UTILIZING GEOGRAPHIC EPIDEMIOLOGY TO DETERMINE HIGH RISK AREAS FOR COCCIDIOIDOMYCOSIS IN TEXAS

by

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I. INTRODUCTION

Coccidioidomycosis, commonly referred to as "valley fever" or "cocci" has been a well-known endemic fungal disease to the southwestern United States since the early 1900s (Hirschmann 2007). Recent dramatic increases in disease incidents since the 1990s however, have initiated a reemergence in interest surrounding the disease's cause as well as its effects on the population (Kirkland and Fierer 1996). Modern epidemiological studies on coccidioidomycosis seek to understand the environmental effects on the growth and dispersal of the fungus that causes the disease, but their results tend to reveal that the factors contributing to the escalation of disease incidents are complex and difficult to isolate (Kolivras and Comrie 2003; Comrie 2005; Park et al. 2005; Baptista-Rosas, Hinojosa, and Riquelme 2007; Comrie and Glueck 2007; Fisher et al. 2007; Talamantes, Behseta, and Zender 2007; Tamerius and Comrie 2011).

Coccidioidomycosis impacts on the human population are profound and range from long-term interruptions in the ability to perform daily activities to severe symptoms that can increase healthcare costs and may be deadly (Kirkland and Fierer 1996; Chiller, Galgiani, and Stevens 2003; Galgiani et al. 2005; Tsang et al. 2010; Tsang et al. 2013). With so little known about the ecological niche of the coccidioidomycosis-causing fungus, it is important to continue conducting research on the environmental determinants of this niche to better understand how the presence of the fungus might contribute to the prevalence of the disease (Fisher et al. 2007; Talamantes, Behseta, and Zender 2007).

II. BACKGROUND, RESEARCH PROBLEM, AND SIGNIFICANCE

Background

Coccidioidomycosis is caused by *Coccidioides immitis* and *Coccidioides posadasii* (Fisher et al. 2002), two species of pathogenic fungi predominantly found in the fine, loamy, sandy soils of the arid southwestern United States, northern Mexico, and parts of Central and South America (Figure 1) (Stevens 1995; Fisher et al. 2007). When these soils are disturbed, either by natural causes or by human activity, the fungal spores are aerosolized and often inhaled by humans, causing infection (Chiller, Galgiani, and Stevens 2003; Arizona Department of Health Services 2012).

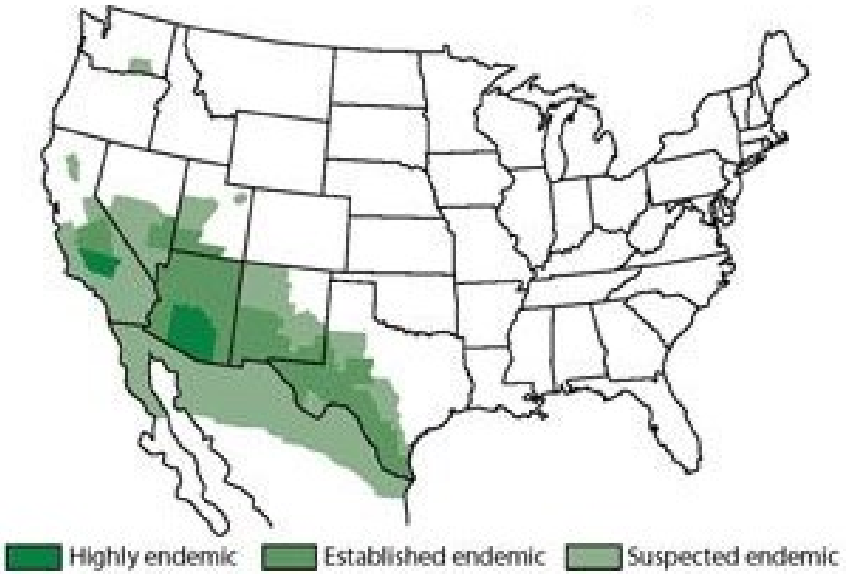


Figure 1. Areas endemic for coccidioidomycosis in the United States.
Source: Centers for Disease Control and Prevention (CDC) 2014.

According to Galgiani et al. (2005), approximately 150,000 people in the United States are infected with coccidioidomycosis each year, and of this infected population, approximately 40 percent experience clinical symptoms that range from common cold or

flu-like symptoms to severe pulmonary distress. In a small percentage of the population, the disease can disseminate to other parts of the body including the skin, bones, joints, and brain, which can be fatal (Kirkland and Fierer 1996; Chiller, Galgiani, and Stevens 2003; Galgiani et al. 2005). Studies have shown that 75 percent of those who experience symptoms report that the disease significantly impacts their abilities to carry out daily activities like attending school or work, and approximately 40 percent require hospitalization (Tsang et al. 2010).

Research Problem

Because of its prevalence and impact on the human population, coccidioidomycosis has been a nationally notifiable disease since 1995. Both Arizona and California have mandated reporting of all incidents of the disease since 1997 and 2010, respectively, and this has greatly contributed to the accuracy in tracking its occurrence (Hector et al. 2011; Arizona Department of Health Services 2012; Tsang et al. 2013). Since the 1990s, coccidioidomycosis cases have increased dramatically (Kirkland and Fierer 1996), and although this is due in part to the improvement in reporting, there is no definitive explanation for the continued upward trend in incidents since 1997 (Park et al. 2005; Sunenshine et al. 2007; Tsang et al. 2013; Arizona Department of Health Services 2013). Researchers (Kolviras and Comrie 2003; Komatsu et al. 2003; Comrie 2005; Park et al. 2005) attribute much of this increase in prevalence to climatic factors, but they also recognize the need for more research on the environmental and human-induced influences on *Coccidioides* growth and dispersal (Kolivras and Comrie 2003; Comrie 2005; Scott, Robbins, and Comrie 2012).

For this study, a quantitative spatial analysis was conducted on coccidioidomycosis to determine high risk areas for the disease in Texas. Using county level, seasonally aggregated, population normalized, reported cases of the disease in California from 2003-2012 as a proxy for the *Coccidioides* fungus, a model was constructed to predict the influence of predetermined environmental and anthropogenic variables on its growth and dispersal. Using geographic information systems (GIS), the model was applied to similar environments in Texas to determine the areas at high risk for the presence of *Coccidioides* and consequently, a high risk for coccidioidomycosis.

Significance and Broader Impact

Texas was chosen as the study area because despite the fact that it is an endemic state for coccidioidomycosis (Centers for Disease Control and Prevention 2012), very little research has been conducted regarding the disease there. The currently accepted delineation of Texas as an endemic state is based upon dated and often incomplete reports of the disease (Gautam et al. 2013). It is possible that since Texas does not mandate the reporting of coccidioidomycosis incidents, many cases go undiagnosed or misdiagnosed, which can lead to an exacerbation in the disease, increased healthcare costs, and in some cases death (Tsang et al. 2010; Tsang et al. 2013). With the increase in disease incidence in other states, it is reasonable to infer that there will be a likely increase in occurrence in Texas as well, and as the population in Texas grows, so too will the risk of exposure to the disease (Galgiani 1999).

The conclusions of this research will potentially provide healthcare professionals and state health officials with new information to better diagnose and manage coccidioidomycosis in Texas. This improvement in diagnosis is likely to lead to more

timely management of the disease, thereby potentially alleviating the complications that arise when it is left untreated. Also, by identifying areas in Texas where *Coccidioides* is likely to occur at higher than normal levels, the conclusions of this study will potentially assist researchers in their attempts to isolate fungal samples in the field for further ecological and biological studies of *Coccidioides* habitat.

III. LITERATURE REVIEW

Understanding the Differences between Medical Geography and Epidemiology and the Contributions of Each

There is much debate in the literature regarding the degree of difference that exists between epidemiology and medical geography and the value that each field contributes to the other. Glass (2000) identifies key differences between the two fields, stating that although the focus of epidemiology lies predominantly in the etiologic (or causal) explanations for disease processes as well as disease diffusion among the human population, medical geography focuses on both the ecological determinants of health as well as disease outcomes among the population.

Alternatively stated, medical geography emphasizes the importance of the human-environment interaction as determinants of many diseases while also focusing on spatial patterns of disease distribution (especially disease clusters), something which epidemiology recognizes but does not explicitly focus upon (Meade, Florin and Gesler 1988). Glass (2000) proposes that the solution for bridging this cross-disciplinary gap lies in the field of environmental epidemiology. He asserts that environmental epidemiology emphasizes the importance of environmental factors as well as the spatial relationships among variables as key components in the etiology of many disease processes, but the methodology remains epidemiologic in nature.

Many researchers, however, consider environmental epidemiology (also referred to as landscape epidemiology or even geographical epidemiology) to be a sub-discipline within the field of medical geography, rather than a distinct field, because of its focus on ecological analysis, or the analysis of spatial relationships between environmental factors and disease (Mayer 1982; Meade, Florin, and Gesler 1988; Kistemann, Dangendorf, and

Schweikart 2002; Young, Tulls, and Cothren 2013). This is especially true for environmentally driven diseases like West Nile virus, Lyme disease, and coccidioidomycosis, to name a few (Young, Tullis, and Cothren 2013).

Regardless of these nuanced interpretations, O'Dwyer and Burton (1998) argue for the cross-disciplinary cooperation between the fields of medical geography and epidemiology because of the value each can contribute to the other. Medical geographers are highly skilled in understanding complex spatial relationships and interactions, especially between humans and the environmental determinants of disease. They are also adept at analyzing these relationships and interactions through the utilization of geospatial technologies like GIS and remote sensing (Meade, Florin, and Gesler 1988; O'Dwyer and Burton 1998; Meade and Earickson 2000; Kistemann, Dangendorf, and Schweikart 2002; Schröder 2006; Young, Tullis, and Cothren 2013). In contrast, epidemiologists possess medical knowledge that geographers may lack but that is necessary to accurately and comprehensively analyze many disease processes (O'Dwyer and Burton 1998).

A prominent example of these commonalities between the two disciplines, and further justification for the need for cross-disciplinary collaboration, is John Snow's famous Broad Street Map (Figure 2), depicting the locations of cholera cases in South London in order to determine the source of the 1853 cholera outbreak. Although John Snow is commonly considered a pioneer in the field of modern epidemiology (Frerichs 2014), it is reasonable to argue that because of his utilization of spatial analysis to determine the source of the disease, he is, as well, a pioneer in the field of modern medical geography.

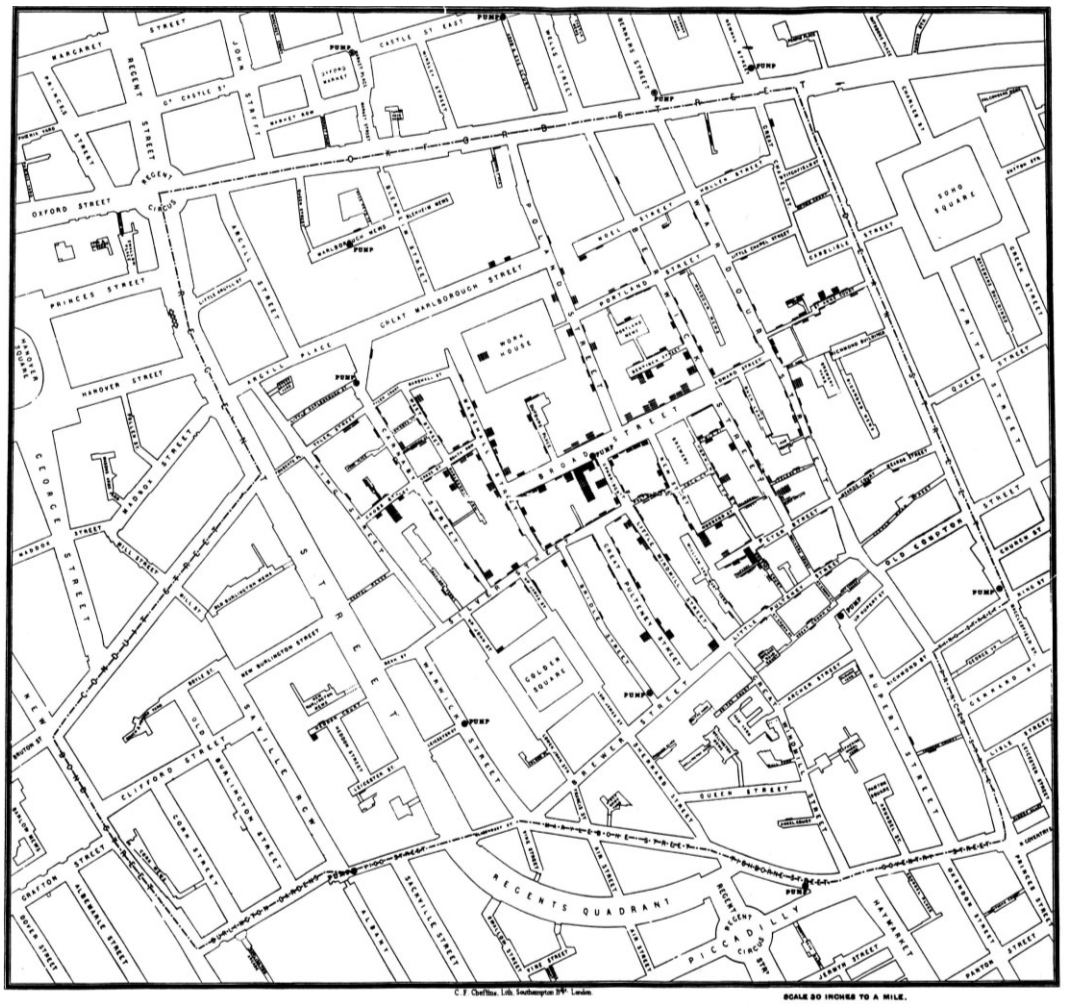


Figure 2. John Snow's map of the locations of cholera incidents in South London, 1853. *Source:* Matrix 2013.

The Object-Centered and Human-Pathogen Coevolution Theories of Medical Geography

To add to this distinction between medical geography and epidemiology, while also emphasizing the need for cross-disciplinary collaboration, Scott, Robbins, and Comrie (2012) assert the importance of object-centered and human-pathogen coevolution theories as foundations of medical geography. An object-centered approach entails directing the primary research focus on a specific object in the broader context of human and environmental interactions. This directed focus on the object of interest encourages

interdisciplinary and cross-disciplinary cooperation because it breaks down the propensity of researchers to strictly adhere to their field-specific methodologies, as this often hinders cooperative efforts among researchers from different fields (Meade, Florin, and Gesler 1988, Scott, Robbins, and Comrie 2012).

A human-pathogen coevolution approach suggests that humans and pathogens will always coexist and will therefore coevolve to adapt to each other (Woolhouse et al. 2002). Although traditional studies incorporating this theory stress the literal (genetic) evolution of humans and pathogens as a result of one another (Woolhouse et al. 2002; Zaneveld et al. 2008; Rehermann 2009), Scott, Robbins, and Comrie (2012) introduce an alternative view of the human-pathogen coevolution theory as it pertains to the human-environment interaction tradition of geography. The cycle begins when humans initially cause or encourage their own exposure to pathogens through institutionally driven actions, i.e. land-use changes, policy guidelines, and waste management practices. The resulting disease outbreaks then spur reactionary human responses, which eventually lead to institutional modifications designed to discourage further exposure. Examples of these include increased education, more aggressive disease monitoring, and the development of new treatments. This theory very closely aligns with Meade, Florin, and Gesler's (1988) concept of the triangle of human ecology in which habitat, population, and behavior are affected by, and therefore systematically respond to, disease within society.

To emphasize how these theories, inherent to medical geography, differ from those of epidemiology, Scott, Robbins, and Comrie (2012) discuss the theoretical approaches commonly applied to epidemiological studies: ecological/evolutionary models and population models. Ecological/evolutionary models are often used to

understand the growth and development of pathogens, while population models are used to assess disease exposure. According to the authors, these traditional epidemiological theories fail to sufficiently incorporate the complex and dynamic human-environmental interactions that result in—and react to—pathogen exposure.

Because of this, the human-pathogen coevolution theory provides an appropriate alternative for studying environmentally determined diseases like coccidioidomycosis. In addition to being environmentally driven, coccidioidomycosis incidents are increasing (Park et al. 2005; Sunenshine et al. 2007; Arizona Department of Health Services 2012; Tsang et al. 2013), and it is likely that human factors such as migration to endemic areas and changes to the landscape play a role in these increased incidents (Meade, Florin, and Gesler 1988; Galgiani 1999). As a result, the human-pathogen coevolution theory provides the most comprehensive means for analyzing and understanding both the disease's prevalence among the population and the institutional changes that will come about as a result of its prevalence (Meade, Florin, and Gesler 1988; Scott Robbins, and Comrie 2012).

The fact that researchers have a very limited understanding of *Coccidioides* niche requirements necessitates an object-centered approach to garner a better understanding of those requirements (Kolivras and Comrie 2003; Comrie 2005; Scott, Robbins, and Comrie 2012). In order to predict the areas of highest exposure risk, it is first necessary to identify where *Coccidioides* is most likely to occur, and this requires a more comprehensive understanding of the environmental factors that support its growth and dispersal (Baptista-Rosas, Hinojosa, and Riquelme 2007; Fisher et al. 2007). The object of interest, in this case, is the *Coccidioides* fungus, and to understand its habitat requires

cross-disciplinary collaboration. The idea is that by focusing on this specific object of interest, researchers can overcome the interdisciplinary rifts that tend to occur as the result of methodology-focused research (Meade, Florin, and Gesler 1988; Scott, Robbins, and Comrie 2012). It is therefore evident that both the object-centered and human-pathogen coevolution theories form the fundamental foundations necessary for the success of this research.

Debates within the Field of Medical Geography

The epistemological debate that exists between medical geography and epidemiology unfortunately continues even within the field of medical geography itself. However, researchers mostly agree that medical geography should be broken down into two traditions: geographical epidemiology (also called landscape epidemiology or ecological analysis) and health systems planning (Mayer 1982; Meade, Florin, and Gesler 1988; Boulos, Roudsari, and Carson 2001; Kistemann, Dangendorf, and Schweikart 2002). Geographical epidemiology involves studying the spatial distribution of diseases as well as the ecological (including human-induced) influences on disease processes. Alternatively, the health systems planning tradition analyzes the spatial perspectives on the access to/delivery of healthcare services planning (Mayer 1982; Meade, Florin, and Gesler 1988; Boulos, Roudsari, and Carson 2001; Kistemann, Dangendorf, and Schweikart 2002).

Some researchers argue that the field of medical geography does not fully account for all geographic perspectives on health and disease and that the field should be further sub-divided. Kearns (1993) proposed, and Cutchin (2007) later supported the need for a new and distinct discipline, which he termed the geography of health. In contrast to

traditional medical geography, which is objective and analytical in nature—a result of its emphasis on the environmental determinants of disease—health geography (as the geography of health is often called) critically analyzes the social, place-based determinants on the overall health of the population (Kearns 1993; Cutchin 2007). These determinants are often measured by the quality of available healthcare services and by the equality of access to those services (Perry and Gesler 2000; Hawthorne and Kwan 2012). In this sense, health geography is similar to the health services planning tradition of medical geography, but it is more critical in nature and has a stronger emphasis on the characteristics of place (Kearns 1993).

Mayer (1994) quickly criticized this perspective as being too narrow in scope and unnecessary. He argued that medical geography is sufficient as a stand-alone discipline because of its flexibility in encompassing social, place-based factors as part of the overall environmental determinants of health. Although this epistemological debate appears to needlessly divide researchers who should otherwise cooperate for the benefit of what each has to offer to the field, it continues to be a noteworthy and ongoing debate (Rosenberg 1998; Kearns and Moon 2002; Kwan 2004; Cutchin 2007).

A Geographical Epidemiology Approach to Coccidioidomycosis Research

Recognizing the debates and the epistemological differences that exist within the fields of epidemiology and medical geography, it is important to emphasize that this study will fall within the ecological analysis, or geographical epidemiology tradition of medical geography, due to the inherent nature of coccidioidomycosis as an environmentally determined disease. Because coccidioidomycosis is caused by the direct inhalation of fungal spores from the surrounding environment, rather than by person-to-

person contact (Chiller, Galgiani, and Stevens 2003; Arizona Department of Health Services 2013), research that focuses on the environmental determinants of the disease must be conducted in order to understand its spatial distribution and associated risk to the human population. This justifies geographical epidemiology as the most appropriate discipline through which to study this disease.

Within this discipline, the literature identifies two common approaches to studying coccidioidomycosis, its spatial distribution, and both its effects on and risks to the population. The first approach entails a direct ecological analysis of the fungus that causes the disease. This involves analyzing the environmental conditions of the sites at which actual *Coccidioides* samples have been isolated to better understand the organism's ecological niche (Baptista-Rosas, Hinojosa, and Riquelme 2007; Fisher et al. 2007). Although many researchers recognize this to be the most accurate method for determining the environmental factors necessary for the growth and survival of *Coccidioides*, they are well aware of its limitations. Chief among these is that in order to conduct this type of analysis, it is first necessary to ascertain the locations of *Coccidioides* in the environment (Kolivras and Comrie 2003; Comrie 2005).

This presents a common problem: although ubiquitous, *Coccidioides* is very elusive, and although multiple sites in endemic areas have been sampled in attempts to isolate colonies of the fungus, very few of those attempts have proven successful (Baptista-Rosas, Hinojosa, and Riquelme 2007). Due to the insufficient number of positively identified samples of *Coccidioides*, it is difficult to make authoritative conclusions about the ecological requirements of the population as a whole. Fisher et al. (2007) found this to be the case when they tested soil samples from the few sites known

to harbor *Coccidioides* in an effort to establish its niche parameters. Their only definitive conclusions were that *Coccidioides* resides in loamy, sandy soils and requires temperatures below 55 degrees Celsius (°C). Had they had a larger sample to study, Fisher et al. (2007) might have been able to present stronger conclusions.

The second, and more common, approach to studying coccidioidomycosis involves an indirect ecological analysis. This type of research uses reported cases of coccidioidomycosis to determine the environmental factors that are associated with the disease exposure (Kolivras and Comrie 2003; Comrie 2005; Park et al. 2005; Comrie and Glueck 2007; Talamantes, Behseta, and Zender 2007; Tamerius and Comrie 2011). This approach focuses less on the spatial distribution of the fungus itself and more on determining the environmental patterns in known endemic areas that have the greatest influence on the increase in coccidioidomycosis incidence. Much of this research involves the use of statistical modeling to predict future outbreaks, and it tends to concentrate heavily on the use of climatic factors as independent variables.

For example, Comrie (2005) developed a multivariate regression model to analyze the effects of seasonal climate patterns of alternating wet and dry periods on coccidioidomycosis exposures in Pima County, Arizona. This study concluded that the most important factor influencing exposure rates was the incidence of precipitation during the typically arid spring in the preceding 1.5-2 years before exposure.

Kolivras and Comrie (2003) developed a regression model to predict future coccidioidomycosis outbreaks. Their results revealed that temperature and precipitation were statistically significant predictors of coccidioidomycosis incidents. Specifically, they concluded that periods of precipitation followed by periods of hot, dry conditions

were associated with the highest incidence of the disease; that winter seasonal climate patterns appeared to have the most significant impact on future outbreaks; and that the months with the highest numbers of reported cases produced the best models for prediction.

Park et al. (2005) developed a Poisson regression model to analyze the association between climatic factors (wind, dust, temperature and precipitation) and coccidioidomycosis incidents. Their results revealed that the most statistically significant variables associated with disease rates were temperatures during the three months prior to reported incidents, average dust levels, and precipitation during the seven months prior to the reported cases.

Although these early studies were successful in explaining coccidioidomycosis incidents with climatic data alone, recent climate-only based studies have failed to explain fully the continued upward trends in reported cases, leading researchers to recognize the need to incorporate non-climatic data such as soil conditions as well as the anthropogenic factors of migration and development into their models (Comrie and Glueck 2007; Talamantes, Behseta, and Zender 2007; Tamerius and Comrie 2011).

No studies have been conducted on the spatial distribution of coccidioidomycosis in places that mandate incidence reporting for the purpose of determining disease risk areas in places that do not. Additionally, there have been no studies incorporating GIS in the analyses of environmental factors that contribute to the growth and dispersal of *Coccidioides* in order to determine high risk areas for coccidioidomycosis. Only one study has systematically attempted to determine current coccidioidomycosis risk areas in Texas, rather than relying on dated and incomplete historical delineations of endemic

areas in the state (Gautam et al. 2013). That study however, used seropositive dogs in Texas as the proxy for *Coccidioides* occurrence, not human cases in other endemic areas.

