse]

IF Q3A OTHER:
3A1. How did you get the fish? [text, DR]

IF Q3A PURCHASED:
3B. Where did you buy the fish? [Local fisherman / Fish market, Grocery Store, Other, Don't know, Refuse]

IF OTHER: 3B1. [text, DR]

4. Do you know where the fish was caught? [YNDR]

IF YES:

4A. Where was the fish caught? [North of island, South of island, Away from Island – North, Away from Island – Southwest, Away from Island – Southeast, Don't know, Refuse]

Next, we have some questions about fish poisoning.

5. Is there a season when fish are more likely to be poisonous? [YNDR]

   IF YES:
   5A. When are fish more likely to be poisonous? [text, DR]

6. Are there certain types of fish that you believe are poisonous? [YNDR]

   IF YES:
   6A. What types of fish do you believe are poisonous? [INT: Do not read. Mark all that apply.] [checkbox
   Barracuda
   Carang
   Grouper
   INT: If "Grouper," prompt for specific type & mark. If specific type not known, just mark "Grouper."
   Black grouper
   Gag
   Red hind
   Red grouper
   Roch hind
   Scamp
   Yellowfin grouper
   Hardnose (Blue Runner)
   Hogfish
   Jack
   INT: If "Jack," prompt for specific type & mark. If specific type not known, just mark "Jack."
   Amber jack
   Bar jack
   Black jack
   Blue runner
   Horse-eye jack
   Yellow Jack
   Olewife ('Old Wife') / Triggerfish
   Mackerel
   INT: If "Mackerel," prompt for specific type & mark. If specific type not known, just mark "Mackerel."
   Cero mackerel
   King mackerel / Kingfish
   'Pot fish' (Small fish caught in fish traps)
   Snapper
   INT: If "Snapper," prompt for specific type & mark. If specific type not known, just mark "Snapper."
   Blackfin snapper
   Cubera snapper
   Dog snapper

Gray snapper
Yellowtail snapper
Other
Don't know
Refuse]

IF "Other"
6A1. Specify 'other' type of fish [text]

6B. Do you avoid eating these types of fish? [YNDR]

7. Is there any way to tell if a fish might be poisonous? [YNDR]

IF YES:
7A. How can you tell if a fish might be poisonous? [INT: Do not read. Mark all that apply.]
[checkbox
Big eyes
Cook silver coin or spoon with the fish
Feed piece of fish to pet
Green flesh
Put fish on ant bed
See if flies land on fish
Taste liver of fish
Other
Don't know
Refuse]

IF "Other"
7A1. Specify 'other' method [text]

8. If you, or someone in your household, got fish poisoning, how would you treat it? [INT: Do not read. Mark all that apply.]
[checkbox
Go to the emergency room
Visit local medical clinic or doctor
Benadryl
Brown sugar
Bush tea
Charcoal
Mauby Bark
Other
Don't know
Refuse]

IF "Other"
8A1. Specify 'other' method [text]

9. *Have you ever been poisoned by fish? [YNDR]

IF NO: GO TO Q18

IF YES:
9A. How many times have you had fish poisoning in your lifetime? [#, DR]

9B. How many times have you had fish poisoning in the past five years? [#, DR]

IF One or More:
9C. How many times have you had fish poisoning in the past year? [#, DR]

Next, we'd like to know a little more about the fish poisoning you had.

IF "One" to Q9A:
9D. *In what month and year did you first have fish poisoning?
Month [January, February, March, April, May, June, July, August, September, October, November, December, Don't know, Refuse]
Year [year, dr]

GO TO Q10

IF "Two":
9E. *In what month and year did you first have fish poisoning?
Month [January, February, March, April, May, June, July, August, September, October, November, December, Don't know, Refuse]
Year [year, dr]

9F. *And, in what month and year did you next have fish poisoning?
Month [January, February, March, April, May, June, July, August, September, October, November, December, Don't know, Refuse]
Year [year, dr]

GO TO Q10

IF "Three":
9G. *In what month and year did you first have fish poisoning?
Month [January, February, March, April, May, June, July, August, September, October, November, December, Don't know, Refuse]
Year [year, dr]

9H. *And, in what month and year did you next have fish poisoning?
Month [January, February, March, April, May, June, July, August, September, October, November, December, Don't know, Refuse]
Year [year, dr]

9I. *And, in what month and year did you next have fish poisoning?
Month [January, February, March, April, May, June, July, August, September, October, November, December, Don't know, Refuse]
Year [year, dr]

GO TO Q10

IF More than three:

Please consider the three most recent times you had fish poisoning.

