INVESTIGATION OF THE DISTRIBUTION OF *AEDES AEGYPTI* IN MARICOPA COUNTY, ARIZONA

By Whitney M. Holeva-Eklund

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Approved:

Crystal Hepp, Ph.D., Chair

Timothy Behrens, Ph.D.

Joseph Mihaljevic, Ph.D.

David C. Folch, Ph.D.

ABSTRACT

INVESTIGATION OF THE DISTRIBUTION OF *AEDES AEGYPTI*

IN MARICOPA COUNTY, ARIZONA

WHITNEY M. HOLEVA-EKLUND

Aedes aegypti is the primary vector of dengue, yellow fever, Zika, and chikungunya viruses. In recent years, mosquito-borne diseases have reemerged as a pressing public health issue around the world, as the geographic distribution of mosquitoes has increased rapidly. Maricopa County, Arizona is at risk for outbreaks of disease caused by viruses transmitted by *Ae. aegypti* due to the established presence of the mosquito vector and the high volume of travelers coming to Arizona from areas with endemic *Ae. aegypti*-borne viruses. Although much research exists on the broad distribution of this mosquito, there is less understanding of the local distribution and range of the vector in a desert climate. This dissertation employs a combination of spatial analysis, statistical analysis, and phylogenomic analysis to develop a better understanding of the local factors that support mosquito populations and the movement of mosquito populations over time and space in Maricopa County, AZ; this is the first time these methods have been used to study the recently established mosquito population in this area. A better understanding of the *Ae. aegypti* population is a critical component of implementing effective public health efforts that address outbreaks of associated disease. The hypothesis of these studies was that *Ae. aegypti* is not uniformly distributed throughout Maricopa County and that genetically distinct populations are separated by short

distances given the commonly held belief that this mosquito travels very short distances during its lifetime. The results indicated that although there are areas within Maricopa County, AZ that appear to be more suitable for the vector, there is more extensive mixture between populations in Maricopa County than expected. Additionally, we found a positive association between *Ae. aegypti* adult female populations and median income and structure age in a given area, suggesting that older, wealthier neighborhoods may provide suitable habitat for this mosquito. Through the phylogenomic analysis, we identified two potential source locations from 2020 that are seeding populations of this vector throughout Maricopa County, AZ. Given these findings, it may be advisable to increase the range of public health and mosquito surveillance efforts related to the detection of *Ae. aegypti*-borne viruses; targeting vector control efforts to source locations or older, wealthier neighborhoods should also be considered. Importantly, it is essential to note that the findings presented in this dissertation are preliminary, and further research is urgently needed to better our understanding of the preferred habitat and range of the vector in this area.

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DEDICATION

This dissertation is dedicated to two people

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My husband, Kurt, for his constant love, support, and encouragement throughout this process (and for keeping me fed and reminding me to go outside when things got busy).

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I hope that I can inspire you to pursue your goals

the way you've inspired me to accomplish mine.

PREFACE

The chapters of this dissertation were originally written to appear as articles in various scientific journals. Combining these articles into dissertation format may have resulted in some redundancies in the information presented in each chapter.

Publication information for each chapter is as follows:

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Chapter 5:

In progress: Phylogeographic Investigation of *Aedes aegypti* in Maricopa County, Arizona

CHAPTER 1: INTRODUCTION

Broad Overview

In 2017, approximately 350 million people around the world were infected with one of the most common mosquito-borne diseases (dengue, malaria, lymphatic filariasis, chikungunya, Zika, yellow fever, Japanese encephalitis, or West Nile fever),[1] and about half of the world's population (nearly 4 billion people) resides in areas where they are at risk of contracting dengue virus alone.[2]

Mosquito-borne diseases are extremely costly, both in the sense of the lives lost or altered by these diseases and also in the amount of financial resources needed to combat their spread. For example, dengue virus, which is transmitted by *Aedes aegypti*, affects a large portion of the world's population at an enormous expense. One study in Puerto Rico revealed that there were about 61,000 suspected dengue fever cases between 2002 and 2010 with a cost of over $38 million a year on average during this time period; the costs increased to over $46 million annually after factoring in the expense of mosquito control efforts.[3] The cost of dengue virus infections alone (not including vector control) in the Americas is estimated to be an average of over $2 billion annually based on data from 2000 to 2007.[4] Worldwide, over 20,000 deaths from dengue fever occur yearly, with over 230 million people suffering through dengue virus infections; the overall expense of these infections is difficult to estimate because of the impacts on so many factors of society such as treatment, lost labor, lost tourism, disruptions to health care for other diseases resulting in lost work, mosquito surveillance, testing, and control, and many other areas.[5] These costs reflect just one

virus transmitted by one mosquito species, *Ae. aegypti*; considering all of the pathogens transmitted by *Ae. aegypti* (such as yellow fever virus, Zika virus, and chikungunya virus) increases the costs associated with the vector substantially.

The global burden of mosquito-borne disease is not spread equally among the world's countries or their populations. Generally, residents of low-resource countries who live in poverty are at the highest risk for contracting vector- or mosquito-borne diseases today,[6] although populations of mosquito vectors are rapidly expanding into additional territory around the globe. Importantly, even within countries or regional areas, the distribution of mosquito vectors and mosquito-borne diseases is not uniform. Many factors like weather patterns, vegetation, moisture, and socioeconomic factors (such as population density, median income, physical infrastructure, and human behaviors that either create or limit mosquito habitat) can influence the presence or abundance of mosquito populations and therefore the risk of associated mosquito-borne diseases.

Background

Historical and Modern Context

Mosquito-borne Disease around the World

Origin

Mosquitoes have existed for hundreds of millions of years,[7–9] and have developed a close relationship to humans and human settlements over millennia.[9,10] Outbreaks of disease caused by pathogens transmitted by *Ae. aegypti* have been described for thousands of years.

Early descriptions of disease possibly attributable to dengue virus were recorded as far back as the Chin Dynasty in China, between 265-420 AD.[11] It is unclear when or where exactly dengue first began to infect human populations, although it is clear that by the late 1700s outbreaks of the disease were occurring regularly in both Asia and the Americas.[12] It is thought that dengue virus first circulated among non-human primates in Asia and Africa before each of the four distinct serotypes independently jumped to humans.[12] The four dengue virus serotypes likely first became established in humans within the last century to no more than 1,500 years ago, with previous infections resulting from incidental encroachment into the sylvatic cycle of the virus.[12–14]

The first time that an outbreak of yellow fever was unmistakably described was in the year 1648 in Mexico; however, outbreaks had occurred long before this with descriptions possibly referring to yellow fever in Haiti in 1495.[15] Yellow fever virus is thought to have originated in Africa, first circulating in sylvatic cycles among non-human primates, and then causing disease among human populations after the domestication of the vector *Ae. aegypti*.[15]

Other diseases, such as those caused by Zika or chikungunya viruses have only recently emerged in human populations, reflecting the ever-evolving relationship between mosquitoes, the viruses they transmit, and humans. Chikungunya virus is thought to have originated in Africa and first been transmitted in an urban cycle some time between 1879 and 1956, when the virus was introduced to Asia,[16] however, it has only become a major threat to global public health in the past two decades.[17] Similarly, Zika virus circulated in sylvatic cycles in Africa causing sporadic incidental human infections until it explosively emerged in a series of outbreaks beginning in the 21st

century.[10] The relationship between mosquitoes and humans has a long history and continues to evolve today.

Past Impacts

Over thousands of years, humans and mosquitoes have developed a close but antagonistic relationship. Humans have impacted the evolution of mosquitoes while mosquitoes and the viruses they transmit have also impacted human history and evolution. For example, human settlements and water storage helped lead to the domestication of the mosquito *Ae. aegypti*.[18] Then, as global trade increased, the domesticated mosquito vector was spread around the world so that today roughly half of the global population is at risk of contracting viruses spread by the mosquito.[2,18] The impact of the relationship between humans and mosquitoes is felt in both directions. Specifically, the gene that causes sickle-cell anemia remains so prevalent in Africa because it provides protection from malaria for those who are heterozygous, despite causing poor health in humans who are homozygous for the gene.[19] However, despite this close relationship that has existed for millennia, only recently have mosquitoes been identified not just as a nuisance but also as a source of disease.

Beliefs

Mosquito-borne diseases have plagued humans throughout history, long before the discovery of their microscopic causative agents. Many people have attempted to explain the causes of such diseases, often citing spiritual or magical origins.[20] Although disputed, the name dengue is possibly derived from the Swahili phrase “Ka-dinga pepo” which refers to an illness caused by an evil spirit.[21] Likewise, for centuries, malaria was thought to be caused by “bad air” consisting of poison or decomposed matter.[20]

Discovery

Yellow fever was the first disease to be linked to mosquitoes. This connection was first suspected by Carlos Finlay, a physician from Cuba, in 1881; however, he was never able to adequately prove this assertion.[22] When the United States Army suffered massive casualties from yellow fever in Cuba during its war with Spain, Walter Reed was sent to investigate the causative agent of the mysterious disease.[22] Through a series of experiments where Dr. Reed infected nonimmune individuals, the link to *Ae. aegypti* was proven, although it would be many more years before the causative agent of yellow fever was identified as a virus.[22] Once the link between yellow fever and *Ae. aegypti* was discovered, massive campaigns in Cuba and Panama eliminated yellow fever in these areas, allowing the successful completion of the Panama Canal.[22,23]

Our current understanding of the spread of mosquito-borne disease has come a long way since the days where magic, spirits, or “bad air” was the suspected cause of these illnesses, and we now have the knowledge necessary to prevent and treat many of these diseases. However, people around the world still continue to suffer greatly from pathogens transmitted by mosquitoes. It remains unclear how or why invasive mosquito species are spreading to new areas, and additional research is urgently needed to prepare for outbreaks in areas that have not recently been affected by mosquito-borne disease.

Current Impacts

Each year, hundreds of millions of people around the world suffer from mosquito-borne diseases, and hundreds of thousands of people lose their lives.[1] The impacts of

dengue, yellow fever, Zika, and chikungunya viruses, which are all transmitted by *Ae. aegypti*, are discussed in detail in subsequent sections of this dissertation.

Other high-impact mosquito-borne diseases include the parasitic infections malaria, which infects over 200 million people annually, and lymphatic filariasis, which infects nearly 40 million people each year.[24] In 2020, malaria killed over 625,000 people.[25] Japanese encephalitis virus causes over 60,000 infections a year with a case fatality rate as high as 30%; in 30-50% of those who survive infection, permanent neurological complications occur, resulting in high levels of morbidity.[26] Over 3 billion people in Asia are at risk of infection with Japanese encephalitis virus.[26] West Nile virus first emerged in the United States in 1999[27] and is now the most common mosquito-borne disease in the country.[28]

Mosquito-borne diseases generally create a huge health burden for impoverished countries and populations throughout the world.[29] Malaria, for example, disproportionately affects the African Region, which was burdened with 95% of the cases and 96% of the deaths from this disease in 2020; most of the deaths occurred in children under five years of age.[25] However, mosquito-borne diseases are also believed to be expanding around the world, both increasing in incidence in endemic areas as well as spreading to new geographic territory.[24] The southwestern United States has recently experienced a boom in invasive *Ae. aegypti* populations as well as the recent identification of locally acquired cases of associated disease such as dengue.[30]

Expansion

Both mosquito populations and the burden of pathogens that they transmit have been expanding around the globe during the 21st century. Many of the mosquitoes that

effectively transmit diseases to humans are considered to be “invasive species” and therefore extremely adept at adapting to new environments and habitats.[31] These species include *Ae. aegypti*, *Ae. albopictus*, and *Culex* species.[31–33]

Importantly, especially for the work presented in this dissertation, it is unclear how invasive mosquito vectors are so easily adapting to thrive in new environments that were previously considered inhospitable.[31] Changing land use and land cover due to human development are leading theories that should be further explored.[31] Whatever the reason for such rapid expansion, the spread of invasive species is projected to increase putting billions of people in regular contact with these disease vectors.[33]

In addition to the rapid global spread of mosquitoes, multiple diseases caused by viruses transmitted by these mosquitoes have also exploded suddenly in new parts of the world. As outlined previously, Zika and chikungunya viruses have caused massive, unexpected outbreaks of great public health importance in new regions during the 21st century.[16,34] As more of the world becomes at risk for mosquito-borne diseases and new threats emerge, it is vital to prepare for additional outbreaks of disease in areas not accustomed to the threat.

Future/Climate Change

Another factor impacting the shifting range of mosquito vectors around the world is the influence of climate change. The success of mosquito populations is greatly dependent on ideal environmental conditions such as temperature and the availability of water for use as breeding habitat, both of which will be affected by a changing climate. However, it is difficult to predict the impacts of global climate change on mosquitoes, who are so dependent on conditions at the neighborhood level, resulting in a lack of

consensus on how climate change will alter the patterns of mosquito-borne diseases globally.[24]

Furthermore, the spread of mosquito vectors and their diseases is a more complex process influenced not only by weather but also by urban development, shifting population dynamics, and changing socioeconomic factors[33] which can be difficult to model and predict. It is challenging, if not impossible and inappropriate, to predict the impacts of climate change on mosquito-borne disease before a good understanding of all of the complex factors that drive the distribution of mosquito vectors is achieved.[35] Although climate change will likely have great impacts on vector populations, these impacts should only be viewed within the context of the much more complex tangle of interacting factors that influence their habitat, behavior, and interaction with hosts.

Vector Biology

Mosquitoes span a wide range of habitats throughout the world—while some species can survive in the arctic tundra, most of the approximately 3,500 species of mosquito reside in tropical and subtropical areas of the world.[36] Both the lifecycle of the mosquito and the transmission cycle of mosquito-borne pathogens depend on climatic factors such as temperature, rainfall, and humidity; however, the favorable conditions for each mosquito species can vary widely,[36] and mosquitoes should not be considered a monolith that can survive in only one single set of climatic conditions. Many mosquito species are also adept at utilizing “microclimates” to propagate their population to the fullest extent possible, even in areas where the general climate may be less than ideal.[36] An exhaustive review of the effects of climatic factors on mosquito vectors and mosquito-borne diseases is not feasible; this overview of the impact of climatological

variables will focus on *Ae. Aegypti*, the focus of this dissertation, and the viruses transmitted by this vector.

Aedes aegypti transmits multiple viruses that cause disease of public health importance, including, but not limited to: dengue, yellow fever, chikungunya, and Zika. The mosquito tends to live in warm, tropical environments as the biological functions of *Ae. aegypti*, such as the ability to take a blood meal, are hampered below a temperature of 14°C.[37] Field experiments have placed the suitable temperature range for survival of *Ae. aegypti* populations between 20-30°C.[38] However, laboratory experiments suggest that minimum and maximum temperatures at which *Ae. aegypti* survive less than one full day are 4°C and 42°C, respectively.[38] *Aedes aegypti* females lay eggs on container walls that can survive long periods of drought before hatching when covered with rainwater; however, too much rainwater can lead to container overflow which destroys the eggs.[39,40] In regions where winter temperatures are not conducive to *Ae. aegypti* survival, winter rains can prove detrimental to *Ae. aegypti* populations in the area.[39] Counterintuitively, areas that have regular dry spells may create breeding habitat for *Ae. aegypti* due to the increased use of water storage containers by human populations which thereby creates breeding habitat for the mosquito vector.[40,41] Laboratory studies suggest that in addition to temperature, relative humidity may impact the ability of *Ae. aegypti* to perform biological functions, such as lay eggs,[42] and the longevity of *Ae. aegypti* was found to be greater under high humidity laboratory conditions as compared to low humidity laboratory conditions.[43] In addition to the effects of climatological variables on the survival of *Ae. aegypti* populations, temperature has also been found to impact the ability of these mosquito vectors to transmit disease. Within the suitable

temperature range for *Ae. aegypti*, higher temperatures resulted in an increased ability for the mosquito vector to transmit dengue virus.[44,45]

Of course, climatological factors are not the only characteristics of the environment that vary from region to region. Natural landscapes, land use, built environment infrastructure, and socioeconomic factors also vary greatly and can impact the relationship between climatological variables and mosquito vectors or mosquito-borne diseases. *Aedes albopictus*, an invasive mosquito species considered to be similar to *Ae. aegypti*, was found to be more abundant in lower-income neighborhoods with more dilapidated infrastructure; however, when rainfall was low, the mosquito vector was more abundant in higher income neighborhoods where container habitats were filled by human activity.[46] Although mosquito vectors rely on aquatic habitat for reproduction, human activity in the arid climate of the desert southwest United States can create artificial container habitats that allow mosquitoes to propagate even when rainfall is limited.[47] Further, in areas with similar climates, disparities in mosquito-borne disease can exist due to differences in knowledge about and practices related to mosquitoes and the prevention of mosquito-borne diseases among groups with different socioeconomic factors.[48] Mosquito populations may rely on different available habitat throughout the year in regions with varying socioeconomic status; the containers available depending on the socioeconomic level of a neighborhood may provide key habitat to mosquito vectors during different times of the year with varying weather patterns, including cooler winter months.[49] Although climatological factors play a large role in the ability of mosquito vectors to survive and limit the range of mosquito vectors to certain regions around the world, small area socioeconomic factors clearly interact

with climate at a local level to influence the abundance of mosquito vectors and the prevalence of mosquito-borne diseases within a region with established mosquito populations.

Aedes aegypti have adapted to be able to survive in environments altered and created by humans, thriving in urban environments where they face little to no threat from natural predators.[50] They primarily reproduce in human-made artificial containers.[50] The preferred container for oviposition is of larger volume,[51] dark in color, exposed to enough sunlight to create ideal water temperature for larval development, and has a minimal amount of decomposing organic matter.[52,53] Female *Ae. aegypti* often attempt to increase the chances of producing successful offspring by laying eggs on the walls of multiple containers; many females choose containers that already contain *Ae. aegypti* larvae, likely responding to conspecific indicators that certain containers are of suitable quality for oviposition.[52,53] See Abreu et al., 2015[52] and Wong et al., 2011[53] and additional studies cited within these papers for a more comprehensive discussion of *Ae. aegypti* oviposition behavior and site selection. Although *Ae. aegypti* are well-suited to living in urban environments throughout the world and the United States, the invasive mosquito species *Ae. albopictus*, which was introduced to the United States in 1985, can impact *Ae. aegypti* populations through interspecies competition.[54,55] In Maricopa County specifically, however, *Ae. albopictus* has never been trapped, indicating that *Ae. aegypti* may face no interspecific competition for habitat and resources.

Aedes aegypti females have a small range, and most remain within about 100 to 200 meters from where they originated[56,57] unless the conditions of the immediate environment are unsuitable for reproduction in which case *Ae. aegypti* females have

been observed to disperse up to 2.5 kilometers from their origination point.[58] The tendency for these mosquitoes to remain in and seek out areas with well-suited habitat indicates that small area, neighborhood level environmental factors, which are influenced by socioeconomic characteristics, likely have a considerable influence on the ability of *Ae. aegypti* to survive in specific areas. This small range may also indicate that populations of this vector remain mostly isolated from one another potentially resulting in genetically distinct populations unique to individual neighborhoods within Maricopa County.

The mosquito vector *Ae. aegypti* is highly anthropophilic and relies nearly exclusively on human blood meals and habitats for reproduction.[10,59] *Aedes aegypti* females feed preferentially on human blood, even if other potential hosts or sugar meals are available.[60] The mosquito is also known to take blood meals from multiple human hosts during one gonotrophic cycle.[61] *Ae. aegypti* is generally most active during daytime hours which increases potential interactions between the mosquito vector and humans.[62] Altogether, these behaviors make the mosquito an extremely efficient vector of disease.

Dengue, yellow fever, and the newly emerged threats of chikungunya and Zika viruses are primarily transmitted in an urban cycle where the virus can be passed from human to mosquito to human.[63] The maintenance of urban transmission cycles of these diseases requires the co-existence of *Ae. aegypti* mosquitoes[10,59,64] and humans[65] in the same geographic spaces. Travelers, including United States residents returning from their travels, can potentially introduce diseases to the established but naïve mosquito populations at their travel destination in the United States because viruses

can be passed from humans to *Ae. aegypti*.[63] In the fall of 2022, a locally acquired case of dengue fever was identified in Maricopa County, demonstrating the feasibility of transmission in this region.[30] In areas where *Ae. aegypti* is present year-round, such as Maricopa County where the mosquito has established a year-round presence only within the last decade, a single introduction could lead to the disease becoming endemic in the mosquito population. The presence of this competent vector species has allowed for viruses such as dengue, Zika, and chikungunya to be introduced to and locally transmitted in the United States in the past.[33] Therefore, concern about these viruses becoming established in an urban transmission cycle in areas of the United States with established *Ae. aegypti* populations is warranted.

Relevant Diseases

Dengue

Over half of the world's population resides in areas that are at risk for outbreaks of dengue.[66] Importantly, the dengue virus has four serotypes, so individuals can be infected more than once and subsequent infections are potentially harsher and more life threatening.[66,67] Although extremely unpleasant, most dengue infections are generally flu-like and self-limiting.[66,67] Infection with dengue virus is typically not lethal; however, infected patients can also present with the much more severe dengue hemorrhagic fever which was first reported in the Americas during an outbreak in Cuba in 1981.[67–69] Untreated severe dengue infections can have a mortality rate as high as 20% and nearly 60% of those who survive severe dengue report persistent symptoms up to two years after the infection occurred.[67]

Due to the widespread occurrence of dengue, the disease has serious impacts both on global health and on the global economy. It is estimated that dengue causes between about 100 million to 400 million infections annually worldwide.[67,70] In 2013, over 13,000 people globally are estimated to have died from dengue, and the global cost of the disease was estimated to be between 8-9 billion USD.[71] A record number of dengue cases, over 2.7 million, were reported in the WHO Region of the Americas in 2019; likewise, many countries in Asia and Africa also reported a higher than previously observed incidence of dengue infections in 2019.[72] Record numbers of reported cases of dengue in the Americas, as well as higher than normal numbers in Asia and Africa led the WHO to declare dengue “the fastest spreading mosquito-borne viral disease in the world” and to include the disease among a list of the world’s top ten threats to public health.[73]

Dengue has expanded its distribution throughout the world in the last few decades, and has caused locally transmitted cases in the United States.[67] Dengue likely circulated locally in Houston, Texas between 2003-2005, although routine dengue surveillance is not common in this area and dengue cases may be generally underreported.[74] Additionally, local transmission of dengue was reported in Key West, Florida in 2009 where, similar to Texas, dengue surveillance is not routine.[75] These outbreaks of dengue virus in Texas and Florida in the last 15 years resulted in 25 and 90 reported cases of dengue infection, respectively.[76] A serosurvey conducted in 2004 in Brownsville, Texas found that 40% of residents had evidence of past infection of dengue,[77] and during the 2009 dengue outbreak in Key West, Florida, a serosurvey

revealed that between 3-5% had evidence of dengue infection.[75] This evidence has raised concerns about the potential for dengue to establish itself in the United States.

In Arizona, seventeen travel-related cases of dengue infection were reported in 2019, twelve of which were identified in Maricopa County.[78] More recently, five (four) cases were reported in Arizona (Maricopa County) in 2020, eight (seven) in 2021, and 9 (6) in 2022, including one locally acquired case in the Phoenix area.[79] Furthermore, as recently as 2014, outbreaks of dengue resulting in nearly 100 reported cases have occurred along the Arizona-Mexico border in Yuma, Arizona which is less than 200 miles from densely populated Maricopa County.[80] In Maricopa County, a locally acquired case of dengue was reported in Fall 2022.[30] Sonora, Mexico, which is just south of the Arizona-Mexico border, recorded 982 and 2,606 probable cases of dengue in 2018 and 2019, respectively.[81] No widespread surveillance has been conducted in Arizona, and it is unknown what proportion of the population has had past exposure to dengue. Additionally, mosquito samples are not regularly tested for dengue virus. Although dengue is not thought to be routinely circulating in Maricopa County, the recent expansion of the *Ae. aegypti* population, travel-related introductions of the virus into this area, and a recently identified locally acquired case of dengue fever has increased the risk of a dengue outbreak in this region.

Yellow Fever

Yellow fever virus first emerged in central Africa approximately 750 years ago.[82] The yellow fever virus lineages circulating in the Americas are an ancestor of the Western African lineage; these lineages diverged during the time the slave trade was active suggesting that yellow fever was imported to the Western Hemisphere on slave

ships.[82] Today, yellow fever infections occur regularly in South America when a person is inadvertently infected by mosquitoes involved in sylvatic transmission cycles with non-human primates; in Africa, urban outbreaks where the virus is transmitted from human to mosquito to human are more common.[83] Diagnosis of yellow fever can be difficult due to similarities with other mosquito-borne diseases in endemic regions. One estimate places the burden of yellow fever in Africa between 63,000-158,000 yearly severe infections and between 29,000-75,000 related deaths and the burden in South America between 4,000-15,000 annual severe infections and between 2,000-7,000 related deaths.[83]

Historically, yellow fever plagued coastal areas in North America from the 18th to 20th centuries as introductions of the virus from endemic areas regularly caused urban outbreaks.[84] Despite the United States being outside of the modern day commonly infected area, yellow fever virus caused an estimated 5,000 deaths in Philadelphia during the summer and fall of 1793.[85] This outbreak illustrates the devastating consequences that occur when the introduction of infected travelers or mosquitoes is combined with the presence of a competent vector species; it also illustrates the possibility of outbreaks at much higher latitudes than commonly occur today. After *Ae. aegypti* mosquitoes were identified as the responsible vector for yellow fever spread in the early 20th century, mosquito control efforts helped to decrease the spread of yellow fever in non-endemic areas.[84]

Those who develop symptoms from infection with yellow fever virus experience fever, vomiting, kidney failure, and hemorrhaging which can lead to death.[84] A vaccine that effectively protects recipients from yellow fever has existed since the 1930s, but

lack of vaccine coverage due to funding issues leading to a shortage of needed doses as well as concerns about adverse reactions has allowed the disease to persist as a major threat to public health around the world as many people remain vulnerable to yellow fever infections.[84,86] An introduction of the virus to a non-endemic area is of great concern, as the population in such a region would have no existing natural or artificial immunity and a large outbreak would strain emergency vaccine supply (the World Health Organization maintains an emergency stockpile of about 7 million doses).[84,86] Overall, the yellow fever vaccination has been a great public health success: between 20 and 60 million doses are administered yearly and it is estimated that vaccinations help to prevent over 100,000 cases of yellow fever annually.[84,87] However, because yellow fever is maintained in sylvatic cycles where the virus is transmitted between non-human primates and mosquitoes, vaccination campaigns can never fully eradicate yellow fever.[83,84] Therefore, mosquito control remains an important component to reducing the burden of yellow fever in areas with potential for an urban outbreak.

Zika

Zika virus was first discovered in Uganda in 1947 during surveillance for yellow fever, and caused mild, sporadic illness in humans prior to the occurrence of large unexpected clinically relevant Zika virus outbreaks beginning in the Pacific islands in 2007.[88,89] It is believed that the virus circulated widely in Africa and Asia prior to the outbreak of 2007, but the disease was thought to be of little clinical importance and therefore few cases had been recorded.[90] Between 2015-2017, a large outbreak of Zika virus in the Americas resulted in over 3,000 cases of microcephaly associated with Zika infection and was estimated to cost between 7 to 18 billion USD during the outbreak

alone.[91,92] To this day, it remains unclear whether Zika virus infections historically caused major medical complications such as microcephaly that went unnoticed due to a lack of surveillance or if these complications were newly acquired features of infection at the time of this outbreak.[90]

The transmission of Zika virus has been extensive, causing outbreaks in over 87 countries.[90] In the mainland United States in 2016, over 200 cases of locally-transmitted Zika were recorded in Florida and 6 locally-acquired cases of Zika were reported in Texas.[93] Zika virus has been circulating autochthonously in Mexico since 2015 and is estimated to have caused over 270,000 human infections since that time.[94,95] Sonora, Mexico, which borders Arizona to the south, recorded over 300 laboratory-confirmed cases of Zika virus (the most cases of all Mexican states) in 2018.[96]

It is estimated that between 50-80% of people infected with Zika virus experience no symptoms.[90] Those who do develop symptoms generally experience mild illness of fever, headache, joint pain, or rash which resolves within about 10 days.[88,97] More severe complications can occur when pregnant women are infected including preterm birth, miscarriage, microcephaly, neurological complications, or physical abnormalities.[88,97,98] Infants that were infected in utero but were not born with microcephaly were observed to be at higher risk for neurodevelopmental delays at 18 months of age suggesting that the long-term complications of Zika infection have yet to be fully realized.[99]

Prior infection with dengue virus has been shown to limit the severity of a Zika infection;[90] however, prior infection with Zika virus increased the risk of contracting a severe case of dengue virus.[100] At the peak of the Zika outbreak in Brazil, it was

estimated that 60% of the population residing in areas exposed to Zika were infected[90] which raises concerns about the risk of future severe dengue outbreaks in the Americas.

Although large outbreaks have not been observed in the Americas since 2017, Zika virus has not disappeared and may even be circulating silently in the Americas.[90] Outbreaks and infections continue to occur regularly in India and Southeast Asia.[90] Large pockets of susceptible populations who were not infected during the previous large outbreak still remain in the Americas, and transmission is still regularly observed in this region.[90] Further, Zika virus RNA has been isolated from non-human primates in Brazil, which raises concerns for the establishment of a sylvatic viral transmission cycle.[90] Although the focus has shifted away from Zika virus in recent years as the large outbreak in the Americas subsided, the virus has not gone away and concern remains for future spread especially as the range of the virus' primary vector, *Ae. aegypti*, expands.

Chikungunya

The spread of chikungunya virus has been poorly recorded and is not well understood, especially because chikungunya symptoms are easily confused with dengue fever which often cocirculates in the same areas.[101,102] Chikungunya virus was first isolated in Tanzania in 1953 (although it is suspected that it circulated in Africa for centuries prior)[103] and is known to cause disease consisting of fever, rash, and debilitating joint pain which can persist in 30-40% of infected individuals for several months and in about 10% of patients for years after infection.[101,102,104] The name of the virus itself is a Swahili word meaning "that which bends up" and refers to the

devastating joint pain associated with the virus that causes those infected to walk hunched over.[105] For the first time during outbreaks of the 21st century, occasional neurological complications or deaths have also been associated with chikungunya infection and neonatal infections resulting in severe morbidity were observed.[101,104] Severe chikungunya is generally observed in vulnerable populations (neonates, the elderly, and those with comorbidities).[102,104] Unlike the other diseases transmitted by *Ae. aegypti*, asymptomatic infections of chikungunya virus are less common, with only 5-25% of those infected experiencing no symptoms.[102]

Historically, since the first documented outbreak of chikungunya in 1953, the virus has caused sporadic infections and larger epidemics throughout southeast Asia and Africa.[101,102] Epidemics tend to be sudden, unanticipated, and large with attack rates of 33-45% observed.[101,104] In the first outbreak in India since 1973, over 1.4 million infections were recorded in 2006.[101,102] Recent outbreaks highlight the lack of knowledge currently held about this virus: it is unclear if the outbreaks were caused by new introductions or changes to the virus or were simply the result of a resurgence of undetected virus circulating between the vector and other mammalian populations.[101]

Chikungunya has developed as a potential global health threat in the past decade, as the disease has emerged rapidly in the Americas beginning with the Caribbean outbreak in 2013.[102,106] In the United States, over 200 infected travelers were reported, and autochthonous transmission was observed in Florida.[102] Given that chikungunya can be transmitted from humans to mosquitoes and back to humans, infected travelers arriving in areas with an established competent vector population can potentially initiate an outbreak, especially in areas where the population has no current

immunity to the disease.[102] Further, the virus can be vectored by both *Ae. aegypti* and *Ae. albopictus*,[102,107] placing large regions in the Americas and Europe at risk for transmission.[103] It remains unclear why outbreaks were not observed in the Americas until 2013 even though ideal conditions were previously present (naive human population, presence of competent vectors, identification of imported cases);[107] however, the subsequent large epidemics observed illustrate that outbreaks are possible when the virus is introduced to areas with an established vector presence. Although promising vaccine candidates have been developed in the past, there is currently no vaccine or treatment available for chikungunya and prevention relies on mosquito control efforts.[101]

Other Diseases

In addition to the diseases that are most relevant to public health around the world discussed in the previous sections (dengue, yellow fever, Zika, and chikungunya viruses), *Ae. aegypti* is potentially capable of transmitting many more viruses to animals or humans. Past studies have shown the potential for the mosquito to act as a vector for emerging viruses such as Mayaro virus,[108–110] western equine encephalomyelitis virus,[111] Ross River virus and Murray Valley encephalitis virus,[112] and Sindbis virus.[113] Although these viruses are not currently associated with significant public health impacts, the rapid emergence of outbreaks associated with *Ae. aegypti* in the past illustrate the need to remain vigilant in preparing for the next epidemic threat, especially as this vector expands its range into new regions and habitats around the world.

Mosquito-borne Disease in the US

Origin

Although mosquito-borne diseases have recently drawn much attention as "emerging" diseases in the United States, they actually have a long history in the Americas, including the United States. Many mosquito species and mosquito-borne diseases were introduced to the western hemisphere during the period of colonization and slave trade that occurred in the 16th and 17th centuries. One example is the introduction of malaria by Europeans and enslaved Africans during this period; subsequently, malaria spread throughout much of the United States and caused routine outbreaks until the 1950s.[114] Similarly, yellow fever was brought to the United States from Africa or the Caribbean on ships beginning in the 17th century; outbreaks were regularly observed as far north as Boston and throughout the southeastern United States.[115] An outbreak of dengue was first described in the United States in 1780 in Philadelphia, Pennsylvania, and epidemics of dengue occurred with regularity in the southern United States until the 20th century.[116]

Although some mosquito populations or diseases have a long history in the United States, others have only been introduced recently. *Aedes albopictus* did not become established in the United States until the 1980s, despite multiple prior introductions of the vector; since the 1980s, the mosquito has spread throughout the country and has an established population in over 27 states.[117] West Nile Virus has become established throughout the country following its introduction into New York City in 1999.[118] It remains unclear exactly when or how the virus was imported into New York City, but from there it was able to spread across the United States within just a few

years.[118] Both long established and recently introduced mosquito-borne viruses have caused human morbidity and mortality in the United States.

Major Outbreaks/History

Although we typically do not think of the United States as a hotbed of mosquito-borne disease in modern times, mosquitoes and the diseases they transmit tormented the country in the past. Outbreaks occurred regularly in North America between the 17th and 19th centuries resulting in hundreds of thousands of deaths and hundreds of millions of dollars in economic loss.[15,115] In the summer of 1793, a large outbreak of yellow fever in Philadelphia, Pennsylvania played a part in the decision to relocate the capital of the United States to Washington.[116,119] During the American Civil War, over 1.3 million infections and 10,000 deaths were attributed to malaria, causing several Union army failures that are blamed for extending the war by several years.[120]

Notable outbreaks of yellow fever include Philadelphia, Pennsylvania in 1793 resulting in about 5,000 deaths (about 8-9% of the city's population at the time), Philadelphia in 1798 resulting in about 3,500 deaths, and New Orleans, Louisiana in 1853 resulting in about 9,000 deaths (about 9% of the city's population).[115] Outbreaks generally occurred in port cities and did not spread inland due to a lack of infrastructure and travel connecting the cities at that time.[115] Large dengue outbreaks were also common. About 40,000 cases were reported in New Orleans, Louisiana in 1873, about 16,000 cases were reported in Austin, Texas in 1885-1886 (the city was home to 22,000 people at that time), and in 1922 there were about half a million dengue cases in Texas.[121] More recently, over 20,000 cases of West Nile Virus disease have been reported across the United States from 2009-2018.[122] Despite this history, we typically

view large and devastatingly deadly outbreaks of mosquito-borne disease in the United States as a relic of the past; however, the threat of mosquito-borne diseases has not completely gone away. This history demonstrates the possibility of outbreaks of mosquito-borne disease throughout the United States and reminds us of the need to remain vigilant and prepared.

Disappearance and Reemergence

Once it was discovered that the diseases causing devastating outbreaks around the country were transmitted by mosquitoes, a massive campaign was initiated to reduce mosquito populations. Beginning in the early 20th century, mechanical efforts (such as improving sanitation or creating drainage) were undertaken across the country to reduce mosquito populations, followed by chemical control efforts (such as the discovery and application of pesticides) in the mid-1900s.[123] Although initially very successful, mosquito control efforts soon fell out of favor as mosquito-borne disease disappeared in the United States, environmental concerns increased, and the willingness to provide funding dwindled.[123] Since widespread mosquito control efforts ended, mosquito populations throughout the country have returned to greater species diversity and abundance.[124] New threats have emerged as invasive species spread to new habitat and new diseases are introduced to the country.

Future/Climate Change

It is nearly impossible to predict the future of mosquito-borne diseases in the United States, since mosquito populations and disease transmission by mosquitoes are impacted by a wide range of factors such as climate, socioeconomic factors, travel, mosquito control efforts, evolution of insecticide resistance or competitively

advantageous traits, and, of course, stochasticity. However, it is clear that new threats have emerged in the 21st century, and it is likely that additional threats will continue to emerge in the future.

There remain many unknowns about how invasive mosquitoes are spreading and adapting to thrive in new urban environments.[31] It is possible that humans are creating selective pressure for additional anthropogenic mosquito populations in urban environments by creating additional artificial breeding habitats and limiting the natural predators of mosquitoes in these areas.[31] It is vital that we continue to conduct surveillance for existing and emerging threats and continue to seek a better understanding of how invasive mosquitoes are thriving in urban environments in the United States. Although we have become accustomed to a low risk for mosquito-borne disease in the United States in recent times, looking to our past makes it clear that we are not immune to the devastating impacts of mosquito-borne diseases, as illustrated by the history of outbreaks that have occurred in this country. We must continue to be vigilant and prepared for the possibility of mosquito-borne disease in the future by studying and understanding the populations of mosquitoes present in our country.

Mosquito-borne Disease in Arizona

History of Mosquitoes and Aedes aegypti in Arizona

Although much of Arizona is a dry, desert habitat, the state is not currently and never has been immune to mosquito-borne disease. Archaeological records indicate that malaria may have been introduced to Southeastern Arizona as early as the 16th century and became endemic by the 18th century.[125] Although no one was aware of the link between mosquitoes and malaria at the time, in the 1800s, multiple military posts

were relocated due to “miasmic air” causing malaria.[125,126] One such fort in what is today Graham County in Eastern Arizona was abandoned in 1871 due to consistent outbreaks of malaria.[127] Malaria is not routinely transmitted in Arizona today, but other mosquito threats have emerged.

Aedes aegypti was trapped in Arizona as far back as 1931 to 1946 in Tucson and in 1951 in Yuma.[128–130] The Arizona Department of Health Services initiated a mosquito surveillance program in the late 1960s, but did not identify any *Ae. aegypti* mosquitoes until the mid-1990s when the vector was again trapped in Tucson.[131] When the mosquito was first reidentified in Tucson in the mid-1990s, it was generally only trapped after the monsoon season.[131] Increased human settlement in the state has resulted in increased artificial mosquito habitat and therefore more abundant mosquito populations. A guide to the mosquitoes of Arizona published in 1973 outlined the various mosquito species present in the state and recognized the link between increasing settlement and the creation of mosquito habitat.[127] In the past decade, populations of *Ae. aegypti* have increased in Maricopa County, Arizona (see Figure 1.1), and the vector is now routinely trapped year round likely owing to the abundance of human-created breeding habitat.

Risk of Aedes aegypti-borne Viruses in Arizona

Arizona is potentially at risk for developing *Ae. aegypti*-borne diseases due to the established presence of the mosquito vector and the high volume of travelers crossing the border into Arizona from areas with endemic *Ae. aegypti*-borne disease such as Mexico and Central America. Travelers, including United States citizens returning from their travels, can potentially introduce disease to the established but naive mosquito

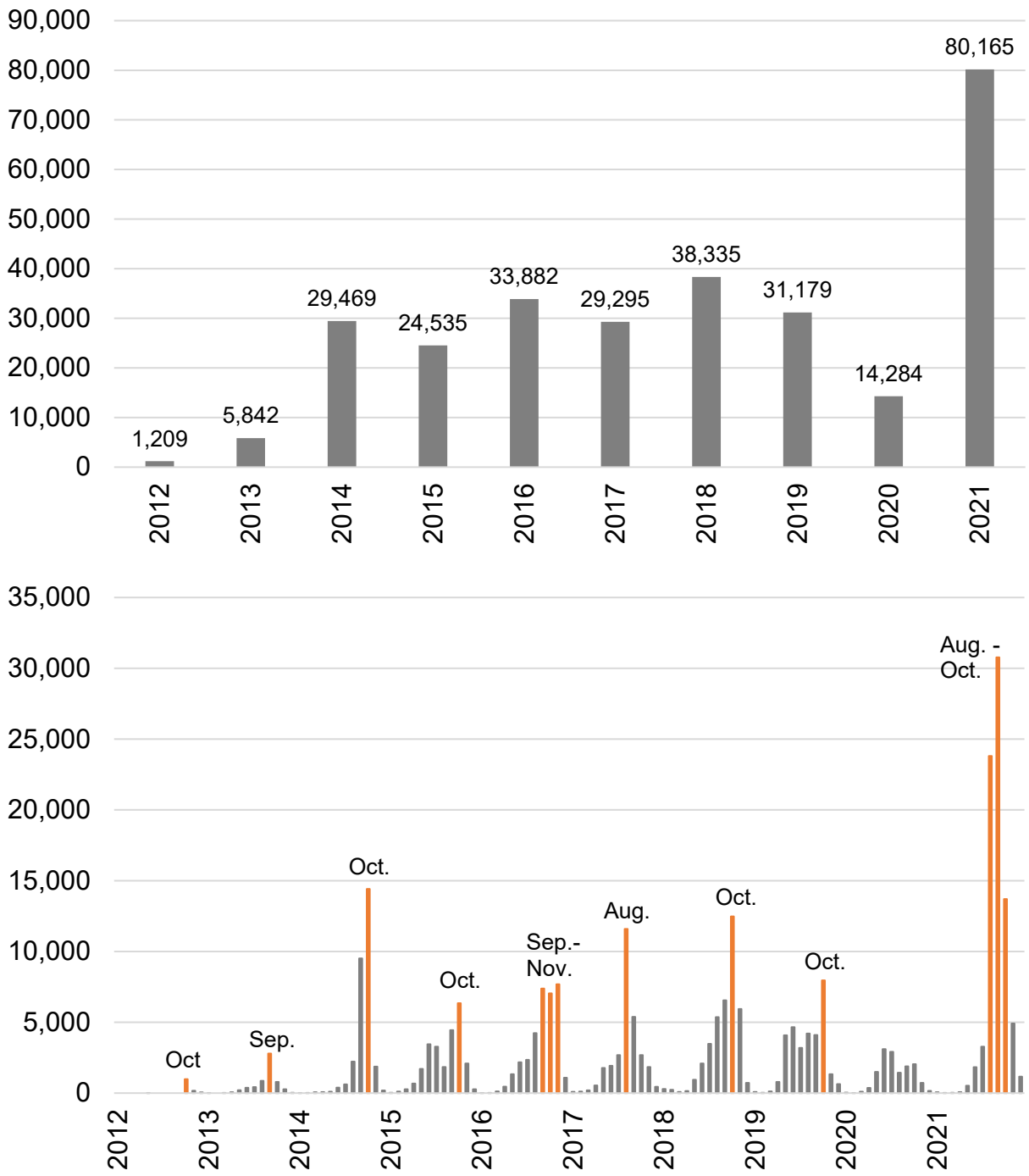

Figure 1.1. Trapping Numbers for *Aedes aegypti* females in Maricopa County, AZ from 2012-2021.Top panel: Yearly sum of female *Aedes aegypti* trapped throughout Maricopa County, Arizona from 2012-2021. Bottom panel: Monthly sum of female *Aedes aegypti* trapped throughout Maricopa County, Arizona from 2012-2021 displaying seasonal pattern of abundance with larger summer populations and smaller winter populations. Peak month(s) are highlighted for all years except 2020, which was an unusually low year.

populations at their travel destination in the United States because viruses can be passed from humans to *Ae. aegypti*.[63] Typically, the United States Bureau of Transportation reports that over 25 million travelers cross the border from Mexico into Arizona each year.[132] Sonora, Mexico, which is just south of the Arizona-Mexico border, recorded over 300 laboratory-confirmed cases of Zika virus (the most cases of all Mexican states)[96] and 982 and 2,606 probable cases of dengue in 2018 and 2019, respectively[81] which raises concerns about these diseases spreading to and becoming established in the *Ae. aegypti* population in nearby Arizona. Within the last decade, *Ae. aegypti* has established a year-round presence in Maricopa County, which could mean a single introduction could lead to the disease becoming endemic in the mosquito population.

Other Mosquito-borne Disease in Arizona

The establishment of other mosquito-borne diseases in Arizona in recent years proves that despite the dry, desert habitat, the state is still at risk for diseases spread by mosquitoes. West Nile Virus, which is spread by *Culex* species mosquitoes, was first observed in Arizona in 2003 and has since become endemic.[27,133] West Nile Virus is generally maintained in a cycle between mosquitoes and avian hosts, while humans and horses are considered “dead-end” hosts who do not establish high enough viremia to pass the virus back to mosquitoes.[27] Regardless, humans are regularly infected with West Nile Virus which can cause serious illness including encephalitis and death.[27] In Arizona in 2021, nearly 1,700 confirmed or probable cases of West Nile Virus infection were reported with 121 fatalities,[134] the worst year on record so far. In addition to West Nile Virus, St. Louis Encephalitis virus has also recently emerged in Arizona. St. Louis

Encephalitis Virus was first identified in Missouri in 1933 and is generally maintained in a cycle between *Culex* species mosquitoes and avian hosts.[135] Prior to 2014, low levels of enzootic circulation of the virus were observed for about 5 decades in Arizona, and one human case occurred between 2010-2014.[135] In 2015, circulation of West Nile Virus and St. Louis Encephalitis virus occurred simultaneously resulting in 23 cases and 1 death from St. Louis Encephalitis Virus infection.[136,137] The emergence of these diseases in Arizona has been unexpected, and illustrates clearly the need to be prepared for the emergence of additional mosquito-borne diseases, including those transmitted by *Ae. aegypti* mosquitoes, in Arizona.

Mosquito-borne Disease Control Strategies

History of Mosquito Control

Once the link between mosquitoes and the diseases they carry was identified, massive efforts were undertaken to reduce or eliminate mosquito populations. Initially, these efforts focused on reducing standing water that mosquitoes could use for breeding habitat by improving sanitation or through massive drainage ditch digging efforts.[123] Other commonly used methods for mosquito control included the use of larvivorous fish, the application of oils to standing water, or the use of screens and nets to reduce contact between humans and mosquitoes.[138] Mechanical control efforts in the United States were supported in large part through New Deal funding and employment programs implemented after the Great Depression.[123]

World War II sparked a rush to identify new ways to protect the United States military from vector-borne diseases while they were fighting abroad which led to the discovery of many new chemical compounds and pesticides that could be used to

reduce mosquito populations.[123] By mid-century, chemicals and pesticides, such as the newly discovered DDT, were regularly used in mosquito control efforts in the United States.[123,138] At the time, the apparent success of mosquito control efforts and the perceived efficacy of chemical control methods sparked an interest in more ambitious goals: namely, the complete eradication of mosquito vectors such as *Ae. aegypti*.

PAHO Eradication Campaign

In 1947, a resolution to completely eradicate the vector *Ae. aegypti* from the Western Hemisphere was adopted by the Pan American Health Organization spurred by the apparent success of mosquito control efforts after the discovery of effective insecticides.[139,140] This campaign was proposed by Brazil after the country had successfully completed its own eradication efforts but was since suffering from reinfestation from neighboring countries; it became obvious that the only way to successfully eradicate the vector from one country was to successfully eradicate the vector from all neighboring countries in the Western Hemisphere such that it could not return to territory from which it had been eradicated.[141] Eradication efforts remained the responsibility of individual countries while the Pan American Health Organization attempted to coordinate such efforts.[141]

The campaign was initially quite successful, and *Ae. aegypti* was declared eradicated from eighteen countries by 1962[140] with many other countries reporting the absence of the mosquito or having eradication campaigns in progress.[141] However, not all countries in the Americas participated equally in the efforts to eradicate *Ae. aegypti*. Most notably, the United States was slow to respond to requests that the country initiate a program aimed at eradicating *Ae. aegypti* and the eventual attempt to establish such a

program lasted only four years.[141,142] The funds for an *Ae. aegypti* eradication program in the United States were not appropriated until 1963 and the program did not actually begin until the summer of 1964; at the time it was anticipated that the vector could be eradicated from the United States within five years of the program's initiation.[143] However, the public health and vector control infrastructure in the United States as well as the political will to fund a total eradication program were lacking, allowing *Ae. aegypti* to persist in the United States and hamstringing the campaign for the entire Western Hemisphere.[141,142]

Additionally, by 1965, financial support and resources for the program began to dwindle causing a lapse in eradication programs in several countries.[140] Due to a lack of coordination among neighboring countries and islands and increasing populations of insecticide resistant mosquitoes, reinfestation of countries that had previously declared eradication began in the 1960s.[140] Although the primary motivation for the lapse of eradication campaigns was the cost, there were also questions about the feasibility of total eradication given insecticide resistance and the threat of reintroduction from Africa even if the vector was completely eradicated from the Americas.[144] There were also questions about the necessity of total eradication given improvements in surveillance and testing as well as the availability of vaccinations.[144] Furthermore, a decrease in morbidity and mortality from *Ae. aegypti*-borne diseases due to the success of the campaign actually increased skepticism for the continued need for eradication efforts.[144]

Although once quite close to success, the program lapsed and beginning in the 1970s the mosquito populations that remained in the Americas began to regain and expand their previous geographic ranges which allowed the vector to remain a threat to

public health in the region.[142] The current spread of mosquitoes and mosquito-borne diseases to further regions causes concern for current and future outbreaks of mosquito-borne disease in areas that are not prepared to handle such a threat.

Current and Future Control Strategies

As outlined in previous sections, past mosquito control efforts focused primarily on infrastructure improvement, drainage of standing water, and the heavy use of insecticides. Mosquito control philosophies have shifted between the pursuit of disease reduction and the ambitious goal of eradicating an entire mosquito species. Today, mosquito control measures differ around the world, depending on the burden of mosquito-borne disease experienced by a country in recent history.

Current mosquito control practices in the United States are similar to those that have been used for over a century, although their application is slightly more sophisticated. Additionally, many insecticides that were once widely used have been removed from the cabinet of mosquito control tools due to environmental concerns or because mosquitoes have developed resistance making them ineffective.[145] Mosquito control operations today aim to be targeted and create the least amount of disruption to the natural environment as possible.

Many mosquito control programs implement a philosophy of control known as Integrated Mosquito Management (IMM). IMM is a mosquito control strategy that uses comprehensive surveillance and control methods to reduce mosquito populations while having the smallest impact on the environment as possible.[146] The American Mosquito Control Association (AMCA) has published guidelines on the best practices for mosquito

control programs.[146] According to the American Mosquito Control Association, IMM Programs include five core pillars:

1. Engaging the community regularly

2. Surveillance, mapping, and rational setting of action thresholds

3. Physical control through manipulation of mosquito habitat

4. Larval and adult mosquito management using multiple tools including source reduction, biological control, and the application of targeted insecticides

5. Monitoring for insecticide efficacy and resistance

The manual of best practices includes detailed recommendations and guidance to help local or regional vector control programs implement each of these five strategies. The AMCA manual emphasizes the need for flexibility and adaptability of mosquito control programs based on local needs and the current status of mosquito populations. Additionally, the widespread use of insecticides without a demonstrated need and without utmost regard to monitoring for resistance, similar to practices of the past, is discouraged.

Given the emphasis of IMM on using surveillance data and mosquito distributions to make control decisions, there is a strong need for additional research aimed at creating a better understanding of mosquito habitat and distributions. Ideally, mosquito control programs could deploy extensive trapping systems to determine the need for mosquito control in real time; however, such programs are labor and cost intensive and therefore are not always feasible for small programs to implement. Modeling the distribution of mosquito vectors to “fill in the gaps” between trapping locations can help to identify additional areas that should be targeted for control efforts or increased

surveillance efforts.[146] Beyond just modeling the current distribution, analysis can also provide a better understanding of the relationship between mosquito populations and local factors, such as weather or socioeconomic characteristics. When multiple years of mosquito trapping data are available, trends of distribution over time can be better understood which allows mosquito control personnel to identify persistent hot spots or new areas of mosquito infestation. The AMCA manual cites many useful studies that map or model the distribution of mosquito populations on pages 52-53.[146] In a world of limited resources for mosquito control, these types of analysis (such as those presented in this dissertation) can be invaluable for targeting efforts to areas where they will be most effective while causing the least amount of harm to the environment.

Dissertation Research

Study Area (Maricopa County, Arizona)

Although *Ae. aegypti* does not currently cause outbreaks of mosquito-borne viral disease in Maricopa County, Arizona it is clear that the possibility of a disease outbreak in the county is ever present based on the newly established presence of the vector species and recent cases of locally acquired dengue fever.[30]

Maricopa County is located in south central Arizona in the southwestern United States. The county comprises approximately 24,000 square kilometers of land and contains Arizona's capital and most populated city, Phoenix, along with over 20 additional recognized cities and towns.[147] The population of Maricopa County is approximately 4.5 million residents.[147] The county is located in a desert climate with generally low humidity. Phoenix has an average annual rainfall of 20.40 cm, an average maximum temperature of 41.2°C for the hottest moth, July, and an average minimum

temperature of 7.1°C for the coldest month, December.[148] Rainfall is scarce and sporadic for most of the year, while monsoon season in July and August can bring torrential rains.[148] Like most desert climates, the temperature can fluctuate drastically between the daytime high and the nighttime low with variations of 15°C or more in one day being common.[148]

Maricopa County Environmental Services Vector Control Division performs regular CO_2 trapping throughout Maricopa County, with the majority of traps concentrated in the Phoenix metropolitan area where the majority of the population resides. Each week, they set up more than 800 overnight traps for a 12-hour period. The trapping program in Maricopa County is one of the most comprehensive programs in the country, both in the amount of area covered and in the regularity with which traps are placed. Through an established partnership between my dissertation committee chair, Dr. Crystal Hepp, and Maricopa County Vector Control, I have been allowed access to this wealth of trapping data for the years 2014-2021. The provided data includes the trapping date, number of adult mosquitoes trapped, species and sex of the mosquitoes, identification number of the trap, and latitude and longitude values. In addition to the trapping data, samples of mosquitoes have also been provided.

Research Purpose

Recently, multiple mosquito-borne viruses such as dengue, chikungunya, and Zika have been introduced or reintroduced into the United States (primarily in Arizona, Texas, and Florida) as the range of mosquito vectors, particularly *Ae. aegypti*, becomes more extensive than ever before.[59] It remains unclear why the range of this vector is rapidly expanding around the globe, but theories include warming temperatures due to

climate change, the adaptation of the vector to new environments, shifting socioeconomic factors and increased urbanization, and further distribution of the vector due to increased global trade and travel.[33,35,59] To help form answers to questions about the expanding range of the mosquito, researchers have begun to employ many techniques to study the distribution and range of the vector, such as statistical analysis, spatial analysis, and phylogenomic analysis (see chapters 3-5 for references to current research in these areas). Given the broad range of skills and knowledge needed to carry out studies in these domains, rarely do these studies overlap to form a more complete picture of the influences on mosquito survival. One goal of this dissertation is to take an interdisciplinary approach that brings together the knowledge that can be gained through each of these individual approaches in order to create a more complete picture of the drivers of the *Ae. aegypti* population in Maricopa County, Arizona. Additionally, these studies will also explore potential connections to socioeconomic factors that may influence the population of *Ae. aegypti*, a highly anthropophilic mosquito vector. Anecdotally, it is believed that *Ae. aegypti* is more abundant in higher income areas of the Phoenix metropolitan area where golf courses, water features, grass lawns, and landscaping are more common; exploring associations with income in these studies will allow us to examine this belief while the phylogeographic analysis will allow us to explore whether *Ae. aegypti* mosquitoes migrate to or from these areas.

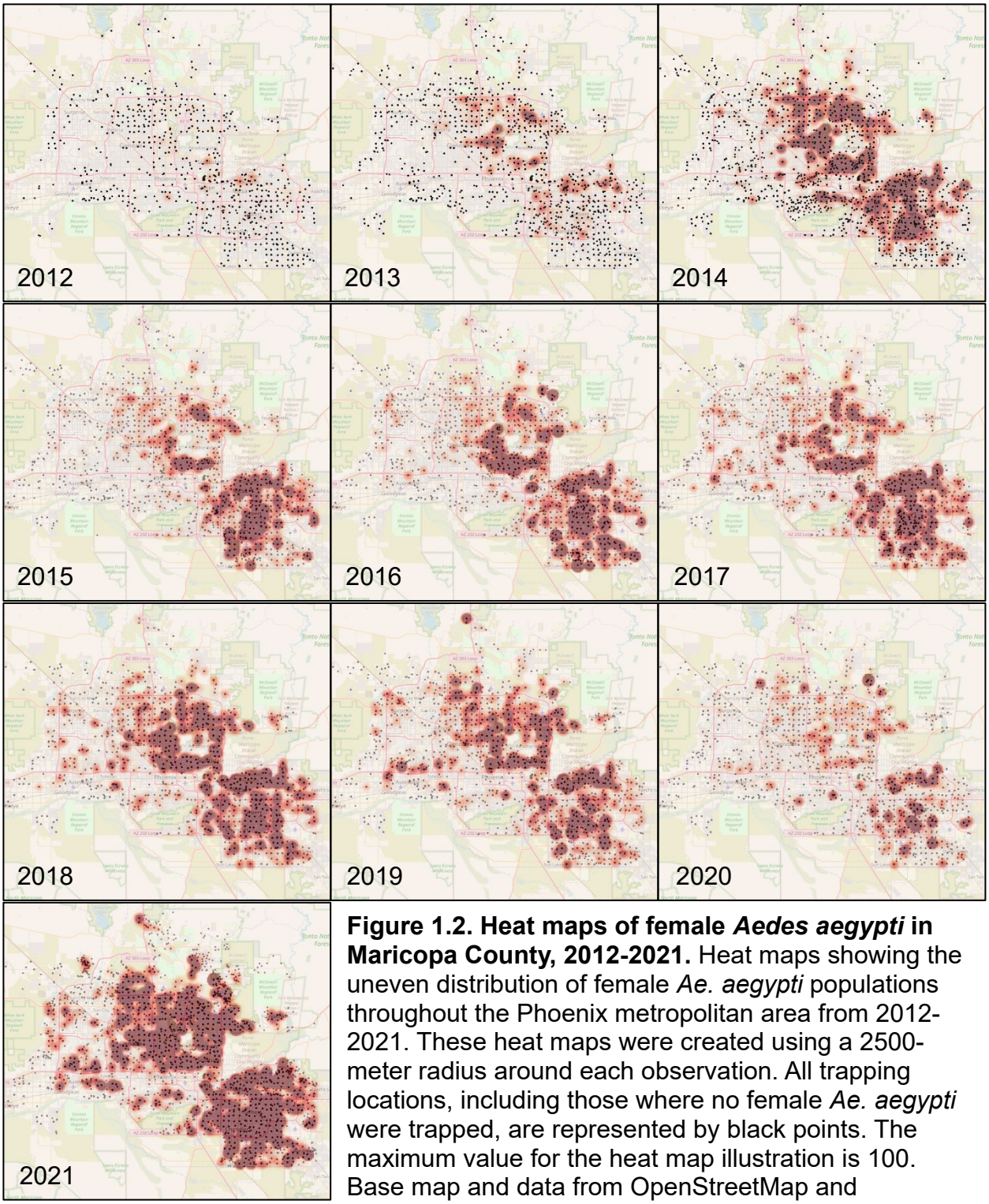

Figure 1.2. Heat maps of female *Aedes aegypti* in Maricopa County, 2012-2021. Heat maps showing the uneven distribution of female *Ae. aegypti* populations throughout the Phoenix metropolitan area from 2012-2021. These heat maps were created using a 2500-meter radius around each observation. All trapping locations, including those where no female *Ae. aegypti* were trapped, are represented by black points. The maximum value for the heat map illustration is 100. Base map and data from OpenStreetMap and OpenStreetMap Foundation (CC-BY-SA). © https://www.openstreetmap.org and contributors.

Aedes aegypti are found throughout the metropolitan Phoenix area; however, some areas of the county support larger populations of *Ae. aegypti* than others (see Figure 1.2). This mosquito relies nearly exclusively on human blood meals and habitat for reproduction, so it is generally found nearby human settlements.[10,50,59,60] Mosquito trapping efforts are concentrated around the main population center in Maricopa County, the Phoenix metropolitan area, where the population of *Ae. aegypti* is unevenly distributed. So far, it is unclear why *Ae. aegypti* populations cluster in certain areas (i.e., whether there are local socioeconomic or environmental characteristics that support larger *Ae. aegypti* populations or how mosquitoes move between local populations).

The projects of this dissertation are a step toward the long-term goal of identifying small area socioeconomic or landscape characteristics that support *Ae. aegypti* populations in Maricopa County, Arizona and more broadly in desert environments. This information has been shared with the Maricopa County Environmental Services Vector Control Division so that interventions designed to reduce mosquito populations and pathogen transmission risk can be implemented in an extremely targeted fashion that conserves resources and reduces the risks associated with the overuse of pesticides. These results can also help to inform a targeted public health response in the event of an outbreak by identifying the range of risk for disease around a trapped mosquito that has tested positive for a virus. Ideally, these studies will be informative for improving public health, because an understanding of the distribution, range, and movement of the mosquito population is a critical component of implementing effective public health efforts.

Aims and Objectives

This dissertation is made up of three distinct studies that utilize a broad range of methods from multiple fields to shine a light on the ways in which *Ae. aegypti* mosquitoes are surviving or even thriving in Maricopa County, Arizona, a desert environment with which the vector was previously thought to be incompatible. In keeping with the spirit of Interdisciplinary Health research, these studies will pull methods and guiding frameworks from the disciplines of public health and health equity, social sciences, ecology, entomology, statistics, geographic information science, biology, and bioinformatics, and they will take inspiration from many other fields. The goal of these studies is to begin the process of understanding the populations of the vector that inhabit this region. To my knowledge, this combination of methods and techniques has never before been used to study populations of this mosquito, and it certainly had not been applied to the *Ae. aegypti* populations of Arizona prior to this dissertation.

The format of this dissertation will proceed as follows: Chapter 2: a literature review exploring the connection between *Ae. aegypti* populations and socioeconomic factors in the mainland United States; then, Chapters 3-5: the three aims, as presented below; and, finally, Chapter 6: an overall discussion and conclusions.

<u>Aim 1:</u> Create species distribution models that characterize landscape traits, such as greenness and moisture, that are associated with *Ae. aegypti* populations. This aim will explore the physical characteristics of a neighborhood that may contribute to mosquito habitat. Maricopa County has a desert climate, so

determining whether constructed green areas contribute to mosquito habitat is important to understanding how mosquitoes thrive in this area.

Aim 2: Characterize weather patterns and neighborhood socioeconomic factors associated with *Ae. aegypti* presence. This aim explores the neighborhood characteristics associated with the presence of mosquito populations and therefore increased interactions between humans and the mosquito vector. To accomplish this aim, I have created a Bayesian mixed-effects statistical model with spatial and temporal random effects to evaluate associations between weather and census-derived socioeconomic characteristics and mosquito populations.

Aim 3: Characterize the origin of and migration between local *Ae. aegypti* mosquito populations within Maricopa County, Arizona. Using mitochondrial genome sequencing data coupled with Bayesian phylogenomic analyses, this aim explores the substructure of the *Ae. aegypti* mosquito population in Maricopa County to determine the mosquito species' range. These findings can help to inform mosquito control practices that are targeted to the ecology of the vector.

Impact

In public health, it is often stated that "an ounce of prevention is worth a pound of cure." Although diseases transmitted by *Ae. aegypti* are not currently routinely circulating in Maricopa County, Arizona, the mosquito vector is now well established in this region and cases of locally acquired dengue fever have been identified as of Fall 2022.[30] Given that *Ae. aegypti*-borne diseases can be transmitted in an urban cycle (that is, passed from humans to mosquitoes and back to humans), it is feasible that a single introduction could set off a chain of events leading to a major outbreak in this

area where the population is likely to have virtually no previous immunity to these diseases. A better understanding of the mosquito vector in this area is urgently required to prepare resources in case a swift and targeted public health response is needed. My goal is that these studies can help reduce the public health and economic burden of a potential outbreak of a virus spread by *Ae. aegypti* by creating an understanding of the local factors that support *Ae. aegypti* populations and the movement of these populations over time and space.

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CHAPTER 2: SYSTEMATIC REVIEW: THE IMPACT OF SOCIOECONOMIC FACTORS ON *AEDES AEGYPTI* MOSQUITO DISTRIBUTION IN THE MAINLAND UNITED STATES

ABSTRACT

Aedes aegypti mosquitoes are primary vectors of dengue, yellow fever, chikungunya and Zika viruses. *Ae. aegypti* is highly anthropophilic and relies nearly exclusively on human blood meals and habitats for reproduction. Socioeconomic factors may influence the spread of *Ae. aegypti* due to its close relationship with humans. This paper describes and summarizes the published literature on how socioeconomic variables influence the distribution of *Ae. aegypti* mosquitoes in the mainland United States. A comprehensive search of PubMed/Medline, Scopus, Web of Science, and EBSCO Academic Search Complete through June 12, 2019 was used to retrieve all articles published in English on the association of socioeconomic factors and the distribution of *Ae. aegypti* mosquitoes. Additionally, a hand search of mosquito control association websites was conducted in an attempt to identify relevant grey literature. Articles were screened for eligibility using the process described in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. Initially, 3,493 articles were identified through the database searches and previously known literature. After checking for duplicates, 2,145 articles remained. 570 additional records were identified through the grey literature search for a total of 2,715 articles. These articles were screened for eligibility using their titles and abstracts, and 2,677 articles were excluded for not meeting the eligibility criteria. Finally, the full text for each of the remaining articles (n = 38) was read to determine eligibility. Through this screening process, 11 articles were identified for inclusion in this review. The findings for these 11 studies

revealed inconsistent relationships between the studied socioeconomic factors and the distribution and abundance of *Ae. aegypti*. The findings of this review suggest a gap in the literature and understanding of the influence of anthropogenic factors on the distribution of *Ae. aegypti* that could hinder efforts to implement effective public health prevention and control strategies should a disease outbreak occur.

Introduction

Although mosquito-borne diseases have recently drawn much attention as "emerging" diseases in the United States, they actually have a long history in the Americas. *Aedes aegypti* (L.) mosquitoes and the viruses transmitted by this vector originated in Africa and were introduced to what would become the United States via ships used in the slave trade around the 17th century [1,2]. Arboviruses such as yellow fever remained widespread in this country as recently as the 19th century; yellow fever caused over 100,000 deaths along the Mississippi River and eastern seaboard of the United States between the 18th and 19th centuries [2]. The decreased prevalence of mosquito-borne disease in the United States can mostly be attributed to improved socioeconomic factors (such as income and infrastructure) that protect against transmission of arboviruses to humans through the widespread use of window screens, the increased use of air conditioning, improved sanitation conditions, as well as the use of pesticides [2]. In addition, members of the Pan American Health Organization approved a resolution in 1947 with the intention of eradicating *Ae. aegypti* from the Americas by decreasing larval habitat and routinely applying insecticides to potential habitat [3].

During the 20th century, the Pan American Health Organization program aimed at mosquito eradication throughout the Americas was initially quite successful, and *Ae. aegypti* was declared eradicated from several Southern and Central American countries [3,4]. This attempt at eradication used insecticides and larval habitat reduction to reduce mosquito populations [4]. However, not all countries in the Americas participated equally in the efforts to eradicate *Ae. aegypti*. Most notably, the United States was slow to respond to requests that the country initiate a program aimed at eradicating *Ae. aegypti* and the eventual attempt to establish such a program lasted only a few years [4]. Additionally, financial support and resources for the program soon began to dwindle throughout the Americas, and *Ae. aegypti* developed resistance to some of the insecticides used in the program [3]. The program soon lapsed and beginning in the 1970s the mosquito populations that remained in the Americas began to regain and expand their previous geographic ranges which allowed *Ae. aegypti* to remain a threat to public health in the Americas [2,4]. The current spread of mosquitoes and mosquito-borne diseases to further regions causes concern for current and future outbreaks of mosquito-borne disease in areas that are not prepared to handle such a threat. Additionally, novel mosquito-borne diseases introduced to the United States from other areas of the world constitute a risk to public health.

The current distribution of *Ae. aegypti* throughout the world is more extensive than has ever been recorded [5]. In the last few decades *Ae. aegypti* has expanded its range in the United States, and this trend is predicted to continue in the coming decades [6]. *Ae. aegypti* live in warm environments, as their biological functions are hampered below a temperature of 14°C [7] and temperatures below 10°C are generally not survivable for

adult or larval *Ae. aegypti* [8]. In nature, female *Ae. aegypti* live for approximately a month, although some have been recorded living up to 45 days [8]. *Ae. aegypti* have adapted to be able to thrive in environments altered and created by humans [9]. This mosquito primarily reproduces in human-made artificial containers and are able to thrive in urban environments where they face little to no threat from natural predators [9]. However, the invasive mosquito species *Ae. albopictus*, which was introduced to the United States in 1985, can impact *Ae. aegypti* populations through interspecies competition [10,11]. Although this review is not primarily focused on the interaction between these two species and instead attempts to characterize the impact of socioeconomic factors on the distribution of the mosquito vector *Ae. aegypti*, it is important to recognize that the presence of *Ae. albopictus* may be important to determining suitable habitat for *Ae. aegypti*.

Ae. aegypti mosquitoes have a very small range, and few stray further than about 100 meters from where they originated [12] unless the conditions of the immediate environment are unsuitable for reproduction in which case *Ae. aegypti* females have been observed to disperse up to 2.5 km from their origination point [13]. The tendency for these mosquitoes to remain in and seek out areas with well-suited habit indicates that small-scale, neighborhood level environmental factors, which are influenced by socioeconomic characteristics, likely have a considerable influence on the ability of *Ae. aegypti* to survive in specific areas.

The mosquito vector *Ae. aegypti* is highly anthropophilic and relies nearly exclusively on human blood meals and habitats for reproduction [5]. *Ae. aegypti* females feed preferentially on human blood, even if other potential hosts or sugar meals are

available [14]. *Ae. aegypti* are generally most active during daytime hours which increases potential interactions between the mosquito vector and humans and in turn increases the potential for the spread of viruses by *Ae. aegypti* [8]. Dengue, yellow fever, and the newly emerged threats of chikungunya and Zika viruses are primarily transmitted in an urban cycle where the virus can be passed from human to mosquito to human [15]. The maintenance of an urban transmission cycles of these diseases requires the co-existence of *Ae. aegypti* mosquitoes [5,16,17] and humans [1] in the same geographic spaces. Travelers can potentially introduce diseases to the established but naïve *Ae. aegypti* populations at their travel destination in the United States because viruses can be passed from humans to *Ae. aegypti* [15]. The presence of this competent vector species has allowed for viruses such as dengue, Zika, and chikungunya viruses, to be introduced to and locally transmitted in the United States in the past [6]. Therefore, concern about these viruses becoming established in an urban transmission cycle the United States is warranted.

As globalization continues to bring our world closer together, it is increasingly important to monitor and prepare for the introduction of additional diseases spread by mosquitoes such as *Ae. aegypti* [2]. Given the generally small range of *Ae. aegypti*, those living or working in areas with suitable habitat for *Ae. aegypti* will be most likely to come in to contact with the mosquito vector and will therefore be at greatest risk of disease [12]. Developing a greater understanding of the populations and areas most at risk of infection by studying the relationship between *Ae. aegypti* and socioeconomic factors may allow for the improvement of existing methods to control mosquito populations and intervene in the life cycle of viruses that have the potential to be

introduced to the United States. Certainly, organizations do currently exist to monitor and control mosquito populations throughout the United States and many states have comprehensive mosquito control and surveillance programs. This paper does not attempt to claim that mosquito control programs are nonexistent, but that they may benefit from an enhanced understanding of underlying relationships between socioeconomic factors and mosquito populations to efficiently allocate resources.

Arboviruses vectored by Aedes aegypti

Dengue has expanded its distribution throughout the world in the last few decades, and has been reported to have caused locally transmitted cases in the United States [18]. Over half of the world's population resides in areas that are at risk for outbreaks of dengue [19]. Importantly, the dengue virus has four subtypes, so individuals can be infected more than once and subsequent infections are potentially harsher and more life threatening [19]. Most dengue infections are generally mild, flu-like, and self-limiting [19]. Although dengue is generally mild, infected patients can also present with the much more severe dengue hemorrhagic fever which was first reported in the Americas during an outbreak in Cuba in 1981 [20,21]. Due to the widespread occurrence of dengue, the disease has serious impacts both on health and on the global economy. It is estimated that dengue causes up to 100 million infections annually worldwide [17]. In 2013, over 13,000 people globally are estimated to have died from dengue, and the global cost of the disease was estimated to be between 8-9 billion USD [22].

Dengue likely circulated locally in Houston, Texas between 2003-2005, although routine dengue surveillance is not common in this area and dengue cases may be generally underreported [23]. Additionally, local transmission of dengue was reported in

Key West, Florida in 2009 where, similar to Texas, dengue surveillance is not routine [24]. These outbreaks of dengue virus in Texas and Florida in the last 15 years have resulted in 25 cases and 90 cases of dengue infection, respectively [17,25]. A serosurvey conducted in 2004 in Brownsville, Texas found that 40% of residents had evidence of past infection of dengue [26], and during the 2009 dengue outbreak in Key West, Florida, a serosurvey revealed that 5% had evidence of dengue infection [24]. This evidence has raised concerns about the potential for dengue to establish itself in the United States.

Yellow fever infections and disease outbreaks typically occur in tropical areas of Africa and South America [27]. Despite the United States being outside of the commonly infected area, yellow fever virus caused an estimated 5,000 deaths in Philadelphia during the summer and fall of 1793 [28]. This is just one of many examples where the presence of a competent vector species combined with the importation of infected vectors or travelers has resulted in a devastating outbreak. Those who develop symptoms from infection with yellow fever virus experience fever, vomiting, kidney failure, hemorrhaging, and in 20-60% of cases, death [27]. A vaccine that effectively protects recipients from yellow fever has existed since the 1930s, but lack of vaccine coverage due to funding issues leading to a shortage of needed doses has allowed the disease to persist as a major threat to public health around the world [27,29].

Chikungunya virus was first isolated in Tanzania in 1953 and is known to cause disease consisting of fever, rash, and debilitating joint pain [30]. Historically, chikungunya virus has caused sporadic cases of infection in Africa and Asia, but has recently caused large outbreaks in Southeast Asia from 2004-2005 and in the

Caribbean in 2013 [31]. Chikungunya has developed as a potential global health threat in the past decade, as the disease has emerged rapidly in the Americas beginning with the Caribbean outbreak in 2013 [5,32]. At this point in time, the spread of chikungunya virus has been poorly recorded and is not well understood [30]. Although there is no evidence of local transmission of chikungunya in the United States, travelers with a viremic load capable of facilitating virus transmission have been identified returning to areas of the United States with established *Ae. aegypti* presence, raising the possibility that chikungunya could be introduced to *Ae. aegypti* populations in the United States [33]. Chikungunya virus is considered to be a potential public health threat should it emerge in the Americas, because the population has no current immunity to the disease [17].

Zika virus was first discovered in Uganda in 1947 during surveillance for yellow fever, and caused mild, sporadic illness in humans prior to the occurrence of unexpected large-scale Zika virus outbreaks beginning in the Pacific islands in 2007 [32,34]. The Zika outbreak in Brazil that began in 2015 introduced widespread concern that Zika infection was linked to severe neurological complications for infants infected during prenatal development [34]. Zika virus has been circulating autochthonously in Mexico since 2015 and is estimated to have caused over 270,000 human cases of Zika virus infection since that time [35,36]. Between 2015-2017, a large outbreak of Zika virus in the Americas resulted in over 3,000 cases of microcephaly associated with Zika infection and was estimated to cost between 7 to 18 billion USD during the outbreak alone [37,38]. In the United States in 2016, over 200 cases of locally-transmitted Zika

were recorded in Florida and 6 locally-acquired cases of Zika were reported in Texas [39].

Framework of socioeconomic factors

Given the limited average dispersal of *Ae. aegypti*, [12], small-scale habitats and built environment characteristics are important for controlling the abundance of mosquito vectors in specific neighborhoods. *Ae. aegypti* have adapted to be able to thrive in environments altered and created by humans [9]. *Ae. aegypti* primarily reproduces in human-made artificial containers and are able to thrive in urban environments [9]. *Ae. aegypti* generally prefer humid environments, but anthropogenic modifications to the environment can create habitats that provide *Ae. aegypti* the ability to flourish even in areas where the natural climate would be inhospitable, such as Arizona [40]. The metropolitan area of Phoenix, Arizona is located in the arid climate of the Sonoran Desert of the southwestern United States [41]. Although the natural environment of Arizona is dry desert that would be inhospitable for *Ae. aegypti*, urban development in the Phoenix metropolitan area has created an “oasis” characterized by increased vegetation and shade trees, grassy lawns, and irrigated fields [41,42]. The abundance and diversity of vegetation as well as water usage is greater in residential areas with higher socioeconomic status in Phoenix [41,43]. Therefore, the potential available habitat for *Ae. aegypti*, which requires water to reproduce and has been associated with more abundant vegetation in a nearby similar desert climate [44], may be influenced by neighborhood socioeconomic factors in areas such as Arizona.

Socioeconomic status can impact a person’s life and health in many ways and is often discussed as a part of a social determinants of health framework. Healthy People

2020 defines social determinants of health as, “conditions in the environments in which people are born, live, learn, work, play, worship, and age that affect a wide range of health, functioning, and quality-of-life outcomes and risks” [45]. As previously mentioned, the socioeconomic status of a neighborhood can influence the neighborhood design, infrastructure, and landscape, which in turn could potentially influence available mosquito habitat. For instance, green areas are found less often in economically disadvantaged areas of a city than in affluent areas which may influence the abundance of *Ae. aegypti* given that this mosquito has been found to be positively associated with vegetation [44,46]. Socioeconomic factors can also influence the way that people live their lives, such as how much time they spend outdoors. This is relevant to *Ae. aegypti* populations because these mosquitoes generally rely on human blood meals to be able to reproduce [5].