IV. RESEARCH METHODS

In an attempt to build upon the direct and indirect ecological analysis foundations mentioned in the previous chapter, this study combined aspects from both in order to capitalize on the strengths of each. Although the literature stressing the importance of determining the ecological niche of *Coccidioides* is very convincing, equally convincing is the infeasibility of using isolated samples to do so. Because of this, it was apparent that the geographic locations of reported cases of coccidioidomycosis were required as a proxy for the spatial distribution of *Coccidioides* in the absence of actual samples. The inherent assumptions in doing so were that individuals remained in the same counties in which they were infected from spore exposure to symptom onset, and therefore, incidents of the disease were reported in the same counties in which the disease was contracted (Meade and Earickson 2000).

These locations were then used to determine the environmental conditions common to the areas where *Coccidioides* is highly likely to be present and cause outbreaks of coccidioidomycosis. The environmental variables were combined with the anthropogenic variable of economic development to construct a statistical model that determined the conditions most likely to contribute to the growth, dispersal, and exposure to the disease-causing fungal spores and consequently, a high risk of coccidioidomycosis.

The statistical model was built combining logistic regression with weighted linear combination in GIS to determine areas in selected counties within California with a high likelihood for the presence of *Coccidioides* to cause an outbreak of coccidioidomycosis. This model used coccidioidomycosis cases reported in California as the dependent variable and environmental and anthropogenic factors (discussed in detail later) as the

independent variables. The model was then applied to areas in Texas with similar environmental and anthropogenic characteristics to predict where *Coccidioides* would be most likely to occur at outbreak levels there.

Similar geographical epidemiological studies have utilized logistic regression techniques to predict high risk areas for diseases such as malaria and Lyme disease (Kleinschmidt et al. 2000; Brownstein, Holford and Fish 2003; de Oliveira et al. 2013). Like coccidioidomycosis, malaria and Lyme disease are environmentally communicable. Both diseases are contracted through contact with infectious organisms from the environment (mosquitoes and ticks, respectively), rather than contact with infected humans, and logistic regression has been successful in determining the relative importance of environmental influences on mosquito and tick proliferation as well as human contact risk (Kleinschmidt et al. 2000; Brownstein, Holford and Fish 2003, de Oliveira et al. 2013). As a result, it was presumed that logistic regression would be an appropriate method for predicting the relative environmental and anthropogenic influences on *Coccidioides* growth, dispersal, and contact with humans as well.

Weighted linear combination is a commonly used suitability analysis technique in GIS in which individual criterion layers are assigned weights and overlaid using map algebra (Bolstad 2008; Drobne and Lisec 2009). The result is a final output layer representing those combined relative weights, which can be used to describe place "suitability" in a risk assessment context. For this study, each of the independent variables was represented in GIS as an individual criterion layer. The final outputs were layers (one for each season of study) illustrating the results of their weighted combination as the dependent variable of where *Coccidioides* would likely occur at outbreak levels.

Although there exist varying techniques for assigning weights to each criterion layer, including arbitrary value assignment and expert opinion (Malczewski 2000; Drobne and Lisec 2009), logistic regression offered an objective and statistical method for doing so and was therefore, the most appropriate for this study (Gaines, Boring, and Porter 2005).

Study Area

The research study area was comprised of two locations: southern California (used to build the statistical model) and West Texas (the target area for determining coccidioidomycosis outbreak risk)

The California study area was comprised of eight counties in California, all of which either fall on, or are located south of the 37 degrees north latitude line (Figure 3). This area was chosen for three reasons. First, the vast majority of reported cases occur in the southern portion of the state. Second, California aggressively monitors and reports all cases of the disease (California Department of Public Health 2011). Finally, the eight counties selected were the only counties for which complete data sets were available. Incomplete data sets were those lacking values for either the environmental or anthropogenic independent variables or coccidioidomycosis cases, during the time period to be studied.

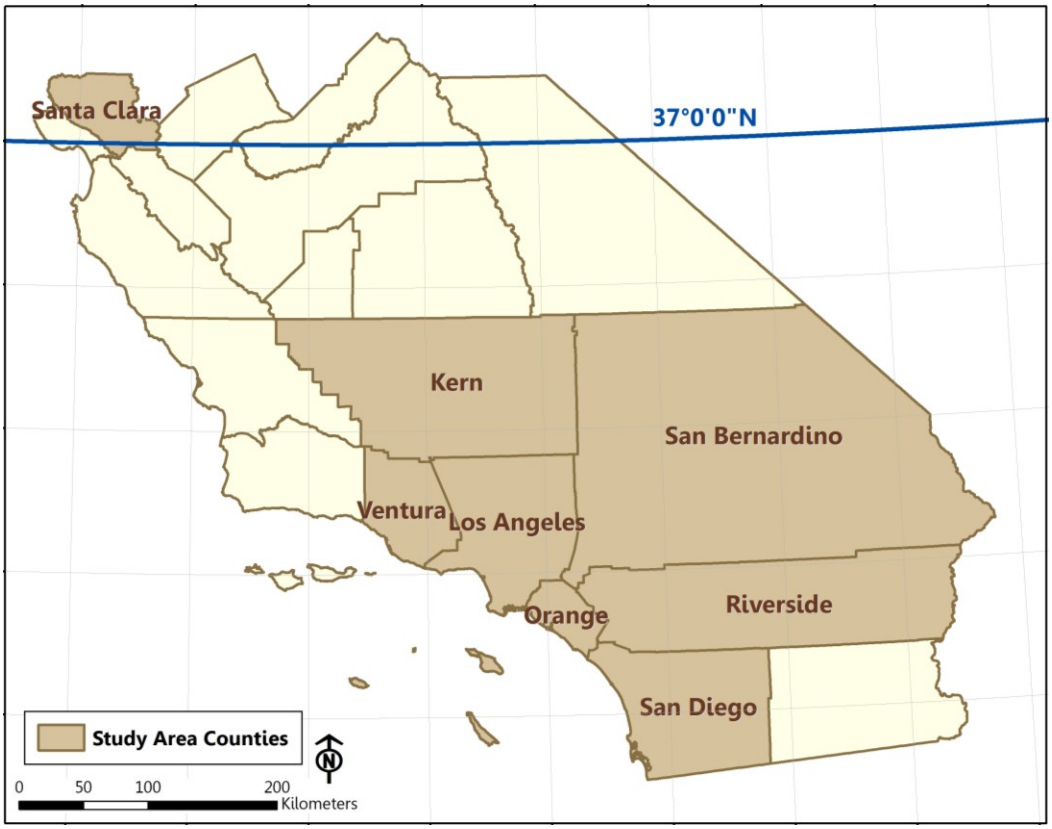


Figure 3. California study area.

The Texas study area was comprised of fifteen counties in Texas, all of which either fall on, or are located west of the 100 degrees west longitude line (Figure 4). Like the California study area, these fifteen counties were the only counties for which a complete data set was available.

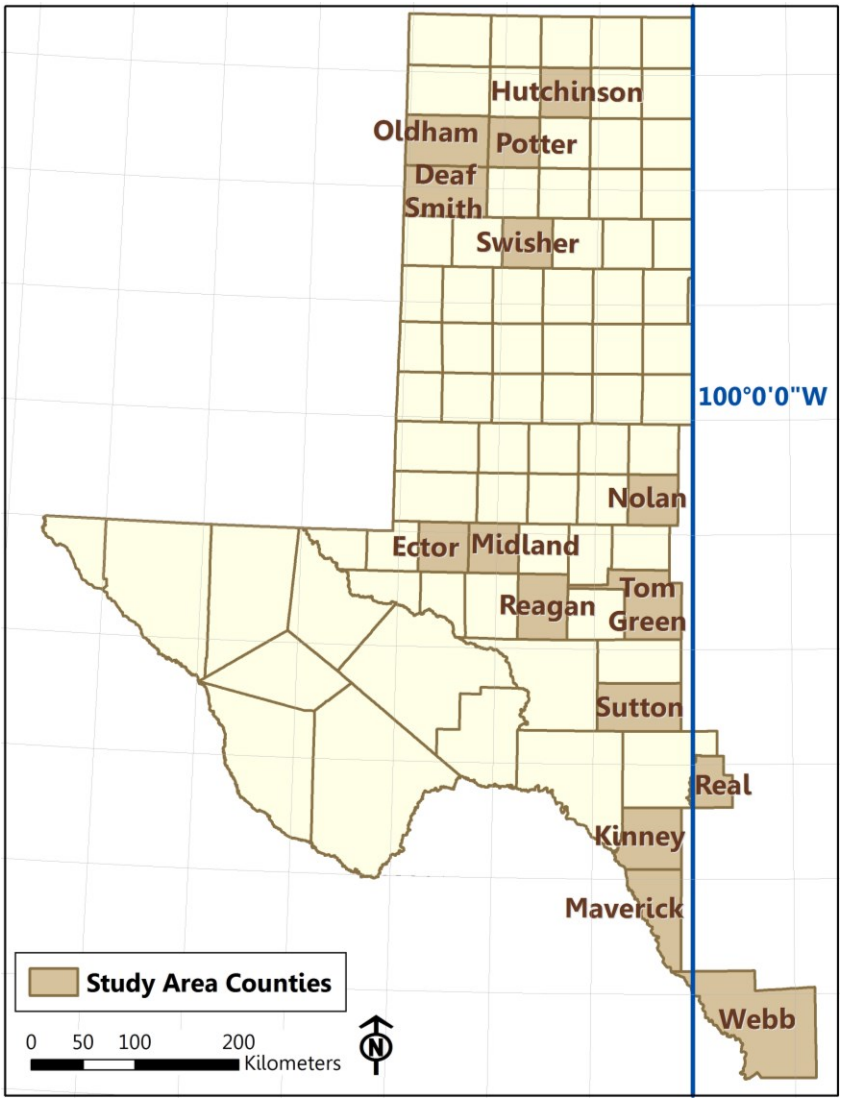


Figure 4. Texas study area.

The West Texas study area was chosen because of its previous delineation as an endemic risk area and its relatively similar climate to southern California. Both West Texas and large parts of southern California fall primarily within the arid (B) Köppen climate zones, the climate in which *Coccidioides* is found (Stevens 1995; Fisher et al. 2007), with some areas located partially within the subtropical mid-latitude (C) Köppen climate zones (Figure 5) (National Weather Service 2011). The fact that both study areas

fall mostly within the same climate zones allows the potential to extrapolate climate-based results from one study area to the other.

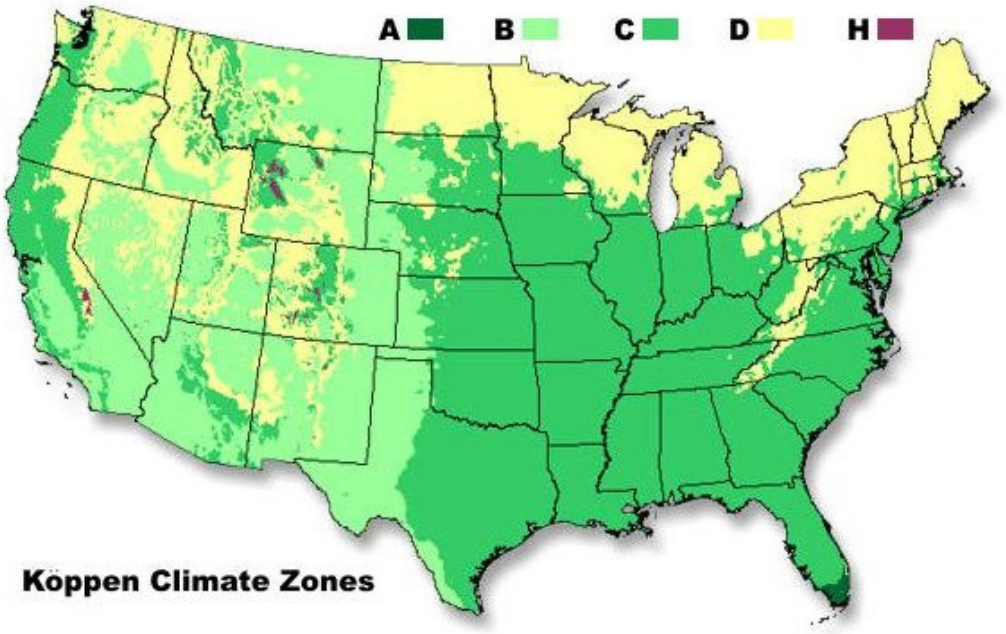


Figure 5. Map of Köppen climate zones for the U.S. [A) Tropical Climates; B) Arid Climates; C) Subtropical Mid-Latitude Climates; D) Continental Mid-Latitude Climates; H) Highland Climates].
Source: National Weather Service 2011.

Dependent Variable

The dependent variable, presence of *Coccidioides* at outbreak levels, was a binary variable coded "1" for "outbreak level," and "0" for "non-outbreak level." In the model, this was represented by the proxy variable, seasonally aggregated, county level, population normalized, rates of coccidioidomycosis in the California study area from 2003-2012. The monthly coccidioidomycosis cases at the county level were obtained directly from individual California county health departments and required seasonal aggregation and population normalization (discussed below).

Disease cases were delivered in varying forms of report dates, such as date of exposure, date of diagnosis, or date of report. Occasionally all three report dates occurred in the same county data set with no explanation of which date type belonged to which value. To account for this, each rate was time-lagged by one month to allow for at least thirty days to occur between spore exposure and diagnosis/report date. Also, because the reported months were aggregated seasonally, it was reasonable to presume that most of the exposure-to-report time would be captured within the ninety days comprising each season, especially when including the one month time lag (Comrie 2005; Tamerius and Comrie 2011).

The World Health Organization (2014) defines disease outbreak as the "occurrence of cases of disease in excess of what would normally be expected in a defined community, geographical area or season." Thus outbreak, for the purpose of this study, referred to seasonally aggregated cases that exceeded the 65th percentile of the combined monthly rates in all counties within the study area from 2003-2012. In view of the absence of an explanation for what constituted a higher than expected occurrence of a disease, the 65th percentile reasonably represented this value, as it accounted for incidents that were at least 15 percent higher than the median.

Determination of Seasons and Rates

Seasons throughout the analysis were aggregated as follows: December-February (winter); March-May (spring); June-August (summer); and September-November (fall). In addition, the time period for all variables, unless otherwise stated, was from 2003-2012.

All rates throughout the analysis were population normalized per 100,000 people according to the 2000 U.S. Census county population data for all dates prior to 2010, and the 2010 U.S. Census county population data for all dates after 2010 (U.S. Census Bureau 2000, 2010).

Independent Variables

Environmental

The environmental independent variables included the average seasonal temperature deviations from the 30-year seasonal normal, in °C and total seasonal precipitation deviations from the 30-year seasonal normal, in millimeters for each California study area county. The actual climate values were obtained from the U.S. National Climatic Data Center (NCDC) (2014), while the 30-year (1981-2010) normal values were obtained from a list compiled by Golden Gate Weather Services (2011). Climographs of the 30-year normal values for each study area county are included in Appendix B.

Temperature and precipitation deviations from normal were used, rather than their absolute values, to allow for extrapolation of the results to Texas, as absolute values would have prevented the possibility of a reference point for comparison between the two study areas. Additionally, because the literature suggests that the increase in coccidioidomycosis incidents is potentially due to climatic changes (Kolviaras and Comrie 2003; Komatsu et al. 2003; Comrie 2005; Park et al. 2005), analyzing the deviations from normal captured the possibility for the change in climate as an influencing factor for *Coccidioides* growth and dispersal, whereas including absolute temperature and precipitation values did not.

Because *Coccidioides* growth is dependent on climatic factors, and because the fungus requires time to develop infectious spores (although there is debate among researchers on the amount of time this process requires) (Fisher et al. 2007), it was imperative to account for the time lag between the climatic influences on the initial growth of *Coccidioides* and the later dispersal of its mature spores. In order to account for this, for each season of disease outbreaks, the temperature and precipitation data were analyzed for the three seasons prior to it. Each of the seasonal independent variables was analyzed for its effect on the dependent variable at time zero (T0), the actual season of study, as well as at each consecutively time-lagged season preceding T0. This accounted for climatic influences on *Coccidioides* growth and dispersal up to a year prior to human spore exposure.

Anthropogenic

The anthropogenic independent variable of seasonal human-induced soil disturbance was represented by county level, population normalized, seasonally aggregated, rates of building permits issued by each California study area county. These data were obtained from the U.S. Census Bureau (2014) and from individual California county permit departments. According to the U.S. Census Bureau (2013), the average length of time between permit issuance and construction initiation was one to three months. Therefore, this variable was analyzed at T0, as well as time-lagged by one season, to account for the possibility of this time lapse (Park et al. 2005).

Both groups of independent variables (environmental and anthropogenic) were continuous variables in the analysis.

Analysis

The variables were initially tested for multicollinearity by conducting a correlation analysis using IBM SPSS software (IBM Corporation 2012). The time-lagged temperature variables were highly correlated with each other, and therefore collinear. These results were anticipated, however, as the values were expected to trend together due to the short time span between seasons. Time lagged building permit rates were also highly correlated with each other, but these results were anticipated as well and for the same reasons as the temperature variables. It was therefore concluded that multicollinearity did not negatively affect this study.

A binary logistic regression analysis was then conducted to build seasonal predictive models for coccidioidomycosis outbreak risk. The enter method was used to determine which independent variables significantly predicted the dependent variable. In this method, all variables were entered into the model in single step and included in the output with their respective results. Significant variables were determined to be only those with $p < 0.05$. An Omnibus Test of Model Coefficients, or Chi Square analysis, tested the model's overall significance; the Nagelkerke pseudo R^2 assessed the amount of variance explained by the independent variables in the model; and the Hosmer and Lemeshow test assessed how well the predicted probabilities matched the observed probabilities (Meyers, Gamst, and Guarino 2013).

The results of the analysis provided an equation representing the dependent variable as the predicted log odds that any observed case belonged to the "1," or "presence of *Coccidioides* at outbreak levels" category given any change in the

independent variables according to their relative predictive strengths, or coefficients (Meyers, Gamst, and Guarino 2013).

These resulting significant independent variable coefficients were used as the relative weights for weighted linear combination in ArcGIS 10.1 (Esri 2012). Using map algebra, these coefficients were multiplied by their corresponding independent variable (criterion) layers, resulting in a layer that represented the log odds of a predicted outbreak. This layer was then transformed by map algebra into a layer representing the probability of the presence of *Coccidioides* at outbreak levels. This analysis was repeated for each season of study to obtain seasonal *Coccidioides* exposure probabilities (Figure 6).

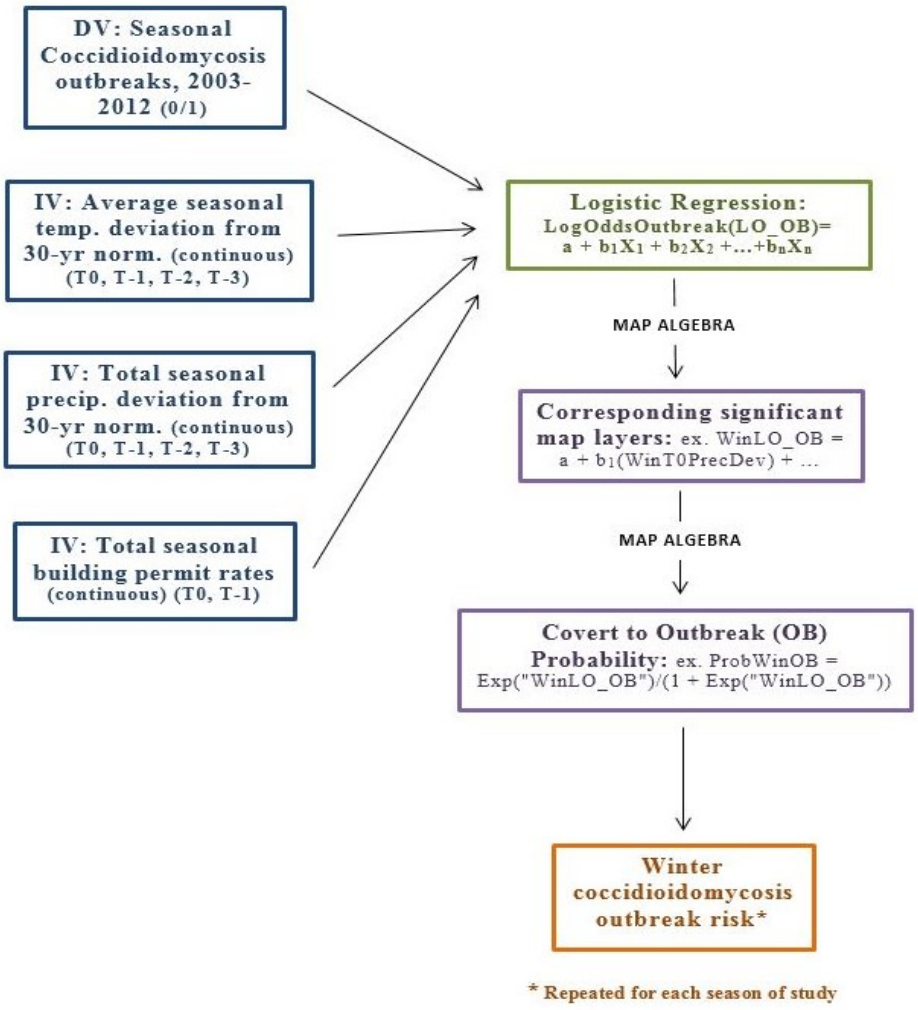


Figure 6. Conceptual model of data analysis.

The results were verified in California using mapped locations of actual outbreaks to compare to areas of high outbreak probability, according to the model results. The model was then applied to the Texas study area by applying weighted linear combination in GIS to the corresponding Texas criterion layers.

V. RESULTS

Winter

The winter season model resulted in a Chi Square (df = 10, N = 80) value of 25.87, $p = 0.004$, indicating that the model provided a statistically significant prediction of success. The Nagelkerke pseudo R^2 indicated that the model accounted for approximately 36 percent of the total variance. The Hosmer and Lemeshow Test indicated an overall prediction success rate of 76.3 percent and correct prediction rates of 50 percent for the "outbreak" group and 88.9 percent for the "no outbreak group." The classification cutoff value for predicting membership in the successful groups was 0.5. Table 1 displays the results of the winter season outbreak model.

Table 1. Winter season model results

Winter Model	B	Wald	Sig.	Exp (B)	95% C.I. for EXP (B)
Win T0 Precip. Dev. (mm)	**-0.008**	4.037	**0.045**	**0.992**	**0.985 - 1**
Win T-1 Precip. Dev. (mm) (Fall)	0.011	1.315	0.252	1.011	0.992 - 1.03
Win T-2 Precip. Dev. (mm) (Sum)	0.042	0.803	0.37	1.043	0.951 - 1.144
Win T-3 Precip. Dev. (mm) (Spr)	-0.003	0.191	0.662	0.997	0.985 - 1.01
Win T0 Temp. Dev. (C)	-0.004	0	0.991	0.996	0.469 - 2.116
Win T-1 Temp. Dev. (C) (Fall)	0.801	2.783	0.095	2.228	0.869 - 5.713
Win T-2 Temp. Dev. (C) (Sum)	-0.638	2.153	0.142	0.528	0.225 - 1.239
Win T-3 Temp. Dev. (C) (Spr)	0.087	0.087	0.767	1.091	0.614 - 1.939
Win T0 Bldg. Permits	**-0.041**	4.671	**0.031**	**0.96**	**0.925 - 0.996**
Win T-1 Bldg. Permits (Fall)	**0.046**	7.048	**0.008**	**1.047**	**1.012 - 1.084**
Constant	**-1.517**	11.233	**0.001**	**0.219**	

Explanations of variable meanings included in Appendix A

Although winter precipitation deviation from normal (Win T0 Precip. Dev. (mm)) and winter building permit rates (Win T0 Bldg. Permits) were significant variables in the

model ($p = 0.045$, $p = 0.031$, respectively), their coefficients were negative, resulting in odds ratios less than one. This means that for winter precipitation deviation from normal, for example, every one unit change in that variable resulted in a -0.008 unit change in the log of the odds for a winter outbreak, or a less than one times (0.992) greater likelihood of an outbreak occurring. Therefore, despite its significance ($p = 0.045$) in the model, it is unlikely that winter temperature deviation from normal has much predictive influence on winter outbreaks (Meyers, Gamst, and Guarino 2013). The winter building permit rates variable can be interpreted in the same manner.

