December 19, 2024

Philip G. Wyels
Assistant Chief Counsel
State Water Resources Control Board
1001 I Street
Sacramento, CA 95814

*Sent Via Email:* *commentletters@waterboards.ca.gov*

**Re: Comments on Draft Dairy Order, SWRCB/OCC FILES A-2283(b)**

Dear Mr. Wyels,

On behalf of researchers at Stanford University, we write to provide important new information relevant to the State Water Resources Control Board's ("State Board") draft order "In the Matter of Review of Waste Discharge Requirements General Order No. R5-2013-0122 for Milk Cow Dairies in the Central Valley Region," published on October 1, 2024 ("Draft Dairy Order"). In particular, the attached preliminary analysis of MediCal data by Dr. Jenny Suckale's research group suggests that certain communities in the Central Valley could be experiencing heightened incidences of infantile methemoglobinemia, or "blue baby syndrome." One of the primary causes of "blue baby syndrome" is ingestion of nitrate-contaminated drinking water.[1] At a minimum, this analysis is grounds for the State Board to act immediately to safeguard the health and safety of affected residents who may not be aware that their drinking water wells are contaminated.

As the Draft Dairy Order correctly recognizes, dairy manure accounts for one-third of total nitrogen applied to agricultural lands in the San Joaquin Valley and the Tulare Lake Basin.[2] Unsurprisingly, the average concentration of nitrate in shallow groundwater beneath dairy operations is 48 mg/L.[3] As the State Board recognizes, such high levels of nitrates in food or

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[1] Jenny Suckale, Basil Seif, I. Avery Bick, "Evidence of elevated risk for blue-baby syndrome and blue spells in the Central Valley, California," A Stanford Sustainability Accelerator Project, unpublished (Dec. 15, 2024) at 1, attached.

[2] California State Water Resources Control Board, Draft Order WQ 2024-00xx, SWRCB/OCC Files A-2283(b), In the Matter of Review of Waste Discharge Requirements General Order NO R5-2013-0122 For Milk Cow Dairies in the Central Valley Region Issued by the California Regional Water Quality Board, Central Valley Region (Oct. 1, 2024) https://www.waterboards.ca.gov/public_notices/petitions/water_quality/docs/r5-2013-0122/a2283bdrftordr.pdf (hereafter, the Draft Dairy Order) at 9 (citing Thomas Harter et al., *Nitrogen Fertilizer Loading to Groundwater in the Central Valley, Final Report to the Fertilizer Research Education Program, Projects 11‑0301 and 15‑0454*, California Department of Food and Agriculture and University of California, Davis (2017) at 106, http://ucanr.edu/sites/groundwaternitrate/files/268749.pdf.

[3] *Id*. at 52.

formula can cause blue baby syndrome – a potentially deadly disease – in otherwise healthy infants.[4]

I. <u>Preliminary data suggests that the Central Valley has a disproportionate number of zip codes with both elevated domestic well water nitrate concentrations and reported blue baby symptoms.</u>

Cyanotic attacks, when prolonged and repeated, can be indicative of blue-baby syndrome.[5] There are several peer reviewed studies directly linking blue-baby syndrome to nitrate overexposure.[6] An area of particular concern is California's Central Valley, where approximately 92,000 households rely on domestic wells.[7]

To better understand Central Valley's situation, researchers at Stanford University, led by Dr. Suckale, explored the prevalence of reported newborn cyanotic attacks and methemoglobinemia, as compared to domestic well nitrate concentrations.[8] The Suckale team used MediCal data from 2011-2019.[9] Notably, the datasets for both cyanotic attacks and methemoglobinemia do not, per se, capture *all* instances of either condition for babies zero to six months old, who are considered highest risk.[10] First, authors estimate that MediCal data only represents about 38% of the 2019 California population.[11] And of that 38%, only those who reported to their doctors and were coded appropriately are reflected.[12] Second, the newborn cyanotic attack code only applies to babies zero to 28 days old, thus excluding high-risk babies 29 days to six months old.[13] Third, while the methemoglobinemia code covers all ages, because the data is linked to MediCal beneficiaries, and it takes time to create a new beneficiary record, doctors may use an adult beneficiary's record, and thus older age, to record a baby's symptoms.[14]