Socioeconomic factors may influence the spread of *Ae. aegypti* due to their reliance on human blood meals and their adaptation to the use of human-created habitat for reproduction. Surveillance efforts should continue to consider social determinants and local challenges to combatting mosquito-borne disease as part of comprehensive mosquito control programs [47] among the many other factors that influence mosquito populations and disease transmission. In order to implement prevention strategies and respond to future disease outbreaks, it is crucial to first understand the distribution of mosquito vectors [16,48]. Given that *Ae. aegypti* has extensive interaction with humans, understanding the distribution of *Ae. aegypti* could be enhanced by an understanding of how *Ae. aegypti* are affected by human socioeconomic factors.

Public health prevention and control efforts targeted toward areas at the greatest risk for disease transmission in the case that one of the aforementioned viruses enters the United States once again do currently exist. However, these programs may be enhanced through a deeper understanding of the influence of socioeconomic conditions on the *Ae. aegypti* distribution throughout the country. We focus solely on the mainland United States because socioeconomic conditions can vary widely around the world, and the results of a study with vastly different conditions in another country cannot be reliably extrapolated to conditions in the United States [17]. This paper summarizes the published literature on how socioeconomic variables influence the distribution of *Ae. aegypti* mosquitoes in the mainland United States and aims to answer the following question: how do socioeconomic factors impact the distribution of *Ae. aegypti*?

Materials and Methods

Search Strategy

A comprehensive search was developed to retrieve all published articles on the association of socioeconomic factors and the distribution of *Ae. aegypti* mosquitoes. The following search query was used: ("Aedes aegypti" OR "*Ae. aegypti*" OR "*A. aegypti*") AND (distribut* OR presence OR prevalence OR density OR geographic* OR habitat OR spatial OR abundance) AND (social OR equity OR justice OR economic OR socioeconomic OR social-ecological OR equality OR disparity OR disparities OR inequality OR inequalities OR environment OR landscape OR income OR neighborhood OR community OR communities). Search results were limited to articles/reviews and publications written in English. Four electronic databases (PubMed/Medline, Scopus, Web of Science, and EBSCO Academic Search Complete) were searched using this

query through June 12, 2019. Additionally, in an attempt to include grey literature published by mosquito control organizations, 24 mosquito control organizations located in the United States were identified using a popular search engine, and their websites were hand searched for articles, newsletters, or other publications that would be relevant to this review. This search was conducted by first identifying articles that named *Ae. aegypti* as the article's subject and then scanning the title or text of the article for references to the distribution of the mosquito or references to the consideration socioeconomic factors.

Article selection

Articles were screened for eligibility using the process described in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [49]. First, all articles discovered by searching the databases named above were downloaded and checked for duplicates using the Mendeley reference manager software (Mendeley Desktop, Version 1.19.4). After removing duplicates, the remaining articles were assessed for eligibility using their titles and abstracts. Articles that met the following criteria were considered relevant to this review: 1) published in English; 2) study specifically evaluated the distribution of *Ae. aegypti* mosquitoes, not a specific disease transmitted by *Ae. aegypti*; 3) study evaluated the influence of socioeconomic factors on the distribution of *Ae. aegypti*; 4) study took place in the mainland United States.

Relevant articles were then read in full to determine their eligibility for this review. Additional articles potentially relevant to this review were identified from the grey literature search, the bibliography of relevant studies, or previously known literature and

were screened for eligibility in the same fashion. Articles eligible for this review were original peer-reviewed studies (i.e., not reviews, commentaries, editorials, abstracts, etc.) or publications of mosquito control organizations from the mainland United States that studied the impact of socioeconomic factors on the distribution of *Ae. aegypti* mosquitoes. See Figure 2.1 for a diagram of the selection process. Once the included articles were identified, each was read in full. The information relevant to location, date of study, survey methods, analysis methods, and socioeconomic factors were summarized for inclusion in this review. Main themes were then determined based on the compiled information.

Results

Initially, 3,461 articles were identified through the database searches conducted, and an additional 32 articles were identified through bibliographies and previously known literature for a total of 3,493 articles. After removing duplicates, 2,145 articles remained. These articles were screened for eligibility for this review using their titles and abstracts, and 2,098 articles were excluded for not meeting the eligibility criteria noted above. Finally, the full text for each of the remaining articles (n = 38) was read to determine eligibility. Through this screening process, 11 articles were identified for inclusion in this review. See Figure 2.1.

The grey literature search resulted in 570 articles, publications, newsletters, or information from national meetings that directly mentioned *Ae. aegypti*. Of these, 6 were identified as potentially relevant to the review because the titles or articles contained some combination of the keywords used in the search process detailed in the methods relating to distribution and socioeconomic factors. These 6 articles were all identified

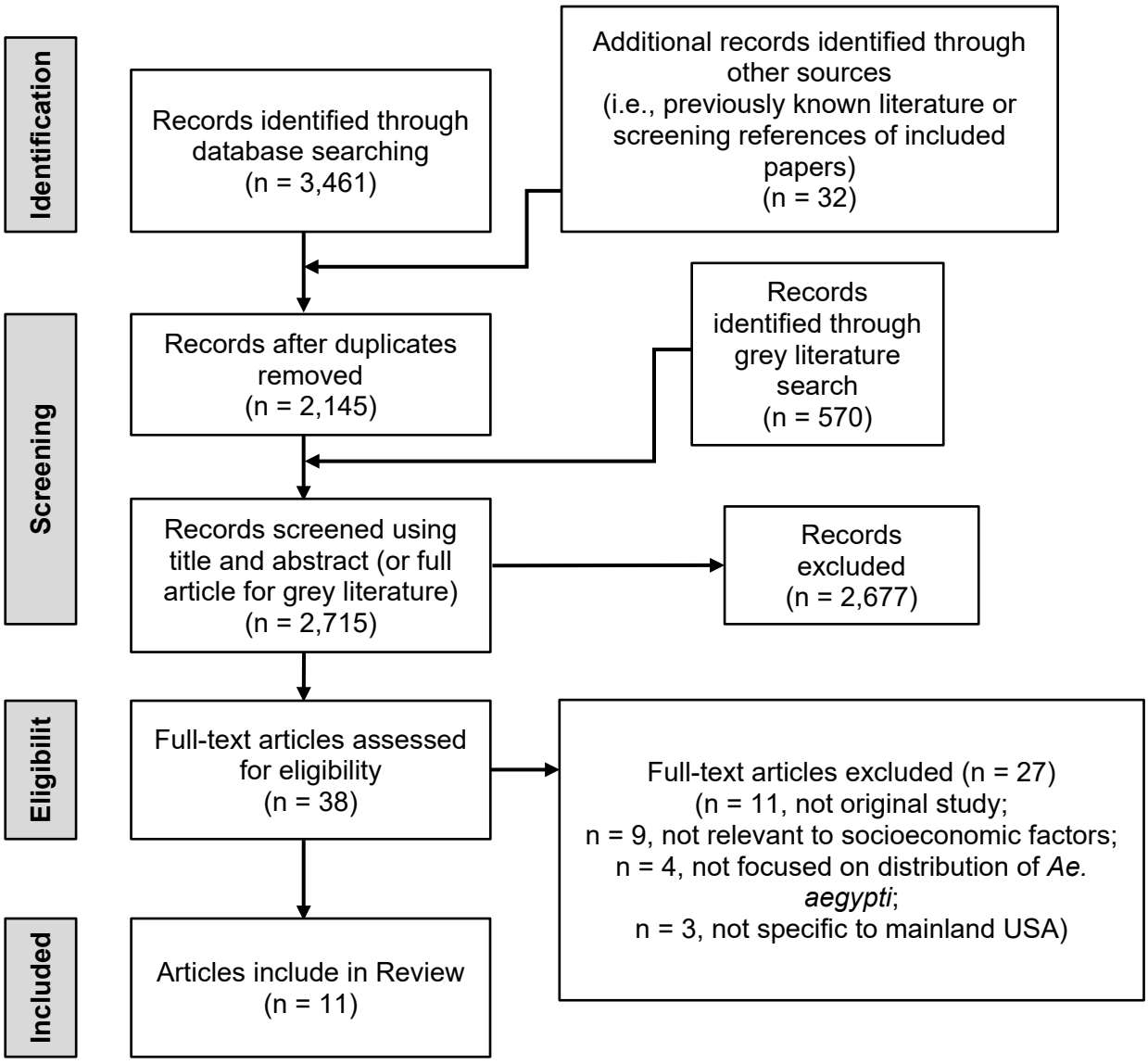

Figure 2.1. Systematic article selection process based on PRISMA guidelines.

through the Journal of the American Mosquito Control Association. The 6 identified articles were further reviewed, and 1 was found to be a duplicate to an already included article that was discovered through database searching, 2 were not research related to the mainland United States, and 3 did not actually address socioeconomic factors. Most publications from these organizations tended to address mosquito biology or the

effectiveness of pesticides rather than the relationship between *Ae. aegypti* and socioeconomic factors. See Table 2.1 for a list of all mosquito control associations that were identified and searched.

The included studies took place in Florida (n = 5), Texas (n = 3), Arizona (n = 2), or Louisiana (n = 1). The dates of the studies ranged from 1984 to 2018. Main themes that emerged from this summary were the inclusion of economic factors, housing and built environment factors, demographic factors, and/or interactions between these factors. See Table 2.2.

Economic factors

The earliest study that related *Ae. aegypti* presence to socioeconomic factors was conducted by Chambers et al. (1986); their results indicated that more containers holding water (potential *Ae. aegypti* habitat) were found in low-income areas as opposed to middle- or high-income and *Ae. aegypti* was only found independently of other mosquito species in low-and middle-income areas as opposed to high-income areas [50].

Most studies identified for this review only sampled *Ae. aegypti* outdoors. However, in one study conducted by Martin et al. (2019), *Ae. aegypti* were found to be more prevalent indoors in low-income communities compared to middle-income communities in South Texas. The abundance of indoor *Ae. aegypti* populations was not influenced by changes in seasonal temperatures as outdoor populations were [49]. No differences were observed for the outdoors abundance of *Ae. aegypti* depending on income; *Ae. aegypti* were found to be much more prevalent outdoors compared to indoors using ovitraps regardless of community income levels [49].

Table 2.1. Mosquito and vector control associations with websites that were searched for grey literature.

Association	Type of Publication Searched	Years Available	Articles mentioning *Ae. aegypti* identified
American Mosquito Control Association	Journal of the American Mosquito Control Association (1985-2019), Mosquito News (1941-1984), Mosquito Systematics (1969-1994)	1941-2019	497
Alabama Vector Management Society	Meeting Agendas	2014-2019	2
Florida Mosquito Control Association	Best Management Practices (2012), Journal of the Florida Mosquito Control Association (2019), Wing Beats Magazine (1990-2019)	1990-2019	8
Georgia Mosquito Control Association	Publications of Interest linked on website, DIDEEBYCHA Newsletters	2010-2019	7
Illinois Mosquito and Vector Control Association	Newsletters	2001-2015	3
Indiana Vector Control Association	No publications available on website	N/A	N/A
Louisiana Mosquito Control Association	Le Maringouin Newsletters	1987-2019	17
Michigan Mosquito Control Association	Skeeter Scanner Newsletters	2007-2018	23
Mid-Atlantic Mosquito Control Association	MAMCA Newsletters	2017-2019	5
Mississippi Mosquito and Vector Control Association	No publications available on website	N/A	N/A
Mosquito and Vector Control Association of California	Mosquito & Vector News (2019), Publications linked on website	2019	4
Nebraska Mosquito and Vector Control Association	Skeeter Newsletters	2008-2019	2
New Jersey Mosquito Control Association	NJMCA Newsletters	1989-2019	7

Table 2.1 continued. Mosquito and vector control associations with websites that were searched for grey literature.

Association	Type of Publication Searched	Years Available	Articles mentioning *Ae. aegypti* identified
North Carolina Mosquito and Vector Control Association	The Biting Times Newsletters	2003-2019	3
North Central Mosquito Control Association	No publications available on website	N/A	N/A
Northeastern Mosquito Control Associations	News linked on website	N/A	0
Northwest Mosquito Vector and Control Association	Newsletters	2017-2019	1
Ohio Mosquito and Vector Control Association	No publications available on website	N/A	N/A
South Carolina Mosquito Control Association	The Landing Rate Count Newsletters	2012-2019	5
Tennessee Mosquito and Vector Control Association	Member Publications listed on website	2009-2016	0
Texas Mosquito Control Association	Newsletter archive “coming soon”	N/A	N/A
Utah Mosquito Abatement Association	Annual Proceedings of the UMAA	1948-2007	1
Virginia Mosquito Control Association	The Skeeter Newsletters	2017-2019	2
West Central Mosquito and Vector Control Association	No publications available on website	N/A	N/A

Income was studied in multiple publications with inconsistent results. In Tucson, Arizona, the presence of *Ae. aegypti* pupae was negatively correlated with household income [38]. In another study in Tucson, Arizona by Walker et al. (2011), *Ae. aegypti* larval abundance was found to be significantly negatively associated with income in a normal rain year but there was no significant association between larval abundance and income in a dry year [52]. A study conducted by Reiter et al. (2003) compared the abundance of *Ae. aegypti* in a city in Texas that straddles the United States—Mexico border and found that *Ae. aegypti* was more abundant in the Texas portion of the city where income was higher [54].

Models of *Ae. aegypti* distribution traditionally rely heavily on climatic variables, without taking into consideration the influence of human interactions; however, a study by Obenauer et al. (2017) found that adding a factor representing poverty to a species distribution model greatly improved its accuracy [55]. These findings indicate that poverty has a meaningful impact on the distribution of *Ae. aegypti* likely due to differences in available habitat based on socioeconomic factors.

Housing and built environment factors

Inconsistent results regarding the influence of land use were observed. A study conducted by Wilke et al. (2018) revealed that construction sites in urban areas of Florida are ideal habitat for *Ae. aegypti* reproduction. *Ae. aegypti* seem to be well suited to utilizing construction sites for reproduction, regardless of other socioeconomic characteristics of the surrounding area [9]. However, another Florida study found that *Ae. aegypti* were found to be more abundant in areas primarily used for residential purposes as opposed to areas used for commercial or industrial purposes in Tampa,

Table 2.2. Summary of relevant information from identified articles studying the relationship between *Ae. aegypti* and socioeconomic factors.

Ref.	Location	Time Period	Study Design	Data Analysis	Socioeconomic Factors	Results
[9]	Miami-Dade County, Florida, USA	July– October 2017 and 2018	Adult survey using CO_2 traps and immature survey using collection of water existing naturally at 11 construction sites	Shannon and Simpson indices; Individual rarefaction curves; Data matrix plot	Presence of construction (indicator of expanding urbanization); sampling conducted across socioeconomically distinct locations; construction workers disproportionately exposed to *Ae. aegypti*	*Ae. aegypti* was most abundant mosquito species at construction sites. Construction sites represent ideal habitat for *Ae. aegypti* regardless of other socioeconomic factors
[51]	South Texas, USA	September 2016 – April 2018	CDC autocidal gravid ovitraps indoors and outdoors for 69 houses in 8 communities	Generalized Linear Mixed Model (GLMM)	Income	Low-income communities had higher abundance of *Ae. aegypti* indoors compared to middle-income communities
[52]	Tampa, Florida, USA	June and September 2006	Ovitraps and immature sampling at cemeteries and surrounding areas	Paired *t*-tests; nested ANOVAs	Built environment (cemetery, residential, commercial, industrial)	*Ae. aegypti* were more abundant in residential sites than in commercial or industrial sites; coexistence with *Ae. albopictus* occurs at residential sites; no differences existed in the abundance of *Ae. aegypti* between cemeteries and surrounding areas

Table 2.2 continued. Summary of relevant information from identified articles studying the relationship between *Ae. aegypti* and socioeconomic factors.

Ref.	Location	Time Period	Study Design	Data Analysis	Socioeconomic Factors	Results
[40]	Tucson, Arizona, USA	August 2012	Outdoor larval habitat container survey of 355 houses in 20 neighborhoods; sampling of immature mosquitoes	Simple linear regression; multiple regression models; log-linear regression with Poisson distribution	Housing type, ownership status (own or rent), house age, household income, number of household residents, presence of children, use of landscaping services	Presence of *Ae. aegypti* pupae positively associated with home ownership and negatively associated with household income regardless of home ownership status
[53]	South Texas, USA	June – September 2010	Ovitraps at 21 sites in 4 cities	ANOVA; linear regression	Rural/suburban/ urban gradient	Presence of *Ae. aegypti* was not influenced by rural/urban land use
[54]	Tucson, Arizona, USA	July – September 2003 and 2004	Outdoor ovitraps at 47 residential sites	Multiple regression; logistic regression	Population density, income, house age	Population density was not associated with *Ae. aegypti* abundance; income was negatively associated with *Ae. aegypti* abundance; house age was positively associated with *Ae. aegypti* abundance
[55]	South Florida, USA	March 2002 – February 2003	Ovitraps at 45 sites throughout 3 counties	ANOVA; Kruskal-Wallis tests; multiple regression	Rural/suburban/ urban gradient and industrial land use	*Ae. aegypti* abundance was positively associated with urban settings compared to rural settings

Table 2.2 continued. Summary of relevant information from identified articles studying the relationship between *Ae. aegypti* and socioeconomic factors.

Ref.	Location	Time Period	Study Design	Data Analysis	Socioeconomic Factors	Results
[56]	Laredo, Texas, USA and Nuevo Laredo, Taumalipas, Mexico	Summer 1999	Household *Ae. aegypti* habitat and larval survey of mosquito-infested containers as measured by the Breteau Index and the House Index	Univariate and multivariate analyses	Income, housing characteristics, number of household residents, housing density	*Ae. aegypti* were more abundant on the Texas side of the border where income is higher, housing density is lower, and number of household residents is lower compared to the Mexico side of the border
[57]	Southeastern USA	1960 – 2014	Use of existing database of *Ae. aegypti* occurrences	Maxent species distribution model	Poverty, population density	Adding poverty and population density factors greatly improves model accuracy
[58]	West Palm Beach and Boca Raton, Florida, USA	September – October 2001	360 ovitraps placed outdoors in varying residential areas	MANOVA and pairwise comparisons; maximum likelihood categorical analyses	Rural/suburban/ urban gradient measured by population density, number of houses, level of sanitation, presence of non-human hosts	*Ae. aegypti* was most abundant in urban areas and co-occurred with *Ae. albopictus* in suburban areas
[50]	East Baton Rouge Parish, Louisiana, USA	May – August 1984	Container habitat and larval survey at 540 households	Split-split-split plot model; ANOVA; two-way contingency chi-square tests	Income	More wet containers (potential habitat) and were found in low-income areas; *Ae. aegypti* larvae were only found independently in low- and middle-income areas

Florida in 2006 [50]. No differences existed in the abundance of *Ae. aegypti* between cemeteries and the surrounding mixed urban environment [50].

Multiple studies evaluated the effects of urban and rural environments on the abundance of *Ae. aegypti*. In southeastern Florida, *Ae. aegypti* was more abundant in urban areas compared to suburban or rural areas and was found to co-occur with *Ae. albopictus* primarily in suburban areas [56]. A study in South Florida, USA found that *Ae. aegypti* abundance was positively associated with variables representing urban environments as opposed to variables representing rural environments in a regression analysis [53]. However, contrary to the Florida studies, a study in South Texas found that the abundance of *Ae. aegypti* was not influenced by whether ovitraps were placed in urban, suburban, or rural locations, although the presence of *Ae. albopictus* due to higher than usual rainfall during the summer of the study (2010) may have influenced the results [51].

The age of infrastructure was considered by two studies that were both conducted in Tucson, Arizona, an arid desert environment. A study by Walker et al. (2011) found that house age was positively associated with *Ae. aegypti* larval abundance in Tucson, Arizona potentially due to more mature vegetation and objects collected in the yards of older homes [52]. A later study in Tucson, Arizona found that house age was not significantly associated with the presence of *Ae. aegypti* larvae or pupae [38].

In one study comparing *Ae. aegypti* abundance in a Texas city on the United States—Mexico border, *Ae. aegypti* was more abundant in the Texas portion of the city where houses and buildings are more likely to be air-conditioned and have window

screens, housing density is lower, and the number of residents living in each household is lower [54].

Demographic factors

A few publications in this review studied the influence of an urban environment compared to a rural environment on the abundance of *Ae. aegypti*, but only one study explicitly evaluated the effects of population density on *Ae. aegypti* abundance. Adding a variable representing population density to a species distribution model for *Ae. aegypti* resulted in a much better fit model of *Ae. aegypti* presence in the southeastern United States compared to a model that relied solely on climate data, reflecting the important interactions between the highly anthropophilic *Ae. aegypti* and humans that influence distribution [55].

The only other demographic factor considered was home ownership status. A study by Walker et al. (2018) found that the presence of *Ae. aegypti* pupae in the arid environment of Tucson, Arizona was significantly higher for homes occupied by the owner compared to rental homes [38].

Interactions between factors

Socioeconomic factors often do not exist independently and may interact to influence *Ae. aegypti* abundance. A study in Tucson, Arizona found the interaction between house age and income to be significant: *Ae. aegypti* larval abundance was higher in older low-income houses than in older high-income houses [52]. The interaction between population density and income was also significant in the study by Walker et al. (2011); this study found that *Ae. aegypti* larval abundance was higher in high-density, low-income areas as compared to high-density, high-income areas [52].

Discussion

The findings for these 11 studies revealed inconsistent relationships between the studied socioeconomic factors and the distribution and abundance of *Ae. aegypti*. Given that *Ae. aegypti* mosquitoes vector multiple significant viruses, are highly anthropophilic, and rely on interactions with human populations to reproduce [5], this area of study is extremely relevant to public health. The findings of this review suggest a gap in the literature which could potentially indicate a need for additional research or a need for better circulation of current findings regarding the influence of socioeconomic factors on the distribution of *Ae. aegypti* that could hinder efforts to implement the most effective public health prevention and control strategies should a disease outbreak occur.

Most studies in the United States are dependent on outdoor sampling, as indoor sampling is considered invasive. This could affect the results of these studies because *Ae. aegypti* have been known to rest and reproduce indoors [15] and areas of high income where houses may be more likely to have air conditioning, well-sealed doors and windows, and intact window screens may have higher populations of *Ae. aegypti* outdoors compared to low-income areas where mosquitoes can find habitat indoors. However, in the United States where the use of air-conditioning is widespread, *Ae. aegypti* that find their way indoors may not be able to successfully reproduce or transmit disease due to the lower temperatures and humidity [54] forcing these mosquito vectors to take blood meals outside.

The results of this review are of course limited by the methods adopted to complete the search of the literature. The search terms used in this review were designed to return comprehensive results, but there are likely studies that were missed in this

search process. Additionally, a systematic review is naturally sensitive to publication bias, as only studies that were accepted by journals and published could have possibly been found through this search. It is possible that there exist many other studies with contradictory or null findings that were never accepted for publication and are therefore not included in this review. Additionally, many mosquito control organizations may already possess a deep understanding of the relationship between *Ae. aegypti* and socioeconomic factors that they use to implement effective mosquito control programs. Unfortunately, much of this knowledge is not published on platforms that are easily accessible. Therefore, despite extensive screening of the grey literature that was available on the websites of 24 mosquito control organizations in the United States, the results of this study may be lacking knowledge accrued by these organizations.

Overall, this review revealed a gap in available literature relating the *Ae. aegypti* population of the mainland United States to anthropogenic and socioeconomic factors. That only 11 articles were identified for this review reveals a need for additional published research into the human and built environment characteristics that contribute to ideal habitat for *Ae. aegypti* and therefore contribute to increased risk of disease transmission so that all involved in mosquito control and surveillance can access this information easily to benefit from this understanding. Additionally, these studies were mainly conducted in three states: Arizona, Florida, and Texas. Given that the survival of *Ae. aegypti* is tied to the local climate, more studies should be conducted in varying areas throughout the United States with an established presence of *Ae. aegypti*. The interaction between socioeconomic factors and the climate will likely vary for each local area. For example, in an arid, desert climate such as Arizona, areas of high

socioeconomic status with greater use of water and more vegetation may create more suitable habitat for *Ae. aegypti* [39,41]. However, in environments with more regular precipitation such as Baltimore, Maryland, areas of low socioeconomic status with poor infrastructure are associated with greater abundance of *Ae. albopictus*, although more research is needed to determine if this relationship holds for *Ae. aegypti* [59]. As the mosquito vector *Ae. aegypti* re-emerges throughout the mainland United States and as diseases transmitted by the vector continue to remain a threat to public health, continuing to improve our understanding of *Ae. aegypti* distributions at a local level will allow public health efforts to continue to be targeted to the most at-risk or vulnerable areas and populations. Future studies should focus on including socioeconomic factors in the evaluation of *Ae. aegypti* distributions to gain a better understanding of the local neighborhood environments that support *Ae. aegypti* populations.

It is imperative that the distribution of *Ae. aegypti* be well understood prior to any potential major disease outbreaks. Understanding the habitat and areas where *Ae. aegypti* thrive will allow for a quicker, more targeted response to control the spread of disease should an outbreak occur. Targeted intervention will also help reduce the costs of any future outbreaks by targeting and therefore conserving prevention and treatment resources, limiting the number of people exposed to disease, and reducing the human cases observed. In order to prepare for potential future outbreaks, it is imperative that additional research be conducted in diverse cities throughout the United States to better understand the presence and distribution of *Ae. aegypti* as related to socioeconomic factors.

Conclusions

This systematic review revealed a lack of prior research regarding the connection between the distribution of *Ae. aegypti* mosquitoes and socioeconomic factors. Given that the life cycle of these mosquitoes is closely linked to human populations and behaviors, it is imperative that this connection is better understood. This mosquito vector transmits many diseases relevant to public health such as dengue, yellow fever, Zika, and chikungunya, and they are found throughout large portions of the United States. In the event that a disease is again introduced to the *Ae. aegypti* population in the United States, many people that live in areas where this mosquito is present could be at risk of contracting the disease. Preparation for a disease outbreak is essential and understanding the distribution of this disease vector is a crucial component to that preparation. More research is needed to better understand how the distribution of *Ae. aegypti* relates to socioeconomic factors in the United States.

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CHAPTER 3: SPECIES DISTRIBUTION MODELING OF *AEDES AEGYPTI* IN MARICOPA COUNTY, ARIZONA FROM 2014 TO 2020

ABSTRACT

Background: *Aedes aegypti* mosquitoes transmit dengue, yellow fever, Zika, and chikungunya viruses. Their range has recently been expanding throughout the world, including into desert regions such as Arizona in the southwestern United States. Little is understood about how these mosquitoes are surviving and behaving in arid environments, habitat that was previously considered inhospitable for the vector. The goal of this study is to create quarterly species distribution models based on satellite imagery and socioeconomic indicators for *Ae. aegypti* in Maricopa County, Arizona from 2014 to 2020. **Methods**: Trapping records for Ae. aegypti in Maricopa County, Arizona from 2014 to 2020 were split into 25 quarterly time periods. Quarterly species distribution models (Maxent) were created using satellite imagery-derived vegetation and moisture indices, elevation, and socioeconomic factors (population density, median income) as predictors. Maps of predicted habitat suitability were converted to binary presence/absence maps, and consensus maps were created that represent “core” habitat for the mosquito over 6 years of time. Results were summarized over census-defined zip code tabulation areas with the goal of producing more actionable maps for vector control. **Results**: Population density was generally the most important predictor in the models while median income and elevation were the least important. All of the 25 quarterly models had high test area under the curve values (>0.90) indicating good model performance. Multiple suburban areas surrounding the Phoenix metropolitan core area were identified as consistent highly suitable habitat. **Conclusion**: We identified

long term “core” habitat for adult female *Ae. aegypti* over the course of 6 years, as well as “hotspot” locations with greater than average suitability. Binary maps of habitat suitability may be useful for vector control and public health purposes. Future studies should examine the movement of the mosquito in this region over time which would provide another clue as to how the mosquito is surviving and behaving in a desert region.

Introduction

Aedes aegypti mosquitoes are vectors of great public health importance as they are capable of transmitting dengue, Zika, chikungunya, and yellow fever viruses (Pialoux et al., 2007; Guzman and Harris, 2015; Monath and Vasconcelos, 2015; Musso and Gubler, 2016). Importantly, although this mosquito initially spread throughout the world hundreds of years ago, their range has rapidly expanded into new regions and environments (Kraemer et al., 2015), putting an even greater number of people at risk of contracting these diseases. This vector lives in close proximity to human settlements, is active during daytime hours, and feeds preferentially on humans for blood meals, making the mosquito an efficient vector of diseases (Christophers, 1960). *Aedes aegypti* mosquitoes need water for larval development and generally reside in warm, tropical regions of the world, as their survival and reproductive cycles are greatly impacted by temperature (Brady et al., 2014). Their range has been expanding into more temperate regions of the world, such as the United States and Europe, driven by human movement, human development, and changes in land use and land cover (Kraemer et al., 2019; Wilke et al., 2020). With some exceptions of greater distances traveled, this mosquito is generally found to have a small range of about 100–200 m over the course

of their lifetime (Harrington et al., 2005; Juarez et al., 2020), so their distribution is generally not homogeneous over an entire urban area but rather depends on habitat availability and microenvironment characteristics.

Past studies have focused on identifying the areas of a city well suited to hosting *Ae. aegypti* and identifying characteristics of the well-suited areas that can be targeted for mosquito control purposes. One approach to these studies has been to utilize species distribution models and satellite imagery to better understand the landscape characteristics that may be associated with *Ae. aegypti* populations. The goal of species distribution modeling is to predict the distribution of a species across a landscape given information about environmental variables (Franklin, 1995). Environmental variables may include weather or climate variables, soil variables, topographic variables, or landscape variables (Franklin, 1995). Species distribution models are based in ecological niche theory, the idea that the distribution of a species is limited by environmental characteristics (Vandermeer, 1972). Maxent is a popular freely available machine learning technique for species distribution modeling that uses presence-only observations of a species along with environmental variables to predict the probability of presence of the species throughout the study region (Phillips et al., 2006; Phillips and Dudík, 2008). This method has been used by several studies in the past in combination with remote sensing to predict the occurrence of *Ae. aegypti* (Arboleda et al., 2012; Espinosa et al., 2016; Estallo et al., 2018; Andreo et al., 2021; Hopperstad et al., 2021). One advantage of this approach is the creation of habitat suitability maps that could be useful for identifying consistent hot spots of the mosquito and for vector control planning.

Past studies using Maxent have been conducted in tropical areas, where diseases caused by pathogens transmitted by *Ae. aegypti* greatly impact populations. In Argentina, two studies used satellite imagery and socioeconomic factors to predict the distribution of larval habitat of *Ae. aegypti*, but seasonal or temporal trends were not evaluated (Espinosa et al., 2016; Estallo et al., 2018) while in Florida one study that combined land cover, climatic variables, and human population data to predict larval habitat suitability for *Ae. aegypti* using 6 weeks of larval collection data found that remotely sensed variables were more predictive than locally collected data (Hopperstad et al., 2021). Other studies created multiple species distribution models for one mosquito season (Andreo et al., 2021) or over multiple years (Arboleda et al., 2012) to identify core larval habitat for the vector and areas of the city that may benefit most from vector control activity. Some studies have used a similar but slightly different approach than the study presented in this manuscript by utilizing climate variables rather than satellite imagery to predict habitat suitability for *Ae. aegypti* using Maxent (Abdelkrim et al., 2021).

The goal of this study is to build on this previous research in order to create quarterly species distribution models based on satellite imagery and socioeconomic indicators for *Ae. aegypti* in Maricopa County, Arizona from 2014 to 2020. Maricopa County is located in the Sonoran Desert, habitat that may not naturally be suitable for the mosquito vector. However, anthropogenic modifications to the environment have created an oasis in the desert that has allowed this mosquito vector to thrive in this area. According to adult mosquito trapping data and information provided by the Maricopa County Environmental Services Vector Control Division (MCESVCD), the *Ae.*

aegypti population in Maricopa County, Arizona has been increasing over the last decade, and the mosquito is now routinely trapped year-round in this region. *Aedes aegypti* has been identified in Arizona as far back as 1931 and 1946 in Tucson (Bequaert, 1947; Murphy, 1953) and 1951 in Yuma (Richards et al., 1956). However, the mosquito was not identified in routine surveillance for decades despite no specific efforts to reduce its population in Arizona (Engelthaler et al., 1997). It is possible that the Pan American Health Organization campaign to eradicate *Ae. aegypti* in the Americas contributed to the mosquito not being detected in Arizona in the mid-20th century, but the exact cause of the perceived disappearance of the mosquito remains unclear (Uribe, 1983; Engelthaler et al., 1997; Hotez, 2016). In the mid-1990s, *Ae. aegypti* was once again trapped in Tucson and along the Arizona-Mexico border (Engelthaler et al., 1997). By studying routine trapping data from the past 15 years, it is now clear that the population of the vector is generally increasing in Maricopa County. In 2020, the number of *Ae. aegypti* trapped decreased substantially, and the reasons for the decrease are unclear; however, 2021 was the biggest year on record as of September.

Past studies have attempted to create multitemporal species distribution models for *Ae. aegypti* using satellite imagery and socioeconomic factors as predictors either by creating multiple models within one mosquito season or by creating yearly models over the course of multiple years. This project has extended this research by creating multiple seasonal models per year over the course of 6 years, which allowed the evaluation of both seasonal and long-term trends in habitat suitability for *Ae. aegypti* in Maricopa County. Similar to previous studies, we hypothesized that we would identify

areas in Maricopa County that consistently support *Ae. aegypti* populations over multiple seasons and years. We also anticipated that, given the close relationship the vector has with human populations, human population density would be an important predictor in the models. Finally, given that the mosquito prefers a humid or tropical environment, we expected that increased vegetation would be associated with increased *Ae. aegypti* presence in Maricopa County.

This project is also the first of its kind, as far as we are aware, to utilize satellite imagery and socioeconomic predictors to predict habitat suitability for *Ae. aegypti* using Maxent in an arid desert environment, habitat into which this vector has recently expanded. This project will be a step toward the long-term objective of developing an understanding of the underlying geographic distribution and movement of the mosquito vector *Ae. aegypti* in Maricopa County, Arizona and, more broadly, in arid desert environments. In addition to contributing to the growing body of research that is attempting to understand the distribution of this vector, especially in territories into which the mosquito has recently expanded, the findings of this study will be beneficial to vector control and public health efforts as the mosquito population increases and outbreaks of disease occur.

Materials and Methods

Maricopa County, Arizona: Study location and climate

Maricopa County is located in south central Arizona in the southwestern United States. The county comprises approximately 24,000 square kilometers of land and contains Arizona's capital and most populous city, Phoenix, along with over 20 additional recognized cities and towns (Maricopa County, 2021). The population of

Maricopa County is approximately 4.5 million residents (Maricopa County, 2021). The county is located in a desert climate with generally low humidity. Phoenix has an average annual rainfall of 20.4 cm, an average maximum temperature of 41.2°C for the hottest month, July, and an average minimum temperature of 7.1°C for the coldest month, December (Schmidli, 1996). Rainfall is scarce and sporadic for most of the year, while monsoon season in July and August can bring torrential rains (Schmidli, 1996). Like most desert climates, the temperature can fluctuate drastically between the daytime high and the nighttime low with variations of 15°C or more in 1 day being common (Schmidli, 1996). For this study, we chose not to include weather predictors due to the relatively small study area that should have fairly consistent weather and climate and also due to the lack of availability of this type of data at the scale of our other predictors (30 m).

Maricopa County, Arizona is an at-risk location for potential importation of *Ae. aegypti*-transmitted pathogens due to the established presence of the mosquito vector and a high volume of travelers crossing the border into Arizona from areas with endemic *Ae. aegypti*-transmitted pathogens, such as Mexico and Central America. On average, over 25 million travelers cross the border from Mexico into Arizona each year (United States Department of Transportation, 2022). Further, all travelers crossing the land border from Mexico into Arizona, regardless of their origin, will cross through an area that regularly experiences outbreaks of disease associated with *Ae. aegypti*, which creates the risk that viremic travelers could introduce pathogens to the mosquito vector population in Arizona. Sonora, Mexico, which is just south of the Arizona-Mexico border, recorded over 300 laboratory-confirmed cases of Zika virus (Secretaría de Salud, 2018)

(the most cases of all Mexican states) in 2018 and 982 and 2,606 probable cases of dengue (Secretaría de Salud, 2019) in 2018 and 2019, respectively, which raises concerns about the pathogens that cause these diseases spreading to and becoming established in the *Ae. aegypti* population in Arizona. In Arizona, seventeen travel-related cases of dengue infection were reported in 2019, twelve of which were identified in Maricopa County (Arizona Department of Health Services-Office of Infectious Disease Services, 2019). Furthermore, as recently as 2014, outbreaks of dengue resulting in nearly 100 reported cases have occurred along the Arizona-Mexico border in Yuma, Arizona which is less than 200 miles from densely populated Maricopa County (Jones et al., 2016).

Trapping data and data organization

MCESVCD performs regular CO_2 trapping of adult mosquitoes throughout Maricopa County, but with traps concentrated in the Phoenix metropolitan area, by setting up more than 800 overnight CO_2 traps for a 12-h period each week.

The trapping program in Maricopa County is one of the most comprehensive programs in the country, both in the amount of area covered and in the regularity with which traps are placed. Through an established partnership with MCESVCD, we gained access to this trapping data for the years 2014–2020. The provided data includes the trapping date, number of adult mosquitoes trapped, species and sex of the mosquitoes, identification number of the trap, and latitude and longitude values.

Quarter	Dates	Number of Obs. Used in Model	Avg. Test AUC	Threshold to Convert to Binary Map	Area Predicted as Suitable (%)	Most Important Predictor / Permutation Importance
1	2/1/14—4/30/14	73	0.942	0.52	9.99	Pop. Dens. / 89.4
2	5/1/14—7/31/14	233	0.950	0.50	7.83	Pop. Dens. / 82.4
3	8/1/14—10/31/14	778	0.900	0.68	12.09	Pop. Dens. / 66.4
4	11/1/14—1/31/15	382	0.900	0.60	14.31	Pop. Dens. / 62.1
5	2/1/15—4/30/15	326	0.928	0.58	10.81	Pop. Dens. / 67.8
6	5/1/15—7/31/15	571	0.917	0.56	13.02	Pop. Dens. / 76.8
7	8/1/15—10/31/15	587	0.913	0.54	11.17	Pop. Dens. / 61.0
8	11/1/15—1/31/16	337	0.924	0.60	10.14	Pop. Dens. / 70.5
9	2/1/16—4/30/16	247	0.933	0.64	8.97	Pop. Dens. / 80.9
10	5/1/16—7/31/16	484	0.921	0.62	9.88	NDMI / 59.5
11	8/1/16—10/31/16	702	0.915	0.56	10.75	Pop. Dens. / 67.8
12	11/1/16—1/31/17	511	0.921	0.56	11.00	Pop. Dens. / 68.9
13	2/1/17—4/30/17	299	0.933	0.54	11.50	Pop. Dens. / 90.8
14	5/1/17—7/31/17	613	0.908	0.60	12.08	Pop. Dens. / 55.0
15	8/1/17—10/31/17	763	0.908	0.62	11.17	Pop. Dens. / 53.1
16	11/1/17—1/31/18	388	0.924	0.60	11.75	Pop. Dens. / 57.8
17	2/1/18—4/30/18	121	0.942	0.60	10.51	Pop. Dens. / 85.4
18	5/1/18—7/31/18	580	0.921	0.58	10.77	Pop. Dens. / 71.0
19	8/1/18—10/31/18	n/a	n/a	n/a	n/a	n/a
20	11/1/18—1/31/19	n/a	n/a	n/a	n/a	n/a
21	2/1/19—4/30/19	304	0.920	0.66	11.23	Pop. Dens. / 84.7
22	5/1/19—7/31/19	711	0.911	0.62	11.33	NDMI / 57.1
23	8/1/19—10/31/19	705	0.900	0.58	13.17	NDMI / 49.4
24	11/1/19—1/31/20	383	0.930	0.58	9.33	Pop. Dens. / 77.8
25	2/1/20—4/30/20	210	0.919	0.52	11.57	Pop. Dens. / 83.8
26	5/1/20—7/31/20	612	0.915	0.62	10.77	NDMI / 47.5
27	8/1/20—10/31/20	479	0.925	0.66	9.43	NDMI / 56.7
28	11/1/20—1/31/21	n/a	n/a	n/a	n/a	n/a

Table 3.1. Quarters with descriptive statistics and results. This table shows the quarter number, dates, number of observations used in model building, average test area under curve (AUC) from Maxent output, the threshold used to convert the suitability output to binary presence/absence data using a 10 percent omission threshold, the percentage of are calculated as suitable after converting to binary data, and the most important predictor with the permutation importance.

To create the multitemporal models for this study, we divided the study period into quarters that roughly reflect four seasons of the year with varying levels of mosquito activity. The quarters were defined as follows: February 1–April 30, May 1–July 31, August 1–October 31, and November 1–January 31 (Table 3.1). To suit the requirements of Maxent, the species distribution model used for this study, trapping data were converted to presence only records for each quarter by creating a list of observations at unique locations defined by latitude and longitude and then removing duplicate observations for each location in each quarter. Due to missing data for three quarters (8/1/2018–10/ 31/2018, 11/1/2018–1/31/2019, and 11/1/2020–1/31/2021), presence only records were available to create 25 quarterly models from 2014 to 2020.

Remote sensing predictors

Google Earth Engine (Gorelick et al., 2017) was used to download Landsat 8 OLI satellite imagery (Irons et al., 2012) clipped to Maricopa County, Arizona. For each quarter, all available Landsat 8 images with top of atmosphere reflectance were downloaded. Then, any pixels with a cloud score of 1 or cloud shadow confidence score of 3 were masked. For each Landsat 8 image available, the Normalized Difference Vegetation Index (NDVI) and the Normalized Difference Moisture Index (NDMI) were calculated using bands 5 and 4 or bands 5 and 6, respectively. Finally, the mean NDVI and mean NDMI values were calculated for each pixel using all Landsat 8 images in that quarter. Landsat 8 imagery has a resolution of 30 m, so the resulting NDVI and NDMI products for each quarter in turn also had a 30-m resolution. Elevation data from the NASA Shuttle Radar Topography Mission (SRTM) were also clipped to Maricopa County, Arizona in Google Earth Engine (Farr et al., 2007). The images were exported

from Google Earth Engine to be used with Maxent. The resample function from the raster package (Version 3.5–11) was used to ensure that the elevation raster matched the extent and cell size of the NDVI and NDMI rasters exactly (Hijmans, 2021).

Socioeconomic predictors

Socioeconomic predictors were also included due to the close relationship that Ae. aegypti mosquitoes have with humans. Socioeconomic predictors were downloaded from the United States Census TIGER/Line Shapefiles with Selected Demographic and Economic Data from the American Community Survey 5-Year Estimates from 2019 at the block group resolution (US Census Bureau, 2021). Data were downloaded for all of Arizona, so only those block groups that have their centroid in Maricopa County were selected for further use using ArcMap (Version 10.7.1).

Socioeconomic predictors of interest were population density and median income. Predictors were chosen based on a priori assumptions about potential influences on the suitability of habitat and the availability of blood meals for the vector. Population density was included because the vector generally prefers to feed on humans for blood meals (Christophers, 1960), so areas with more people may be better able to support *Ae. aegypti* populations. Further, a similar study found human population density was the most influential factor for predicting habitat suitability for *Ae. aegypti* in an Argentinian city (Estallo et al., 2018). Median income was included after conversations with MCESVCD staff indicated a potential correlation between *Ae. aegypti* populations and higher income areas, potentially due to an increased use of water for landscaping, water features, or pools.

Population density was calculated by dividing the population of each block group by the area of each block group in square kilometers. The polygon layers for these two variables of interest were converted to rasters using the Polygon to Raster tool in ArcMap (Version 10.7.1) using the setting MAXIMUM_AREA; extent and cell size was set to match that of the NDVI rasters downloaded from Google Earth Engine. The rasters for population density and median income were exported from ArcMap (Version 10.7.1) in ASCII format. Before continuing with further analysis, the socioeconomic predictor rasters were imported to RStudio (Version 1.4.1717) along with the NDVI, NDMI, and elevation rasters (R Core Team, 2021). The resample function from the raster package (Version 3.5-11) was used to ensure that the socioeconomic rasters matched the extent and cell size of the NDVI, NDMI, and elevation rasters exactly (Hijmans, 2021).

Modeling/Maxent

The first step in the modeling process involved evaluating the correlation of the five rasters (NDVI, NDMI, elevation, population density, median income) from each quarter to ensure that no rasters had a correlation of >0.7, as was done in Estallo et al. (2018) and Abdelkrim et al. (2021). Next, we determined the best settings with which to run Maxent for each quarter individually using the ENMeval package (Version 2.0.2) in RStudio (Version 1.4.1717) using 10-fold cross validation (Kass et al., 2021; R Core Team, 2021). The possible settings from which we chose the best model included the features L, LQ, H, LQH, LQHP, LQHPT (L, Linear; Q, Quadratic; P, Product; H, Hinge; T, Threshold) with a regularization multiplier between 1 and 5 (Phillips, 2005; Merow et al., 2013). The best settings for each quarter were chosen based on the model with the

lowest delta corrected Akaike Information Criterion (AICc) (Hurvich and Tsai, 1989). Using the ENMeval package, a bias file was also created based on the observations for each quarter. Bias files help address the issues that arise when sampling is not random throughout the study area by biasing the background points selected to be in the same area where the majority of observations occurred, thereby reducing potential bias towards predicting higher suitability in areas that are simply more accessible and therefore more sampled. This approach is preferred over filtering observations when the species is expected to be spatially clumped, as is the case for *Ae. aegypti*, which would be expected to have greater populations around densely populated areas (Kramer-Schadt et al., 2013).

Next, we ran Maxent (version 3.4.0) for each quarter using the bias file created for each quarter and the best settings possible as described above. Each Maxent model was created using 10-fold cross validation, and the average output across all 10 folds was further evaluated. Supplementary Table S3.1 for the feature settings and regularization multiplier used for each quarter.

Output manipulation

The Maxent output included habitat suitability maps for Maricopa County with values ranging from 0 to 1 representing the estimated habitat suitability for *Ae. aegypti* mosquitoes for each 30-m by 30-m square in the county, based on the observations for that quarter (Phillips, 2005). These maps were then converted to binary presence/absence maps based on the 10 percent omission threshold determined using the package SDMtools (Version 1.1-221.2) in RStudio (Version 1.4.1717) (VanDerWal

Consensus Map	Included Quarters	Dates	Area Predicted as Suitable (%)	Omission Rate (%)
First Season	1, 5, 9, 13, 17, 21, 25	All 2/1—4/30 quarters	5.24	38.0
Second Season	2, 6, 10, 14, 18, 22, 26	All 5/1—7/31 quarters	6.11	35.1
Third Season	3, 7, 11, 15, 23, 27	All 8/1—10/31 quarters	7.41	27.4
Fourth Season	4, 8, 12, 16, 24	All 11/1—1/31 quarters	6.88	27.5
Year 1	1, 2, 3, 4	2/1/14—1/31/15	5.61	36.2
Year 2	5, 6, 7, 8	2/1/15—1/31/16	8.11	21.9
Year 3	9, 10, 11, 12	2/1/16—1/31/17	7.42	25.3
Year 4	13, 14, 15, 16	2/1/17—1/31/18	8.11	20.5
Year 5	17, 18	2/1/18—7/31/18	9.03	14.7
Year 6	21, 22, 23, 24	2/1/19—1/31/20	7.48	25.3
Year 7	25, 26, 27	2/1/20—10/31/20	7.52	22.2
All Quarters	All 25 quarters	2/1/14—7/31/18 and 2/1/19—10/31/20	4.17	53.8

Table 3.2. Consensus map aggregations with descriptive statistics and results. This table shows the consensus aggregation with the quarters used for each, the dates for each consensus map, the percentage of area predicted as suitable after converting to a binary map, and the omission rate of the binary map.

et al., 2019; R Core Team, 2021) (Table 3.1; Supplementary Figures S3.1–S3.25). We chose to use the 10 percent omission threshold to create binary maps such that the area that is identified as suitable would encompass nearly all observations. However, this threshold also delineates a smaller area that is considered suitable by removing observations in areas with conditions in which the mosquito is not as consistently trapped. Other species distribution model studies have also utilized this approach (Radosavljevic and Anderson, 2014; Hopperstad et al., 2021).

After the suitability maps were converted to binary values, we calculated the percentage of area in the county that was deemed suitable for each quarter by dividing

the number of pixels deemed suitable by the total number of pixels in the study area (Table 3.1). Further, consensus maps were created by overlaying the binary maps for each year, each season, and for all maps as described above (Figure 3.2; Supplementary Figures S3.26–S3.36). Areas that were predicted as consistently suitable in each of the quarterly maps were considered suitable for the consensus maps (Arboleda et al., 2012). For the consensus maps, the percent of area predicted as suitable and the omission rate, or percentage of positive observations that were not predicted based on the suitable area, was calculated (Table 3.2).

Consensus maps were created for each year (e.g., year 1 was an aggregate of quarter 1, quarter 2, quarter 3, and quarter 4) and for each season (e.g., all February–April quarters; all May–July quarters; all August–October quarters; and all November–January quarters) by averaging the predicted suitability by pixel (Supplementary Figures S3.26–S3.36). Additionally, an overall consensus map was created by averaging the predicted suitability values for all 25 quarterly maps (Figure 3.1).

Maps of major freeways were downloaded from the AZGeo Data Hub to use as location references for the maps produced in this study. The data for the freeways maps was provided by the Maricopa Association of Governments and is publicly available and free to download as a shapefile (https://azgeo-data-hub-agic.hub.arcgis.com/).

Using the binary maps, we were able to calculate the percentage of area in Maricopa County that was determined to be suitable for *Ae. aegypti* for each quarter as well as for all of the consensus maps. We were also able to aggregate the results for block groups, tracts, and zip code tabulation areas (ZCTAs) in two different ways in order to produce more actionable maps for vector control, since individual 30-m by 30-m

pixels would be difficult to target for mosquito control. First, using the original habitat suitability output (with values ranging 0–1), we were also able to determine the average suitability for the aggregate areas for each quarter and for the consensus maps. We produced these average maps for each quarter and again for all consensus average predicted suitability maps (Figure 3.1; Supplementary Figures S3.1–S3.36). Second, using the quarterly and consensus binary maps, we are able to determine the proportion of area that was predicted to be suitable within block groups, tracts, and ZCTAs (Figure 3.2; Supplementary Figures S3.1–S3.36). The 2019 shapefiles for the various census areas were downloaded from the United States Census Bureau (https://www.census.gov/geographies/mapping-files/time-series/geo/tiger-line-file.2019.html), then imported to RStudio (Version 1.4.1717) where we used the function “zonal” from the raster (Version 3.5–11) package to determine the mean suitability value and the proportion of area predicted as suitable for each aggregate area. Maps were then created using ggplot2 (Version 3.3.5) and the sf (Version 1.0–5) packages or using the raster (Version 3.5–11) package (Wickham, 2011; Pebesma, 2018; Hijmans, 2021; R Core Team, 2021).

Results

Trapping observations from 2014 to 2020 were split into 28 quarterly time periods, with full data available for only 25 quarters (Table 3.1). The number of observations varied for each quarter from a low of 73 locations (2/1/2014–4/30/2014) to a high of 778 locations (8/1/2014–10/31/2014) (Table 3.1). Overall, for all 25 quarters for which data was available, there were 11,399 locations at which *Ae. aegypti* was observed, although the locations were not unique for each quarter. The mean number of

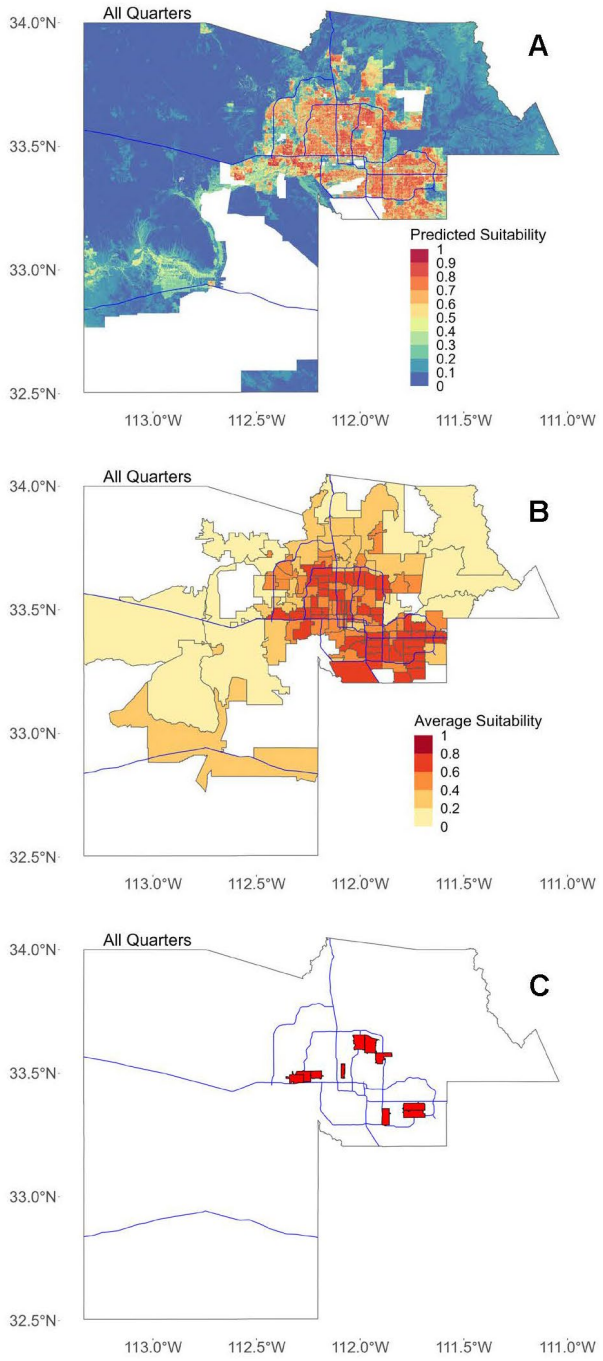

Figure 3.1. Average predicted suitability for all quarters. In all figures, blue lines represent major freeways in Maricopa County as a spatial reference. (**A**) Map showing the mean predicted suitability for each 30-meter by 30-meter pixel, calculated as the mean of the predicted suitability for all 25 quarters. Areas with missing data where suitability was not predicted are shown in white. (**B**) Predicted suitability for all quarters averaged by ZCTA. (**C**) The location of ten ZCTAs with the highest average suitability for all quarters.

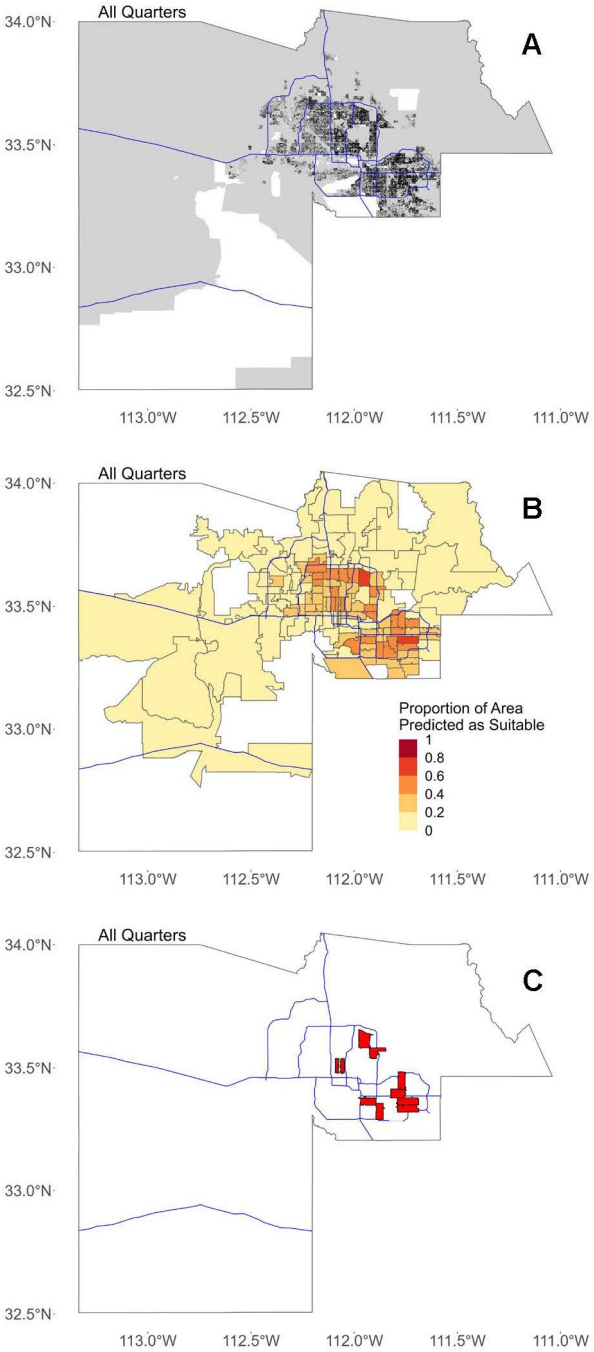

Figure 3.2. Binary maps for all quarters. In all figures, blue lines represent major freeways in Maricopa County as a spatial reference. (**A**) The consensus binary map for all quarters created by overlaying the binary map for all 25 quarters. Areas with missing data where suitability was not predicted are shown in white. (**B**) Proportion of area in each ZCTA predicted as suitable based on binary map in (A). (**C**) The location of ten ZCTAs with the highest proportion of area predicted as suitable for all quarters.

locations at which Ae. aegypti was observed per quarter was 456 (standard deviation: 203).

The following five predictors were used: NDVI, NDMI, elevation (range: 125–2,304 m, mean: 498 m, standard deviation: 258 m), population density (range: 0–14,657 people per square kilometer, mean: 182 people per square kilometer, standard deviation: 625 people per square kilometer), and median income (range: $10,716–$250,001, mean: $73,046, standard deviation: $33,123). The range, mean, and standard deviation values for NDVI and NDMI for each quarter can be found in Supplementary Table S3.2. The importance for each predictor varied from quarter to quarter, but population density was almost always the most important predictor (20/25 models) (Table 3.1) while median income (16/25 models) or elevation (9/25 models) was the least important predictor for all quarters. NDMI was the most important predictor for five quarters: quarters 10, 22, 23, 26, and 27. Increased human population density appears to be associated with greater suitability for *Ae. aegypti* while increased NDVI also appears to be associated with greater suitability for the mosquito up to a certain point, likely because extremely vegetated areas are more likely to have lower human population density (Supplementary Figures S3.37–S3.61).

Output included an image showing the pixel-by-pixel habitat suitability value on a scale of 0–1 (with 1 being highest suitability) (Supplementary Figures S3.1–S3.25), response curves for each predictor (Supplementary Figures S3.37–S3.61), the value for the average permutation importance for each predictor across all folds (Phillips, 2005; Phillips et al., 2006), a receiver operating characteristic (ROC) curve, and test area under curve (AUC) value (Estallo et al., 2018) which provides a threshold-independent

approach to evaluating model performance (Table 3.1). All quarterly models had high (≥0.90) test AUC, indicating excellent model fit (Estallo et al., 2018) (Table 3.1). Suitability was generally high in the Phoenix metropolitan area and lower in the rural areas of the county; however, there did exist quite a bit of variation in suitability throughout the Phoenix area, with the eastern and southeastern portions of the metropolitan area generally having the highest predicted suitability.

After the suitability maps were converted to binary values, we calculated the percentage of area in Maricopa County that was found to be suitable for each quarter (Table 3.1). For the consensus maps, the percentage of area in Maricopa County found to be suitable and the omission rate was calculated (Table 3.2). For the quarterly maps, the area deemed suitable ranged from 7.83% to 14.31% of Maricopa County. For the quarterly consensus maps, the percentage of area of Maricopa County deemed suitable for each quarter was: 5.24% in the February–April quarter, 6.11% for the May–July quarter, 7.41% for the August–October quarter, and 6.88% for the November–January quarter. For the yearly consensus maps, the area of Maricopa County deemed suitable for each year was: 5.61% for year 1, 8.11% for year 2, 7.42% for year 3, 8.11% for year 4, 9.03% for year 5, 7.48% for year 6, and 7.52% for year 7. The overall consensus map had 4.17% of the area of Maricopa County as suitable. For each of the 25 quarterly binary maps, the omission rate was approximately 10% as that is how the threshold was selected; for the consensus maps, the omission rate was calculated by overlaying the observations for all maps combined onto the consensus binary map. The quarterly omission rates were: 38.0% in the February–April quarter, 35.1% for the May–July quarter, 27.4% for the August–October quarter, and 27.5% for the November–January

quarter. The yearly omission rates were: 36.2% for year 1, 21.9% for year 2, 25.3% for year 3, 20.5% for year 4, 14.7% for year 5, 25.3% for year 6, and 22.2% for year 7. The omission rate for the overall binary map was 53.8%.

The top 10 block groups, tracts, and ZCTAs in terms of overall average suitability were spread throughout the Phoenix metropolitan area in the southeastern, northeastern, central, and southwestern areas (Figure 3.1). All of the top 10 block groups, tracts, and ZCTAs in terms of the proportion of area predicted as suitable are located in the central Phoenix or the eastern/southeastern Phoenix metropolitan areas (Figure 3.2).

Discussion

Through the creation of species distribution models for 25 quarterly time periods over 6 years, we were able to identify potential long term “core” habitat for the mosquito vector, as well as some “hotspot” locations with greater than average suitability that could potentially be targeted for vector control activity. We confirmed our hypotheses by identifying areas in Maricopa County that consistently support *Ae. aegypti* populations, by determining that human population density is an important predictor for the presence of *Ae. aegypti* populations, and by determining that increased vegetation, up to a certain point, is associated with the presence of *Ae. aegypti* populations in Maricopa County. One of the greatest strengths of this study is the ability to look at seasonal trends over the course of 6 years, providing further insight into the long-term habits of the vector in this region. Furthermore, this is the first study, as far as we are aware, that has evaluated species distribution models for the vector *Ae. aegypti* in a desert region.

Binary maps, especially the consensus binary maps, are potentially great tools for vector control planning purposes. Distilling 6 years of trapping data down into one map that shows locations with consistent habitat suitability for *Ae. aegypti* populations can help to provide an overall summary of the activity of *Ae. aegypti* since it has become strongly established in this region. It also helps to “fill in the gaps” between trapping locations and to identify additional areas that may have high suitability for the vector but are not currently being as intensively trapped or observed. Of course, the threshold that is chosen to create the binary maps has a substantial impact on the areas that are identified as suitable compared to the areas that are not.

We found that the omission rate was much higher for the consensus maps than it was for quarterly maps, indicating that there is a consistent area that is suitable for the vector, but that a lot of mosquito activity is also observed outside of this core area. This study does not provide insight into preferred larval habitat as the distribution maps were based solely on trapping data for adult mosquitoes, although it is reasonable to assume that the presence of adult female mosquitoes may indicate the presence of suitable larval habitat in which eggs can be deposited. Future studies should examine the movement of the mosquito in this region over time which would provide another clue as to how the mosquito is surviving and behaving in a desert region.

Tract and ZCTA aggregations should be interpreted with caution since the census data for population density and median income were both collected at the block group level. Some tracts and ZCTAs have missing data due to 50 census block groups having missing median income information. Further, the census tracts and ZCTAs may not have the same composition as the block groups that made up the predictors, but

instead are an aggregate of all characteristics in that area. In particular, the ZCTA results may be skewed because ZCTAs are not meant to represent a homogenous population. However, the results are still useful for vector control purposes because they provide an easier tool for planning instead of individual 30-m by 30-m pixels, and in the event of an outbreak predicted habitat suitability for *Ae. aegypti* can quickly be linked to human case data which is generally reported at the ZCTA level. Importantly, the overall characteristics of the tract or ZCTA may not reflect the smaller areas that are actually suitable for the vector.

Our study, like the Argentina-based findings published by Estallo et al., 2018 and the Florida-based findings published by Hopperstad et al. (2021), indicated that human population density is an important factor when determining habitat suitability for *Ae. aegypti*. Given that this mosquito vector is highly anthropophilic, this is an expected finding. Like Andreo et al. (2021) and Arboleda et al. (2012), we were able to create species distribution models for multiple time periods which could then be converted to binary suitability maps and overlaid to determine the areas that are consistently suitable for the vector over a longer time period. Similarly, we hope that these maps can be helpful for vector control purposes by identifying core areas that serve as consistent habitat for the vector over a longer time period. As in Arboleda et al. (2012), we found that the omission rate was much higher for the consensus maps than it was for individual maps, indicating that there is a consistent area that is suitable for the vector over time, but that populations of the vector are also observed in different areas outside of this core habitat depending on the year and season.

Although the maps produced in this study may be helpful for vector control and public health purposes, the results may suffer from the modifiable areal unit problem (MAUP) due to the scale of the predictors used compared to the range of the mosquito that we attempted to model (Openshow, 1979; Jelinski and Wu, 1996; Wong, 2004). The MAUP can be broken down into two primary issues: 1) that the results of any analysis are dependent on the scale of the inputs; and 2) that the results of an analysis will differ based on how areal units are "zoned," even when they are the same size. For example, the results of this analysis may have been different had we used finer or coarser resolution satellite imagery or socioeconomic predictors at the census tract or ZCTA level rather than the census block group level. Additionally, even if the information used in the analysis remained at the same scale, there could be differences in the results based on how the areal units were grouped together. Furthermore, the results could vary based on how they are aggregated after the analysis is performed, so it is wise to interpret all results and conclusions with caution until more research has been conducted and we have a better understanding of these relationships.

One limitation of this study was that trapping data was represented only as presence data. This means that outputs that represent suitability do not account for differences in abundance throughout the county (Elith et al., 2011). Some areas that are predicted to be suitable may only have small or transient populations of *Ae. aegypti* whereas others may have large, consistent populations of the vector and therefore a large increase in the potential risk of pathogen transmission by the mosquito. Presence only data also may not account for fluctuations in populations due to interventions such as insecticide application, which were not accounted for in this study, although

MCESVCD regularly uses pyrethroids to control mosquito populations throughout the county. Future studies that explore species distribution models that account for abundance could be helpful to more specifically identify areas that have large populations of *Ae. aegypti* where people may be more likely to be exposed to pathogens that cause disease. Additionally, models that explicitly account for interventions could help to evaluate the effectiveness of these interventions.

As of yet, we cannot determine whether the findings presented in this study for highly suitable areas would be correlated with risk of disease in the event of an outbreak, although findings by Arboleda et al. indicate that areas predicted as suitable by a species distribution model are correlated with human cases of dengue (Arboleda et al., 2012). In the event of a future outbreak, it will be important to evaluate the relationship between our suitability maps and the incidence of human cases of disease; however, past studies suggest that the maps produced by this study could be helpful for a public health response during an outbreak of disease vectored by *Ae. aegypti*. It is our hope that preparing this information ahead of time could help to reduce the burden and cost of disease in Maricopa County if an outbreak does occur.

The goal of this study was to create quarterly species distribution models based on satellite imagery and socioeconomic indicators for *Ae. aegypti* in Maricopa County, Arizona from 2014 to 2020. This project was intended to be a step toward the long-term objective of developing an understanding of the underlying geographic distribution and movement of the mosquito vector *Ae. aegypti* in Maricopa County, Arizona and, more broadly, in arid desert environments. As the vector continues to expand its range throughout the world, including rapid expansions into the desert southwestern United

States, further understanding of the mosquito's behavior in these regions will be needed in order to prepare for a potential outbreak of disease. It is our goal to create a better understanding of the distribution and behavior of the vector in this region to aid public health and vector control efforts aimed at reducing the risk and burden of disease in the event an outbreak occurs.

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CHAPTER 4: SPATIOTEMPORAL BAYESIAN MODELING OF THE PRESENCE OF *AEDES AEGYPTI* MOSQUITOES IN MARICOPA COUNTY, ARIZONA

ABSTRACT

Aedes aegypti mosquitoes transmit dengue, Zika, yellow fever, and Zika viruses. This mosquito has been increasing its range globally, and it has recently become established in Maricopa County, Arizona. In the Fall of 2022, cases of locally-acquired dengue fever were identified in Maricopa County, raising concerns for the possibility of outbreaks of disease caused by viruses transmitted by *Ae. aegypti* in this region. There is an urgent need for additional research and understanding of *Ae. aegypti* populations in this area. This study uses mosquito trapping data from 2014-2021 and Bayesian mixed-effects modeling methods in R-INLA to create a zero-inflated binomial model with spatial and temporal random effects that predicts the presence of female *Ae. aegypti* mosquitoes in Maricopa County, Arizona with reasonable accuracy. Our choice of weather, vegetation, and socioeconomic predictors allowed us to evaluate the relationship between mosquito presence and various small-scale neighborhood characteristics. We found a positive association between median income, population density, median house age, landscape greenness, and vapor pressure with the presence of female *Ae. aegypti* while precipitation and maximum temperature had negative associations with presence. We mapped spatial effects across the study area to identify locations with higher odds of mosquito presence. Overall, this study demonstrated the feasibility of this approach and developed a framework that can be extended for use as a tool to prioritize vector control and public health resources in this area.

Introduction

The mosquito *Aedes aegypti,* vector of dengue, Zika, yellow fever, and chikungunya viruses, likely originated and became domesticated in Africa before spreading throughout the world to the Americas and then to the Pacific and Asia via ships between the 1400s and 1700s.[1] The current global distribution of the vector covers more geographic territory than at any point in recorded history and continues to grow.[2] Typically, this mosquito lives in areas with a warm climate, as temperatures below 14°C negatively impact their biological functions,[3] temperatures below 10°C are considered unsuitable for adults and larvae and disrupt reproduction.[4] *Ae. aegypti* thrive in humid or tropical conditions, but this species is also adept at taking advantage of niche habitats created by anthropogenic environmental modifications even in areas with an unsuitable natural climate, such as the dry Arizona desert.[5] This mosquito tends to seek blood meals during daytime hours which increases their contact with humans, their preferred blood meal host.[4]

Aedes aegypti are skilled at utilizing environments created by human settlement and land development.[6] In urban environments, the mosquito readily reproduces in artificial containers and faces little to no threat from natural predators.[6] In many areas, the invasive mosquito species *Ae. albopictus*, which was introduced to the United States in 1985, provides competition for breeding spaces.[6,7] However, at this time in Maricopa County, Arizona, *Ae. albopictus* has never been trapped which limits the competition for *Ae. aegypti*, possibly allowing the population to grow even larger.

Aedes aegypti females require blood meals for reproduction, which they take almost exclusively from human hosts.[2] The mosquito feeds preferentially on humans,

even if other potential hosts or sugar meals are available.[8] Individual humans are varyingly attractive to the females depending on a range of physical and olfactory cues.[9] *Ae. aegypti* mosquitoes have a very small range, and few stray further than about 100 meters from where they originated[10] unless the conditions of the immediate environment are unsuitable for reproduction in which case the females have been observed to disperse up to 2.5 km from their origination point.[11] The tendency for mosquitoes to remain in and seek out areas with well-suited habitat indicates that small-scale, neighborhood level environmental factors likely have a considerable influence on the ability of *Ae. aegypti* to survive in specific areas.

Public Health Relevance of Aedes aegypti

Aedes aegypti mosquitoes are primary vectors of dengue,[12] yellow fever,[13] and the newly emerged threats of chikungunya and Zika viruses.[2,14,15] These diseases are primarily transmitted between mosquito and human populations, which raises concerns about infected travelers introducing the disease to a naïve mosquito population at their travel destination, such as Maricopa County.[16] In recent years, mosquito-borne diseases have reemerged as a pressing public health issue in many countries around the world, as the geographic range of mosquitoes has increased rapidly.[2] In the last few decades *Ae. aegypti*, which was thought to be eradicated from the United States, has been increasing in population, and new viruses (Zika, chikungunya) have been introduced to areas around the country.[2,17]

Dengue has expanded its distribution throughout the world in the last few decades and has been reported to have caused locally transmitted cases in the United States.[12] In Arizona, seventeen travel-related cases of dengue infection were reported

in 2019, twelve of which were identified in Maricopa County. Furthermore, as recently as 2014, outbreaks of dengue resulting in nearly 100 reported cases have occurred along the Arizona-Mexico border in Yuma, Arizona which is less than 200 miles from densely populated Maricopa County.[18] In October 2022, two cases of locally-acquired dengue virus were identified in Maricopa County.[19] **Yellow fever** cases typically occur in Africa and South America[13] and result in fever, vomiting, kidney failure, jaundice, hemorrhaging, and in 20-60% of severe cases, death.[13] There is currently no treatment available for yellow fever infection.[13] **Chikungunya** has developed as a potential global health threat in the past decade, as the disease has emerged rapidly in the Americas.[2,20] Chikungunya virus is considered to be a potential public health threat should it emerge in the Americas, because the population has no current immunity to the disease.[15] **Zika** virus was first discovered in Uganda in 1947, and caused mild, sporadic illness in humans prior to the occurrence of unexpected large Zika virus outbreaks beginning in the Pacific islands in 2007.[20,21] The outbreak in Brazil that began in 2015 introduced widespread concern that Zika infection was linked to severe neurological complications for infants infected prenatally.[21] Zika virus has been circulating autochthonously in Mexico since 2015 and has been estimated to have caused over 270,000 human cases of Zika virus infection during that time.[22,23] Between 2015-2017, a large outbreak of Zika virus in the Americas resulted in over 3,000 cases of microcephaly associated with Zika infection and was estimated to cost between 7 to 18 billion USD during the outbreak alone.[24,25]

Risk of transmission in Maricopa County

Maricopa County, Arizona is an at-risk location for potential importation of *Ae. aegypti*-transmitted viruses due to the established presence of the mosquito vector and high volume of travelers crossing the border into Arizona from areas with endemic *Ae. aegypti*-borne viruses, such as Mexico and Central America. On average, over 25 million travelers (including United States citizens returning from their travels) cross the border from Mexico into Arizona each year.[26] Sonora, Mexico, which is just south of the Arizona-Mexico border, recorded over 300 laboratory-confirmed cases of Zika virus (the most cases of all Mexican states) in 2018 and 982 and 2,606 probable cases of dengue in 2018 and 2019, respectively, [27] which raises concerns about these diseases spreading to and becoming established in the *Ae. aegypti* population in Arizona. Although much research exists on the broad distribution of mosquito vectors, there is less understanding of the small area climate and socioeconomic factors that create habitat for *Ae. aegypti* in an arid climate such as Maricopa County, Arizona.

Socioeconomic Factors

Given that *Ae. aegypti* mosquitoes have such a close relationship to humans, the population density of a neighborhood is likely to impact the ability of the vector to inhabit that area. Furthermore, the socioeconomic status of a neighborhood can influence the neighborhood design, infrastructure, and landscape, which in turn could potentially influence available mosquito habitat. For instance, green areas are found less often in economically disadvantaged areas of a city than in affluent areas.[28] In metropolitan Phoenix, the area comprising much of Maricopa County, Arizona, more affluent neighborhoods had more abundant and more diverse vegetation in residential areas

than did less affluent neighborhoods.[29] In another area of Arizona with a similar climate, *Ae. aegypti* was found to be associated with increased vegetation,[30] so the relationship between neighborhood socioeconomic status and mosquito populations deserves more attention and investigation.[31]

Models for Understanding Aedes aegypti in the Southwest US

A limited number of studies have attempted to model *Ae. aegypti* distributions in the arid desert climate of the Southwestern United States, only one of which used a combination of climate and socioeconomic predictors to model mosquito abundance. A paper published by Monaghan et al. (2018) included temperature and humidity variables in a Gaussian mixed effects model for the log-transformed count of *Ae. aegypti* to predict the potential abundance of the mosquito in Maricopa County, Arizona one month in advance for the years 2006-2015.[32] Although the model developed in this publication is simple to use and useful for determining the potential suitability of habitat for *Ae. aegypti*, the authors also acknowledge that the inclusion of "non-climatic factors" such as "the presence of humans and availability of container habitats" may improve model performance.[32] Multiple studies conducted nearby Maricopa County, Arizona, have attempted to model the relationship between *Ae. aegypti* mosquito presence and socioeconomic factors. One such study conducted in nearby Tucson, Arizona used log-linear or logistic regression models to understand the relationship between immature *Ae. aegypti* and household characteristics such as housing type, ownership status, house age, house landscaping/vegetation, number of household residents, and household income; this study found that immature forms of the mosquito were positively associated with home ownership and negatively associated with household income.[5]

Another study conducted in Tucson, Arizona used multiple and logistic regression to study the relationship between *Ae. aegypti* immatures and socioeconomic factors such as population density, income, house age, and vegetation cover; this study found that immature mosquito abundance was positively associated with house age while income was negatively correlated with abundance in a normal rain year but not in a dry year.[33] One study that measured abundance of the vector in Tucson, Arizona, and both Nogales, Arizona, and Nogales, Mexico, included climate data recorded at trapping sites as well as housing and vegetation characteristics of the trapping site.[30] This study utilized multiple logistic regression models and found that the mosquito was positively correlated with rainfall in Tucson, Arizona and with vegetation abundance, although this relationship was complicated by seasonal weather patterns.[30]

Spatiotemporal Models for Understanding Mosquito Presence

All of the studies discussed above did not account for the spatial and temporal dependency of mosquito observations when constructing models to predict *Ae. aegypti* presence or abundance in this region. Although no studies exist that account for these dependencies in models for *Ae. aegypti* in desert regions, there are a few studies that have utilized statistical modeling approaches, namely the Integrated Nested Laplace Approximation with Stochastic Partial Differential Equation (INLA-SPDE) method, a Bayesian modeling approach, for *Ae. aegypti* in other regions. Myer and colleagues have produced a study from 2020 that models *Ae.* aegypti counts in Brownsville, Texas using this approach.[34] In central California, Marcantonio et al. used R-INLA to model the results of a mark-release-recapture study.[35] Myer and colleagues also produced two studies that model the presence of West Nile Virus positive mosquitoes in two New York

counties in 2017 and 2019 that we used to inform the creation of our models.[36,37]

This study extends the limited literature in this area to model the presence of *Ae. aegypti* females across Maricopa County, Arizona from 2014-2021 by 1) utilizing a modeling approach that accounts for both spatial and temporal dependencies and 2) incorporating both weather and socioeconomic predictors. The goal of this study is to better understand the relationship between the presence of the mosquito vector and small-scale environmental and socioeconomic factors in the arid desert climate of Arizona. In order to implement prevention strategies and respond to future disease outbreaks, it is crucial to understand characteristics that drive the distribution of mosquito vectors.[14,38] Additionally, we have constructed our models in a way that would allow predictions one week in advance during mosquito season.