The fall building permit rates variable (Win T-1 Bldg. Permits (Fall)), however, was predictive. Not only was it significant ($p = 0.008$), but also it contained a positive coefficient and an odds ratio greater than one. For every one unit increase in fall building permit rates, there was a 0.046 increase in the log of the odds for a winter outbreak, or a 1.047 times (CI = 1.012 - 1.084) greater likelihood of a winter outbreak occurring, controlling for all other variables (Meyers, Gamst, and Guarino 2013).

This may mean that when building permits are issued in the fall, construction (a likely cause of soil disturbance and subsequent spore aerosolizing) often does not begin until the winter season. These results align with Park et al.'s (2005) study, which concluded that although building permits at T0 were not significant predictors of coccidioidomycosis cases, it was possible that this was due to the time lapse between permit issuance and construction initiation (U.S. Census Bureau 2013).

These results may also indicate that permit issuance and construction initiation occur in the same season, but the time lapse between spore exposure and seeking medical care spans an entire season.

Verification

Verification for the winter model was conducted on four randomly selected years of the study time period, 2004, 2008, 2011, and 2012. The results of the model were mapped using weighted linear combination in GIS and compared to the mapped locations of actual reported winter outbreaks during those years (Figures 7 – 10).

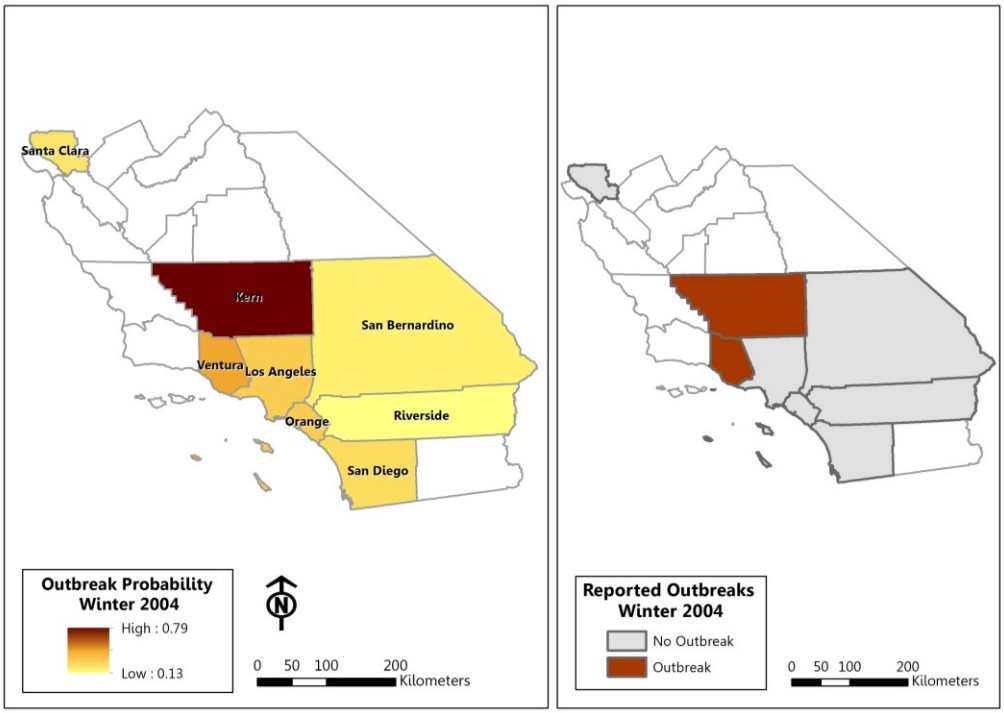


Figure 7. California winter 2004 outbreak probabilities, based on model results, compared to actual outbreaks.

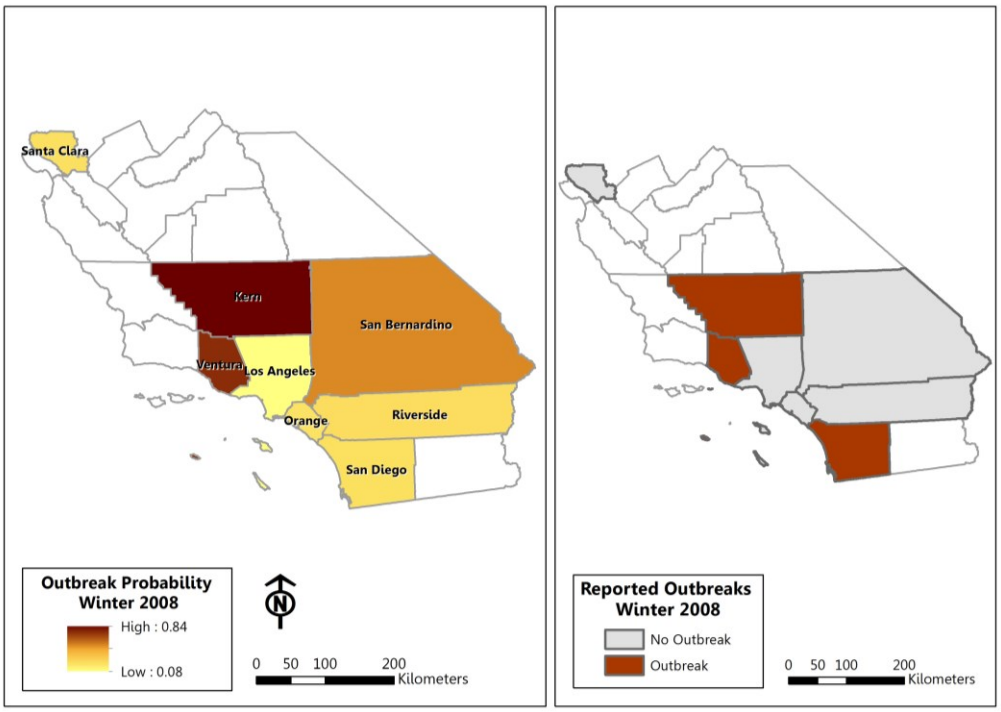


Figure 8. California winter 2008 outbreak probabilities, based on model results, compared to actual outbreaks.

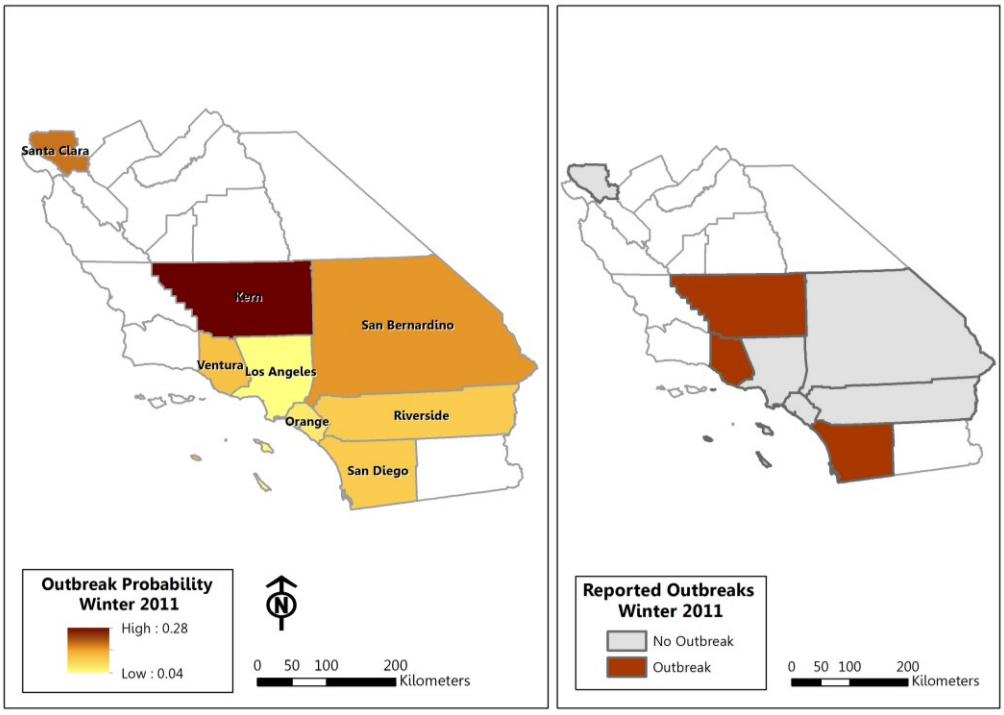


Figure 9. California winter 2011 outbreak probabilities, based on model results, compared to actual outbreaks.

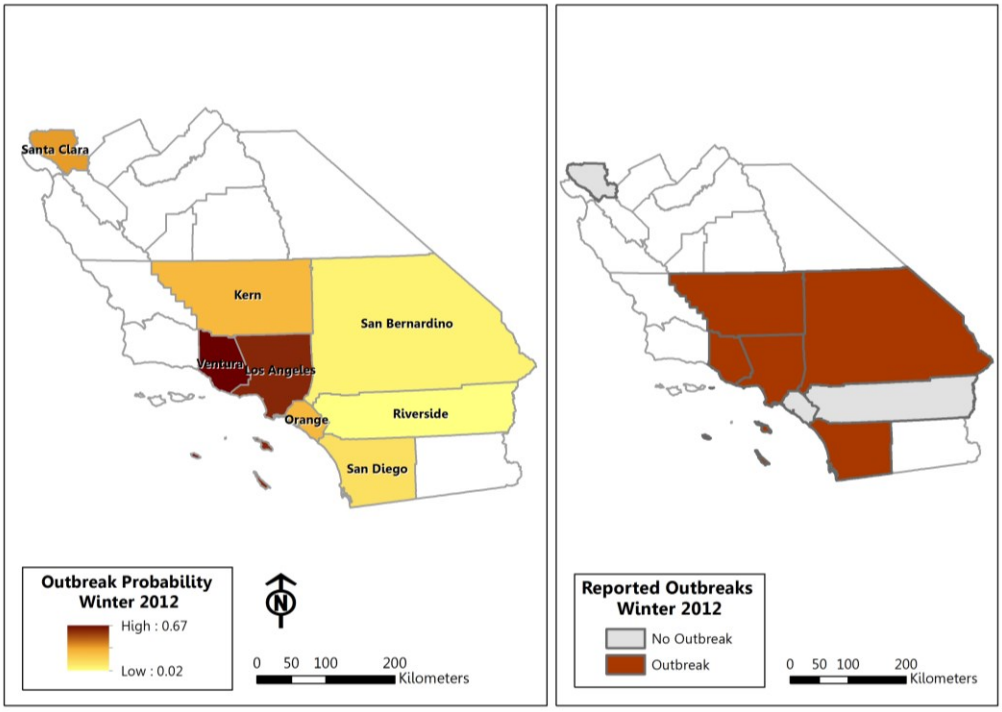


Figure 10. California winter 2012 outbreak probabilities, based on model results, compared to actual outbreaks.

Model-based winter probabilities revealed moderate accuracy when compared to the actual reported outbreaks, especially in the northwestern portion of the study area during 2004, 2008, and 2012. The poor results apparent in 2011 were appropriate when considering that the highest probability of any value was only 28 percent. The overall mediocre results of the verification were expected, considering that although three variables were significant in the model (winter precipitation deviations from normal, winter building permit rates, and fall building permit rates), only one variable (fall building permit rates) displayed predictive power. It is evident from these results that its predictive strength as a standalone variable was rather weak.

Spring

The spring season, model resulted in a Chi Square (df = 10, N = 80) value of 11.835, $p = 0.296$, indicating that the model did not provide a statistically significant prediction of success. This model was therefore discarded, and no results could be gathered nor any predictions made for the spring season.

Summer

The summer season model resulted in a Chi Square (df = 10, N = 80) value of 24.158, $p = 0.007$, indicating that the model provided a statistically significant prediction of success. The Nagelkerke pseudo R^2 indicated that the model accounted for approximately 37 percent of the total variance. The Hosmer and Lemeshow Test indicated an overall prediction success rate of 75 percent and correct prediction rates of 41.7 percent for the "outbreak" group and 89.3 percent for the "no outbreak group." The classification cutoff value for predicting membership in the successful groups was 0.5. Table 2 displays the results of the summer season outbreak model.

Table 2. Summer season model results

Summer Model	B	Wald	Sig.	Exp (B)	95% C.I. for EXP (B)
Sum T0 Precip. Dev. (mm)	0.010	.057	0.811	1.010	0.929 – 1.099
Sum T-1 Precip. Dev. (mm) (Spr)	-0.014	2.633	0.105	0.986	0.969 – 1.003
Sum T-2 Precip. Dev. (mm) (Win)	**-0.007**	4.395	**0.036**	**0.993**	**0.986 – 1**
Sum T-3 Precip. Dev. (mm) (Fall)	0.017	2.118	0.146	1.017	0.994 – 1.041
Sum T0 Temp. Dev. (C)	-0.445	1.535	0.215	0.641	0.317 – 1.295
Sum T-1 Temp. Dev. (C) (Spr)	-0.295	.710	0.399	0.744	0.375 – 1.479
Sum T-2 Temp. Dev. (C) (Win)	0.586	1.648	0.199	1.796	0.735 – 4.393
Sum T-3 Temp. Dev. (C) (Fall)	0.442	1.547	0.214	1.556	0.775 – 3.122
Sum T0 Bldg. Permits	**0.055**	6.426	**0.011**	**1.057**	**1.013 – 1.103**
Sum T-1 Bldg. Permits (Spr)	**-0.047**	5.410	**0.020**	**0.954**	**0.917 - .993**
Constant	**-1.669**	12.608	**< 0.001**	0.188	

Explanations of variable meanings included in Appendix A

Similar to the winter model, the summer model revealed three variables to be significant, but only one to have predictive power. Winter precipitation deviation from normal (Sum T-2 Precip. Dev. (mm) (Win)) and spring building permit rates (Sum T-1 Bldg. Permits (Spr)) both contained negative coefficients and odds ratios less than one, meaning that despite their significance in the model ($p = 0.036$, $p = 0.02$, respectively), it is unlikely that either variable had much predictive influence on summer outbreaks (Meyers, Gamst, and Guarino 2013).

The summer building permit rates variable (Sum T0 Bldg. Permits), however, was significant ($p = 0.011$) and contained a positive coefficient and an odds ratio greater than one. For every one unit increase in summer building permit rates, there was a 0.055 increase in the log of the odds for a summer outbreak, or a 1.057 times (CI = 1.013 – 1.103) greater likelihood of winter outbreak occurring, controlling for all other variables (Meyers, Gamst, and Guarino 2013).

These results counter the winter results in that they indicate that either construction begins in the same season of permit issuance during the summer, or that there is less of a time lapse between spore exposure and seeking medical care during the summer. It may be possible that people expect to be sick more during the winter and may not seek medical attention right away. This may be especially true considering coccidioidomycosis can mimic symptoms of the common cold (Kirkland and Fierer 1996; Chiller, Galgiani, and Stevens 2003; Galgiani et al. 2005), an illness for which many people do not seek medical care at all. It is generally considered far less common to become sick in the summer, however, leading people to possibly seek medical attention more rapidly if they do develop symptoms. Although merely speculation, this explanation does account for the discrepancy in the results between the winter and summer seasons.

The increased rate of soil desiccation in the dry summer offers another explanation for the discrepancy in results. Because of southern California's predominantly wetter winters, it is possible that the soil requires longer to dry out than it does in the summer. Soil disturbance in the winter may not generate the same volume of aerosolized dust as it would in the summer, so even the immediate initiation of construction upon the receipt of building permits would not necessarily lead to the same rates of spore exposure in the winter as it would in the summer.

Verification

Verification for the summer model was conducted using the same weighted linear combination in GIS technique on the same four years as the winter model (Figures 11 – 14).

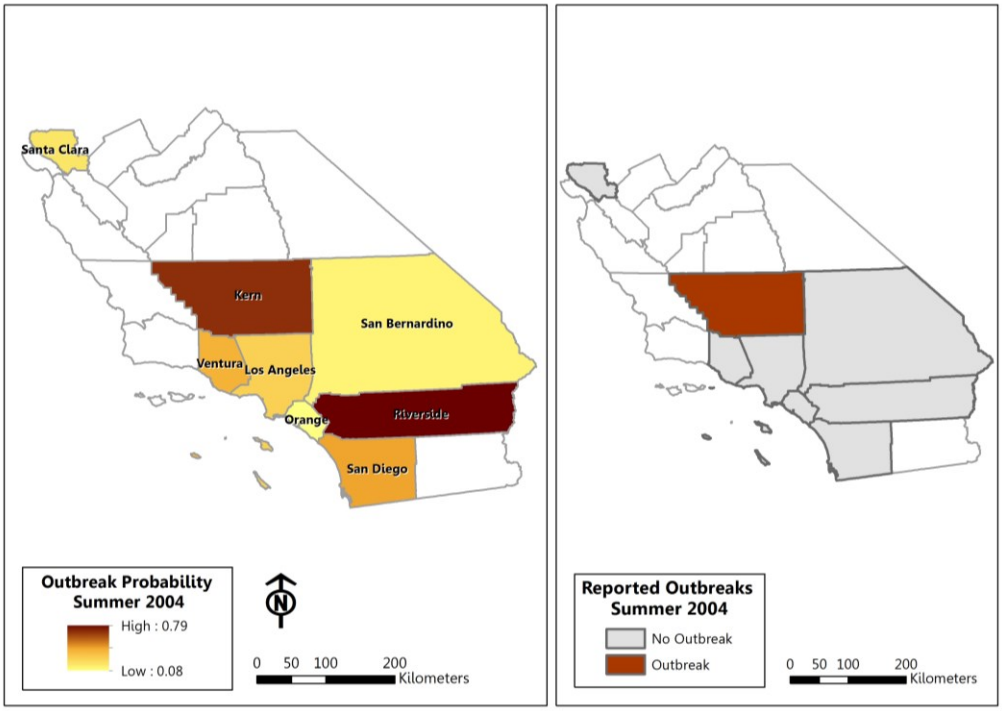


Figure 11. California summer 2004 outbreak probabilities, based on model results, compared to actual outbreaks.

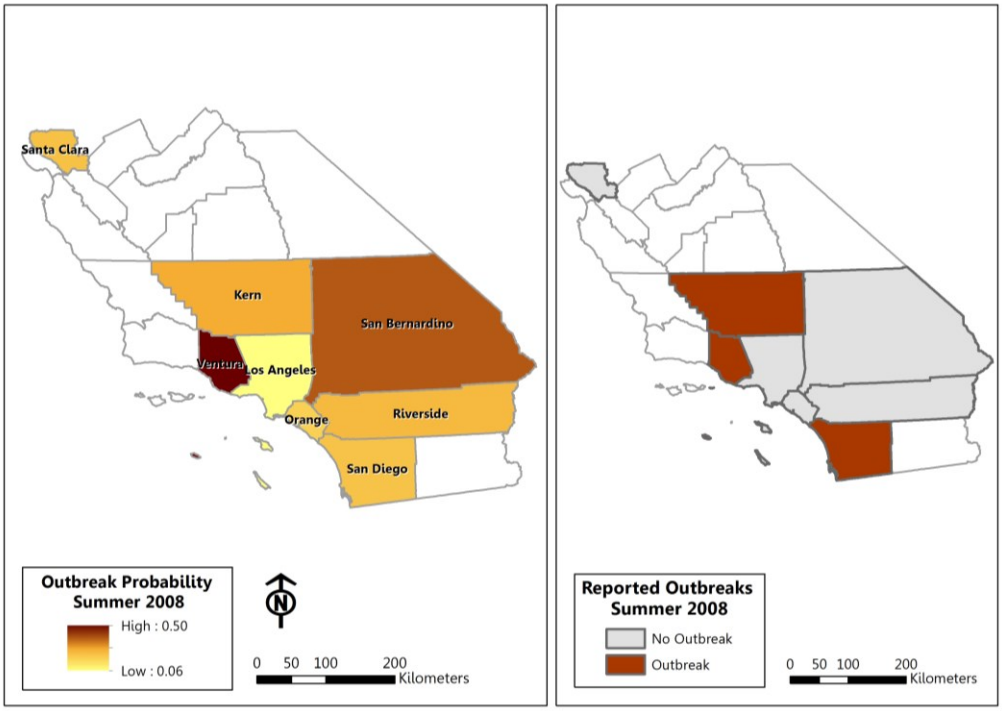


Figure 12. California summer 2008 outbreak probabilities, based on model results, compared to actual outbreaks.

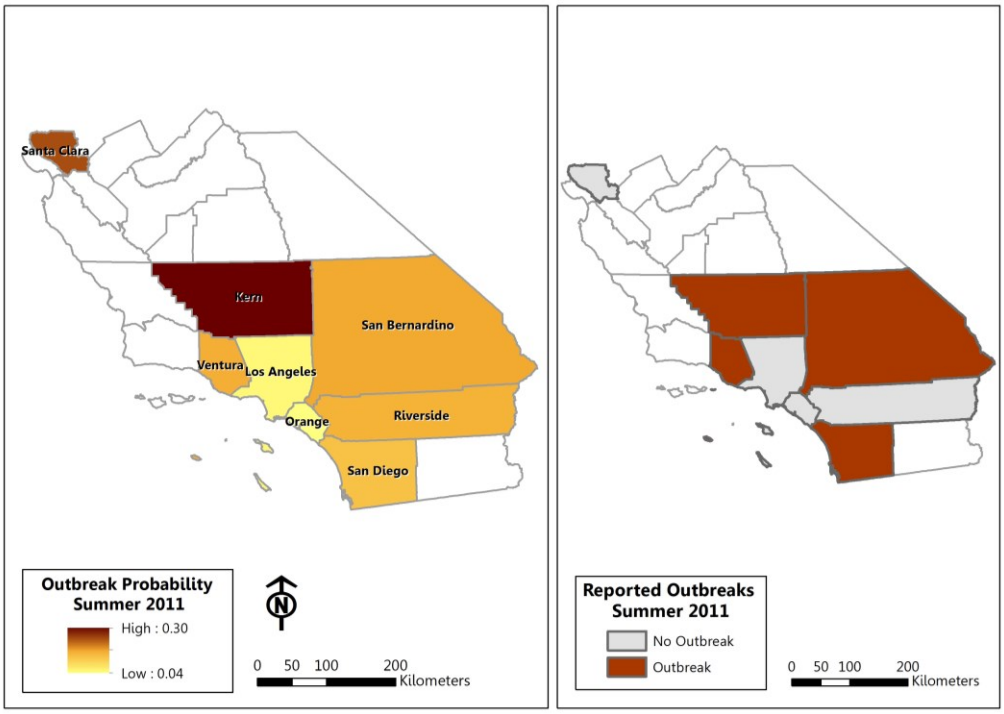


Figure 13. California summer 2011 outbreak probabilities, based on model results, compared to actual outbreaks.

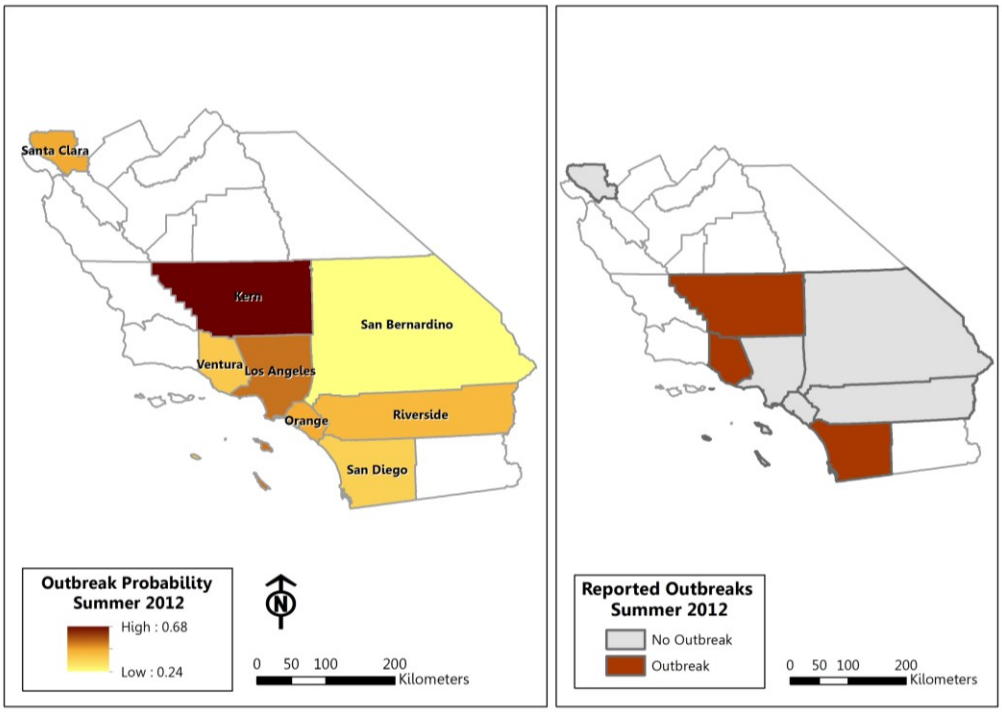


Figure 14. California summer 2012 outbreak probabilities, based on model results, compared to actual outbreaks.