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[4] *Id.* at 29-30.
[5] Suckale at 2.
[6] *Id.* at 1 (it was in part due to such studies that the EPA set the maximum contaminant level for nitrate to 10 mg/L).
[7] *Id.* at 2.
[8] *Id.* at 2-3 (emphasizing that using both codes for methemoglobinemia and cyanotic attacks provides a more accurate picture of all instances where babies with bluish discoloration are coded. "Cyanotic attacks" are "a sudden manifestation of this bluish discoloration in a newborn with previously normal skin color" and "methemoglobinemia" is when "a higher-than-normal amount of methemoglobin is found in the blood" though the code is recorded when submitting the request for blood testing).
[9] *Id.* at 2 (this was the most recent data available).
[10] Draft Dairy Order at 30.
[11] Suckale 3 (furthermore, the cyanotic attack medical codes do not indicate severity, thus, the data does not give us a sense of how pronounced the symptoms were in any given child or in any particular zip code. This would be a valuable tool to better gauge highest risk areas).
[12] *Id.* at 3 (specifically, MediCal Health Care targets low-income households, though there are other eligibility criteria).
[13] *Id.* at 3.
[14] *Id.* at 4 (here, of the 1,730 cases of methemoglobinemia, 117 cases are from baby-beneficiaries zero to one year old, 46 cases are between one and two years, 1,529 cases are associated with all other ages, and 38 cases lacked age data).

Together, this information suggests that the true counts of both conditions in those zero to six months old – that is, those most at risk for severe or deadly impacts – are even higher.[15]

Despite the likely underestimate, Suckale's team found that both methemoglobinemia and cyanotic attacks cluster in several Central Valley counties with high nitrate concentrations in domestic wells.[16] The data shows that more than half of California's zip codes have one or no reported cyanotic attacks and that 90% of reported cases are clustered around dense urban areas or agricultural regions, including the Central Valley.[17] Of reported cyanotic attacks and methemoglobinemia, many are from repeat patients–suggesting clustered high-risk areas.[18] The 1,730 cases of methemoglobinemia among MediCal beneficiaries from 2011-2019 are associated with a mere 499 beneficiaries.[19] Similarly, the 23,330 cases of newborn cyanotic attacks are associated with only 9,411 beneficiaries. Among these 9,411 beneficiaries, 44% experienced several cyanotic attacks.[20] This is notable because repeated cyanotic attacks could be indicative of a persistent, unresolved problem, such as nitrate exposure.[21]

With regards to this Dairy Order, the State Board is most concerned with the municipal and domestic sources of water that exceed the federal maximum contaminant level of 10 mg/L for nitrates.[22] Already, as the State Board recognizes through its Groundwater Ambient Monitoring and Assessment Program (GAMA), 21.7% of California's domestic wells have a mean nitrate concentration over 10 mg/L.[23] The counties highlighted in Dr. Suckale's work are some of the most worrying. In the four counties Dr. Suckale highlights (Tulare, Fresno, Madera, and San Joaquin), many wells exceeded the 10 mg/L maximum contaminant level by more than five times.[24] And, both case counts and rates of cyanotic attacks in these counties were heterogeneously dispersed, often near high-nitrate wells.[25] This finding suggests discrete nitrate

[15] Suckale at 1, 4.
[16] *Id.* at 7.
[17] *Id.* at 5 (If everyone had the same risk of exposure, results would have shown clusters only around highly populated areas. It did not. Instead, affected MediCal beneficiaries largely clustered in a few ZIP Codes many of which were in the Central Valley).
[18] *Id.* at 5.
[19]*Id.* at 3.
[20] *Id.* at 5.
[21] *Id.* at 1, 3 (cyanotic attacks are not uncommon among newborns and are thus not typically accompanied by a blood test).
[22] Draft Dairy Order at 13 ("We are most concerned here with the water quality objective to support the municipal and domestic supply (MUN) beneficial use, the maximum contaminant level (MCL) of 10 milligrams per liter (mg/L) for nitrates.").
[23] Suckale at 3, 8 (Stanford researchers emphasize that many domestic wells are missing from the GAMA dataset potentially making some cyanotic attack locations look unconnected to elevated groundwater nitrate levels); *see also* Ate Visser, Graham E. Fogg, and Thomas Harter, "Effect of Groundwater Age and Recharge Source on Nitrate Concentrations in Domestic Wells in the San Joaquin Valley Giovanni Castaldo," Environmental Science & Technology (2021) 55 (4), 2265-2275, doi: 10.1021/acs.est.0c03071.
[24] Suckale at 8.
[25] *Id.* at 5-8 (Suckale reported rates in addition to case counts since case counts cluster in areas with more MediCal beneficiaries).