9J. *In what month and year did you most recently have fish poisoning?
Month [January, February, March, April, May, June, July, August, September, October, November, December, Don't know, Refuse]
Year [year, dr]
9K. *And, in what month and year did you most recently have fish poisoning prior to that?
Month [January, February, March, April, May, June, July, August, September, October, November, December, Don't know, Refuse]
Year [year, dr]

9L. *And, in what month and year did you most recently have fish poisoning before that?
Month [January, February, March, April, May, June, July, August, September, October, November, December, Don't know, Refuse]
Year [year, dr]

GO TO Q10

For the next few questions, please consider the most recent time you had fish poisoning.

10. *What type of fish do you believe caused your symptoms? [INT: Do not read. Mark ONE.]
[checkbox
Barracuda
Carang
Grouper
INT: If "Grouper," prompt for specific type & mark. If specific type not known, just mark "Grouper."
Black grouper
Gag
Red hind
Red grouper
Roch hind
Scamp
Yellowfin grouper
Hardnose (Blue Runner)
Hogfish
Jack
INT: If "Jack," prompt for specific type & mark. If specific type not known, just mark "Jack."
Amber jack
Bar jack
Black jack
Blue runner
Horse-eye jack
Yellow Jack
Olewife ('Old Wife') / Triggerfish
Mackerel
INT: If "Mackerel," prompt for specific type & mark. If specific type not known, just mark "Mackerel."
Cero mackerel

King mackerel / Kingfish
'Pot fish' (Small fish caught in fish traps)
Snapper
INT: If "Snapper," prompt for specific type & mark. If specific type not known, just mark "Snapper."
Blackfin snapper
Cubera snapper
Dog snapper
Gray snapper
Yellowtail snapper
Other
Don't know
Refuse]

IF "Other"
10A. Specify 'other' type of fish [text]

11. *Did you eat that fish at home, at a restaurant, or somewhere else? [Home, Restaurant, Other, Don't know, Refuse]

IF OTHER:
11A. *Where was that? [text, DR]

IF Q11 NOT RESTAURANT:
11B. *Did you buy the fish or did someone in your household catch the fish? [Buy, Catch, Other (describe), Don't know, Refuse]

IF Q11B OTHER:
11B1. *How did you get the fish? [text, DR]

IF Q11B PURCHASED:
11C. *Where did you buy the fish? [Local fisherman / Fish market, Grocery Store, Other, Don't know, Refuse]

IF OTHER: 11C1. [text, DR]

12. *Do you know where the fish was caught? [YNDR]

IF YES:
12A. *Where was the fish caught? [North of island, South of island, Away from Island – North, Away from Island – Southwest, Away from Island – Southeast, Don't know, Refuse]

13. How soon after you ate the fish did your first symptoms of fish poisoning appear? [text, DR]

14. *What symptoms of fish poisoning did you have? [INT: Do NOT read. Mark ALL that apply.] [checkbox
Abdominal pain
Diarrhea
Hot and cold reversal
Tingling / numbness in hands or feet
Weakness

Other
Don't know
Refuse]

IF OTHER: 14A. Describe 'other' symptoms [text, DR]

FOR EACH RESPONSE GIVEN:
14B. How many days did you have [symptom]? [#, DR]

15. *Did the symptoms cause you to take to bed? [YNDR]

IF YES:
15A. *How many days did you stay in bed? [#, DR]

16. Did the symptoms make you miss work? [YNDR]

IF YES:
16A. How many days of work did you miss? [#, DR]

17. How did you treat your symptoms from fish poisoning? [INT: Prompt if needed. Do not read. Mark ALL that apply.]
[checkbox
Went to the emergency room
Visited a local medical clinic or doctor
Benadryl
Brown sugar
Bush tea
Charcoal
Mauby Bark
Other over-the-counter medicine
Other
Don't know
Refuse]
IF "Went to the emergency room" or "Visited a local medical clinic or doctor":
17A. Did your trip to the emergency room, doctor, or clinic cost you any money? [YNDR]

IF YES:
17A1. How much money did you spend to go to the emergency room, doctor, or clinic? [$, DR]

17B. Were you prescribed any medication by the emergency room, doctor, or clinic? [YNDR]

IF YES:
17B1. How much money did you spend on the prescriptions? [$, DR]

Next, we have a few questions about fish poisoning among other members of your household.