The model-based summer probabilities were relatively inaccurate when compared to the actual reported outbreaks, especially when compared to the results from the winter model verification. The overall high probability values are lower as well; the high values for 2008 and 2011 were 50 percent and 30 percent, respectively. This indicates a rather weak model overall and offers partial explanation for the poor results. Kern County appears to be the most consistently, accurately predicted county for outbreak risk, while all other study area counties vary in both accuracy and consistency.

Similar to the winter model, the poor results of the summer verification can likely also be explained by the fact that only one variable (summer building permit rates) displayed predictive power and that its predictive strength as a standalone variable was rather weak.

Fall

The fall season model resulted in a Chi Square (df = 10, N = 80) value of 25.699, $p = 0.004$, indicating that the model provided a statistically significant prediction of success. The Nagelkerke pseudo R^2 indicated that the model accounted for approximately 37 percent of the total variance. The Hosmer and Lemeshow Test indicated an overall prediction success rate of 73.8 percent and correct prediction rates of 66.7 percent for the "outbreak" group and 79.5 percent for the "no outbreak group." The classification cutoff value for predicting membership in the successful groups was 0.5. Table 3 displays the results of the fall season outbreak model.

Table 3. Fall season model results

Fall Model	B	Wald	Sig.	Exp (B)	95% C.I. for EXP (B)
Fall T0 Precip. Dev. (mm)	-0.012	1.930	0.165	0.988	0.971 – 1.005
Fall T-1 Precip. Dev. (mm) (Sum)	-0.005	0.014	0.907	0.995	0.920 – 1.077
Fall T-2 Precip. Dev. (mm) (Spr)	-0.003	0.300	0.584	0.997	0.985 – 1.009
Fall T-3 Precip. Dev. (mm) (Win)	-0.002	0.630	0.427	0.998	0.994 – 1.003
Fall T0 Temp. Dev. (C)	0.435	1.375	0.241	1.545	0.747 – 3.195
Fall T-1 Temp. Dev. (C) (Sum)	**-1.050**	5.496	**0.019**	**0.350**	**0.146 – 0.842**
Fall T-2 Temp. Dev. (C) (Spr)	0.365	1.272	0.259	1.440	0.764 – 2.714
Fall T-3 Temp. Dev. (C) (Win)	0.438	1.296	0.255	1.549	0.729 – 3.292
Fall T0 Bldg. Permits	0.003	0.047	0.828	1.003	0.974 – 1.034
Fall T-1 Bldg. Permits (Sum)	0.010	0.624	0.430	1.011	0.985 – 1.037
Constant	**-1.427**	9.301	**0.002**	**0.240**	

Explanations of variable meanings included in Appendix A

The fall model revealed poor results overall. The only significant variable, summer temperature deviation from normal ($p = 0.019$), too contained a negative coefficient and odds ratio less than one. This indicates that it did not have much predictive influence on fall outbreaks.

Verification

Because it was significant, however, it was still verified using the same technique and years as the previous verifications (Figures 15 – 18).

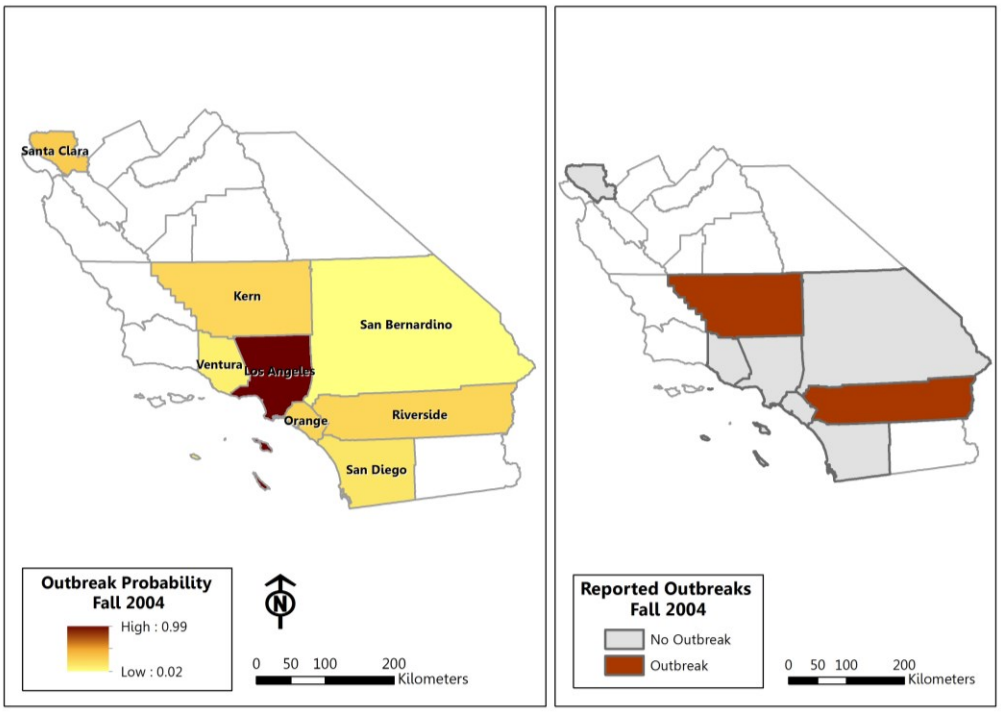


Figure 15. California fall 2004 outbreak probabilities, based on model results, compared to actual outbreaks.

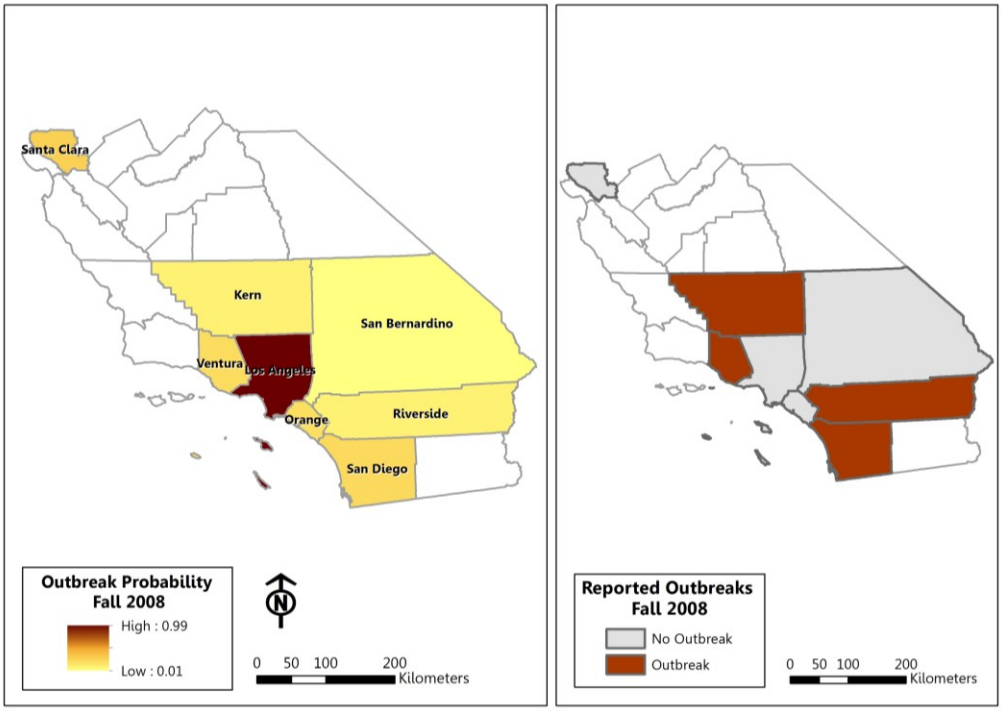


Figure 16. California fall 2008 outbreak probabilities, based on model results, compared to actual outbreaks.

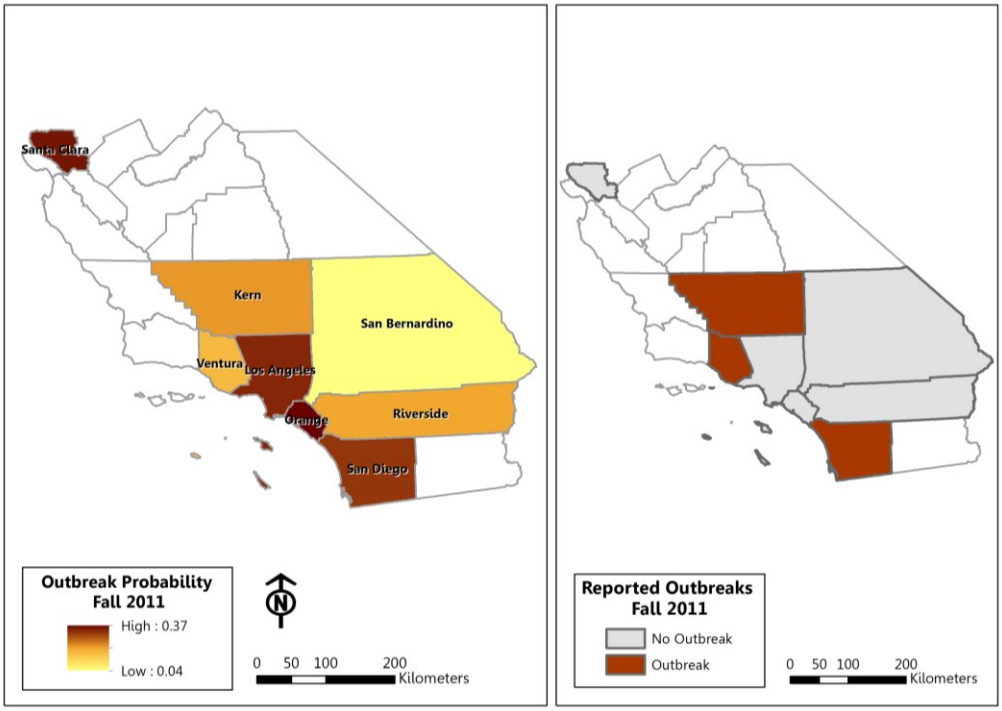


Figure 17. California fall 2011 outbreak probabilities, based on model results, compared to actual outbreaks.

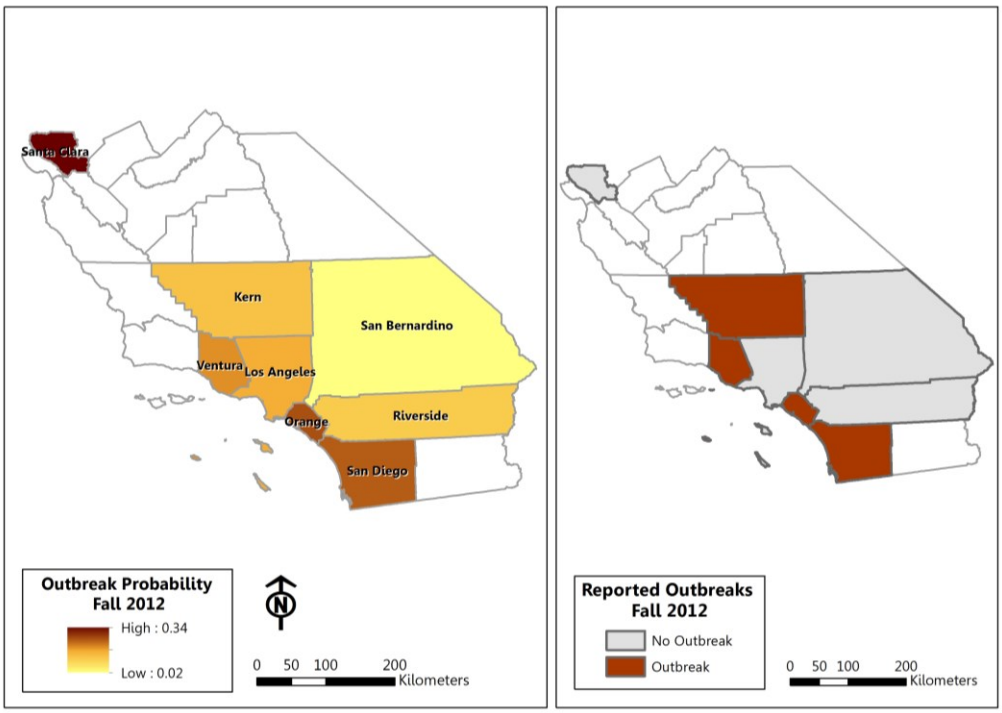


Figure 18. California fall 2012 outbreak probabilities, based on model results, compared to actual outbreaks.

The model-based results of the fall verification were poor, as expected, considering the general weakness of the model. The overall high probability values are low for 2011 and 2012 (37 percent and 34 percent, respectively), and although exceptionally high for 2004 and 2008 (99 percent for both), they were highly inaccurate. No counties were consistently, accurately predicted for outbreak risk, but these results were expected due to the fact that the model contained no strongly predictive variables.

Texas

The seasonal model built from the California study area data was then applied to West Texas using weighted linear combination in GIS to map predicted risk areas for *Coccidioides* at outbreak levels there. All Texas county data were obtained from the same sources as the California data, and their values were seasonally aggregated and population normalized using the same methods previously defined (Figures 19 – 21).

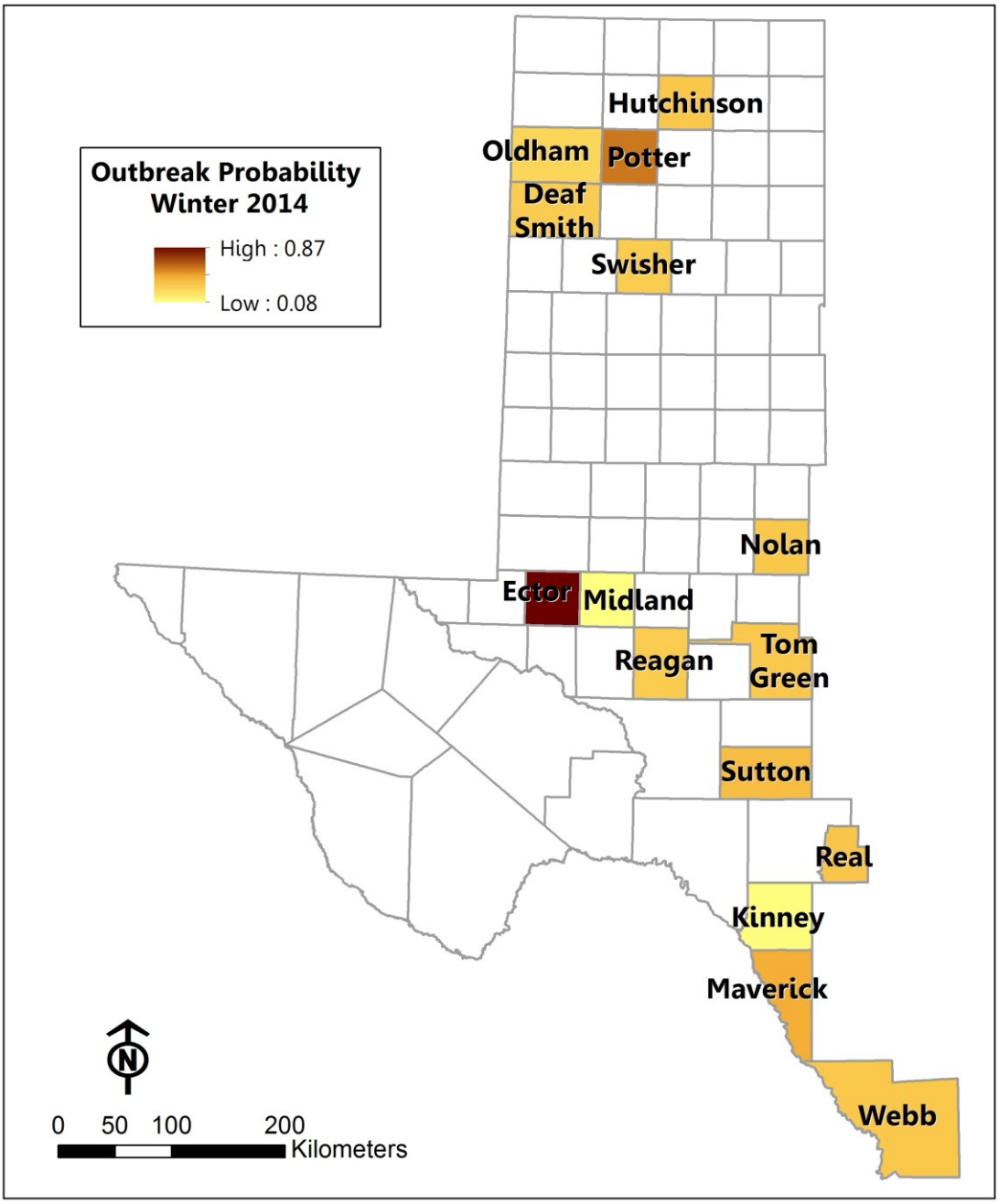


Figure 19. Texas winter 2014 outbreak probabilities, based on model results.

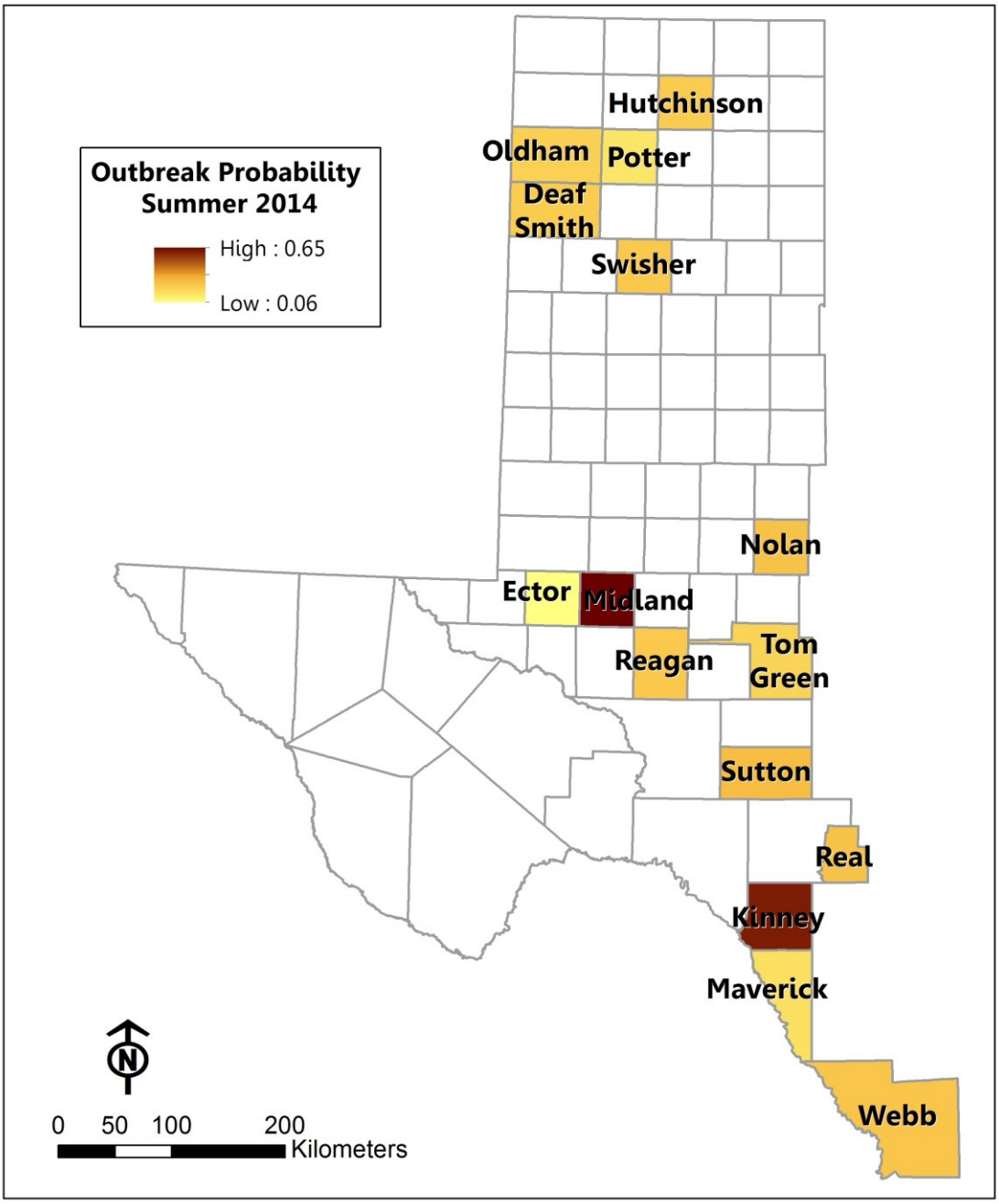


Figure 20. Texas summer 2014 outbreak probabilities, based on model results.

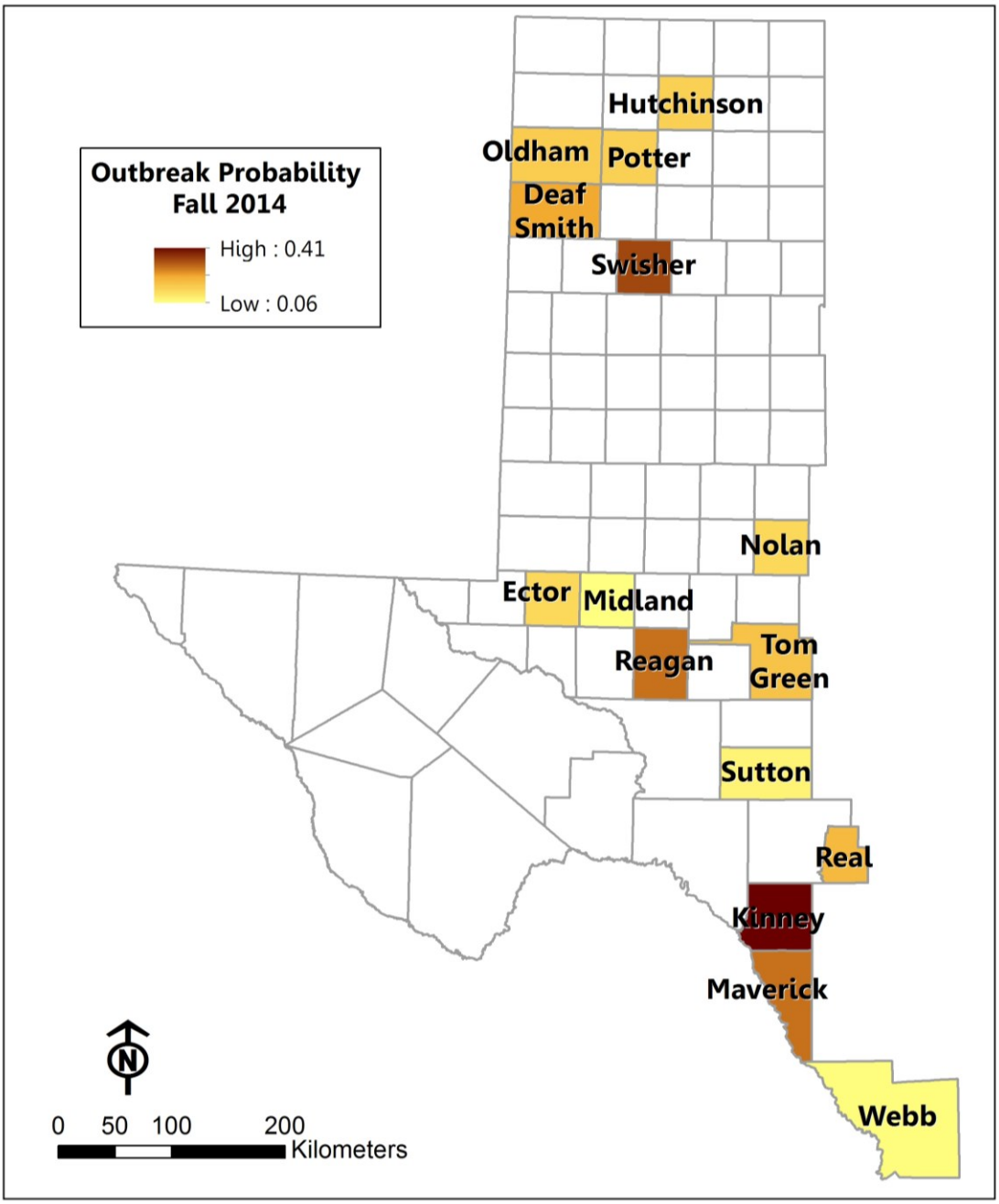


Figure 21. Texas fall 2014 outbreak probabilities, based on model results.