pollution sources. While complex groundwater flows makes confirming nitrate sources difficult, the zip code hot spots are roughly aligned with dairy locations.[26] USDA's most recent 2022 farm census likewise suggests a connection between nitrate-contaminated well water and dairies. Per the census, Tulare County has about 30% of California's dairy cows, with Madera, Fresno, and San Joaquin counties following closely behind.[27] These are the same counties that Suckale's team found to have some of the highest rates of methemoglobinemia and cyanotic attacks.[28]

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[26] *See generally,* Christopher Vincent Henri, Thomas Harter, "Stochastic Assessment of Nonpoint Source Contamination: Joint Impact of Aquifer Heterogeneity and Well Characteristics on Management Metrics," *Advancing Earth and Space Sciences,* 55:8 (Jul. 23, 2019) https://doi.org/10.1029/2018WR024230; "Own Motion Review of WDRS General Order No. R5-2013-0122 For Existing Milk Cow Dairies SWRCB/OCC File A-2283(b)," State Water Resources Control board, https://www.waterboards.ca.gov/public_notices/petitions/water_quality/r5-2013-0122.html.

[27] Aaron Smith, "Where are California's Dairy Cows?" *Ag Data News: UC Davis* (Feb. 16, 2024) (citing "QuickStats" United States Department of Agriculture (2022) https://www.nass.usda.gov/Quick_Stats/.

[28] Suckale at 7-8.

**Cyanotic Attack Case Counts and Average Rates as Compared to Domestic Well Mean Nitrate Concentrations in Four Central Valley Counties, 2011-2019**