18. I first need to ask, how many total people live in your household including yourself? [#, R]

IF ONE (OR REFUSE): GO TO Q22

IF MORE THAN ONE, Continue

19. In the past five years, has anyone else in your household had fish poisoning? [YNDR]

    IF NO, DON'T KNOW, REFUSE GO TO Q22

IF YES, Continue

20. How many total episodes of fish poisoning have other people in your household had in the past five years? [#, DR]

IF One or More:

21. And, how many total episodes of fish poisoning have other people in your household had in just the past year? [#, DR]

Finally, I just have a few demographic questions for statistical purposes.

22. *Gender [Don't ask; just record] [Male, Female]

23. What area of the island do you live in? [North, South, East, West, Charlotte Amalie, DK, R]

24. *What is your age in years? [#, R]

25. *Were you born in the Caribbean? [YNDR]
    IF NO:
    25A. Where were you born? [text, R]
    IF YES:
    25B. On which island were you born? [INT: Do not read. Mark ONE response.]
    [check box:
    Anegada
    Anguilla
    Antigua
    Barbados
    Dominca
    Haiti / Dominican Republic (Santo Domingo)
    Jamaica
    Jost Van Dyke
    Puerto Rico
    St. Croix
    St. John
    St. Kitts/Nevis
    St. Lucia
    St. Marteen
    St. Thomas
    Tortola
    Vigin Gorda
    Other
    Don't know]

25C. **IF 'Other'**: [text]

26. *What is the highest level of education you have completed? [Some high school or less, High school graduate, Some college, College graduate, Refuse]

27. Is your household's total yearly income before taxes $35,000 or less, or more than $35,000? [$35,000 or less, More than $35,000, DK, R]

    IF $35,000 or less:
    27A. And is that: [Less than $20,000; $20,000 up to $30,000; $30,000 up to $35,000; DK; R]

    IF More than $35,000:
    27B. And is that: [$35,001 up to $50,000; $50,000 up to $75,000; $75,000 up to $100,000; more than $100,00; DK; R]

28. Do you have a working cell phone? [YNDR]

    IF NO:
    28A. Does anyone in your household have a working cell phone? [YNDR]

29. *How often do you currently have a drink containing alcohol [INT: Prompt if needed – "any alcoholic beverage including beer, wine, and liquor"]? [Never; Once a month; 2 to 4 times a month; 2 to 3 times a week; 4 or more times a week; Other (describe); DK; R]

    IF NOT 'Never'
    29A. *How often do you drink more than five drinks containing alcohol at one time [INT: Prompt if needed – "in one sitting," or "on one occasion"]? [1 to 3 times per week; Less than once a week, but at least once a month; Less than once a month; More than 4 times per year; Fewer than 4 times per year; Never; DK; R]

30. *Do you currently smoke tobacco [INT: Prompt if needed – "cigarettes, pipe, cigars"]? [YNDR]

    IF NO:
    30A. Are you a former smoker who quit smoking, or were you never a smoker? [Former smoker; Never smoked; Refuse]

31. *Have you ever had any of the following medical problems?

    A. Diabetes [YNDR]
    B. Cancer [YNDR]
    C. Stroke [YNDR]
    D. Kidney disease [YNDR]
    E. Heart problem [YNDR]
    F. High blood pressure [YNDR]
    G. Jaundice or hepatitis [YNDR]

32. Would you like to add any other comments about fish poisoning? [YNDR]

    IF YES: 32A. Comments [text]

33. Do you have any questions regarding this study or your rights as a participant? [YNDR]

IF YES: *For questions regarding this study you may contact Dr. Mike Scicchitano at the Florida Survey Research Center toll free at 866-392-3475. For questions regarding your rights as a participant you may contact the University of Florida Institutional Review Board at 352-392-0433*.

That concludes our survey, thank you very much for your time and participation.

APPENDIX B
FLORIDA CIGUATERA CASE DEFINITION AND DATA COLLECTION FORM[d]

Case Definition

A. Clinical description

Symptoms include abdominal cramps, nausea, vomiting, diarrhea, numbness and paresthesia of lips and tongue, paresthesias of the extremities, metallic taste, arthralgia, myalgia, and blurred vision. Paradoxical temperature sensation is sometimes seen. The illness is associated with the consumption of reef or bottom-dwelling fish such as barracuda, amberjack, grouper, or snapper.