Based on the results of the California verifications, it is reasonable to conclude that the winter Texas risk map is likely the most accurate, followed by the summer map. The fall map is likely very poor, and its results cannot be considered accurate nor can any meaningful information be gathered from them. The spatial distribution of risk appears

sporadic, resulting in difficulty analyzing true high risk areas. This is likely due to the scattered spatial distribution of the counties for which data were available. Had data been available from more, or even spatially clustered counties, the results would likely have been easier to interpret. In addition, the fact that seasonal building permit rates were the only predictive variables in both the winter and summer models, presents difficulty in analyzing risk areas because some of the Texas counties reported no building permits at all.

When compared to the map of known and suspected endemic areas in Texas (Figure 1), the model-based high risk areas correspond with previously established high risk areas. These areas include Ector and Midland Counties, which had both the highest populations and the highest numbers of building permits of all the counties in the study area (U.S. Census Bureau 2010, 2014). These higher populated, higher developed areas fit the factors necessary for contracting coccidioidomycosis: soil disturbance and a human population to inhale the fungal spores (Chiller, Galgiani, and Stevens 2003; Arizona Department of Health Services 2012).

Kinney County reported its highest number of building permits in the summer of 2014 (U.S. Census Bureau 2014), which would explain it being a high risk area in the summer and low risk in the winter, when it reported no building permits the fall prior to it (its predictor variable).

Potter County displayed particularly high winter risk, likely due to its high population growth and development patterns (Galgiani 1999, U.S. Census Bureau 2010, 2014), as it is the location of a major university. This county location is not included in even the suspected coccidioidomycosis risk areas in the original endemic area map. This

may mean that either healthcare professionals are unaware of the potential risk there, causing the disease to go underdiagnosed, or that since disease cases are not reported in Texas, the map is simply out of date. The endemic area may have expanded because of population changes since the last establishment of Texas risk areas, and this may warrant an updated map. Further research will need to be conducted in this area, however, to establish whether coccidioidomycosis risk is as high as the model predicts.

Limitations

There were a number of limitations that likely negatively affected the accuracy of the results of this study. First, the availability of data for research was very poor. This study originally intended to include California counties south of the 37 degrees north latitude line, all Arizona counties, Texas counties west of the 100 degrees west longitude line as the study area, as well as aerial dust concentrations and soil types and independent variables in the model. Incomplete and imprecise data sets (or lack of data altogether), however, necessitated the removal of over half of the original study area and two variables from the study. This likely resulted in a substantial decline in quality of results.

The availability of coccidioidomycosis cases in varying forms of report dates presented difficulty in determining the appropriate season in which to aggregate the cases to ensure accuracy of results. In many cases, it was impossible to determine with any certainty the date of exposure, and this likely had a profound negative effect on the quality of results. Without knowing the actual dates of exposure to Coccidioides spores, it is very difficult to assess with any certainty the environmental and anthropogenic factors with the highest contributions to that exposure.

The climate differences between the California and Texas study areas limited the ability to extrapolate the results from one location to another. Although both climates are considered mostly arid, southern California experiences Mediterranean climate patterns, which result in wet winters and dry summers, whereas West Texas has much drier winters and is wetter in the spring through fall seasons (National Weather Service 2011) (Appendix B). Ideally, identical climates, or at least more-similar climates, would be analyzed and compared with one another, likely producing superior results. However, of the two states that mandate reporting (Arizona and California), only California would release its coccidioidomycosis data for research.

Finally, and most importantly, both the coccidioidomycosis data and climate data were aggregated to the county scale, an exceptionally coarse scale (especially in California) created by human delineated political boundaries that ignore the naturally occurring climate patterns and landscape changes that have significant impacts on disease patterns. These unnatural lines of demarcation inaccurately group data into false aggregates and likely distort the results (Brooker, Hay, and Bundy 2002; Brownstein, Holford and Fish 2003).

A potentially more accurate method for determining disease risk areas would be to determine the influence of climate patterns, interpolated from weather stations across a continuous landscape, on individually reported coccidioidomycosis cases that have been geocoded to actual sites of contamination. This would also create the potential to include additional environmental independent variables, such as slope and aspect, which are inappropriate at the county scale because of their high spatial variability.

Unfortunately, due to healthcare laws like the Health Insurance Portability and Accountability Act of 1996 as well as state policy guidelines, it is often impossible to obtain reported disease cases at the individual level (U.S. Department of Health and Human Services 2014). Therefore, the only available option is to obtain rates that have been aggregated to scales delineated by political boundaries.

VI. CONCLUSION

Despite its limitations, this study established that building permits are significant predictors of seasonal disease risk in the winter and summer seasons. It also identified the area around Potter County as a potentially new area of risk for coccidioidomycosis. This presents an opportunity for further research that includes attempting to isolate *Coccidioides* in the environment at this location in order to further study its niche requirements, as well as an assessment of whether people reporting coccidioidomycosis symptoms are being tested for the disease, and if so, how frequently those tests are returning positive results.

This study also successfully utilized GIS to analyze and model coccidioidomycosis risk—an approach, which until now, had not been attempted. With higher quality data that include a more comprehensive study area, a standardized method of reporting the date of disease exposure, a complete climate data set, building permit data set, and aerial dust concentration data set, and a more precise soil data set, it is likely that an accurate and predictive model could be constructed to determine disease risk in the future.

This could potentially assist in the enhanced diagnosis and management of coccidioidomycosis in West Texas endemic areas, which in turn, could aid in alleviating complications that commonly arise when the disease is left untreated, thereby saving money and even lives (Kirkland and Fierer 1996; Chiller, Galgiani, and Stevens 2003; Galgiani et al. 2005; Tsang et al. 2010; Tsang et al. 2013).

APPENDIX SECTION

APPENDIX A: LIST OF VARIABLE NAMES WITH EXPLANATIONS

Win T0 Precip. Dev. (mm) – Winter precipitation deviation from 30-year normal, at time-zero (T0), in millimeters.

Win T-1 Precip. Dev. (mm) (Fall) – Winter precipitation deviation from 30-year normal, time-lagged by one season, in millimeters.

Win T-2 Precip. Dev. (mm) (Sum) – Winter precipitation deviation from 30-year normal, time-lagged by two seasons, in millimeters.

Win T-3 Precip. Dev. (mm) (Spr) – Winter precipitation deviation from 30-year normal, time-lagged by three seasons, in millimeters.

Win T0 Temp. Dev. (C) – Winter temperature deviation from 30-year normal, at T0, in °C.

Win T-1 Temp. Dev. (C) (Fall) – Winter temperature deviation from 30-year normal, time-lagged by one season, in °C.

Win T-2 Temp. Dev. (C) (Sum) – Winter temperature deviation from 30-year normal, time-lagged by two seasons, in °C.

Win T-3 Temp. Dev. (C) (Spr) – Winter temperature deviation from 30-year normal, time-lagged by three seasons, in °C.

Win T0 Bldg. Permits – Winter building permit rates, at T0.

Win T-1 Bldg. Permits (Fall) – Winter building permit rates, time-lagged by one season.

Sum T0 Precip. Dev. (mm) – Summer precipitation deviation from 30-year normal, at T0, in millimeters.

Sum T-1 Precip. Dev. (mm) (Spr) – Summer precipitation deviation from 30-year normal, time-lagged by one season, in millimeters.

Sum T-2 Precip. Dev. (mm) (Win) – Summer precipitation deviation from 30-year normal, time-lagged by two seasons, in millimeters.

Sum T-3 Precip. Dev. (mm) (Fall) – Summer precipitation deviation from 30-year normal, time-lagged by three seasons, in millimeters.

Sum T0 Temp. Dev. (C) – Summer temperature deviation from 30-year normal, at T0, in °C.

Sum T-1 Temp. Dev. (C) (Spr) – Summer temperature deviation from 30-year normal, time-lagged by one season, in °C.

Sum T-2 Temp. Dev. (C) (Win) – Summer temperature deviation from 30-year normal, time-lagged by two seasons, in °C.

Sum T-3 Temp. Dev. (C) (Fall) – Summer temperature deviation from 30-year normal, time-lagged by three seasons, in °C.

Sum T0 Bldg. Permits – Summer building permit rates, at T0.

Sum T-1 Bldg. Permits (Spr) – Summer building permit rates, time-lagged by one season.

Fall T0 Precip. Dev. (mm) – Fall precipitation deviation from 30-year normal, at T0, in millimeters.

Fall T-1 Precip. Dev. (mm) (Sum) – Fall precipitation deviation from 30-year normal, time-lagged by one season, in millimeters.

Fall T-2 Precip. Dev. (mm) (Spr) – Fall precipitation deviation from 30-year normal, time-lagged by two seasons, in millimeters.

Fall T-3 Precip. Dev. (mm) (Win) – Fall precipitation deviation from 30-year normal, time-lagged by three seasons, in millimeters.

Fall T0 Temp. Dev. (C) – Fall temperature deviation from 30-year normal, at T0, in °C.

Fall T-1 Temp. Dev. (C) (Sum) – Fall temperature deviation from 30-year normal, time-lagged by one season, in °C.

Fall T-2 Temp. Dev. (C) (Spr) – Fall temperature deviation from 30-year normal, time-lagged by two seasons, in °C.

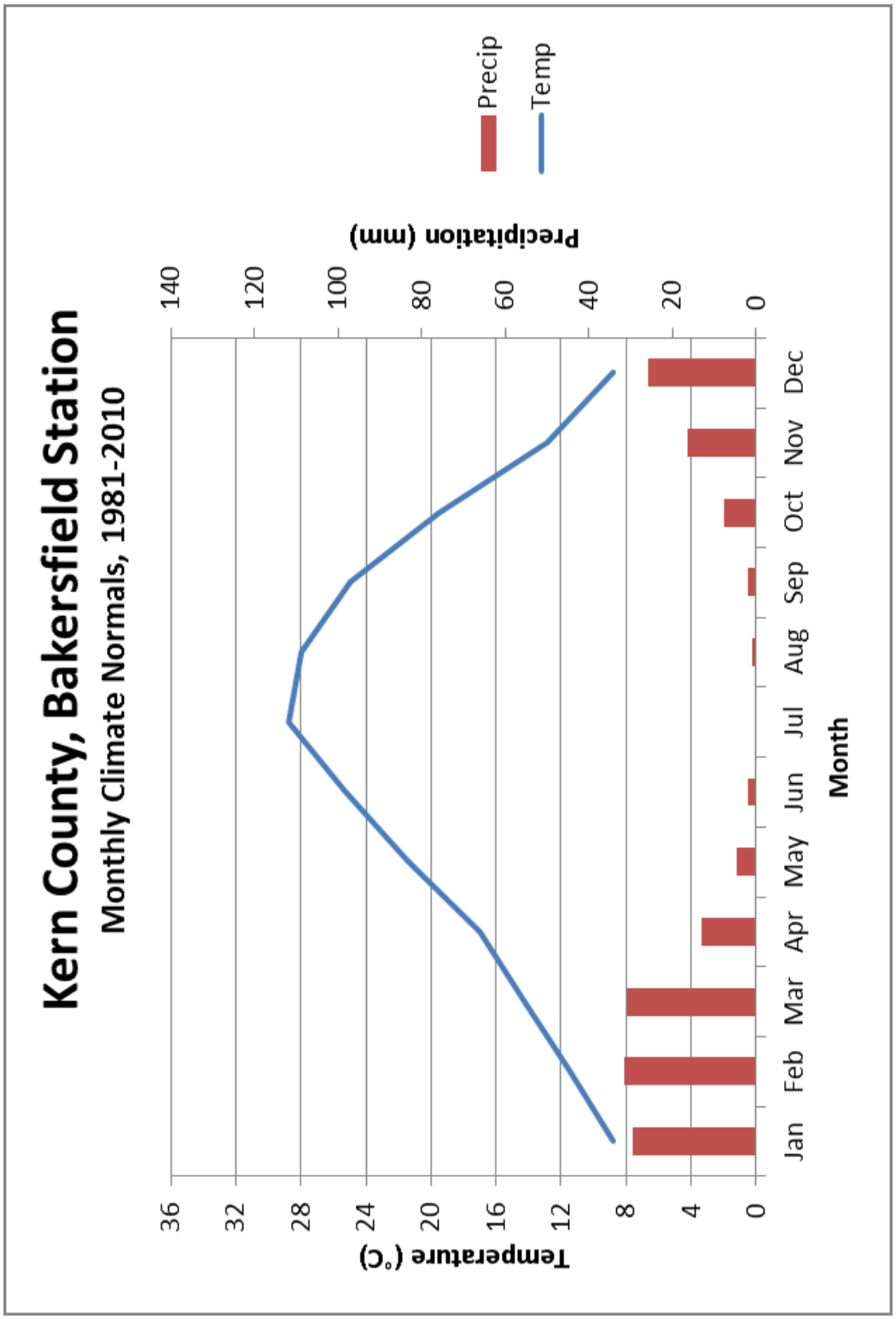
Fall T-3 Temp. Dev. (C) (Win) – Fall temperature deviation from 30-year normal, time-lagged by three seasons, in °C.

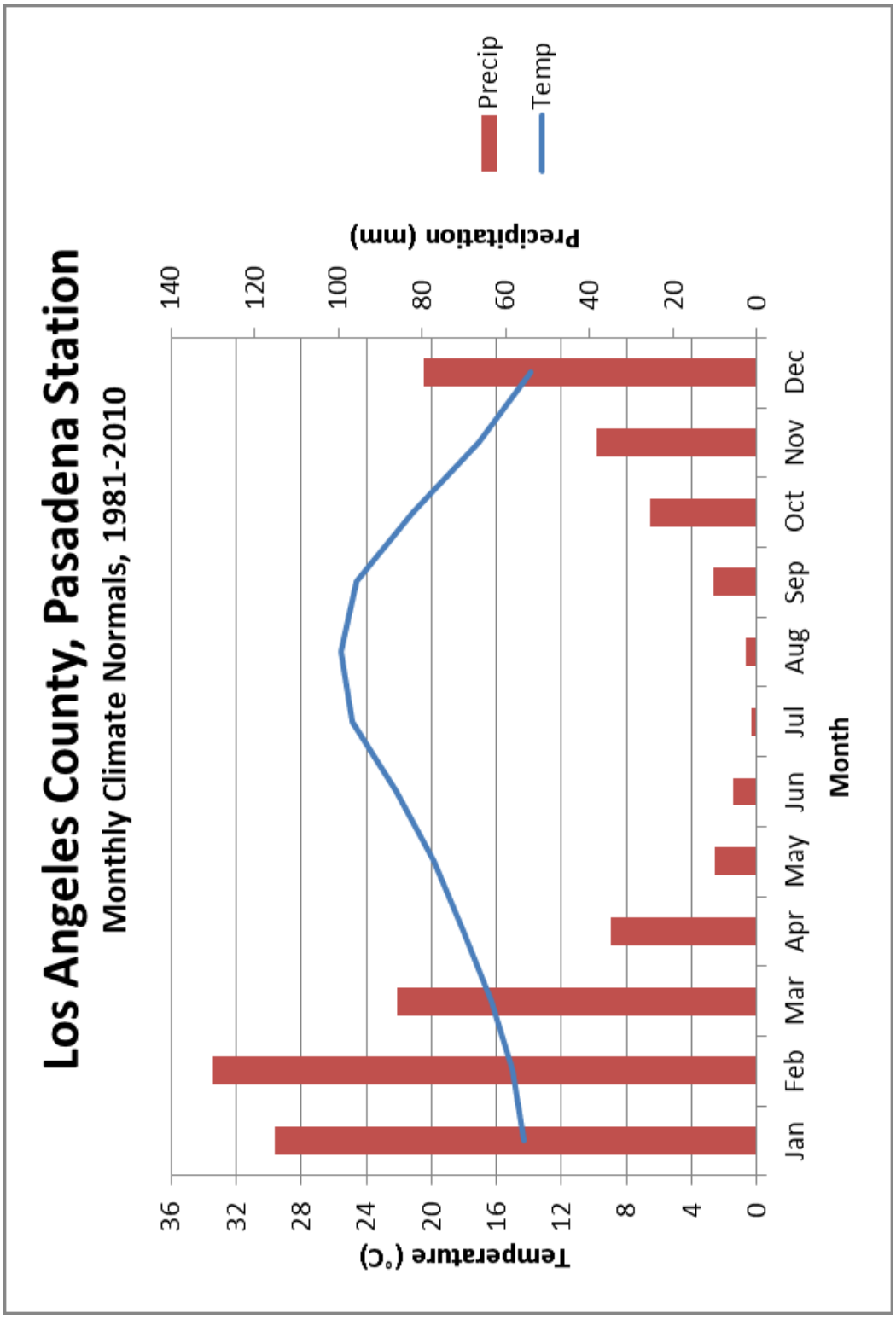
Fall T0 Bldg. Permits – Fall building permit rates, at T0.

Fall T-1 Bldg. Permits (Sum) – Fall building permit rates, time-lagged by one season.