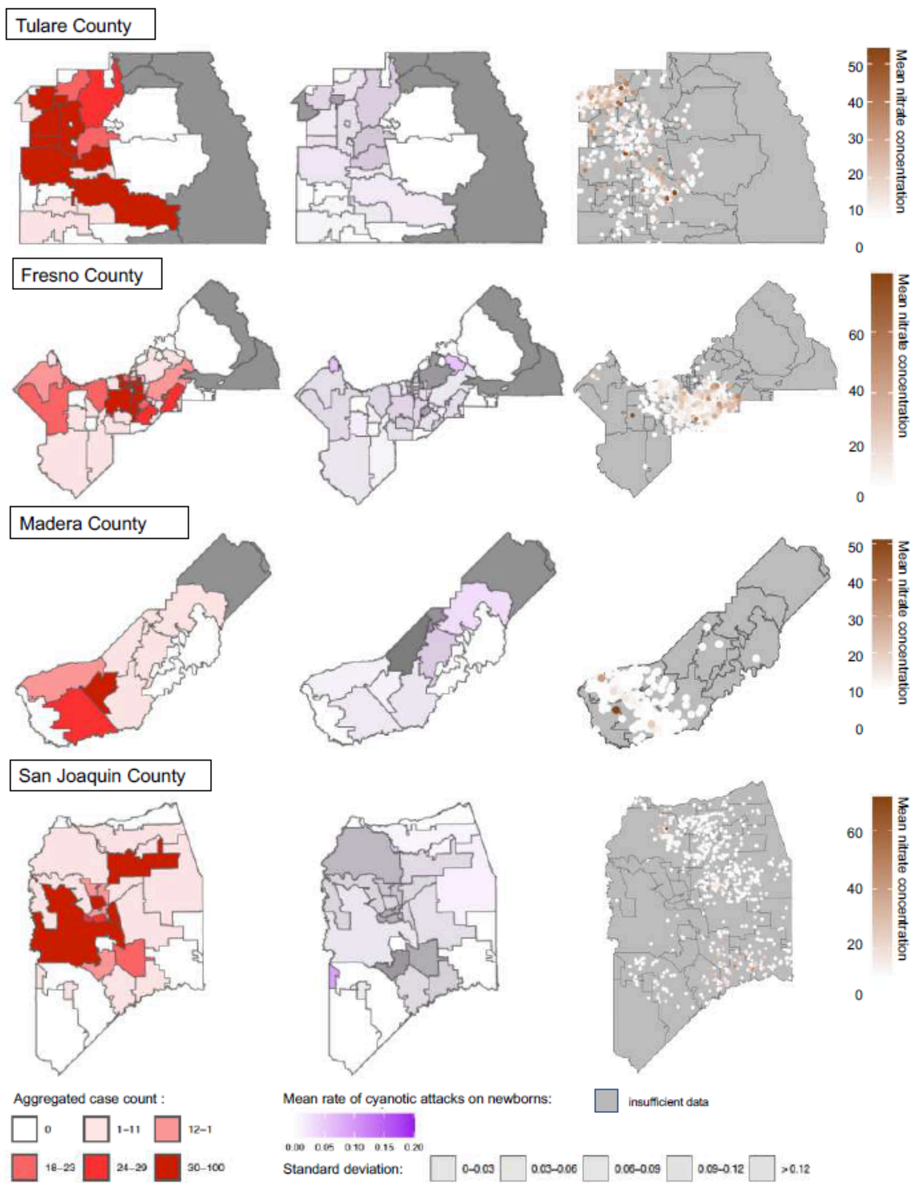


Figure 4: Aggregated case counts (left) and average rates (middle) of cyanotic attacks on newborns by ZIP code for Tulare, Fresno, Madera and San Joaquin County, 2011-2019, as compared to the mean nitrate concentration in domestic wells (right) from the GAMA data set.