B. Laboratory criteria for diagnosis

There is no laboratory testing method to detect ciguatoxin in humans. Therefore, fish testing is strongly encouraged when a leftover sample is available and the clinical and epidemiologic evidence are consistent with CFP.

Detection of ciguatoxin in implicated fish is strongly suggestive, but is not necessary for case confirmation.

C. Case definition

Confirmed: a clinically compatible illness in a patient with a history of fish consumption in the 24 hours before onset of symptoms

D. Comment

Even single sporadic cases should be reported as a single case outbreak to the regional environmental epidemiologist and be recorded on the case report form: Record of Ciguatera Intoxication. Testing for the toxin in implicated fish is available from the FDA.

[d] Reprinted from Florida Department of Health's Surveillance Case Definitions: http://www.doh.state.fl.us/disease_ctrl/epi/surv/CaseDefinitions/2013CaseDef_FINAL.pdf

Case Report Form

The current case report form has been in use since 2011 and is available at http://www.doh.state.fl.us/disease_ctrl/epi/surv/Ciguatera_CRF_v30.pdf or Figures B-1 and B-2. Prior to 2011, ciguatera specific information collected was more limited.

Ciguatera Case Report Form V30

This form is designed to be filled out electronically and attached to the case in Merlin, FDOH Reportable Disease Database.

*Blue fields are REQUIRED

Merlin case number: _____ County number: _____ Investigator: _____

PROFILE DETAILS

*Last name: _____ First name: _____ Middle: _____

Parent or guardian name: _____

*Gender: ☐ Male ☐ Female ☐ Unk *Birth (mm/dd/yy): _____ Death (mm/dd/yy): _____ *Race: ☐ American Indian/Alaska Native ☐ Asian/Pacific Islander ☐ Black ☐ White ☐ Other ☐ Unk *Ethnicity: ☐ Hispanic ☐ Non-Hispanic ☐ Unk

Street address: _____

City: _____ *State: _____ *Zip code: _____ *County: _____

Home phone: _____ Other phone: _____ Emergency phone: _____

CASE INFORMATION

*Imported: ☐ Acquired in FL ☐ Acquired in US, not in FL ☐ Acquired outside US ☐ Unk Origin: _____

*Outbreak: ☐ Outbreak-associated ☐ Sporadic ☐ Unk

Outbreak ID: _____ *Case classification: ☐ Primary ☐ Secondary ☐ Unk

Reporter type: _____ Reporter's name: _____

CLINICAL

Case definitions can be found on the Bureau of Epidemiology Internet site: http://www.doh.state.fl.us/disease_ctrl/epi/surv/CaseDefAug2008_ver1-2.pdf

*DX status: ☐ Confirmed ☐ Probable ☐ Suspect ☐ Unk Date onset (mm/dd/yy): _____

Follow-up status: ☐ Interviewed ☐ Investigated, not interviewed ☐ Not investigated Lab report date (mm/dd/yy): _____

Final known outcome: ☐ Died ☐ Ill at time of reporting ☐ Recovered ☐ Unk Date diagnosis (mm/dd/yy): _____

*Hospitalized: ☐ Yes ☐ No ☐ Unk Date reported to CHD (mm/dd/yy): _____

Prophylaxed: ☐ Yes ☐ No ☐ Unk ☐ N/A Date investigation initiated (mm/dd/yy): _____

Did patient visit an emergency department for this illness? ☐ Yes ☐ No ☐ Unk

SENSITIVE EMPLOYMENT/ATTENDANCE INFORMATION

*Day care: ☐ No ☐ Attendee ☐ Staff ☐ Unk

Company: _____ Last date attended (mm/dd/yy): _____ Phone: _____

Address: _____ City: _____ State: _____ Zip code: _____

*Occupation: ☐ No ☐ Food handler ☐ Healthcare worker ☐ Unk

Company: _____ Last date attended (mm/dd/yy): _____ Phone: _____

Address: _____ City: _____ State: _____ Zip code: _____

PROVIDER INFORMATION

Physician or medical facility name: _____

Address: _____ City: _____ State: _____ Zip code: _____

Phone: _____ Fax: _____ Email: _____

If hospitalized, specify dates: _____

SUMMARY OF INTOXICATION

When was the fish eaten (mm/dd/yyyy): _____ What time was fish eaten (military time ie: 16:50): _____

When did symptoms begin (mm/dd/yyyy): _____ What time did symptoms begin (military time): _____

Type of Fish Consumed: ☐ Grouper ☐ Snapper ☐ Barracuda ☐ Amberjack ☐ Hogfish Other: _____ ☐ Unk.