APPENDIX B: CLIMOGRAPHS OF 30-YEAR MONTHLY NORMALS FOR EACH STATION IN STUDY

California (Golden Gate Weather Services 2011)**:**




Los Angeles County, Pasadena Station
Monthly Climate Normals, 1981-2010
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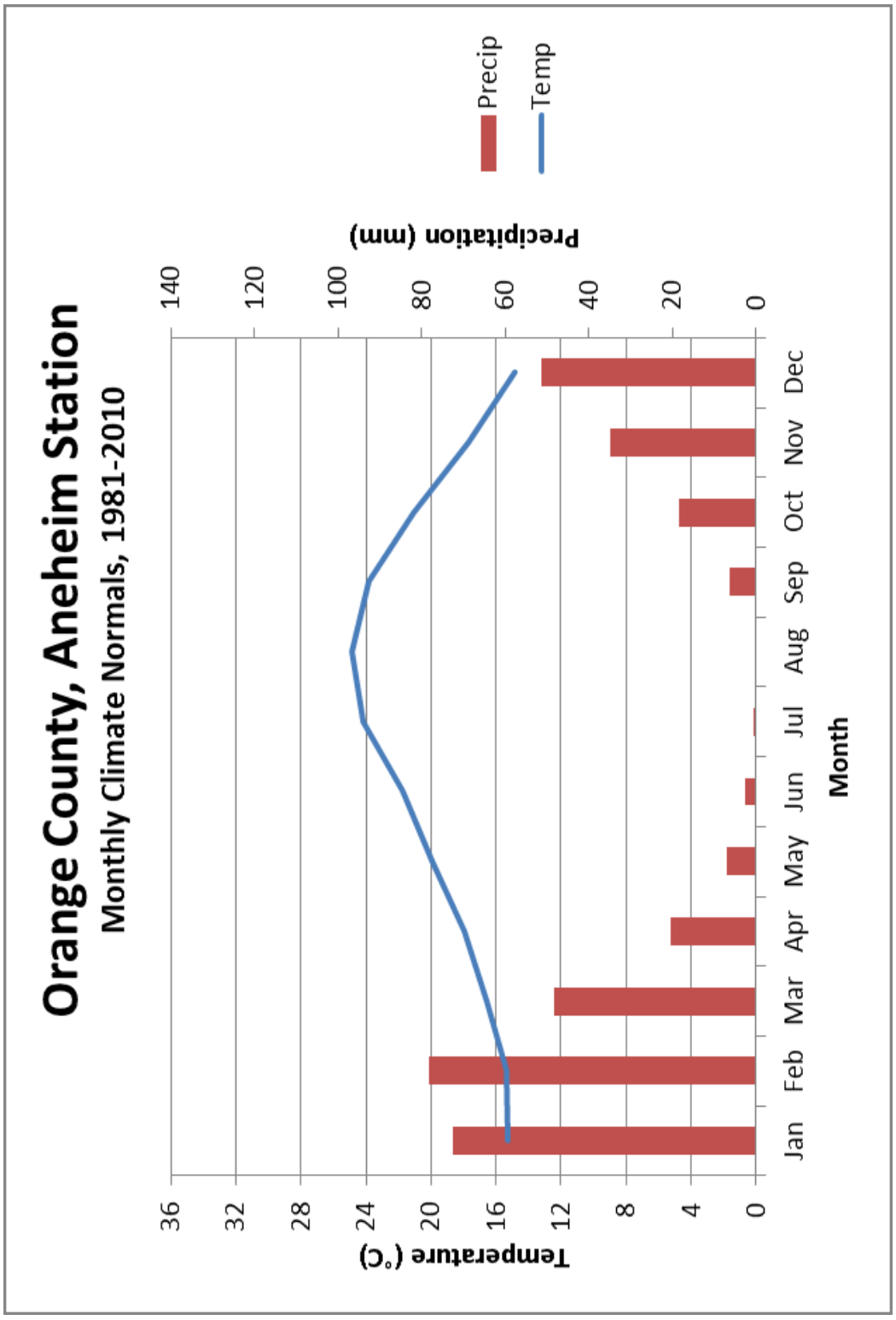
Orange County, Aneheim Station
Monthly Climate Normals, 1981-2010
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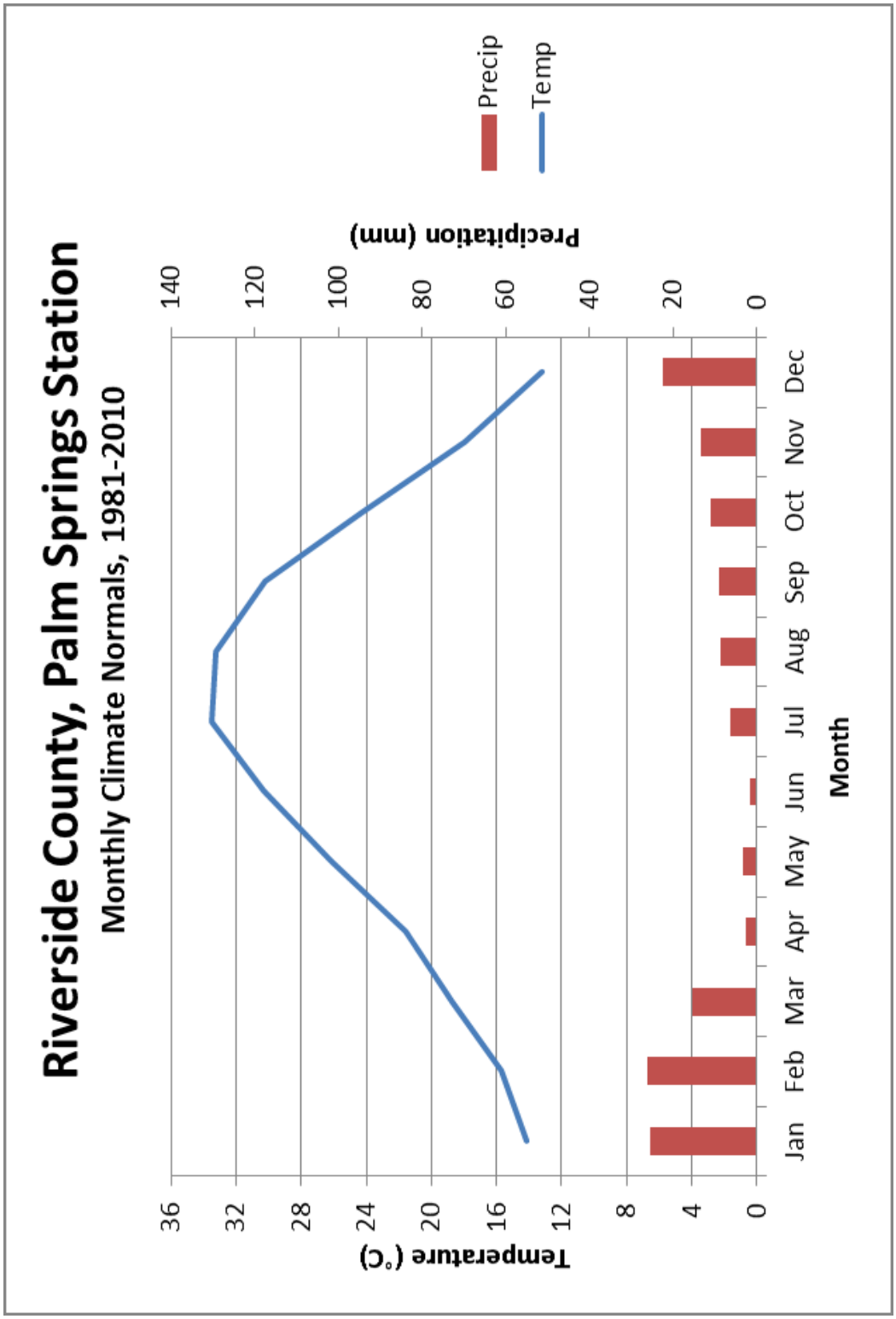
Riverside County, Palm Springs Station
Monthly Climate Normals, 1981-2010
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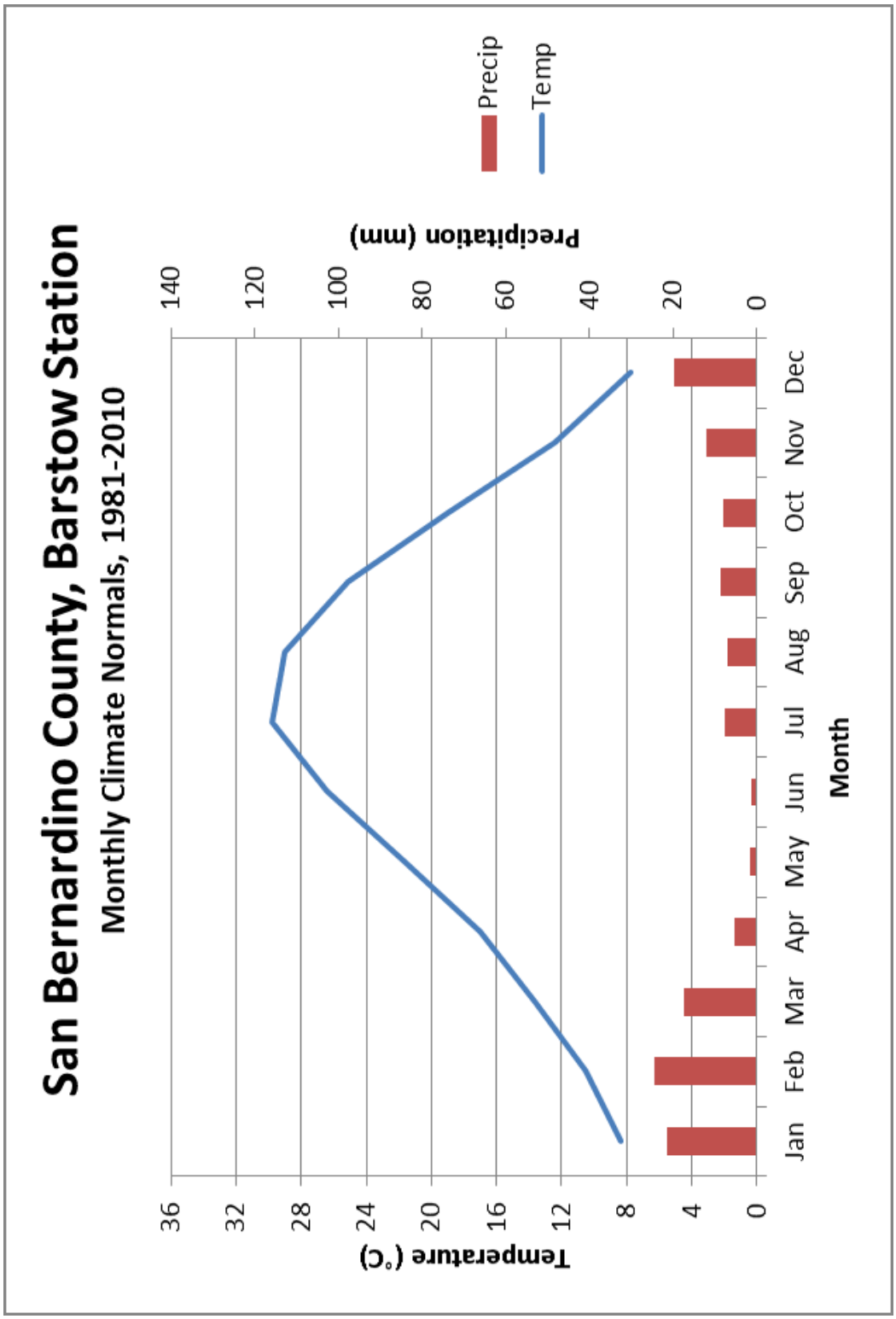
San Bernardino County, Barstow Station
Monthly Climate Normals, 1981-2010
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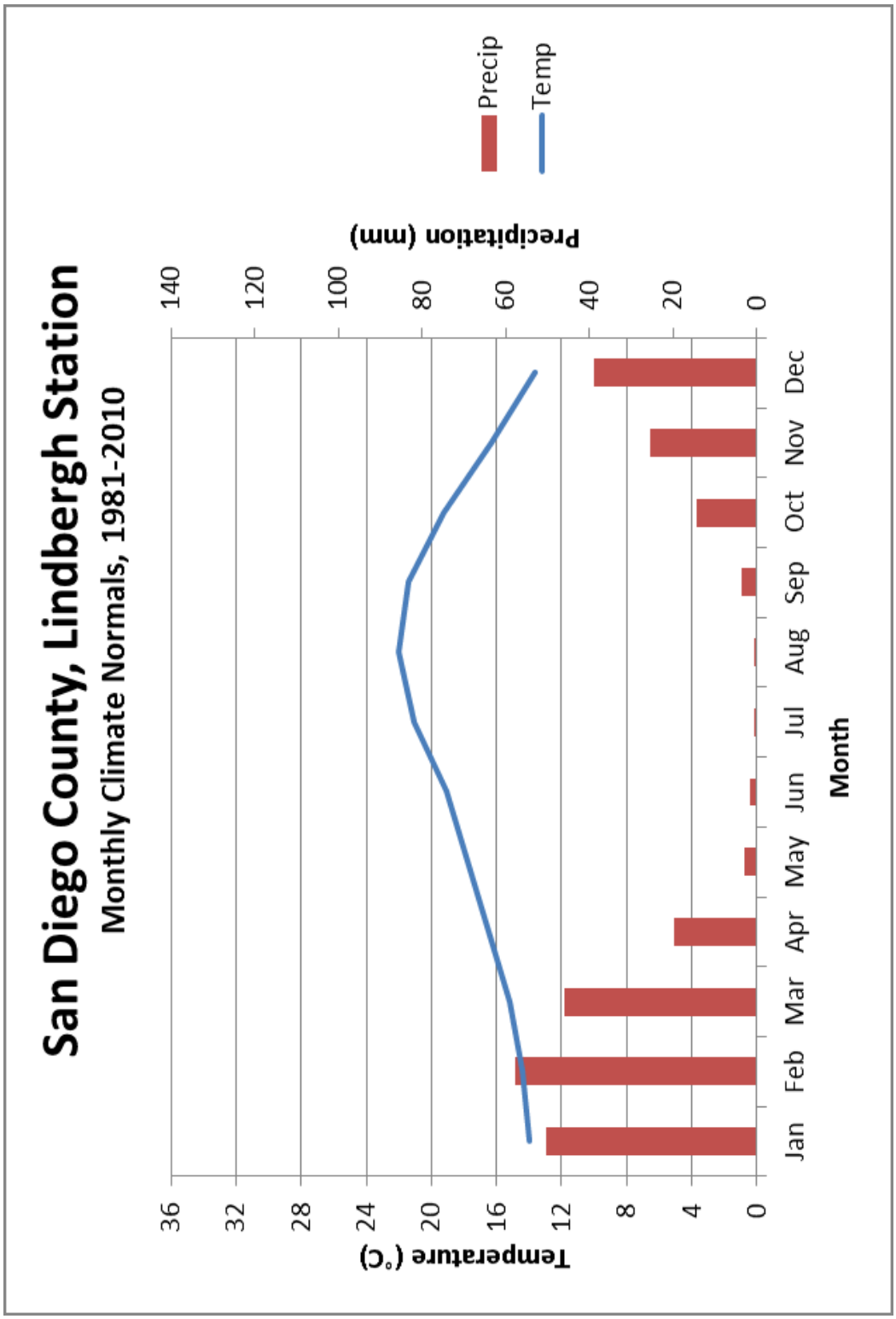
San Diego County, Lindbergh Station
Monthly Climate Normals, 1981-2010
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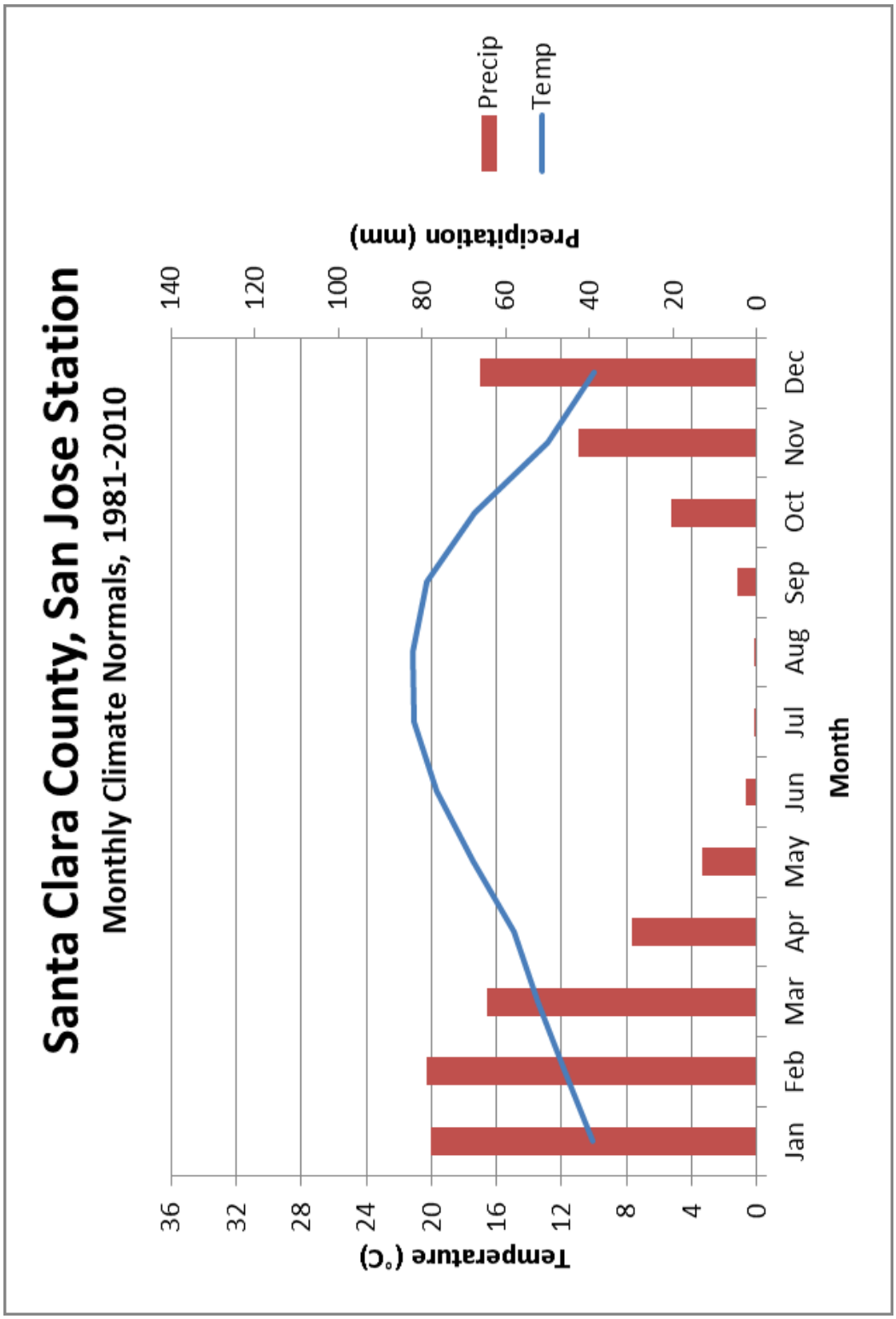
Santa Clara County, San Jose Station
Monthly Climate Normals, 1981-2010
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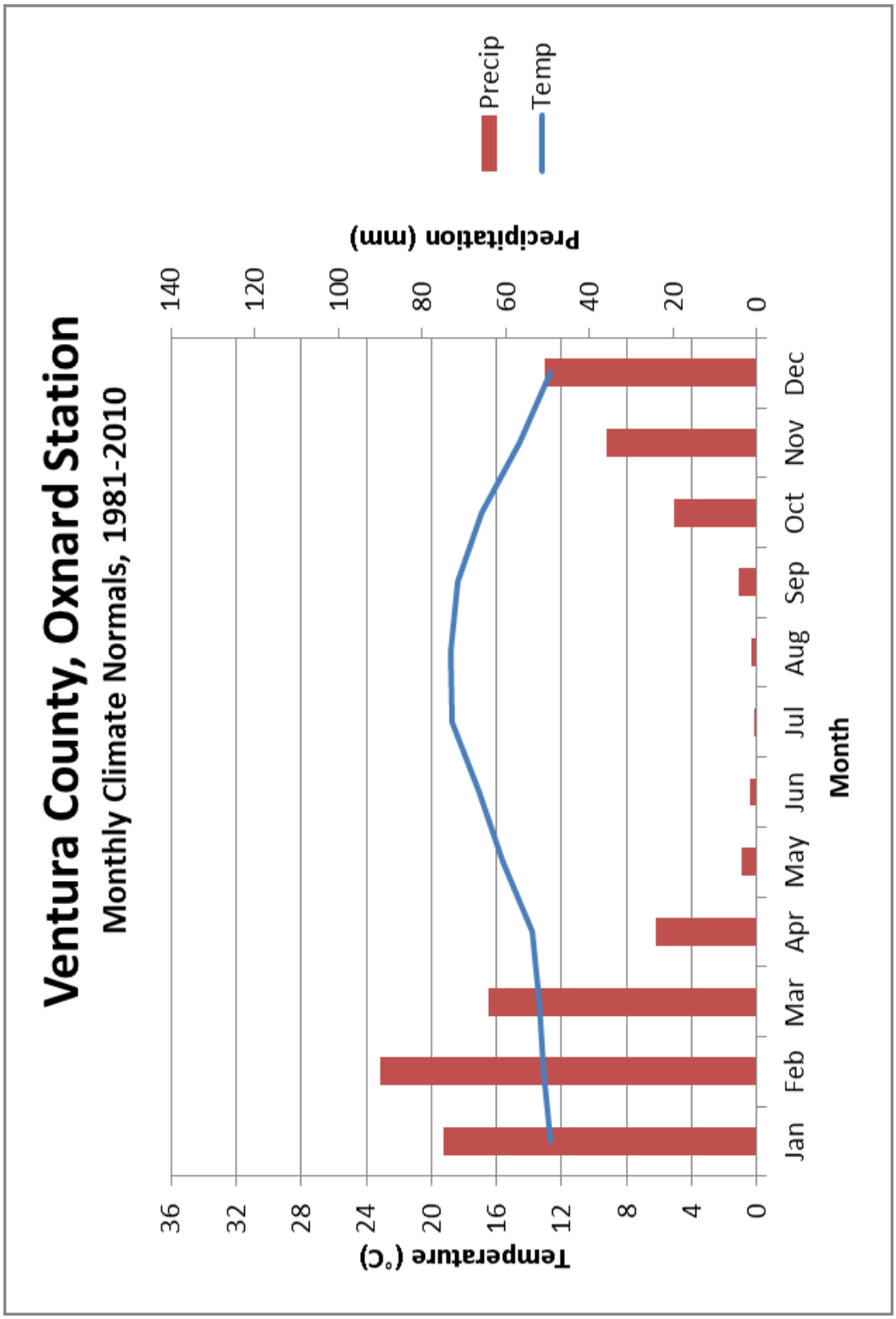
Ventura County, Oxnard Station
Monthly Climate Normals, 1981-2010
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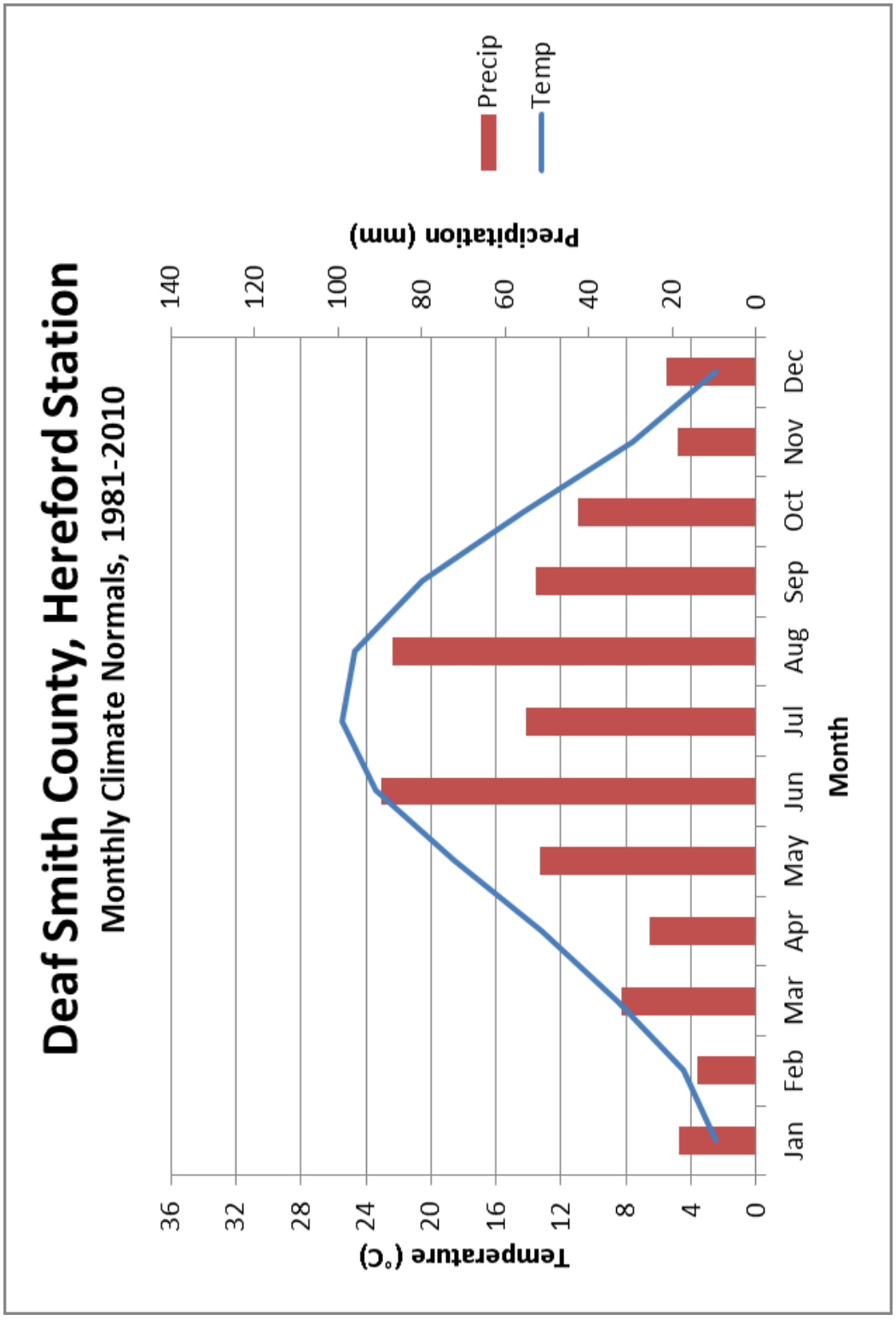
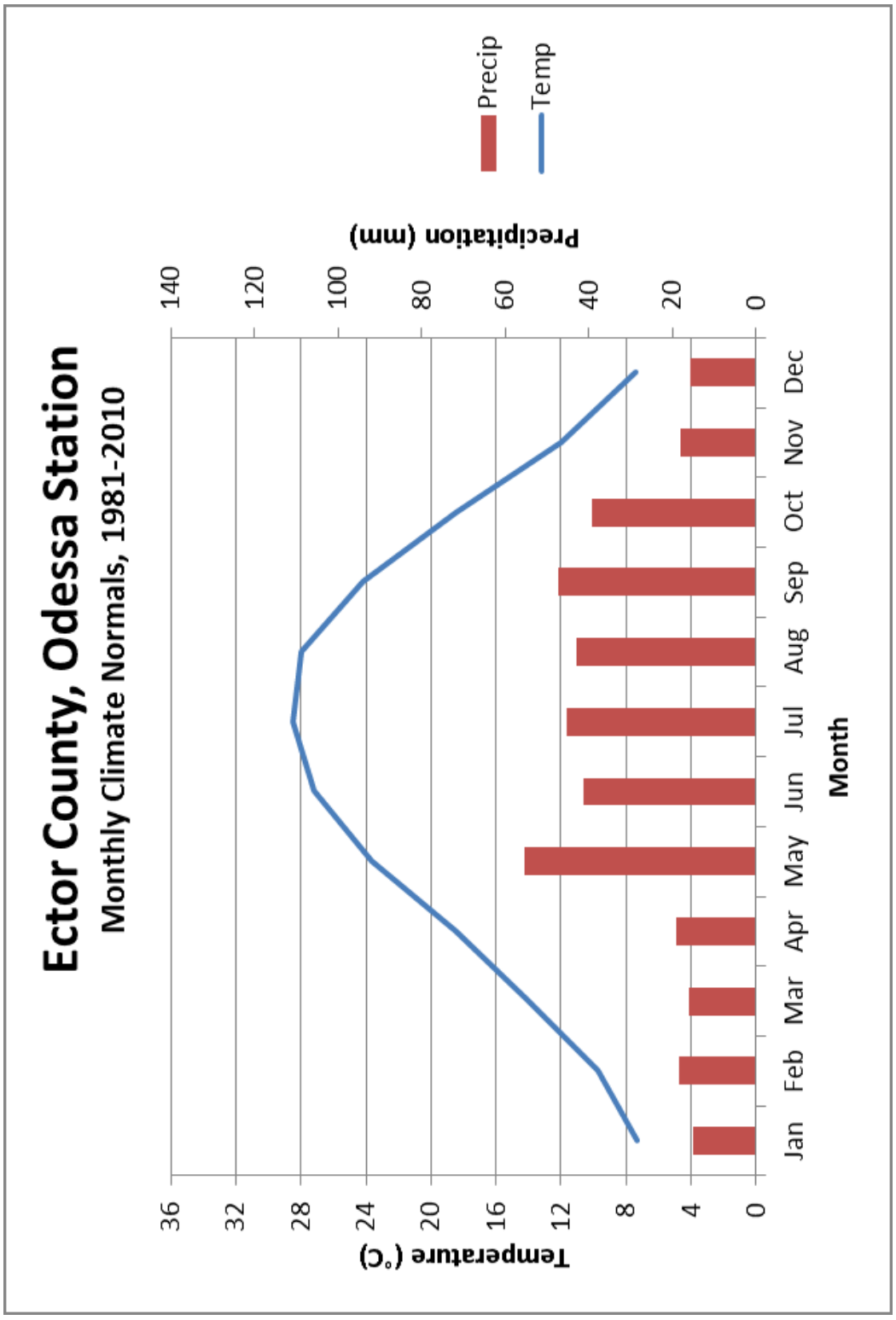
Texas (Golden Gate Weather Services 2011)**:**