Due to the recent increase in range and disease transmission of this mosquito vector throughout the world, especially into desert regions that were previously thought to be inhospitable to the vector, increased efforts to understand how the environment influences mosquito habitat in areas with an established presence of the vector are justified in order to improve preparedness for potential disease outbreaks. A better understanding of how socioeconomic characteristics influence *Ae. aegypti* habitat and movement can help to inform control strategies in order to reduce the burden and cost of future disease outbreaks by facilitating a swift, targeted response. Additionally, the results of our model may help to identify areas that are “hot spots” for *Ae. aegypti* presence, which may help to inform additional surveillance efforts.

Methods

Study Area

Maricopa County, which comprises approximately 23,828 square kilometers of land, is located in south central Arizona, USA with a population of approximately 4.5 million residents as of 2019.[39] Arizona's capital and most populous city, Phoenix, is located within Maricopa County as one of the county's 24 recognized cities and towns.[39] Phoenix has a desert climate with generally low humidity, an average annual rainfall of 20.40 cm, an average maximum temperature of 41.17°C for the hottest month, July, and an average minimum temperature of 7.11°C for the coldest month, December.[40] Sporadic rainfall generally occurs during the winter months of November through March, while monsoons in July and August bring heavy rains.[40]. Typical of a desert climate, temperature fluctuations between the daytime high and the nighttime low temperature can vary by 15°C or more.[40]

Mosquito Sampling

Maricopa County Environmental Services Vector Control Division conducts routine CO_2 trapping throughout Maricopa County, but focused mainly on the Phoenix metropolitan area, by deploying nearly 800 traps overnight for a 12-hour period on a weekly basis. See Figure 4.1 for trapping locations; see Supplementary Figure 4.1 for positive trapping locations per year. Through an established partnership with Maricopa County Vector Control, we gained access to this trapping data for the years 2012-2021. The provided data includes the trapping date, number of adult mosquitoes trapped, species and sex of the mosquitoes, identification number of the trap, and latitude and longitude values (which we transformed to the Universal Transverse Mercator Zone 12 North projection for more accurate distance calculations). We then filtered this data to include

only trapping observations for *Ae. aegypti* females. To facilitate analysis, the presence or absence of *Ae. aegypti* females was summarized by trap location and epidemiological week. Although the mosquito trapping record is close to complete for all weeks between 2012-2021, there are occasional missing data due to holidays for vector control staff or data storage issues. We have retained all observations of zero *Ae. aegypti* females; however, where data were missing we have excluded those locations and epidemiological weeks from the models. Our model utilizes trapping data from the years 2014-2021, after *Ae. aegypti* seems to have become more well established in Maricopa County (see Figure 4.2). The response variable was coded as 0 for trap observations where no female *Ae. aegypti* were observed and 1 for trap observations where one or more female *Ae. aegypti* were observed.

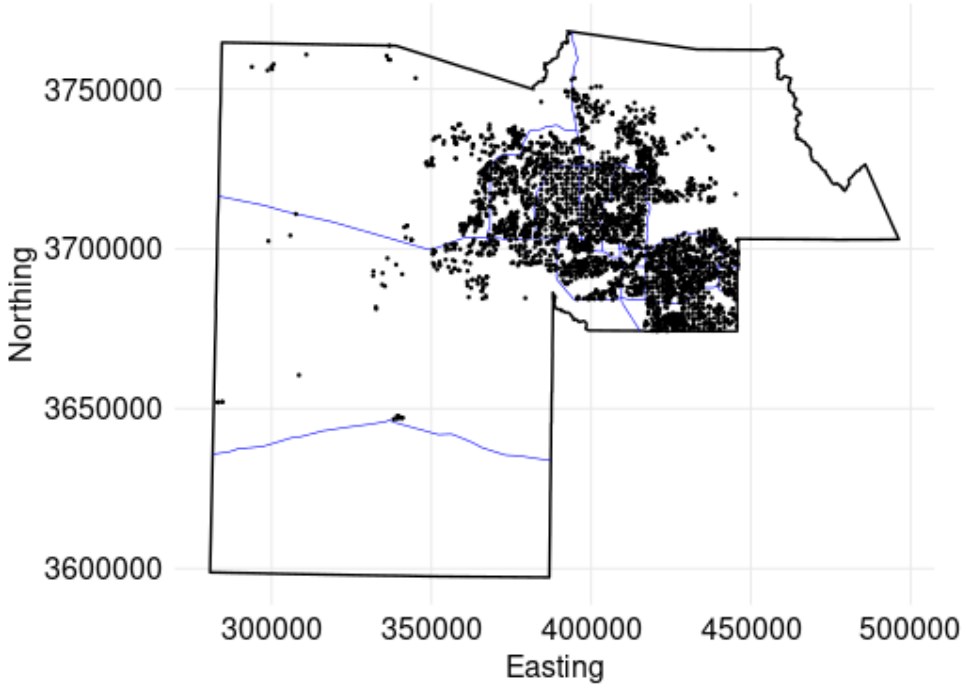

Figure 4.1. Trap locations for Maricopa County from 2014-2021. Major freeways are shown as blue lines to provide a location reference. Each black dot represents one or more trap observation.

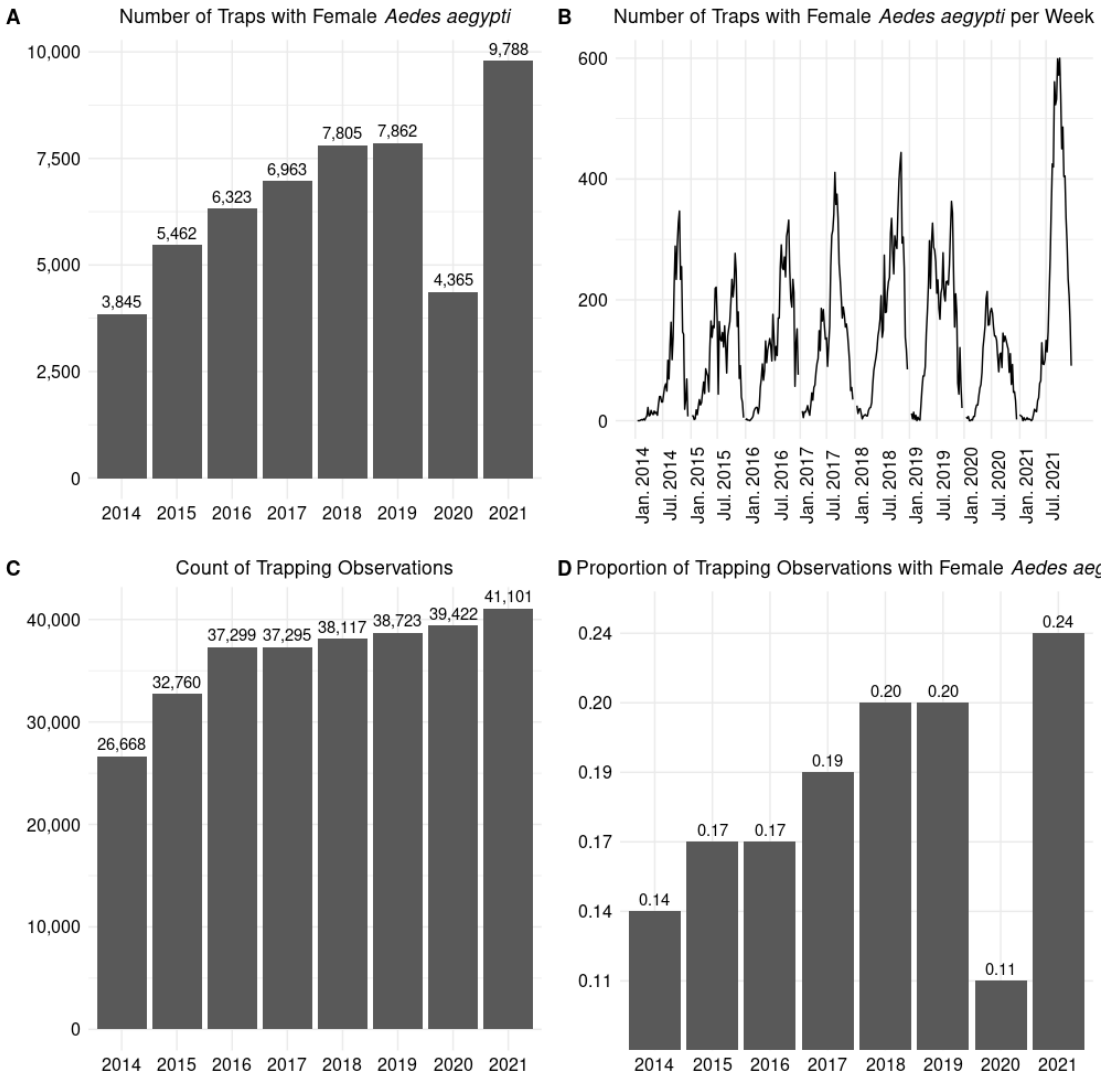

Figure 4.2. Descriptive graphs of *Aedes aegypti* presence in Maricopa County, AZ from 2014-2021. (A) The number of trap observations per year that recorded one or more *Ae. aegypti* females; these values do not represent unique locations. **(B)** The number of trap observations per week that recorded one or more *Ae. aegypti* females; these values represent unique locations per week. **(C)** The total number of trapping observations, regardless of whether *Ae. aegypti* females were recorded. **(D)** The proportion of trapping observations from **(C)** that recorded one or more *Ae. aegypti* females **(A)** per year.

Weather and Land Cover Data

Daily gridded weather data for 2014-2021 were obtained by downloading Daymet variables from Google Earth Engine at a 1-kilometer resolution for the state of Arizona.[41]

The following variables were obtained from Daymet: maximum temperature, precipitation, and vapor pressure. Daily variables were summarized by epidemiological week to match to the mosquito data. Precipitation was summed, while the weekly mean was calculated for minimum temperature, maximum temperature, and vapor pressure. Weekly mosquito observations were matched to the weekly summarized precipitation, maximum temperature, and vapor pressure data from the previous week (hereafter referred to as lag 1) and to the precipitation data for two weeks prior (hereafter referred to as lag 2) for each trapping location. We chose to lag the weather predictors for two reasons: 1) weather data was summed to weekly values, and trap observations could take place at any day during the week. This means that if a trap observation was recorded Monday but a rain event occurred Thursday, that rain event would have no relationship with the trap observation for that week. By lagging the weather predictors, we ensure that weather events predate all trap observations. And 2) in the future, we could use this model to predict mosquito presence for the upcoming week by using lagged weather information. If we used current week weather information as a predictor in our model, we could not predict mosquito presence in advance. Additionally, MODIS satellite imagery data representing the vegetation ground cover were downloaded via Google Earth Engine: Enhanced Vegetation Index (EVI).[42,43] These images are produced at 16-day intervals and were downloaded at a 250-meter resolution over the state of Arizona. Weekly mosquito observations were matched to the most recent available MODIS data for the previous week at each trapping location. Again, we chose to match to the previous week to retain the possibility of predicting mosquito presence in advance.

Census Data

Census data of interest (population, median income, and median year that structures were constructed) were downloaded at the census block group resolution for the state of Arizona from the 2012-2016 and the 2017-2021 American Community Survey 5-year Estimate Data using the tidycensus R package.[44–46] Additionally, the land area for each block group was obtained using the tigris R package.[47] The population density for each census block group was calculated by dividing the population by the area of the block group in square kilometers. The median age of structures was calculated by subtracting the median year structures were built from the year of the mosquito observation; negative values (e.g., mosquito observation from 2017 while median year structure built in that block group is 2019) were rounded to zero.

Predictor Selection

Predictors were selected using *a priori* knowledge of potential relationships and then assessing the multicollinearity of the variables by calculating the variance inflation factor (VIF) for socioeconomic predictors and for greenness/weather predictors to ensure that all selected predictors had a VIF < 3. After ensuring multicollinearity was not an issue, the predictors were scaled by subtracting the mean value and dividing by the standard deviation to improve model convergence and interpretation of predictor-response relationships for covariates on different scales.

Statistical Analysis

We utilized the Bayesian mixed-effects approach in R-INLA, as it has the capability of employing both spatial and temporal random effects simultaneously.[48–51] We evaluated binomial and zero-inflated binomial models with no random effects,

spatial random effects, temporal random effects, and both spatial and temporal random effects. To decrease model and computational complexity, we incorporated spatial and temporal random effects as a purely spatial term and a purely temporal term, according to the the separability hypothesis.[52] We compared models using the deviance information criterion (DIC) as well as the area under curve (AUC) value computed by integrating the area under the receiver-operating characteristic (ROC) curve which is created by plotting the sensitivity by 1 – specificity for a range of "cutoff" values that could be used to calculate presence or absence from the binomial model output. Predictive power of the models was tested by withholding all observations from 2021 from model training, then evaluating model predictions for that year. Models with a lower

Table 4.1. Penalized complexity priors for hyperparameters of the spatiotemporal zero-inflated binomial INLA SPDE model.

Hyperparameter	Prior specification	Initial Values	Interpretation
Mean for spatial range *r*	(Mean, p<)	(10,000, 0.9)	The probability that the mean posterior marginal range of the spatial effect will be less than 10,000 meters is 0.9.
Spatial standard deviation σ_u	(Mean, p>)	(1, 0.5)	The probability that the mean posterior marginal standard deviation of the spatial variance will be greater than 1 is 0.5.
Precision of innovation term for AR(1) θ_1	(τ, p>)	(0.5, 0.5)	The probability that the mean posterior marginal value of the AR(1) innovation term is greater than 0.5 is 0.5. θ_1 is an internal parameter calculated as $\log(\tau(1-\rho^2))$.
AR(1) autocorrelation θ_2	(ρ, p>)	(0.5, 0.9)	The probability that the AR(1) autocorrelation parameter is greater than 0.5 is 0.9. θ_2 is an internal parameter calculated as $\log((1+\rho)/(1-\rho))$.
Zero-inflation probability θ_p	(Mean, S.D.)	(0.5, 0.5)	The mean posterior marginal value of the zero-inflation probability will be 0.5 with standard deviation 0.5.

DIC and higher AUC were considered better fits; we chose the best model based on *a priori* knowledge and model performance for further evaluation.

Spatial random effects were explored by creating a triangulation mesh that overlays the study area from the trapping observation locations (see Figure 4.3). A continuous field of spatial random effects is interpolated between the vertices of the mesh. The main advantage of using R-INLA is the reduction in computational intensity achieved through the use of sparse matrix algebra to estimate spatial effects.[50,51] Spatial random effects are calculated for each vertex in the mesh, and then can be interpolated between vertices to create a spatial random field for the entire study area. Temporal random effects were explored by fitting an autoregressive order 1 (AR(1)) model to the data by epidemiological week. Temporal correlation as defined by the AR(1) model is linearly dependent on the observation of the previous week plus an error term.

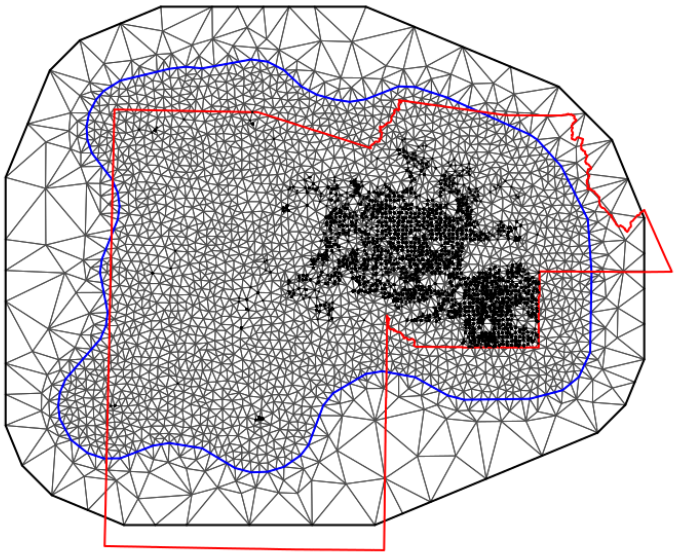

Figure 4.3. Triangulation mesh used by INLA-SPDE model. The boundary of Maricopa County is shown in red for reference. The trapping locations are represented by black points, and the boundary between the inner and out mesh is shown as a blue line. The mesh was created with a 20,000 meter buffer between trapping points and the inner boundary, the inner mesh has a maximum edge length of 5,000 meters while the outer mesh has a maximum edge length of 25,000 meters. The outer mesh is at least 20,000 meters wide. The mesh has 3,548 nodes.

Weakly informative penalized complexity (PC) priors were chosen for all hyperparameters to allow our large dataset to strongly inform the model fit (see Table 4.1).[53] Default priors, defined in R-INLA as a gamma distribution with shape parameter set to 1 and scale parameter set to 0.00001, were used for all fixed effects. The usefulness of the spatial and temporal random effects was evaluated by comparing the DIC and AUC values for each model with random effects to a model with no random effects.

Model accuracy of the best model was assessed by choosing the cutoff point that maximized the Youden's index value (calculated by sensitivity + specificity – 1) to convert model output to a binary response. A confusion matrix of binary predictions versus observed values was created, and the accuracy, true positive rate, true negative rate, false positive rate, and false negative rate were calculated. We utilized R-INLA's projection function to plot the spatial random effect mean and standard deviation of the best model over the study area to visually identify potential hot spots or cold spots of mosquito presence. We also plotted the Matérn correlation function to visualize the relationship between spatial correlation and distance. We visualized the temporal trend of the best model by plotting the log odds over each week of the year. Additionally, the intraclass correlation (ICC), which is the correlation between observations at the same physical location or at the same time after accounting for fixed effects, was calculated for the best model to determine the relative strength of the temporal and spatial random effects.[37,54] We visualized the prior and posterior distributions for all hyperparameters and plotted the posterior distributions for the fixed effects.

All analyses were performed using the high-performance computing cluster

(Aspen) at the Translational Genomics Research Institute.

Results

Predictor Selection and Descriptive Statistics

The following socioeconomic predictors were included in the model: median income, population density, and median house age. The following greenness and weather predictors were included in the model: Modis EVI lagged 1 week, the sum of precipitation, mean maximum temperature, and mean vapor pressure all lagged 1 week, and the sum of precipitation lagged 2 weeks. See Table 4.2 for descriptive statistics of all predictors. All socioeconomic predictors and all greenness/weather predictors had a VIF < 3, so no variables were removed from the model (see Supplementary Table 1).

Table 4.2. Descriptive statistics of variables included in each model.

	Unit	Mean	SD	Min	Max
Median Income	Dollars	92,859	41,403	8,723	250,001
Population Density	People/ Km^2	1,369	1,222	0.09	9,633
Median House Age	Years	27	15	0	82
EVI Lag 1	EVI	0.164	0.066	-0.001	0.975
Sum Precip. Lag 1	mm	4.3	10.9	0.0	149.7
Mean Max Temp Lag 1	°C	31.6	8.0	10.2	46.7
Mean VP Lag 1	Pa	1,115	531	259	3,604
Sum Precip. Lag 2	mm	4.2	11.0	0.0	149.7

After removing observations with any NA data, 250,284 observations remained in our training data set from years 2014-2020, while 41,101 observations remained in the test data set from 2021. Of the 250,284 observations in the training data set, 42,625 were positive for female *Ae. aegypti* (17.0%), while of the 41,101 observations in the test data set, 9,788 were positive for female *Ae. aegypti* (23.8%).

Zero Inflation

We evaluated the inclusion of a zero-inflation parameter in the model by fitting

binomial models with and without zero-inflation and comparing model DIC and AUC (see Table 4.3). Adding a zero-inflation parameter to the model did not result in improved DIC or AUC; however, given the extremely large number of zeroes present in our dataset (83.0% of training observations and 76.2% of test observations), we decided to retain the zero-inflation parameter in our model. The zero-inflation parameter of our final model (zero-inflated binomial with both spatial and temporal random effects) had a mean posterior value of 0.020 with a 95% credible interval of (0.013, 0.029) indicating the presence of very weak zero-inflation. The mean posterior value indicates that about 2% of trapping observations in our model are structural zeroes.

Fixed Effects

The mean posterior coefficients for all fixed effects included in the model are presented as log odds along with their 95% credible intervals in Table 4.3; these values represent the estimated effect of one standard deviation increase in the predictor due to the standardization that we applied to all covariates. Median income, population density, median house age, Modis EVI lagged at 1 week, and mean vapor pressure lagged at 1 week were all positively associated with the presence of Ae. aegypti females. Mean vapor pressure had the strongest positive effect (mean log odds: 0.478; 95% credible interval: (0.457, 0.499)) followed by median house age (mean log odds: 0.375; 95% credible interval: (0.305, 0.445)). The sum of precipitation lagged by 1 week, mean maximum temperature lagged by 1 week, and the sum of precipitation lagged by 2 weeks were all negatively associated with the presence of female Ae. aegypti. The mean maximum temperature had the strongest negative effect (mean log odds: -0.824; 95% credible interval: (-0.870, -0.778). Only one predictor had a 95% credible interval

Table 4.3. Regression Results for Binomial and Zero-Inflated Binomial Models with and Without Spatial, Temporal, and Both Spatial and Temporal Random Effects. Model Performance metrics and posterior mean values and 95% credible intervals for fixed effects presented as log odds and for hyperparameter estimates. Our final chosen model, the zero-inflated binomial with spatial and temporal random effects is bolded.

	Binomial No Spatial or Temporal	Binomial Spatial	Binomial Temporal	Binomial Spatial & Temporal
DIC	207,596	180,669	195,039	167,041
Training AUC	0.718 (0.715, 0.721)	0.816 (0.813, 0.819)	0.765 (0.762, 0.768)	0.852 (0.849, 0.854)
Test AUC	0.814 (0.809, 0.820)	0.850 (0.845, 0.855)	0.859 (0.854, 0.863)	0.891 (0.887, 0.895)
Optimal Youden Index Point from Training Data	0.159504	0.177370	0.178910	0.184873
Zero-inflation Probability θ_p	NA	NA	NA	NA
Mean for spatial range *r*	NA	3,167 (2,745, 3,645)	NA	2,978 (2,572, 3,458)
Spatial standard deviation σ_u	NA	1.653 (1.556, 1.755)	NA	1.685 (1.587, 1.791)
AR(1) autocorrelation ρ	NA	NA	0.986 (0.964, 0.997)	0.984 (0.963, 0.996)
Precision of innovation term for AR(1) τ	NA	NA	0.329 (0.072, 0.834)	0.288 (0.096, 0.608)
Intercept	-1.742 (-1.754, -1.730)	-2.510 (-2.724, -2.308)	-4.120 (-7.854, -0.877)	-5.115 (-8.993, -1.764)
Median Income	0.257 (0.246, 0.268)	0.122 (0.061, 0.184)	0.263 (0.251, 0.274)	0.127 (0.064, 0.191)
Population Density	0.223 (0.212, 0.235)	0.126 (0.048, 0.203)	0.233 (0.222, 0.245)	0.112 (0.034, 0.190)
Median House Age	0.187 (0.175, 0.198)	0.220 (0.154, 0.287)	0.202 (0.190, 0.214)	0.376 (0.307, 0.445)
EVI Lag 1	0.086 (0.075, 0.097)	0.115 (0.095, 0.135)	0.077 (0.066, 0.088)	0.034 (0.013, 0.056)
Sum Precip. Lag 1	-0.038 (-0.049, -0.027)	-0.050 (-0.061, -0.038)	-0.071 (-0.083, -0.059)	-0.090 (-0.103, -0.077)
Mean Max. Temp. Lag 1	0.260 (0.245, 0.275)	0.279 (0.263, 0.294)	-0.676 (-0.717, -0.635)	-0.818 (-0.863, -0.773)
Vapor Pressure Lag 1	0.576 (0.560, 0.591)	0.680 (0.663, 0.698)	0.375 (0.357, 0.393)	0.471 (0.451, 0.492)
Sum Precip. Lag 2	0.029 (0.018, 0.040)	0.034 (0.022, 0.046)	-0.007 (-0.018, 0.005)	-0.007 (-0.020, 0.006)

Table 4.3 continued. Regression Results for All Binomial, Zero-Inflated Binomial Models with and Without Spatial, Temporal, and Both Spatial and Temporal Random Effects.

	Zero-Inflated Binomial No Spatial or Temporal	Zero-Inflated Binomial Spatial	Zero-Inflated Binomial Temporal	**Zero-Inflated Binomial Spatial & Temporal**
DIC	206,679	180,630	195,050	**167,057**
Training AUC	0.718 (0.715, 0.721)	0.816 (0.814, 0.819)	0.765 (0.762, 0.768)	**0.852 (0.849, 0.854)**
Test AUC	0.814 (0.808, 0.819)	0.851 (0.846, 0.856)	0.859 (0.854, 0.863)	**0.891 (0.887, 0.895)**
Optimal Youden Index Point from Training Data	0.360761	0.190844	0.196203	**0.188979**
Zero-inflation Probability θ_p	0.552 (0.536, 0.567)	0.084 (0.063, 0.106)	0.067 (0.036, 0.109)	**0.020 (0.013, 0.029)**
Mean for spatial range *r*	NA	3,105 (2,659, 3,583)	NA	**2,942 (2,531, 3,392)**
Spatial standard deviation σ_u	NA	1.719 (1.614, 1.830)	NA	**1.697 (1.598, 1.802)**
AR(1) autocorrelation ρ	NA	NA	0.985 (0.963, 0.997)	**0.976 (0.251, 0.650)**
Precision of innovation term for AR(1) τ	NA	NA	0.321 (0.071, 0.810)	**0.410 (0.251, 0.650)**
Intercept	-0.571 (-0.641, -0.502)	-2.409 (-2.629, -2.200)	-4.041 (-7.994, -0.723)	**-5.026 (-8.092, -2.172)**
Median Income	0.381 (0.361, 0.402)	0.128 (0.064, 0.193)	0.271 (0.258, 0.285)	**0.128 (0.064, 0.192)**
Population Density	0.373 (0.349, 0.398)	0.134 (0.053, 0.215)	0.243 (0.229, 0.256)	**0.114 (0.035, 0.193)**
Median House Age	0.292 (0.270, 0.313)	0.220 (0.150, 0.290)	0.209 (0.196, 0.222)	**0.375 (0.305, 0.445)**
EVI Lag 1	0.132 (0.112, 0.151)	0.119 (0.098, 0.140)	0.079 (0.068, 0.091)	**0.035 (0.013, 0.056)**
Sum Precip. Lag 1	-0.067 (-0.088, -0.047)	-0.053 (-0.065, -0.040)	-0.071 (-0.083, -0.058)	**-0.090 (-0.104, -0.077)**
Mean Max. Temp. Lag 1	0.443 (0.414, 0.472)	0.291 (0.275, 0.308)	-0.688 (-0.731, -0.645)	**-0.824 (-0.870, -0.778)**
Vapor Pressure Lag 1	0.914 (0.879, 0.950)	0.720 (0.699, 0.741)	0.386 (0.367, 0.407)	**0.478 (0.457, 0.499)**
Sum Precip. Lag 2	0.072 (0.053, 0.091)	0.048 (0.035, 0.061)	-0.004 (-0.016, 0.009)	**-0.005 (-0.018, 0.008)**

that crossed 0, indicating that it was less important to the prediction of the presence of female *Ae. aegypti*: the sum of precipitation lagged at 2 weeks (mean log odds: -0.005; 95% credible interval: (-0.018, 0.008). In Supplementary Table 4.2, the coefficients of the fixed effects are presented as the estimated percent change in response as a result of one standard deviation increase in the predictor. In Supplementary Figure 4.2, the posterior distributions for each fixed effect parameter are displayed.

Random Effects and Hyperparameters

Spatial random effects and temporal random effects were evaluated for inclusion in the model by fitting models with and without these effects and comparing model DIC and AUC (see Table 4.3). Comparing just the zero-inflated binomial models, temporal random effects resulted in a decreased DIC (195,050) compared to models with no random effects (206,679), while spatial random effects resulted in a decreased DIC (180,630) compared to models with no random effects and with temporal random effects. Models that included both temporal and spatial random effects resulted in a lower DIC (167,057) than models with no random effects or with temporal or spatial random effects alone. The AUC value showed the same trend as DIC (see Table 4.3).

The posterior mean and standard deviation of the spatial random effect was projected onto a map of Maricopa County, Arizona by interpolating the values between the nodes of the mesh (see Figure 4.4). The spatial random effect was greatest in the north central and southeast Phoenix metropolitan areas, while suburban areas to the west generally had decreased odds. The standard deviation of the spatial effect was lower in areas where more trapping data was observed, mainly the Phoenix metropolitan area, and higher around the more rural, less trapped areas of the county.

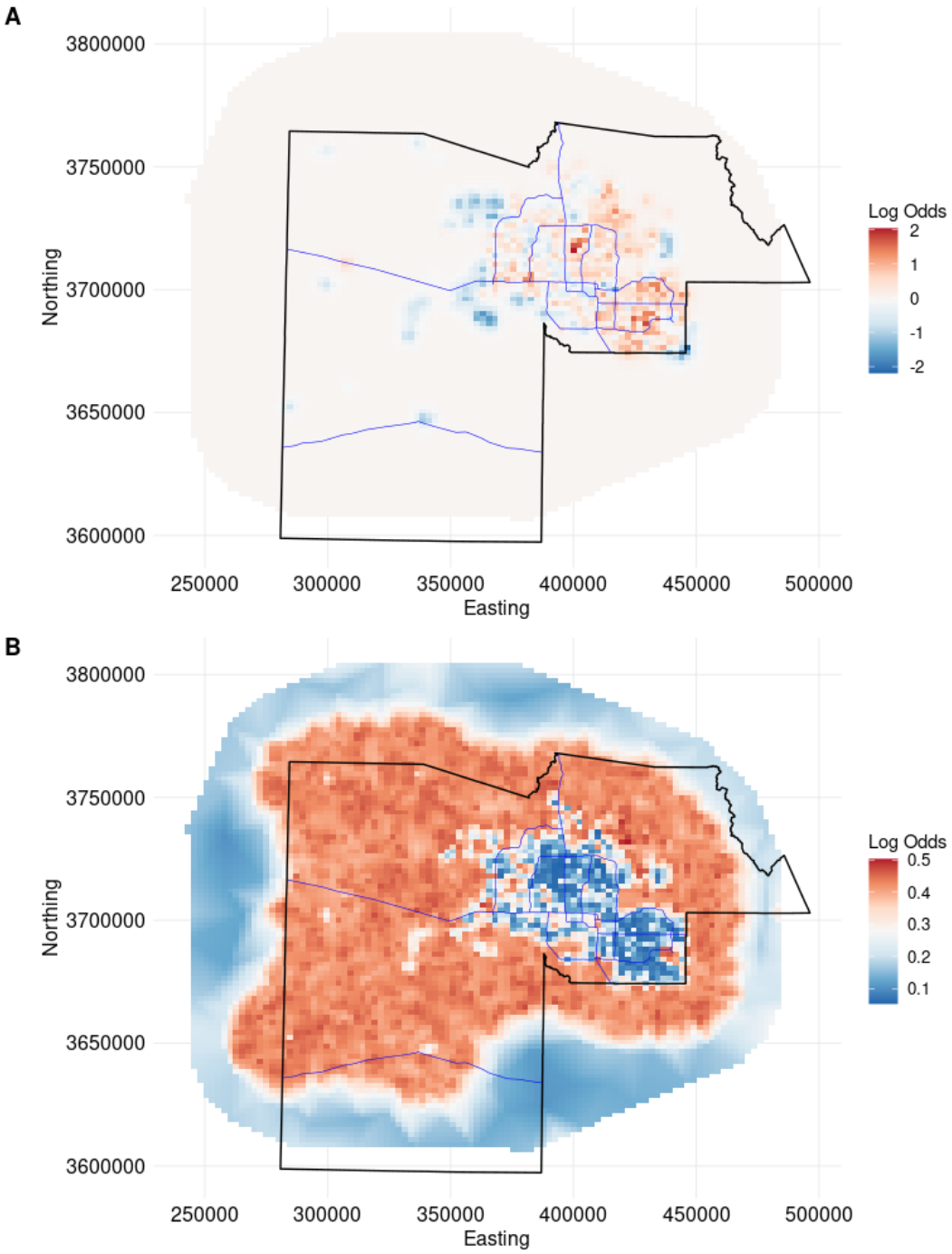

Figure 4.4. The mean (A) and standard deviation (B) of the spatial random effect mapped across Maricopa County, Arizona. Major freeways are shown as blue lines to provide a location reference. Areas with higher odds of female *Aedes aegypti* presence occur in the North Central Phoenix and southeastern Phoenix metropolitan areas while areas of lower odds of presence occur in the western suburbs.

The range (the distance value at which the mean spatial correlation decreases to 0.13) was 2,942 (95% credible interval: (2,531, 3,392) meters which describes a spatial random effect that decreases at a short distance (see Figure 4.5), which is to be expected for *Ae. aegypti*, a vector with a generally small range. The mean σ_u for the spatial effect was estimated at 1.697 (95% credible interval: 1.598, 1,802) indicating the presence of an important spatial effect in our trapping observations. The prior distributions were plotted against the posterior distributions for the spatial range and spatial variance (see Figure 4.6).

The posterior mean of the autocorrelation parameter was 0.976 (95% credible interval: (0.958, 0.986) indicating that there was a strong autocorrelation effect in the model; this indicates that observations change slowly from week to week and the current week's observation depends strongly on the previous week's observation. The posterior mean for the innovation term for the temporal trend was 0.410 (95% credible

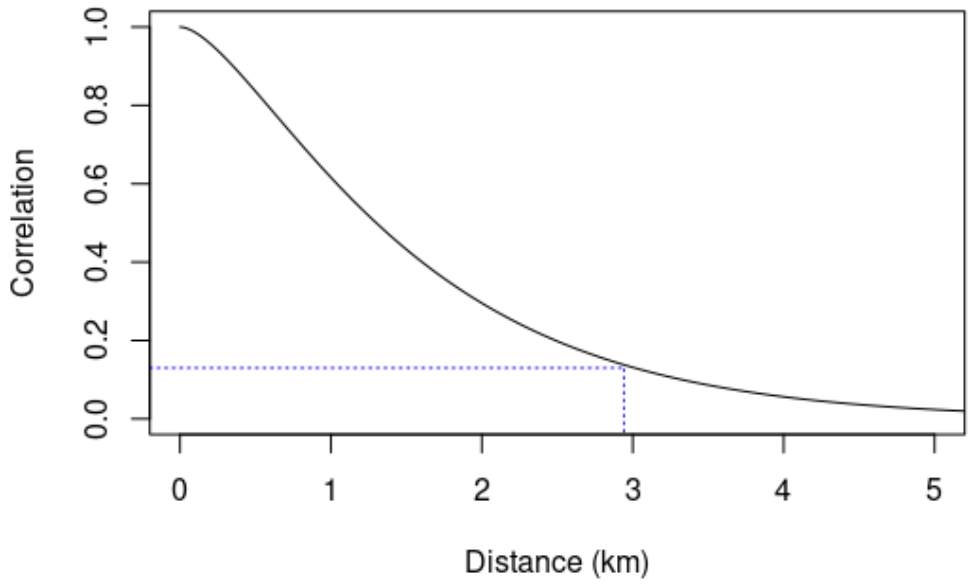

Figure 4.5. Matérn correlation function of the spatial effect. The spatial effect decreases to approximately 0 at about 5 km. The range (distance at which the spatial correlation decreases to 0.13) is denoted at 2,942 meters using blue dashed lines.

interval: (0.251, 0.650) indicating that the week-on-week trend was relatively stable; however, the large credible interval suggests that there is some variation in the size of changes in observations from one week to the next. The prior distributions were plotted against the posterior distributions for the autocorrelation parameter and the temporal innovation parameter (see Figure 4.6). The posterior mean and 95% credible interval for the time trend was plotted against the epidemiological weeks of the year (see Figure 4.7).

The time trend shows a negative yet increasing effect in the beginning of the year, followed by a positive and increasing effect from approximately week 12 to week

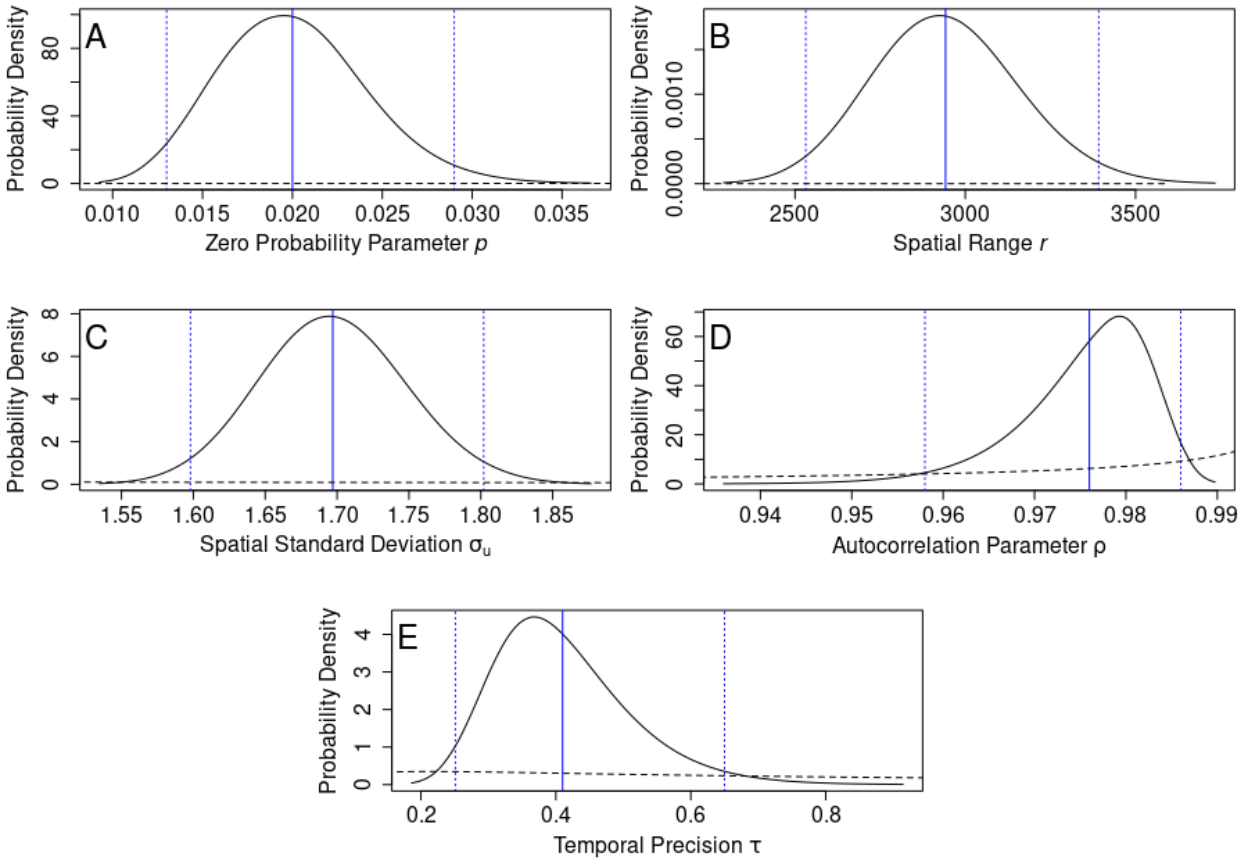

Figure 4.6. Prior (dashed) and posterior (solid) distributions of model hyperparameters for the zero-inflated binomial model with both spatial and temporal random effects. The mean marginal posterior value and 95% credible interval for each parameter is highlighted by the solid and dashed blue lines, respectively.

22. The trend is then positive but stable from approximately week 23 through week 42, followed by a positive yet decreasing trend from approximately week 43 through the end of the year. From weeks 19 to 46, the 95% credible interval does not cross 0 indicating the presence of an important positive temporal effect from approximately June through October.

We evaluated the ICC for spatial and temporal random effects and found that the ICC accounting for both spatial and temporal effects was 0.48, which means that, after accounting for all fixed effects, the correlation that can be attributed to spatiotemporal random effects between two observations from the same trap site in the same week is 0.48. The temporal ICC was 0.03, meaning that, after accounting for all fixed effects, the correlation that can be contributed to temporal effects between two observations in the

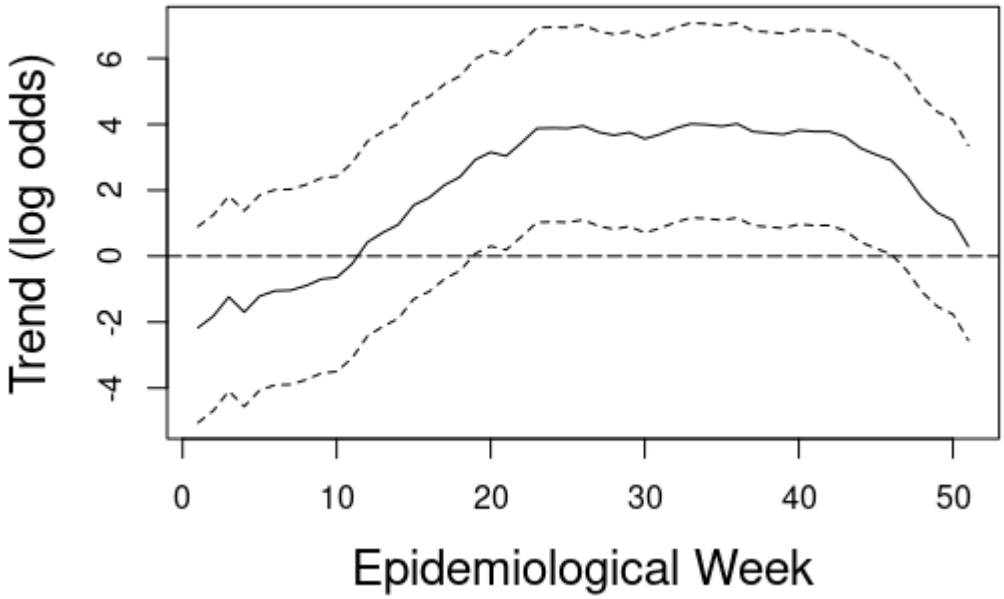

Figure 4.7. Temporal random effect. Mean (solid line) and 95% credible interval (dashed lines) plotted against the epidemiological week of the year. At the beginning of the year, the trend is negative yet increasing, followed by a positive and increasing effect from approximately week 12 to week 22. The trend is positive and stable from weeks 23 to 42, followed by a positive yet decreasing effect from approximately week 43 through the end of the year.

same week, but at different trapping locations is 0.03. Finally, the spatial ICC was 0.45, which means that, after accounting for all fixed effects, the correlation that can be attributed to spatial effects between two observations from the same trapping location but different weeks is 0.45.

We chose to retain the zero-inflation parameter in the model due to the abundance of zero observations in our data set. The posterior mean of the zero-inflation parameter was 0.020 (95% credible interval: 0.013, 0.029) indicating that zero-inflation was present but minimal in the model. The prior distribution was plotted against the posterior distribution for the zero-inflation parameter (see Figure 4.6). About 2% of the observations were excess zeroes, or zero observations that are not otherwise predicted by the covariates included in our model. This may be because female *Ae. aegypti* were present but not trapped, because they were trapped but misidentified or otherwise not recorded, or because the habitat was suitable but they were not present (perhaps due to mosquito control efforts).

Model Performance and Evaluation

Given the improved model performance from spatial and temporal random effects and our decision to retain the zero-inflation parameter, the final model that we selected for evaluation was the zero-inflated binomial model with both spatial and temporal random effects.

We evaluated the performance of the model on both the training (2014-2020) and testing (2021) data sets. We plotted the ROC curve (see Figure 4.8) and calculated the AUC (see Tables 4.4 and 4.5) for the training data altogether (2014-2020), for the test data (2021), and separately for each year in the training data set (see Supplementary

Figures 4.3 to 4.9 and Supplementary Tables 4.3 to 4.9). The AUC value for the training data set (2014-2020) was 0.852 (95% credible interval: 0.849, 0.854) while the AUC value for the test data set (2021) was 0.891 (95% credible interval: 0.887, 0.895). To convert the output of the binomial model to predictions of presence or absence, we used the cutoff that maximized the Youden's index value for the entire training data set (calculated as sensitivity + specificity – 1), 0.188979 to classify predictions for both the training data set and the test data set.

After classifying model predictions into presence or absence classes based on our chosen cutoff, we constructed confusion matrices for the training data (2014-2020) and the test data (2021) as well as for each year in the training data set separately (see Tables 4.4 and 4.5 and Supplementary Tables 4.3 to 4.9). The accuracy of the predictions for the training data was 0.752; the sensitivity was 0.798 and the specificity was 0.743. The accuracy for the predictions for the test data was 0.775; the sensitivity was 0.875 and the specificity was 0.743. We also calculated the precision, negative predictive value, false positive rate, and false negative rate (see Tables 4.4 and 4.5 and Supplementary Tables 4.3 to 4.9). To further explore spatial and temporal trends in our predictions, we plotted the classification of predictions (true positive, false positive, false negative, and true negative) against space and time for all training data (see Figures 4.9 and 4.11), all testing data (see Figures 4.10 and 4.11), and each year separately (see Supplementary Figures 4.10 to 4.17).

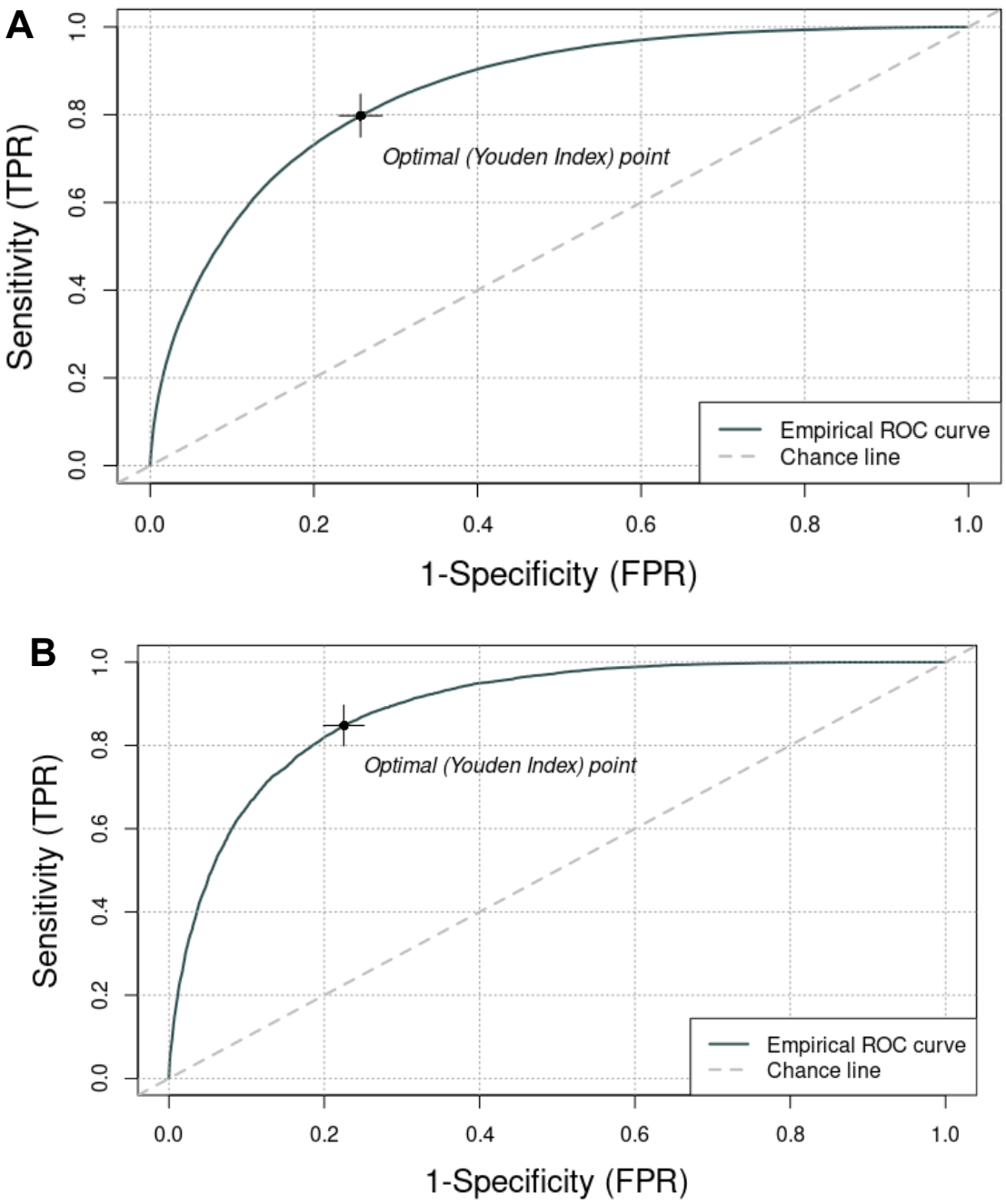

Figure 4.8. ROC curve for training data (A) and testing data (B). The Optimal Youden Index point (where sensitivity + specificity – 1 is maximized) is marked on each plot with dot and crosshairs. For the training data **(A)** this value is 0.188979 while for the test data **(B)** this value is 0.218722. For classification, the training Optimal Youden Index Point was used for all data, both training and test.

Table 4.4. Confusion matrix and performance metrics for all training data, 2014-2020. Classification was based on a cutoff value of 0.1893954.

	True Positive	True Negative	Total
Predicted Positive	34,001	53,373	87,374
Predicted Negative	8,624	154,286	162,910
Total	42,625	207,659	250,284

	Estimate	95% Credible Interval
AUC	0.852	(0.849, 0.854)

	Value	Derivation	Calculation
Accuracy	0.752	(TP + TN) / (P + N)	(34,001 + 154,286) / (42,625 + 207,659)
Sensitivity	0.798	TP / (TP + FN)	34,001 / (34,001 + 8,624)
Specificity	0.743	TN / (FP + TN)	154,286 / (53,373 + 154,286)
Precision	0.389	TP / (TP + FP)	34,001 / (34,001 + 53,373)
Negative Predictive Value	0.947	TN / (TN + FN)	154,286 / (154,286 + 8,624)
False Positive Rate	0.257	FP / (FP + TN)	53,373 / (53,373 + 154,286)
False Negative Rate	0.202	FN / (FN + TP)	8,624 / (8,624 + 34,001)

Table 4.5. Confusion matrix and performance metrics for test data, 2021. Classification was based on a cutoff value of 0.1893954.

	True Positive	True Negative	Total
Predicted Positive	8,562	8,037	16,599
Predicted Negative	1,226	23,276	24,502
Total	9,788	31,313	41,101

	Estimate	95% Credible Interval
AUC	0.891	(0.887, 0.895)

	Value	Derivation	Calculation
Accuracy	0.775	(TP + TN) / (P + N)	(8,562 + 23,276) / (9,788 + 31,313)
Sensitivity	0.875	TP / (TP + FN)	8,562 / (8,562 + 1,226)
Specificity	0.743	TN / (FP + TN)	23,276 / (8,037 + 23,276)
Precision	0.516	TP / (TP + FP)	8,562 / (8,562 + 8,037)
Negative Predictive Value	0.950	TN / (TN + FN)	23,276 / (23,276 + 1,226)
False Positive Rate	0.257	FP / (FP + TN)	8,037 / (8,037 + 23,276)
False Negative Rate	0.125	FN / (FN + TP)	1,226 / (1,226 + 8,562)

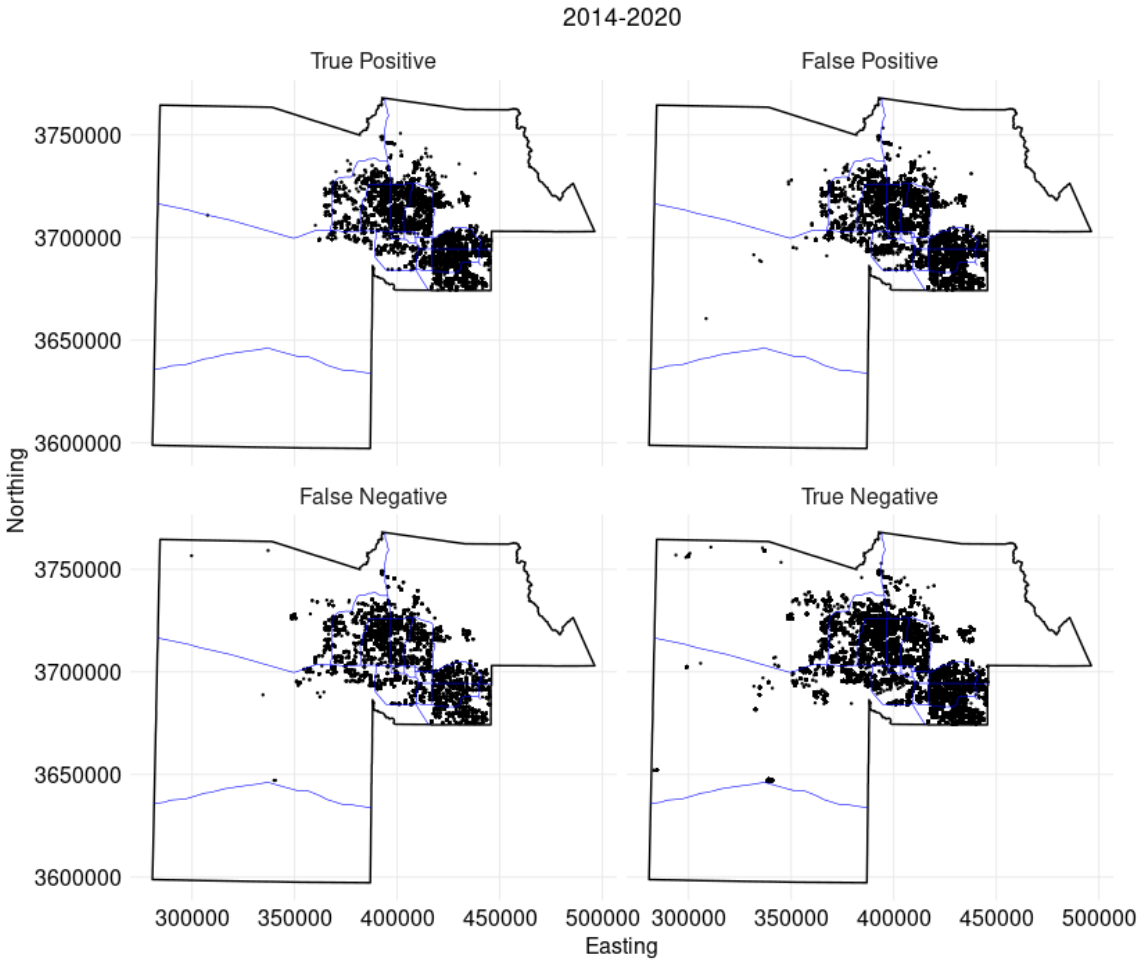

Figure 4.9. The location of predictions by classification status for all training data, 2014-2020. Major freeways are shown as blue lines to provide a location reference. No obvious spatial patterns are present.

Discussion

Using Bayesian mixed-effects modeling in R-INLA, we were able to create a zero-inflated binomial model with spatial and temporal random effects that predicts the presence of female *Ae. aegypti* mosquitoes in Maricopa County, Arizona with reasonable accuracy. Our choice of weather, vegetation, and socioeconomic predictors allowed us to evaluate the relationship between mosquito presence and various small-scale neighborhood characteristics. Furthermore, our strategic selection of weather and

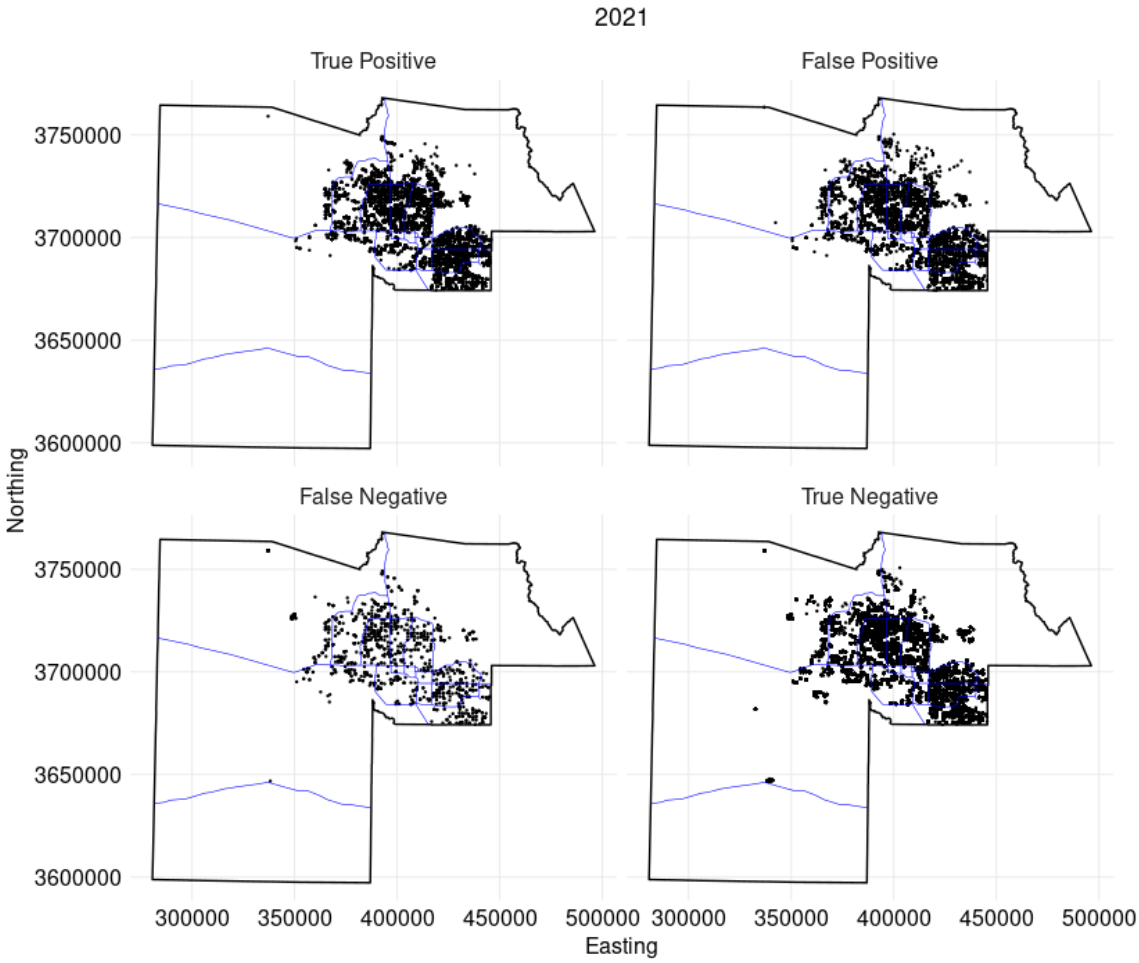

Figure 4.10. The location of predictions by classification status for test data, 2021. Major freeways are shown as blue lines to provide a location reference. No obvious spatial patterns are present.

greenness data from previous weeks will allow the model to be adapted for use as a near real-time predictor of mosquito presence in this area.

Our results indicated that median income, population density, and median house age were important predictors of female *Ae. aegypti* presence in this region. All three socioeconomic predictors had a positive relationship with mosquito presence, indicating that areas with denser human populations, areas with higher median income, and areas with older houses are all associated with a greater likelihood of *Ae. aegypti* presence.

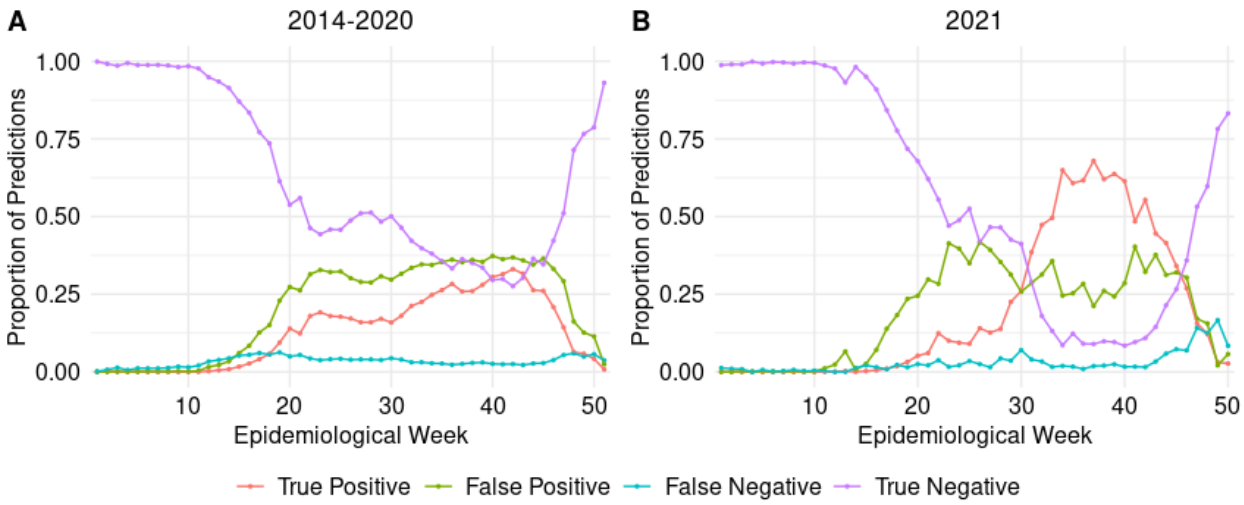

Figure 4.11. Proportion of predictions by classification status for all training data, 2014-2020 (A) and for all test data, 2021 (B). The increase in false positive rate during the summer months indicates that our model overpredicts positive occurrences during that time.

The positive relationship between population density and mosquito presence was expected, given the close relationship that this vector has to humans. Further, the positive relationship between median income and mosquito presence was expected due to the relationship between income and vegetation in the Phoenix metropolitan area[29] and findings from past studies that indicate that *Ae. aegypti* was associated with increased vegetation in a nearby desert area.[30] Anecdotally, the positive relationship between median house age and mosquito presence was not surprising, as older neighborhoods in the Phoenix area may have more established vegetation, larger backyards, and outdated water drainage systems, although this relationship certainly deserves more attention in future studies especially since it was the second strongest predictor of *Ae. aegypti* presence in our model.

The relationship between vegetation (EVI) and mosquito presence was positive but relatively weak. The positive relationship was expected given the findings of past

studies.[30] We attempted to use the most up-to-date satellite data available to create the vegetation predictor for each week while also maintaining our desire to use data from previous weeks so that our model could be used to create real time predictions. This resulted in a lag in the vegetation that may have affected this relationship. Further, we evaluated the vegetation solely at the trap location, future studies may consider evaluating a larger area of vegetation around each trap location, as the trap site may not be representative of the surrounding area.

Our results indicated that the sum of precipitation from the previous week, the mean maximum temperature from the previous week, and the sum of precipitation from two weeks ago were all negatively associated with *Ae. aegypti* presence while the mean vapor pressure from the previous week was positively associated with *Ae. aegypti* presence. All weather predictors besides the sum of precipitation from two weeks ago were important. The negative relationship between the precipitation variables and *Ae. aegypti* presence was surprising, given that the mosquito requires water for reproduction; however, it is possible that increased rain actually leads to spillover of water from containers, which would negatively impact the ability of the mosquito larvae to develop, especially if the mosquito generally relies on containers filled with water by humans.[55] The negative relationship between mean maximum temperature and mosquito presence was also surprising, given that the mosquito cannot survive lower temperatures: temperatures below 14°C negatively impact their biological functions[3] and temperatures below 10°C are considered unsuitable and disrupt reproduction.[4] However, temperatures in Maricopa County regularly exceed 40°C, which may contribute to the desiccation of eggs and the evaporation of water from breeding

containers. Laboratory studies suggest that *Ae. aegypti* survive less than one full day at 42°C[56] indicating that this region may simply get too hot for the mosquito in the summers unless it can seek out more appropriate microclimates.[57] Future studies should explore a non-linear relationship between temperature and mosquito presence that allows for a positive relationship between presence and temperature at intermediate temperatures and a negative relationship at extreme cold or hot temperatures.[58] Finally, mosquito presence was strongly positively associated with vapor pressure from the previous week, which is a measure of the moisture content of the air. This finding was not surprising as previous studies have demonstrated a greater ability for *Ae. aegypti* to lay eggs and survive for longer periods of time in more humid conditions.[59,60]

Our model included spatial and temporal random effects that helped to explain the presence of the mosquito after accounting for the fixed effects. Comparing the DIC and AUC values of the models with and without spatial, temporal, and both spatial and temporal random effects indicated that including spatial and temporal random effects resulted in improved model fit. We were able to plot the spatial effect across the study area to identify locations with greater odds of mosquito presence. Locations in the central Phoenix and southeastern Phoenix metropolitan areas generally had higher odds of mosquito presence while areas in the western Phoenix metropolitan area generally had lower odds. These results were expected based on the results of our trapping data and from the experience of vector control professionals in Maricopa County. The areas with greater odds of mosquito presence should be studied further to generate a better understanding of mosquito behavior in these locations (are they acting

as source or sink locations?). Plotting the class of predictions against space did not identify any structure in correct or incorrect predictions. The range at which the spatial correlation between traps diminished to below 0.13 was 2,942 meters, suggesting the possibility that the mosquito may have a larger range than what is typically expected (about 100 meters) [10] in the desert habitat of Maricopa County. The range value is slightly larger than what has been previously identified as the top range of the mosquito (2,500 meters),[11] although there is a lack of research on the behavior of the vector in desert habitats where the species has recently become established. There is a great opportunity for additional research on the flight range of the mosquito in this region.

We were also able to plot the temporal effects across the weeks of the year which identified an important positive temporal effect from approximately June through October. This was an expected finding based on the general trend of the trapping data in Maricopa County from our study period. This finding indicates that there may be an opportunity for important population reduction work in the winter months when the mosquito population is generally lower, while vector control efforts in the summer may be better concentrated on risk reduction. By plotting the class of predictions by week, it is obvious that our model overpredicts positive occurrences during summer months (due to the increase in the false positive rate). One explanation for this is that the species has only recently become established in this area and may not have exploited the full extent of suitable habitat at this point; in other words, the false positive predictions identify areas where the mosquito may become established in the near future. Another explanation is that the model is simply incorrect and overpredicts mosquito presence in areas that are not suitable, perhaps due to an inappropriate

model or missing covariates that could better explain presence and absence.

The location and time of an observation accounts for about 48% of the variation in observations of female *Ae. aegypti* with location accounting for much more of this effect (45%) than time (3%). This finding may suggest the possibility of the existence of hotspots (which may be acting as potential source locations) that consistently support *Ae. aegypti* populations and may be good candidates for targeted vector control efforts.

Comparing our model to others that have modeled *Ae. aegypti* in this region, our results suggesting a positive relationship between income and mosquito presence are contradictory to two past studies conducted in Tucson, AZ that found a negative relationship between income and mosquito abundance.[5,33]. On the other hand, our findings regarding a positive association with house age were consistent.[33] Our finding of a positive association with vegetation was consistent with another study conducted in Tucson; however, our findings of a negative association with rainfall were contradictory with this study.[30] The only other published model of *Ae. aegypti* in Maricopa County used minimum temperature and vapor pressure to predict monthly abundance of the mosquito; our findings were consistent for a positive relationship with vapor pressure, but contradictory for a positive relationship with temperature (although this study used minimum temperature while our model used maximum temperature).[32] It is important to note that none of these studies accounted for spatial or temporal dependency which may have skewed the results.

Only two other studies have used R-INLA to create models of *Ae. aegypti* that account for spatial or temporal dependency in the United States; these studies were conducted in Brownsville, TX and central California.[34,35] Comparing our results to the

results of the Texas study, our findings were consistent regarding a negative relationship with temperature and a positive relationship with humidity.[34] The spatial range identified in this model, 900 m, was much smaller than our spatial range of 2,942 meters, which deserves further investigation to determine if *Ae. aegypti* are behaving differently in Maricopa County, AZ than in other locations. The temporal trends between the model in this study and our model also differed, indicating the importance of constructing models that account for local population dynamics. It is difficult to compare our results to the California study due to major differences in study design.[35] The findings of the California study modeling mark-release-recapture results highlighted the importance of temperature and wind speed (both negative predictors of recapture) in *Ae. aegypti* dispersal and found that the actual mean distance traveled by recaptured mosquitoes was 232 m, while the model predicted a mean distance traveled of up to 422 m. R-INLA has also been employed to create models of *Ae. aegypti* in Singapore,[58] Indonesia,[61] and Brazil.[62] Although these studies are interesting and important, comparison of their results to ours may not be appropriate due to the wide difference in climate and habitat between Maricopa County, AZ and these locations.

Like any other model, ours is not without limitations. First, our decision to average all mosquito counts and weather predictors to the week time scale provided more simplicity in a computationally intensive model, but decreased the resolution of our model. Furthermore, our decision to extract weather and greenness variables only at the trap site also provided more simplicity, but may have skewed the results by not accounting for the areas immediately around trapping locations. Although Maricopa County, Arizona has a well-deserved reputation as a sunny location, cloud cover in the

satellite imagery data may have resulted in missing EVI data which would have resulted in mosquito observations being thrown out. Given that EVI was only weakly associated with mosquito presence, it may be worth considering the exclusion of this predictor. Additionally, we did not investigate non-linear relationships between the predictors and mosquito presence. Future models may benefit from evaluating potential non-linear relationships with the socioeconomic and weather predictors.[58] Moreover, we included the spatial and temporal random effects as separate terms to simplify model complexity; future studies should consider evaluating the spatiotemporal random effects as an interaction between space and time. It is possible that the spatiotemporal effects could vary depending on the location (e.g., if some areas of Maricopa County provide more suitable habitat for overwintering). Finally, the model likely overestimates the presence of *Ae. aegypti* resulting in increased false positive predictions, because the species has only recently become established in this area during the study period and may not have realized the full extent of its potential habitat yet. This is supported by the higher accuracy of predictions for the test year (2021) when there were more positive observations compared to training years (2014-2020).

We believe that our study has demonstrated the feasibility of using Bayesian mixed-effects modeling in R-INLA to create a zero-inflated binomial model with spatial and temporal random effects that predicts the presence of female *Ae. aegypti* in Maricopa County, Arizona with reasonable accuracy. We would like to build on this model in the future by exploring the ability to predict mosquito presence a week in advance, creating models that could predict mosquito abundance rather than presence, incorporating fogging and mosquito control activity in the model, and exploring the

inclusion of additional predictors (such as wind speed and direction)[35] or additional time lags for weather predictors. Furthermore, in addition to building on this model, we also plan to conduct analyses to help identify potential source and sink locations in this region.

Conclusions

Our study has extended a very limited collection of literature related to 1) Bayesian mixed-effects modeling in R-INLA for *Ae. aegypti* mosquitoes and 2) models of *Ae. aegypti* in the southwestern United States by creating a zero-inflated binomial model with spatial and temporal random effects that predicts the presence of female *Ae. aegypti* in Maricopa County, Arizona. Our approach demonstrated the feasibility of using weather and socioeconomic predictors from previous weeks to predict the presence of the mosquito with reasonable accuracy using a 7-year training data set (2014-2020) and 1-year testing data set (2021). We identified and mapped spatial effects from the model to identify areas that have higher odds of *Ae. aegypti* presence and characterized relationships between mosquito presence and median income, population density, median house age, greenness, precipitation, temperature, and vapor pressure. This approach is an improvement over models of *Ae. aegypti* populations in the southwestern United States that have been previously published. By characterizing the relationships between socioeconomic and weather predictors and identifying spatial and temporal effects, we have developed a framework that can be extended for use as a tool to prioritize vector control and public health resources in this area.

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CHAPTER 5: PHYLOGEOGRAPHIC INVESTIGATION OF *AEDES AEGYPTI* IN MARICOPA COUNTY, ARIZONA

ABSTRACT

Aedes aegypti, the primary vector of dengue, yellow fever, chikungunya, and Zika viruses, has recently become well-established in Maricopa County, Arizona and the broader desert southwest United States. Recently identified cases of locally-acquired dengue fever have sparked concern about viruses transmitted by *Ae. aegypti* being imported to Maricopa County, an area with over 4.5 million residents, most of whom are naïve to viruses transmitted by this mosquito. Our study contributes to the growing body of literature on the phylogenetic structure of *ae. Aegypti* populations by providing the first collection of 94 mitochondrial genome sequences from the Maricopa County, Arizona population of the mosquito after its recent population expansion in this region. We employed phylogeographic techniques to investigate the spatial distribution and movement of the mosquito vector of interest in Maricopa County. *Aedes aegypti* has historically been thought to have a very small range (about 100-200m), so we expected to find a strong relationship between sampling location and genetic similarity. Surprisingly, no distinct clades related to geographic location were identified, and we found no relationship between geographic distance and genetic distance. These findings suggest that population mixture exists throughout the county regardless of geographic distance which has implications for vector control and public health practice in this region. Importantly, this is the first study of its kind in this region, so additional resolution may be achieved as additional samples are sequenced.

Introduction

Concerns about the public health impact of the mosquito vector *Aedes aegypti* are growing as the global range of this vector is more extensive than at any point in history and is continuing to expand.[1,2] These mosquitoes are the primary vector of four viruses that cause extensive morbidity and mortality in human populations: dengue,[3] yellow fever, [4] chikungunya, and Zika.[1,2,5]. *Aedes aegypti* have a close relationship with humans, relying almost exclusively on human hosts for blood meals that facilitate reproduction[1,6] and on artificial containers and human-created infrastructure for habitat to lay eggs.[1,7] This mosquito thrives in urban environments where threats from natural predators are nearly nonexistent.[7]

Generally, *Ae. aegypti* mosquitoes are best suited to a warm, humid tropical climate; temperatures below 10°C (50°F) are typically lethal for adults and larvae.[8] They also must live in a habitat with small bodies or containers of standing water to facilitate the hatching of eggs. However, given their close relationship with humans, they can become established in areas that would otherwise be naturally inhospitable so long as anthropogenic modifications to the habitat create favorable conditions.[9] Like many species of mosquito, *Ae. aegypti* are adept at utilizing “microclimates” to propagate their population to the fullest extent possible, even in areas where the general climate may be less than ideal.[10] This ability is evident throughout the arid American Southwest, especially in the hot, dry region of Maricopa County, Arizona.

In recent years, the geographic range of mosquitoes has increased rapidly raising renewed concerns about the public health impact of diseases vectored by *Ae. aegypti*.[1] The viruses carried by *Ae. aegypti* are primarily transmitted between humans

and the mosquito, so an infected traveler can introduce the disease to a naïve mosquito population at their travel destination or upon their return home.[11] These mosquitoes are effective vectors of viruses given their close relationship to humans and their tendency to remain active during daytime hours, which increases the likelihood of contact between the mosquito and humans.[8] Furthermore, this mosquito is known to take blood meals from multiple hosts during one reproductive cycle, facilitating further spread of viruses that the vector may be carrying.[12] At one point, *Ae. aegypti* was thought to be eradicated from the United States, but populations of the mosquito have been increasing in the past few decades, and new viruses (Zika, chikungunya) have been introduced to areas of the country with established populations of the mosquito.

Public Health

Dengue

Over half of the world's population resides in areas that are at risk for outbreaks of dengue.[13] It is estimated that dengue causes between about 100 million to 400 million infections annually worldwide.[3,14] In 2013, over 13,000 people globally are estimated to have died from dengue, and the global cost of the disease was estimated to be between 8-9 billion USD.[15] In Arizona in 2019, there were seventeen travel-related cases of dengue infection, twelve of which occurred in Maricopa County. Additionally, outbreaks of dengue occurred in Yuma, Arizona in 2014, resulting in nearly 100 reported cases.[16] In October 2022, two cases of locally acquired dengue virus along with one mosquito pool positive for dengue virus were identified in Maricopa County.[17]

Yellow fever

Yellow fever infections occur regularly in South America when a person is inadvertently infected by mosquitoes involved in sylvatic transmission cycles with non-human primates; in Africa, urban outbreaks where the virus is transmitted from human to mosquito to human are more common.[18] Diagnosis of yellow fever can be difficult due to similarities with other mosquito-borne diseases in endemic regions. One estimate places the burden of yellow fever in Africa between 63,000-158,000 yearly severe infections and between 29,000-75,000 related deaths and the burden in South America between 4,000-15,000 annual severe infections and between 2,000-7,000 related deaths.[18]

Chikungunya

The spread of chikungunya virus has been poorly recorded and is not well understood, especially because a chikungunya infection is easily confused with an infection of dengue which has similar symptoms and often cocirculates in the same areas.[19,20] Historically, since the first documented outbreak of chikungunya in 1953, the virus has caused sporadic infections and larger epidemics throughout southeast Asia and Africa.[19,20] Epidemics tend to be sudden, anticipated, and large with attack rates of 33-45% observed.[19,21] Chikungunya has developed as a potential global health threat in the past decade, as the disease has emerged rapidly in the Americas beginning with the Caribbean outbreak in 2013.[20,22] In the United States, over 200 infected travelers were reported, and autochthonous transmission was observed in Florida.[20]

Zika

Between 2015-2017, a large, unexpected outbreak of Zika virus in the Americas resulted in over 3,000 cases of microcephaly associated with Zika infection and was estimated to cost between 7 to 18 billion USD during the outbreak alone.[23,24] In the mainland United States in 2016, over 200 cases of locally-transmitted Zika were recorded in Florida and 6 locally-acquired cases of Zika were reported in Texas.[25] Zika virus has been circulating autochthonously in Mexico since 2015 and is estimated to have caused over 270,000 human infections since that time.[26,27] Although large outbreaks have not been observed in the Americas since 2017, Zika virus has not disappeared; large pockets of susceptible populations who were not infected during the previous outbreak still remain in the Americas, and transmission is still regularly observed in this region.[28]

Maricopa County

Maricopa County, Arizona has an established presence of *Ae. aegypti* and a large number of travelers crossing the border into Arizona from areas with endemic *Ae. aegypti*-borne disease, such as Mexico and Central America. These conditions put the region at risk for an outbreak of disease spread by the mosquito. Approximately 25 million travelers cross the southern land border from Mexico into Arizona each year.[29] All travelers that traverse the land border from Sonora, Mexico into Arizona are coming from an area that regularly experiences cases of dengue and Zika viruses.