Where was fish obtained: ☐ Restaurant ☐ Fisher ☐ Grocer/Market ☐ Institution ☐ Unk.

Name of vendor: _____ Location: _____ ☐ Self Harvested

When was fish harvested (mm/dd/yyyy): _____ Length of Whole Fish: _____ (Approx. in Inches) ☐ Unk.

Weight of Whole Fish: _____ (Approx. in Lbs.) ☐ Unk. Location: _____ GPS location: _____

How did the fish taste: ○ Good ○ Foul Did you consume alchohol while you ate the fish: ○ Yes ○ No

Parts of Fish Consumed: _____ Any left over fish: ○ Yes ○ No

Amount of Fish Consumed: _____ (Approx. Ounces; 3 oz fish = checkbook) Was fish Shared: ○ Yes ○ No

Figure B-1. Florida Ciguatera Case Report Form, page 1

SUMMARY OF INTOXICATION (CONTINUED)

If others ate fish, please note names and contact information of those people:

Did others who consumed the fish get sick: ◯ Yes ◯ No If yes, note names and contact information of people:

REVIEW OF SYMPTOMS

(1) ☐ Nausea/Vomiting	(11) ☐ Chest Tightness	(21) ☐ Visual Difficulties
(2) ☐ Diarrhea	(12) ☐ Joint/Muscle Pain/Weakness	(22) ☐ Hallucinations
(3) ☐ Abdominal Pain	(13) ☐ Coordination/Dexterity Problems	(23) ☐ Headaches
(4) ☐ Loss of Appetite	(14) ☐ Difficulty Speaking/Articulating	(24) ☐ Tremors/Seizures
(5) ☐ Dry Mouth	(15) ☐ Difficulty breathing	(25) ☐ Attention/Concentration Problems
(6) ☐ Excessive Salivation	(16) ☐ Pain/difficulty urinating	(26) ☐ Depression
(7) ☐ Metallic Taste	(17) ☐ Dizziness/Vertigo	(27) ☐ Anxiety
(8) ☐ Itching/Rash	(18) ☐ Tingling/Numbness /Pain in Hands and/or Feet	(28) ☐ Irritability
(9) ☐ Slowed Heart Beat	(19) ☐ Tingling/Numbness/Pain in Teeth, Gums and/or Mouth	(29) ☐ Insomnia
(10) ☐ Rapid Heart Beat	(20) ☐ Temperature Reversal: Hot Feels Cold; Cold feels Hot	(30) ☐ Lack of Sex Drive

Which symptom was the chief complaint (use number associated with above symptoms, if possible):

Which three symptoms occurred first (use numbers associated with above symptoms, if possible):

Were there any delayed symptoms: ◯ Yes ◯ No

If so, which ones (use numbers associated with above symptoms, if possible):

Did they receive medical treatment: ◯ Yes ◯ No If yes, when:

Where was treatment received:

HEALTH AND MEDICAL INFORMATION

Has a physician diagnosed ciguatera: ◯ Yes ◯ No

If yes, where:

Was the fish sent for testing for ciguatera: ◯ Yes ◯ No

Sent by whom:

Are there results: ◯ Yes ◯ No

If yes, are they willing to provide lab results: ◯ Yes ◯ No

Have you had ciguatera before: ◯ Yes ◯ No

If yes, when:

Known allergies/sensitivities:

Were you recently exposed to insecticides or herbicides: ◯ Yes ◯ No If Yes, what kind:

If Yes, where:

If yes, when:

Interviewer:

Date of Interview:

Additional Comments:

Referral Source:

Figure B-2. Florida Ciguatera Case Report Form, page 2

APPENDIX C
CIGUATERA QUESTIONNAIRE FOR RECREATIONAL FISHERMEN

- Have you ever been diagnosed with ciguatera fish poisoning after eating saltwater fish?
    - Yes (skip to question 3)
    - No
    - Not sure

- Have you ever experienced vomiting and/or diarrhea combined with numbness around the mouth or hands, weakness in the legs, or reversal of hot and cold sensations after eating saltwater fish?
    - Yes
    - No (skip to question 18)
    - Not sure

- Did you or someone you know catch the fish that caused your symptoms?
    - Yes
    - No (skip to question 7)

- Where did you or someone else catch the fish that caused your symptoms?
    - Florida
    - Not in Florida (skip to question 6)
    - Not sure

- If in Florida, what was the nearest county to the location where the fish was caught? (drop down list of Florida coastal counties) (skip to question 11)

- If not in Florida, please specify where the fish was caught: (skip to question 11)

- Where did you obtain the fish that caused your symptoms?
    - Restaurant
    - Grocery store
    - Fish market
    - Other

- If other, where did you obtain the fish:

- Did you obtain the fish that caused your symptoms in Florida or outside Florida?
    - Florida (skip to question 11)
    - Not in Florida

- If not in Florida, where did you obtain the fish?