Ector County, Odessa Station
Monthly Climate Normals, 1981-2010
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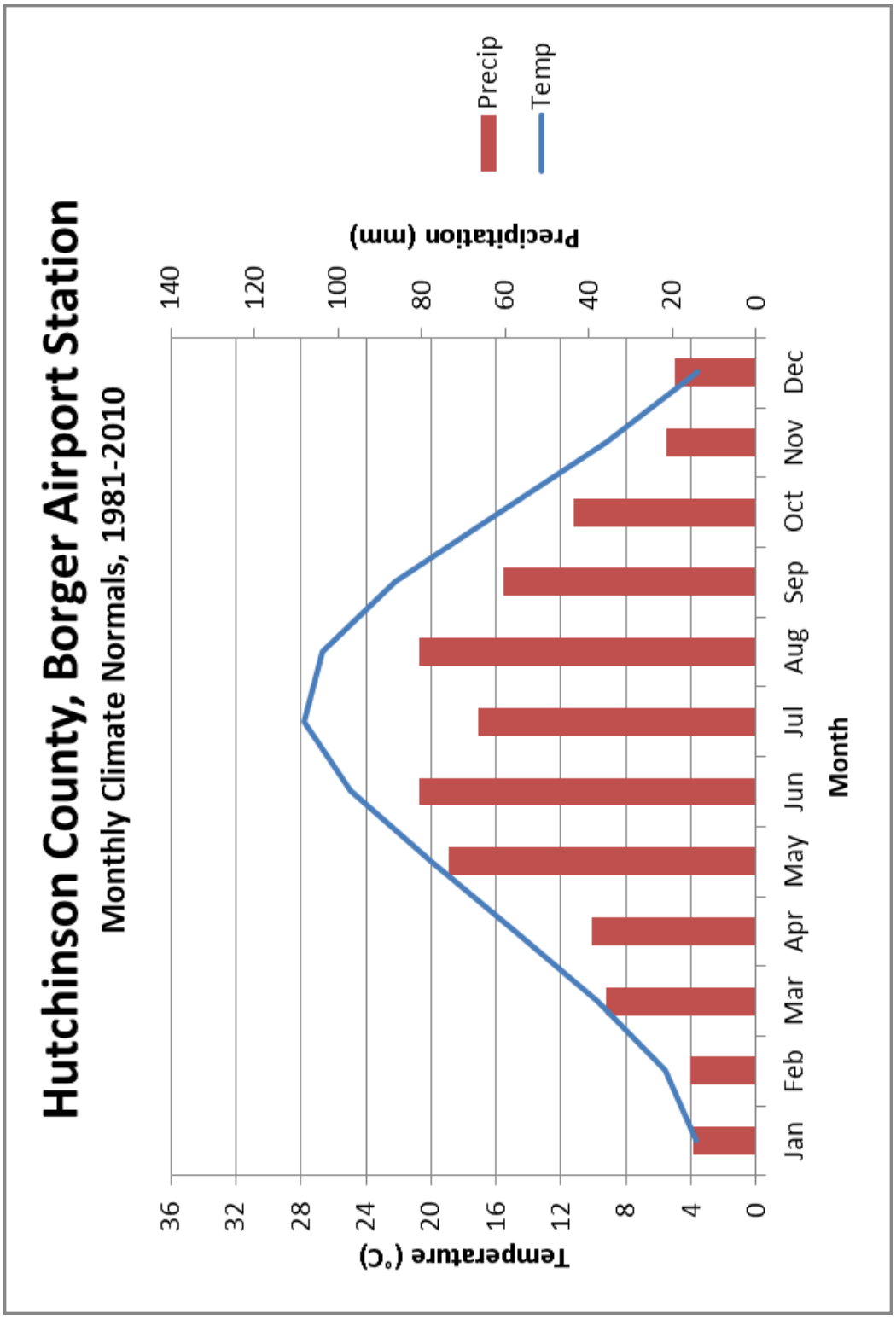
Hutchinson County, Borger Airport Station
Monthly Climate Normals, 1981-2010
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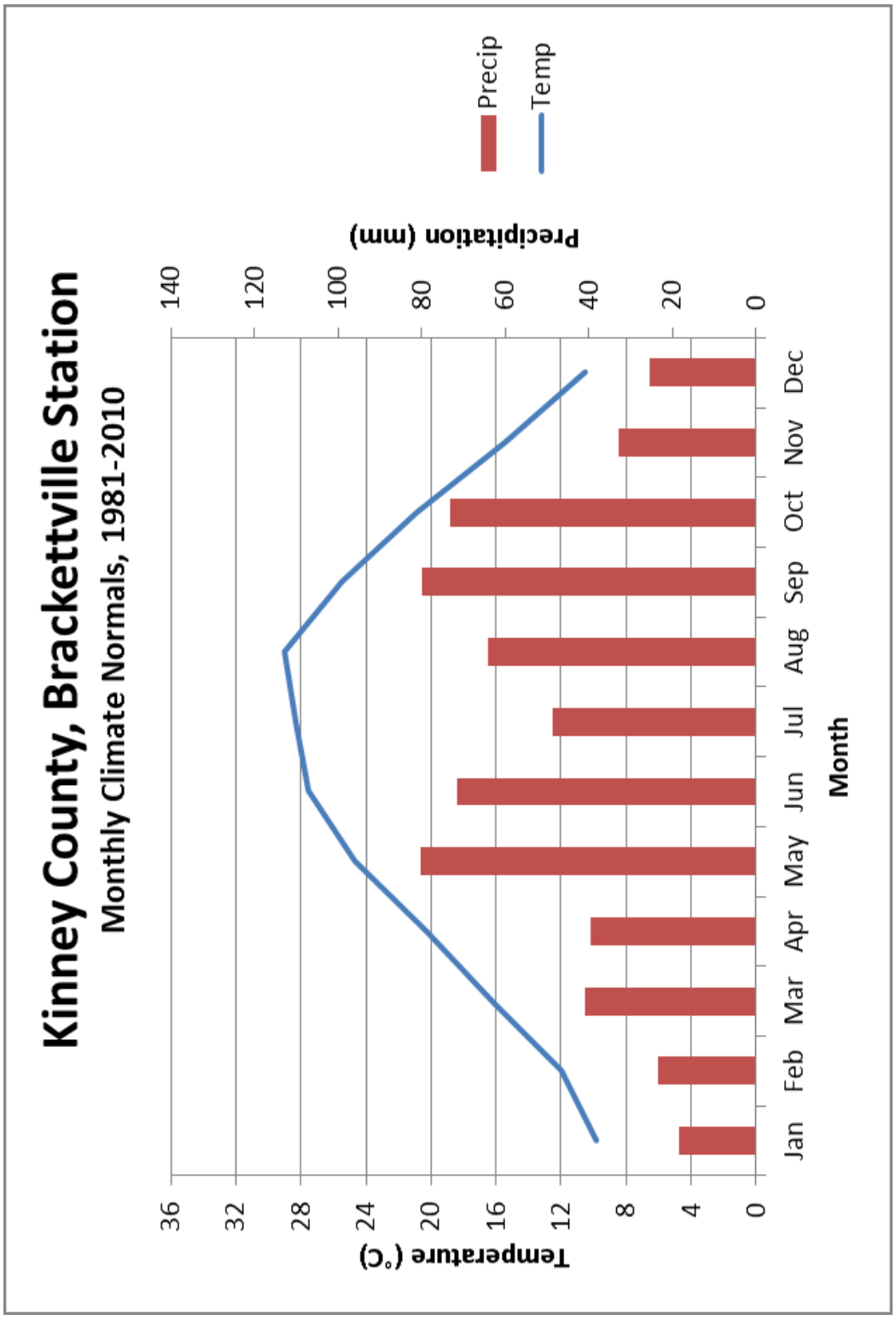
Kinney County, Brackettville Station
Monthly Climate Normals, 1981-2010
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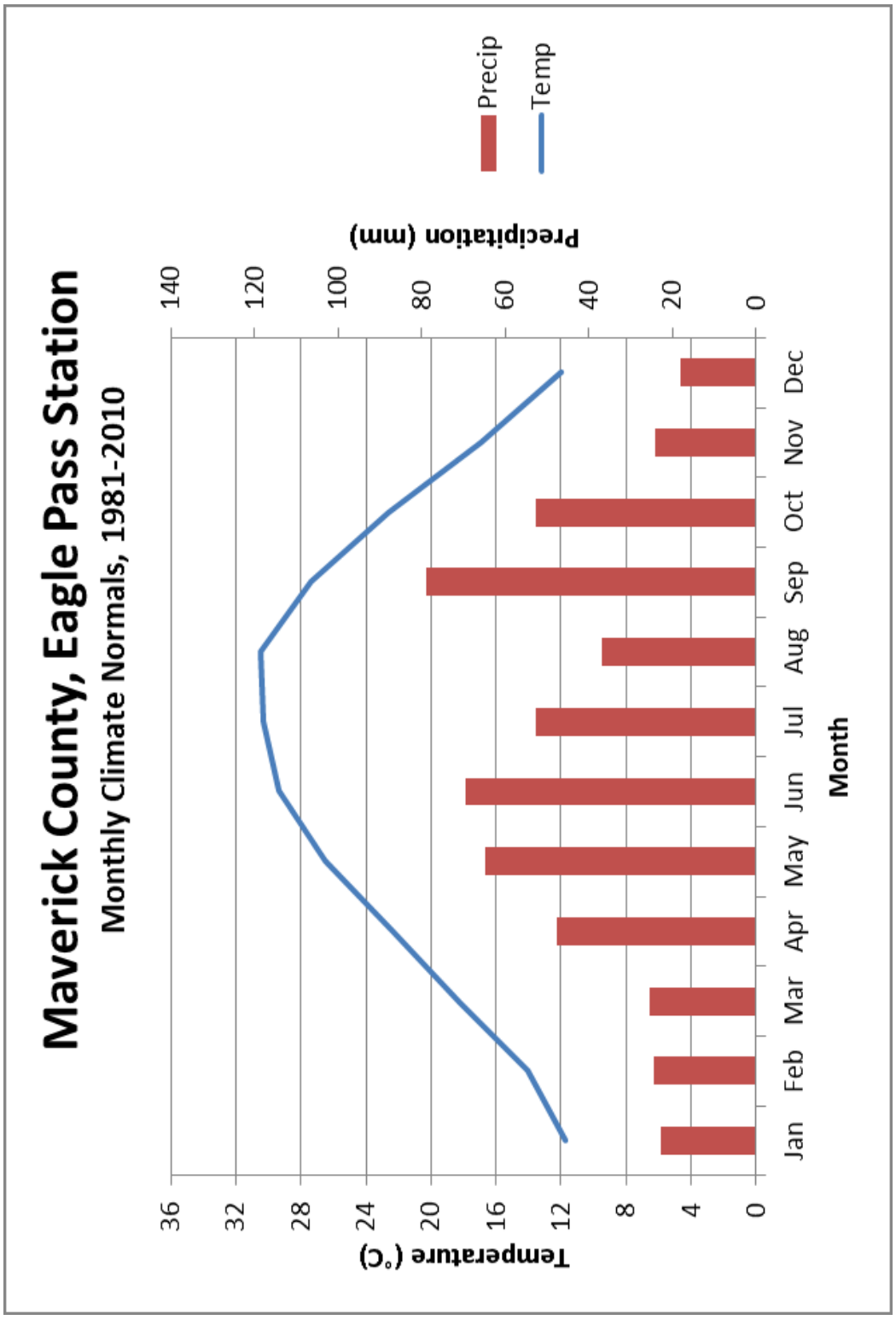
Maverick County, Eagle Pass Station
Monthly Climate Normals, 1981-2010
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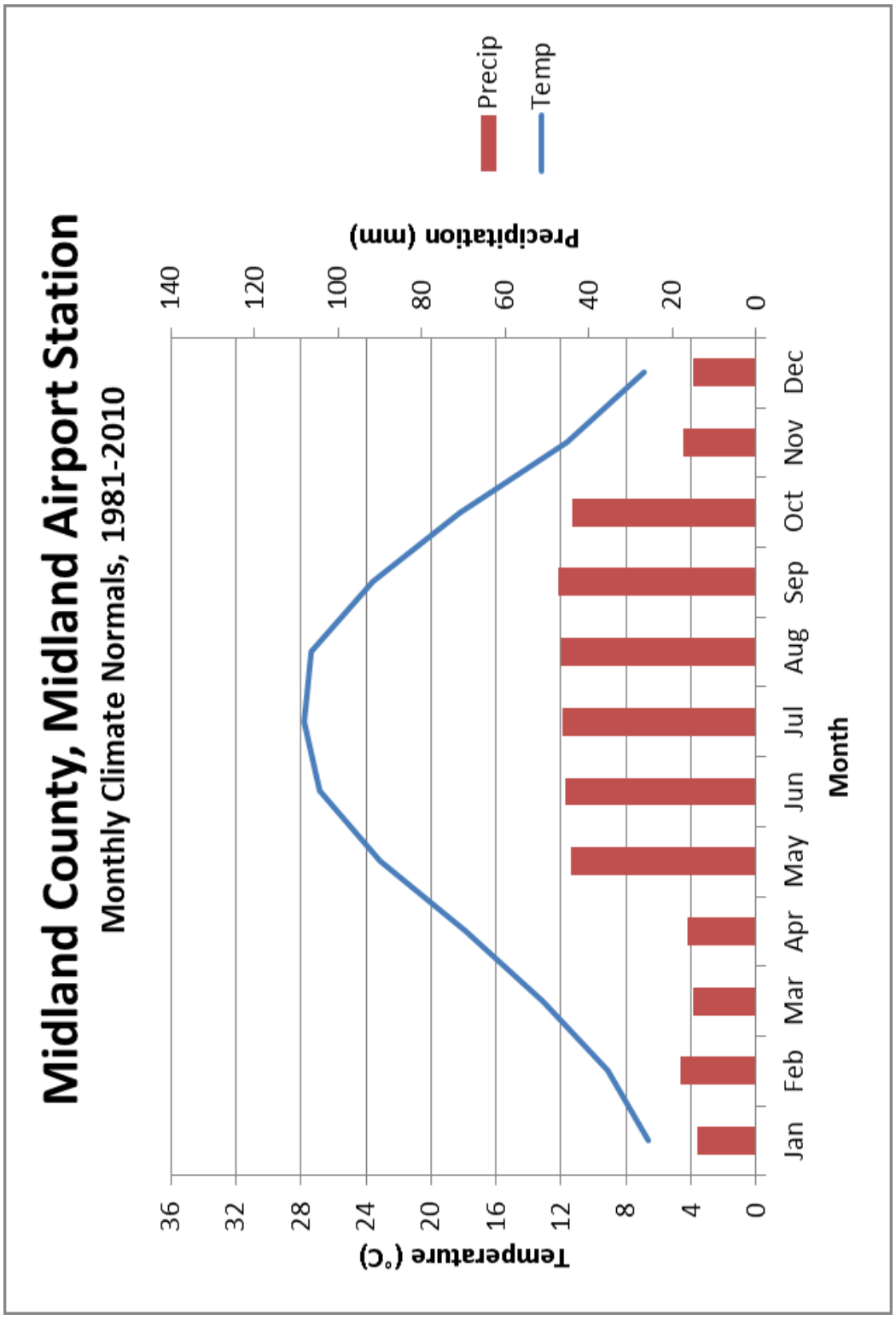
Midland County, Midland Airport Station
Monthly Climate Normals, 1981-2010
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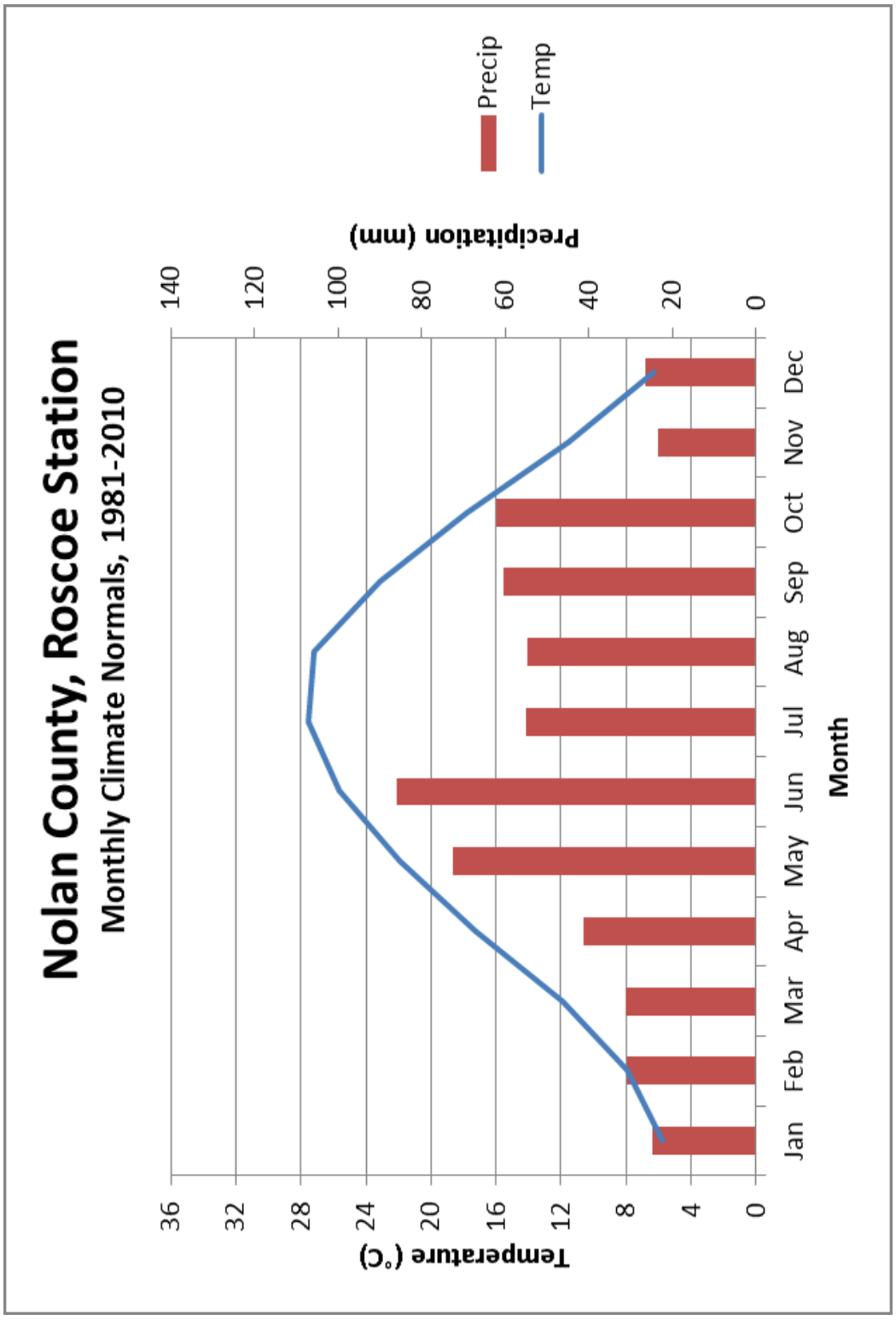
Nolan County, Roscoe Station
Monthly Climate Normals, 1981-2010
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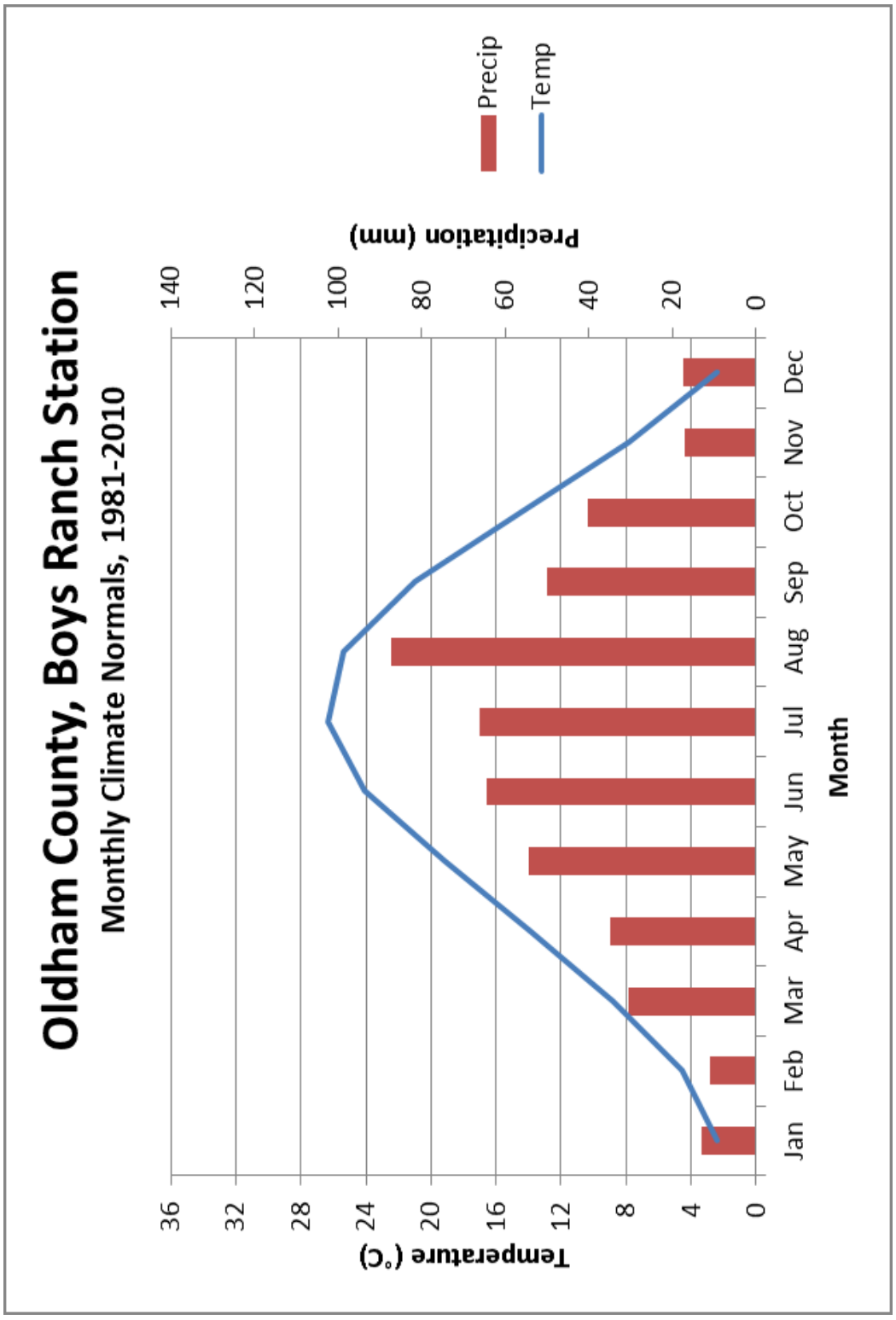
Oldham County, Boys Ranch Station
Monthly Climate Normals, 1981-2010
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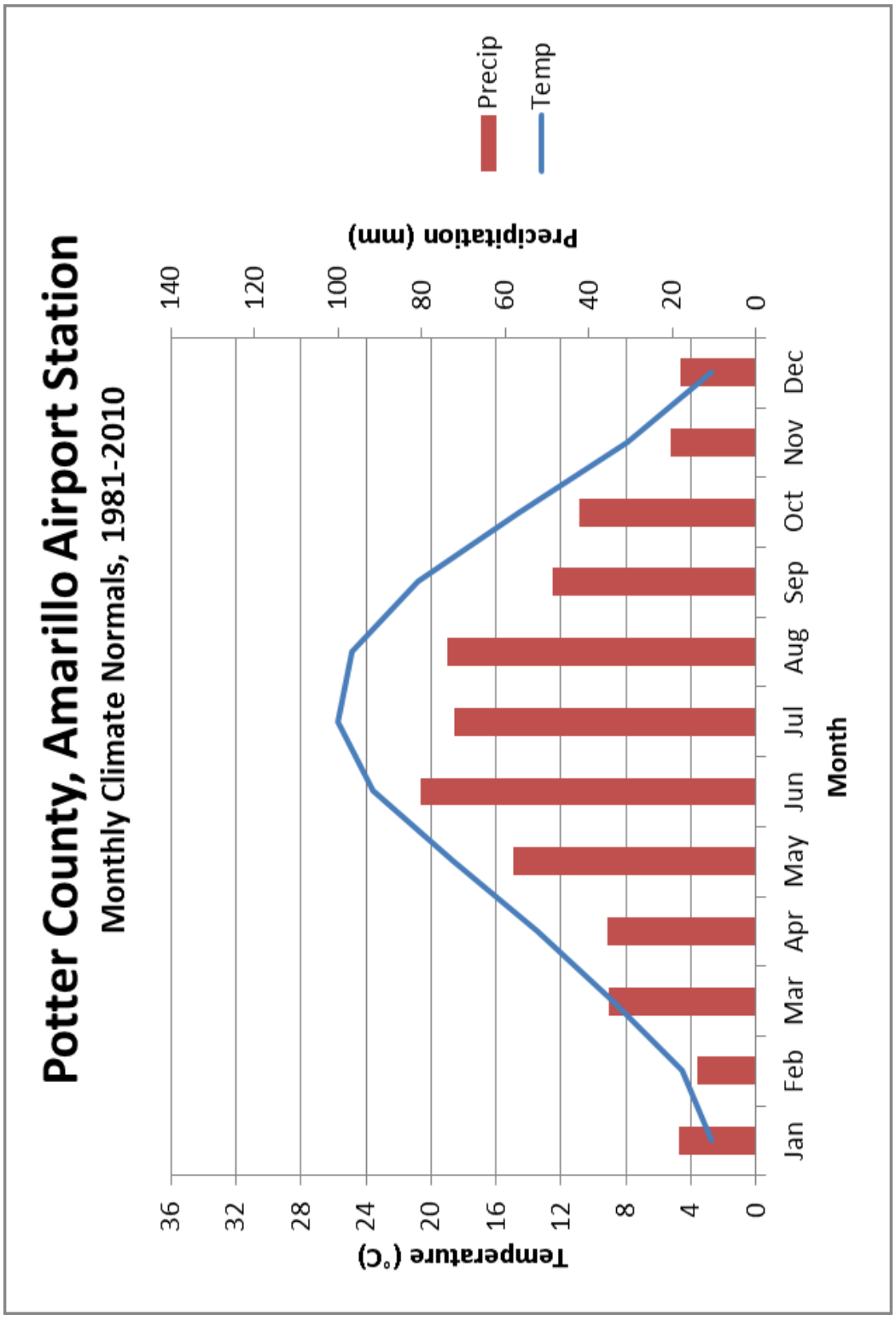