**Methemoglobinemia Case Counts for MediCal Beneficiaries, 2011-2019**

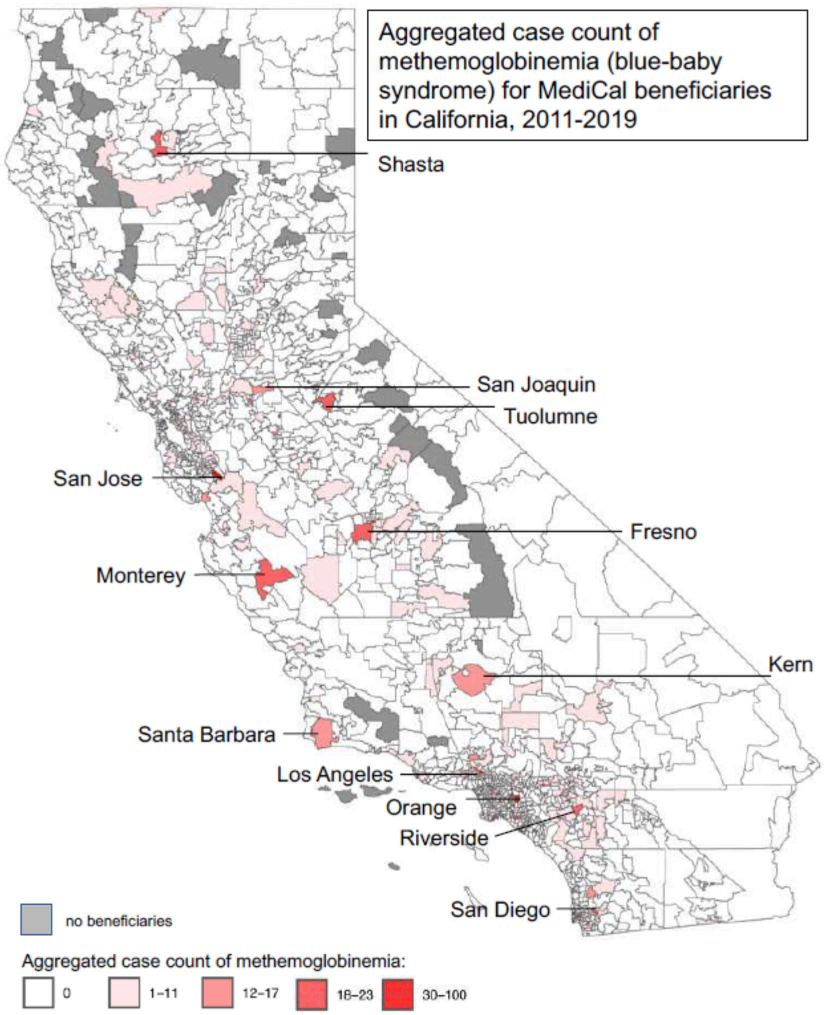


Figure 1: Aggregated case counts of methemeglobinemia (blue-baby syndrome) among MediCal beneficiaries at the ZIP-code level in California, 2011-2019.

Ultimately, while the dataset is preliminary, there are two key takeaways from this research. First, looking at case counts (regardless of zip code population), there are clusters of reported methemoglobinemia and cyanotic attacks in the Central Valley. And second, this clustering occurs in counties with high domestic well nitrate concentrations.[29]

II. Given this preliminary data, the State Board should act now.

In 2019, the State Board directed the Central Valley Regional Water Board to "ensure that affected residents in localized areas within management zones with nitrate concentrations exceeding 10 mg/L ("hot spots") are identified and provided access to drinking water."[30] Because

[29] Suckale at 8.
[30] Draft Dairy Order at 27 (citing State Water Board Resolution No. 2019-0057).

this preliminary data captures MediCal beneficiaries from 2011-2019, we cannot comment on any potential impact that the 2019 directive may have had on Central Valley cyanotic attacks. However, given the directive's unclear timeline and enforcement and the potentially severe health impacts implicated by the Suckale team's work, we urge the State Board to take immediate action to protect at-risk communities.

The Draft Dairy Order allows regional water boards to give dairies substantial time to come into compliance with existing water quality requirements.[31] Such delayed compliance only ensures that the contamination problem will continue to worsen in the interim. Regardless of the final compliance dates, the State Board has an obligation to immediately protect at-risk communities, especially those marginalized residents – and their children – who may be unaware of the contamination of their drinking water.

## III. Recommended Immediate Next Steps

We support the Draft Dairy Order's efforts to address dairy-linked nitrate contaminated well water in the short and long term.[32] However, a critical first step is more comprehensive well water testing and data collection. The Suckale lab shines a light on the present Central Valley public health crisis even without data on many domestic wells.[33] To intervene thoughtfully and effectively, the State Board must prioritize Central Valley domestic well water testing and dataset updates. To that end, we urge the State Board to prioritize collaboration between its many programs related to domestic well water quality and their relevant data collection efforts.[34] Simultaneously, we urge the State Board to prioritize community-level education and outreach regarding the Central Valley blue baby risk. Suckale's lab mapped several zip codes with elevated well water nitrate, suggesting many families are unaware of the myriad of health risks that nitrate overexposure poses.

Lastly, given the present threat to human health, we suggest a bifurcated process that addresses nitrate's current harms and the root causes of its elevated levels. For wells with nitrate

[31] Draft Dairy Order at 45 ("Nonpoint Source Policy Key Element #3 provides for regional water board allowance of time to growers for compliance with water quality requirements (the groundwater limitation), so long as the regional board specifies a time schedule with corresponding "quantifiable milestones" of progress (p.34); Water Code Sec. 13263(c) allows for waste discharges to become compliant with water quality objectives over a specified time schedule, even if the discharges 'will likely temporarily continue to cause or contribute to the exceedances of water quality objectives'").

[32] *See e.g.,* Draft Dairy Order at 74 ("That 'all dairies that are causing or contributing to exceedances of 10 mg/L nitrate in groundwater must provide alternative water supplies to any residents that rely on that groundwater'...The regional water boards shall take into account the information and experience gained by the CV-SALTS program and the SAFER program, and work with our staff to ensure dairies are notified of their obligation to comply with this requirement, domestic wells impacted by nitrates from dairy operations are identified and tested, and residents reliant on affected water are provided with safe replacement water').

[33] Suckale at 8 (emphasizing the need for more water monitoring and increased community awareness); Visser at 2265.

[34] For instance, SAFER, CV Salts, ILRP, SGMA, and DRIP.

concentrations above the federal safety level, the State Board should prioritize immediate access to safe drinking water. Simultaneously, the regulatory reform and remediation work must also continue.