The *Ae. aegypti* population in Maricopa County, Arizona has been increasing over the last decade, and the mosquito is now routinely trapped year-round in this region. In many locations around the world, the invasive mosquito species *Ae.*

albopictus, which was introduced to the United States in 1985, can impact *Ae. aegypti* populations through interspecies competition.[30,31] However, in Maricopa County, Arizona, *Ae. albopictus* has never been trapped and is not considered to be an established species, limiting the competition that *Ae. aegypti* faces in this region. *Aedes aegypti* has been identified in Arizona as far back as 1931 and 1946 in Tucson[32,33] and 1951 in Yuma.[34] However, the mosquito was not identified in routine surveillance for decades despite no specific efforts to reduce its population in Arizona.[35,36] It is possible that the Pan American Health Organization campaign to eradicate *Ae. aegypti* in the Americas contributed to the mosquito not being detected in Arizona in the mid-20th century, but the exact cause of the perceived disappearance of the mosquito remains unclear.[35–37] In the mid-1990s, *Ae. aegypti* was once again trapped in Tucson and along the Arizona-Mexico border. [35] Using routine trapping data from the past ten years, it is now clear that the population of the vector is generally increasing in Maricopa County (see Figure 5.1). In 2020, the number of *Ae. aegypti* trapped decreased substantially, and the reasons for the decrease are unclear; however, 2021 was the biggest year on record.

Although much work has been done to record locations where the mosquito is present throughout Maricopa County through extensive trapping, there is less understanding of the population structure or movement of the mosquito, as well as whether source locations exist in the county. These mosquitoes have historically been thought to stay close to their emergence point (within about 100 meters),[38] however, if conditions are not suitable for reproduction in their immediate environment, there is evidence that the female mosquito can travel much further to seek out appropriate

habitat with observations of dispersal distances up to 2.5 kilometers from their origination point.[39] The tendency for these mosquitoes to remain close to the area where they originate could contribute to a population substructure within this region, allowing a phylogeographic analysis to identify the mixture of subpopulations and the movement of mosquitoes throughout Maricopa County.

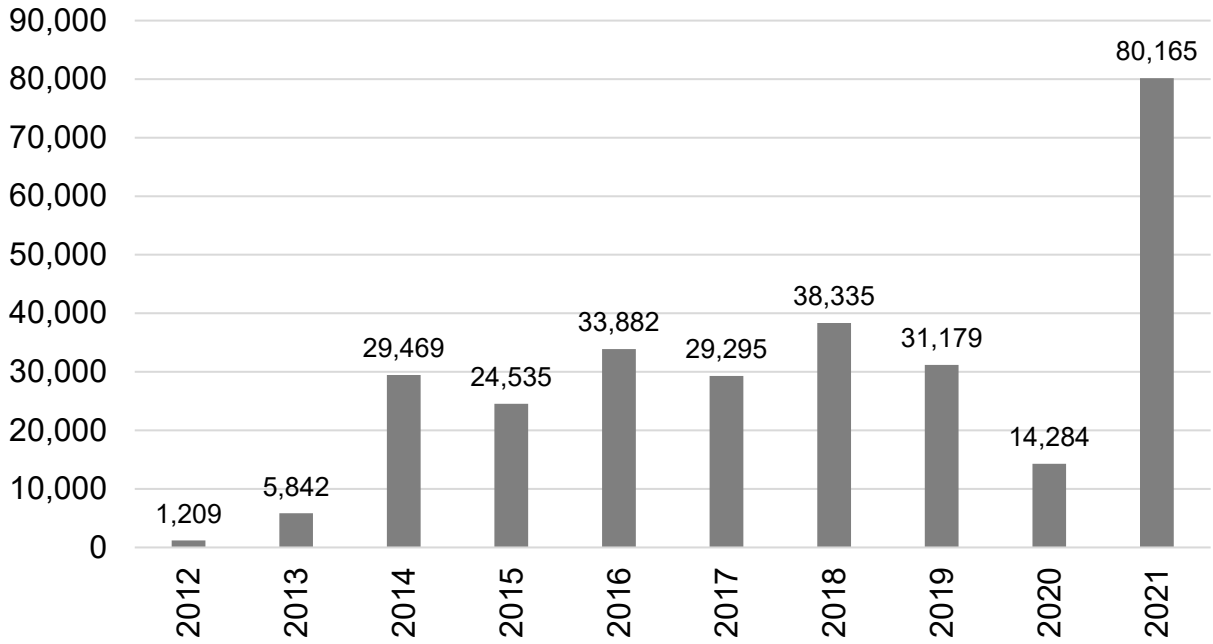

Figure 5.1 Trapping Numbers for *Aedes aegypti* females in Maricopa County, AZ from 2012-2021. Yearly sum of female *Aedes aegypti* trapped throughout Maricopa County, Arizona from 2012-2021.

Past Research and Similar Studies

A limited number of studies exist that have conducted similar analyses around the world, including a few studies from the United States. Many of these studies have been conducted in tropical regions of the world, in habitat that has traditionally been associated with *Ae. aegypti*. These studies have identified population structures and

distinct lineages that help to inform vector control strategies that account for differences in vector behavior or insecticide resistance.

One study, published by Fernando and colleagues in 2020, sequenced the COI (460 bp) and ND4 (349 bp) mitochondrial genes to study the ancestral origin of *Ae. aegypti* and was able to determine the origin of the species as well as the rate of mixture between various regions of the world.[40] A study with similar goals conducted in Bolivia by Paupy and colleagues in 2012 used sequences of nine microsatellites as well as the COI (860 bp) and ND4 (400 bp) mitochondrial genes to reveal the population of *Ae. aegypti* in this country had recently undergone a large expansion and two distinct lineages occur.[41] In a 2008 study based out of Brazil, researchers sequenced the COI (852 bp) mitochondrial gene from a sample of 163 individual *Ae. aegypti* mosquitoes to determine the population structure and gene flow between multiple regions of the country as well as within one city. They determined that two distinct lineages of the mosquito population existed throughout the country due to multiple introductions, geographic barriers, control activities, and passive dispersal.[42] In both Bolivia and Brazil, the presence of two distinct lineages of the vector could influence mosquito behavior or vector competence and therefore could have an impact on public health in the event of an outbreak of disease vectored by this mosquito. The findings from these studies are crucial for informing vector control and surveillance efforts by providing information on the mixture of populations in the region.

Phylogeographic studies have previously been conducted in the United States in Florida, California, and Arizona. A study conducted by Damal et al. in 2013 sequenced the ND4 (342 bp) and ND5 (418 bp) mitochondrial genes to reveal significant gene flow

between *Ae. aegypti* populations on the East and West coasts of Florida, suggesting that human-aided dispersal is common.[43] They also found that two distinct lineages were present on both coasts and theorized that this could be the result of multiple introduction events into Florida. Likewise, a study conducted by Brown and colleagues in 2013, using microsatellites, found that *Ae. aegypti* mosquitoes readily migrate between the Florida Keys and Southeastern Florida mainland, likely aided by human travel in this region.[44]

Two studies have thus far been conducted in the southwestern United States. In a study conducted in California in 2019, whole genome sequencing of 46 *Ae. aegypti* individuals (the first time this method was utilized with field-collected *Ae. aegypti*) revealed evidence for the existence of distinct, isolated populations of the vector throughout California, likely brought to the region in multiple introduction events.[45] Finally, an Arizona focused study was conducted in 2005 by Merrill and colleagues, which employed amplified fragment length polymorphism.[46] They found that populations of *Ae. aegypti* from multiple towns and cities in southeastern Arizona were genetically differentiated into three regions suggesting that populations rarely migrated between the regions but were occasionally mixed due to human transport. It is important to note that this study included only one sample site in Maricopa County, the primary area of interest for this study, and was conducted prior to the mass colonization of Maricopa County by *Ae. aegypti* that has been observed in the past decade.

Interestingly, the studies conducted in Florida suggest that *Ae. aegypti* populations from nearby cities or towns are genetically mixed despite the presence of geographic barriers that may prevent their movement between these regions. However,

the two available studies from the more arid regions of California and Arizona suggest that the populations of *Ae. aegypti* remain genetically differentiated between the towns and cities that were sampled. This difference in population structure could possibly be explained by chance, due to the small number of studies available, but additional research is needed to explore the possibility that the behavior of *Ae. aegypti* differs between tropical and arid environments. This study provides an abundance of additional data on the movement of *Ae. aegypti* in a desert region by sequencing the entire mitochondrial genome (16,665 bp) of *Ae. aegypti* mosquitoes from 94 samples collected throughout the Phoenix metropolitan area in 2020.

Study Objectives

Our study contributes to the growing body of literature on the phylogenetic structure of *Ae. aegypti* populations by providing the first collection of mitochondrial genome sequences from the Maricopa County, Arizona population of the mosquito after it has recently become established in this region. We employed phylogeographic techniques to investigate the spatial distribution and movement of the mosquito vector of interest in Maricopa County. Phylogeography as a field is principally concerned with the spatial and temporal distributions of genetic information, specifically within a single species or among a few closely related species. The methods of phylogeography work especially well in species with limited movement capabilities, as populations of such species are easily isolated and thus develop genetic distinctions and population substructure.[47] In the case of *Ae. aegypti*, the mosquito vector tends to have a very small range, often identified as 100 to 200 meters from where the mosquito originated,[38,48] which may contribute to population substructure across Maricopa

County, Arizona. However, the barriers between populations should be thought of as semi-permeable as mosquitoes may have a larger range than expected or be transported between populations by human movement or monsoon storm events with strong winds. Phylogeographic techniques allow the mixture between populations to be explored, providing valuable insight into the movement of populations and potential population substructure within Maricopa County.[47] Furthermore, the spatiotemporal evolution of the mosquito vector was evaluated by projecting the phylogenetic tree constructed in this study in the geographic space of Maricopa County.[49]

The goal of this project is to utilize whole mitochondrial genome sequencing to study the relationship between *Ae. aegypti* collected across Maricopa County, Arizona from 2020. Three research questions are addressed in this study. The first question is: what is the population structure of *Ae. aegypti* in Maricopa County? The second question is: what is the extent of mixture of the *Ae. aegypti* population between various locations throughout Maricopa County, Arizona? And, finally, the third question is: are there source locations in Maricopa County, Arizona that consistently contribute to populations of *Ae. aegypti* throughout the county? Our hypothesis is that, given the typically small range of the mosquito, we will see distinct clusters of *Ae. aegypti* mosquito sequences dependent on location, and a positive relationship between geographic distance and genetic distance.

The resulting analyses provide a better understanding of the movement of the vector within this area, as well as identify potential locations where the mosquito population is well-maintained. This project is a step toward the long-term objective to develop an understanding of the underlying geographic distribution and movement of

the mosquito vector *Ae. aegypti* in Maricopa County, Arizona and, more broadly, in arid desert environments. The findings presented in this study will be beneficial to vector control and public health efforts as this mosquito continues to expand its range and outbreaks of disease occur. A better understanding of the distribution, movement, and potential source locations of *Ae. aegypti* in an arid desert environment before any viruses are introduced to the naïve vector population can help inform control strategies in order to reduce the burden and cost of disease should an outbreak occur.

Methods

Study area

Maricopa County, located in South Central Arizona, is approximately 23,828 square kilometers (9,200 square miles). The county had a population of approximately 4.5 million residents as of 2019. Arizona's capital, Phoenix, is located within Maricopa County as one of the county's 24 recognized cities and towns that comprise part of the state's largest metropolitan area.[50] Phoenix has a desert climate with generally low humidity, an average annual rainfall of 20.4 cm (8.0 inches), an average maximum temperature of 41.2°C (106.1°F) for the hottest month, July, and an average minimum temperature of 7.1°C (44.8°F) for the coldest month, December. Rainfall rarely occurs during the winter months of November through March, while monsoons in July and August typically bring heavy rains and dust storms called haboobs. Typical of a desert climate, temperature fluctuations between the daytime high and the nighttime low can be 15°C (30°F) or more.

Mosquito Sampling

Maricopa County Environmental Services Vector Control Division conducts routine CO_2 trapping throughout Maricopa County, focusing mainly on the Phoenix metropolitan area, by deploying more than 800 traps overnight for a 12-hour period on a weekly basis. The trapping program in Maricopa County is one of the most robust programs in the country, both in the amount of area covered and in the regularity with which traps are placed. Through an established partnership with Maricopa County Vector Control, we gained access to this trapping data for 2020. The provided data includes the trapping date, number of adult mosquitoes trapped, species and sex of the mosquitoes, identification number of the trap, and latitude and longitude values.

In addition to the trapping records, we have access to mosquito pools collected throughout Maricopa County from 2020. Due to sample availability and fallout during sample processing, our initial analysis presented in this study includes only samples from May to November 2020, for a total of 94 mosquito pools from 30 trapping locations. We continue to work diligently on sequencing additional samples from 2019-2021 to further our analysis. The trap locations were selected to maximize sample availability. The locations include both trap clusters separated by short distances and trap locations separated by longer distances (see Figure 5.2).

Sample Processing

We arrayed individual mosquitoes from each available sample of interest into Zymo Research Lysis racks containing 2.0mm beads, then added 800uL of Zymo Research 1X DNA/RNA shield to each of the wells of the lysis rack. Each lysis rack contained 90 individuals and 6 reagent blanks to ensure sample sterility. Samples were

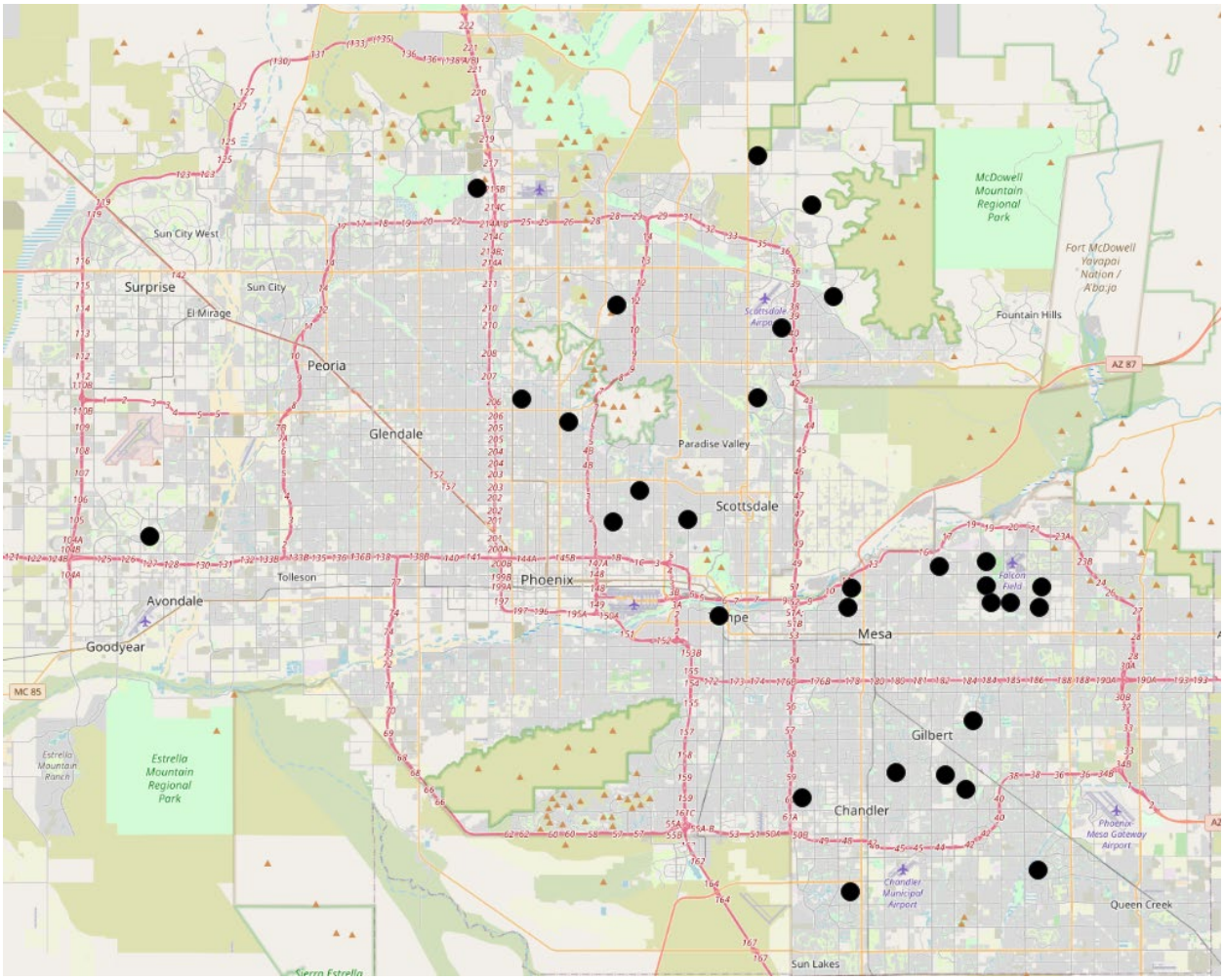

Figure 5.2 Location of 30 traps from which *Aedes aegypti* mitochondrial genome samples were sequenced. Base map and data from OpenStreetMap and OpenStreetMap Foundation (CC-BY-SA). © https://www.openstreetmap.org and contributors.

homogenized on a Qiagen TissueLyser II at maximum speed in four 1-minute intervals for a total homogenization time of 4 minutes. Following complete homogenization, all samples (n = 180) underwent DNA/RNA extraction using Zymo Research Quick-DNA/RNA Pathogen MagBead kit on a ThermoFisher Scientific KingFisher Flex instrument. PCR amplification was performed on the resulting DNA/RNA elutions using a newly designed tiled-amplicon assay targeting the mitochondrial genome of *Ae. aegypti*. The 2,200 bp amplicons were visualized on 1.0% agarose gels using New

England Biolabs Quick-Load 1kb DNA Ladder. All samples with correct amplicon size (n = 102) were cleaned using AMPureXP beads at 0.8X concentration and quantified with an Invitrogen Quant-iT High Sensitivity dsDNA kit on a BioTek Synergy LX plate reader. Quantified samples were normalized to 100ng using Tris-HCl, pH8 for a final volume of 40 uL. Normalized samples were put through the WatchMaker Genomics Watchmaker DNA Library Prep Kit with Fragmentation following manufacturer recommendation with minor modifications. The IDT xGen stubby adapters and IDT xGen UDI 10nt primers were used for adapter ligation and indexing during the WatchMaker library prep. Indexed samples underwent a size-selection clean-up using 0.4x and 1.0x AMPure XP beads. Size-selected samples (n = 94) were pooled equal-molar and final QC was performed. All samples were sequenced with a NexSeq1000 P1 600 cycle sequencing kit on a NextSeq 1000 sequencer at the Translational Genomics Research Institute, North in Flagstaff, Arizona.

Genomic Processing

To generate consensus sequences needed for further analysis, the sequencing reads were first processed using BBDuk—a tool integrated into the BBMap package[51]—to remove Illumina adapter and primer sequences. The trimmed reads were mapped against the California reference genome, MH348176, using Bowtie2.[52] The mapped reads were sorted and indexed using Samtools 1.16.1.[53] Consensus sequences were generated using iVar 1.0 with a minimum of 10X coverage and a majority base proportion of 0.8.[53,54]

Phylogenetic Analysis

Consensus sequences created from the previous step were aligned using the software Multiple Alignment using Fast Fourier Transform (MAFFT).[55] A maximum parsimony tree was reconstructed using the Molecular Evolutionary Genetics Analysis (MEGA) software.[56] The pairwise geographic distance and the proportional pairwise genetic distance were calculated for all samples, [56] and a simple linear regression was performed to evaluate the relationship between geographic and genetic distance. A Nextstrain phylogeny was created with the intent to examine the spatial distribution of sites.[49] StrainHub was used to describe the network of connections between trapping locations based on the maximum parsimony phylogenetic tree, which allowed us to identify potential source locations of mosquito populations in Maricopa County.[57]

A total of 14,217 positions were included in the final analyses. Ten equally parsimonious maximum parsimony trees were created using the 94 mitochondrial genomes sequenced as part of this study and one reference genome from California. The bootstrap consensus tree shows all clusters that were supported by at least 5 of the 10 equally parsimonious trees (see Figure 5.3). The samples from 2020 were genetically similar across Maricopa County with no obvious separation into distinct clades based on geographic location. The relationship between pairwise geographic distance and pairwise genetic distance was very weak (adjusted R-squared = 0.0199) indicating population mixture throughout the region (see Figure 5.4).

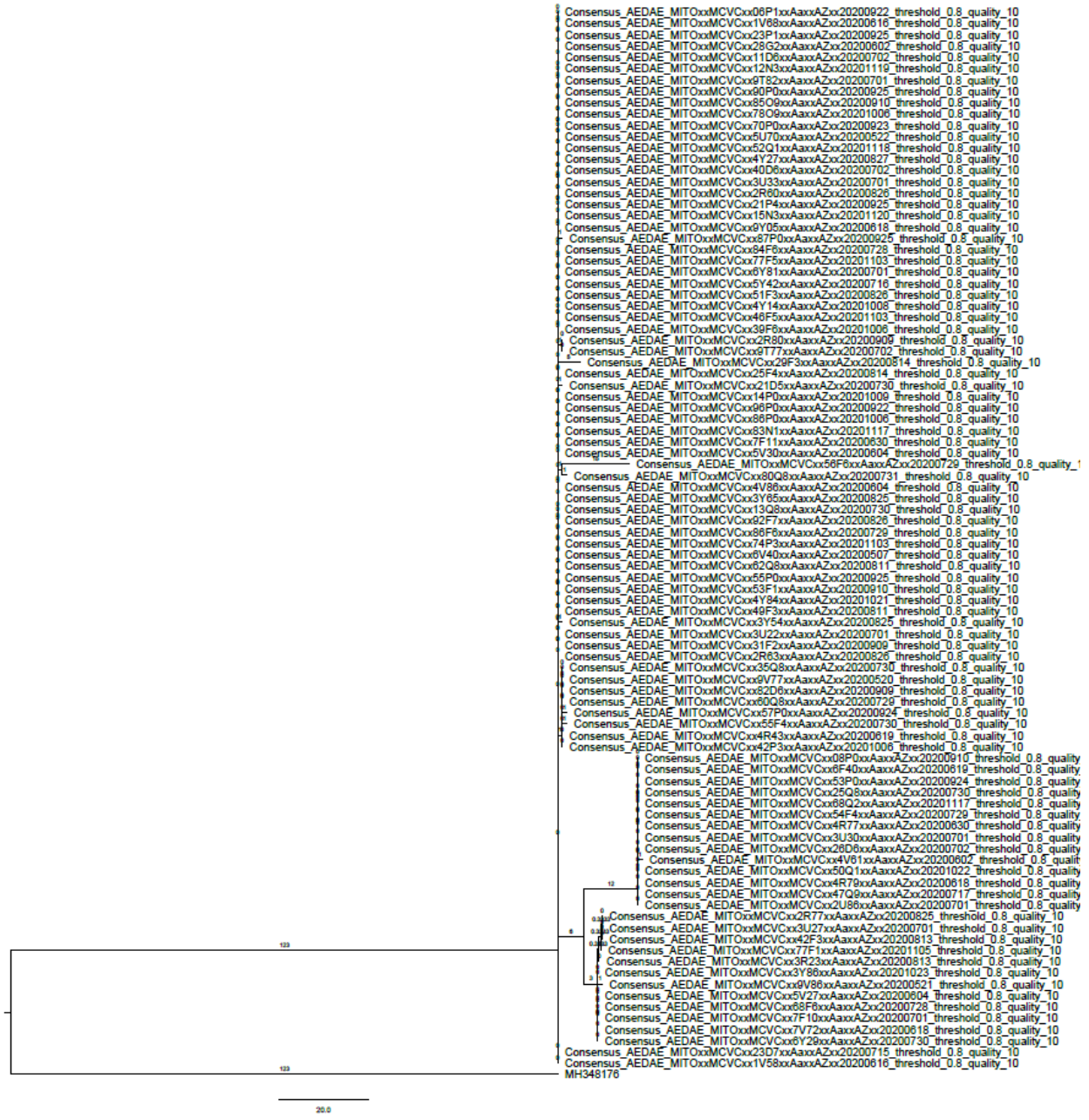

Figure 5.3. Bootstrap consensus phylogenetic tree showing the relationship between 94 *Aedes aegypti* mitochondrial genomes from May-November 2020 in Maricopa County, AZ. Ten equally parsimonious trees were created, and the bootstrap consensus tree shows all clusters that were supported by at least 5 of the 10 equally parsimonious trees. All samples were genetically similar indicating a mixture of populations throughout Maricopa County regardless of geographic distance. Branch labels indicate the number of substitutions.

Results

The Nextstrain phylogeny and map indicated the presence of genetic relatedness between samples throughout the Phoenix metropolitan area (see Figure 5.5). When examining some of the most closely related mitochondrial genomes for one clade, we still observe relationships between samples that are over 30 kilometers apart (see Figure 5.6).

The StrainHub analysis showed connections between trap locations throughout Maricopa County. Further, two locations stood out as potential source locations with 10 (RT151) and 13 (RT555) connections to other trap locations around the county. RT151 was in the north central portion of the Phoenix metropolitan area while RT555 was in the southeastern portion of the Phoenix metropolitan area (see Figure 5.7).

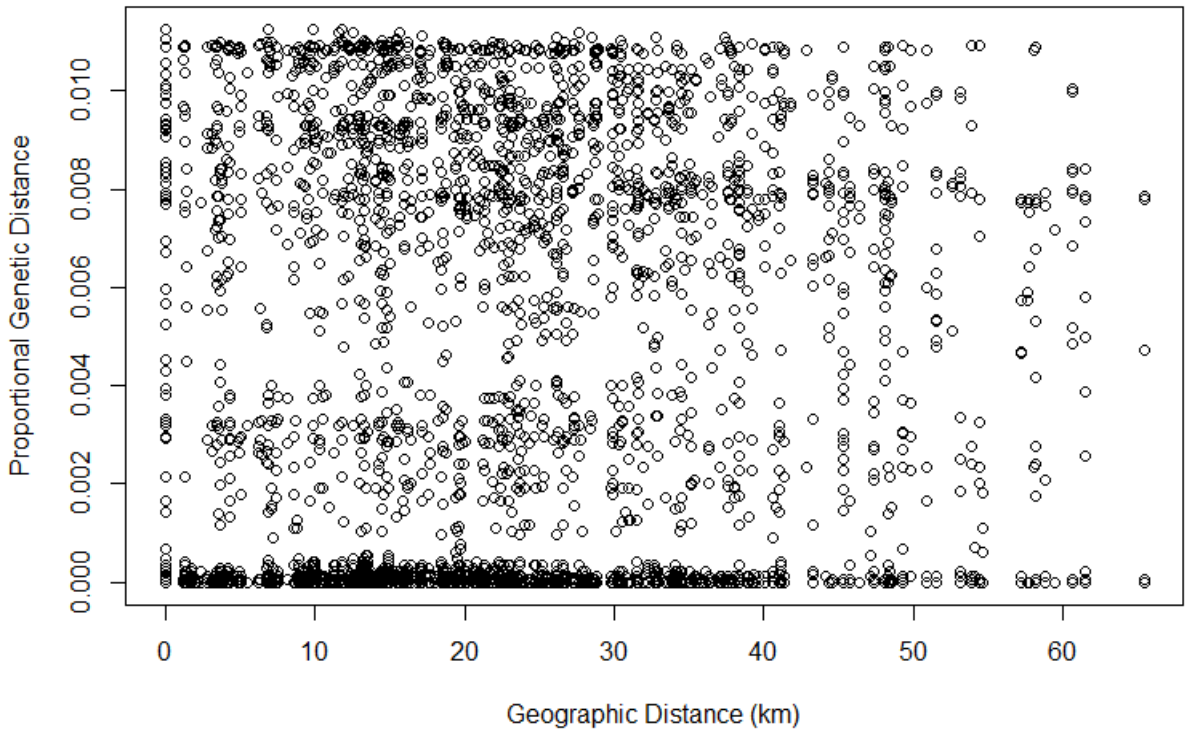

Figure 5.4 Plot of geographic distance against proportional genetic distance. No clear relationship is present indicating that there is a mixture of populations in Maricopa County, AZ regardless of distance.

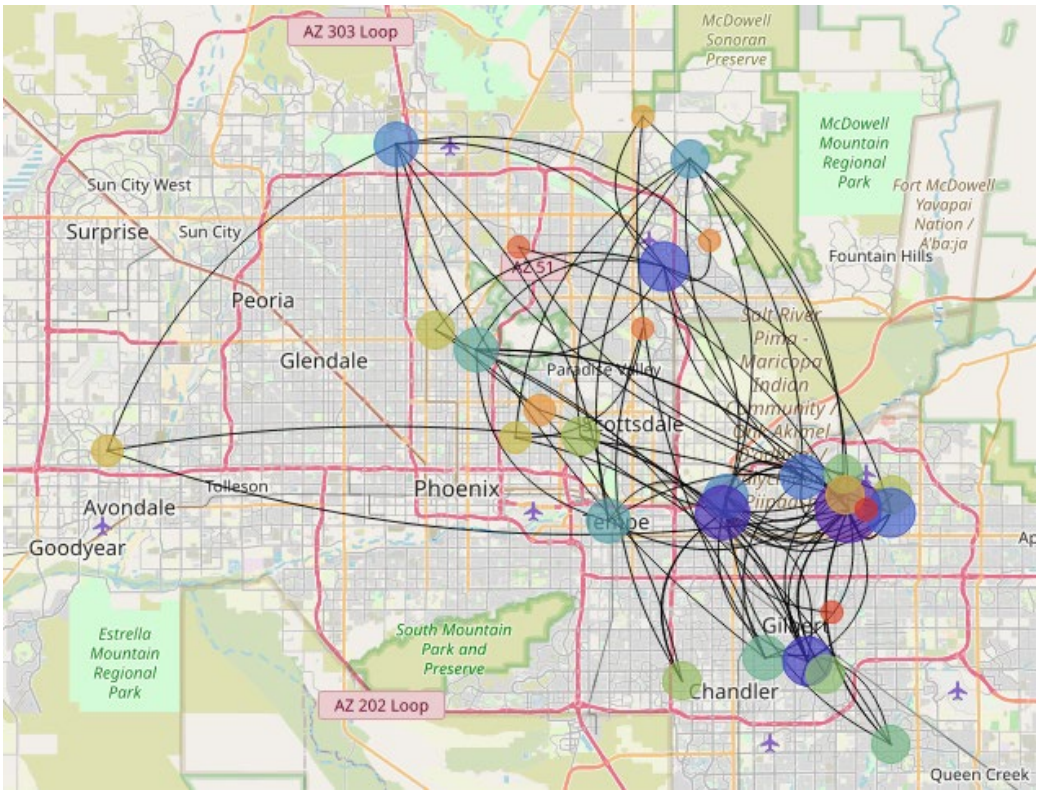

Figure 5.5 Map representing Nextstrain phylogeny. Lines represent genetic connections between samples from locations throughout Maricopa County. The connections between locations throughout this area suggest that populations are not isolated based on distance.

Discussion

We sequenced the mitochondrial genomes of 94 *Ae. aegypti* female mosquitoes trapped at 30 sampling locations throughout the Phoenix metropolitan area in Maricopa County, AZ from May to November 2020. We found no evidence of genetic isolation based on geographic location.

We hypothesized that we would find distinct clades based on geographic location due to historical beliefs that this mosquito travels a very short distance. Past studies have held to the belief that most *Ae. aegypti* mosquitoes remain within about 100 meters of their origination point.[38] Findings from a 1938 study that claimed that this

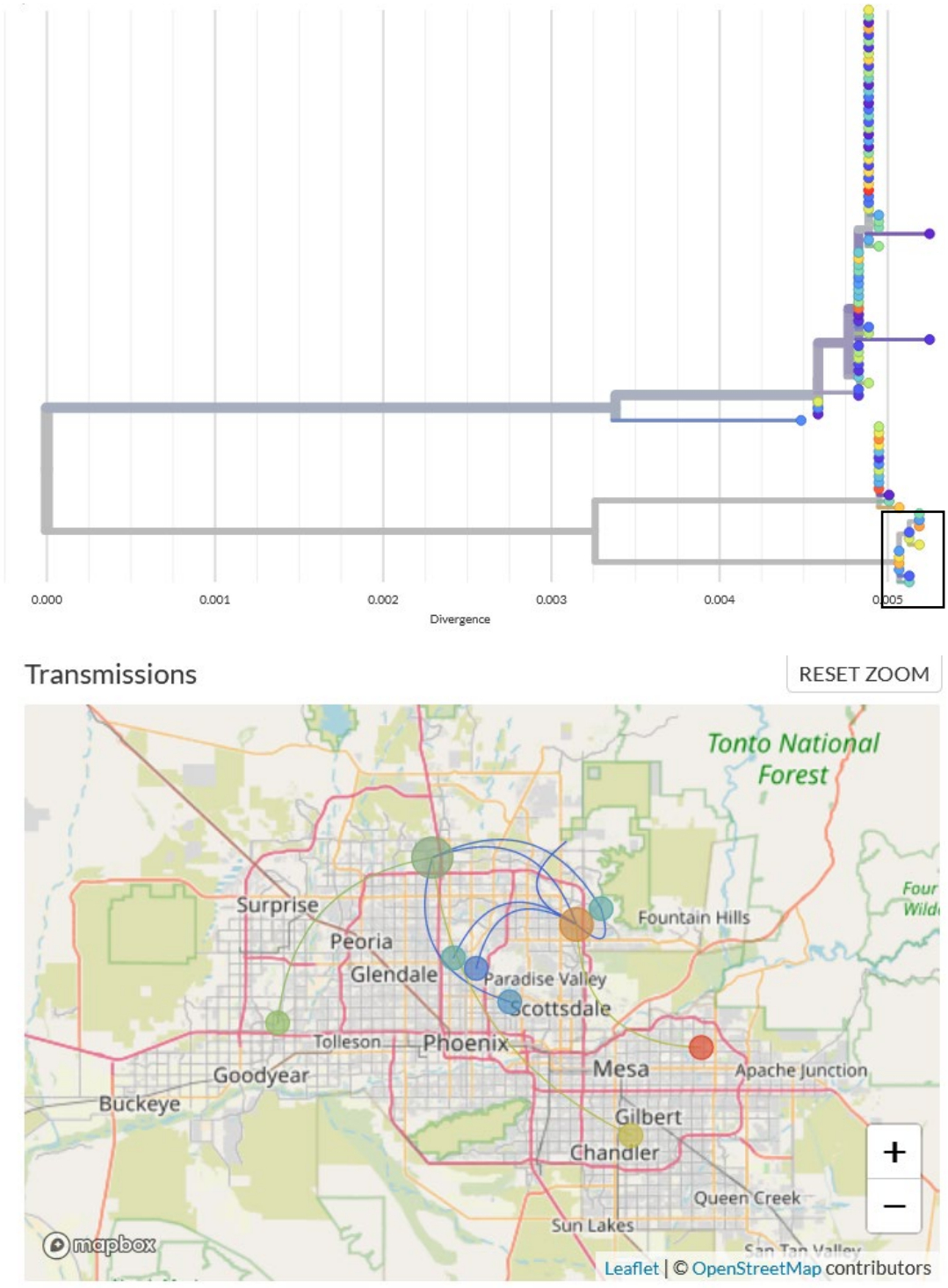

Figure 5.6. Map of one clade of *Aedes aegypti* mitochondrial genome sequences. Top panel: Full phylogeny created in Nextstrain with one clade of 12 samples shown in a black box at the bottom. Bottom panel: Map showing the location and connections between the 12 samples from one closely related clade. Despite their close genetic relatedness, these samples were from throughout the Phoenix metropolitan area.

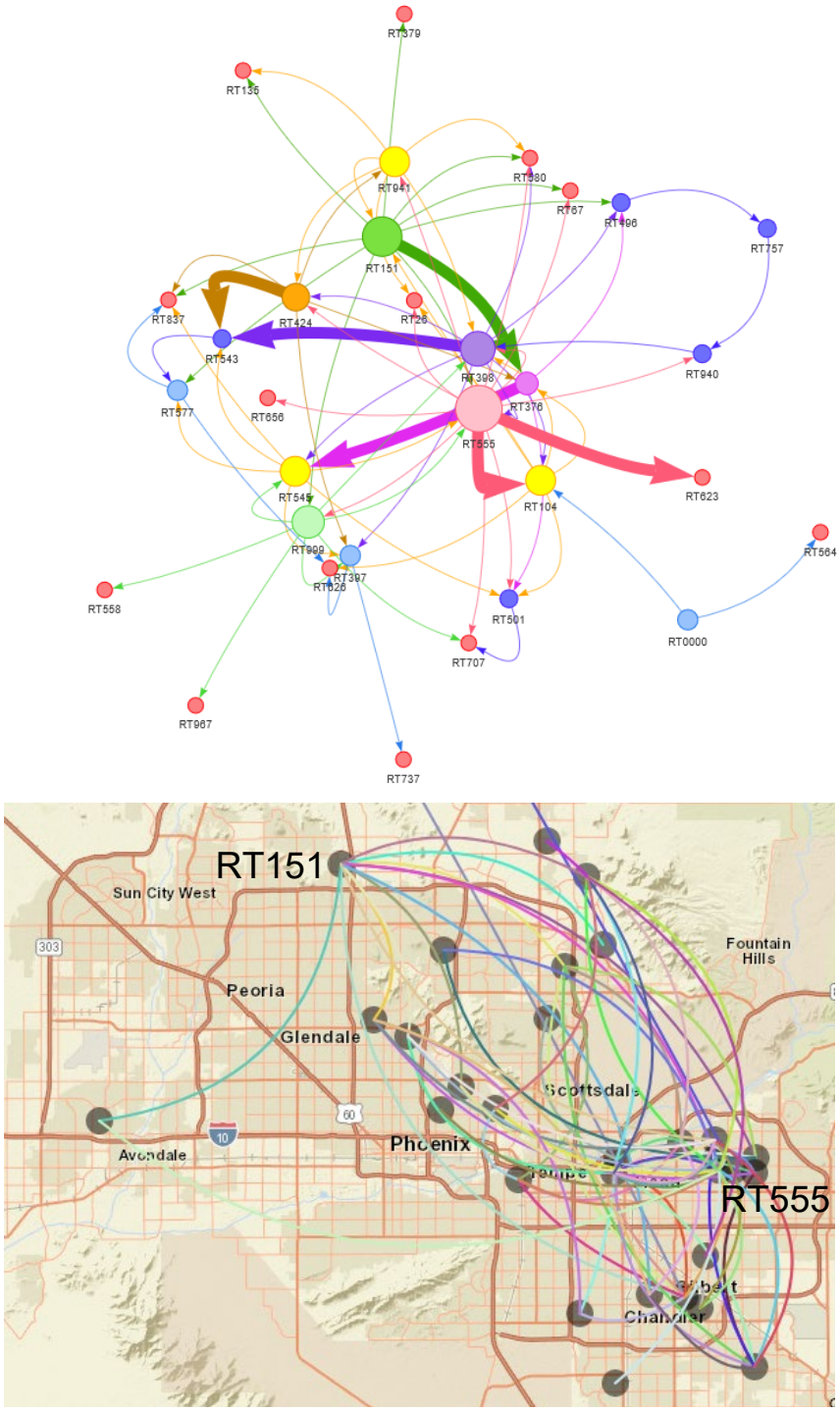

Figure 5.7. StrainHub analysis results showing connections between trapping locations. Top panel: Network showing the number of connections from each trap to other traps. Traps RT151 and RT555 stood out as potential source locations with 10 and 13 connections to other trapping locations, respectively. Bottom panel: StrainHub network analysis results displayed over a map of the Phoenix metropolitan area. The two potential source locations (RT151 and RT555) are labeled in the north central and southeastern Phoenix metropolitan area, respectively.

mosquito generally travels no further than 25-30 meters have continued to influence beliefs and control practices related to *Ae. aegypti* despite other studies finding the mosquito capable of traveling between 1,000-2,500 meters in the field and upwards of 11km in laboratory studies[39].

Based on the groupings in the phylogenetic trees constructed from these 94 samples, our findings indicate that populations of this mosquito are related throughout Maricopa County at locations that are over 30-50km away from one another. This indicates that there is population mixture far beyond the distance that this mosquito is typically believed to travel. Furthermore, a network analysis based on the maximum parsimony tree constructed in this study revealed many connections between trapping locations throughout Maricopa County. Additionally, this analysis allowed us to identify two potential source locations of mosquito populations with many connections to other traps around the Phoenix metropolitan area. Importantly, however, this analysis cannot tell us whether the mosquito is moving great distances around Maricopa County of its own power or if other forces are working to transport the mosquitoes over long distances.

Similar to findings from Bolivia, we found no evidence of a relationship between genetic and geographic distance of our samples.[41] Likewise, a study from Brazil found that *Ae. aegypti* populations were genetically distinct between regions thousands of kilometers apart, but showed evidence of population mixture within regions connected by busy trade and travel routes (with samples taken hundreds to thousands of kilometers apart), and strong gene flow within cities (with samples taken between 4-13km apart).[42] Consistent with our results, two studies in Florida found evidence for

gene flow and population mixture over long distances (between cities on the east and west coast of the state[43] and between Key West and Miami).[44] Between the results of these studies and our analysis, there is evidence that *Ae. aegypti* mosquitoes may be mixing at greater distances than previously thought, whether by their own power or with the help of outside forces such as human travel. On the other hand, a study conducted in California found that populations of *Ae. aegypti* appeared to be isolated between regions based on an analysis of the nuclear genome but not an analysis of the mitochondrial genome, indicating that the mitochondrial genome may not capture recent population divergence.[45] It is possible that the populations of *Ae. aegypti* in Maricopa County are isolated, but that this isolation occurred too soon after a recent introduction event to appear in our analysis of mitochondrial genomes.

Overall, we presented the first collection of 94 mitochondrial genome sequences from the Maricopa County, AZ population of *Ae. aegypti* after its recent population expansion in this region. These samples were from 30 trapping locations throughout the Phoenix metropolitan area from May to November 2020. We employed phylogeographic techniques to investigate the spatial distribution and movement of the mosquito vector of interest in Maricopa County. We found that the samples from 2020 were genetically similar across Maricopa County with no obvious separation into distinct clades based on geographic location. Although *Ae. aegypti* females have historically been thought to have a very small range, we found population mixture throughout the county regardless of geographic distance between sample locations suggesting a greater extent of movement and population mixture than what was previously believed to be possible.

Importantly, this is the first study of its kind in this region, so additional resolution may be achieved as additional samples are sequenced and analyzed.

Our findings indicate that the range of the mosquito may be larger than previously thought. Given these results, it may be advisable to increase the range of public health outreach and mosquito surveillance efforts in the event that a mosquito is found to be carrying a virus or a human tests positive for a virus transmitted by the mosquito. Unfortunately, a larger range may also suggest that localized mosquito control efforts are less likely to be effective as the mosquito may not be restricted to a small range and could seek out more suitable habitat further away. Further research is urgently needed to continue exploring the range of the vector in this area.

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CHAPTER 6: CONCLUSION

Within the last decade, a large population of *Ae. aegypti* mosquitoes has become well-established in Maricopa County, Arizona, as the vector quickly expands its range around the world. Concerns about the public health impacts of the mosquito have continued to increase; threats of dengue and yellow fever viruses remain a risk, while outbreaks of newly emerged viruses such as Zika and chikungunya have created new challenges. There is a growing interest in the public health impact of this mosquito in Arizona, especially since the first cases of locally-transmitted dengue virus were identified in Maricopa County in Fall 2022. Viruses transmitted by this mosquito can be passed in a cycle from human to mosquito and then back to human, so it is possible for just one infected traveler to introduce a virus to the *Ae. aegypti* population in Maricopa County, an area where the vast majority of residents are naive to dengue, yellow fever, chikungunya, or Zika viruses. Despite the rising concerns surrounding the vector in this region, there are still many unanswered questions about the behavior of the mosquito in a desert environment.

The first step toward addressing the growing population of *Ae. aegypti* and preparing for potential public health threats in Maricopa County is to gain a better understanding of the underlying drivers of the habitat supporting this mosquito population. It is also crucial to establish a better understanding of the range and movement of the vector in this region so that a “range of risk” can be defined for virus transmission and pesticides and other control tactics can be deployed in a targeted fashion. Maricopa County Environmental Services Vector Control Division has managed a robust mosquito surveillance program throughout the county, providing weekly

mosquito trapping observations from over 800 locations for over a decade. This program plays a crucial role in gaining a better understanding of mosquito presence and movement patterns in this region. From the trapping data, it is obvious that the *Ae. aegypti* population is not uniformly distributed throughout the county. The goal of this dissertation was to use this data to expand our understanding of mosquito presence beyond trapping locations, or “fill in the gaps” between traps, and to better understand the locations where the mosquito was or was not present.

This dissertation is comprised of three distinct studies that utilized methods from various fields to characterize the relationship between socioeconomic factors, weather patterns, and landscape characteristics and *Ae. aegypti* mosquito populations. Furthermore, the first mitochondrial genome sequences from this population were produced, providing valuable insight into the genetic diversity and relatedness of mosquitoes trapped at various locations throughout Maricopa County. Taken together, these three studies provide the first glimpse into the mechanisms supporting this mosquito population in an area that was recently thought to be inhospitable for the vector. We hope that the results of these studies can be useful for informing targeted vector control or public health practice, which can help to reduce the burden and cost of disease, especially in the event of an outbreak.

Summary of Findings

Chapter 2

In Chapter 2, a comprehensive literature search was conducted using relevant keywords to retrieve published articles and gray literature related to the impact of socioeconomic factors on *Ae. aegypti* populations in the United States. Four electronic

databases and the websites of 24 mosquito control organizations located in the United States were searched through June 12, 2019. The articles were screened for eligibility using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. The relevant articles were then read in full to determine their eligibility for the review. The selected articles were original peer-reviewed studies or publications of mosquito control organizations from the mainland United States that studied the impact of socioeconomic factors on the distribution of *Ae. aegypti* mosquitoes. The location, date of study, survey methods, analysis methods, and socioeconomic factors were summarized for inclusion in the review. The main themes were determined based on the compiled information.

Through this search, 11 articles were identified that investigated the relationship between socioeconomic factors and the distribution of *Ae. aegypti* in the mainland United States. These articles focused on economic factors, housing and built environment factors, and demographic factors. The review found inconsistent results regarding the impact of socioeconomic factors such as income, land use, housing age, and population density on the distribution of *Ae. aegypti*. The results of this review emphasize the need for further research to understand the impact of socioeconomic factors on the distribution of *Ae. aegypti* and to develop effective strategies for mosquito control.

Chapter 3

In Chapter 3, we used trapping data from 2014-2020 to create quarterly species distribution models for female *Ae. aegypti.* Trapping observations were converted to quarterly presence-only records of the mosquito resulting in 25 separate data sets and

models. Quarterly species distribution models (Maxent) were created using satellite imagery-derived vegetation and moisture indices, elevation, and socioeconomic factors (population density, median income) as predictors. Maxent is a popular freely available machine learning technique for species distribution modeling that uses presence-only observations of a species along with environmental variables to predict the probability of presence of the species throughout the study region. Maps that displayed predicted habitat suitability for 30-meter squares throughout the county were created for each quarter. These maps were summarized to binary predictions and also summarized to create consensus maps over multiple quarters.

Population density was generally the most important predictor in the models while median income and elevation were the least important. Increased human population density was associated with greater suitability for *Ae. aegypti* while increased greenness also appeared to be associated with greater suitability for the mosquito up to a certain point while extremely high values of landscape greenness were associated with lower predicted habitat suitability, likely because extremely vegetated areas are more likely to have lower human population density. Multiple suburban areas surrounding the Phoenix metropolitan core area were identified as consistent highly suitable habitat throughout the six-year study period. We also created binary maps of habitat suitability that may be useful for vector control and public health purposes.

Chapter 4

In Chapter 4, we used records of the presence and absence of *Ae. aegypti* females from 2014 to 2020 to create Bayesian hierarchical models with spatial and temporal random effects using R-INLA. We matched the mosquito trapping records to

socioeconomic predictors (income, population density, housing age), weather predictors (temperature, precipitation, and vapor pressure), and satellite imagery data (Enhanced Vegetation Index). Our choice of weather, vegetation, and socioeconomic predictors allowed us to evaluate the relationship between mosquito presence and various small-scale neighborhood characteristics; the choice to lag predictors by one week provides the opportunity to expand this model for use as a real-time predictor. We compared models with no random effects, with temporal random effects, with spatial random effects, and with both temporal and spatial random effects; the best performing model included both spatial and temporal random effects.

We found a positive association between median income, population density, and median house age, landscape greenness, and vapor pressure with the presence of female *Ae. aegypti* while precipitation and maximum temperature had negative associations with presence. We mapped spatial effects across the study area to identify locations with higher odds of mosquito presence. We found that the range (the distance at which the spatial correlation decreases to 0.13) was 2,942 meters. The autocorrelation parameter for the AR(1) model was 0.976 indicating that observations depend heavily on the previous week; there was an important positive temporal effect from approximately June through October. However, it is important to note that the model overpredicted positive observations during the summer months (possibly because the species has only recently become established in this area and may not have exploited the full extent of suitable habitat at this point or the model is simply incorrect or includes inappropriate or missing covariates and overpredicts mosquito presence in areas that are not suitable). This study demonstrated the feasibility of this

approach and developed a framework that can be extended for use as a tool to prioritize vector control and public health resources in this area.

Chapter 5

In Chapter 5, we presented the first collection of mitochondrial genome sequences from the Maricopa County, AZ population of *Ae. aegypti* after its recent population expansion in this region. The 94 mitochondrial genomes included in the analysis were from 30 trapping locations throughout the Phoenix metropolitan area from May to November 2020. We employed phylogeographic techniques to investigate the spatial distribution and movement of the mosquito vector of interest in Maricopa County.

The samples from 2020 were genetically similar across Maricopa County with no obvious separation into distinct clades based on geographic location. Although *Ae. aegypti* females have historically been thought to have a very small range, we found population mixture throughout the county regardless of geographic distance between sample locations suggesting a greater extent of movement and population mixture than what was previously believed to be possible. Importantly, this is the first study of its kind in this region, so additional resolution may be achieved as additional samples are sequenced.

Comparison of Studies and Conclusions

In Chapter 3, we created Maxent models based only on the presence records of *Ae. aegypti* females for each quarter from 2014-2020. Although these models resulted in useful maps of predicted habitat suitability, this approach was unable to account for temporal trends or negative observations. Summarizing observations to quarterly time periods resulted in a loss of resolution in the findings and an inability to link mosquito

observations to weather patterns. Furthermore, due to the structure of the models (using the average Normalized Difference Vegetation Index value as a predictor for each quarter), it would not be possible to predict future habitat suitability. The models presented in Chapter 4 addressed some of these issues: we were able to use both presence and absence records of *Ae. aegypti* females, and we retained resolution to the week time scale. Additionally, the use of lagged weather predictors creates the opportunity to use this model to predict mosquito presence in real time.

Similarly, the results of both Chapter 3 and Chapter 4 indicated that population density is an important predictor of habitat suitability for *Ae. aegypti* presence. In both chapters, increased vegetation was also linked to presence. In Chapter 4 but not in Chapter 3, median income was found to be an important predictor of presence. Despite the different approaches employed by the two studies, very similar areas were identified as being favorable habitat for female *Ae. aegypti* in both chapters (see Figure 6.1).

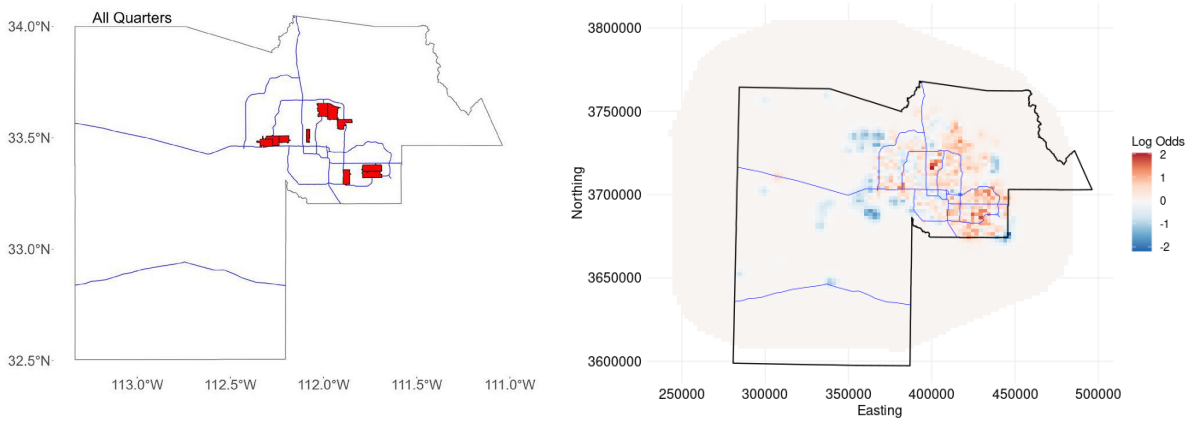

Figure 6.1 Comparison of predicted habitat suitability from Chapter 3 and Chapter 4. On left, Panel C from Figure 3.1 depicts the location of the ten Zip Code Tabulation Areas (ZCTAs) with the highest average suitability for all quarters. On the right, Panel A from Figure 4.4 depicts the mean of the spatial effect mapped across Maricopa County. Both figures show areas of higher suitability in the southeastern Phoenix metropolitan area, the north central metropolitan area, and an area of higher suitability west of downtown Phoenix.

In Chapter 5, a phylogenomic approach was taken to study the connection of *Ae. aegypti* female populations between multiple trapping locations in the Phoenix metropolitan area. The results of this study suggested that there is much more mixture between populations at further distances than what we might expect if the vector had a small range of movement in this desert region. This study did not examine the links between mosquito populations and weather or socioeconomic factors, so a direct comparison of suitable areas like the one between Chapters 3 and 4 is difficult to make. The results from Chapter 4 suggested correlation of the likelihood of presence of *Ae. aegypti* females between trap sites up to about 2,942 m while the results from Chapter 5 suggest that there is population mixture between traps 30 km apart or more. Taken together, these findings suggest that it may be time to rethink the commonly held belief that *Ae. aegypti* females travel very small distances over the course of their lifetime. However, it is important to note that our studies do not directly evaluate the flight range of the mosquito in this area; it is possible that these connections exist because the mosquito is being moved by humans or some other force. Additional research is needed to clarify how the vector is moving far distances between trap locations in the Phoenix metropolitan area.

Implications for Practice

The findings of these studies have identified areas within Maricopa County, AZ that appear to be more suitable for the vector. These areas should be targeted for increased disease surveillance, vector control, and public health outreach. Additional research may clarify if these areas are source locations. In the event that source locations are identified, heavily targeting those areas for vector control may help to

decrease populations of the mosquito for the entire region, especially if the source locations are targeted during the offseason, when small fractions of the mosquito population overwinter in the area. However, given our findings that the range of the mosquito may be larger than previously thought, it may be advisable to increase the range of public health outreach and mosquito surveillance efforts in the event that a mosquito is found to be carrying a virus or a human tests positive for a virus transmitted by the mosquito. Unfortunately, a larger range may also suggest that localized mosquito control efforts are less likely to be effective as the mosquito may have the ability to seek out more suitable habitat further away. Further research is urgently needed to better our understanding of the preferred habitat and range of the vector in this area.

Limitations and Further Research

Although these studies represent a great starting point for understanding the distribution and behavior of *Ae. aegypti* in a desert environment, more work needs to be done to continue to gain knowledge on the habitat being used by this vector. Additional field studies that identify larval habitat could be helpful to determine how the mosquito is breeding in these conditions. Furthermore, fieldwork studies that help understand the behavior of the mosquito, such as mark-release-recapture studies could provide a better understanding of how the mosquito is moving throughout this area. We would also like to extend these methods to modeling the abundance of the vector throughout this region, rather than just the presence or absence. Finally, analyzing additional mitochondrial genomes will provide better resolution on the movement of mosquito populations throughout this area, including the possible identification of source or sink locations.

One big limitation of these studies is that we were unable to link our findings to the presence of viruses transmitted by this mosquito because, fortunately, no large outbreaks of these viruses have occurred in Maricopa County, AZ at this point in time. Although we assume that increased mosquito presence would be associated with increased mosquito-human interaction and therefore increased risk of disease transmission, we cannot guarantee that areas of greater habitat suitability have any connection to increased viral transmission. Additional work will be required to understand the connection between the results of our studies and disease incidence in the event of an outbreak.

Overall, the results of these studies provide an initial understanding of the mosquito population in Maricopa County. These studies are helpful because they identify areas of potentially greater habitat suitability which can help inform vector control or public health priorities or provide a way to narrow down locations that may be ideal for fieldwork studies within the nearly 24,000 square kilometers of Maricopa County. Further work is urgently needed to continue expanding our knowledge of this vector before a large outbreak of disease occurs.

APPENDIX TABLE OF CONTENTS

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Supplementary Material for Chapter 4 ..... *A68*
Supplementary Data and Code A68
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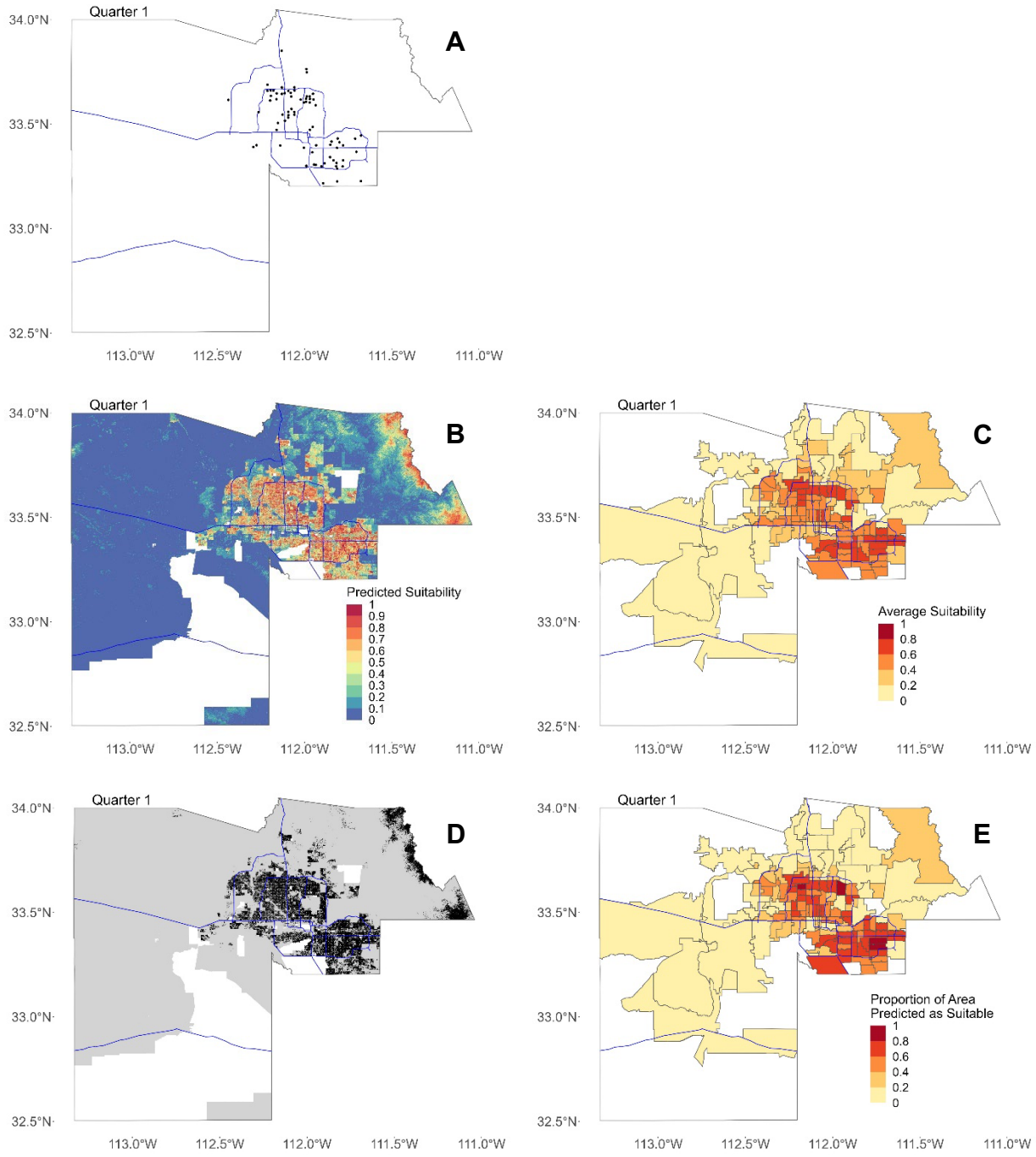
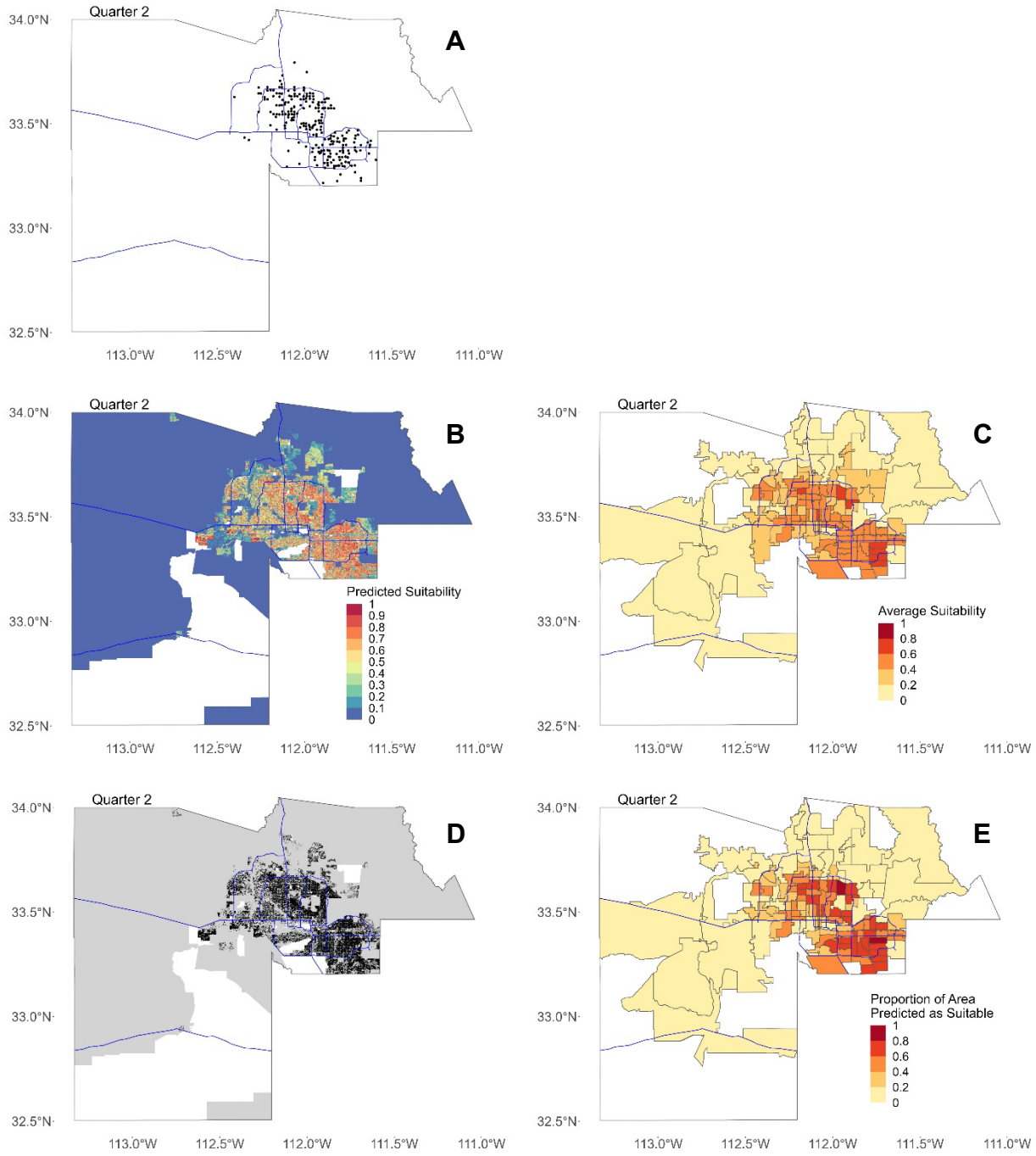
SUPPLEMENTARY DATA AND CODE FOR CHAPTER 3: SPECIES DISTRIBUTION MODELING OF *AEDES AEGYPTI* IN MARICOPA COUNTY, ARIZONA FROM 2014 TO 2020

All data and code used in this analysis is available in a public Google Drive at https://drive.google.com/drive/folders/1Hrqs-Vpv-9w64rtBBXuKq9Po51D3A3-G?usp=sharing. All descriptions of .R code, as well as an intended file structure and workflow can be found in the README folder. Data provided for each quarter are the observations of Ae. aegypti in Maricopa County. Latitude and longitude values have been truncated to the hundredths digit and jittered to address concerns of trap theft or destruction.

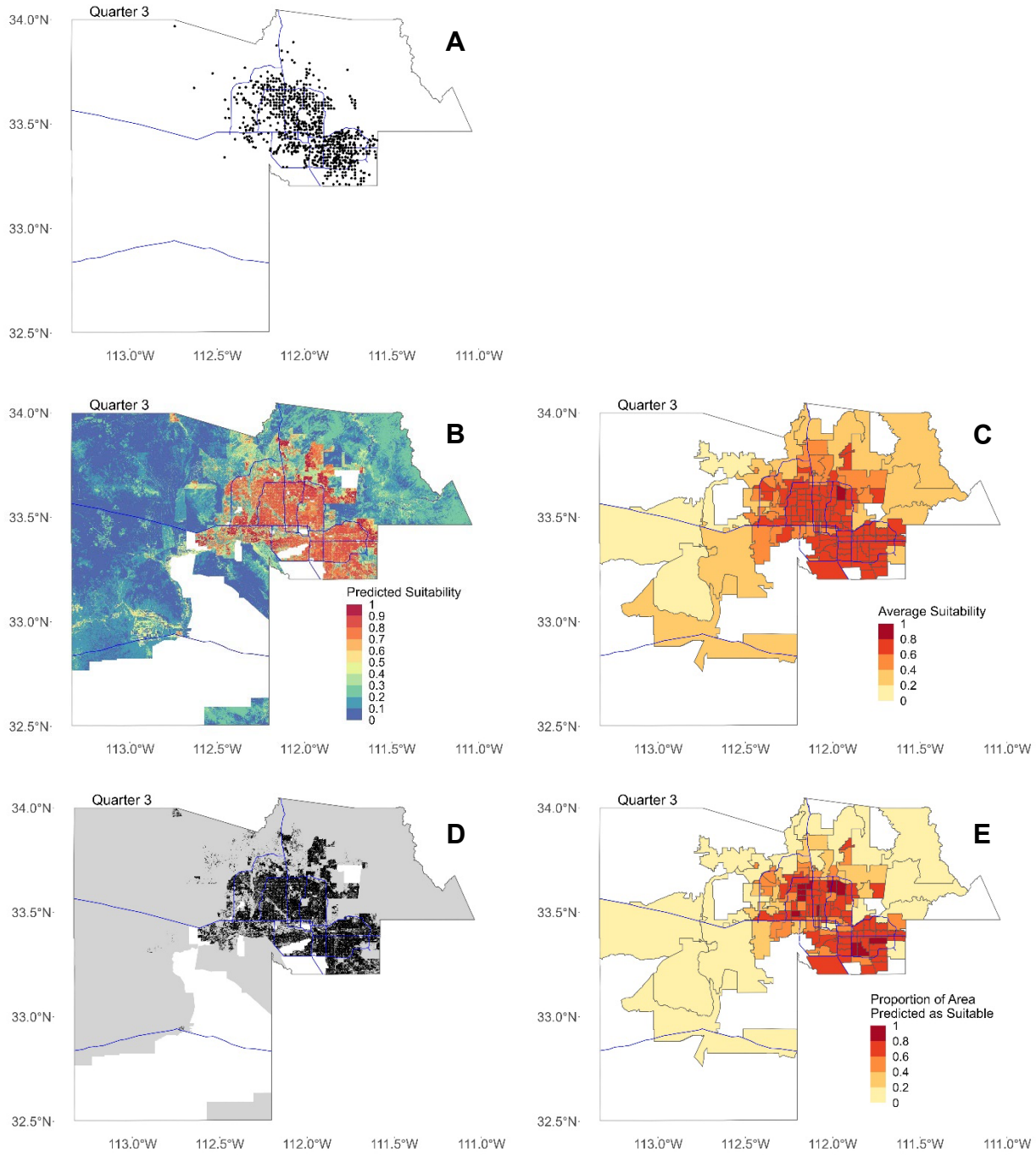
SUPPLEMENTARY FIGURES FOR CHAPTER 3: SPECIES DISTRIBUTION MODELING OF *AEDES AEGYPTI* IN MARICOPA COUNTY, ARIZONA FROM 2014 TO 2020



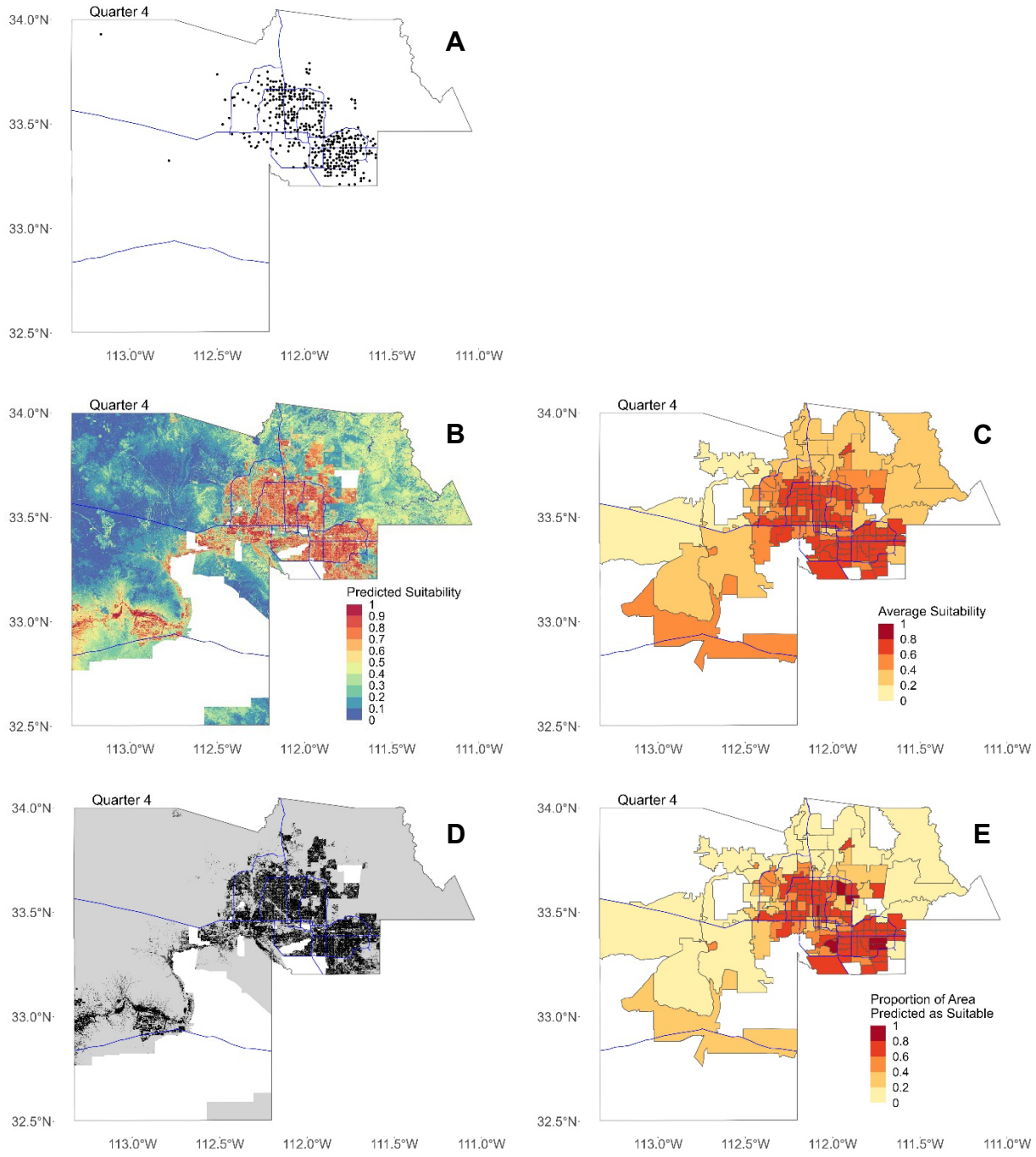
Supplementary Figure 3.1. Maps for Quarter 1 (2/1/14—4/30/14). In all figures, blue lines represent major freeways in Maricopa County. (**A**) Map of all locations where Ae. aegypti females were trapped in Maricopa County in Quarter 1. (**B**) Maxent output showing predicted suitability for 30-meter by 30-meter pixels. (**C**) Predicted suitability averaged by ZCTA. (**D**) Binary map showing areas predicted as suitable in black and not suitable in gray. In (B) and (C), areas with missing data where suitability was not predicted are shown in white. (**E**) Proportion of area in each ZCTA predicted as suitable after converting to binary map.



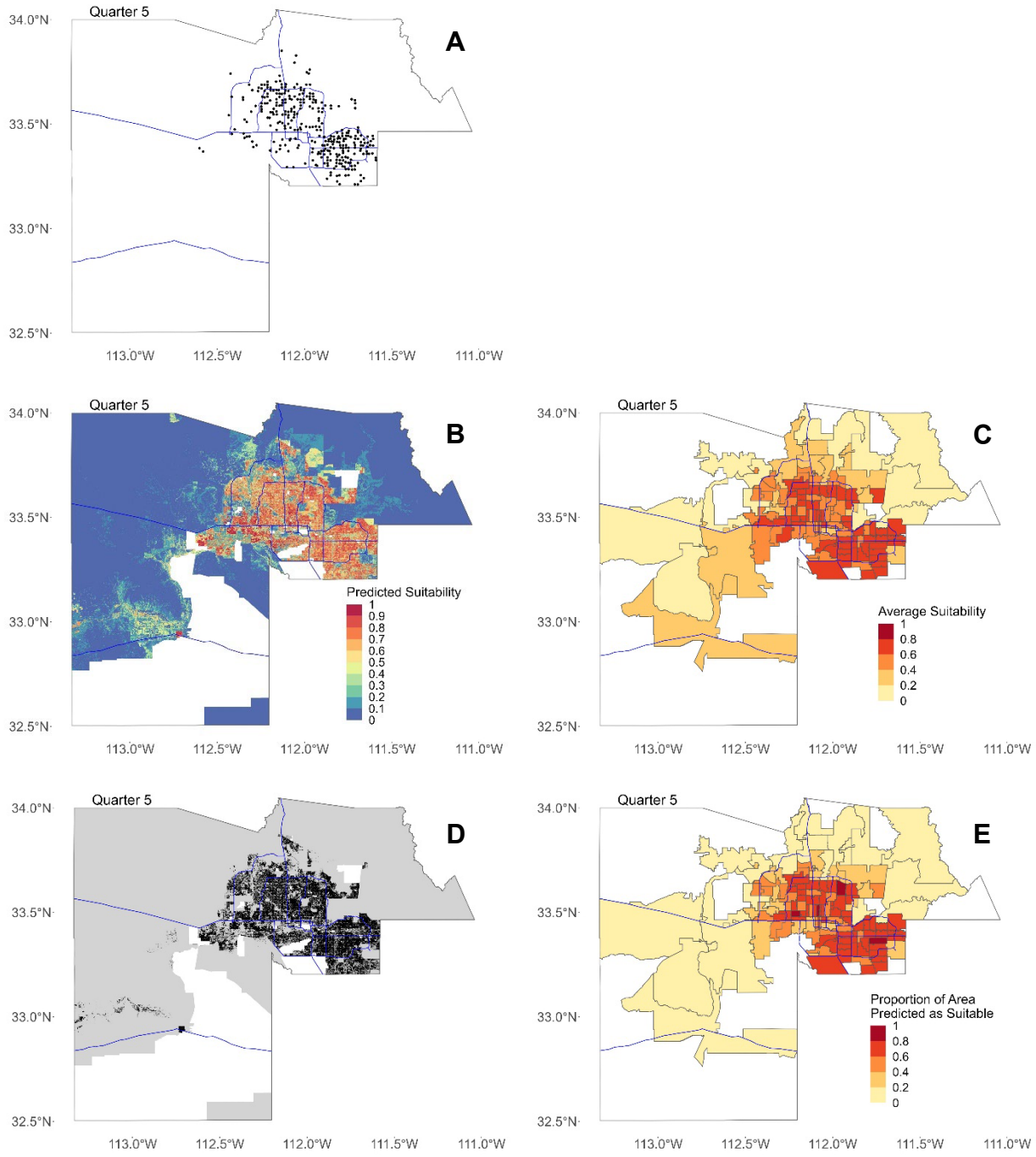
Supplementary Figure 3.2. Maps for Quarter 2 (5/1/14—7/31/14). In all figures, blue lines represent major freeways in Maricopa County. (**A**) Map of all locations where Ae. aegypti females were trapped in Maricopa County in Quarter 2. (**B**) Maxent output showing predicted suitability for 30-meter by 30-meter pixels. (**C**) Predicted suitability averaged by ZCTA. (**D**) Binary map showing areas predicted as suitable in black and not suitable in gray. In (B) and (C), areas with missing data where suitability was not predicted are shown in white. (**E**) Proportion of area in each ZCTA predicted as suitable after converting to binary map.