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Monthly Climate Normals, 1981-2010
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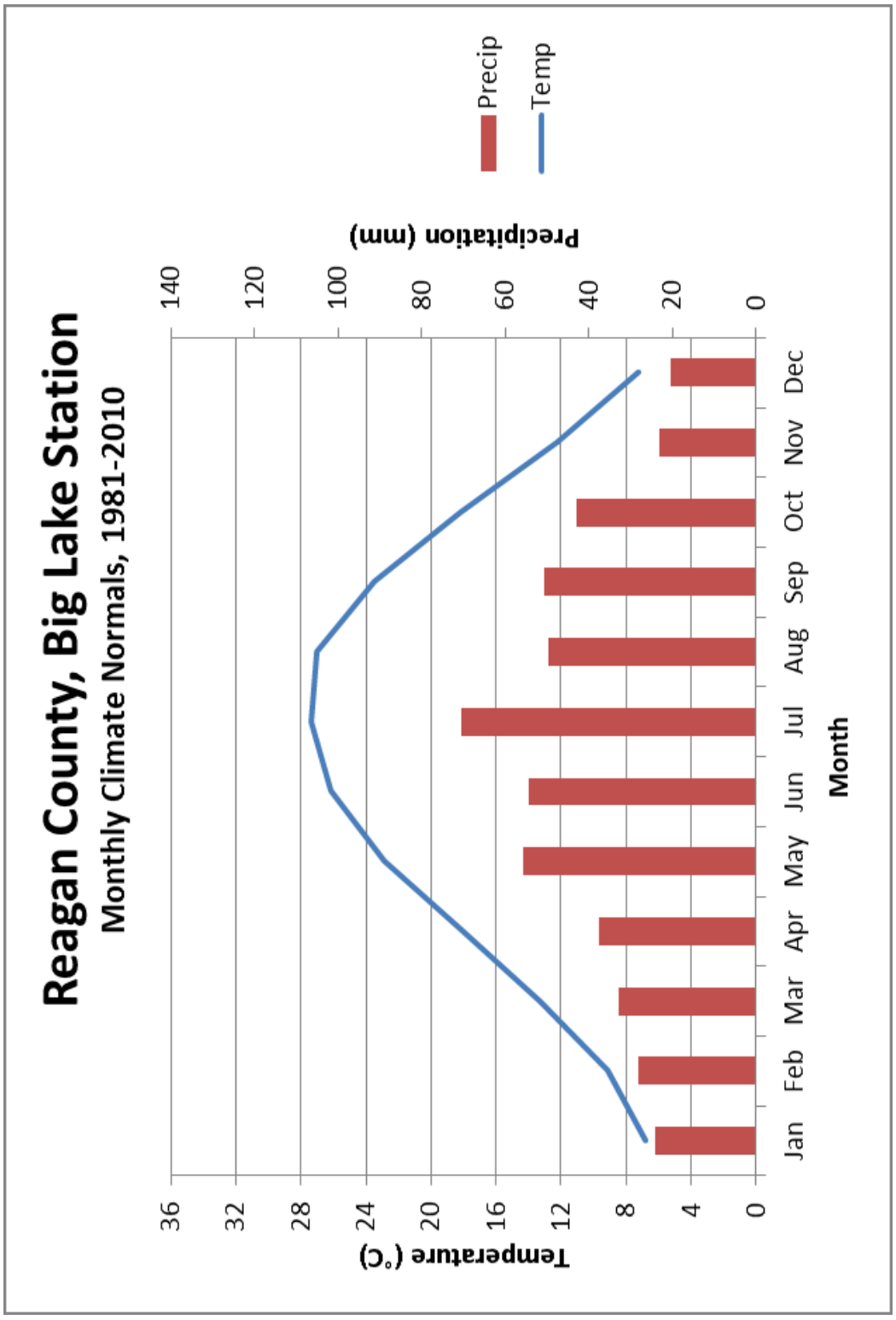
Reagan County, Big Lake Station
Monthly Climate Normals, 1981-2010
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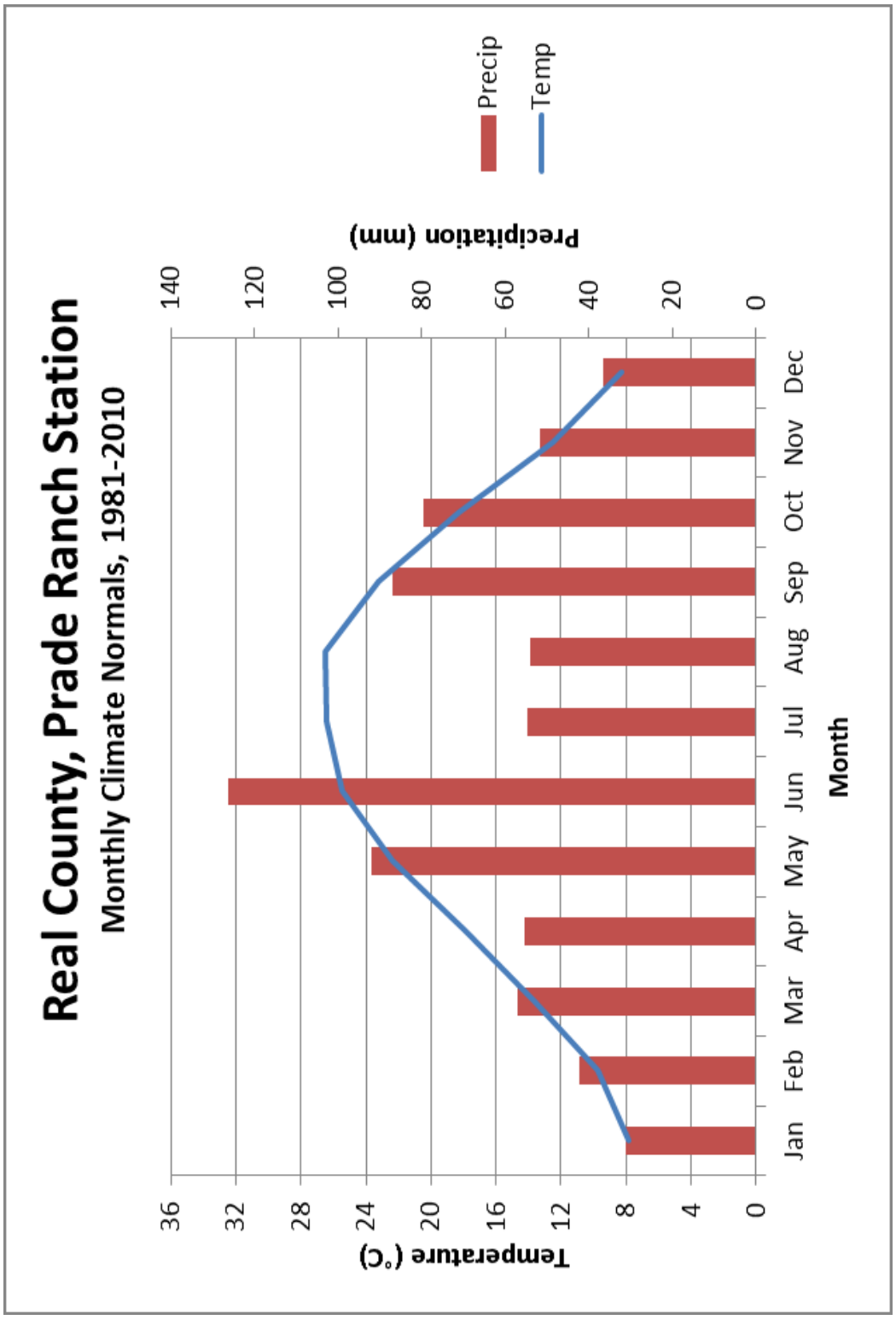
Real County, Prade Ranch Station
Monthly Climate Normals, 1981-2010
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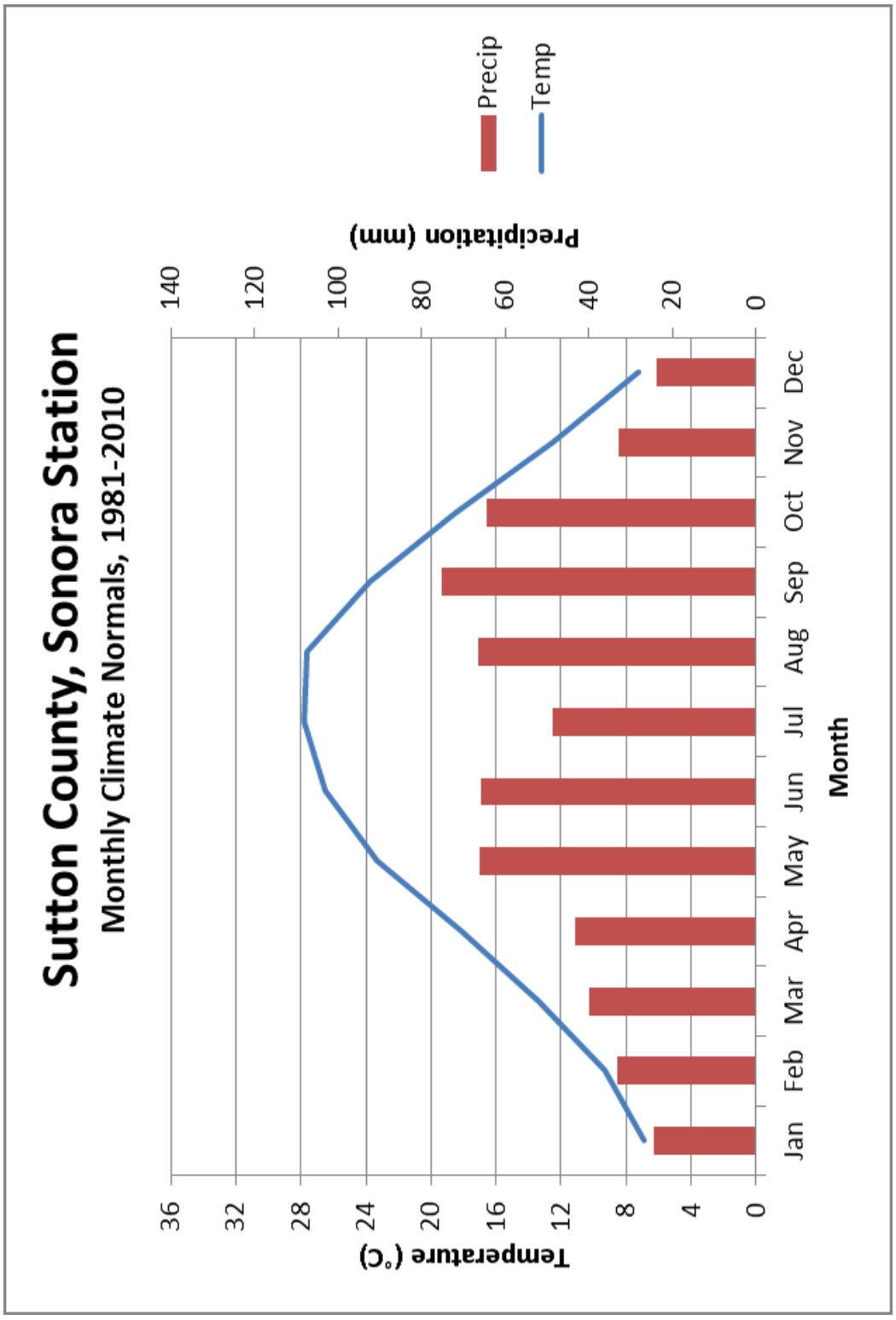
Sutton County, Sonora Station
Monthly Climate Normals, 1981-2010
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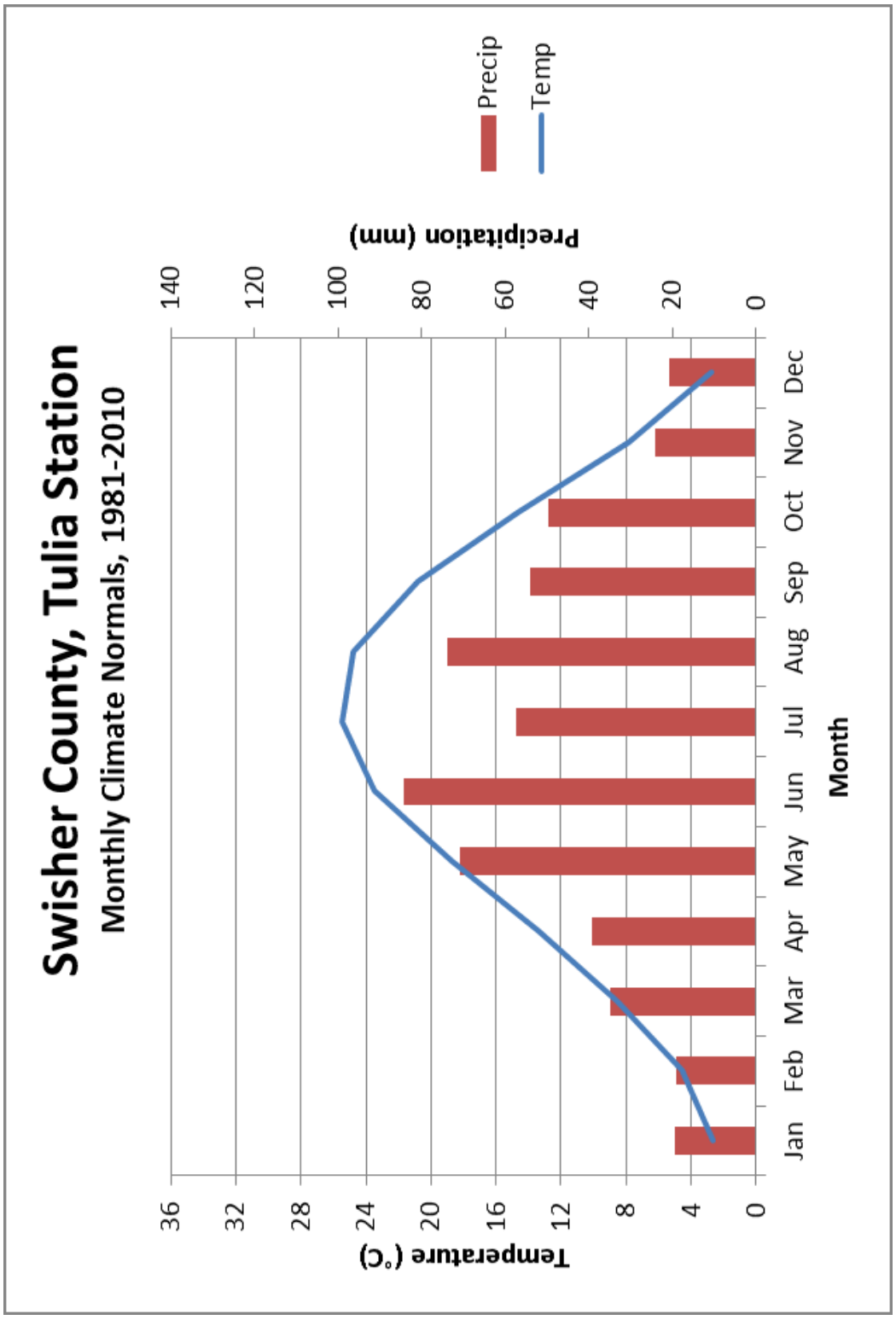
Swisher County, Tulia Station
Monthly Climate Normals, 1981-2010
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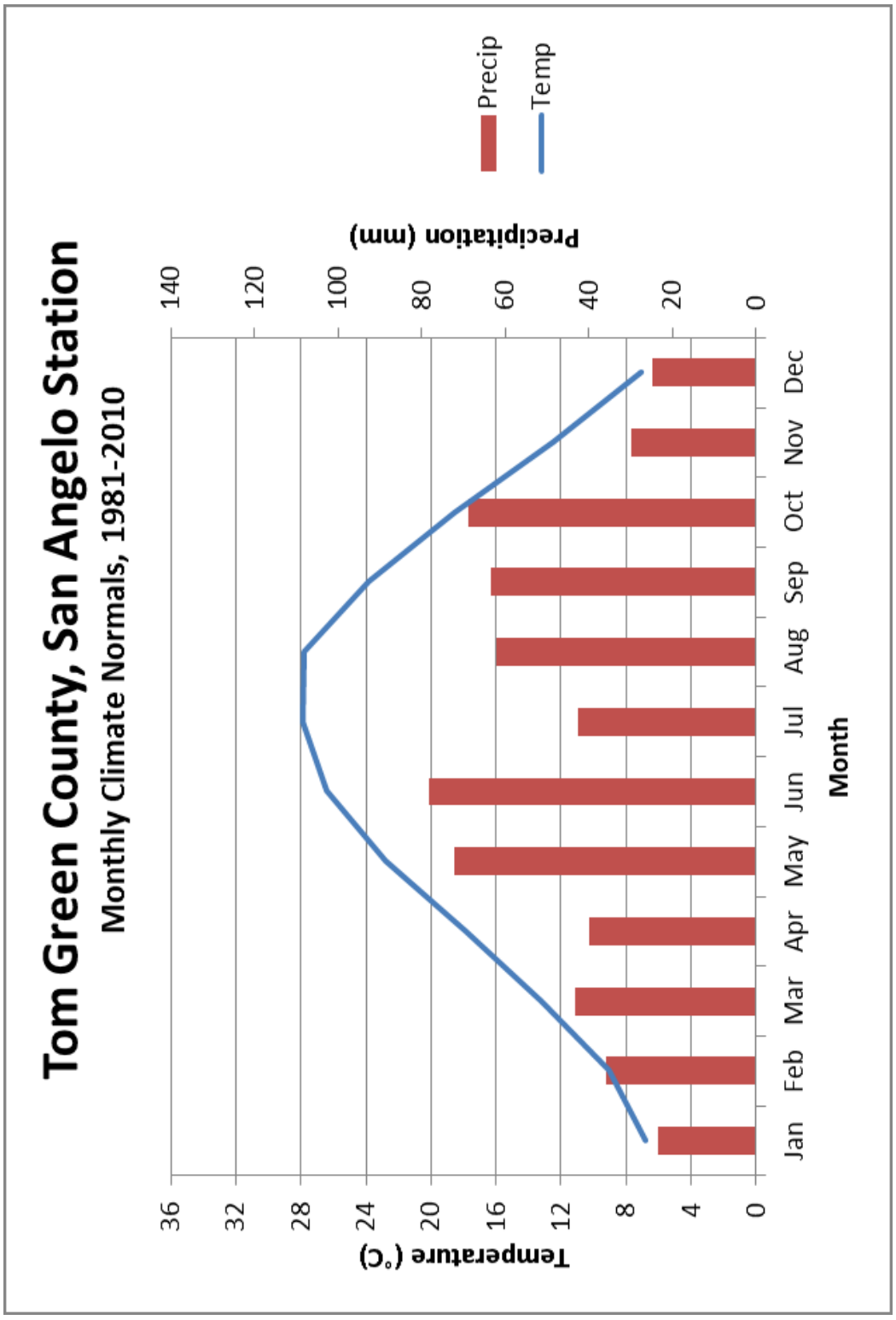
Tom Green County, San Angelo Station
Monthly Climate Normals, 1981-2010
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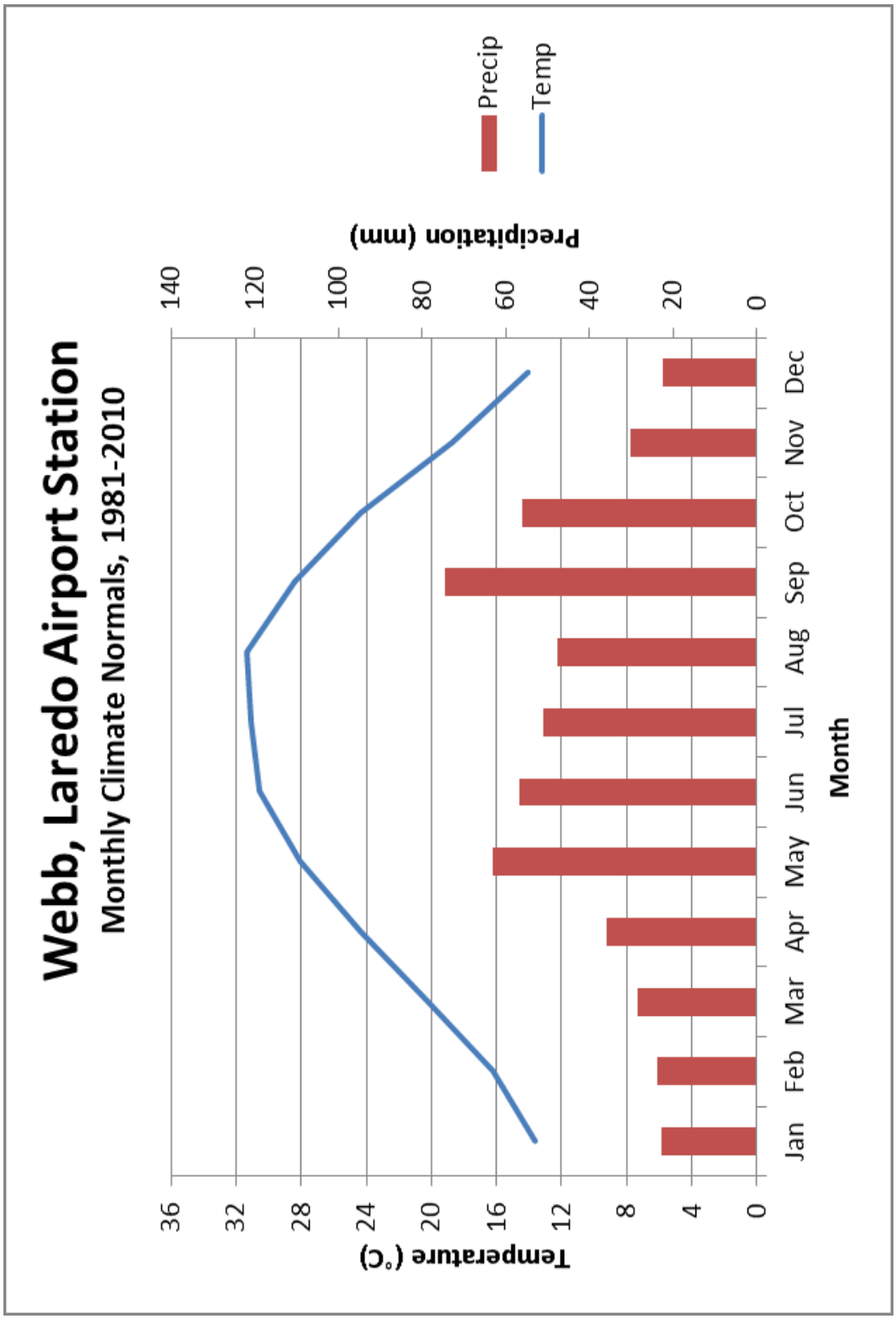
Webb, Laredo Airport Station
Monthly Climate Normals, 1981-2010
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