There are several approaches to providing safe drinking water to contaminated domestic well water users. We urge the State Board to prioritize consulting impacted communities regarding intervention options, and to swifty implement preferred interventions. Three of the most common interventions are a) providing bottled water, b) connecting contaminated-well water communities to the public water system, and c) installing reverse osmosis or ion exchange units to faucets.[35] We emphasize, however, that prioritizing immediate access to safe drinking water should not come at the expense of addressing the root causes of the Central Valley's elevated nitrate levels and the State Board's duty to implement long-term remediation efforts.

## III. Conclusion

Given the State Board's duty to safeguard our water, we urge the State Board to move forward with immediate community level action. The State Board rightfully acknowledges that:

> [D]airies are a major contributor to the widespread nitrate groundwater contamination and many rural households in the Central Valley are plagued with nitrate-contaminated drinking water, resulting in severe health, economic, and quality-of-life impacts. We therefore believe that shifting the predominant paradigm is critically important.[36]

These comments provide further details of this grim reality and emphasize that while working to shift the paradigm, the State Board should also prioritize immediate community-level blue baby syndrome education and well-water testing; and collaborate with communities, now, to mitigate nitrate overexposure's likely existing harms.

Thank you for considering these comments.
Respectfully submitted,

Gina Hervey, JD, MS
Deborah A Sivas JD, MS

[35] "Nitrates in Drinking Water," *PenState Extension* (Aug. 26, 2022), https://extension.psu.edu/nitrates-in-drinking-water (Reverse osmosis pushes nitrate contaminated water through a high pressure pump and reverse osmosis membrane to filter out nitrate ions). "Nitrates in Drinking Water," *PenState Extension* (Aug. 26, 2022), https://extension.psu.edu/nitrates-in-drinking-water (ion exchange units move the contaminated water through a resin that exchanges chloride ions for nitrate and sulfate ions).
[36] Draft Dairy order at 7.

Michael Wara, JD, PhD
Michael Mastrandrea, PhD
Amanda Zerbe JD, MS
Cassandra Jurenci JD, MS

*Researchers from the Environmental and Natural Resources Law and Policy Program, Stanford Law School Climate and Energy Policy Program, Stanford Woods Institute For the Environment*

# Evidence of elevated risk for blue-baby syndrome and blue spells in the Central Valley, California

Jenny Suckale, Basil Seif, I. Avery Bick

December 19th, 2024

**We show that case counts of methemoglobinemia (blue-baby syndrom) and cyanotic attacks on newborns tend to cluster in parts of the Central Valley and Southern California using individual-level health data for MediCal beneficiaries in California during years 2011 to 2019. Our data suggests that newborns in these areas could have elevated risk for these two conditions.**

## 1 Background

Blue-baby syndrome was first described in 1945 by pediatric resident Hunter Comly[1]. Officially termed infantile methemoglobinemia, its main symptom is cyanosis, or the development of a blue-gray skin color. The two described cases were related to the digestion of well water with nitrate levels of 90 mg/L and 140 mg/L. Intake of nitrate through water or vegetables rich in nitrate can cause methemoglobinemia, because nitrate, $NO_3^-$, reduces to nitrite, $NO_2^-$, in the intestine. When nitrite is absorbed into the bloodstream, it oxidizes hemoglobin to methemoglobin, a substance that does not bind and transport oxygen, reducing the ability of the bloodstream to supply oxygen to tissues and resulting in a blue-gray skin color[2].

[1] Hunter H Comly. Cyanosis in infants caused by nitrates in well water. *Journal of the American Medical Association*, 129(2):112–116, 1945

[2] Deepanjan Majumdar. The blue baby syndrome: nitrate poisoning in humans. *Resonance*, 8(10):20–30, 2003

After the discovery of blue-baby syndrome, independent surveys in the Midwest states identified numerous other cases related to nitrate exposure. In 1951, Walton compiled a synthesis report of the 48 states, plus what were then the territories of Alaska and Hawaii, listing 278 cases with 39 deaths[3]. None of the cases was related to wells containing 10 mg / L or less nitrate, and only 2.3 % of the cases involved wells with nitrate concentrations between 10 and 20 parts mg/L. Based in part on the Walton report, the US Environmental Protection Agency set the maximum contaminant limit for nitrate at 10 mg/L in the Safe Drinking Water Act and its subsequent amendments. However, cases of blue-baby syndrome associated with exposure to nitrate persist[4] despite regulatory efforts.