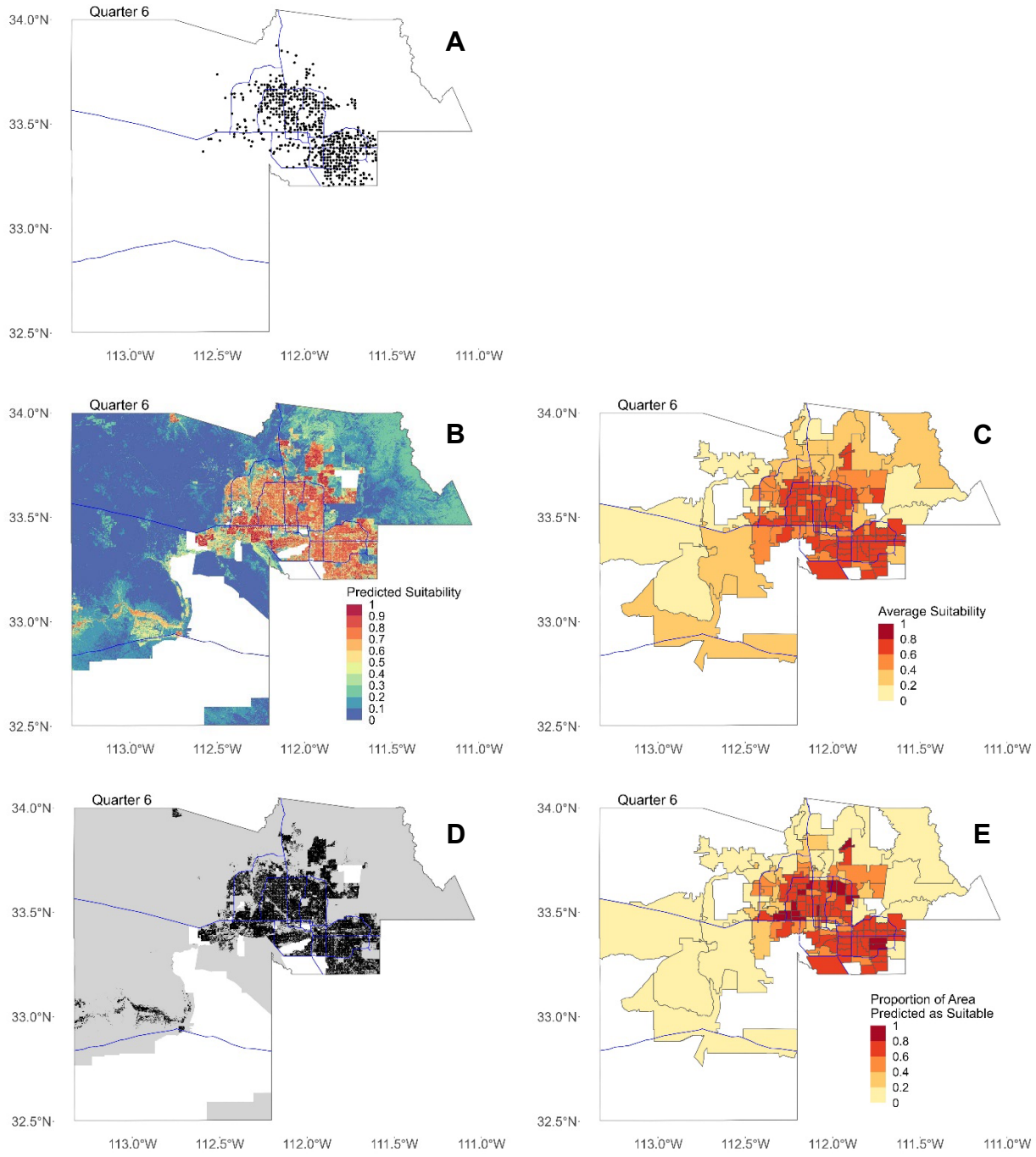
Supplementary Figure 3.3. Maps for Quarter 3 (8/1/14—10/31/14). In all figures, blue lines represent major freeways in Maricopa County. (**A**) Map of all locations where Ae. aegypti females were trapped in Maricopa County in Quarter 3. (**B**) Maxent output showing predicted suitability for 30-meter by 30-meter pixels. (**C**) Predicted suitability averaged by ZCTA. (**D**) Binary map showing areas predicted as suitable in black and not suitable in gray. In (B) and (C), areas with missing data where suitability was not predicted are shown in white. (**E**) Proportion of area in each ZCTA predicted as suitable after converting to binary map.



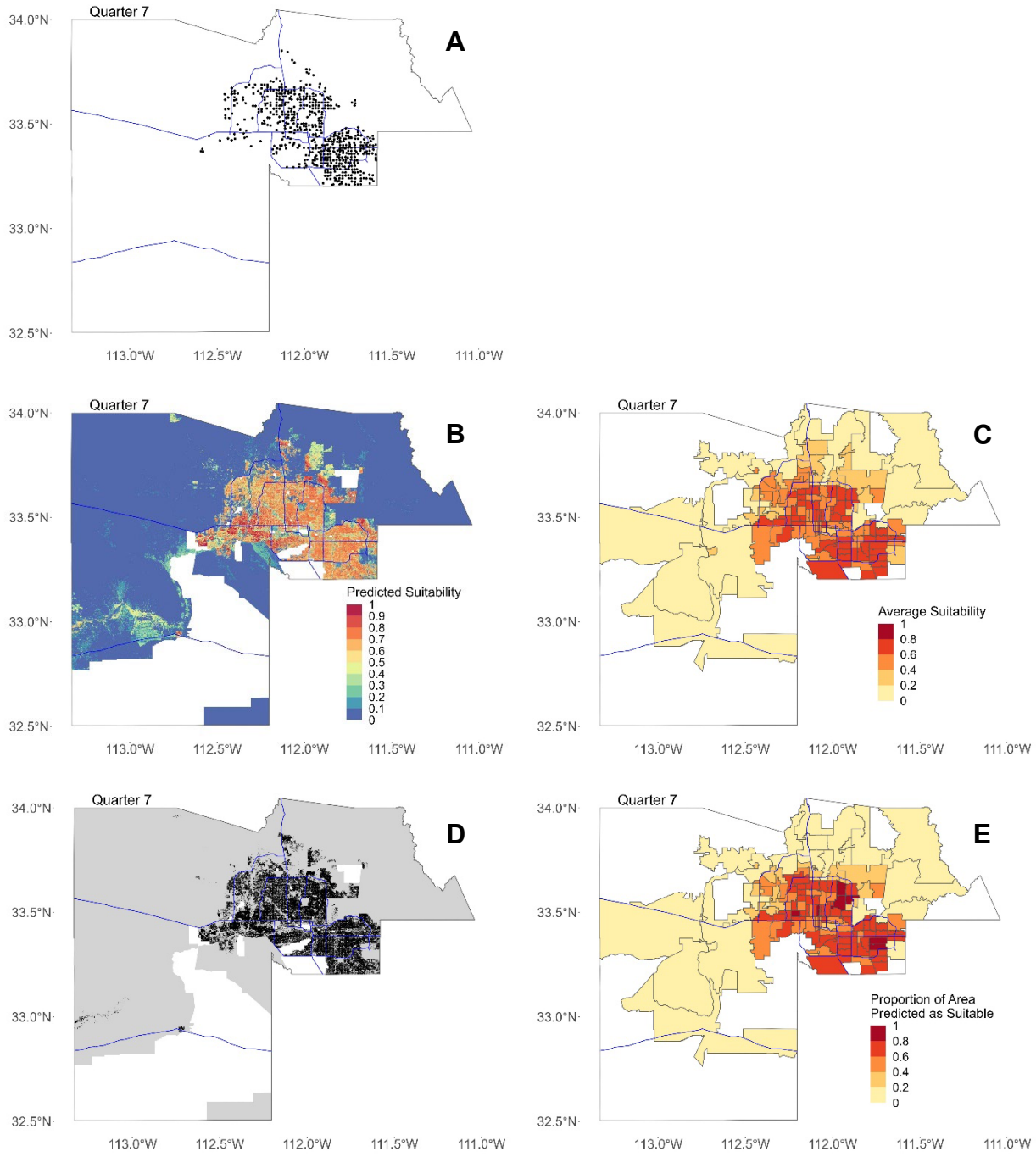
Supplementary Figure 3.4. Maps for Quarter 4 (11/1/14—1/31/15). In all figures, blue lines represent major freeways in Maricopa County. (**A**) Map of all locations where Ae. aegypti females were trapped in Maricopa County in Quarter 4. (**B**) Maxent output showing predicted suitability for 30-meter by 30-meter pixels. (**C**) Predicted suitability averaged by ZCTA. (**D**) Binary map showing areas predicted as suitable in black and not suitable in gray. In (B) and (C), areas with missing data where suitability was not predicted are shown in white. (**E**) Proportion of area in each ZCTA predicted as suitable after converting to binary map.



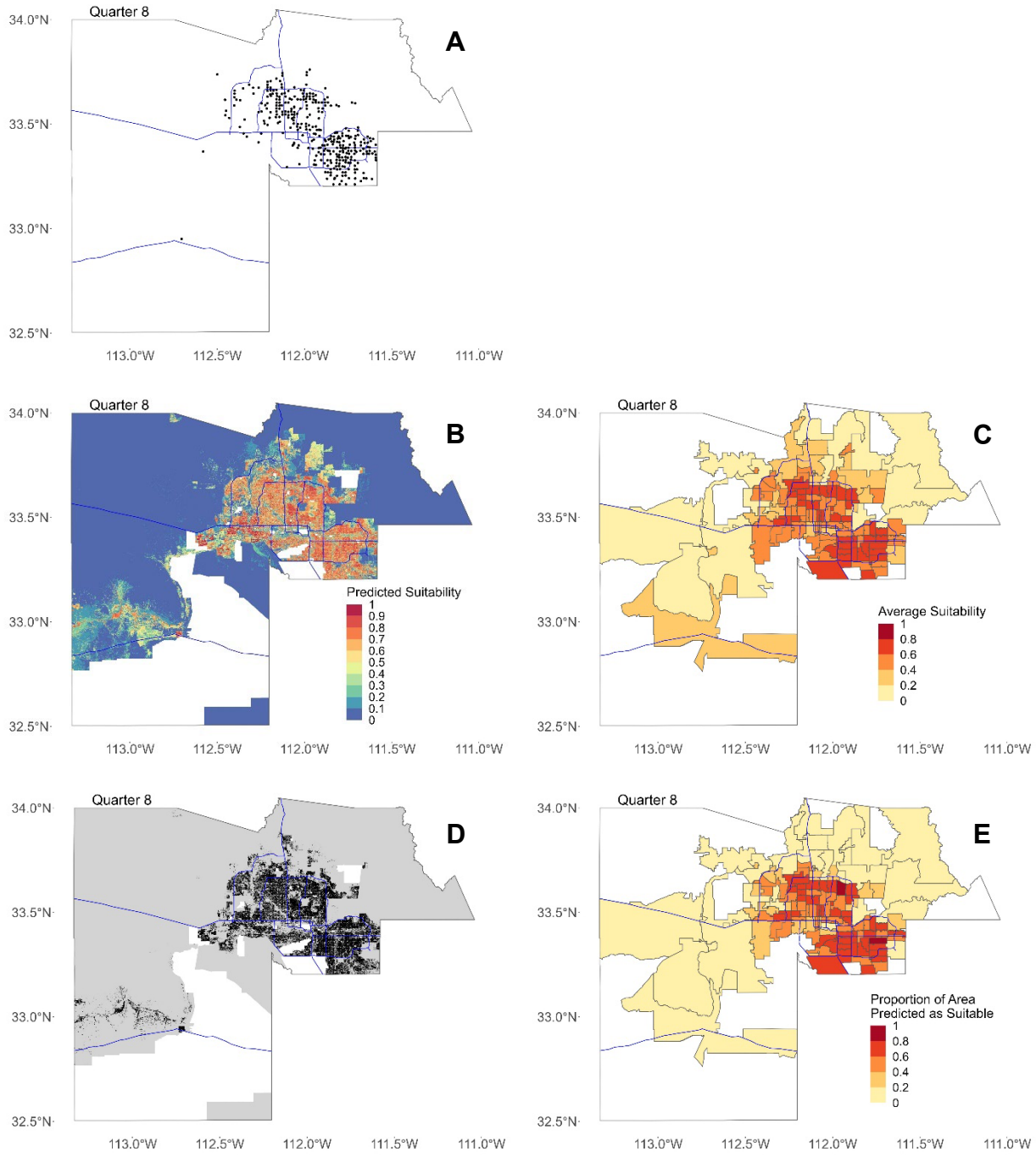
Supplementary Figure 3.5. Maps for Quarter 5 (2/1/15—4/30/15). In all figures, blue lines represent major freeways in Maricopa County. (**A**) Map of all locations where Ae. aegypti females were trapped in Maricopa County in Quarter 5. (**B**) Maxent output showing predicted suitability for 30-meter by 30-meter pixels. (**C**) Predicted suitability averaged by ZCTA. (**D**) Binary map showing areas predicted as suitable in black and not suitable in gray. In (B) and (C), areas with missing data where suitability was not predicted are shown in white. (**E**) Proportion of area in each ZCTA predicted as suitable after converting to binary map.



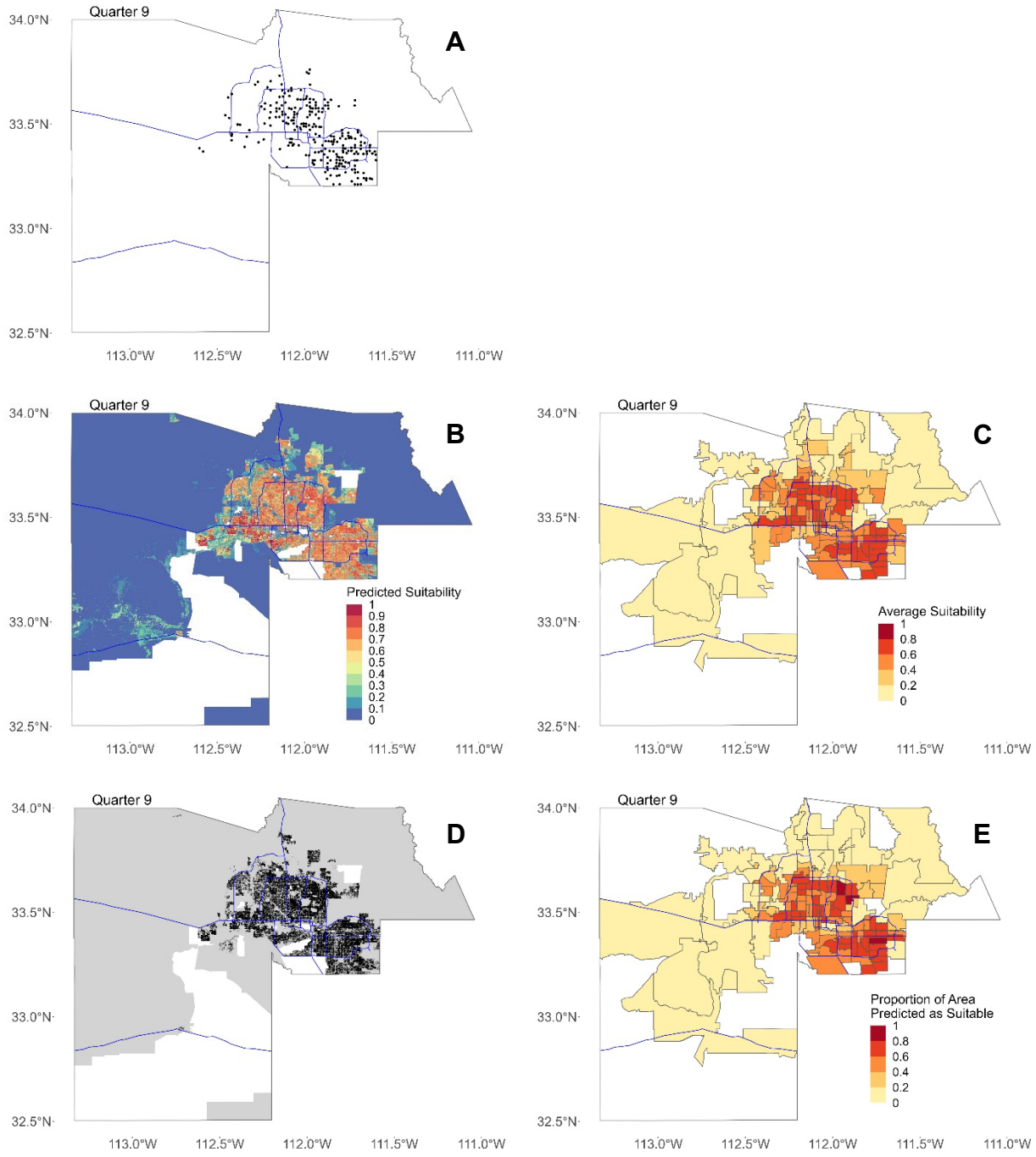
Supplementary Figure 3.6. Maps for Quarter 6 (5/1/15—7/31/15). In all figures, blue lines represent major freeways in Maricopa County. (**A**) Map of all locations where Ae. aegypti females were trapped in Maricopa County in Quarter 6. (**B**) Maxent output showing predicted suitability for 30-meter by 30-meter pixels. (**C**) Predicted suitability averaged by ZCTA. (**D**) Binary map showing areas predicted as suitable in black and not suitable in gray. In (B) and (C), areas with missing data where suitability was not predicted are shown in white. (**E**) Proportion of area in each ZCTA predicted as suitable after converting to binary map.



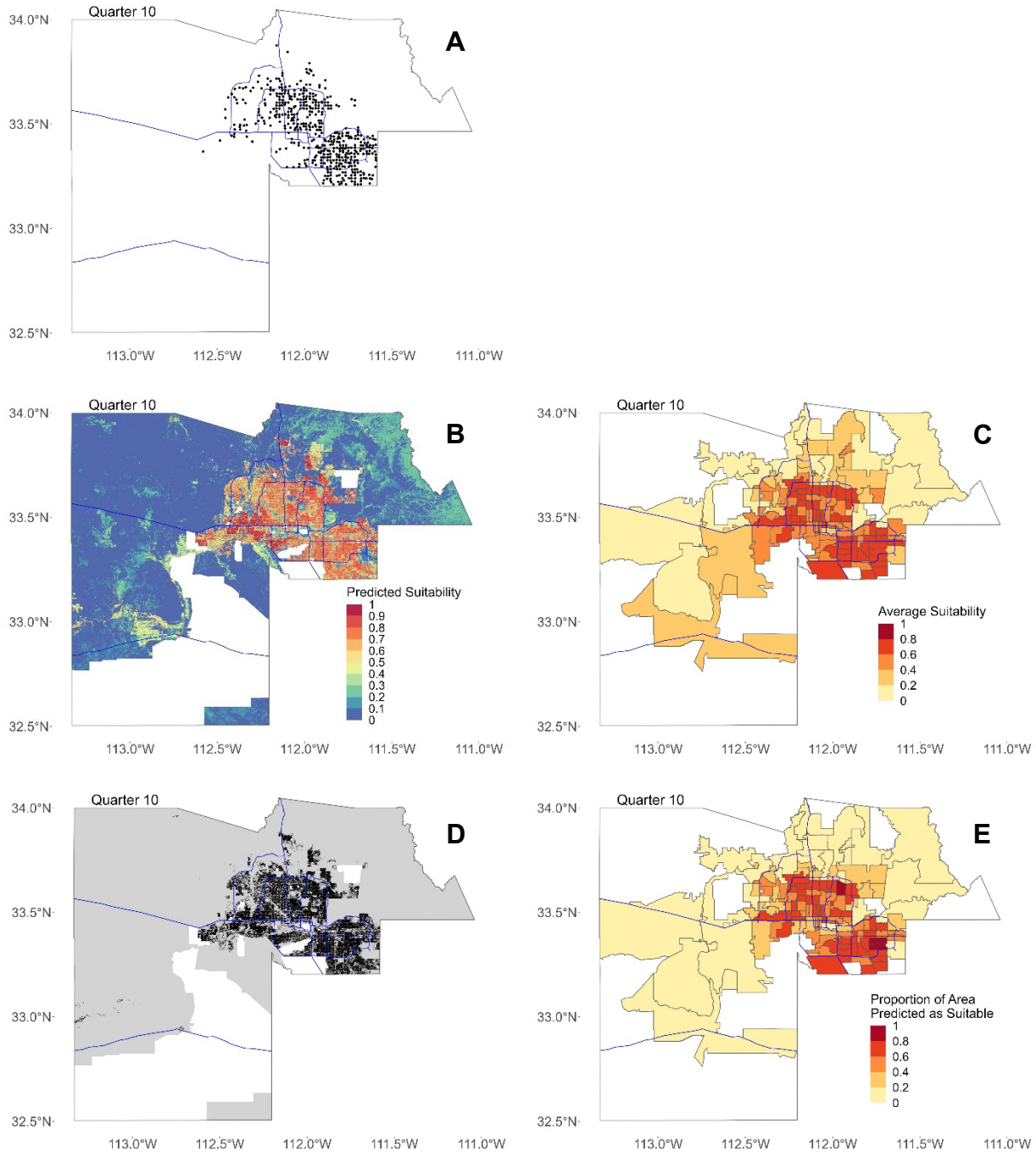
Supplementary Figure 3.7. Maps for Quarter 7 (8/1/15—10/31/15). In all figures, blue lines represent major freeways in Maricopa County. (**A**) Map of all locations where Ae. aegypti females were trapped in Maricopa County in Quarter 7. (**B**) Maxent output showing predicted suitability for 30-meter by 30-meter pixels. (**C**) Predicted suitability averaged by ZCTA. (**D**) Binary map showing areas predicted as suitable in black and not suitable in gray. In (B) and (C), areas with missing data where suitability was not predicted are shown in white. (**E**) Proportion of area in each ZCTA predicted as suitable after converting to binary map.



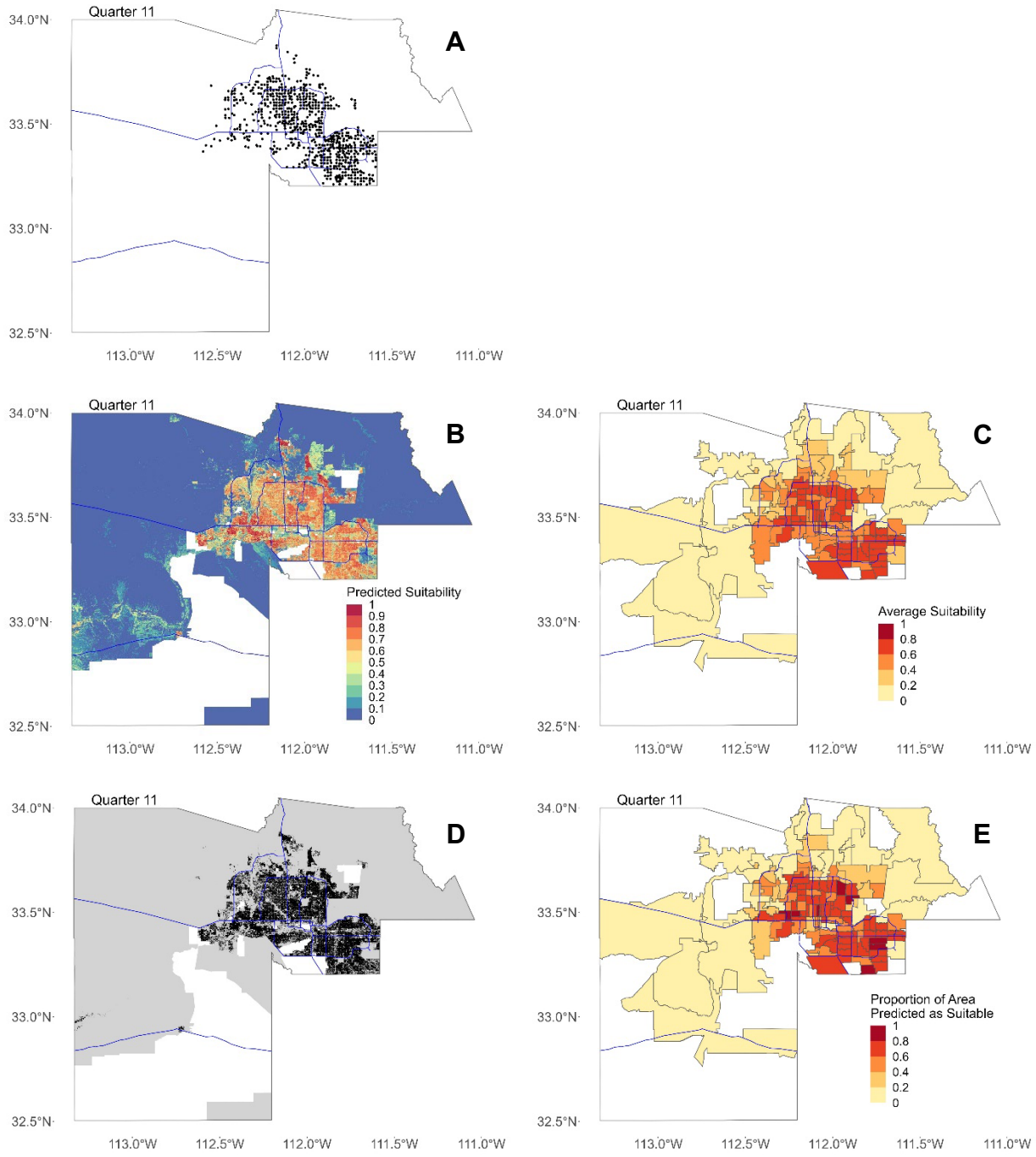
Supplementary Figure 3.8. Maps for Quarter 8 (11/1/15—1/31/16). In all figures, blue lines represent major freeways in Maricopa County. (**A**) Map of all locations where Ae. aegypti females were trapped in Maricopa County in Quarter 8. (**B**) Maxent output showing predicted suitability for 30-meter by 30-meter pixels. (**C**) Predicted suitability averaged by ZCTA. (**D**) Binary map showing areas predicted as suitable in black and not suitable in gray. In (B) and (C), areas with missing data where suitability was not predicted are shown in white. (**E**) Proportion of area in each ZCTA predicted as suitable after converting to binary map.



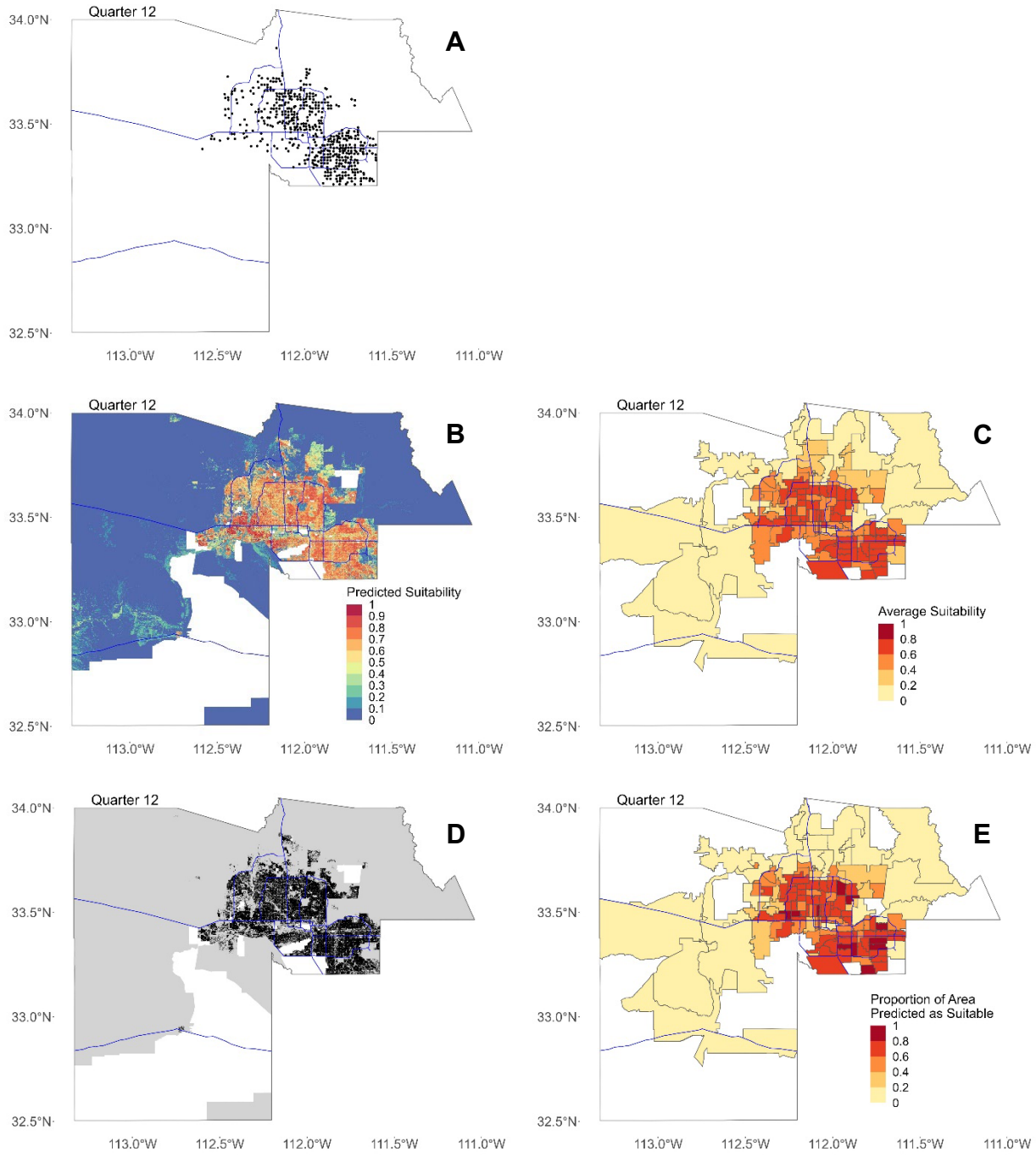
Supplementary Figure 3.9. Maps for Quarter 9 (2/1/16—4/30/16). In all figures, blue lines represent major freeways in Maricopa County. (**A**) Map of all locations where Ae. aegypti females were trapped in Maricopa County in Quarter 9. (**B**) Maxent output showing predicted suitability for 30-meter by 30-meter pixels. (**C**) Predicted suitability averaged by ZCTA. (**D**) Binary map showing areas predicted as suitable in black and not suitable in gray. In (B) and (C), areas with missing data where suitability was not predicted are shown in white. (**E**) Proportion of area in each ZCTA predicted as suitable after converting to binary map.



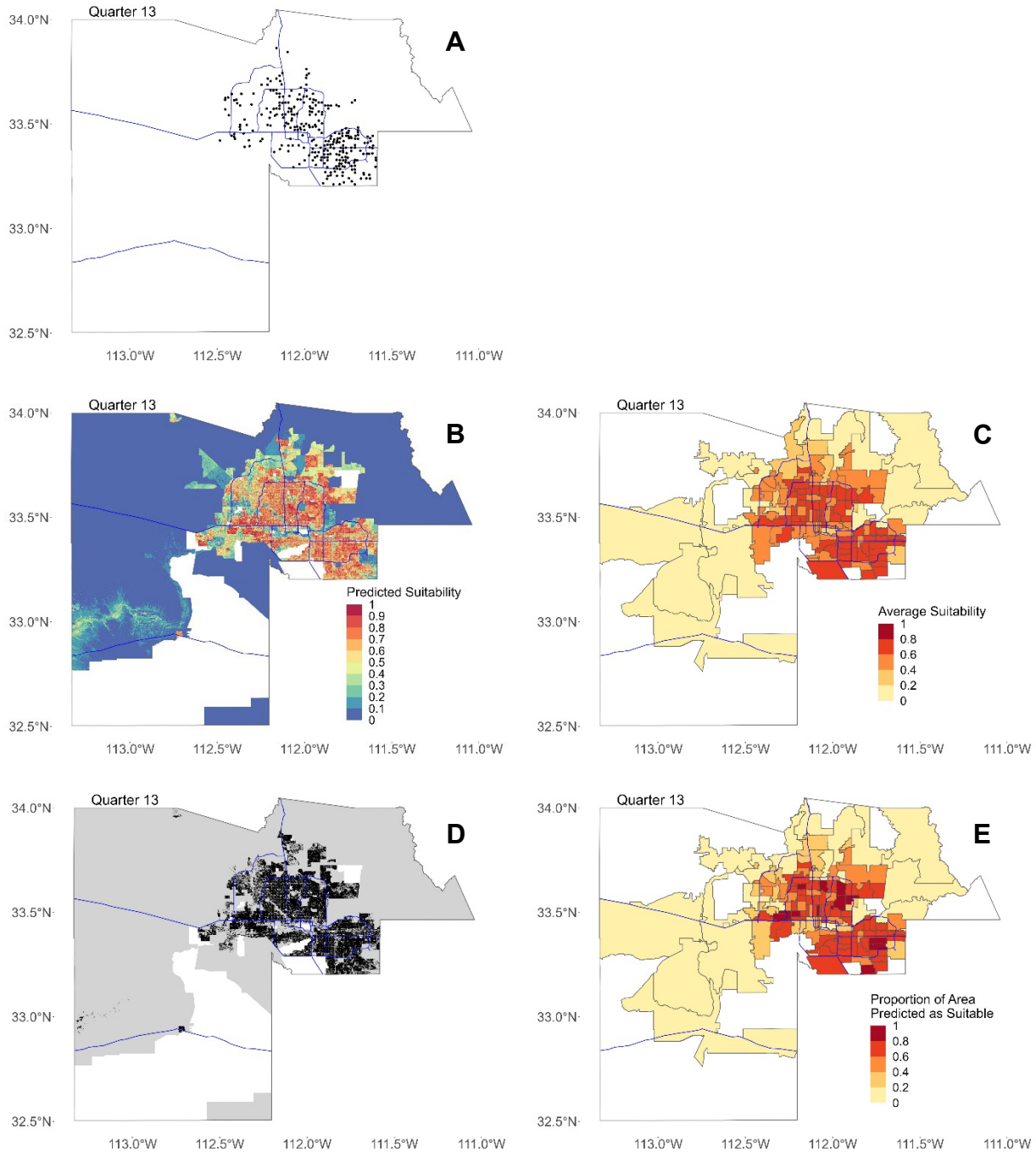
Supplementary Figure 3.10. Maps for Quarter 10 (5/1/16—7/31/16). In all figures, blue lines represent major freeways in Maricopa County. (**A**) Map of all locations where Ae. aegypti females were trapped in Maricopa County in Quarter 10. (**B**) Maxent output showing predicted suitability for 30-meter by 30-meter pixels. (**C**) Predicted suitability averaged by ZCTA. (**D**) Binary map showing areas predicted as suitable in black and not suitable in gray. In (B) and (C), areas with missing data where suitability was not predicted are shown in white. (**E**) Proportion of area in each ZCTA predicted as suitable after converting to binary map.



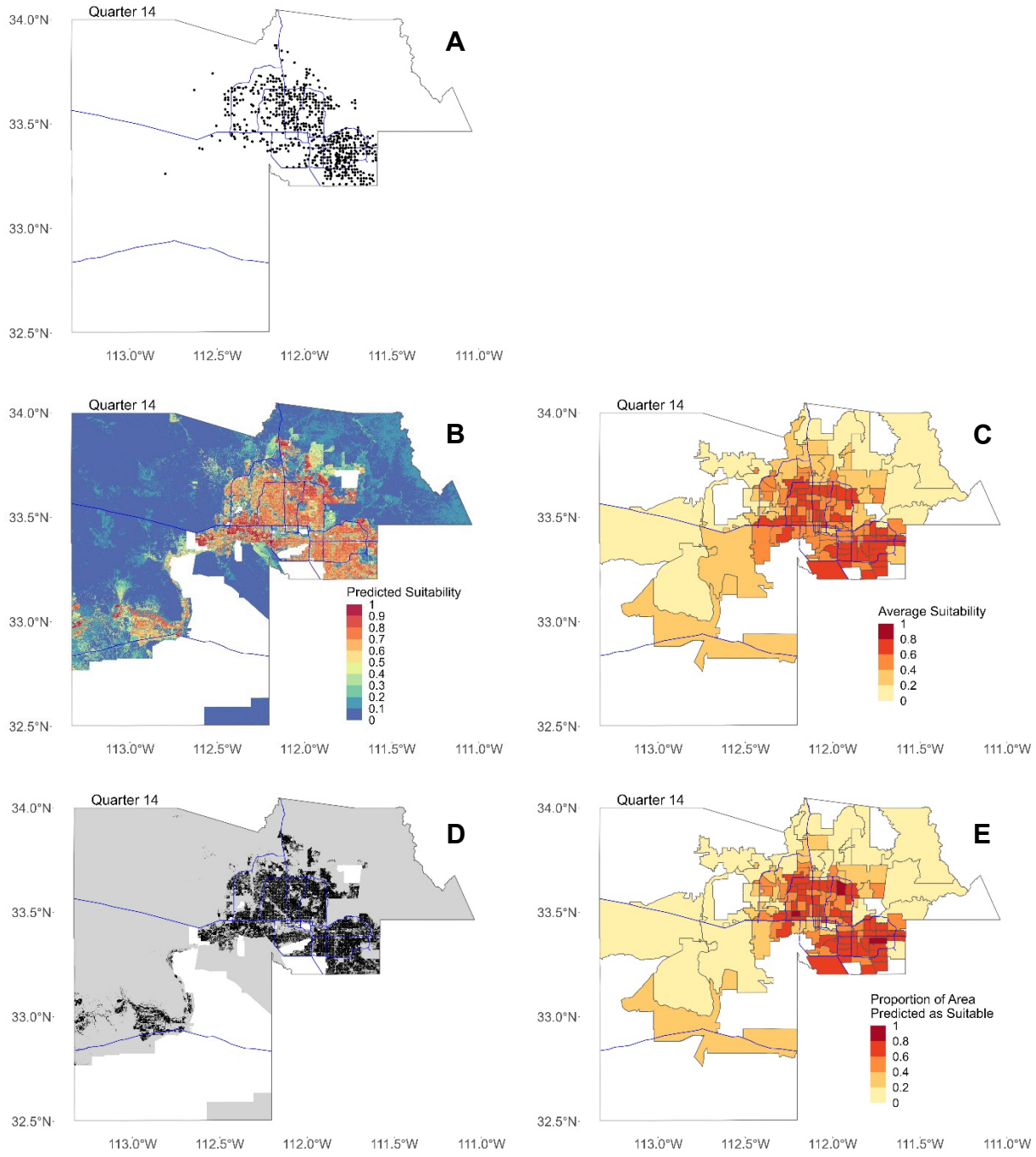
Supplementary Figure 3.11. Maps for Quarter 11 (8/1/16—10/31/16). In all figures, blue lines represent major freeways in Maricopa County. (**A**) Map of all locations where Ae. aegypti females were trapped in Maricopa County in Quarter 11. (**B**) Maxent output showing predicted suitability for 30-meter by 30-meter pixels. (**C**) Predicted suitability averaged by ZCTA. (**D**) Binary map showing areas predicted as suitable in black and not suitable in gray. In (B) and (C), areas with missing data where suitability was not predicted are shown in white. (**E**) Proportion of area in each ZCTA predicted as suitable after converting to binary map.



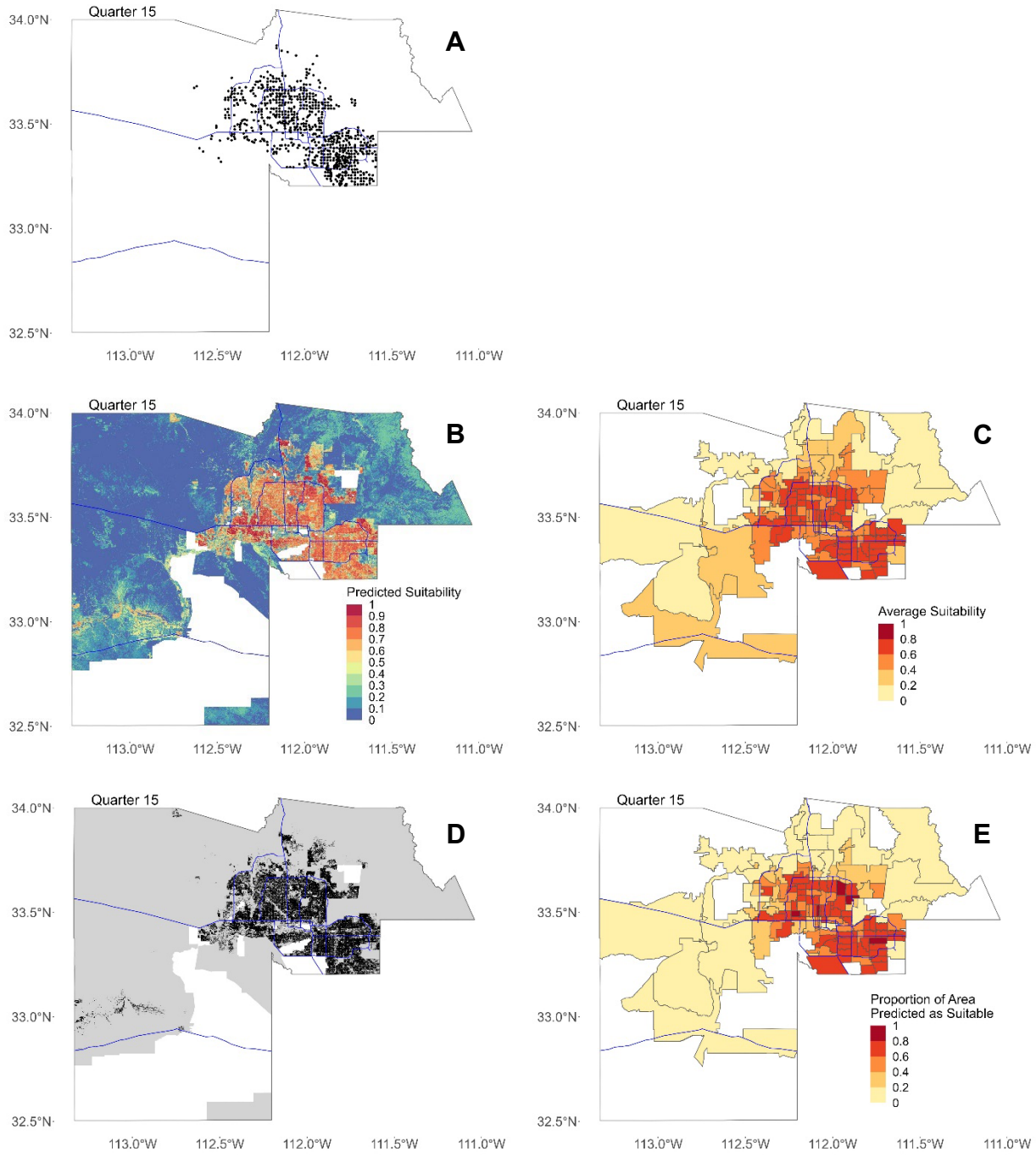
Supplementary Figure 3.12. Maps for Quarter 12 (11/1/16—1/31/17). In all figures, blue lines represent major freeways in Maricopa County. (**A**) Map of all locations where Ae. aegypti females were trapped in Maricopa County in Quarter 12. (**B**) Maxent output showing predicted suitability for 30-meter by 30-meter pixels. (**C**) Predicted suitability averaged by ZCTA. (**D**) Binary map showing areas predicted as suitable in black and not suitable in gray. In (B) and (C), areas with missing data where suitability was not predicted are shown in white. (**E**) Proportion of area in each ZCTA predicted as suitable after converting to binary map.



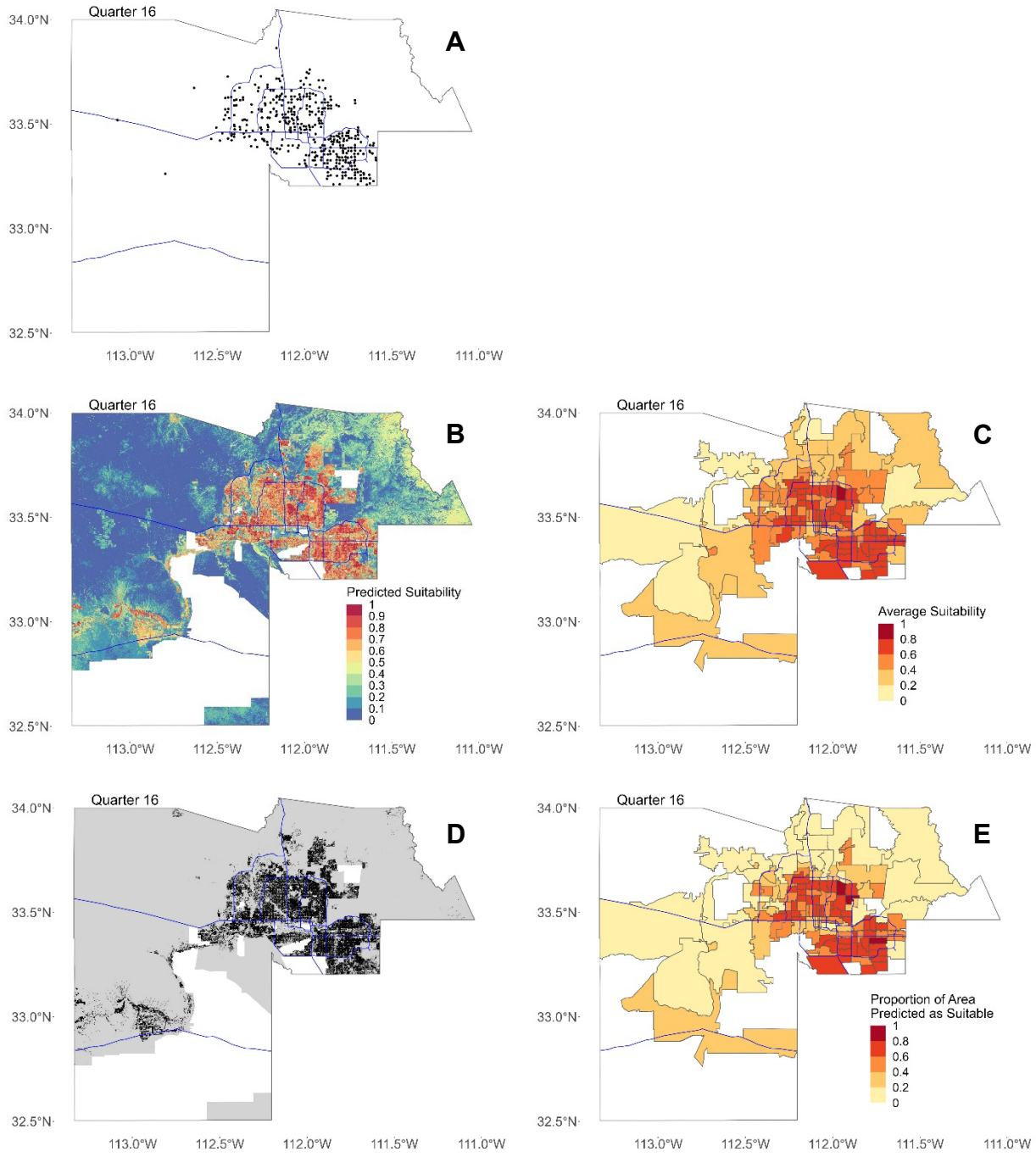
Supplementary Figure 3.13. Maps for Quarter 13 (2/1/17—4/30/17). In all figures, blue lines represent major freeways in Maricopa County. (**A**) Map of all locations where Ae. aegypti females were trapped in Maricopa County in Quarter 13. (**B**) Maxent output showing predicted suitability for 30-meter by 30-meter pixels. (**C**) Predicted suitability averaged by ZCTA. (**D**) Binary map showing areas predicted as suitable in black and not suitable in gray. In (B) and (C), areas with missing data where suitability was not predicted are shown in white. (**E**) Proportion of area in each ZCTA predicted as suitable after converting to binary map.



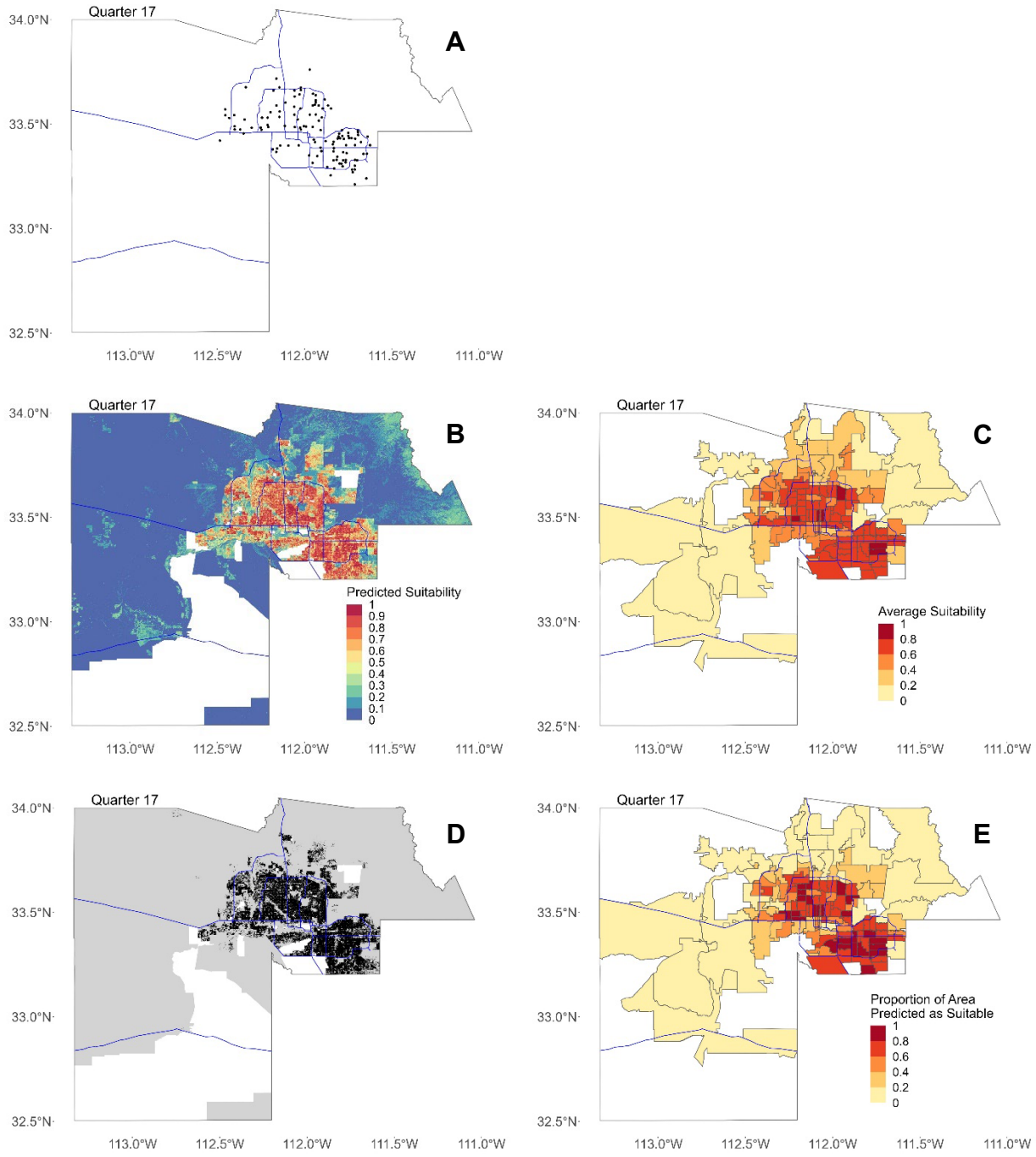
Supplementary Figure 3.14. Maps for Quarter 14 (5/1/17—7/31/17). In all figures, blue lines represent major freeways in Maricopa County. (**A**) Map of all locations where Ae. aegypti females were trapped in Maricopa County in Quarter 14. (**B**) Maxent output showing predicted suitability for 30-meter by 30-meter pixels. (**C**) Predicted suitability averaged by ZCTA. (**D**) Binary map showing areas predicted as suitable in black and not suitable in gray. In (B) and (C), areas with missing data where suitability was not predicted are shown in white. (**E**) Proportion of area in each ZCTA predicted as suitable after converting to binary map.



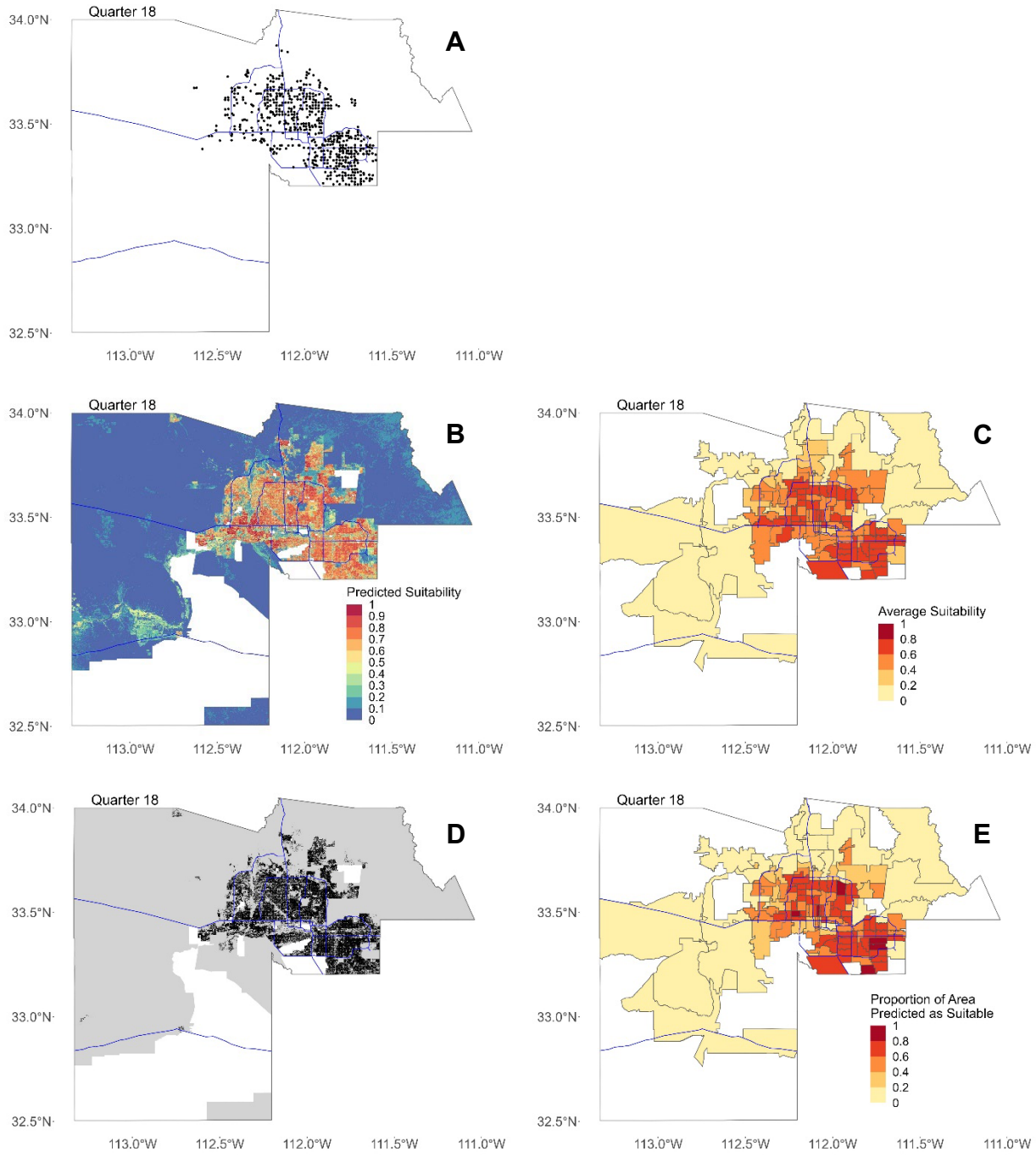
Supplementary Figure 3.15. Maps for Quarter 15 (8/1/17—10/31/17). In all figures, blue lines represent major freeways in Maricopa County. (**A**) Map of all locations where Ae. aegypti females were trapped in Maricopa County in Quarter 15. (**B**) Maxent output showing predicted suitability for 30-meter by 30-meter pixels. (**C**) Predicted suitability averaged by ZCTA. (**D**) Binary map showing areas predicted as suitable in black and not suitable in gray. In (B) and (C), areas with missing data where suitability was not predicted are shown in white. (**E**) Proportion of area in each ZCTA predicted as suitable after converting to binary map.



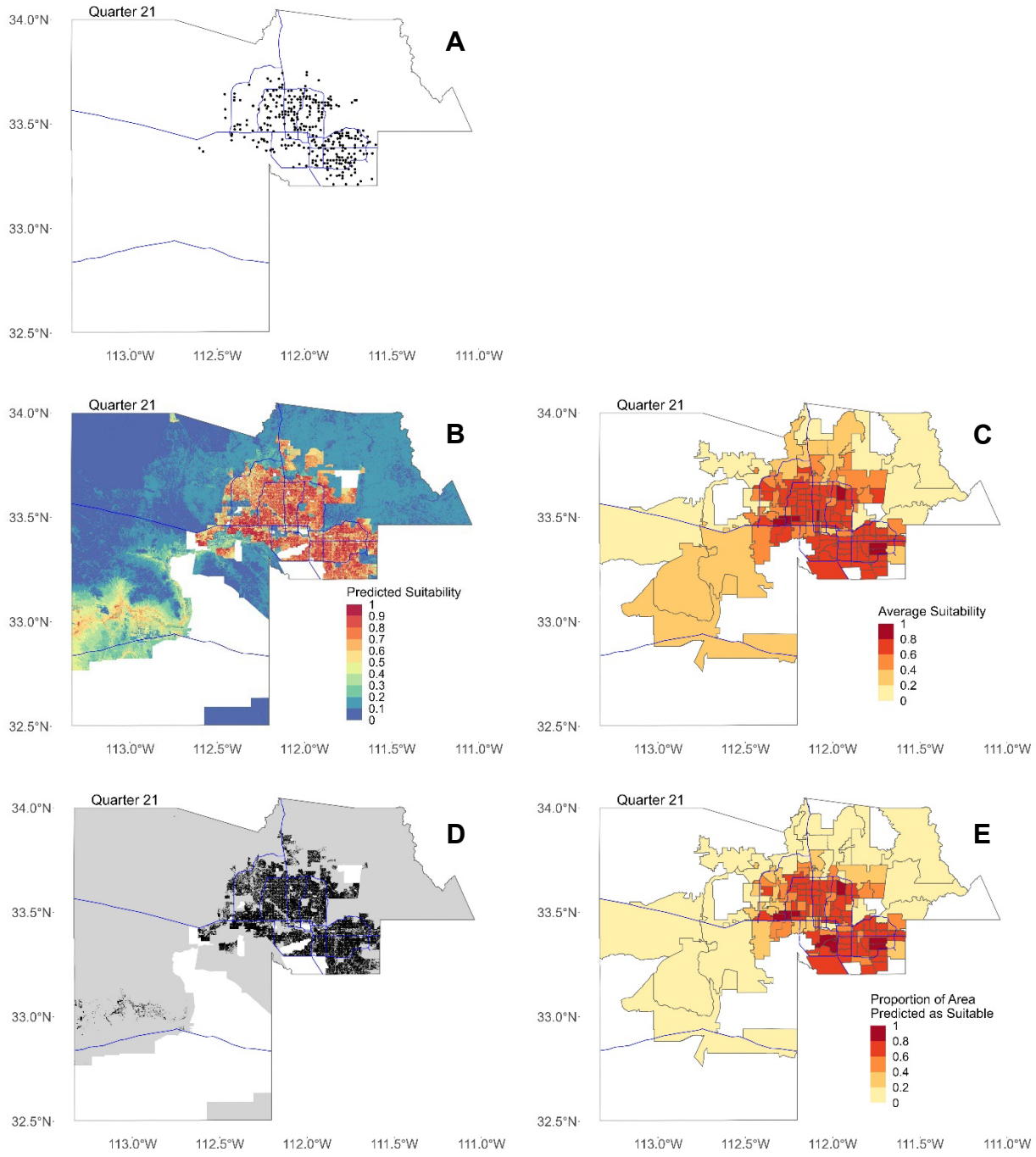
Supplementary Figure 3.16. Maps for Quarter 16 (11/1/17—1/31/18). In all figures, blue lines represent major freeways in Maricopa County. (**A**) Map of all locations where Ae. aegypti females were trapped in Maricopa County in Quarter 16. (**B**) Maxent output showing predicted suitability for 30-meter by 30-meter pixels. (**C**) Predicted suitability averaged by ZCTA. (**D**) Binary map showing areas predicted as suitable in black and not suitable in gray. In (B) and (C), areas with missing data where suitability was not predicted are shown in white. (**E**) Proportion of area in each ZCTA predicted as suitable after converting to binary map.



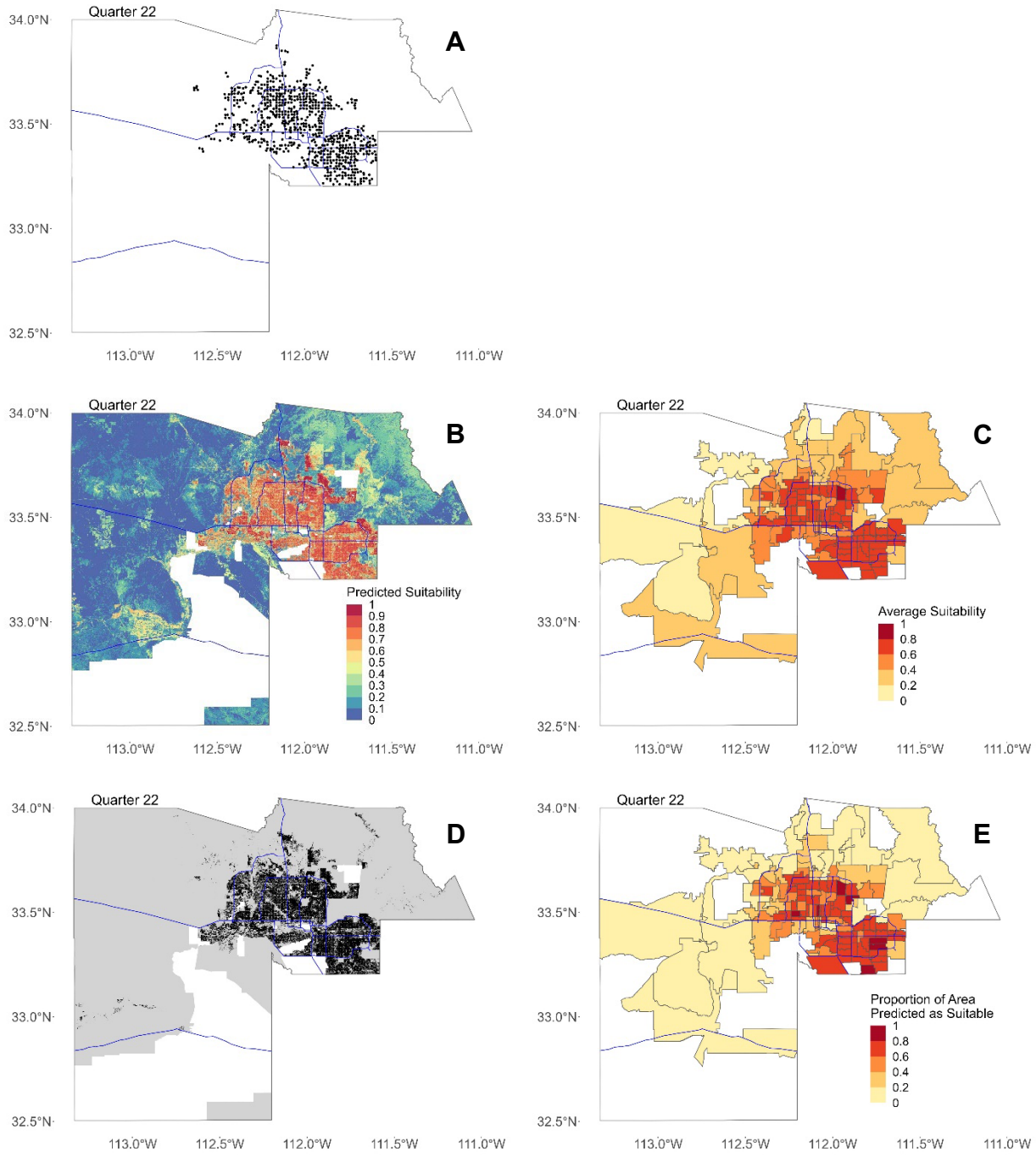
Supplementary Figure 3.17. Maps for Quarter 17 (2/1/18—4/30/18). In all figures, blue lines represent major freeways in Maricopa County. (**A**) Map of all locations where Ae. aegypti females were trapped in Maricopa County in Quarter 17. (**B**) Maxent output showing predicted suitability for 30-meter by 30-meter pixels. (**C**) Predicted suitability averaged by ZCTA. (**D**) Binary map showing areas predicted as suitable in black and not suitable in gray. In (B) and (C), areas with missing data where suitability was not predicted are shown in white. (**E**) Proportion of area in each ZCTA predicted as suitable after converting to binary map.



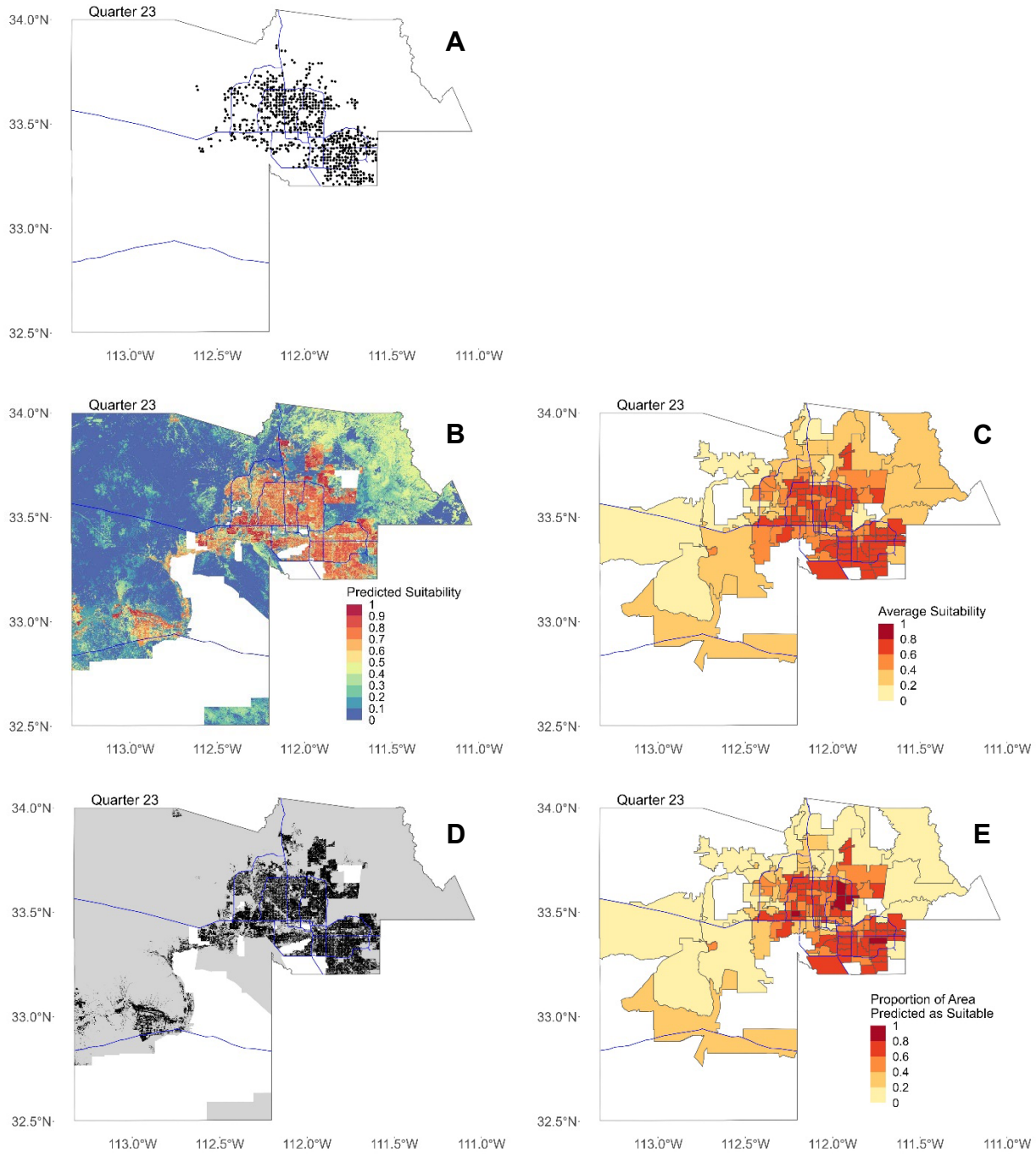
Supplementary Figure 3.18. Maps for Quarter 18 (5/1/18—7/31/18). In all figures, blue lines represent major freeways in Maricopa County. (**A**) Map of all locations where Ae. aegypti females were trapped in Maricopa County in Quarter 18. (**B**) Maxent output showing predicted suitability for 30-meter by 30-meter pixels. (**C**) Predicted suitability averaged by ZCTA. (**D**) Binary map showing areas predicted as suitable in black and not suitable in gray. In (B) and (C), areas with missing data where suitability was not predicted are shown in white. (**E**) Proportion of area in each ZCTA predicted as suitable after converting to binary map.



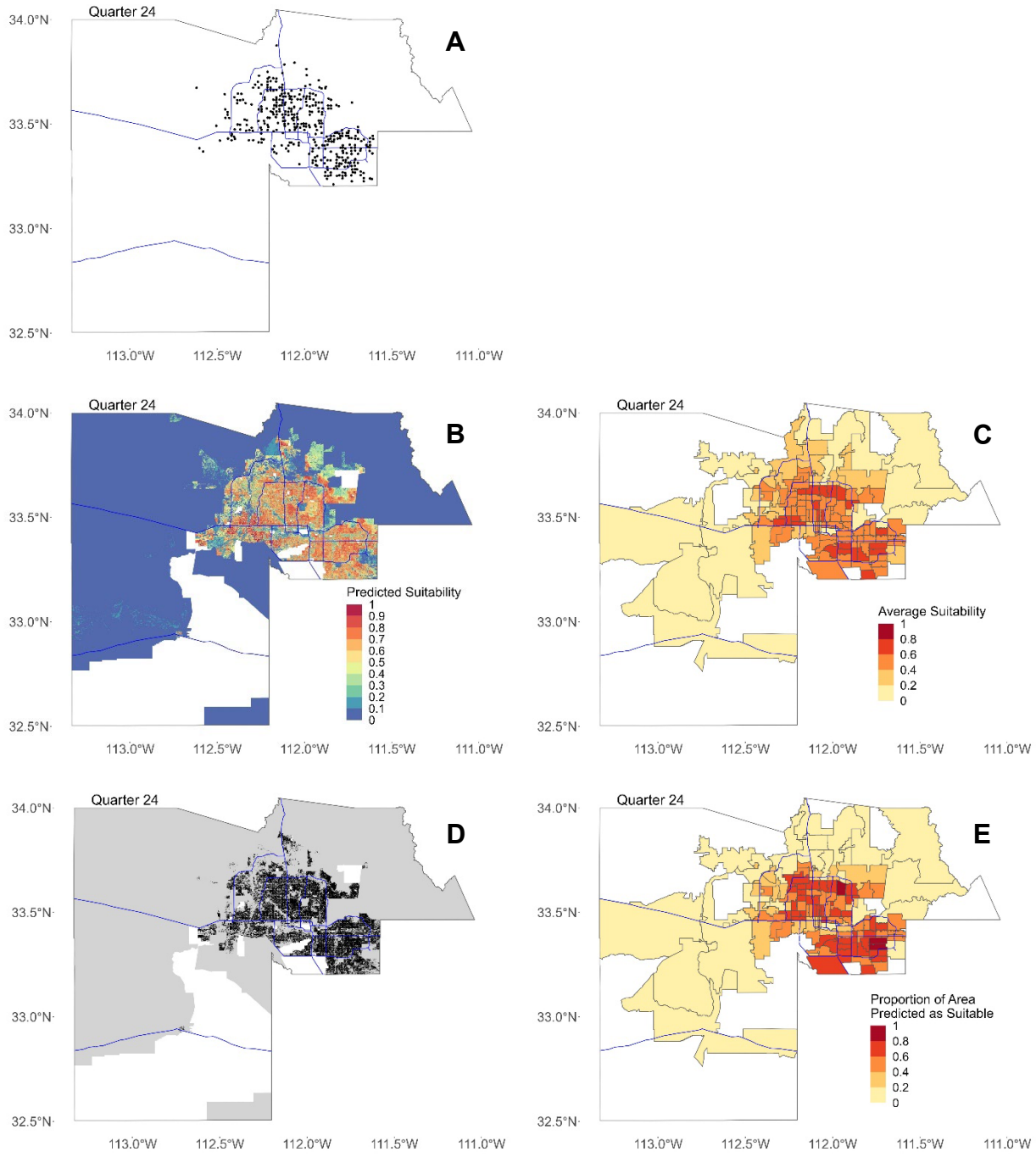
Supplementary Figure 3.19. Maps for Quarter 21 (2/1/19—4/30/19). In all figures, blue lines represent major freeways in Maricopa County. (**A**) Map of all locations where Ae. aegypti females were trapped in Maricopa County in Quarter 21. (**B**) Maxent output showing predicted suitability for 30-meter by 30-meter pixels. (**C**) Predicted suitability averaged by ZCTA. (**D**) Binary map showing areas predicted as suitable in black and not suitable in gray. In (B) and (C), areas with missing data where suitability was not predicted are shown in white. (**E**) Proportion of area in each ZCTA predicted as suitable after converting to binary map.



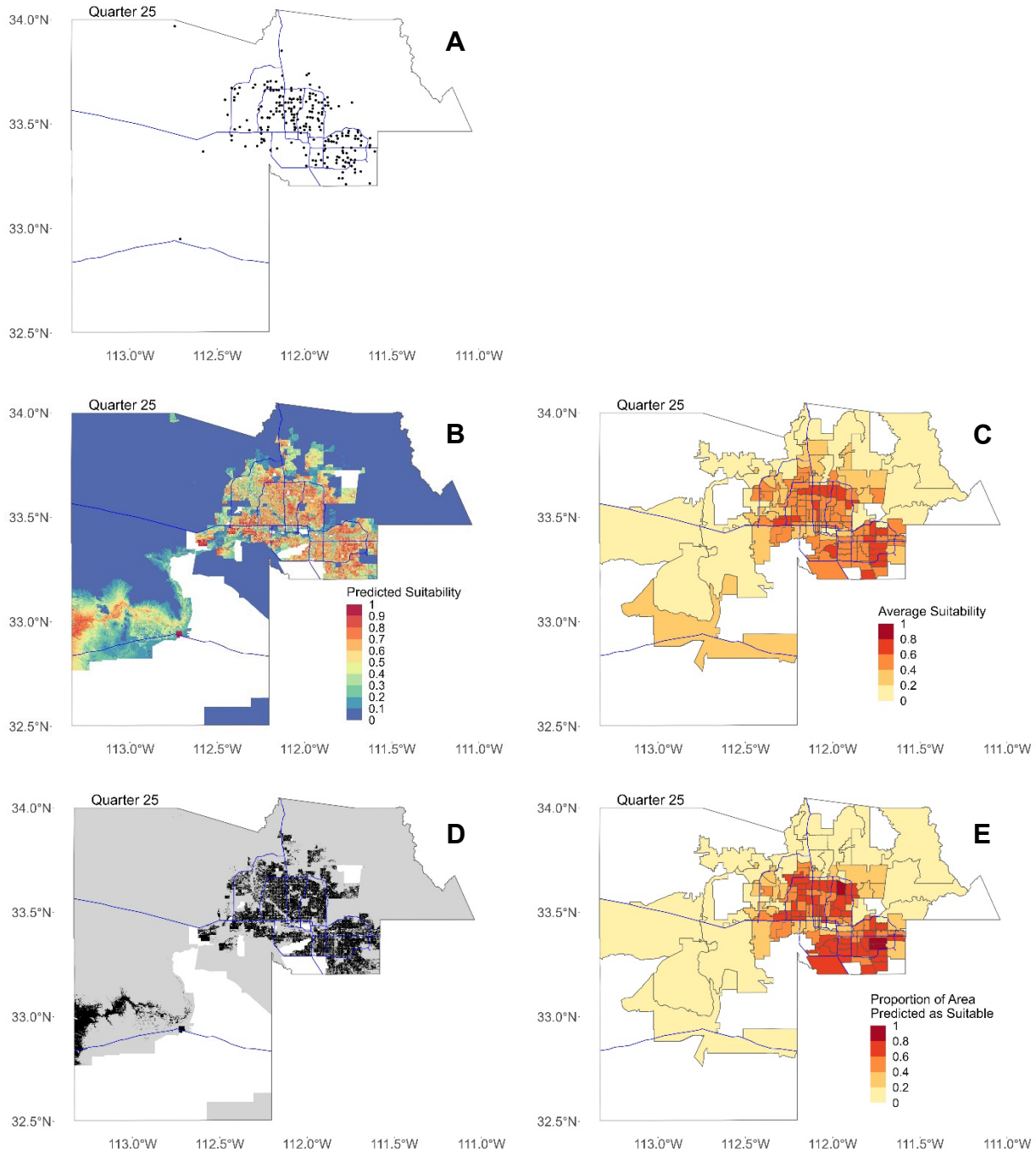
Supplementary Figure 3.20. Maps for Quarter 22 (5/1/19—7/31/19). In all figures, blue lines represent major freeways in Maricopa County. (**A**) Map of all locations where Ae. aegypti females were trapped in Maricopa County in Quarter 22. (**B**) Maxent output showing predicted suitability for 30-meter by 30-meter pixels. (**C**) Predicted suitability averaged by ZCTA. (**D**) Binary map showing areas predicted as suitable in black and not suitable in gray. In (B) and (C), areas with missing data where suitability was not predicted are shown in white. (**E**) Proportion of area in each ZCTA predicted as suitable after converting to binary map.