- What type of fish caused your symptoms?

- How long ago did your illness occur?
    - Within the past year
    - More than one year, but less than five years ago
    - More than five years ago
    - Not sure

- Were you a Florida resident when your illness occurred?
    - Yes
    - No

- Did you seek medical attention for your illness (select all that apply)
    - Went to emergency room
    - Went to private physician
    - Called poison control
    - Other
    - None (skip to question 17)

- Was any of this medical attention obtained in Florida?
    - Yes
    - No
- If other, please specify what medical attention you sought:

- How long did your symptoms last?
    - One week or less
    - More than one week but less than one month
    - 1-2 months
    - 3-4 months
    - 5-6 months
    - More than 6 months but less than one year
    - One year or more

- Do you take any measures to avoid ciguatera fish poisoning? If so, what measures do you take?

- Are there any ways you can tell whether a fish might be poisonous? What are they?

- Do you have any other comments about ciguatera fish poisoning?

- What is your zip code?

- Are you of Hispanic or Latino origin?

- First and Last Name (if Yes to question 1 or 2)

- Date of birth (MM-DD-YYY) (if Yes to question 1 or 2)

APPENDIX D
ROLES OF COAUTHORS

Ciguatera Incidence in the U.S. Virgin Islands Has Not Increased Over a 30 Year Time Period, Despite Rising Seawater Temperatures

- Elizabeth G. Radke: co-designed survey questionnaire and medical record review abstraction form; designed and performed all analyses and data management; managed IRB approvals; wrote entire draft

- Lynn M. Grattan: obtained study funding, co-designed medical record review abstraction form; reviewed survey questionnaire; commented on draft

- Robert L. Cook: provided input to analyses; commented on draft

- Tyler B. Smith: reviewed survey questionnaire; commented on draft

- Don M. Anderson: obtained study funding, reviewed survey questionnaire; commented on draft

- J. Glenn Morris: obtained study funding, co-designed survey questionnaire and medical record review abstraction form; commented on draft

- Non-author contributors: Margaret Abbott (performed medical record review); Vasu Misra (provided seawater temperature data); Florida Survey Research Center (performed telephone survey)

Influence of Cardiac Disease and Alcohol Use on the Development of Severe Ciguatera Illness

- Elizabeth G. Radke: contributed to development of data collection forms on cases; added questions to telephone survey questionnaire for purpose of analysis; designed and performed all analyses and data management; managed IRB approvals; wrote entire draft

- Lynn M. Grattan: obtained study funding, co-designed and managed enrollment and follow up of cases for analysis as a cohort (separate study); co-designed data collection forms; commented on draft

- J. Glenn Morris: obtained study funding, co-designed and managed enrollment and follow up of cases for cohort; co-designed data collection forms; commented on draft

- Non-author contributors: Margaret Abbott (study coordinator, performed data collection on cases); Sparkle Roberts

Epidemiology of Ciguatera in Florida

- Elizabeth G. Radke: designed survey questionnaire and performed email survey; obtained fisheries data; designed and performed all analyses and data management; managed IRB approvals; wrote entire draft

- Andrew Reich: provided surveillance data from FDOH, reviewed survey questionnaire, commented on draft; will perform data linkage between email survey and FDOH database

- J. Glenn Morris: reviewed survey questionnaire; commented on draft

- Non-author contributors: Kevin Hanson (assisted with distribution of email survey)

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Elizabeth Radke received her Bachelor of Science in Animal Sciences from the University of Kentucky in 2006 and her Master of Public Health in Epidemiology at the University of Pittsburgh in 2008. She then worked as the Arbovirus Surveillance Coordinator at the Florida Department of Health from 2009 to 2010. She received her Ph.D. in Epidemiology from the University of Florida in the spring of 2013. She also serves as the Editor of the One Health Newsletter.