[3] Graham Walton. Survey of literature relating to infant methemoglobinemia due to nitrate-contaminated water. *American Journal of Public Health and the Nations Health*, 41:986–996, 1951

Not all reported cases of blue-baby syndrome appear to have been associated with nitrate exposure. In 1980, several cases were reported for which the cause of high methemoglobin levels was never determined[5]. Potential explanations included exposure to unidentified nitrate, bacterial infection, or exposure to another toxic substance in drinking water, such as copper[6]. These cases highlight how challenging it can be to correctly diagnose blue-baby syndrome. In addition to performing a blood test to determine the methemoglobin level, doctors would need to become aware of an baby's exposure to nitrate and other pollutants through interviews with parents or caregivers and water tests.

[4] Lynda Knobeloch, Barbara Salna, Adam Hogan, Jeffrey Postle, and Henry Anderson. Blue babies and nitrate-contaminated well water. *Environmental health perspectives*, 108(7):675–678, 2000

[5] Emanuel Hegesh and Joseph Shiloah. Blood nitrates and infantile methemoglobinemia. *Clinica Chimica Acta*, 125(2):107–115, 1982

[6] Deana M Manassaram, Lorraine C Backer, and Deborah M Moll. A review of nitrates in drinking water: maternal exposure and adverse reproductive and developmental outcomes. *Environmental health perspectives*, 114(3):320–327, 2006

Given these diagnoses challenges and the general rarity of blue-baby syndrome, it is possible that blue-baby syndrome is underdiagnosed, particularly in areas where healthcare facilities are short on resources and staff. In recognition of this possibility, we complement our analysis of the case count of blue-baby syndrome with an analysis of cyanotic attacks on newborns. Cyanotic attacks, also known as blue spells, are defined as a sudden bluish discoloration of a newborn's skin with previously normal skin color. They can last from a few moments to an extended period of time at which point caregivers are likely to seek medical attention.

We emphasize that cyanotic attacks are a common health condition, particularly in premature babies, and can have multiple different causes[7]. Short cyanotic attacks tend to pass without medical intervention, but prolonged and repeated cyanosis could be a symptom of blue-baby syndrome. Given that nitrate concentrations in domestic wells in California commonly exceed the federally mandated threshold of 10 mg/L, it is informative to evaluate whether the prevalence of cyanotic attacks is elevated in regions with high water pollution. An area of particular concern is the Central Valley, where approximately 92,000 households rely on private, often unmonitored wells[8].

[7] RS Illingworth. Cyanotic attacks in newborn infants. *Archives of Disease in Childhood*, 32(164):328, 1957

[8] Tyler D Johnson and Kenneth Belitz. Identifying the location and population served by domestic wells in california. *Journal of Hydrology: Regional Studies*, 3:31–86, 2015

## 2 Data

We analyze the individual-level data set of inpatient and outpatient services for 100% of MediCal beneficiaries in California in the years 2011-2019[9,10,11]. We currently do not have access to these data from recent years. The MediCal data base uses ICD codes to classify and record diseases, symptoms, and procedures. The International Classification of Diseases (ICD) is a standardized system that allows for consistent data collection and comparison worldwide. In 2015, the ICD codes were updated from ICD-9 to ICD-10.