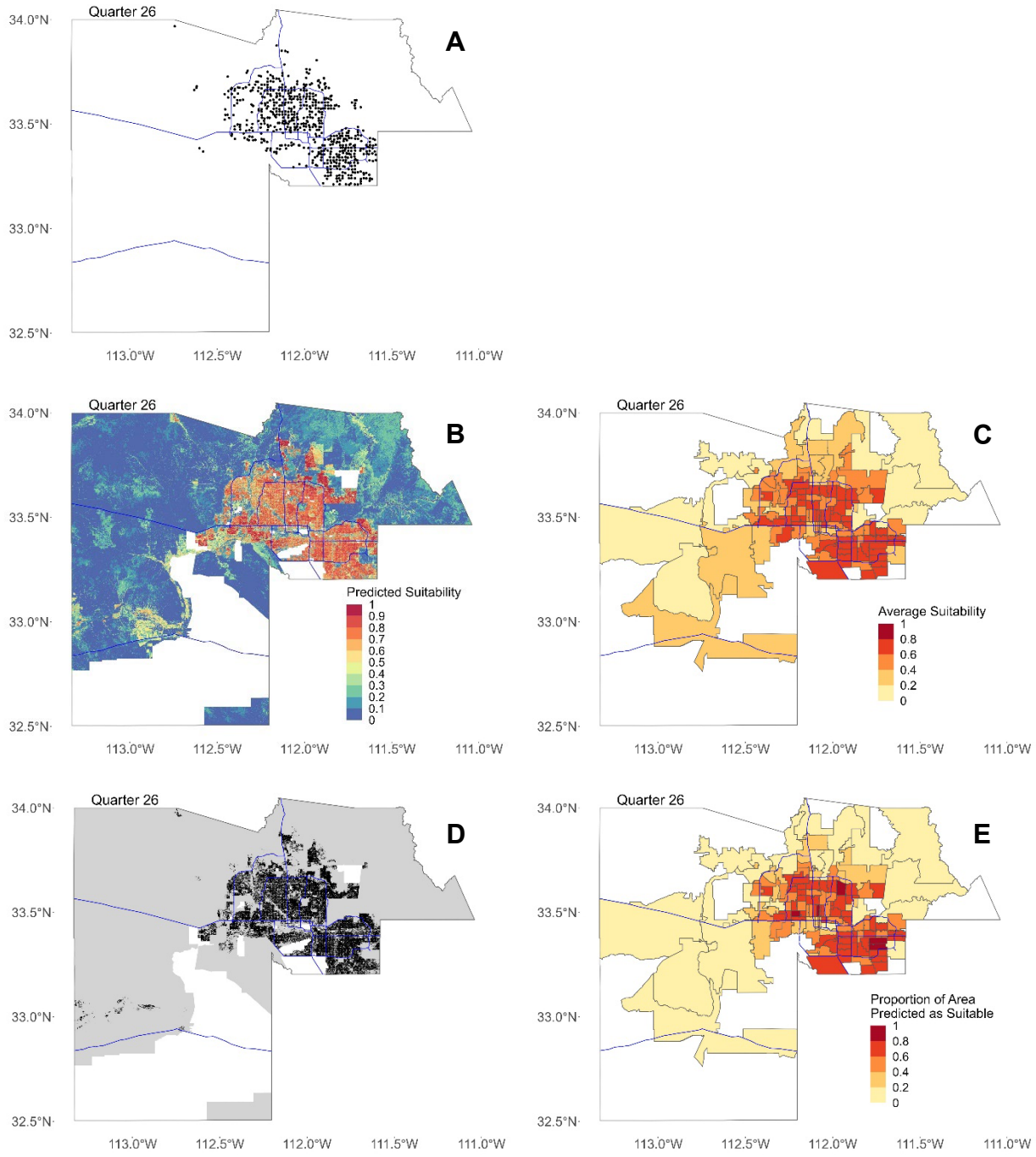
Supplementary Figure 3.21. Maps for Quarter 23 (8/1/19—10/31/19). In all figures, blue lines represent major freeways in Maricopa County. (**A**) Map of all locations where Ae. aegypti females were trapped in Maricopa County in Quarter 23. (**B**) Maxent output showing predicted suitability for 30-meter by 30-meter pixels. (**C**) Predicted suitability averaged by ZCTA. (**D**) Binary map showing areas predicted as suitable in black and not suitable in gray. In (B) and (C), areas with missing data where suitability was not predicted are shown in white. (**E**) Proportion of area in each ZCTA predicted as suitable after converting to binary map.



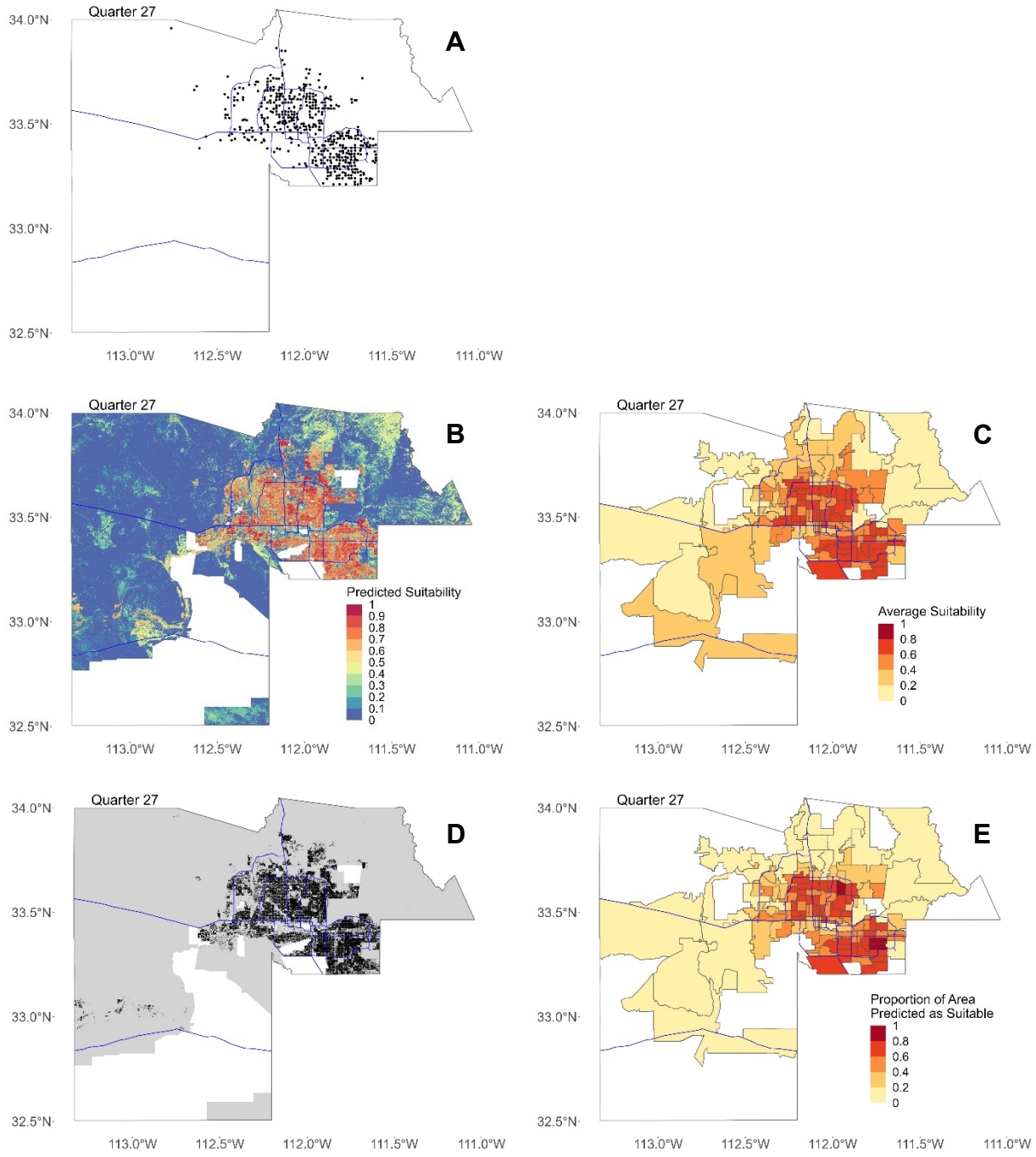
Supplementary Figure 3.22. Maps for Quarter 24 (11/1/19—1/31/20). In all figures, blue lines represent major freeways in Maricopa County. (**A**) Map of all locations where Ae. aegypti females were trapped in Maricopa County in Quarter 24. (**B**) Maxent output showing predicted suitability for 30-meter by 30-meter pixels. (**C**) Predicted suitability averaged by ZCTA. (**D**) Binary map showing areas predicted as suitable in black and not suitable in gray. In (B) and (C), areas with missing data where suitability was not predicted are shown in white. (**E**) Proportion of area in each ZCTA predicted as suitable after converting to binary map.



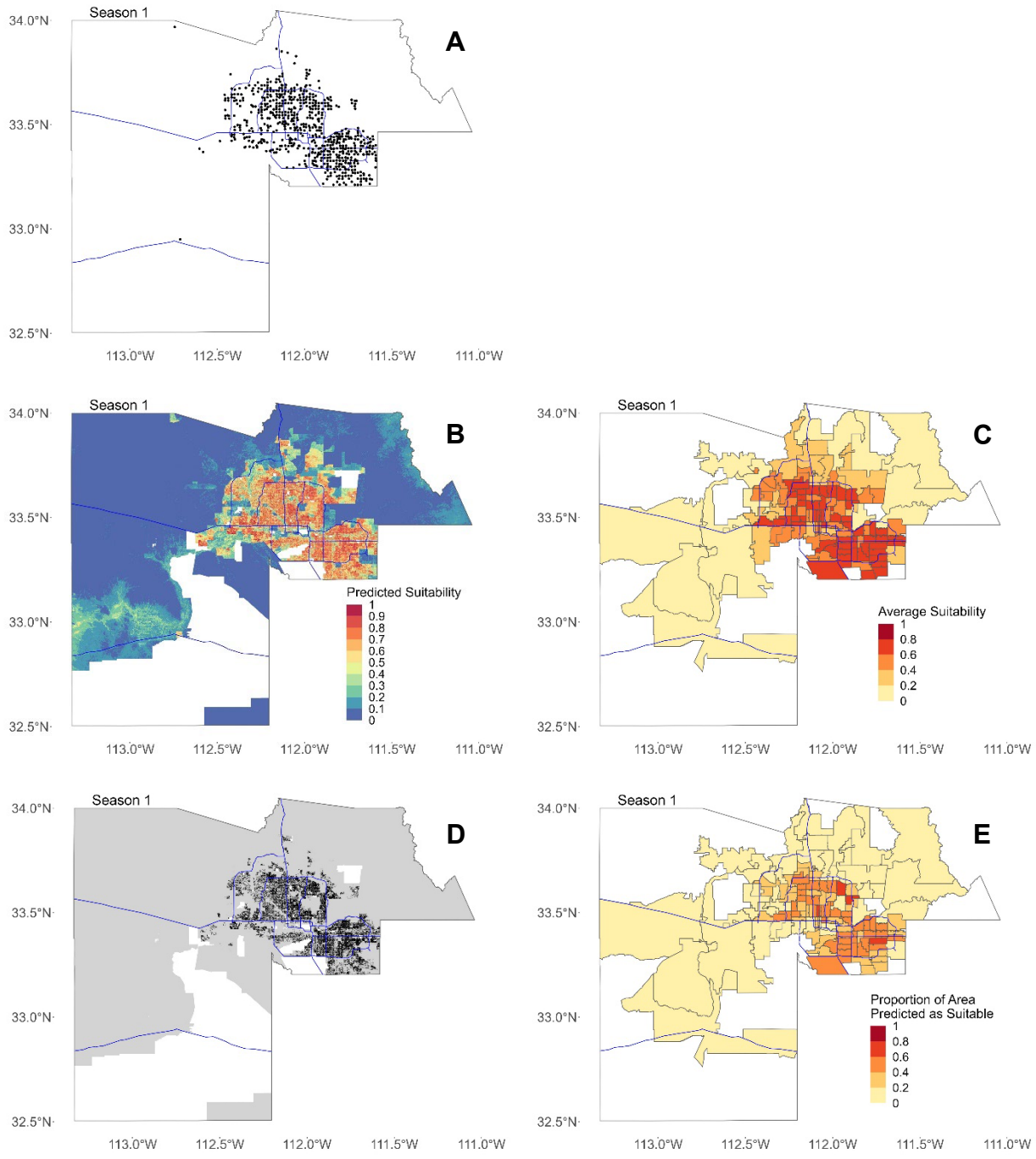
Supplementary Figure 3.23. Maps for Quarter 25 (2/1/20—4/30/20). In all figures, blue lines represent major freeways in Maricopa County. (**A**) Map of all locations where Ae. aegypti females were trapped in Maricopa County in Quarter 25. (**B**) Maxent output showing predicted suitability for 30-meter by 30-meter pixels. (**C**) Predicted suitability averaged by ZCTA. (**D**) Binary map showing areas predicted as suitable in black and not suitable in gray. In (B) and (C), areas with missing data where suitability was not predicted are shown in white. (**E**) Proportion of area in each ZCTA predicted as suitable after converting to binary map.



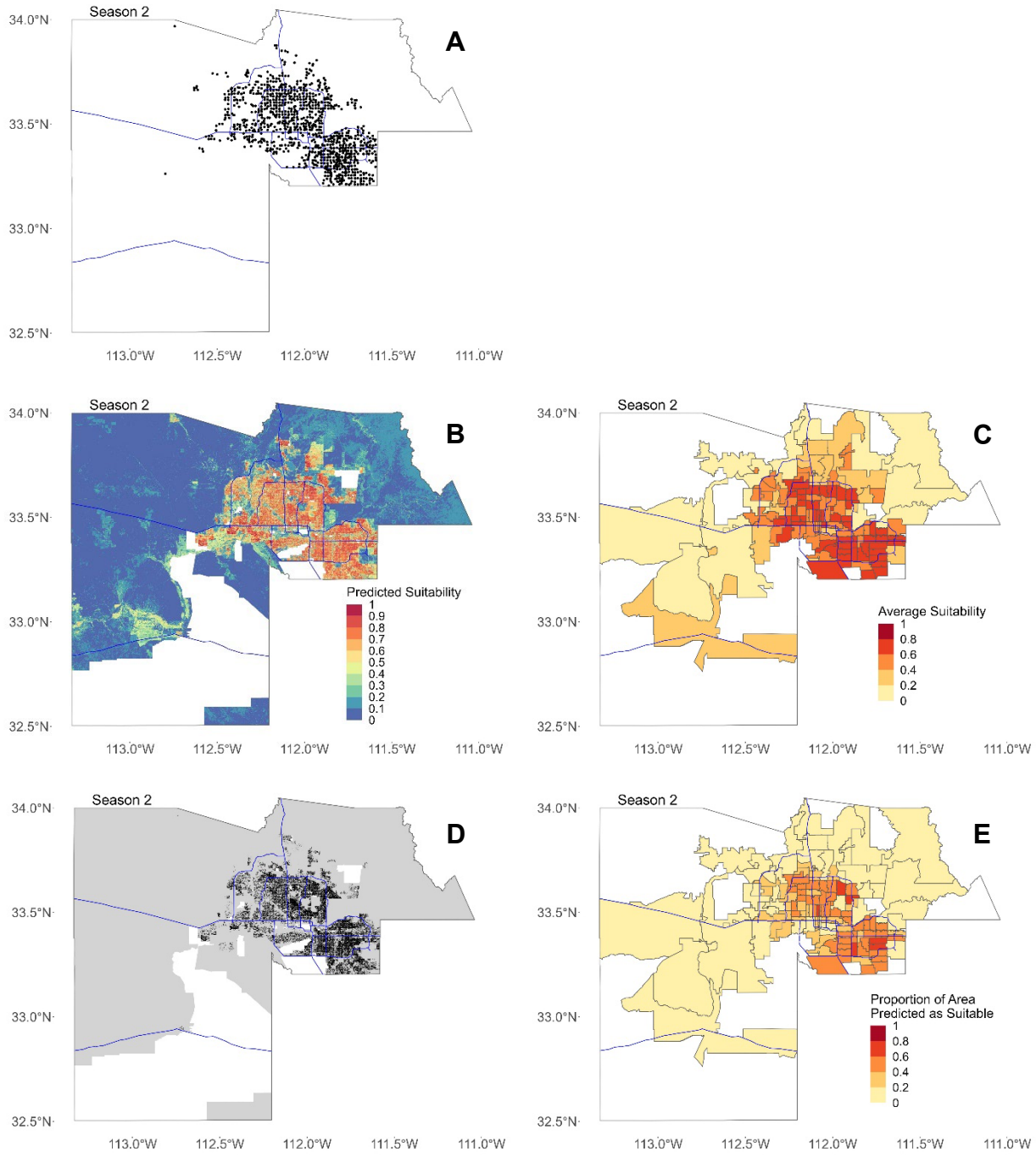
Supplementary Figure 3.24. Maps for Quarter 26 (5/1/20—7/31/20). In all figures, blue lines represent major freeways in Maricopa County. (**A**) Map of all locations where Ae. aegypti females were trapped in Maricopa County in Quarter 26. (**B**) Maxent output showing predicted suitability for 30-meter by 30-meter pixels. (**C**) Predicted suitability averaged by ZCTA. (**D**) Binary map showing areas predicted as suitable in black and not suitable in gray. In (B) and (C), areas with missing data where suitability was not predicted are shown in white. (**E**) Proportion of area in each ZCTA predicted as suitable after converting to binary map.



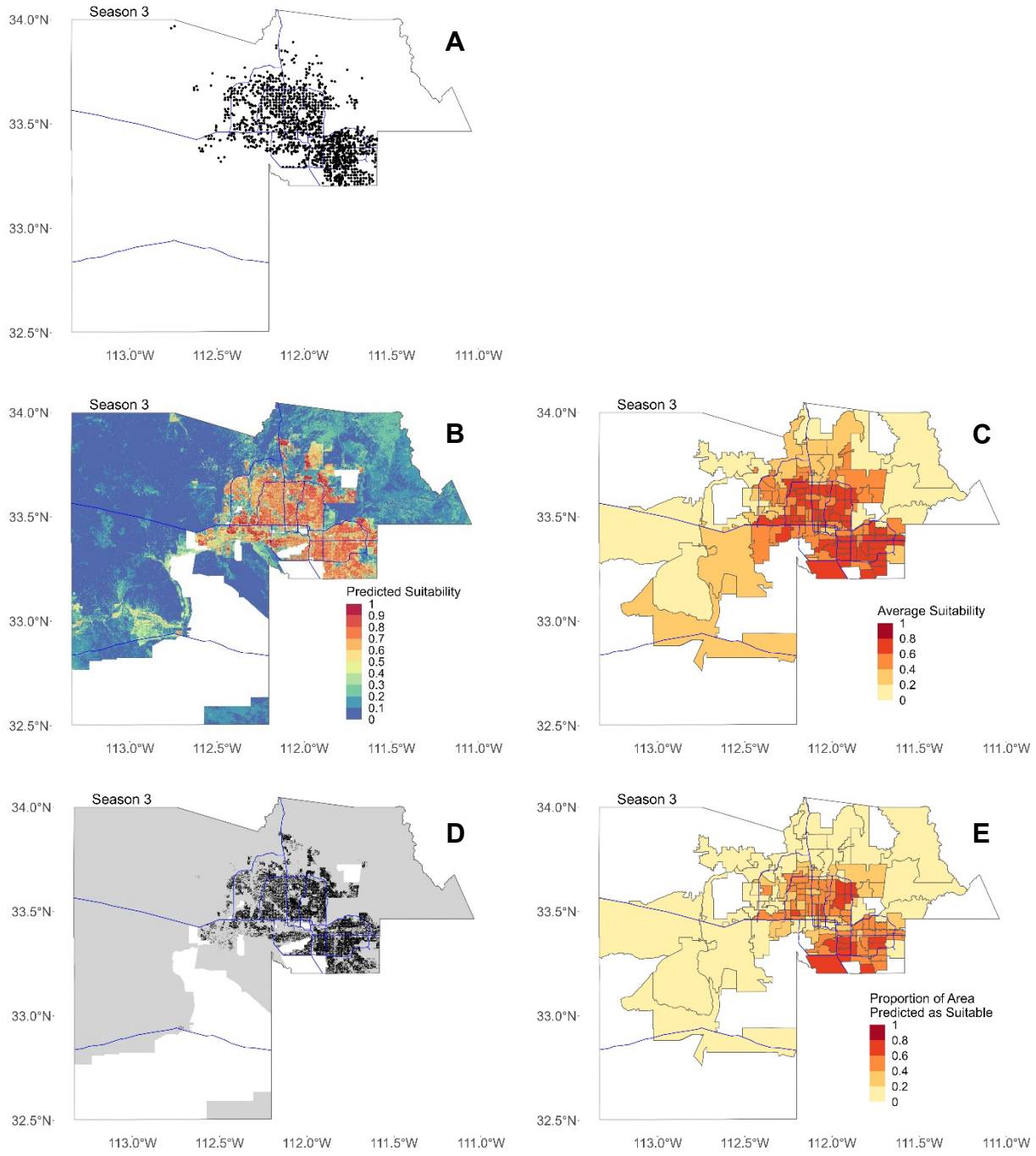
Supplementary Figure 3.25. Maps for Quarter 27 (8/1/20—10/31/20). In all figures, blue lines represent major freeways in Maricopa County. (**A**) Map of all locations where Ae. aegypti females were trapped in Maricopa County in Quarter 27. (**B**) Maxent output showing predicted suitability for 30-meter by 30-meter pixels. (**C**) Predicted suitability averaged by ZCTA. (**D**) Binary map showing areas predicted as suitable in black and not suitable in gray. In (B) and (C), areas with missing data where suitability was not predicted are shown in white. (**E**) Proportion of area in each ZCTA predicted as suitable after converting to binary map.



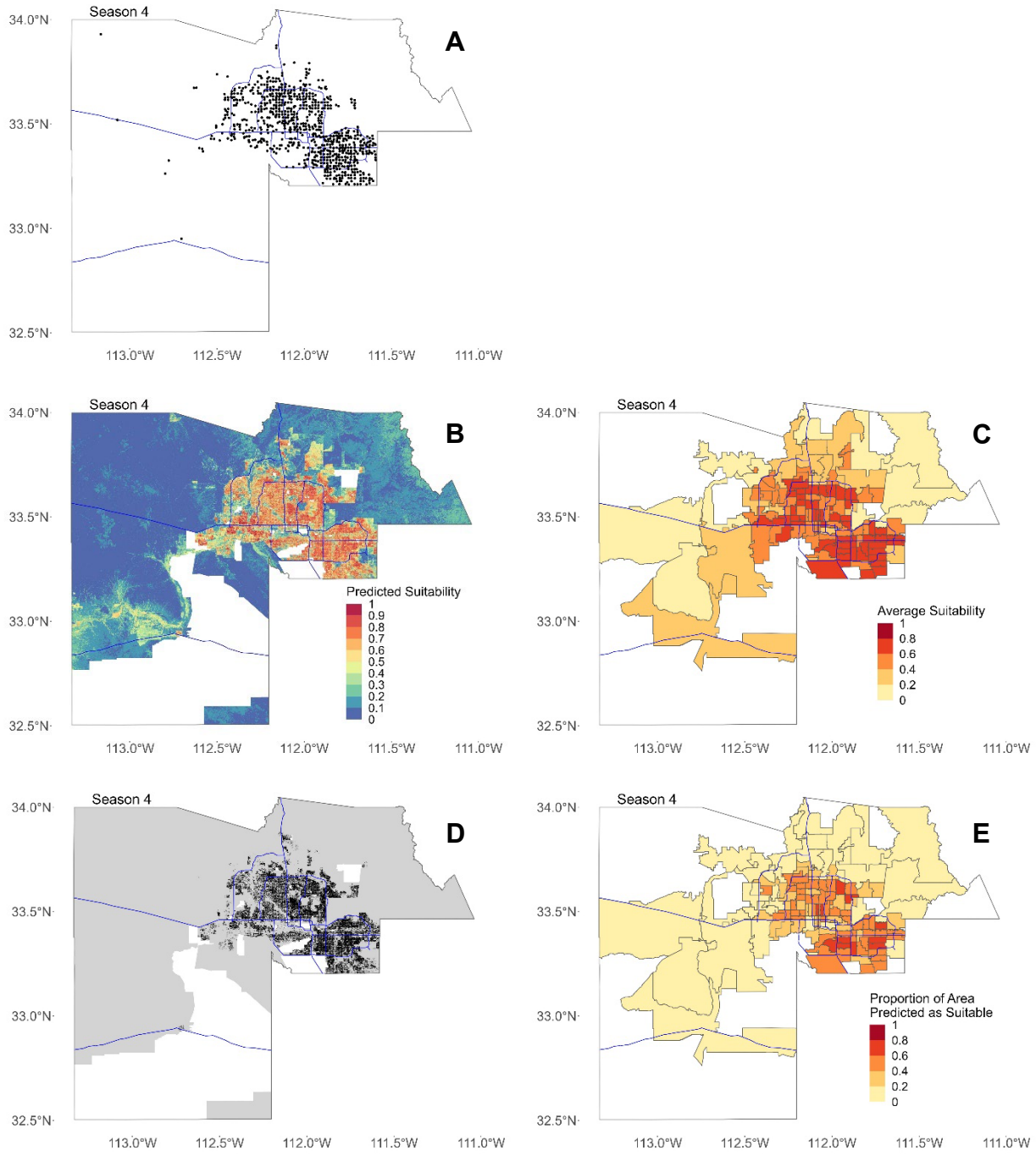
Supplementary Figure 3.26. Maps for Season 1 (2/1-4/30 quarters). In all figures, blue lines represent major freeways in Maricopa County. (**A**) Map of all locations where Ae. aegypti females were trapped in Maricopa County in Season 1. (**B**) Map showing mean predicted suitability for 30-meter by 30-meter pixels. (**C**) Mean predicted suitability averaged by ZCTA. (**D**) Binary map showing areas predicted as suitable for all quarters in black and not suitable in gray. In (B) and (C), areas with missing data where suitability was not predicted are shown in white. (**E**) Proportion of area in each ZCTA predicted as suitable after converting to binary map.



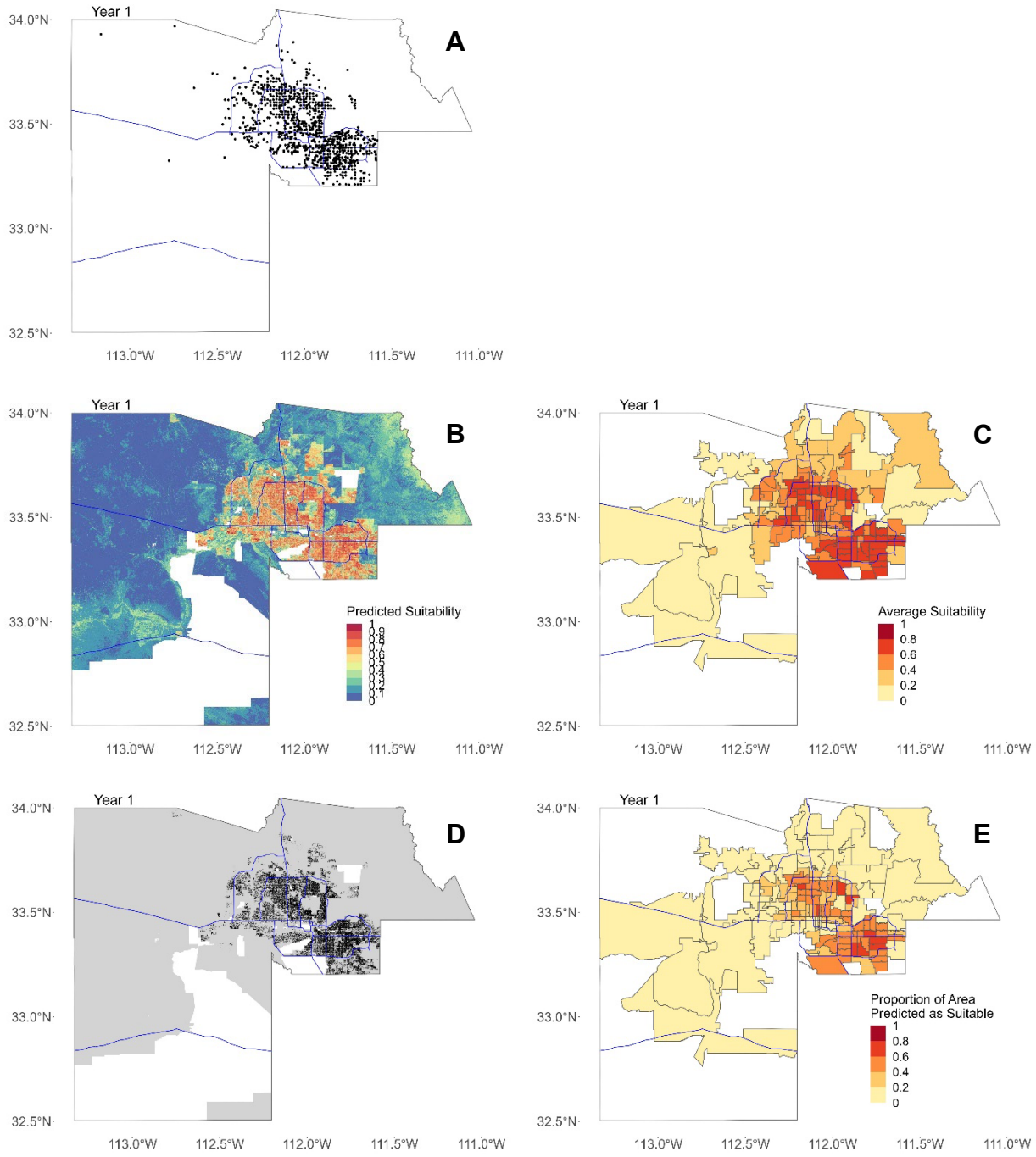
Supplementary Figure 3.27. Maps for Season 2 (5/1-7/31 quarters). In all figures, blue lines represent major freeways in Maricopa County. (**A**) Map of all locations where Ae. aegypti females were trapped in Maricopa County in Season 2. (**B**) Map showing mean predicted suitability for 30-meter by 30-meter pixels. (**C**) Mean predicted suitability averaged by ZCTA. (**D**) Binary map showing areas predicted as suitable for all quarters in black and not suitable in gray. In (B) and (C), areas with missing data where suitability was not predicted are shown in white. (**E**) Proportion of area in each ZCTA predicted as suitable after converting to binary map.



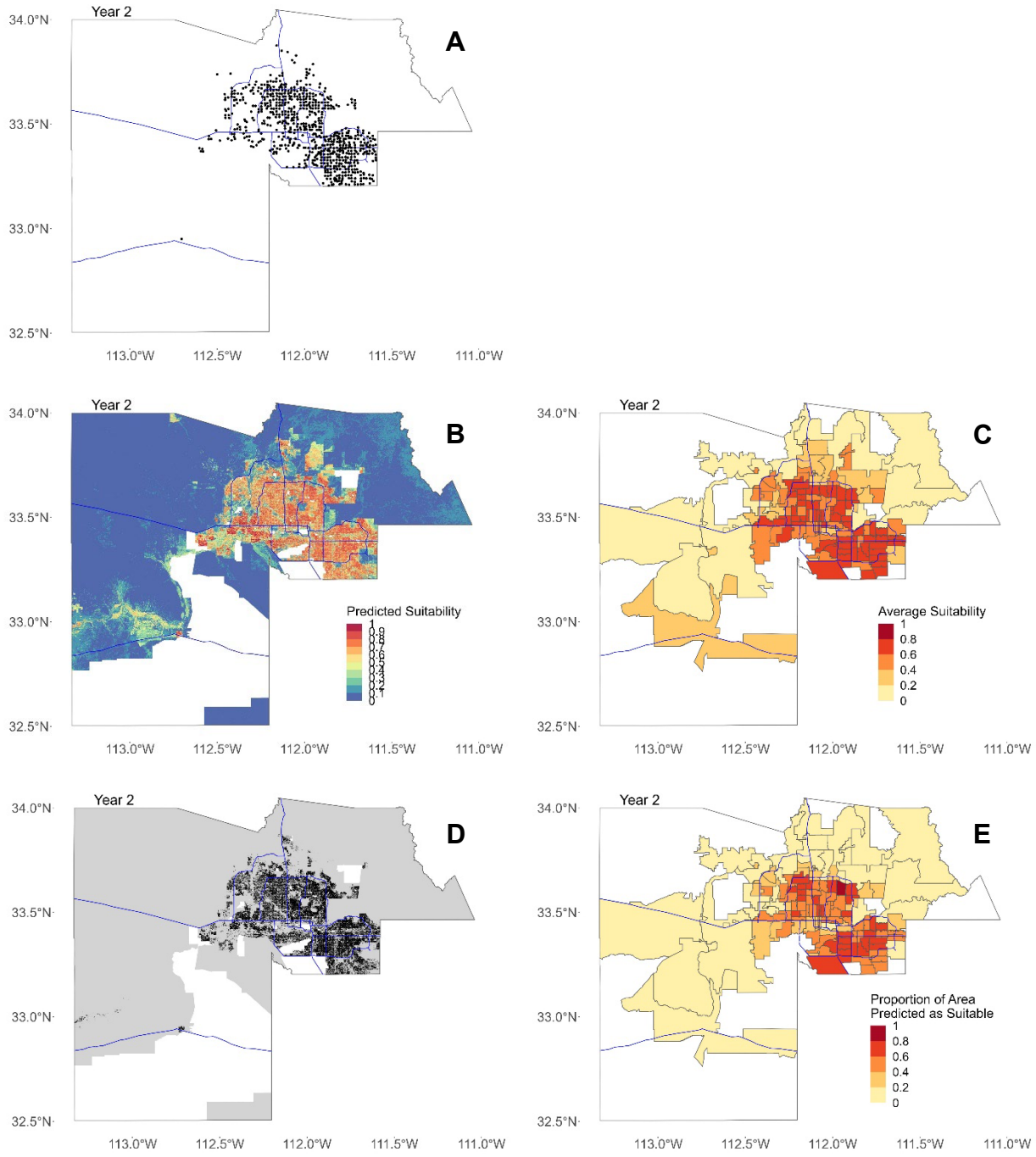
Supplementary Figure 3.28. Maps for Season 3 (8/1-10/31 quarters). In all figures, blue lines represent major freeways in Maricopa County. (**A**) Map of all locations where Ae. aegypti females were trapped in Maricopa County in Season 3. (**B**) Map showing mean predicted suitability for 30-meter by 30-meter pixels. (**C**) Mean predicted suitability averaged by ZCTA. (**D**) Binary map showing areas predicted as suitable for all quarters in black and not suitable in gray. In (B) and (C), areas with missing data where suitability was not predicted are shown in white. (**E**) Proportion of area in each ZCTA predicted as suitable after converting to binary map.



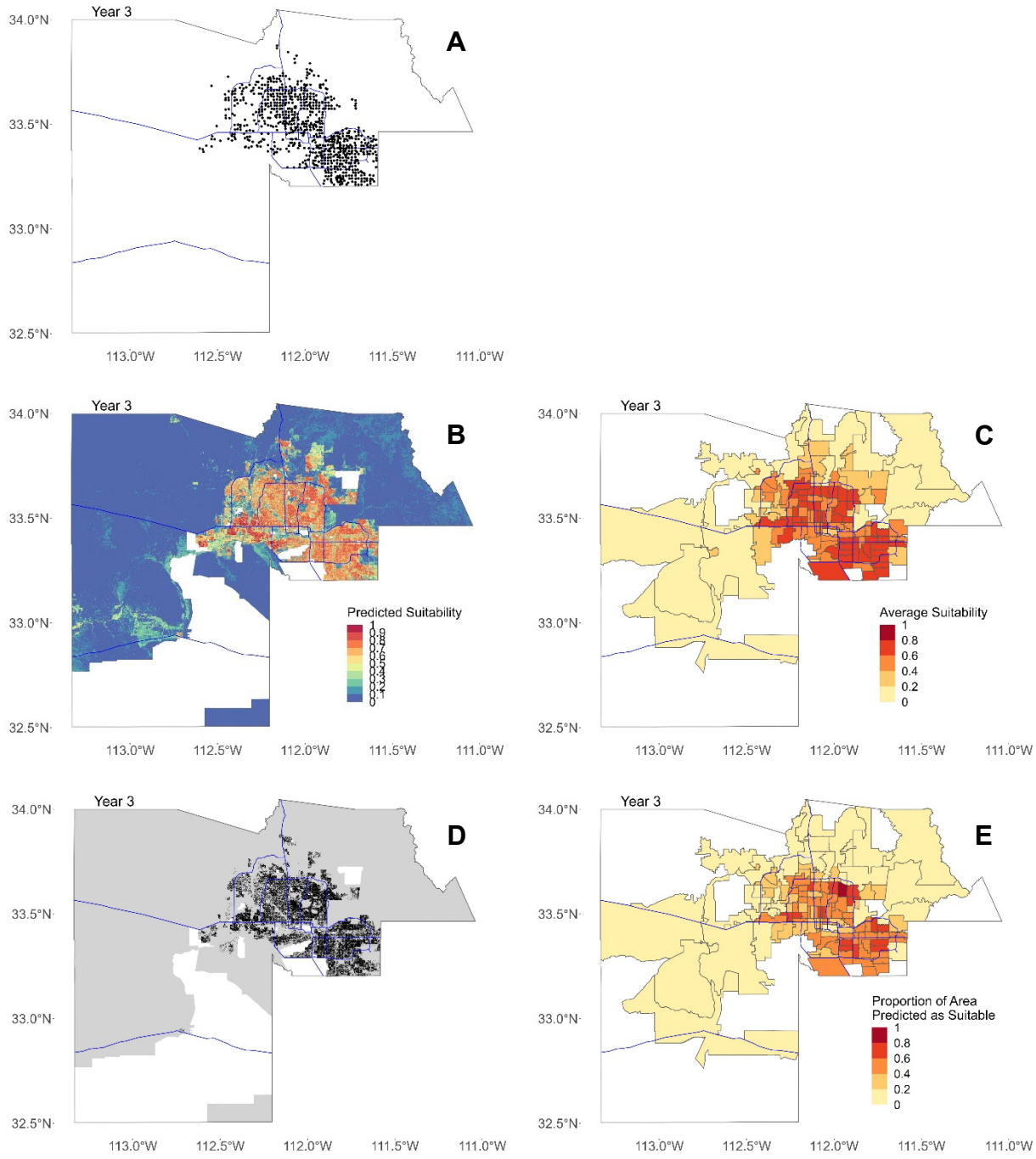
Supplementary Figure 3.29. Maps for Season 4 (11/1-1/31 quarters). In all figures, blue lines represent major freeways in Maricopa County. (**A**) Map of all locations where Ae. aegypti females were trapped in Maricopa County in Season 4. (**B**) Map showing mean predicted suitability for 30-meter by 30-meter pixels. (**C**) Mean predicted suitability averaged by ZCTA. (**D**) Binary map showing areas predicted as suitable for all quarters in black and not suitable in gray. In (B) and (C), areas with missing data where suitability was not predicted are shown in white. (**E**) Proportion of area in each ZCTA predicted as suitable after converting to binary map.



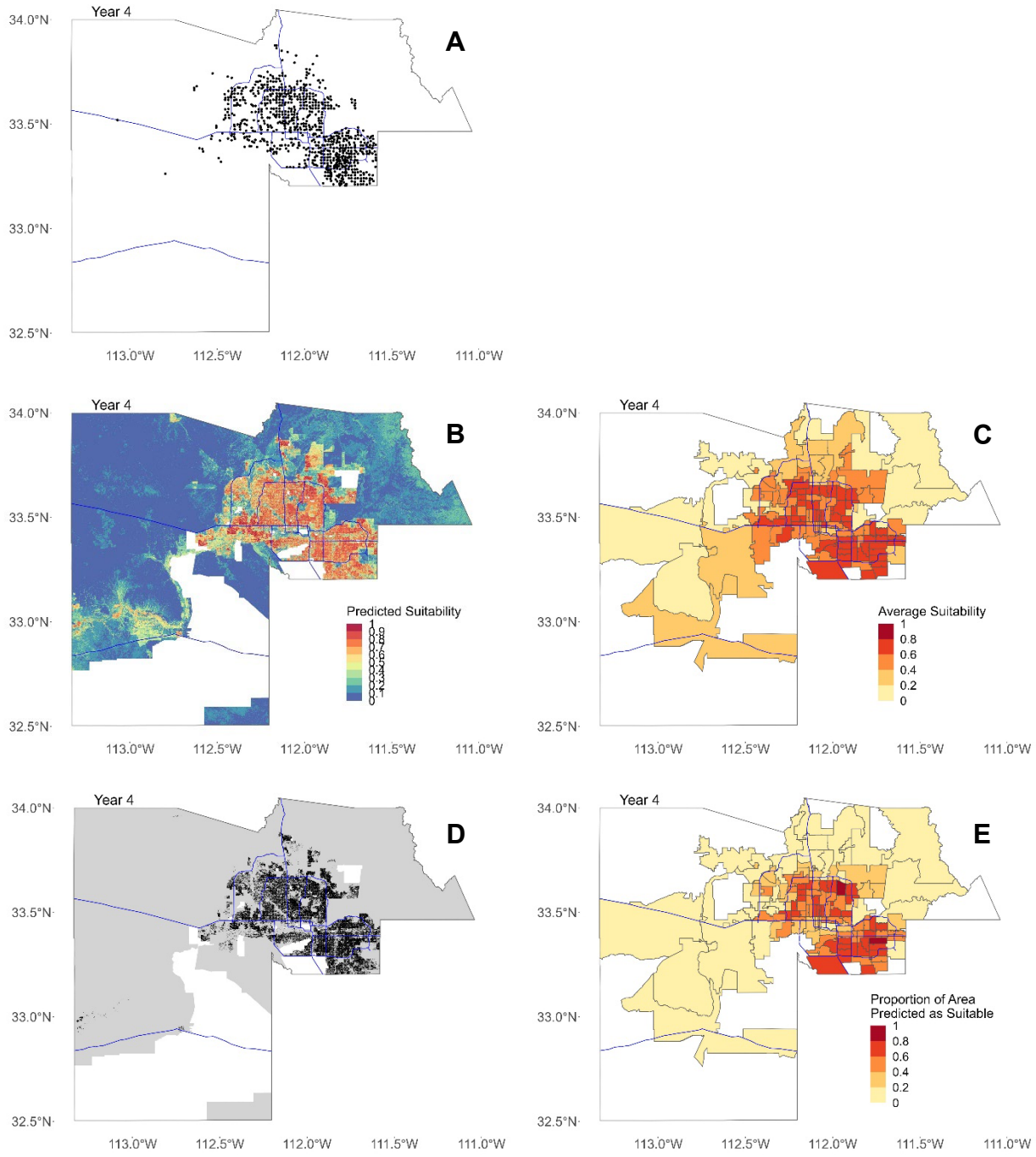
Supplementary Figure 3.30. Maps for Year 1 (2/1/14-1/31/15). In all figures, blue lines represent major freeways in Maricopa County. (**A**) Map of all locations where Ae. aegypti females were trapped in Maricopa County in Year 1. (**B**) Map showing mean predicted suitability for 30-meter by 30-meter pixels. (**C**) Mean predicted suitability averaged by ZCTA. (**D**) Binary map showing areas predicted as suitable for all quarters in black and not suitable in gray. In (B) and (C), areas with missing data where suitability was not predicted are shown in white. (**E**) Proportion of area in each ZCTA predicted as suitable after converting to binary map.



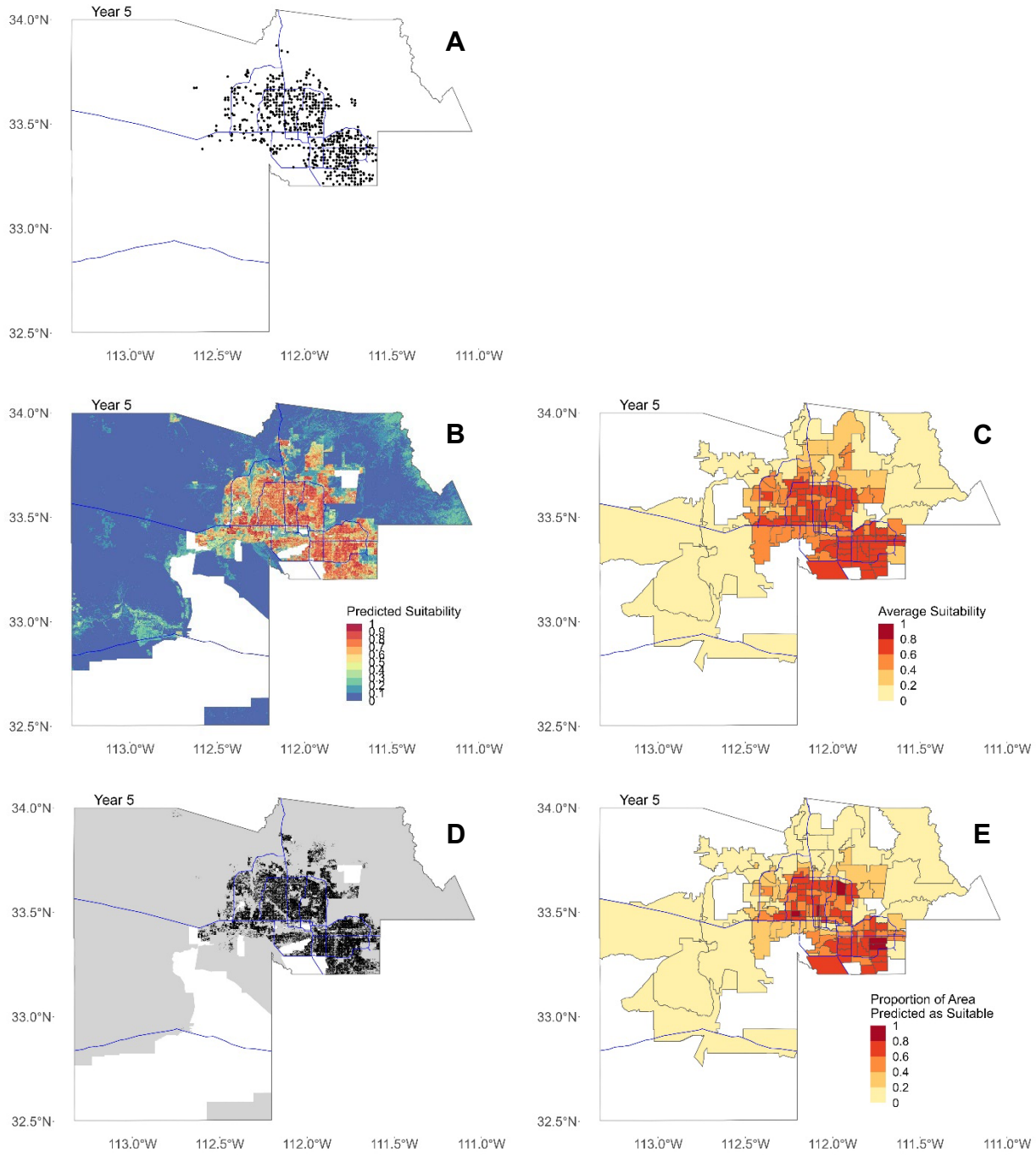
Supplementary Figure 3.31. Maps for Year 2 (2/1/15-1/31/16). In all figures, blue lines represent major freeways in Maricopa County. (**A**) Map of all locations where Ae. aegypti females were trapped in Maricopa County in Year 2. (**B**) Map showing mean predicted suitability for 30-meter by 30-meter pixels. (**C**) Mean predicted suitability averaged by ZCTA. (**D**) Binary map showing areas predicted as suitable for all quarters in black and not suitable in gray. In (B) and (C), areas with missing data where suitability was not predicted are shown in white. (**E**) Proportion of area in each ZCTA predicted as suitable after converting to binary map.



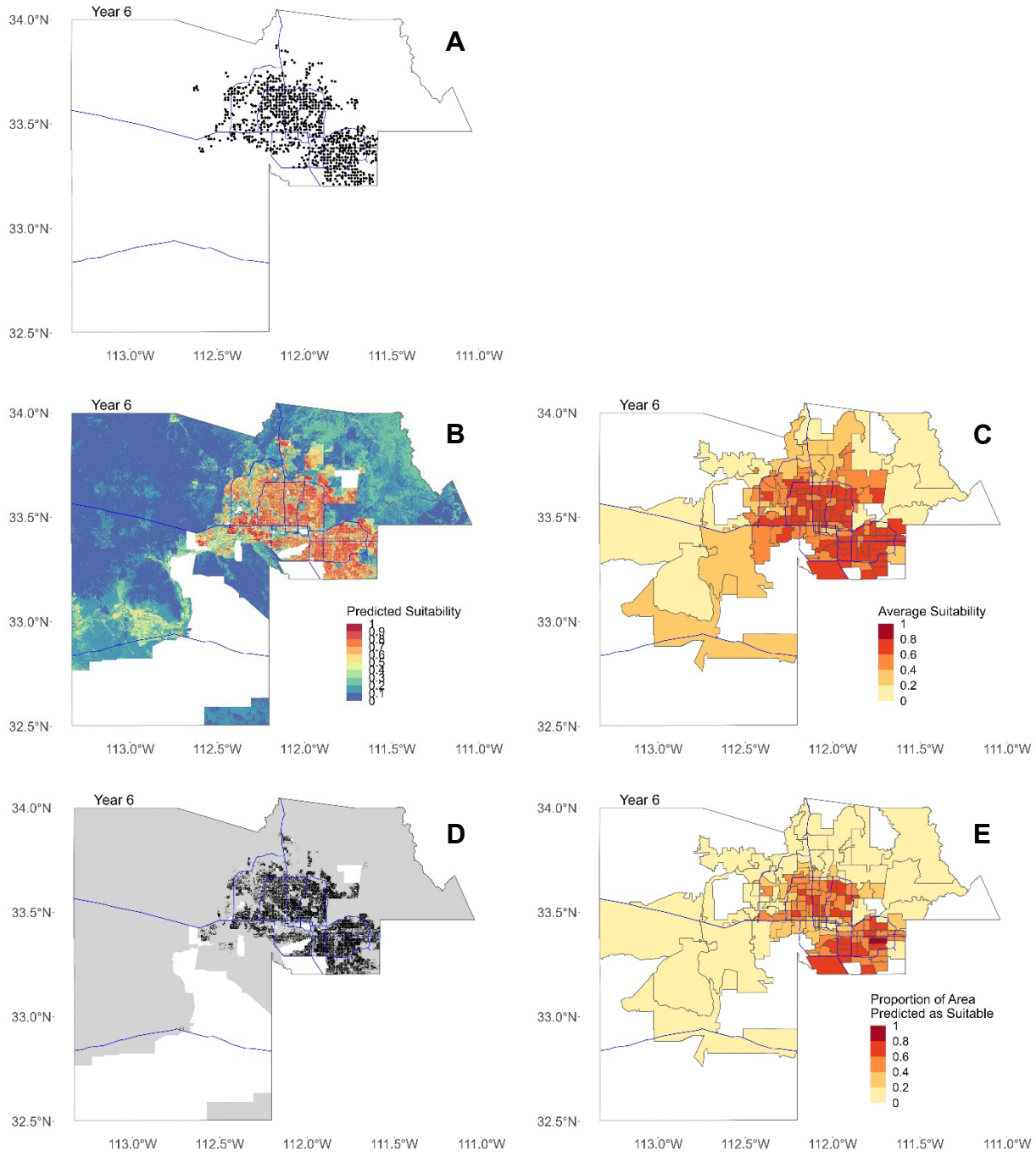
Supplementary Figure 3.32. Maps for Year 3 (2/1/16-1/31/17). In all figures, blue lines represent major freeways in Maricopa County. (**A**) Map of all locations where Ae. aegypti females were trapped in Maricopa County in Year 3. (**B**) Map showing mean predicted suitability for 30-meter by 30-meter pixels. (**C**) Mean predicted suitability averaged by ZCTA. (**D**) Binary map showing areas predicted as suitable for all quarters in black and not suitable in gray. In (B) and (C), areas with missing data where suitability was not predicted are shown in white. (**E**) Proportion of area in each ZCTA predicted as suitable after converting to binary map.



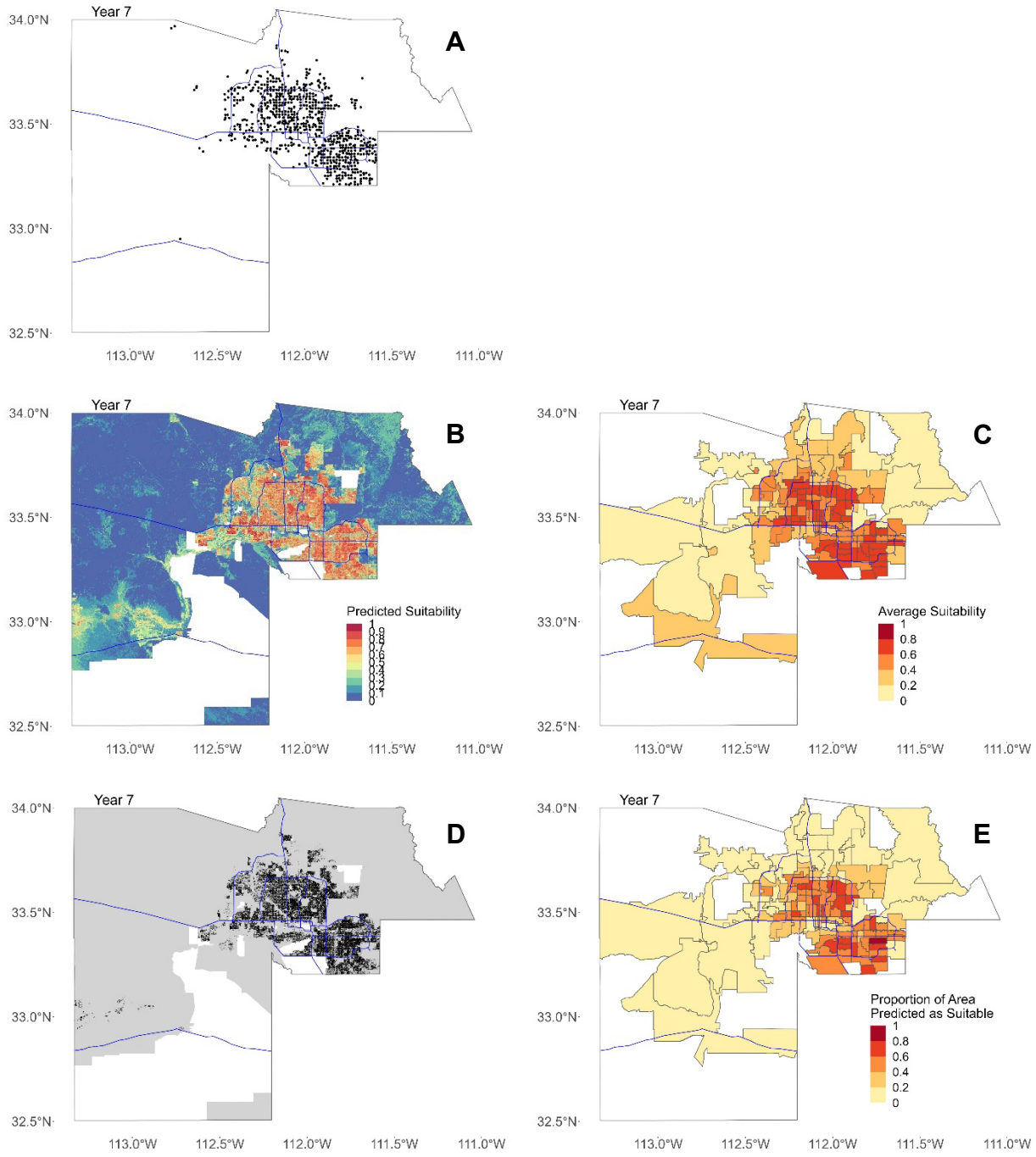
Supplementary Figure 3.33. Maps for Year 4 (2/1/17-1/31/18). In all figures, blue lines represent major freeways in Maricopa County. (**A**) Map of all locations where Ae. aegypti females were trapped in Maricopa County in Year 4. (**B**) Map showing mean predicted suitability for 30-meter by 30-meter pixels. (**C**) Mean predicted suitability averaged by ZCTA. (**D**) Binary map showing areas predicted as suitable for all quarters in black and not suitable in gray. In (B) and (C), areas with missing data where suitability was not predicted are shown in white. (**E**) Proportion of area in each ZCTA predicted as suitable after converting to binary map.



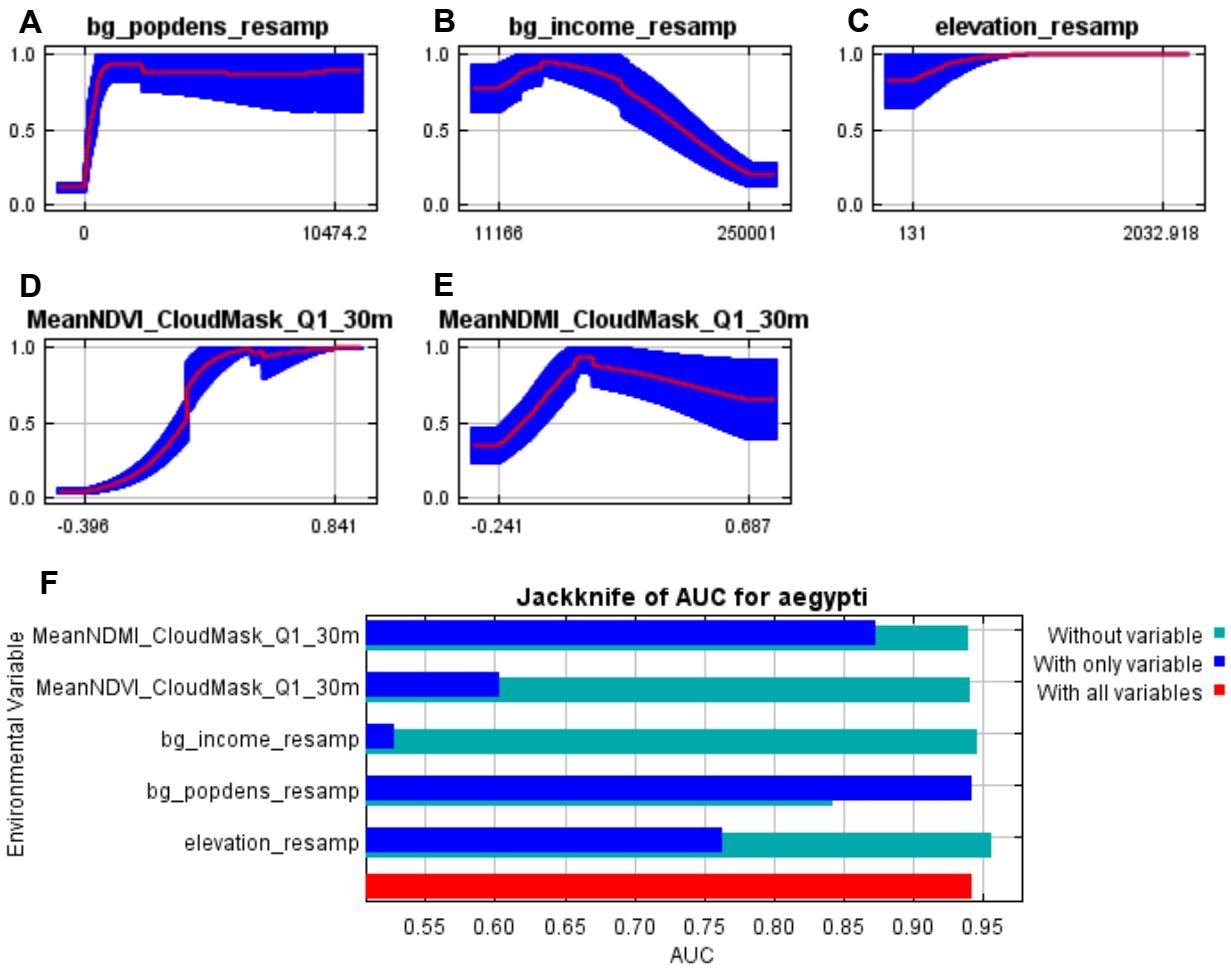
Supplementary Figure 3.34. Maps for Year 5 (2/1/18-7/31/18). In all figures, blue lines represent major freeways in Maricopa County. (**A**) Map of all locations where Ae. aegypti females were trapped in Maricopa County in Year 5. (**B**) Map showing mean predicted suitability for 30-meter by 30-meter pixels. (**C**) Mean predicted suitability averaged by ZCTA. (**D**) Binary map showing areas predicted as suitable for all quarters in black and not suitable in gray. In (B) and (C), areas with missing data where suitability was not predicted are shown in white. (**E**) Proportion of area in each ZCTA predicted as suitable after converting to binary map.



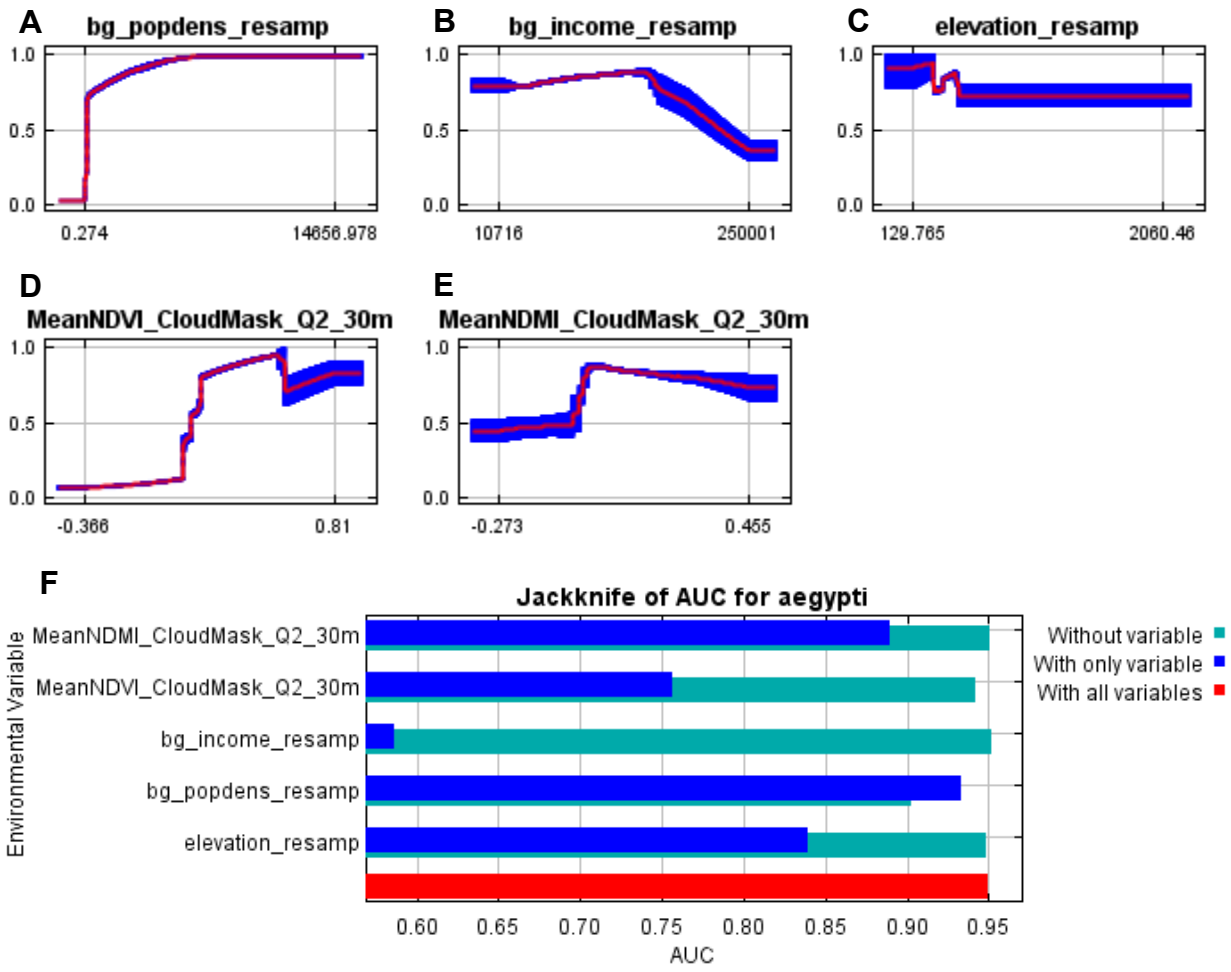
Supplementary Figure 3.35. Maps for Year 6 (2/1/19-1/31/20). In all figures, blue lines represent major freeways in Maricopa County. (**A**) Map of all locations where Ae. aegypti females were trapped in Maricopa County in Year 6. (**B**) Map showing mean predicted suitability for 30-meter by 30-meter pixels. (**C**) Mean predicted suitability averaged by ZCTA. (**D**) Binary map showing areas predicted as suitable for all quarters in black and not suitable in gray. In (B) and (C), areas with missing data where suitability was not predicted are shown in white. (**E**) Proportion of area in each ZCTA predicted as suitable after converting to binary map.



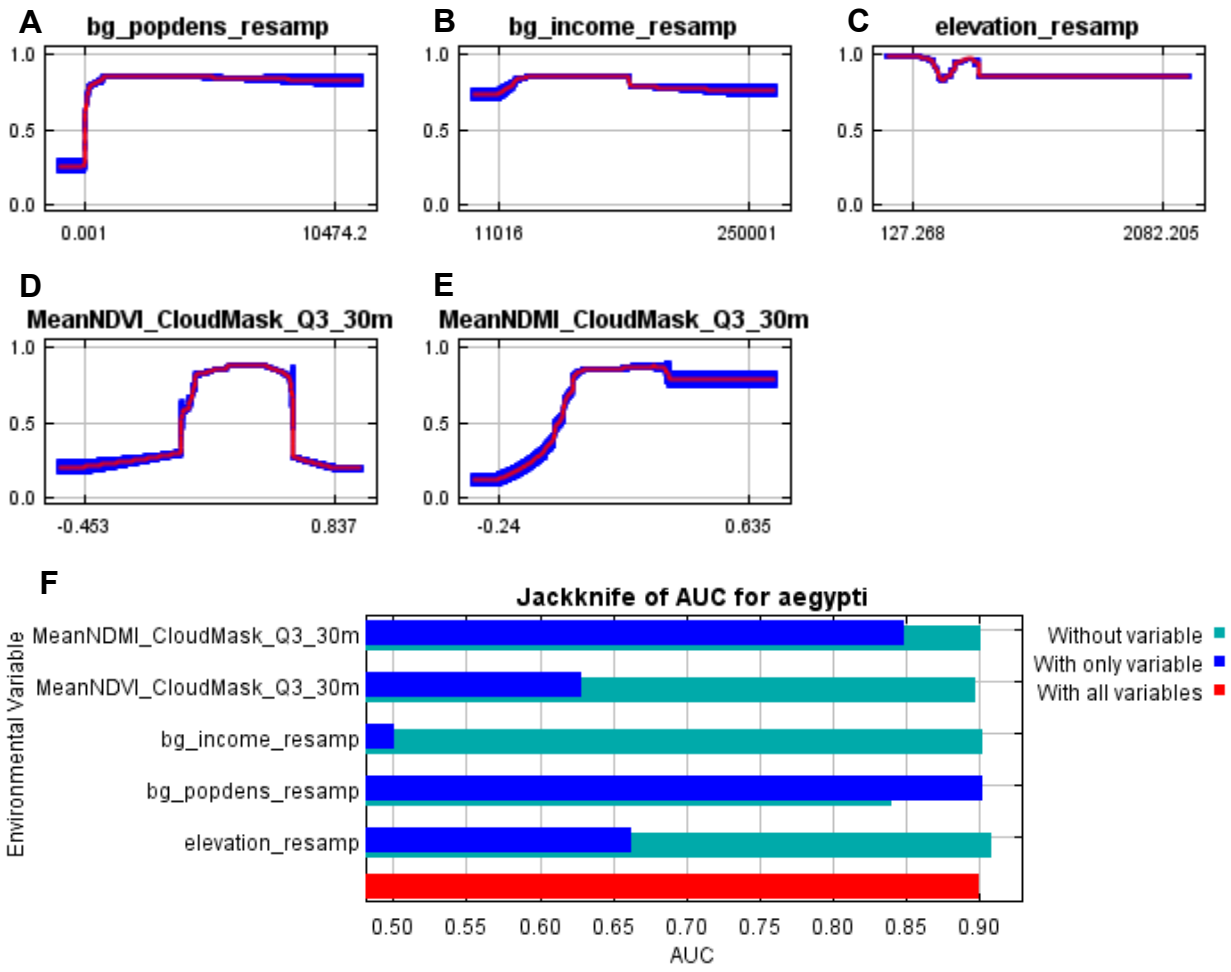
Supplementary Figure 3.36. Maps for Year 7 (2/1/20-10/31/20). In all figures, blue lines represent major freeways in Maricopa County. (**A**) Map of all locations where Ae. aegypti females were trapped in Maricopa County in Year 7. (**B**) Map showing mean predicted suitability for 30-meter by 30-meter pixels. (**C**) Mean predicted suitability averaged by ZCTA. (**D**) Binary map showing areas predicted as suitable for all quarters in black and not suitable in gray. In (B) and (C), areas with missing data where suitability was not predicted are shown in white. (**E**) Proportion of area in each ZCTA predicted as suitable after converting to binary map.



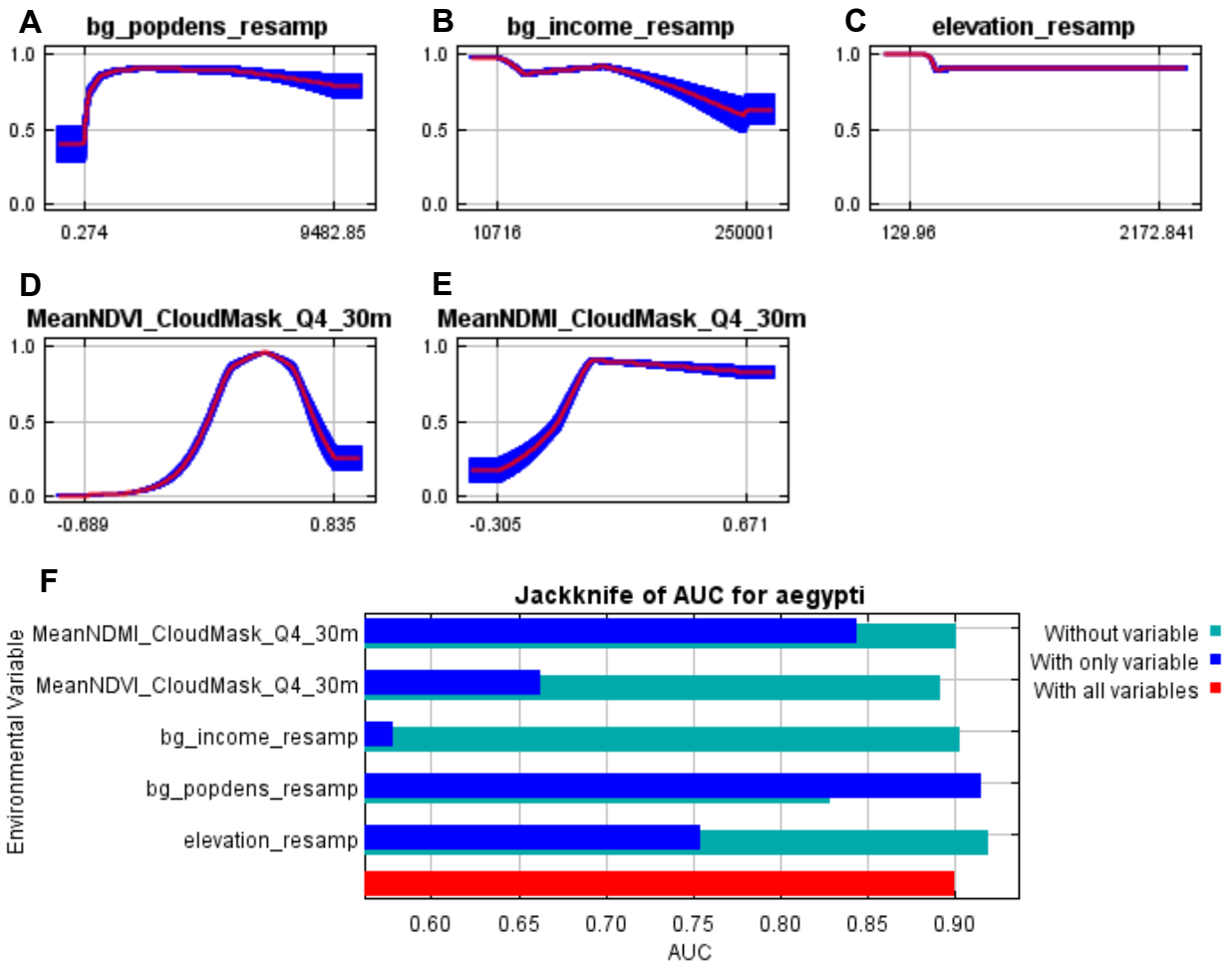
Supplementary Figure 3.37. Response curves for Quarter 1 (2/1/14—4/30/14). (**A**) through (**E**) show Maxent response curves for the predictors Population Density, Median Income, Elevation, mean Normalized Difference Vegetation Index (NDVI), and mean Normalized Difference Moisture Index (NDMI). Response curves are shown for each predictor when all other predictors are held constant. Mean response from 10 folds is shown with a red line, and +/- one standard deviation is shown in blue. (**F**) Maxent output showing the average change in the Area Under Curve (AUC) value when only that predictor is included (dark blue), when only that predictor is removed (green), and when all predictors were included (red).



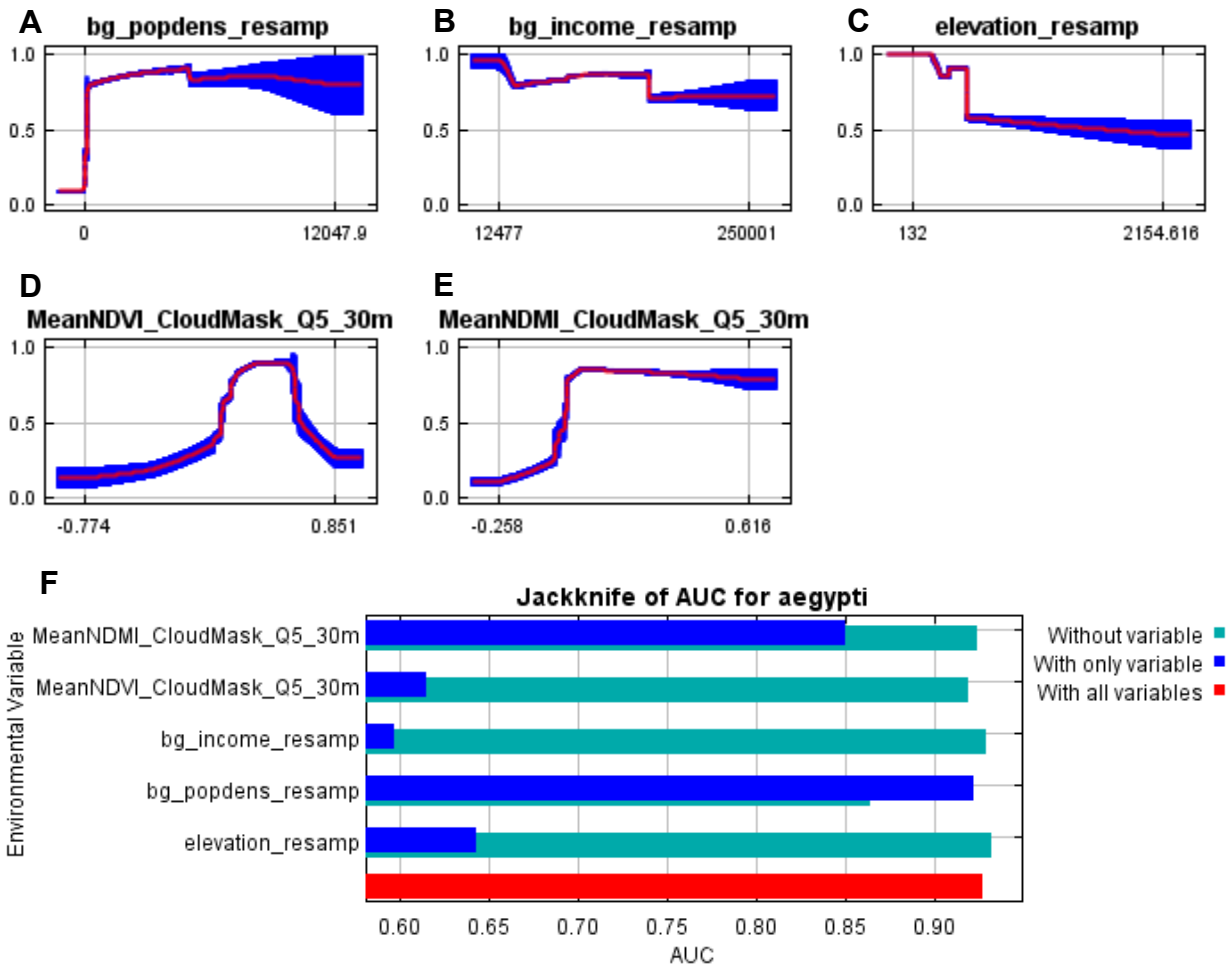
Supplementary Figure 3.38. Response curves for Quarter 2 (5/1/14—7/31/14). (**A**) through (**E**) show Maxent response curves for the predictors Population Density, Median Income, Elevation, mean Normalized Difference Vegetation Index (NDVI), and mean Normalized Difference Moisture Index (NDMI). Response curves are shown for each predictor when all other predictors are held constant. Mean response from 10 folds is shown with a red line, and +/- one standard deviation is shown in blue. (**F**) Maxent output showing the average change in the Area Under Curve (AUC) value when only that predictor is included (dark blue), when only that predictor is removed (green), and when all predictors were included (red).



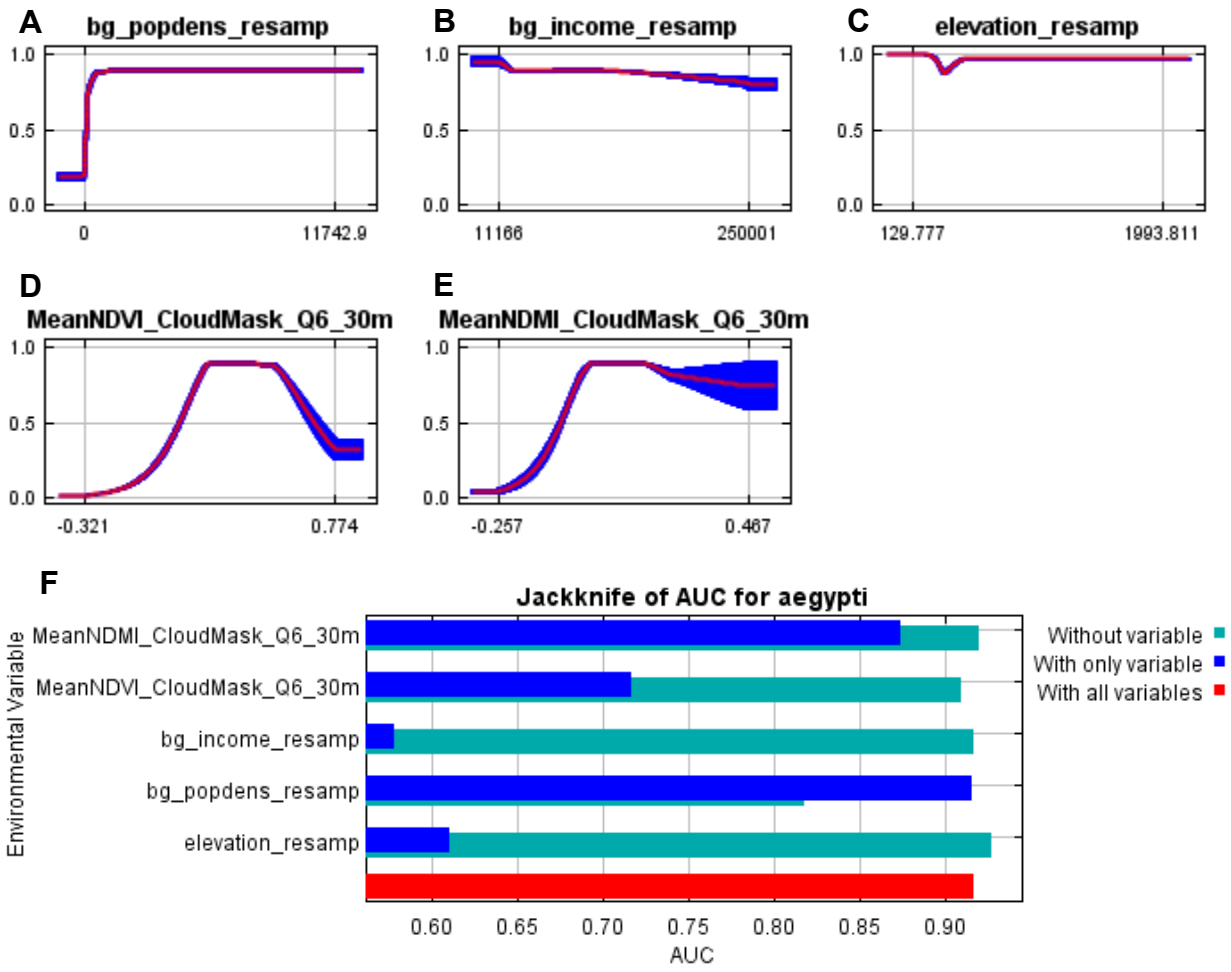
Supplementary Figure 3.39. Response curves for Quarter 3 (8/1/14—10/31/14). (**A**) through (**E**) show Maxent response curves for the predictors Population Density, Median Income, Elevation, mean Normalized Difference Vegetation Index (NDVI), and mean Normalized Difference Moisture Index (NDMI). Response curves are shown for each predictor when all other predictors are held constant. Mean response from 10 folds is shown with a red line, and +/- one standard deviation is shown in blue. (**F**) Maxent output showing the average change in the Area Under Curve (AUC) value when only that predictor is included (dark blue), when only that predictor is removed (green), and when all predictors were included (red).



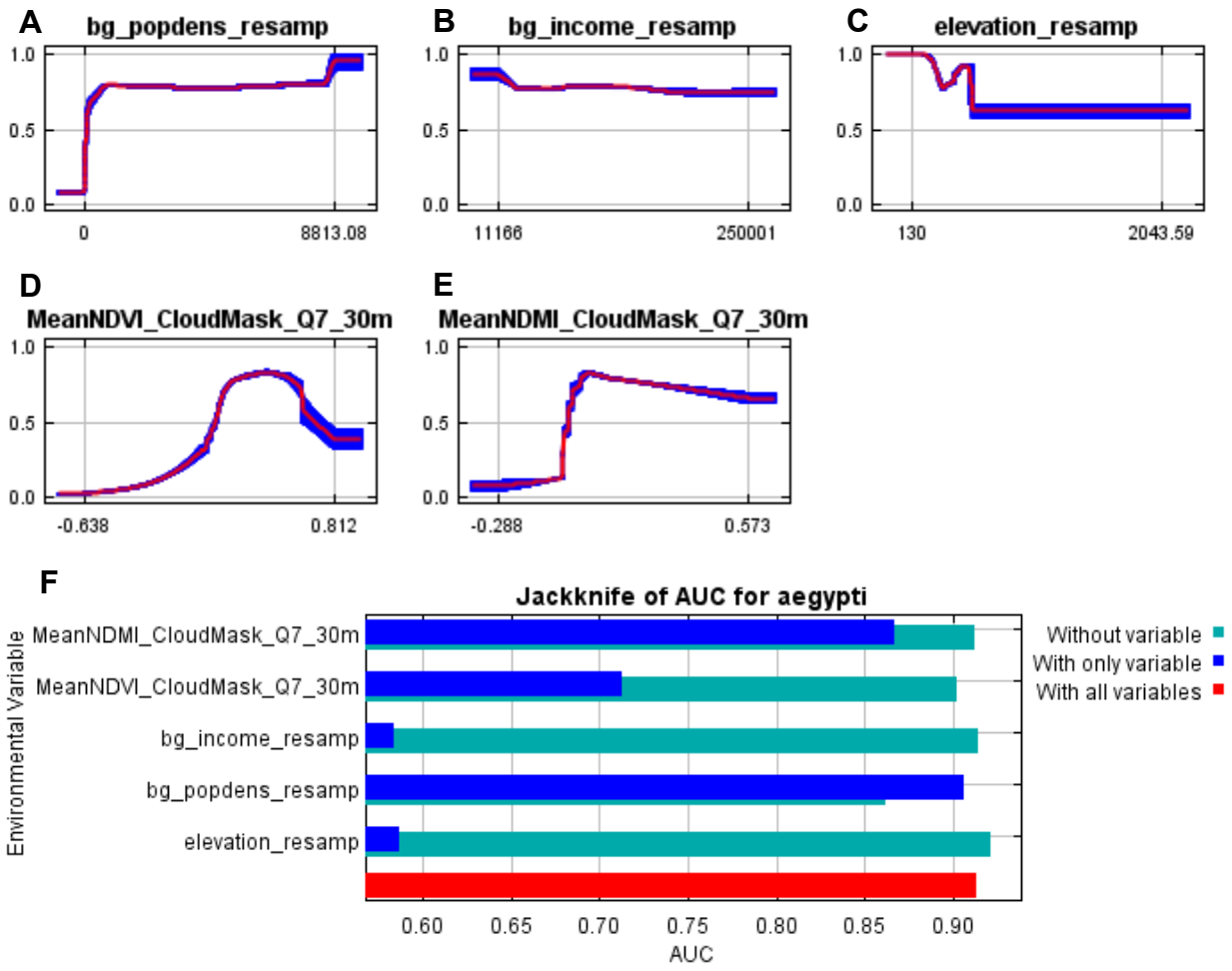
Supplementary Figure 3.40. Response curves for Quarter 4 (11/1/14—1/31/15). (**A**) through (**E**) show Maxent response curves for the predictors Population Density, Median Income, Elevation, mean Normalized Difference Vegetation Index (NDVI), and mean Normalized Difference Moisture Index (NDMI). Response curves are shown for each predictor when all other predictors are held constant. Mean response from 10 folds is shown with a red line, and +/- one standard deviation is shown in blue. (**F**) Maxent output showing the average change in the Area Under Curve (AUC) value when only that predictor is included (dark blue), when only that predictor is removed (green), and when all predictors were included (red).



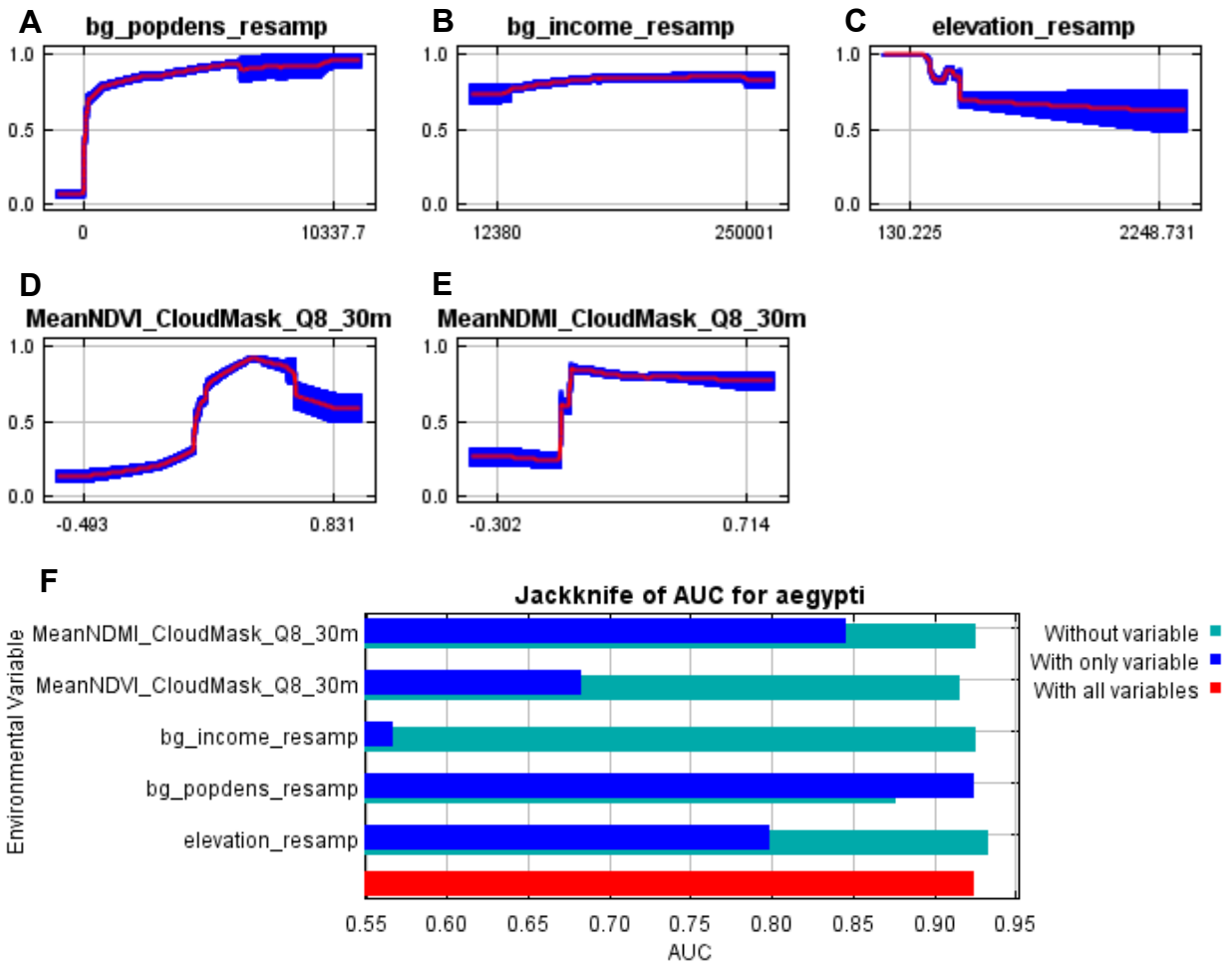
Supplementary Figure 3.41. Response curves for Quarter 5 (2/1/15—4/30/15). (**A**) through (**E**) show Maxent response curves for the predictors Population Density, Median Income, Elevation, mean Normalized Difference Vegetation Index (NDVI), and mean Normalized Difference Moisture Index (NDMI). Response curves are shown for each predictor when all other predictors are held constant. Mean response from 10 folds is shown with a red line, and +/- one standard deviation is shown in blue. (**F**) Maxent output showing the average change in the Area Under Curve (AUC) value when only that predictor is included (dark blue), when only that predictor is removed (green), and when all predictors were included (red).



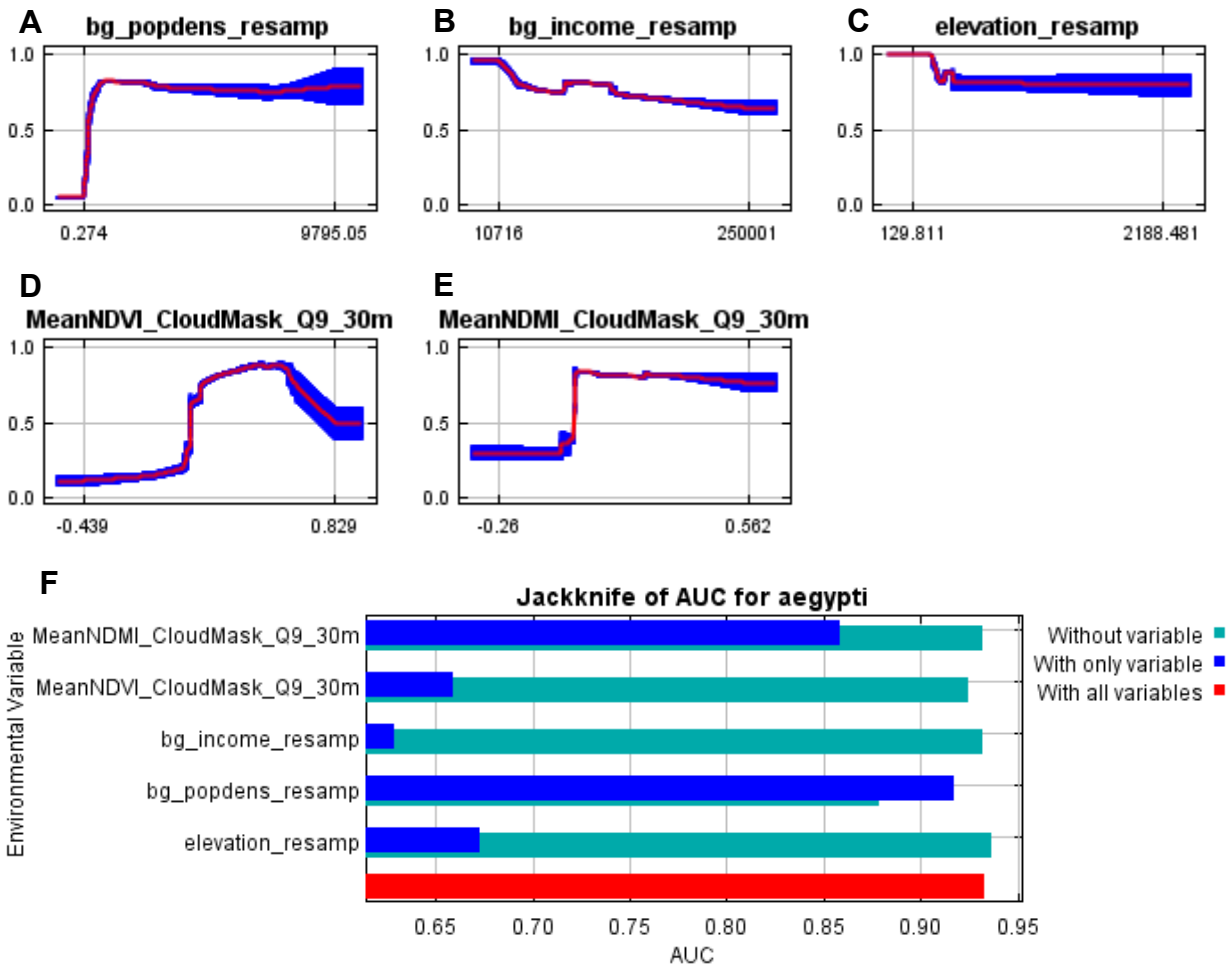
Supplementary Figure 3.42. Response curves for Quarter 6 (5/1/15—7/31/15). (**A**) through (**E**) show Maxent response curves for the predictors Population Density, Median Income, Elevation, mean Normalized Difference Vegetation Index (NDVI), and mean Normalized Difference Moisture Index (NDMI). Response curves are shown for each predictor when all other predictors are held constant. Mean response from 10 folds is shown with a red line, and +/- one standard deviation is shown in blue. (**F**) Maxent output showing the average change in the Area Under Curve (AUC) value when only that predictor is included (dark blue), when only that predictor is removed (green), and when all predictors were included (red).



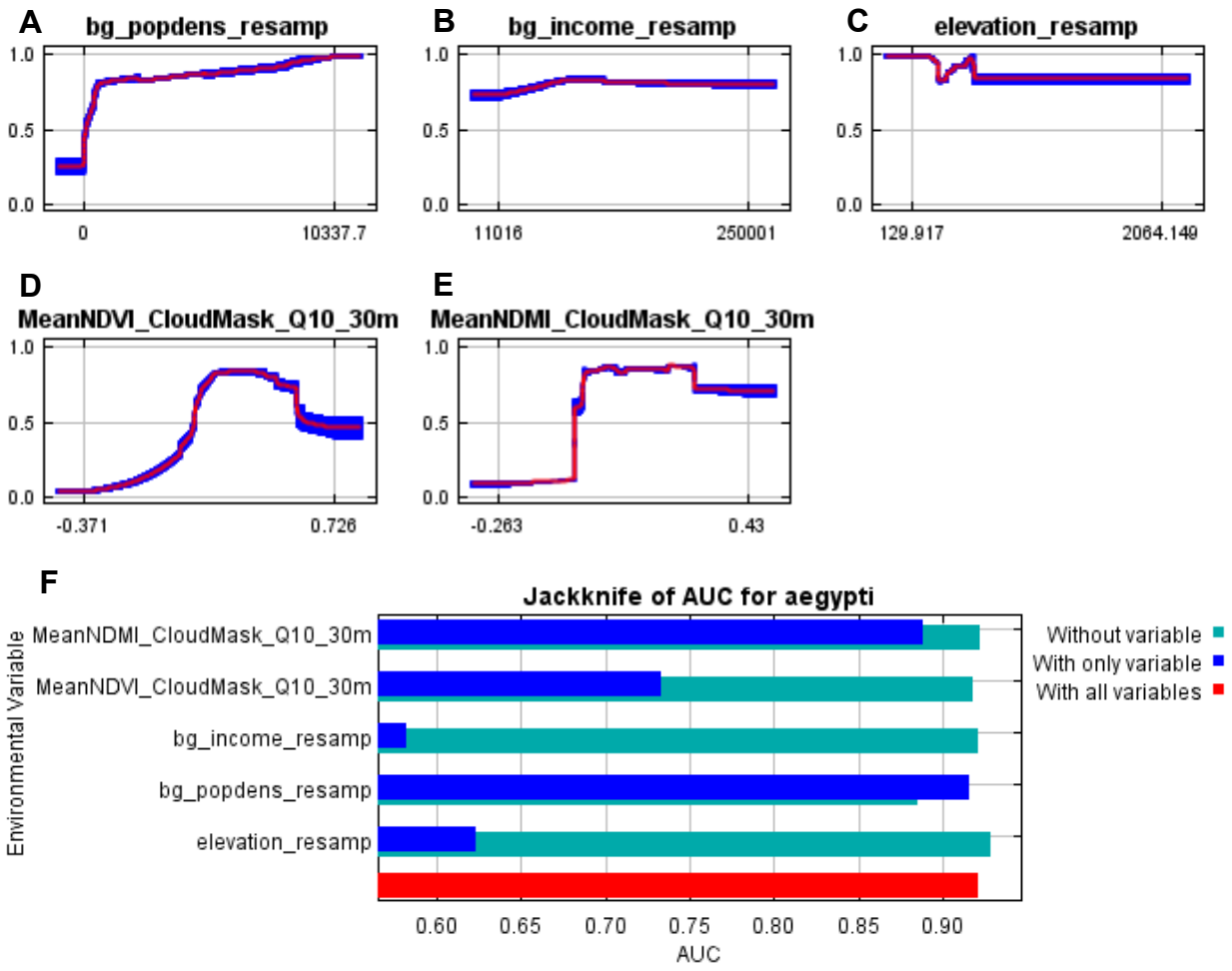
Supplementary Figure 3.43. Response curves for Quarter 7 (8/1/15—10/31/15). (**A**) through (**E**) show Maxent response curves for the predictors Population Density, Median Income, Elevation, mean Normalized Difference Vegetation Index (NDVI), and mean Normalized Difference Moisture Index (NDMI). Response curves are shown for each predictor when all other predictors are held constant. Mean response from 10 folds is shown with a red line, and +/- one standard deviation is shown in blue. (**F**) Maxent output showing the average change in the Area Under Curve (AUC) value when only that predictor is included (dark blue), when only that predictor is removed (green), and when all predictors were included (red).



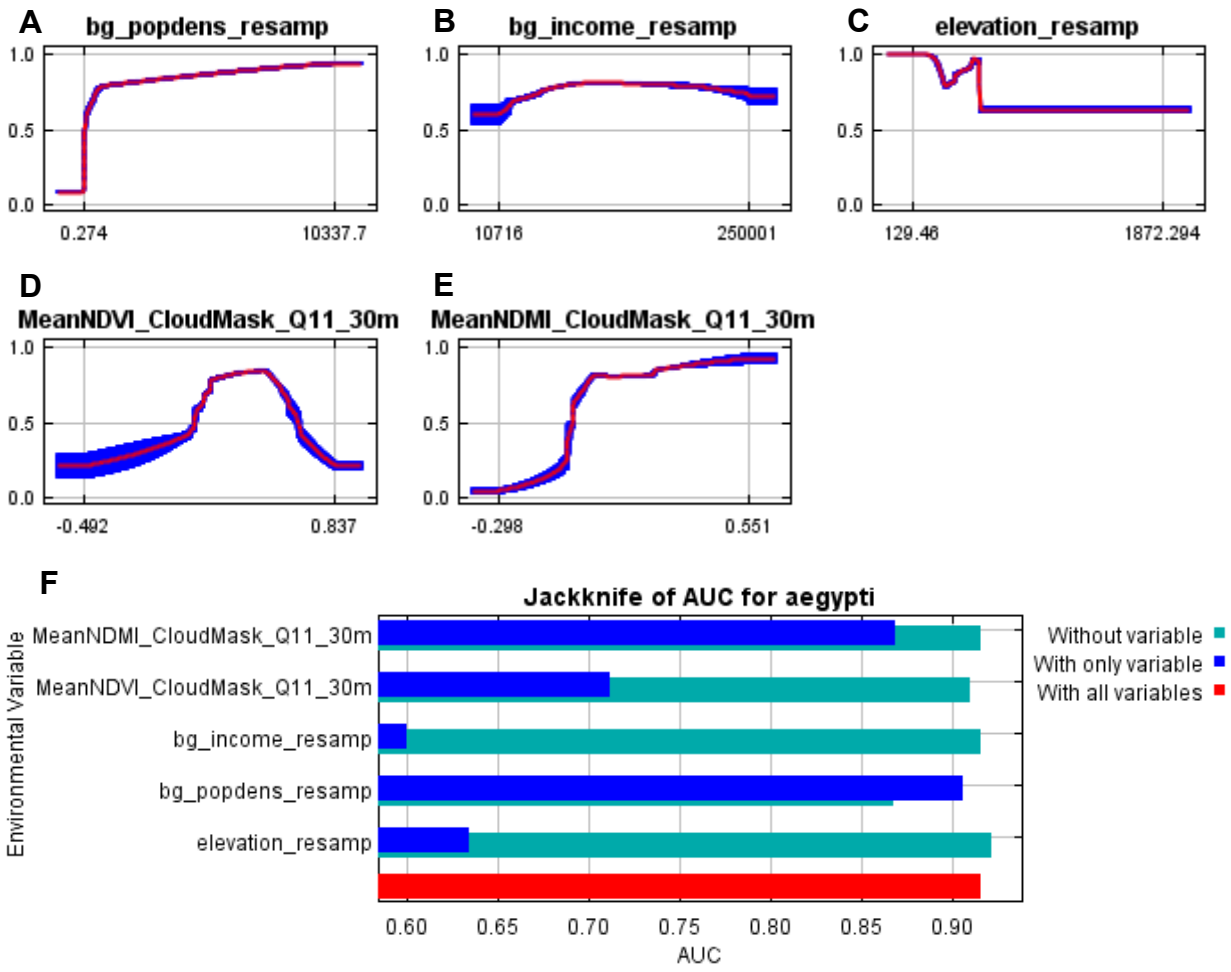
Supplementary Figure 3.44. Response curves for Quarter 8 (11/1/15—1/31/16). (**A**) through (**E**) show Maxent response curves for the predictors Population Density, Median Income, Elevation, mean Normalized Difference Vegetation Index (NDVI), and mean Normalized Difference Moisture Index (NDMI). Response curves are shown for each predictor when all other predictors are held constant. Mean response from 10 folds is shown with a red line, and +/- one standard deviation is shown in blue. (**F**) Maxent output showing the average change in the Area Under Curve (AUC) value when only that predictor is included (dark blue), when only that predictor is removed (green), and when all predictors were included (red).



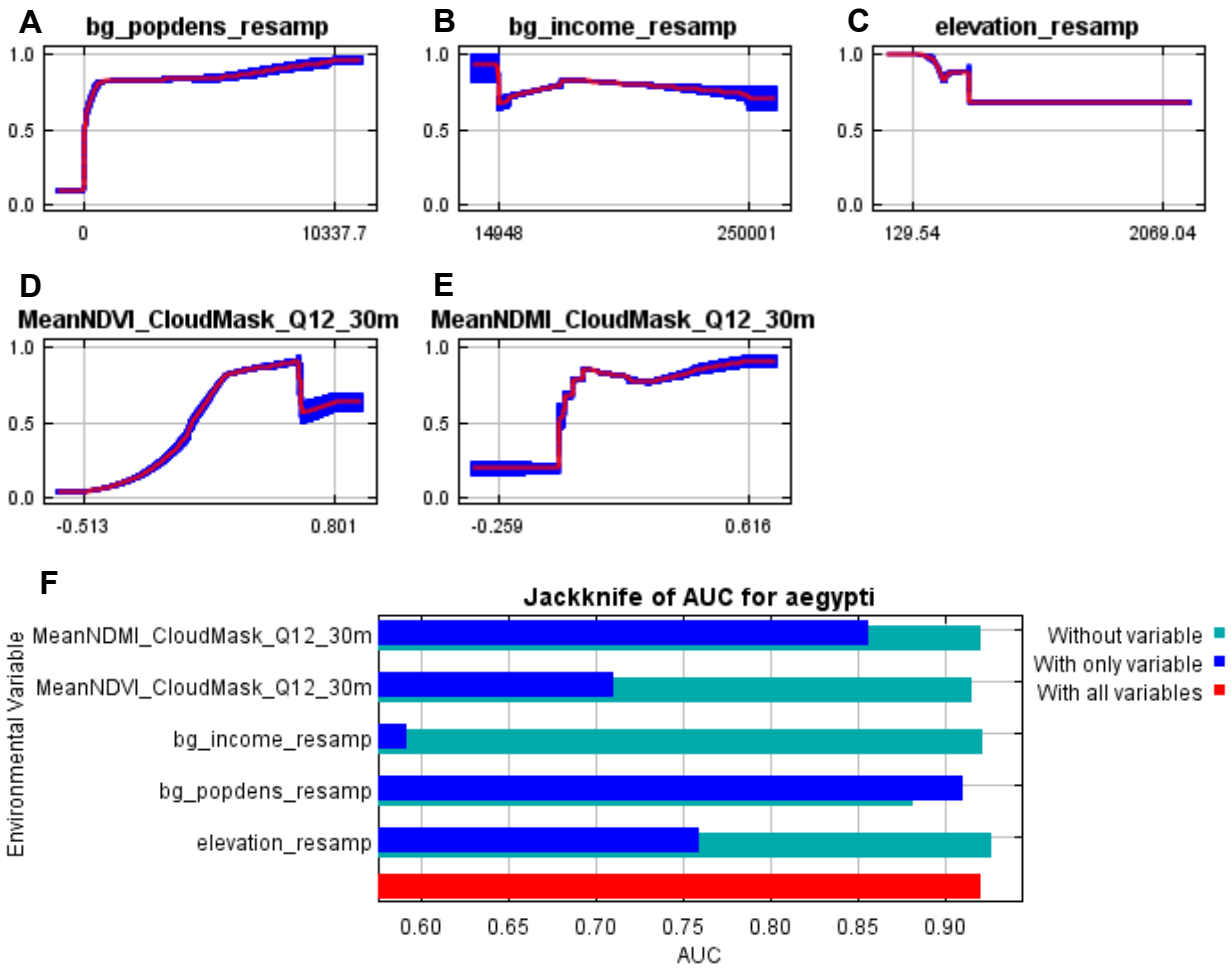
Supplementary Figure 3.45. Response curves for Quarter 9 (2/1/16—4/30/16). (**A**) through (**E**) show Maxent response curves for the predictors Population Density, Median Income, Elevation, mean Normalized Difference Vegetation Index (NDVI), and mean Normalized Difference Moisture Index (NDMI). Response curves are shown for each predictor when all other predictors are held constant. Mean response from 10 folds is shown with a red line, and +/- one standard deviation is shown in blue. (**F**) Maxent output showing the average change in the Area Under Curve (AUC) value when only that predictor is included (dark blue), when only that predictor is removed (green), and when all predictors were included (red).



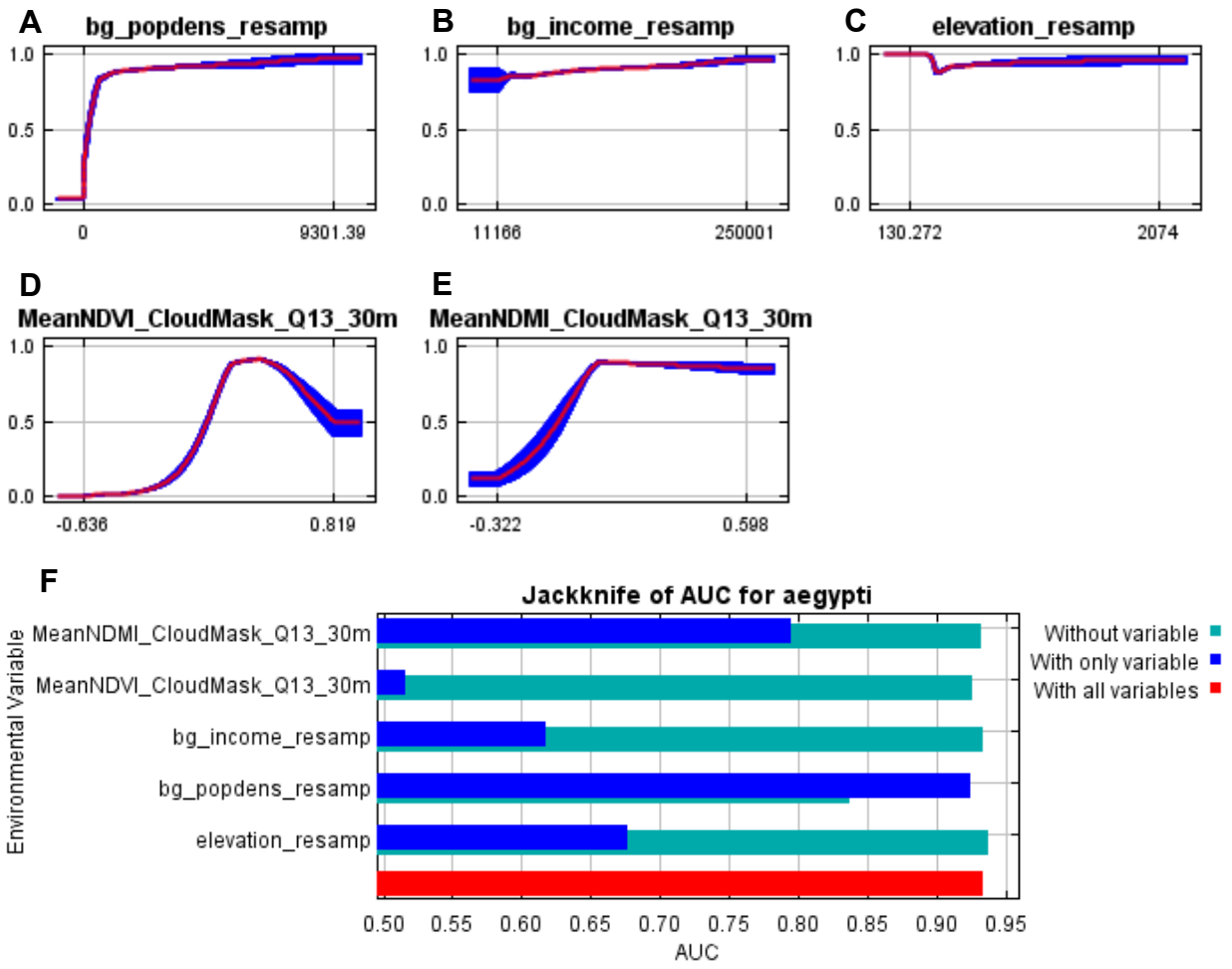
Supplementary Figure 3.46. Response curves for Quarter 10 (5/1/16—7/31/16). (**A**) through (**E**) show Maxent response curves for the predictors Population Density, Median Income, Elevation, mean Normalized Difference Vegetation Index (NDVI), and mean Normalized Difference Moisture Index (NDMI). Response curves are shown for each predictor when all other predictors are held constant. Mean response from 10 folds is shown with a red line, and +/- one standard deviation is shown in blue. (**F**) Maxent output showing the average change in the Area Under Curve (AUC) value when only that predictor is included (dark blue), when only that predictor is removed (green), and when all predictors were included (red).



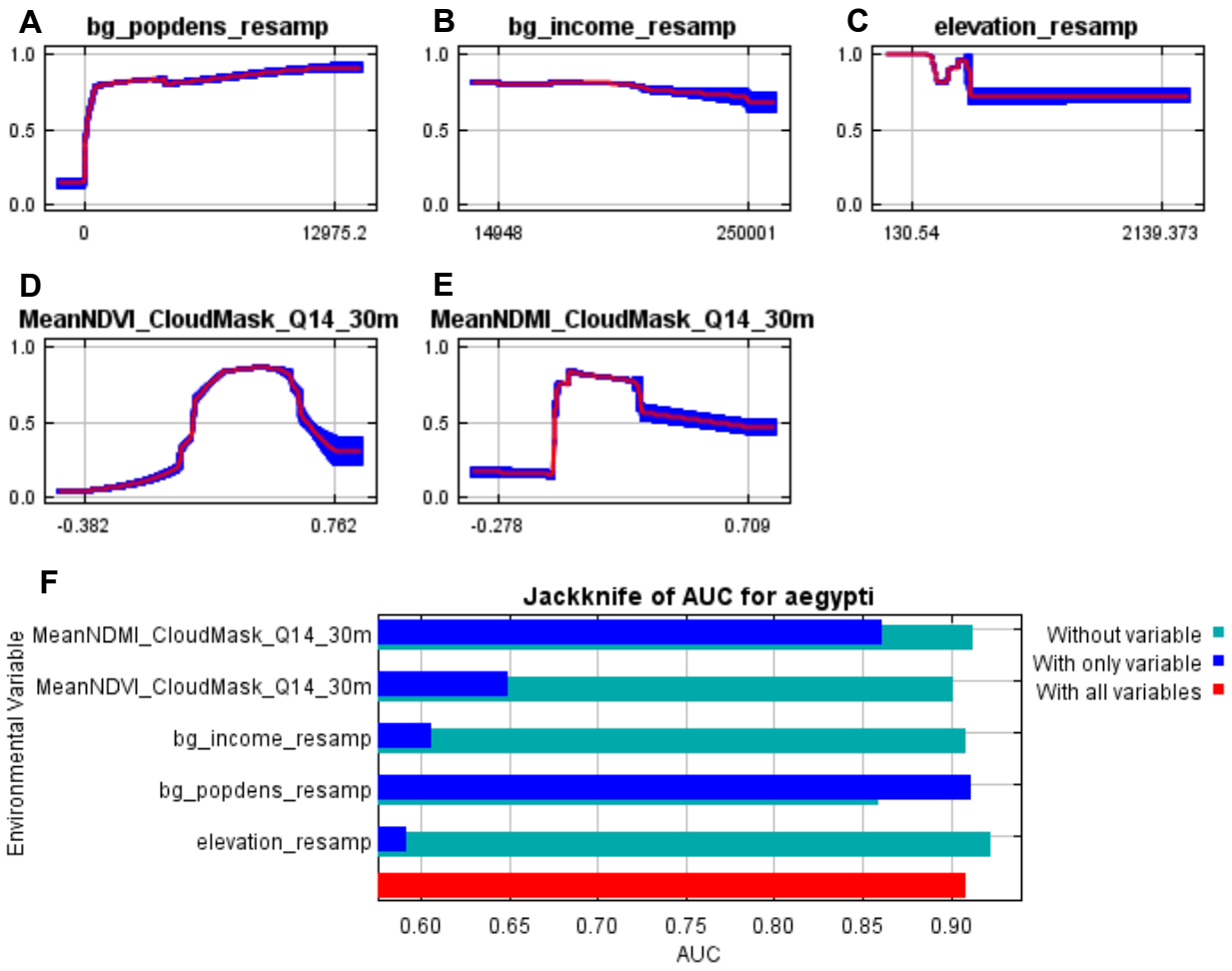
Supplementary Figure 3.47. Response curves for Quarter 11 (8/1/16—10/31/16). (**A**) through (**E**) show Maxent response curves for the predictors Population Density, Median Income, Elevation, mean Normalized Difference Vegetation Index (NDVI), and mean Normalized Difference Moisture Index (NDMI). Response curves are shown for each predictor when all other predictors are held constant. Mean response from 10 folds is shown with a red line, and +/- one standard deviation is shown in blue. (**F**) Maxent output showing the average change in the Area Under Curve (AUC) value when only that predictor is included (dark blue), when only that predictor is removed (green), and when all predictors were included (red).



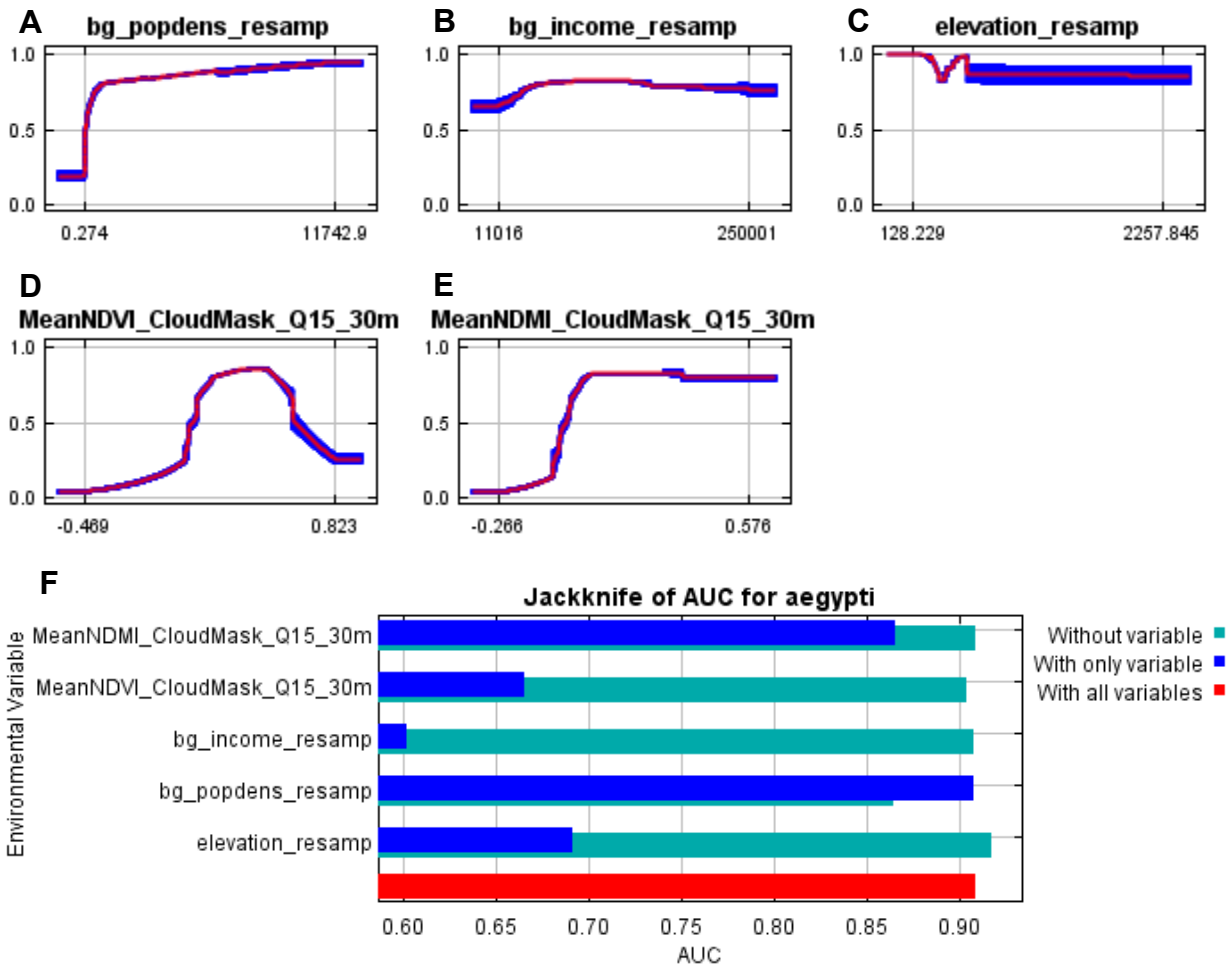
Supplementary Figure 3.48. Response curves for Quarter 12 (11/1/16—1/31/17). (**A**) through (**E**) show Maxent response curves for the predictors Population Density, Median Income, Elevation, mean Normalized Difference Vegetation Index (NDVI), and mean Normalized Difference Moisture Index (NDMI). Response curves are shown for each predictor when all other predictors are held constant. Mean response from 10 folds is shown with a red line, and +/- one standard deviation is shown in blue. (**F**) Maxent output showing the average change in the Area Under Curve (AUC) value when only that predictor is included (dark blue), when only that predictor is removed (green), and when all predictors were included (red).



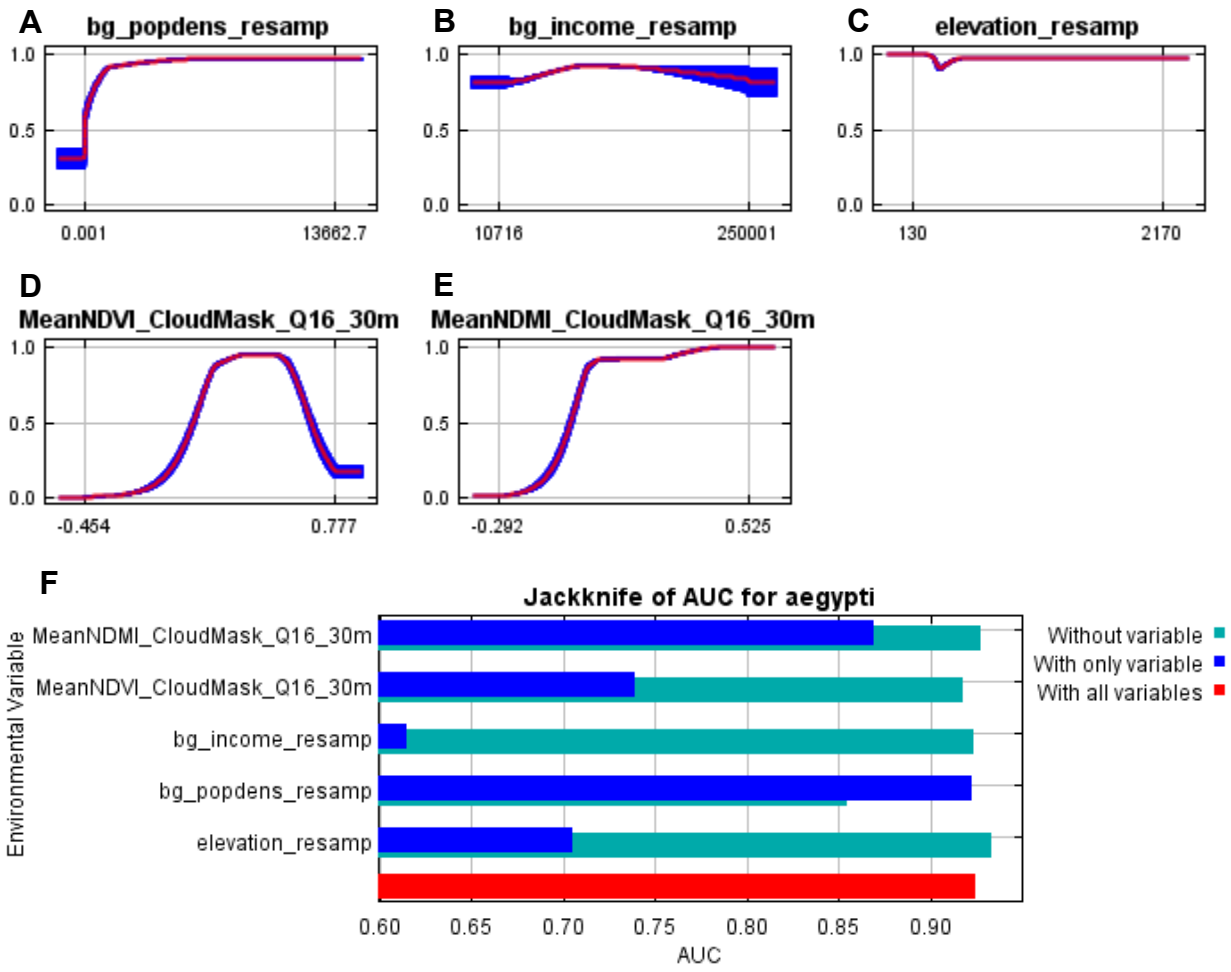
Supplementary Figure 3.49. Response curves for Quarter 13 (2/1/17—4/30/17). (**A**) through (**E**) show Maxent response curves for the predictors Population Density, Median Income, Elevation, mean Normalized Difference Vegetation Index (NDVI), and mean Normalized Difference Moisture Index (NDMI). Response curves are shown for each predictor when all other predictors are held constant. Mean response from 10 folds is shown with a red line, and +/- one standard deviation is shown in blue. (**F**) Maxent output showing the average change in the Area Under Curve (AUC) value when only that predictor is included (dark blue), when only that predictor is removed (green), and when all predictors were included (red).



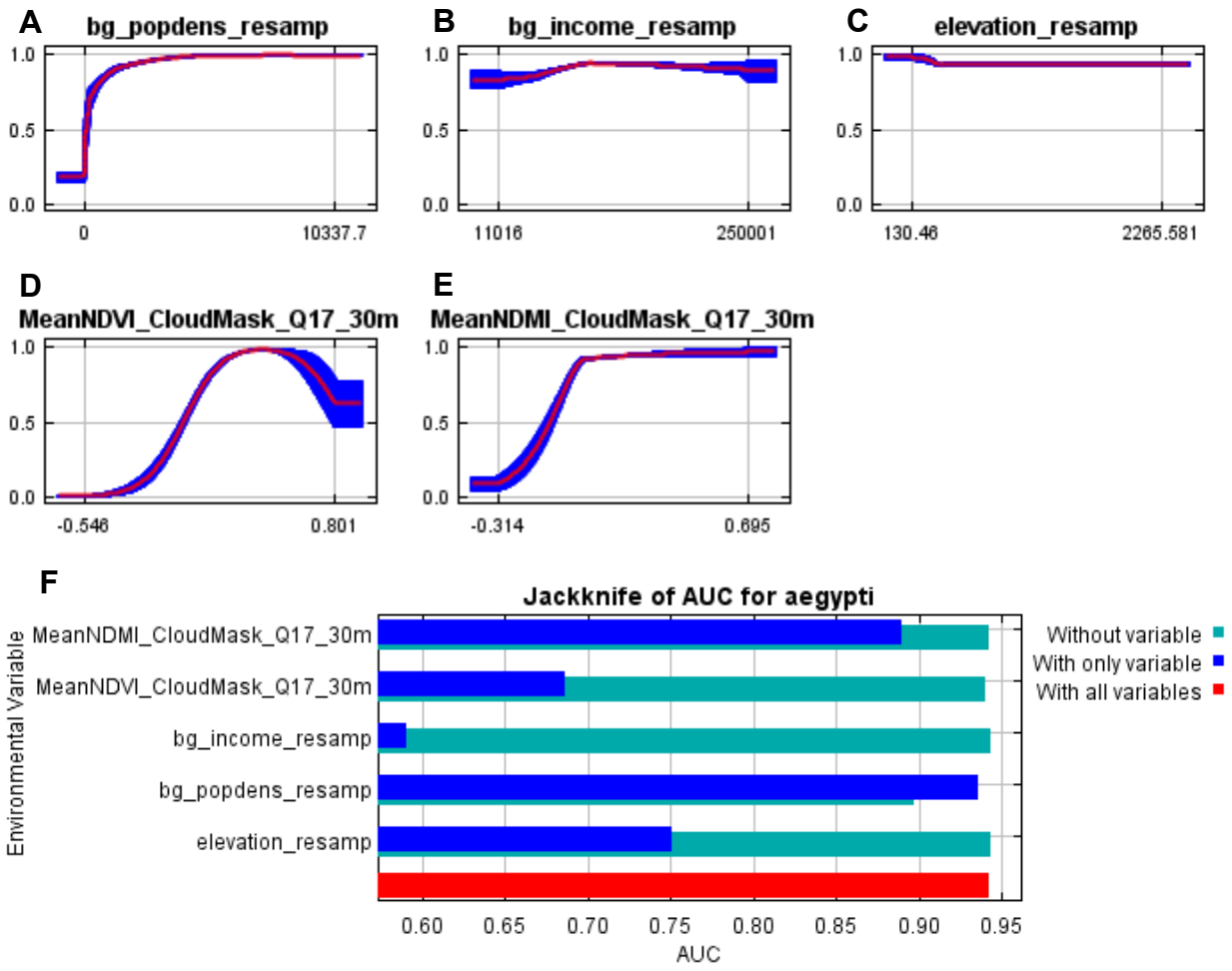
Supplementary Figure 3.50. Response curves for Quarter 14 (5/1/17—7/31/17). (**A**) through (**E**) show Maxent response curves for the predictors Population Density, Median Income, Elevation, mean Normalized Difference Vegetation Index (NDVI), and mean Normalized Difference Moisture Index (NDMI). Response curves are shown for each predictor when all other predictors are held constant. Mean response from 10 folds is shown with a red line, and +/- one standard deviation is shown in blue. (**F**) Maxent output showing the average change in the Area Under Curve (AUC) value when only that predictor is included (dark blue), when only that predictor is removed (green), and when all predictors were included (red).



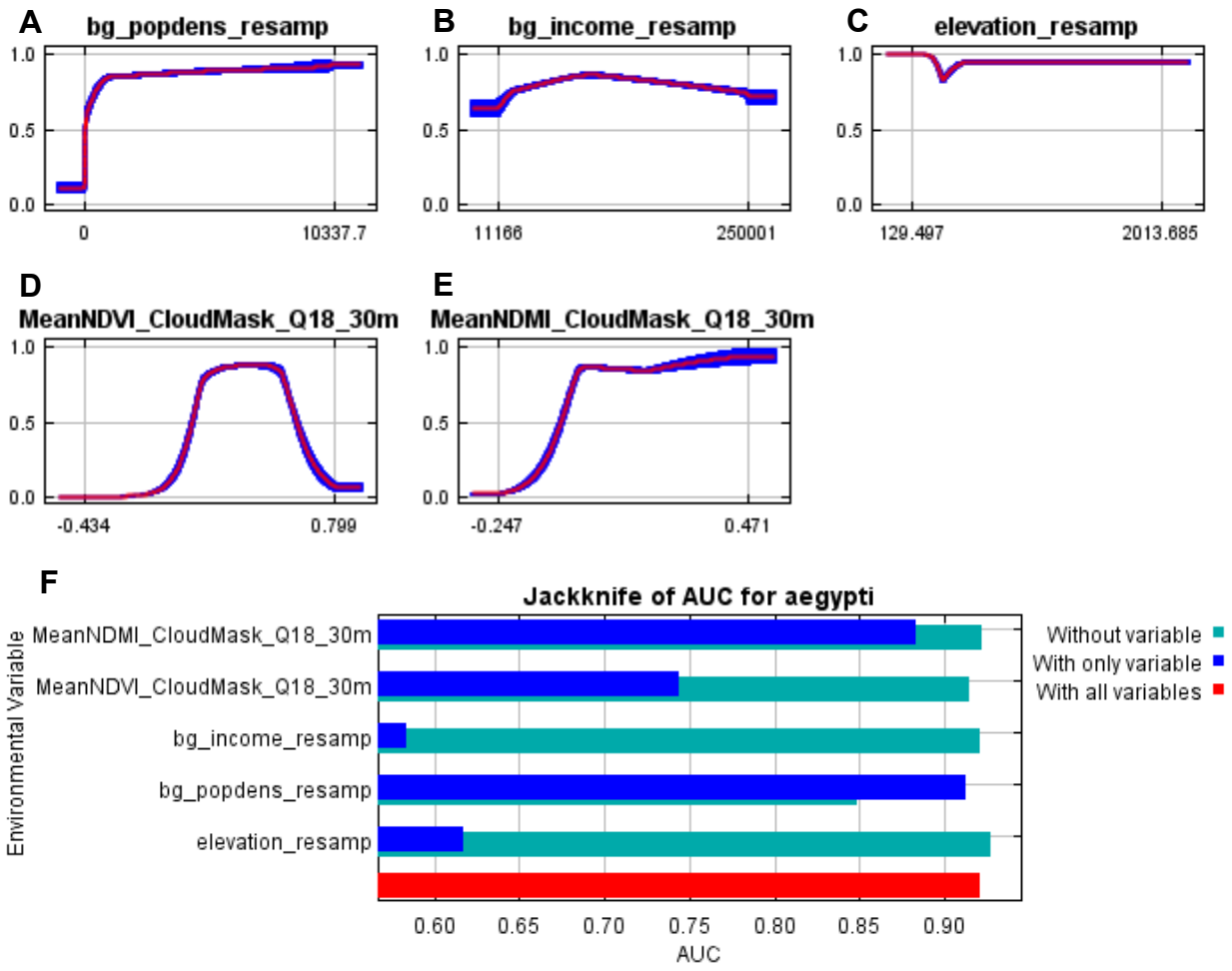
Supplementary Figure 3.51. Response curves for Quarter 15 (8/1/17—10/31/17). (**A**) through (**E**) show Maxent response curves for the predictors Population Density, Median Income, Elevation, mean Normalized Difference Vegetation Index (NDVI), and mean Normalized Difference Moisture Index (NDMI). Response curves are shown for each predictor when all other predictors are held constant. Mean response from 10 folds is shown with a red line, and +/- one standard deviation is shown in blue. (**F**) Maxent output showing the average change in the Area Under Curve (AUC) value when only that predictor is included (dark blue), when only that predictor is removed (green), and when all predictors were included (red).



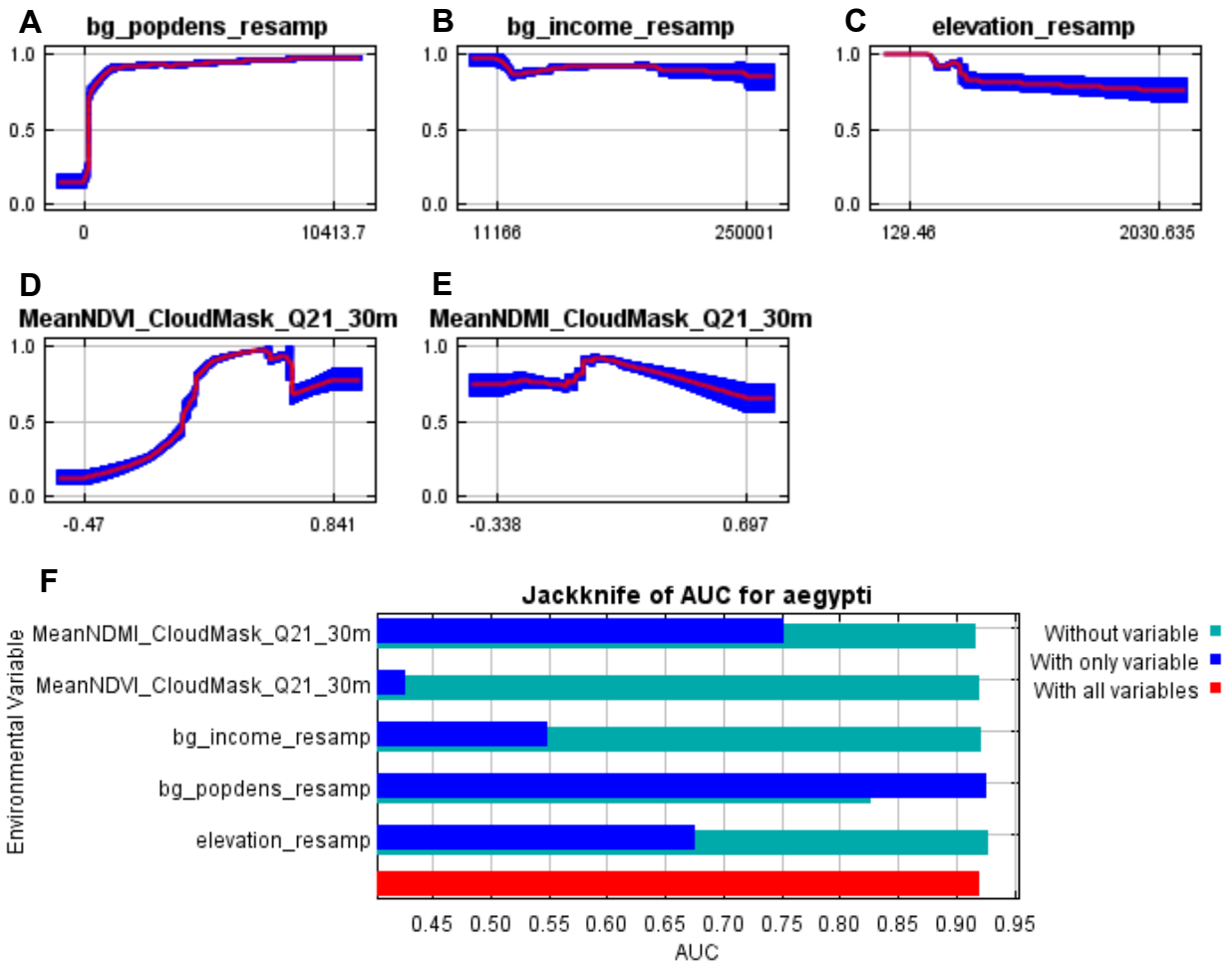
Supplementary Figure 3.52. Response curves for Quarter 16 (11/1/17—1/31/18). (**A**) through (**E**) show Maxent response curves for the predictors Population Density, Median Income, Elevation, mean Normalized Difference Vegetation Index (NDVI), and mean Normalized Difference Moisture Index (NDMI). Response curves are shown for each predictor when all other predictors are held constant. Mean response from 10 folds is shown with a red line, and +/- one standard deviation is shown in blue. (**F**) Maxent output showing the average change in the Area Under Curve (AUC) value when only that predictor is included (dark blue), when only that predictor is removed (green), and when all predictors were included (red).



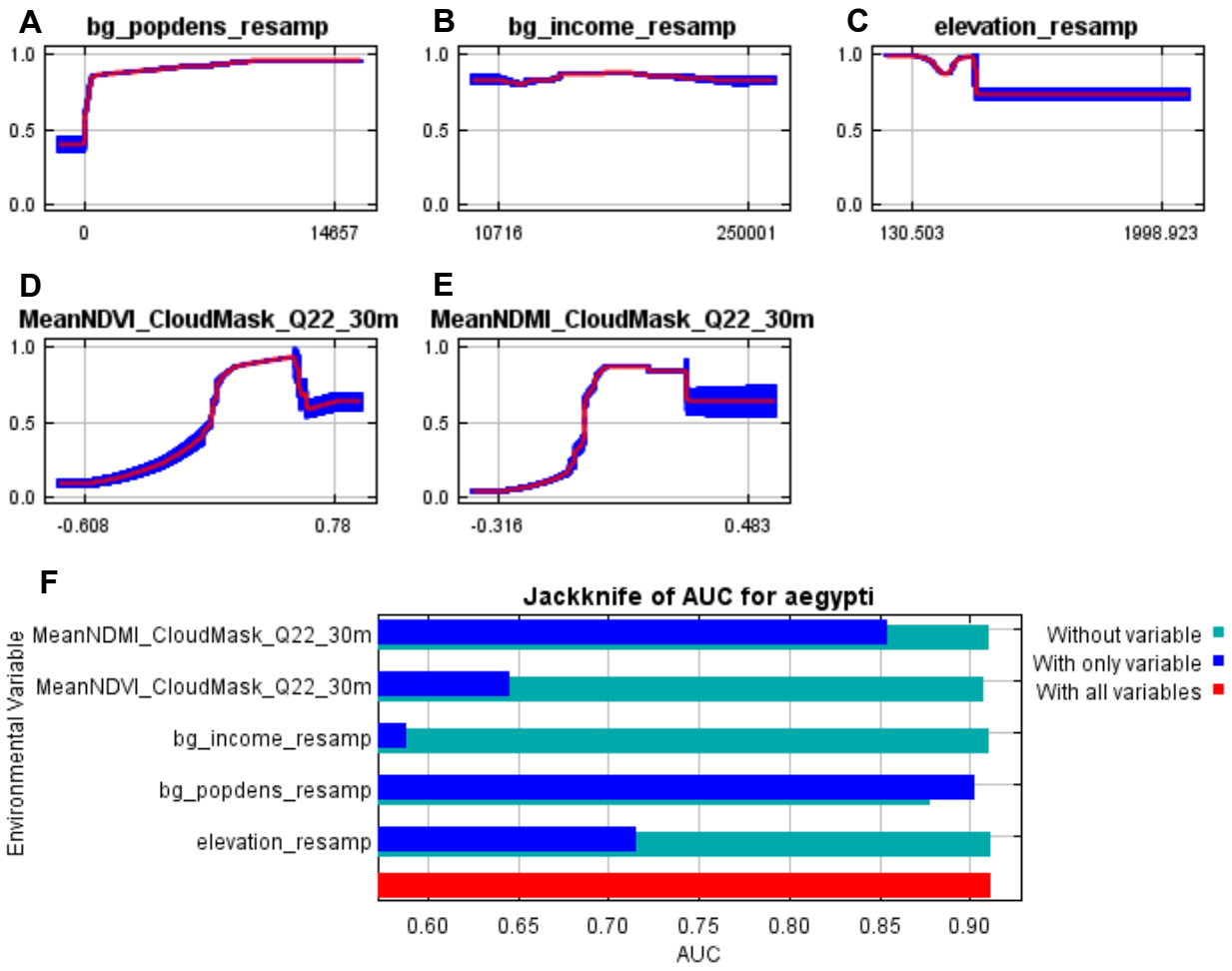
Supplementary Figure 3.53. Response curves for Quarter 17 (2/1/18—4/30/18). (**A**) through (**E**) show Maxent response curves for the predictors Population Density, Median Income, Elevation, mean Normalized Difference Vegetation Index (NDVI), and mean Normalized Difference Moisture Index (NDMI). Response curves are shown for each predictor when all other predictors are held constant. Mean response from 10 folds is shown with a red line, and +/- one standard deviation is shown in blue. (**F**) Maxent output showing the average change in the Area Under Curve (AUC) value when only that predictor is included (dark blue), when only that predictor is removed (green), and when all predictors were included (red).



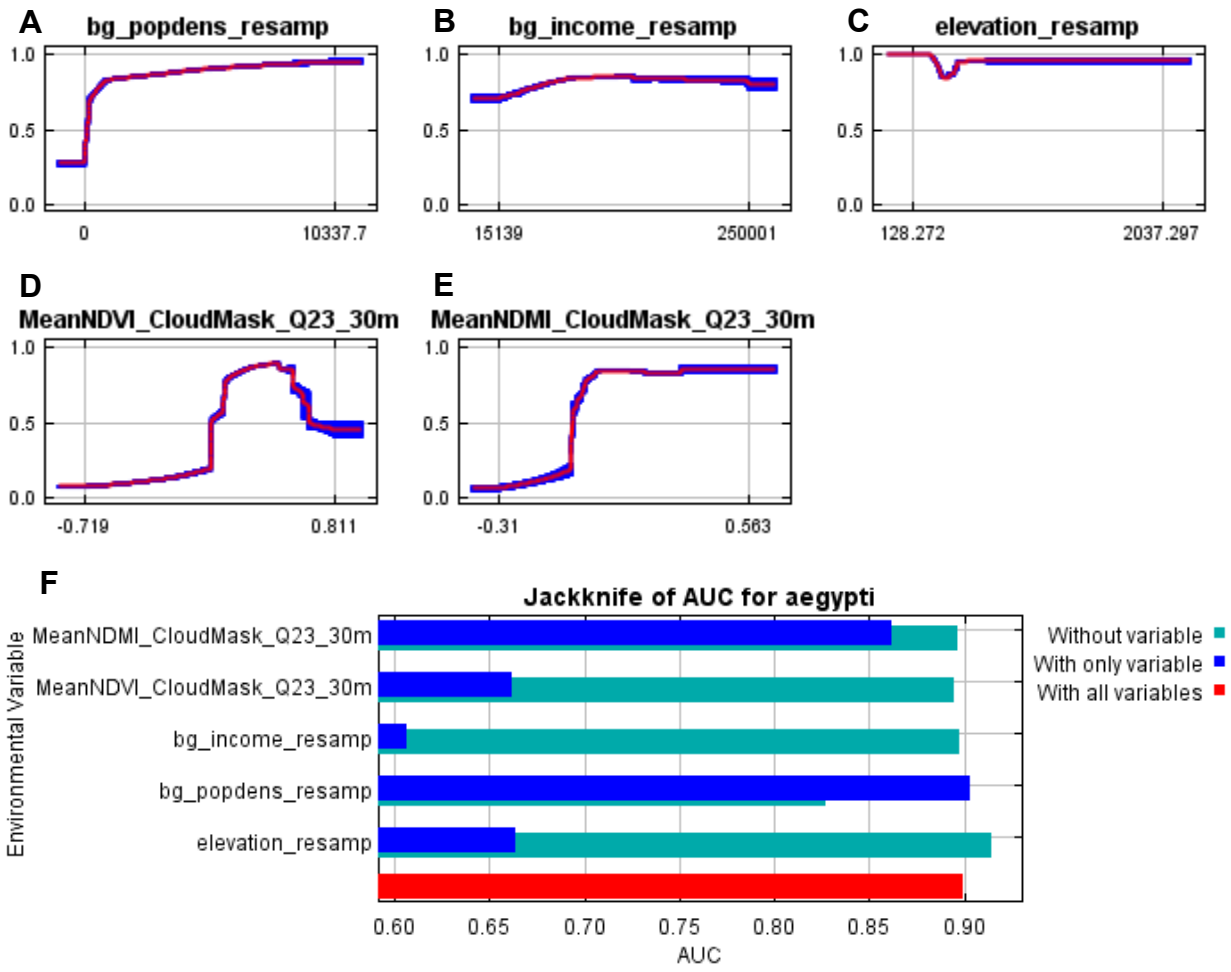
Supplementary Figure 3.54. Response curves for Quarter 18 (5/1/18—7/31/18). (**A**) through (**E**) show Maxent response curves for the predictors Population Density, Median Income, Elevation, mean Normalized Difference Vegetation Index (NDVI), and mean Normalized Difference Moisture Index (NDMI). Response curves are shown for each predictor when all other predictors are held constant. Mean response from 10 folds is shown with a red line, and +/- one standard deviation is shown in blue. (**F**) Maxent output showing the average change in the Area Under Curve (AUC) value when only that predictor is included (dark blue), when only that predictor is removed (green), and when all predictors were included (red).



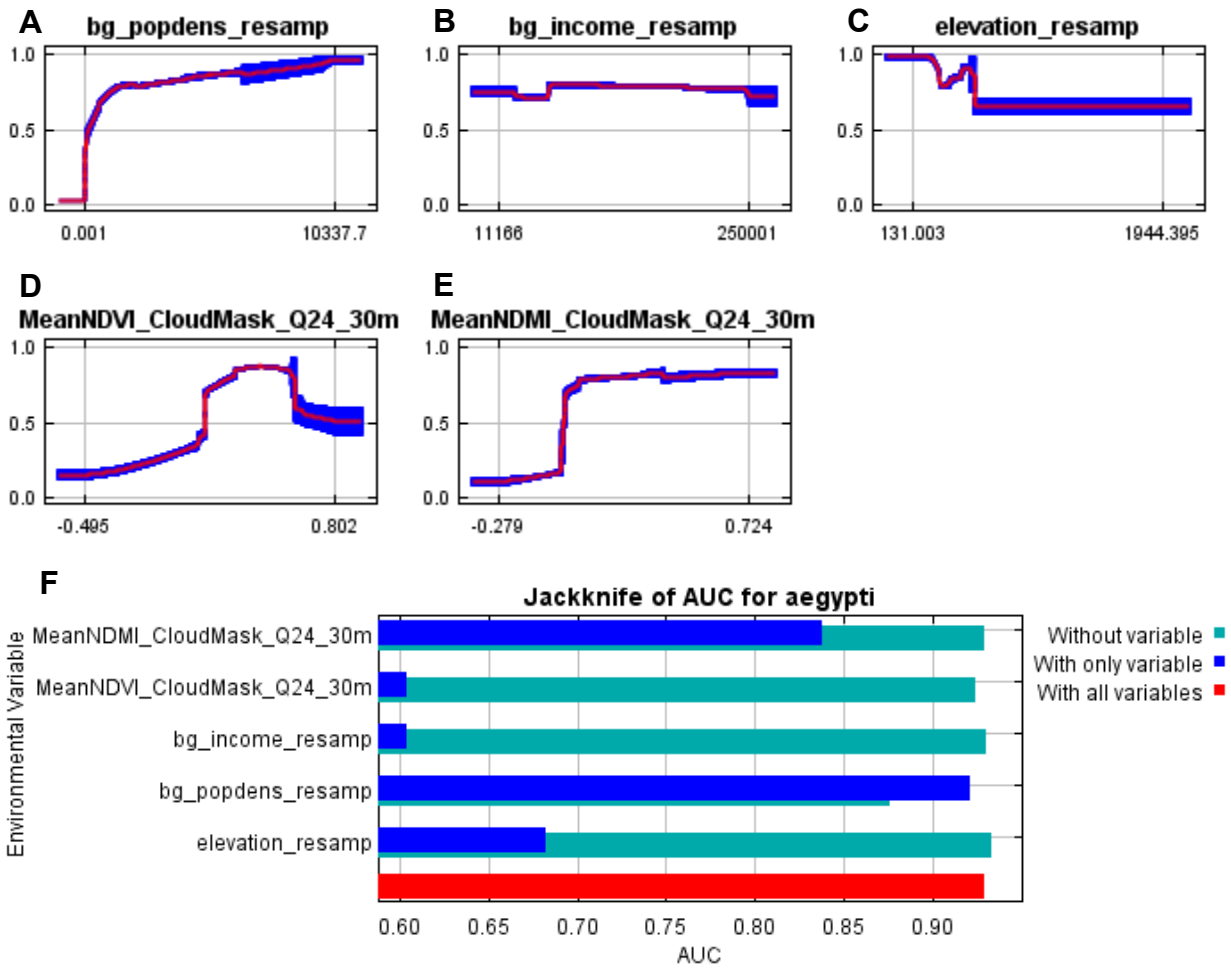
Supplementary Figure 3.55. Response curves for Quarter 21 (2/1/19—4/30/19). (**A**) through (**E**) show Maxent response curves for the predictors Population Density, Median Income, Elevation, mean Normalized Difference Vegetation Index (NDVI), and mean Normalized Difference Moisture Index (NDMI). Response curves are shown for each predictor when all other predictors are held constant. Mean response from 10 folds is shown with a red line, and +/- one standard deviation is shown in blue. (**F**) Maxent output showing the average change in the Area Under Curve (AUC) value when only that predictor is included (dark blue), when only that predictor is removed (green), and when all predictors were included (red).



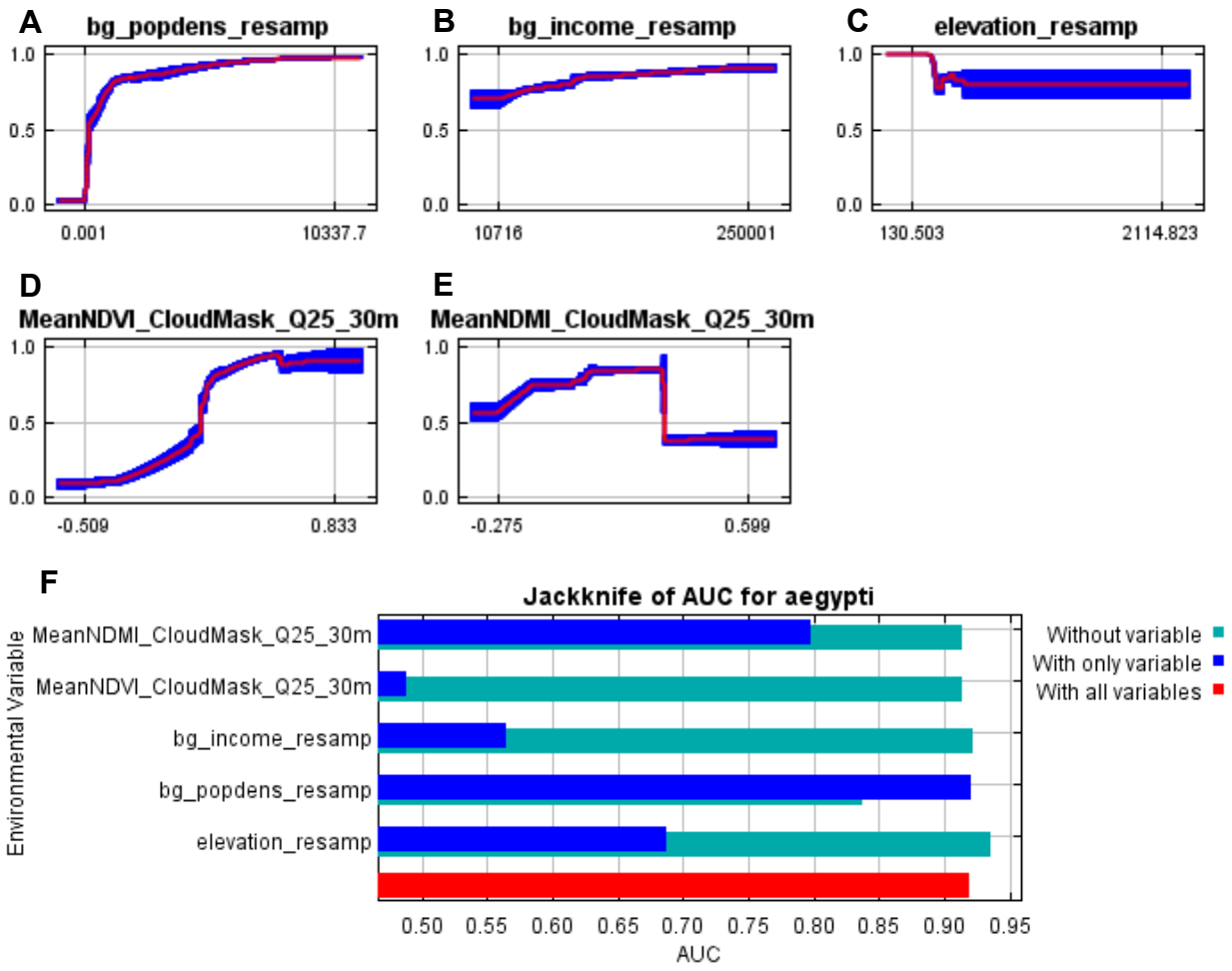
Supplementary Figure 3.56. Response curves for Quarter 22 (5/1/19—7/31/19). (**A**) through (**E**) show Maxent response curves for the predictors Population Density, Median Income, Elevation, mean Normalized Difference Vegetation Index (NDVI), and mean Normalized Difference Moisture Index (NDMI). Response curves are shown for each predictor when all other predictors are held constant. Mean response from 10 folds is shown with a red line, and +/- one standard deviation is shown in blue. (**F**) Maxent output showing the average change in the Area Under Curve (AUC) value when only that predictor is included (dark blue), when only that predictor is removed (green), and when all predictors were included (red).



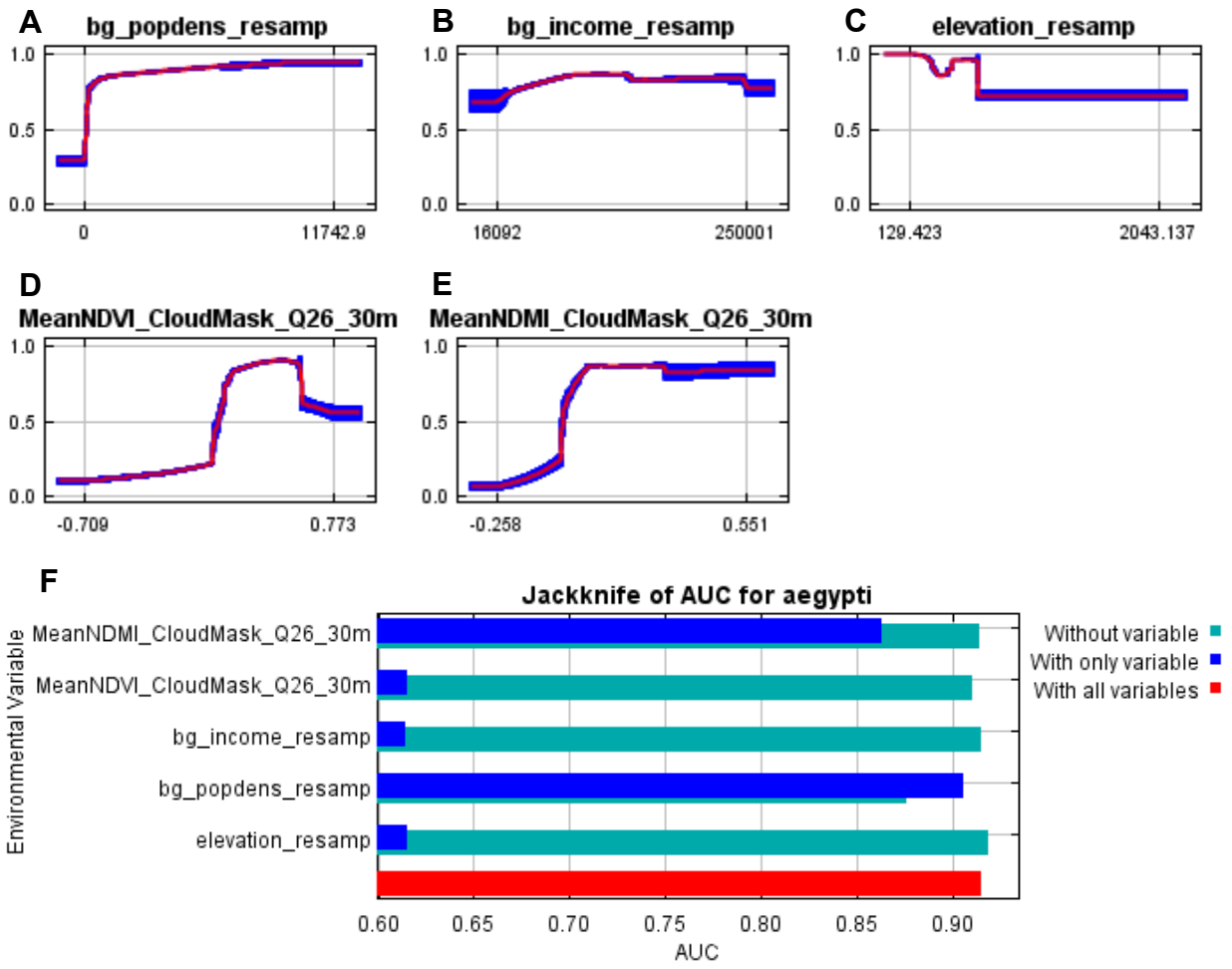
Supplementary Figure 3.57. Response curves for Quarter 23 (8/1/19—10/31/19). (**A**) through (**E**) show Maxent response curves for the predictors Population Density, Median Income, Elevation, mean Normalized Difference Vegetation Index (NDVI), and mean Normalized Difference Moisture Index (NDMI). Response curves are shown for each predictor when all other predictors are held constant. Mean response from 10 folds is shown with a red line, and +/- one standard deviation is shown in blue. (**F**) Maxent output showing the average change in the Area Under Curve (AUC) value when only that predictor is included (dark blue), when only that predictor is removed (green), and when all predictors were included (red).



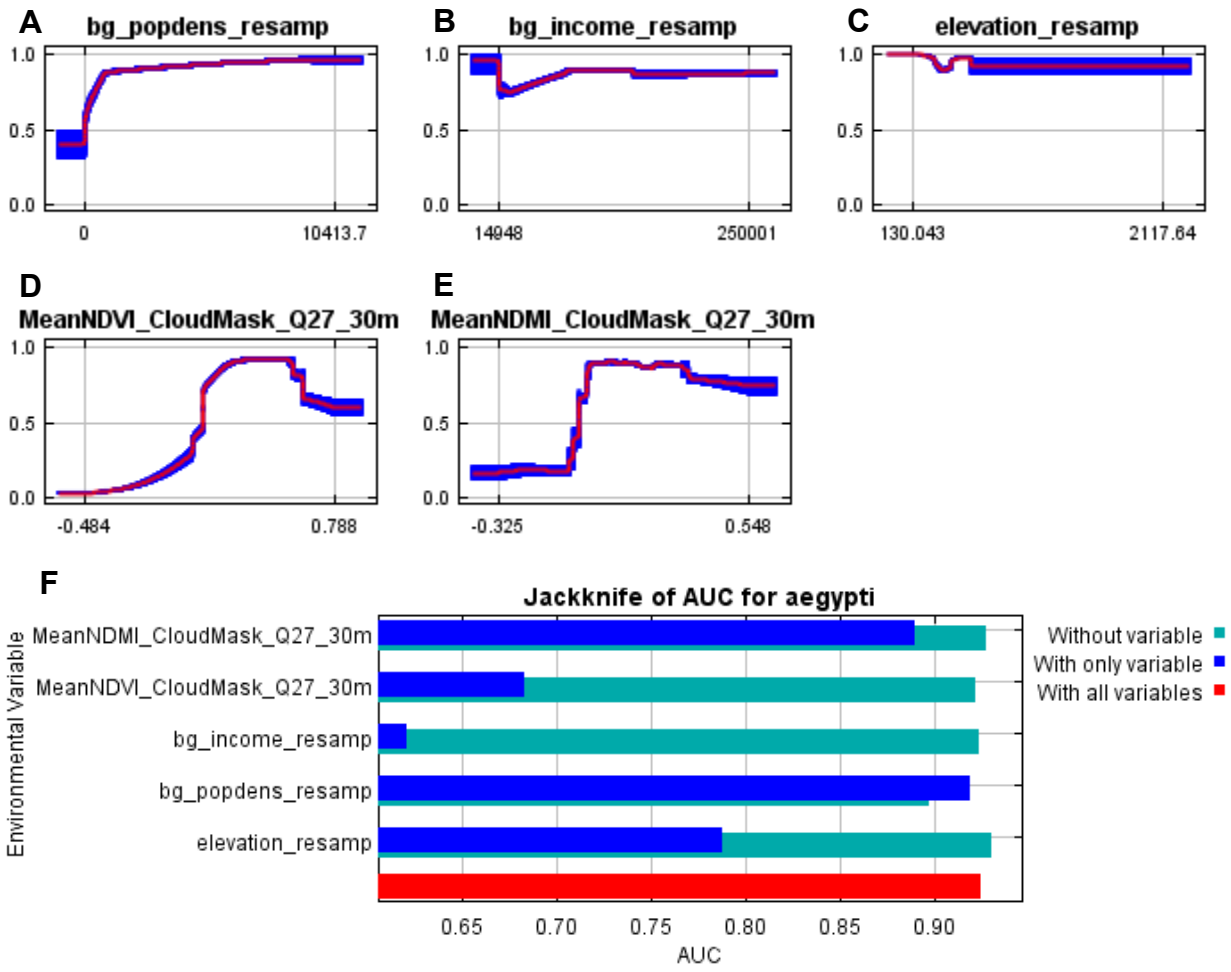
Supplementary Figure 3.58. Response curves for Quarter 24 (11/1/19—1/31/20). (**A**) through (**E**) show Maxent response curves for the predictors Population Density, Median Income, Elevation, mean Normalized Difference Vegetation Index (NDVI), and mean Normalized Difference Moisture Index (NDMI). Response curves are shown for each predictor when all other predictors are held constant. Mean response from 10 folds is shown with a red line, and +/- one standard deviation is shown in blue. (**F**) Maxent output showing the average change in the Area Under Curve (AUC) value when only that predictor is included (dark blue), when only that predictor is removed (green), and when all predictors were included (red).



Supplementary Figure 3.59. Response curves for Quarter 25 (2/1/20—4/30/20). (**A**) through (**E**) show Maxent response curves for the predictors Population Density, Median Income, Elevation, mean Normalized Difference Vegetation Index (NDVI), and mean Normalized Difference Moisture Index (NDMI). Response curves are shown for each predictor when all other predictors are held constant. Mean response from 10 folds is shown with a red line, and +/- one standard deviation is shown in blue. (**F**) Maxent output showing the average change in the Area Under Curve (AUC) value when only that predictor is included (dark blue), when only that predictor is removed (green), and when all predictors were included (red).



Supplementary Figure 3.60. Response curves for Quarter 26 (5/1/20—7/31/20). (**A**) through (**E**) show Maxent response curves for the predictors Population Density, Median Income, Elevation, mean Normalized Difference Vegetation Index (NDVI), and mean Normalized Difference Moisture Index (NDMI). Response curves are shown for each predictor when all other predictors are held constant. Mean response from 10 folds is shown with a red line, and +/- one standard deviation is shown in blue. (**F**) Maxent output showing the average change in the Area Under Curve (AUC) value when only that predictor is included (dark blue), when only that predictor is removed (green), and when all predictors were included (red).



Supplementary Figure 3.61. Response curves for Quarter 27 (8/1/20—10/31/20). (**A**) through (**E**) show Maxent response curves for the predictors Population Density, Median Income, Elevation, mean Normalized Difference Vegetation Index (NDVI), and mean Normalized Difference Moisture Index (NDMI). Response curves are shown for each predictor when all other predictors are held constant. Mean response from 10 folds is shown with a red line, and +/- one standard deviation is shown in blue. (**F**) Maxent output showing the average change in the Area Under Curve (AUC) value when only that predictor is included (dark blue), when only that predictor is removed (green), and when all predictors were included (red).

SUPPLEMENTARY TABLES FOR CHAPTER 3: SPECIES DISTRIBUTION MODELING OF *AEDES AEGYPTI* IN MARICOPA COUNTY, ARIZONA FROM 2014 TO 2020

Quarter	Feature Settings	Regularization Meter
1	LQHPT	1
2	LQHPT	1
3	LQHPT	1
4	LQHP	1
5	LQHPT	1
6	H	1
7	LQHPT	1
8	LQHPT	1
9	LQHPT	1
10	LQHPT	1
11	LQHPT	1
12	LQHPT	1
13	LQHP	1
14	LQHPT	1
15	LQHPT	1
16	H	1
17	LQH	1
18	LQHP	1
19	n/a	n/a
20	n/a	n/a
21	LQHPT	1
22	LQHPT	1
23	LQHPT	1
24	LQHPT	1
25	LQHPT	1
26	LQHPT	1
27	LQHPT	1
28	n/a	n/a

Supplementary Table 3.1. Maxent settings used for each quarter. Abbreviations for feature settings are as follows: L = linear, Q = quadratic, H = hinge, P = product, T = threshold. The feature settings determine the mathematical transformations of the predictors. The regularization multiplier is a penalty that is used to reduce model overfitting.

	NDVI				NDMI			
Quarter	Min.	Max.	Mean	S.D.	Min.	Max.	Mean	S.D.
1	-0.83	0.86	0.21	0.10	-0.48	0.88	0.00	0.08
2	-0.80	0.85	0.17	0.09	-0.47	0.84	-0.04	0.08
3	-0.83	0.85	0.21	0.11	-0.55	0.93	-0.01	0.09
4	-0.84	0.87	0.20	0.10	-0.61	0.95	0.00	0.09
5	-0.85	0.86	0.21	0.11	-0.53	0.85	-0.01	0.09
6	-0.78	0.81	0.18	0.09	-0.45	0.83	-0.04	0.08
7	-0.83	0.85	0.18	0.10	-0.55	0.86	-0.03	0.09
8	-0.91	0.87	0.18	0.10	-0.60	0.97	-0.02	0.10
9	-0.82	0.87	0.19	0.10	-0.54	0.89	-0.02	0.09
10	-0.72	0.82	0.16	0.09	-0.50	0.80	-0.04	0.08
11	-0.84	0.86	0.17	0.10	-0.71	0.90	-0.03	0.08
12	-0.91	0.87	0.17	0.10	-0.61	0.97	-0.02	0.09
13	-0.84	0.88	0.23	0.11	-0.54	0.92	0.01	0.08
14	-0.74	0.85	0.18	0.09	-0.47	0.87	-0.04	0.08
15	-0.80	0.85	0.18	0.10	-0.58	0.88	-0.03	0.09
16	-0.84	0.85	0.17	0.09	-0.50	0.89	-0.02	0.09
17	-0.89	0.86	0.16	0.09	-0.46	0.88	-0.04	0.08
18	-0.78	0.84	0.16	0.09	-0.45	0.89	-0.05	0.08
19	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a
20	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a
21	-0.85	0.86	0.25	0.11	-0.54	0.89	0.04	0.08
22	-0.77	0.82	0.19	0.09	-0.57	0.83	-0.03	0.08
23	-0.77	0.84	0.19	0.10	-0.58	0.95	-0.03	0.09
24	-0.81	0.85	0.22	0.10	-0.55	0.99	0.01	0.10
25	-0.84	0.87	0.26	0.11	-0.59	0.92	0.03	0.09
26	-0.81	0.83	0.20	0.09	-0.57	0.90	-0.03	0.08
27	-0.75	0.82	0.18	0.09	-0.51	0.76	-0.05	0.08
28	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a

Supplementary Table 3.2. Range, mean, and standard deviation of NDVI and NDMI values for each quarter.

SUPPLEMENTARY DATA AND CODE FOR CHAPTER 4: SPATIOTEMPORAL BAYESIAN MODELING OF THE PRESENCE OF *AEDES AEGYPTI* MOSQUITOES IN MARICOPA COUNTY, ARIZONA

Data and code used in this analysis is available in a public Google Drive at https://drive.google.com/drive/folders/1AwMr29aQjNJeiqculCxtrVkXSZVlQ5c9?usp=share_link. Latitude and longitude values have been truncated to the hundredths digit and jittered to address concerns of trap theft or destruction.

SUPPLEMENTARY TABLES FOR CHAPTER 4: SPATIOTEMPORAL BAYESIAN MODELING OF THE PRESENCE OF *AEDES AEGYPTI* MOSQUITOES IN MARICOPA COUNTY, ARIZONA

Supplementary Table 4.1. Variance Inflation Factor to evaluate multicollinearity of model predictors. Census predictors were evaluated separately from greenness and weather predictors. No predictors had a high VIF (>3) that would indicate multicollinearity.

Census Predictors	VIF		Greenness and Weather Predictors	VIF
Median Income	1.13		EVI Lag 1	1.00
Population Density	1.23		Sum Precip. Lag 1	1.15
Median House Age	1.26		Mean Max. Temp. Lag 1	1.66
			Vapor Pressure Lag 1	1.83
			Sum Precip. Lag 2	1.15

Supplementary Table 4.2. Interpretation of fixed effects from zero-inflated binomial model with spatial and temporal random effects. For each variable, an increase by one standard deviation results in the mean percent change of odds of *Aedes aegypti* presence, holding the other variables constant.

	S.D.	Mean Percent Change	95% Credible Interval
Median Income	41,403	13.7	(6.6, 21.2)
Population Density	1,222	12.1	(3.6, 21.3)
Median House Age	15	45.5	(35.7, 56.0)
EVI Lag 1	0.066	3.6	(1.3, 5.8)
Sum Precip. Lag 1	10.9	-8.6	(-9.9, -7.4)
Mean Max Temp Lag 1	8.0	-56.1	(-58.1, -54.1)
Mean VP Lag 1	531	61.3	(57.9, 64.7)
Sum Precip. Lag 2	11.0	-0.5	(-1.8, 0.8)

Supplementary Table 4.3. Confusion matrix and performance metrics for 2014.
Classification was based on a cutoff value of 0.188979.

	True Positive	True Negative	Total
Predicted Positive	3,362	6,585	9,947
Predicted Negative	483	16,238	16,721
Total	3,845	22,823	26,668

	Estimate	95% Credible Interval
AUC	0.876	(0.869, 0.883)

	Value	Derivation	Calculation
Accuracy	0.735	(TP + TN) / (P + N)	(3,362 + 16,238) / (3,845 + 22,823)
Sensitivity	0.874	TP / (TP + FN)	3,362 / (3,362 + 483)
Specificity	0.712	TN / (FP + TN)	16,238 / (6,585 + 16,238)
Precision	0.338	TP / (TP + FP)	3,362 / (3,362 + 6,585)
Negative Predictive Value	0.971	TN / (TN + FN)	16,238 / (16,238 + 483)
False Positive Rate	0.289	FP / (FP + TN)	6,585 / (6,585 + 16,238)
False Negative Rate	0.126	FN / (FN + TP)	483 / (483 + 3,362)

Supplementary Table 4.4. Confusion matrix and performance metrics for 2015.
Classification was based on a cutoff value of 0.188979.

		True Positive	True Negative	Total
Predicted Positive		4,197	7,456	11,653
Predicted Negative		1,265	19,842	21,107
Total		5,462	27,298	32,760
	Estimate	95% Credible Interval		
AUC	0.825	(0.818, 0.832)		
		Value	Derivation	Calculation
Accuracy		0.734	(TP + TN) / (P + N)	(4,197 + 19,842) / (5,462 + 27,298)
Sensitivity		0.768	TP / (TP + FN)	4,197 / (4,197 + 1,265)
Specificity		0.727	TN / (FP + TN)	19,842 / (7,456 + 19,842)
Precision		0.360	TP / (TP + FP)	4,197 / (4,197 + 7,456)
Negative Predictive Value		0.940	TN / (TN + FN)	19,842 / (19,842 + 1,265)
False Positive Rate		0.273	FP / (FP + TN)	7,456 / (7,456 + 19,842)
False Negative Rate		0.232	FN / (FN + TP)	1,265 / (1,265 + 4,197)

Supplementary Table 4.5. Confusion matrix and performance metrics for 2016.
Classification was based on a cutoff value of 0.188979.

	True Positive	True Negative	Total
Predicted Positive	4,977	7,288	12,265
Predicted Negative	1,346	23,688	25,034
Total	6,323	30,976	

	Estimate	95% Credible Interval
AUC	0.860	(0.854, 0.866)

	Value	Derivation	Calculation
Accuracy	0.769	(TP + TN) / (P + N)	(4,977 + 23,688) / (6,323 + 30,976)
Sensitivity	0.787	TP / (TP + FN)	4,977 / (4,977 + 1,346)
Specificity	0.765	TN / (FP + TN)	23,688 / (7,288 + 23,688)
Precision	0.406	TP / (TP + FP)	4,977 / (4,977 + 7,288)
Negative Predictive Value	0.946	TN / (TN + FN)	23,688 / (23,688 + 1,346)
False Positive Rate	0.235	FP / (FP + TN)	7,288 / (7,288 + 23,688)
False Negative Rate	0.213	FN / (FN + TP)	1,346 / (1,346 + 4,977)

Supplementary Table 4.6. Confusion matrix and performance metrics for 2017. Classification was based on a cutoff value of 0.188979.

	True Positive	True Negative	Total
Predicted Positive	5,253	7,186	12,439
Predicted Negative	1,710	23,146	24,856
Total	6,963	30,332	37,295

	Estimate	95% Credible Interval
AUC	0.843	(0.837, 0.849)

	Value	Derivation	Calculation
Accuracy	0.762	(TP + TN) / (P + N)	(5,253 + 23,146) / (6,963 + 30,332)
Sensitivity	0.754	TP / (TP + FN)	5,253 / (5,253 + 1,710)
Specificity	0.763	TN / (FP + TN)	23,146 / (7,186 + 23,146)
Precision	0.422	TP / (TP + FP)	5,253 / (5,253 + 7,186)
Negative Predictive Value	0.931	TN / (TN + FN)	23,146 / (23,146 + 1,710)
False Positive Rate	0.237	FP / (FP + TN)	7,186 / (7,186 + 23,146)
False Negative Rate	0.246	FN / (FN + TP)	1,710 / (1,710 + 5,253)

Supplementary Table 4.7. Confusion matrix and performance metrics for 2018.
Classification was based on a cutoff value of 0.188979.

		True Positive	True Negative	Total
Predicted Positive		6,571	7,796	14,367
Predicted Negative		1,234	22,516	23,750
Total		7,805	30,312	38,117
	Estimate	95% Credible Interval		
AUC	0.873	(0.868, 0.878)		
		Value	Derivation	Calculation
Accuracy		0.763	(TP + TN) / (P + N)	(6,571 + 22,516) / (7,796 + 30,312)
Sensitivity		0.842	TP / (TP + FN)	6,571 / (6,571 + 1,234)
Specificity		0.743	TN / (FP + TN)	22,516 / (7,796 + 22,516)
Precision		0.457	TP / (TP + FP)	6,571 / (6,571 + 7,796)
Negative Predictive Value		0.948	TN / (TN + FN)	22,516 / (22,516 + 1,234)
False Positive Rate		0.257	FP / (FP + TN)	7,796 / (7,796 + 22,516)
False Negative Rate		0.158	FN / (FN + TP)	1,234 / (1,234 + 6,571)

Supplementary Table 4.8. Confusion matrix and performance metrics for 2019.
Classification was based on a cutoff value of 0.188979.

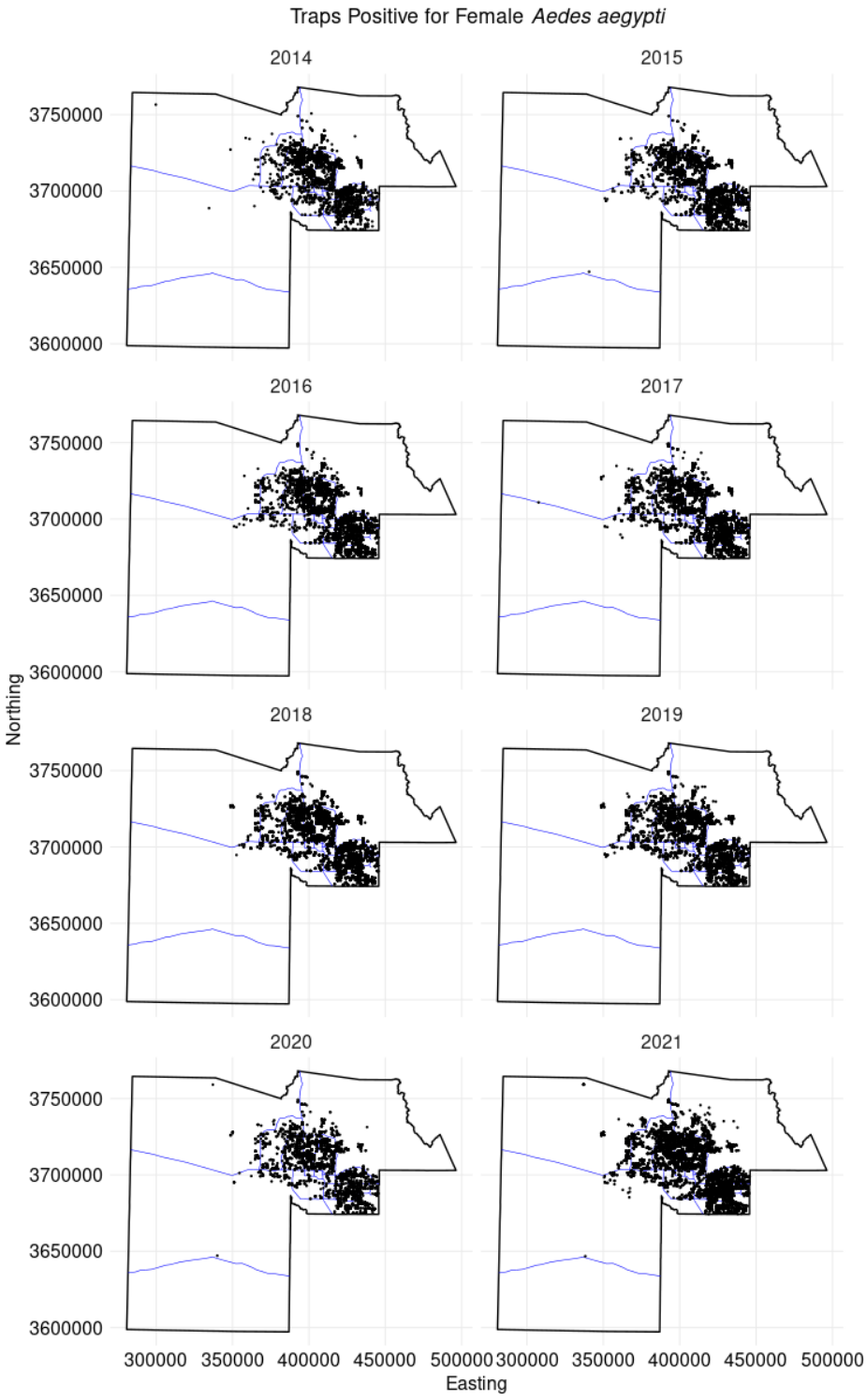
		True Positive	True Negative	Total
Predicted Positive		6,209	7,761	13,970
Predicted Negative		1,653	23,100	24,753
Total		7,862	30,861	38,723
	Estimate	95% Credible Interval		
AUC	0.851	(0.846, 0.857)		

	Value	Derivation	Calculation
Accuracy	0.757	(TP + TN) / (P + N)	(6,209 + 23,100) / (7,862 + 30,861)
Sensitivity	0.790	TP / (TP + FN)	6,209 / (6,209 + 1,653)
Specificity	0.749	TN / (FP + TN)	23,100 / (7,761 + 23,100)
Precision	0.445	TP / (TP + FP)	6,209 / (6,209 + 7,761)
Negative Predictive Value	0.933	TN / (TN + FN)	23,100 / (23,100 + 1,653)
False Positive Rate	0.252	FP / (FP + TN)	7,761 / (7,761 + 23,100)
False Negative Rate	0.210	FN / (FN + TP)	1,653 / (1,653 + 6,209)

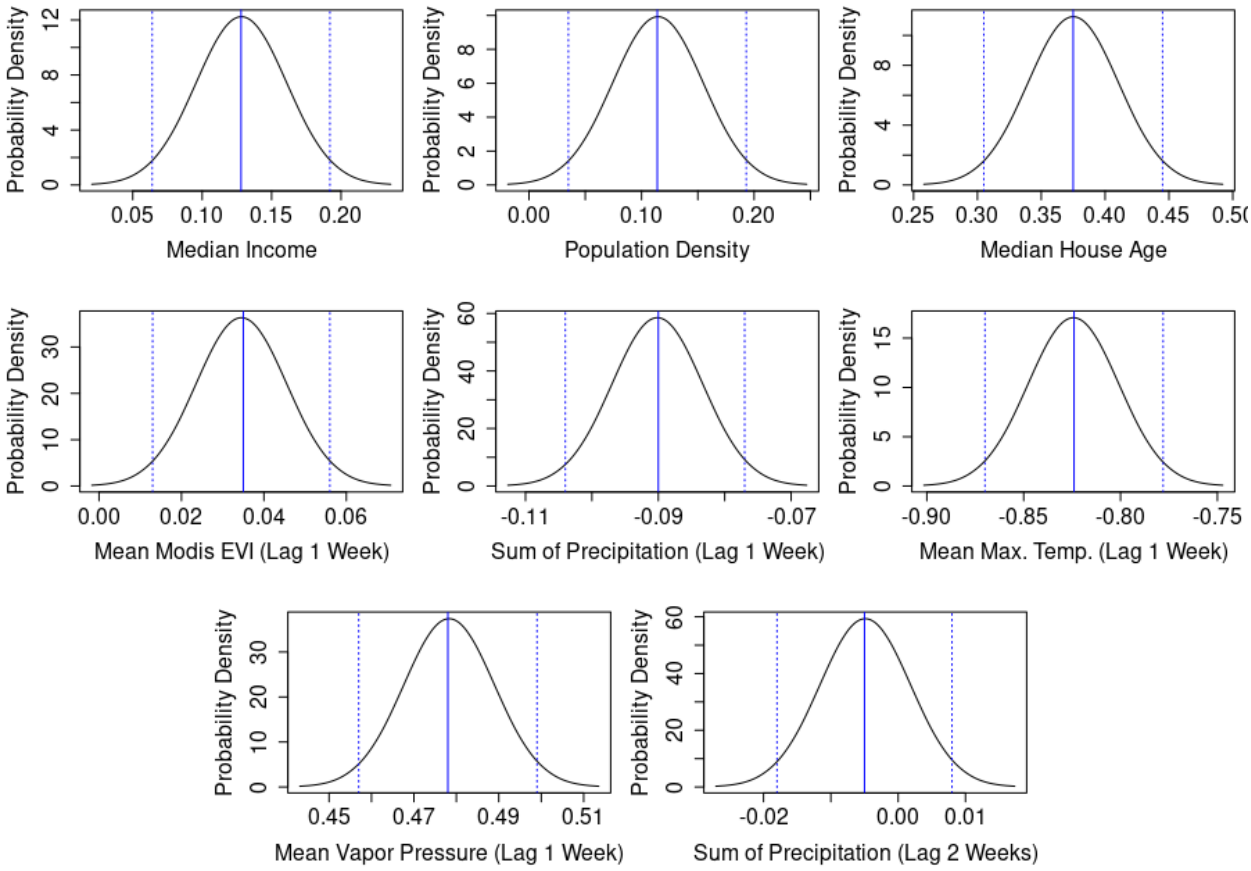
Supplementary Table 4.9. Confusion matrix and performance metrics for 2020.
Classification was based on a cutoff value of 0.188979.

		True Positive	True Negative	Total
Predicted Positive		3,432	9,301	12,733
Predicted Negative		933	25,756	26,689
Total		4,365	35,057	39,422
	Estimate	95% Credible Interval		
AUC	0.840	(0.832, 0.847)		
		Value	Derivation	Calculation
Accuracy		0.740	(TP + TN) / (P + N)	(3,432 + 25,756) / (4,365 + 35,057)
Sensitivity		0.786	TP / (TP + FN)	3,432 / (3,432 + 933)
Specificity		0.735	TN / (FP + TN)	25,756 / (9,301 + 25,756)
Precision		0.270	TP / (TP + FP)	3,432 / (3,432 + 9,301)
Negative Predictive Value		0.965	TN / (TN + FN)	25,756 / (25,756 + 933)
False Positive Rate		0.265	FP / (FP + TN)	9,301 / (9,301 + 25,756)
False Negative Rate		0.214	FN / (FN + TP)	933 / (933 + 3,432)

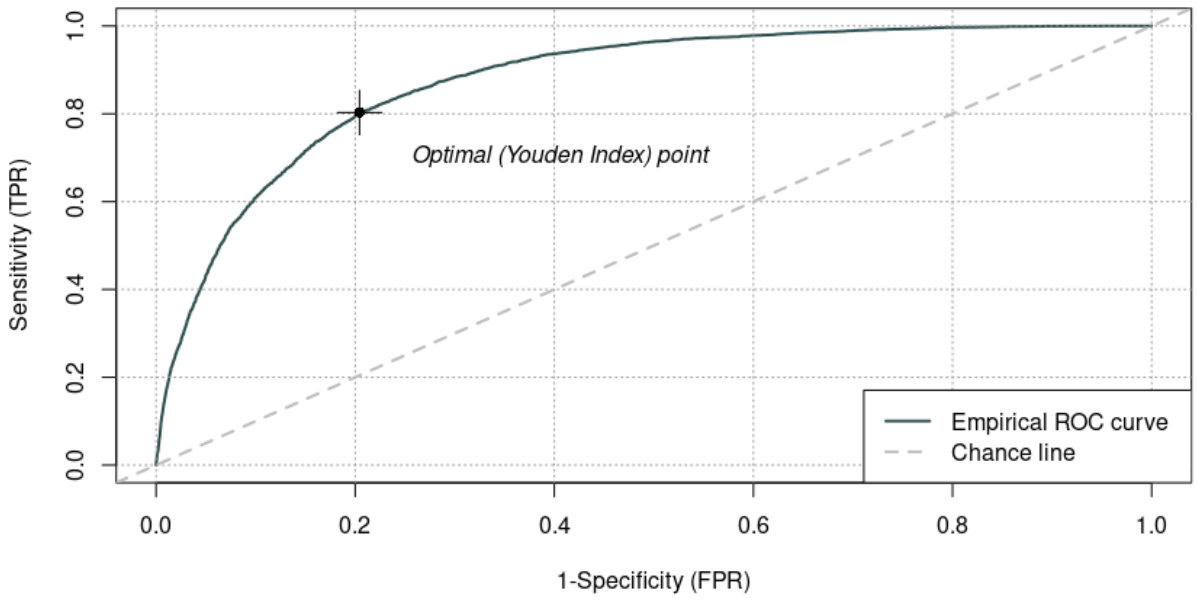
SUPPLEMENTARY FIGURES FOR CHAPTER 4: SPATIOTEMPORAL BAYESIAN MODELING OF THE PRESENCE OF *AEDES AEGYPTI* MOSQUITOES IN MARICOPA COUNTY, ARIZONA



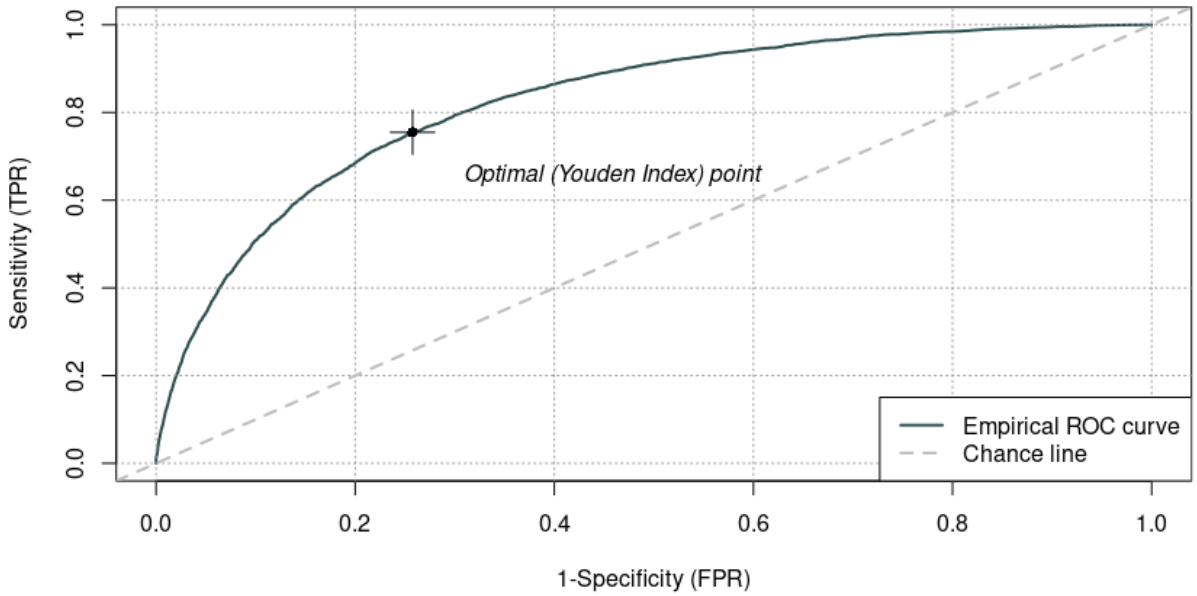
Supplementary Figure 4.1. Location of traps positive for female *Ae. aegypti* per year, 2014-2021. Major freeways are shown as blue lines to provide a location reference. Each dot represents one or more observation of *Ae. aegypti* at that location.



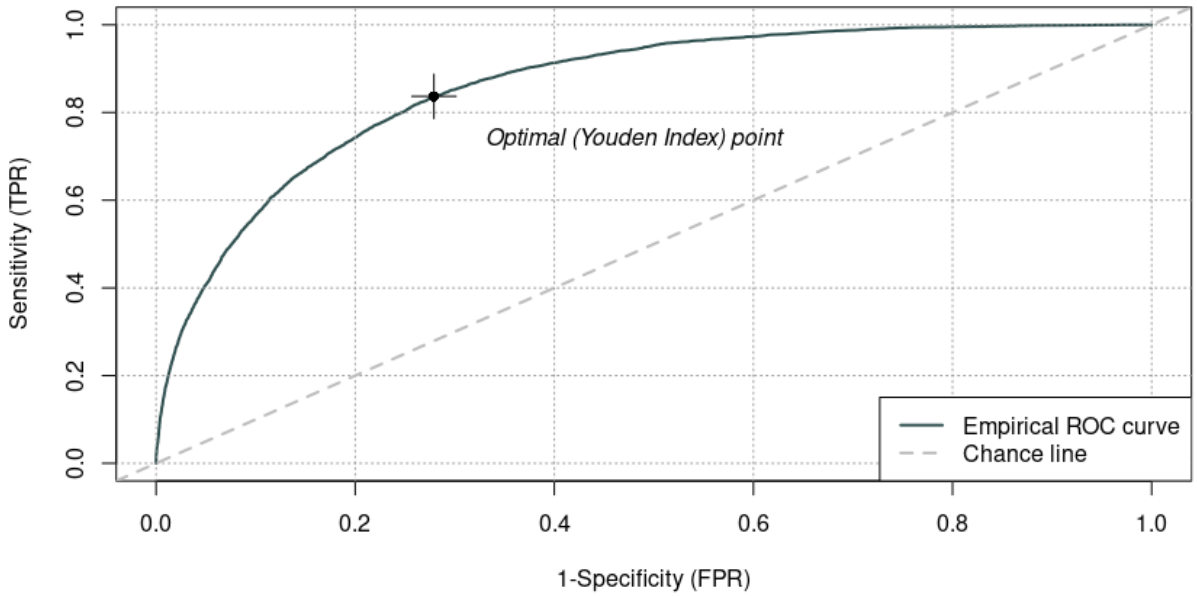
Supplementary Figure 4.2. Posterior distributions of fixed effects for the zero-inflated binomial model with both spatial and temporal random effects. The mean marginal posterior value and 95% credible interval for the log odds for each parameter is highlighted by the solid and dashed blue lines, respectively. Default priors (defined in R-INLA as a gamma distribution with shape parameter set to 1 and scale parameter set to 0.00001) were used for initial values for all fixed effects.



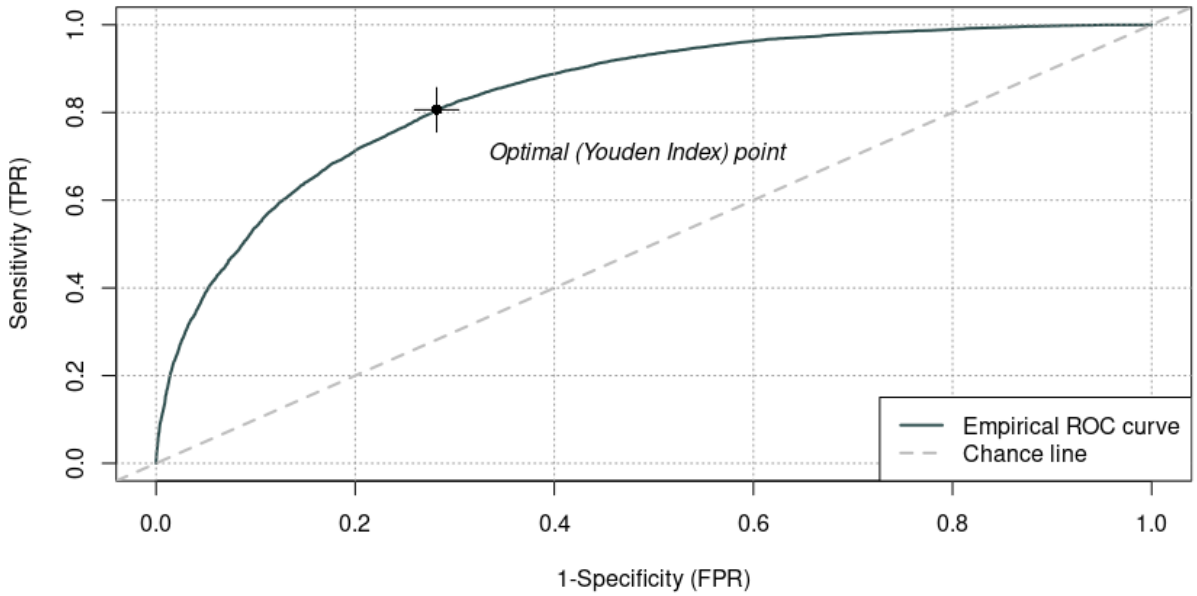
Supplementary Figure 4.3. ROC curve for 2014.



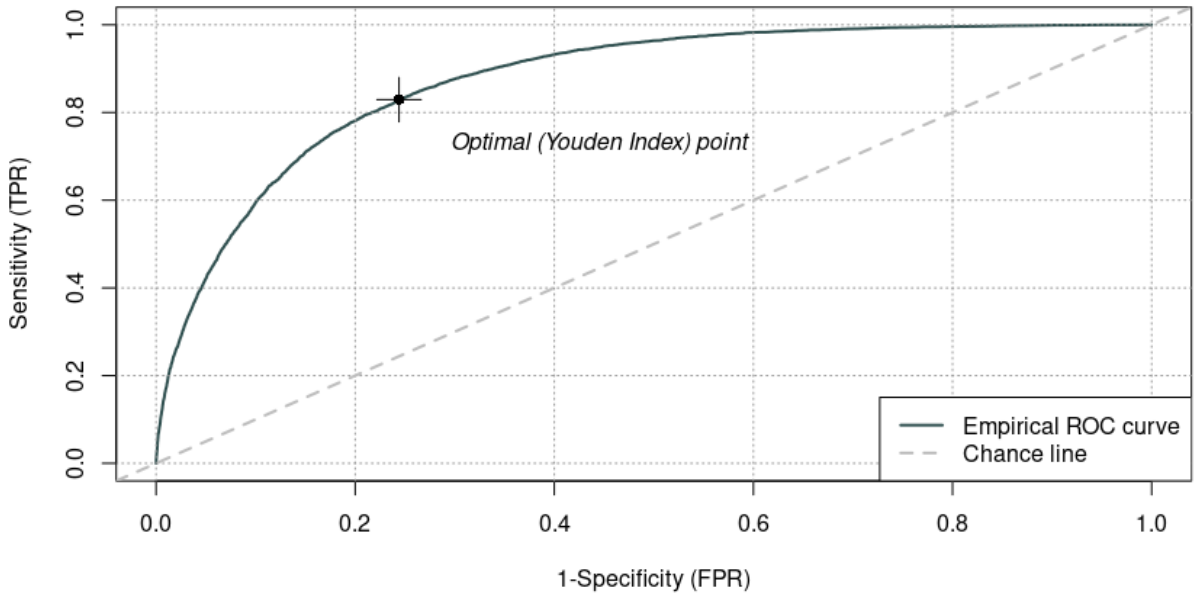
Supplementary Figure 4.4. ROC curve for 2015.



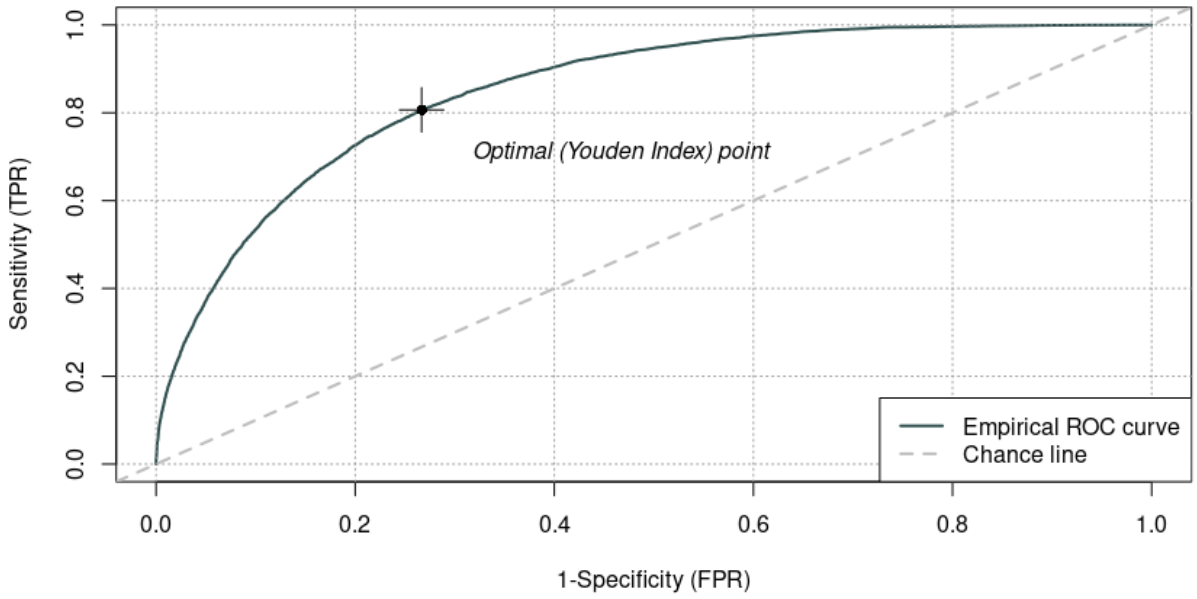
Supplementary Figure 4.5. ROC curve for 2016.



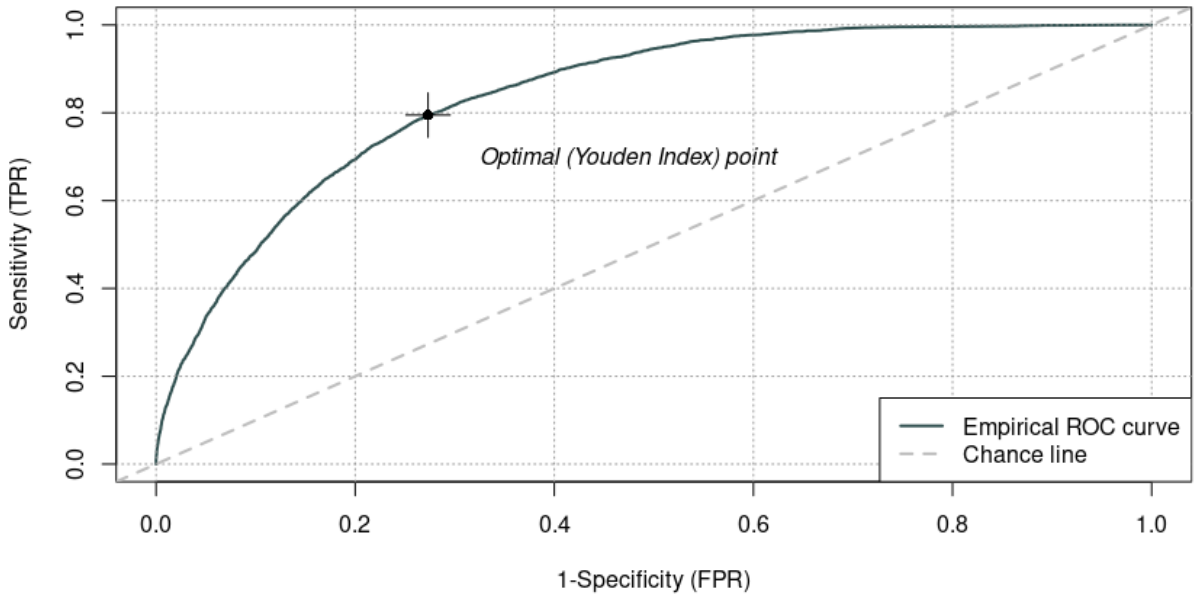
Supplementary Figure 4.6. ROC curve for 2017.



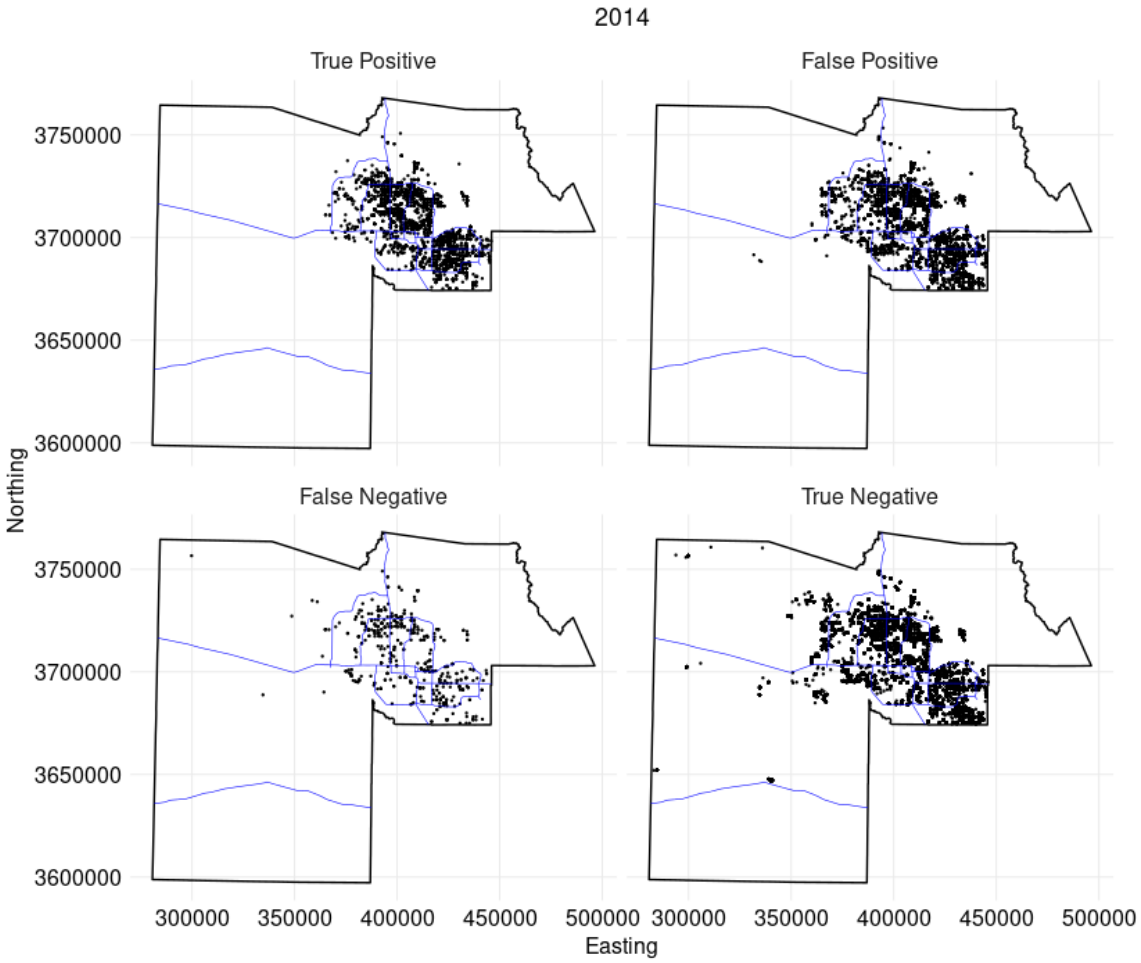
Supplementary Figure 4.7. ROC curve for 2018.



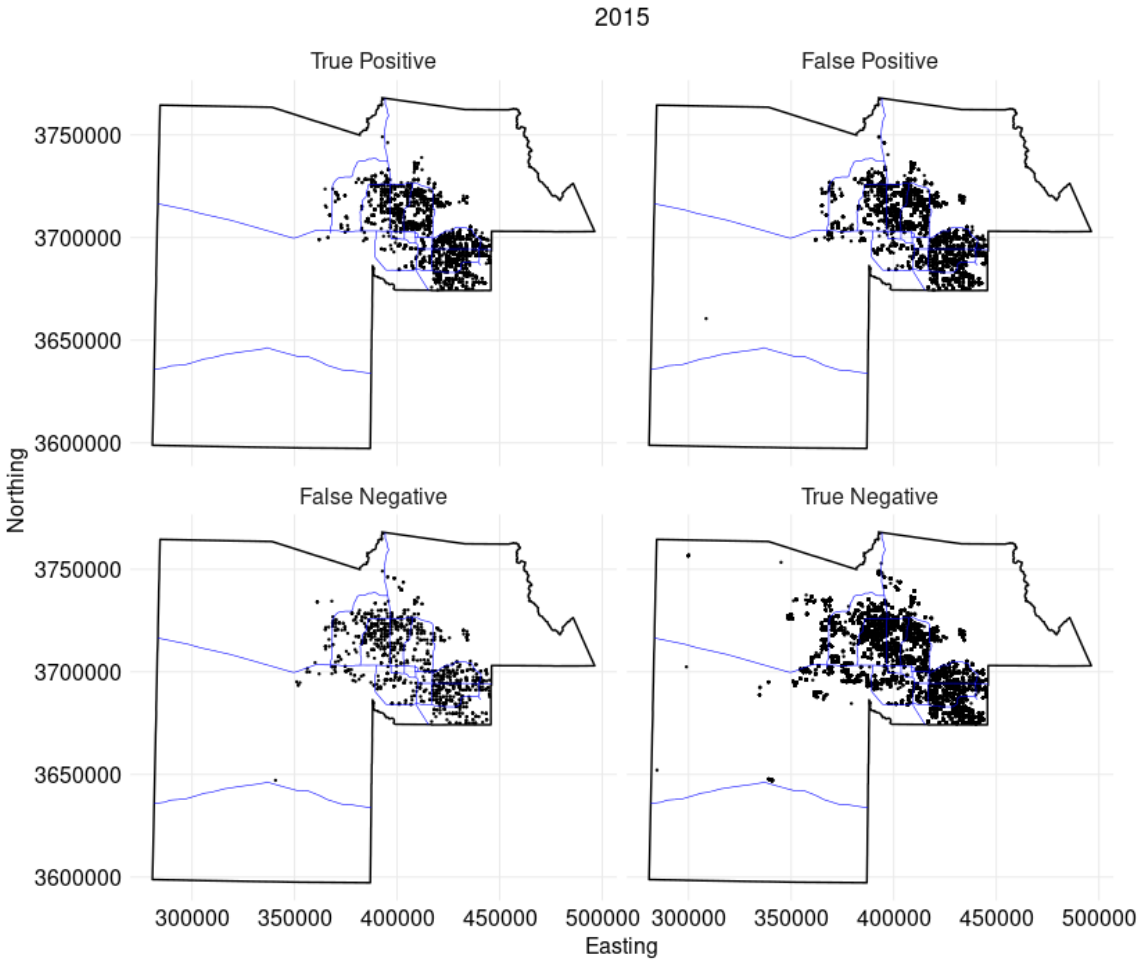
Supplementary Figure 4.8. ROC curve for 2019.



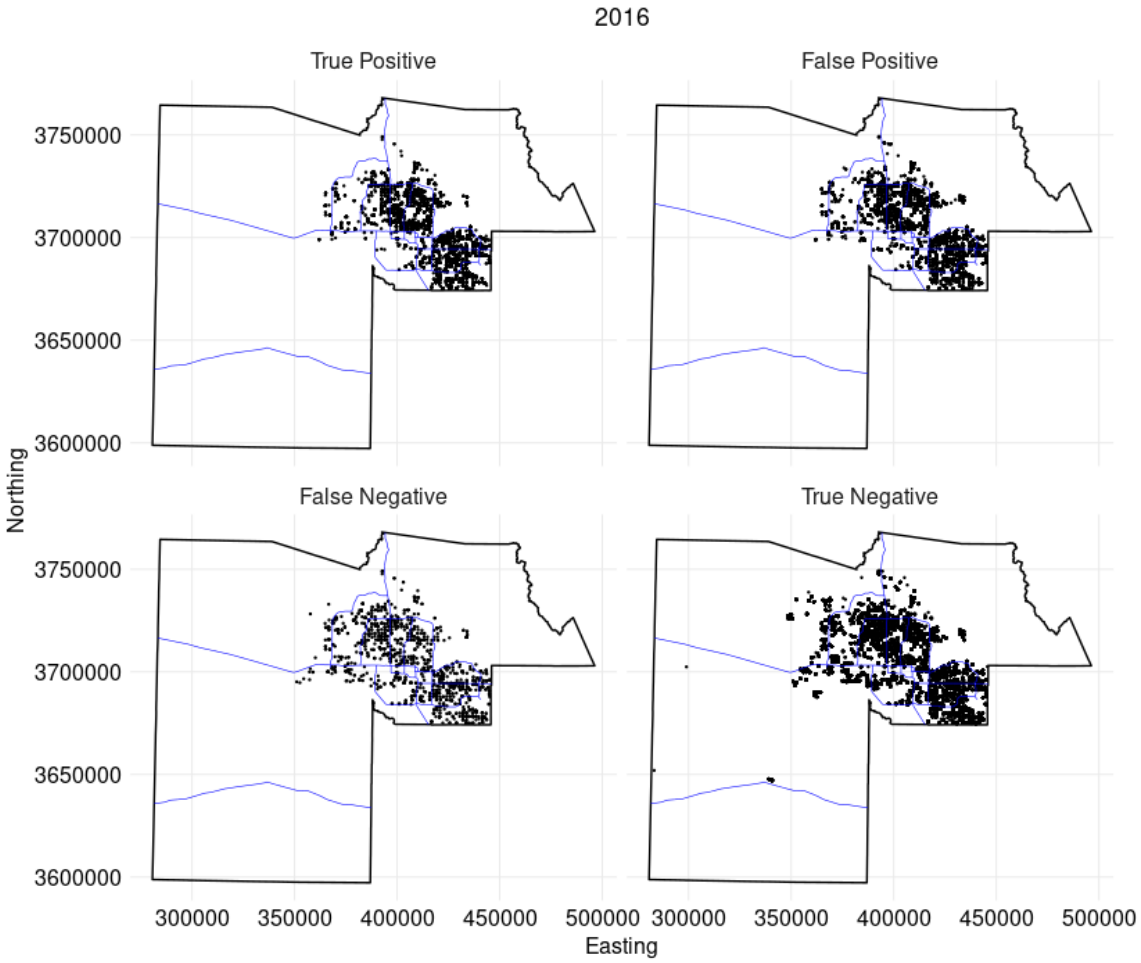
Supplementary Figure 4.9. ROC curve for 2020.



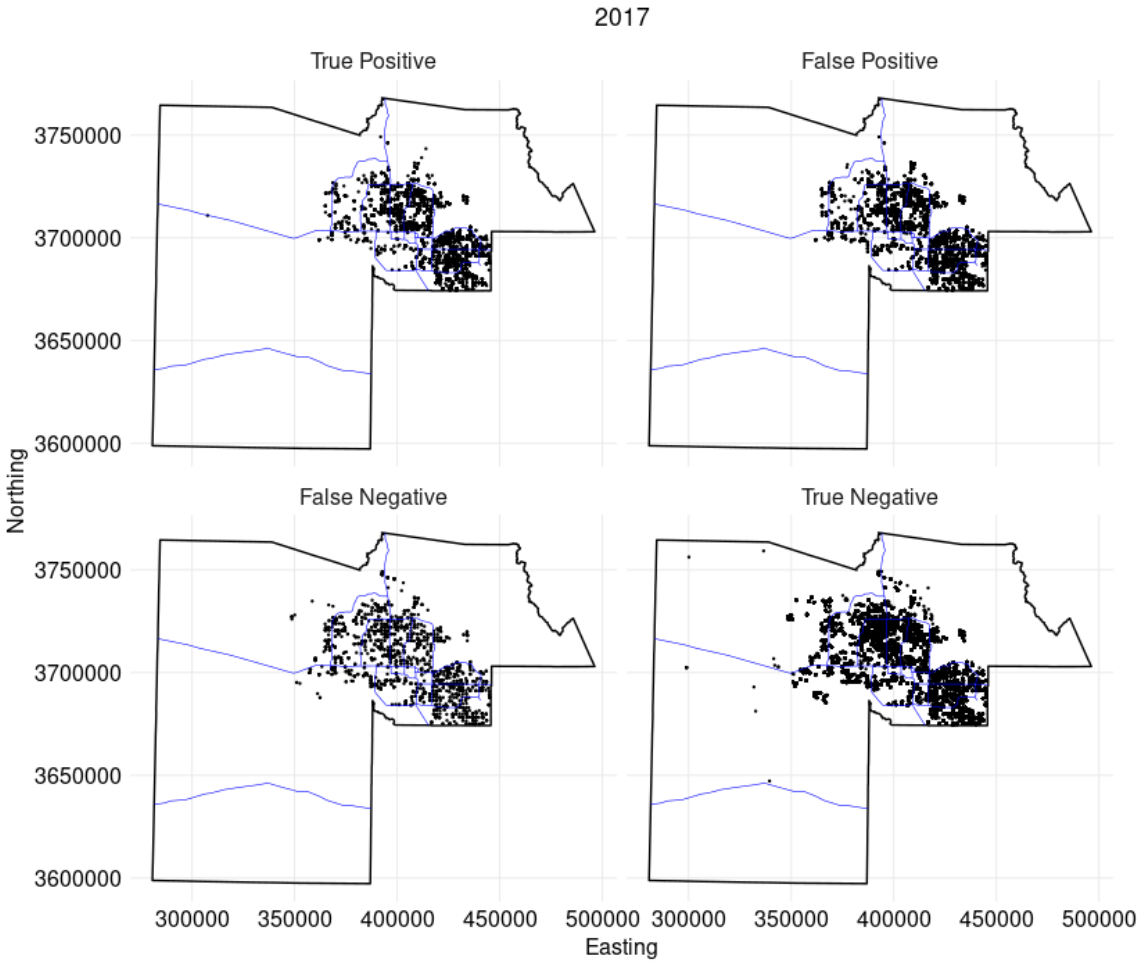
Supplementary Figure 4.10. The location of predictions by classification status for 2014. Major freeways are shown as blue lines to provide a location reference. No obvious spatial patterns are present.



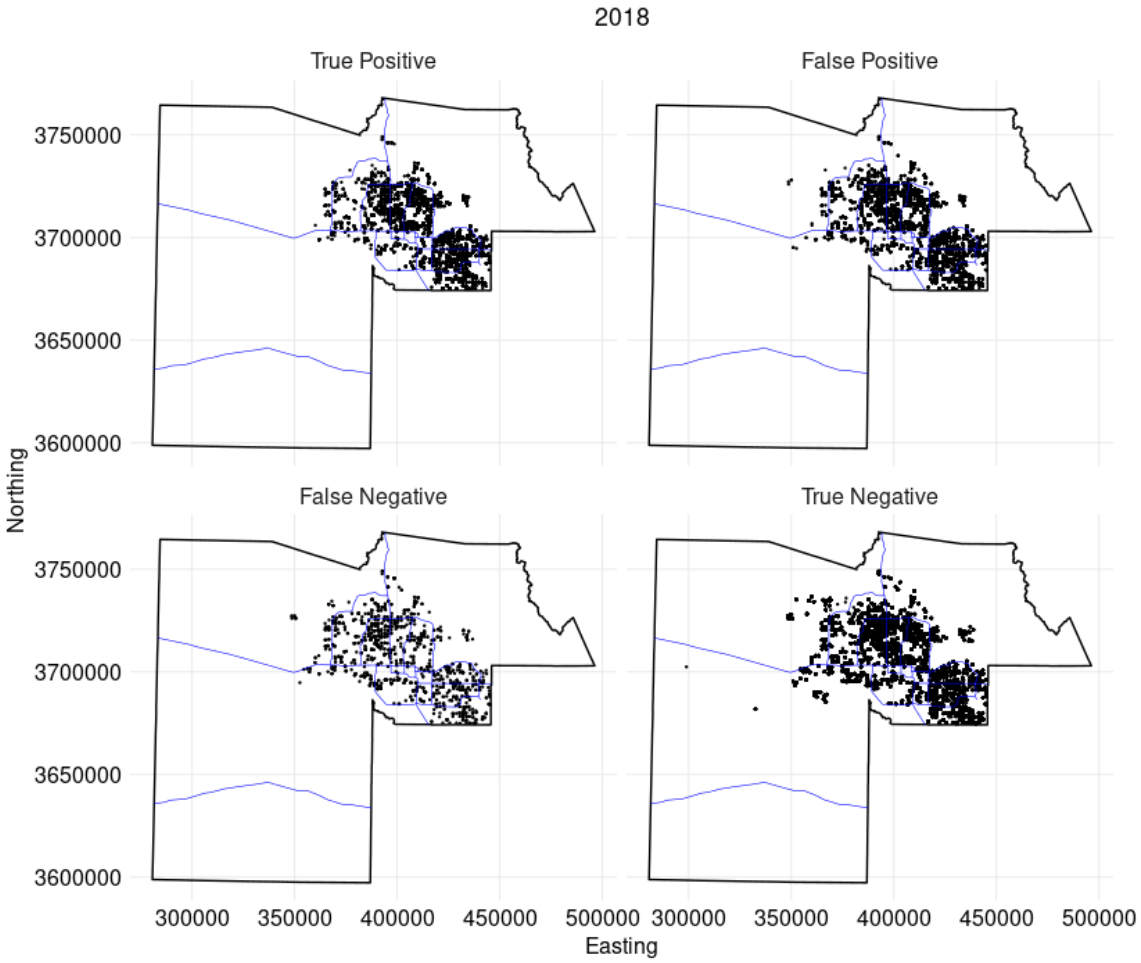
Supplementary Figure 4.11. The location of predictions by classification status for 2015. Major freeways are shown as blue lines to provide a location reference. No obvious spatial patterns are present.



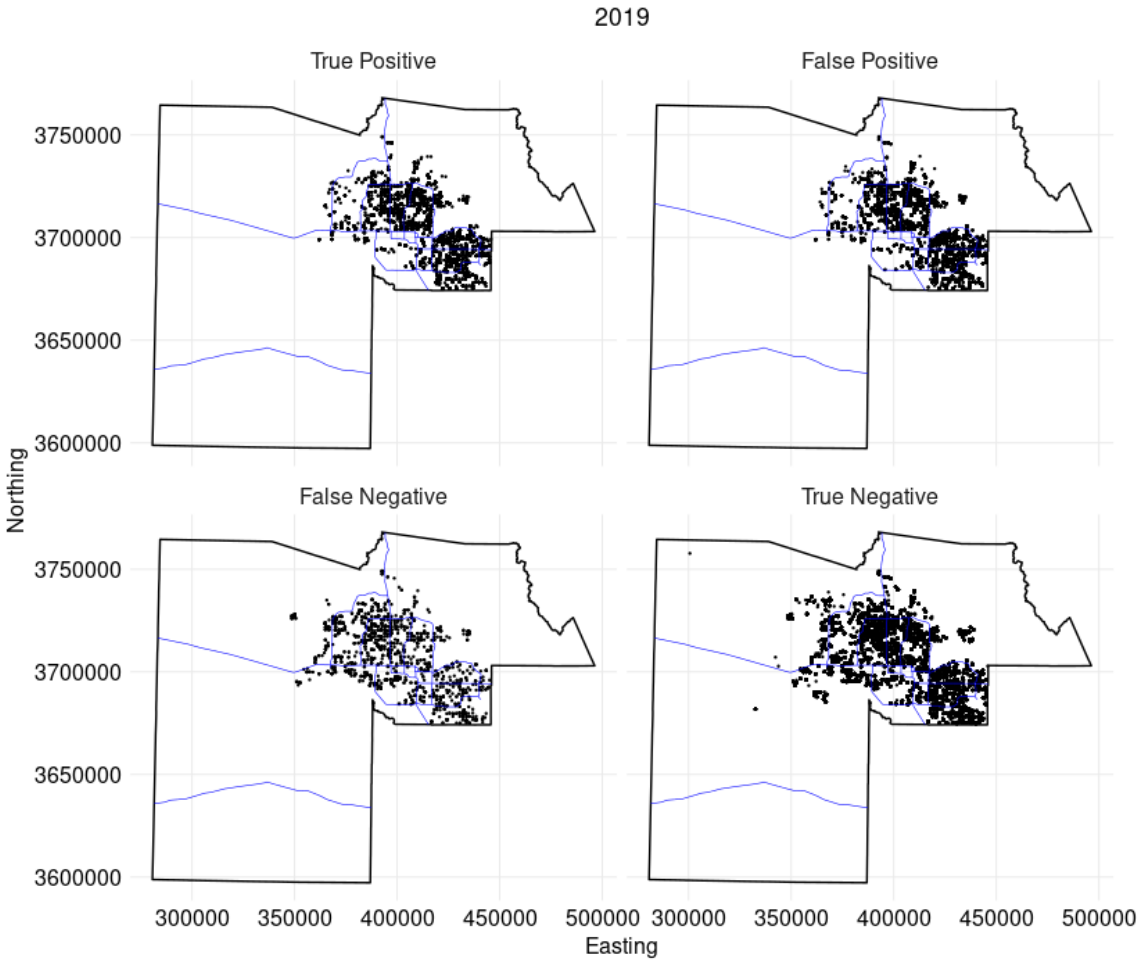
Supplementary Figure 4.12. The location of predictions by classification status for 2016. Major freeways are shown as blue lines to provide a location reference. No obvious spatial patterns are present.



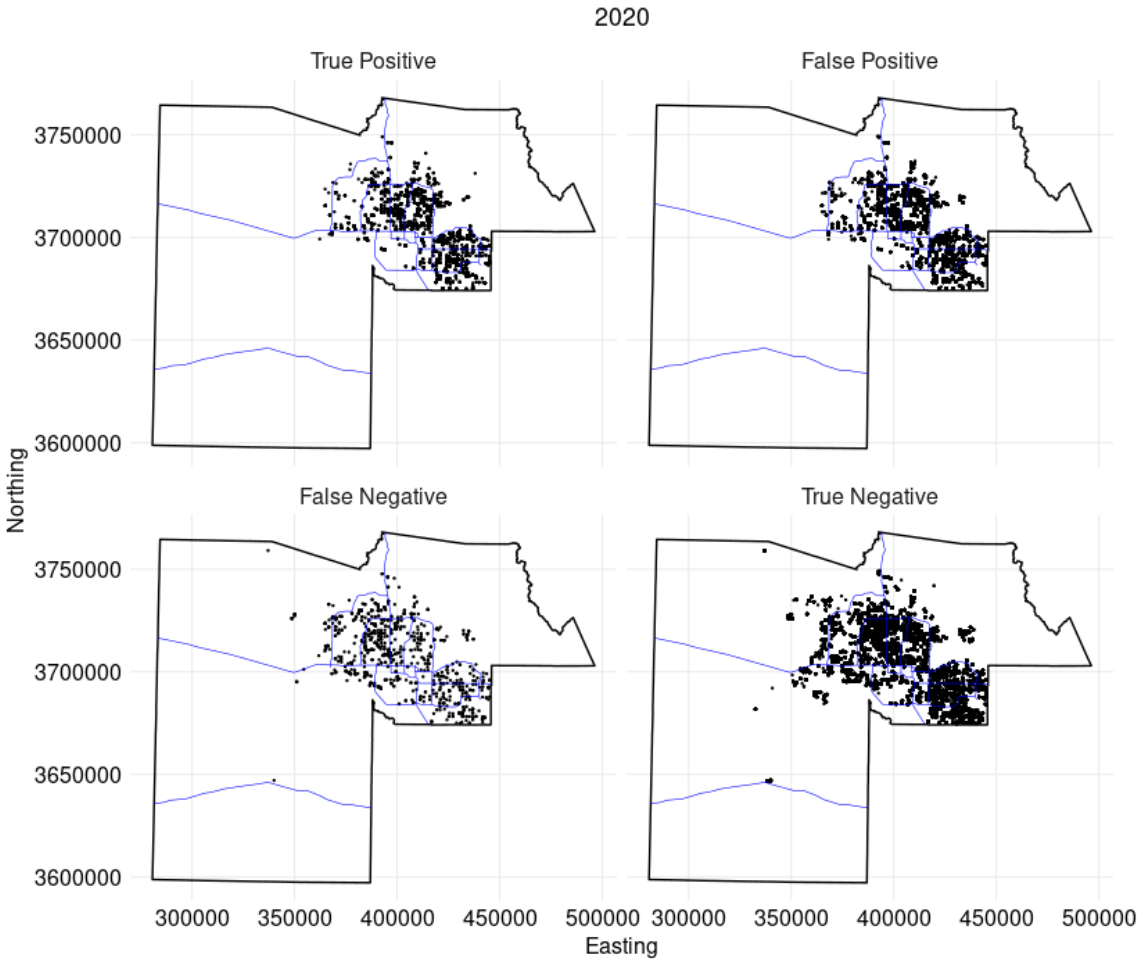
Supplementary Figure 4.13. The location of predictions by classification status for 2017. Major freeways are shown as blue lines to provide a location reference. No obvious spatial patterns are present.



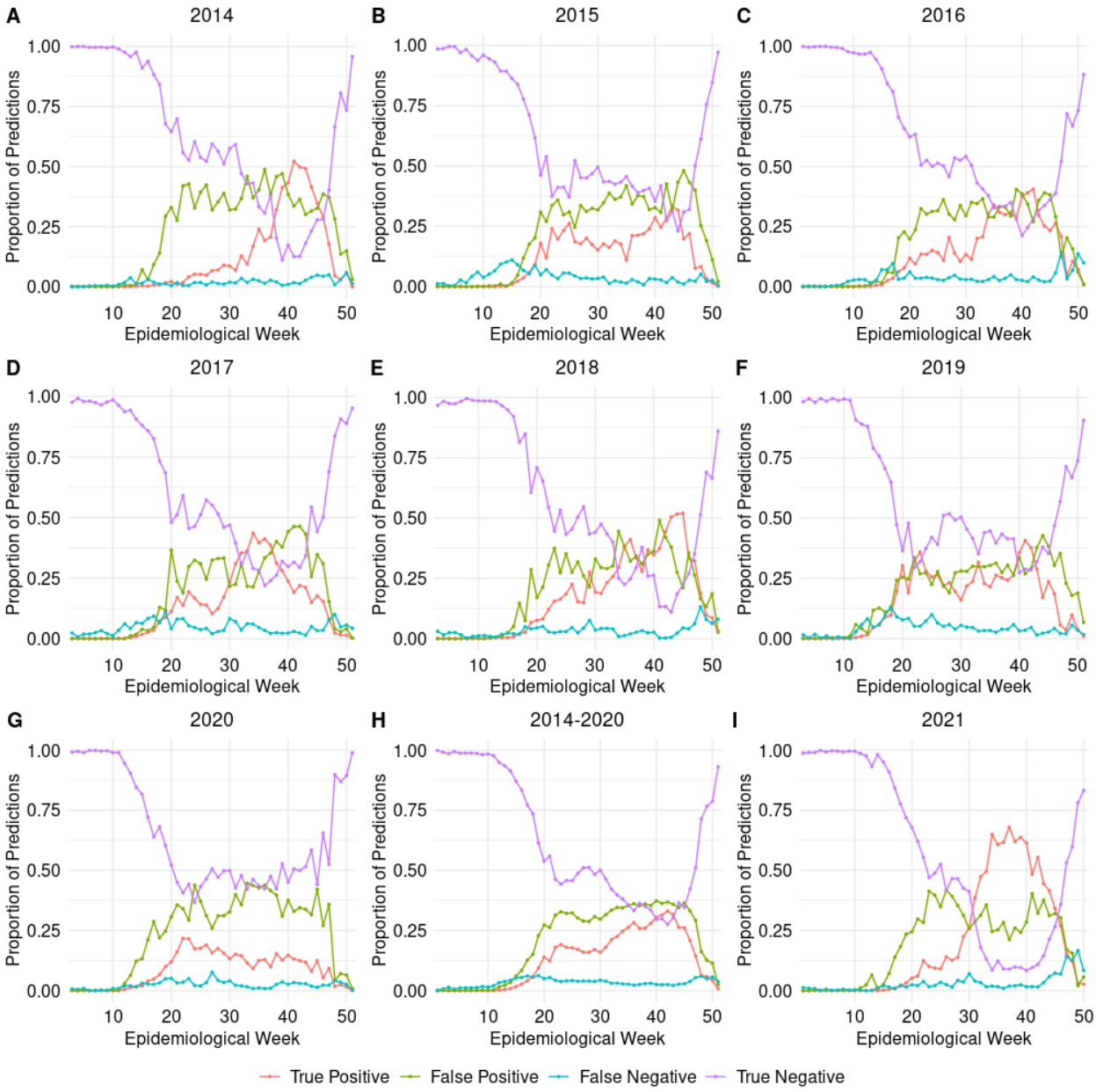
Supplementary Figure 4.14. The location of predictions by classification status for 2018. Major freeways are shown as blue lines to provide a location reference. No obvious spatial patterns are present.



Supplementary Figure 4.15. The location of predictions by classification status for 2019. Major freeways are shown as blue lines to provide a location reference. No obvious spatial patterns are present.



Supplementary Figure 4.16. The location of predictions by classification status for 2020. Major freeways are shown as blue lines to provide a location reference. No obvious spatial patterns are present.



Supplementary Figure 4.17. Proportion of predictions by classification status for each year in the training data set, 2014-2020 (A-G), all training data together (H), and for 2021 test data (I). The increase in false positive rate during the summer months indicates that our model overpredicts positive occurrences during that time.