[9] Stanford Center for Population Health Sciences. Medicaid 100% [2011-2019] personal summary (ps)/demographic & eligibility (de) (version 3.1) [dataset]. Redivis, 2023c

[10] Stanford Center for Population Health Sciences. Medicaid 100% [2011-2019] inpatient (ip) (version 2.0) [dataset]. Redivis, 2023a

[11] Stanford Center for Population Health Sciences. Medicaid 100% [2011-2019] other services (ot) (version 3.0) [dataset]. Redivis, 2023b

We evaluate the prevalence of two health conditions, "Methemoglobinemia" and "Cyanotic attacks on newborns". We identify "Methemoglobinemia" through ICD-10 code D74 and the ICD-9 code 289.7. According to the ICD system, methemeglobinemia is defined as "A condition in which a higher than normal amount of methemoglobin is found in the blood. Methemoglobin is a form of hemoglobin that cannot carry oxygen. In methemoglobinemia, the tissues cannot get enough oxygen. Symptoms may include headache, dizziness, fatigue, shortness of breath, nausea, vomiting, rapid heartbeat, loss of muscle coordination, and blue-colored skin. Methemoglobinemia can be caused by injury or being exposed to certain drugs, chemicals, or foods. It can also be an inherited condition. [..]"

We identify "cyanotic attacks on newborns" through the ICD-10 code P28.2 and the ICD-9 code 770.83, both representing "cyanotic attacks on newborns". According to the ICD system, a cyanotic attack is different from cyanosis: "Cyanosis is a bluish discoloration of the nail beds, skin and/or mucus membranes due to low hemoglobin levels in the capillary beds and is a fairly common finding in a newborn. Cyanotic attacks are defined as a sudden manifestation of this bluish discoloration in a newborn with a previously normal skin color. The episodes usually last less than 30 minutes with the infant's color returning to normal without intervention. [..]"

We evaluate both conditions because they both represent possible ways through which a baby with blue-ish discoloration of its skin could be encoded in the MediCal data base. There are three main differences in the usage of the two codes. First, the ICD codes P00-P96 specifically refer to the perinatal period defined as the first 28 days of a baby's life. According to the coding manager at the Lucille Packard Children's Hospital, health conditions occurring during the perinatal period would tend to be encoded using these codes, which include P28.2 and 770.83. Older babies are not captured in this code. Second, a blood test is required to measure the methemoglobin level in the blood of a baby, but blood tests are not routinely performed during the perinatal period. Third, ICD codes D74 and 289.7 are billing codes used to order blood tests when a doctor suspects elevated levels of methemoglobin in the blood of a patient. These codes do not confirm that methemoglobin was indeed elevated.

Our analysis underestimates the actual case count for both conditions in California because we focus only on MediCal beneficiaries. To be included in the MediCal database, the newborn or one of the parents must be enrolled in the MediCal Health Care Program. MediCal targets low-income households, although there are other eligibility criteria, such as disability. The number of beneficiaries changed during the years available to us with approximately 15 million beneficiaries in 2019, which corresponds to about 38% of the Californian population in 2019. There are likely to be more cases of methemoglobinemia and cyanotic attacks on newborns in the medium to high income range.

We compare the prevalence of cyanotic attacks with the concentration of nitrates in domestic wells available through the Groundwater Ambient Monitoring and Assessment Program (GAMA) of the State Water Resources Control Board[12]. The data set includes 5,179 domestic wells where 21.7% have mean nitrate concentrations that exceed the maximum contaminant limit of 10 mg/L for nitrate. It is important to note that many domestic wells are not included in the GAMA data set and are not currently monitored.

[12] Jennifer L Shelton and Elias Tejeda. California groundwater ambient monitoring and assessment (gama) program priority basin project: Domestic-supply assessment. Technical report, US Geological Survey, 2024

## 3 Results

Our database contains a total of 1,730 cases of methemeglobinemia among MediCal beneficiaries in California for years 2011-2019. These cases are associated with 499 unique beneficiaries, which implies that several beneficiaries were diagnosed with this condition multiple times. Of the 1,730 cases, 29 cases lack information about ZIP code or county. We show the spatial distribution of the remaining 1,701 cases in Figure 1. ZIP codes without MediCal beneficiaries are colored gray. The vast majority of ZIP codes does not have a single case of methemeglobinemia.

Recorded cases tend to cluster in a few ZIP codes, many of which fall into the Central Valley including Shasta (Redding area), San Joaquin, Tuoloumne, Fresno and Kern. Two other clusters in San Jose (Gilroy area) and Monterey/San Benito counties also fall into agricultural areas. The remaining cases are clustered in the population centers of Santa Barbara, Riverside, Irvine, and Los Angeles County. These clusters are not necessarily unexpected because rare conditions like methemeglobinemia tend to cluster in population

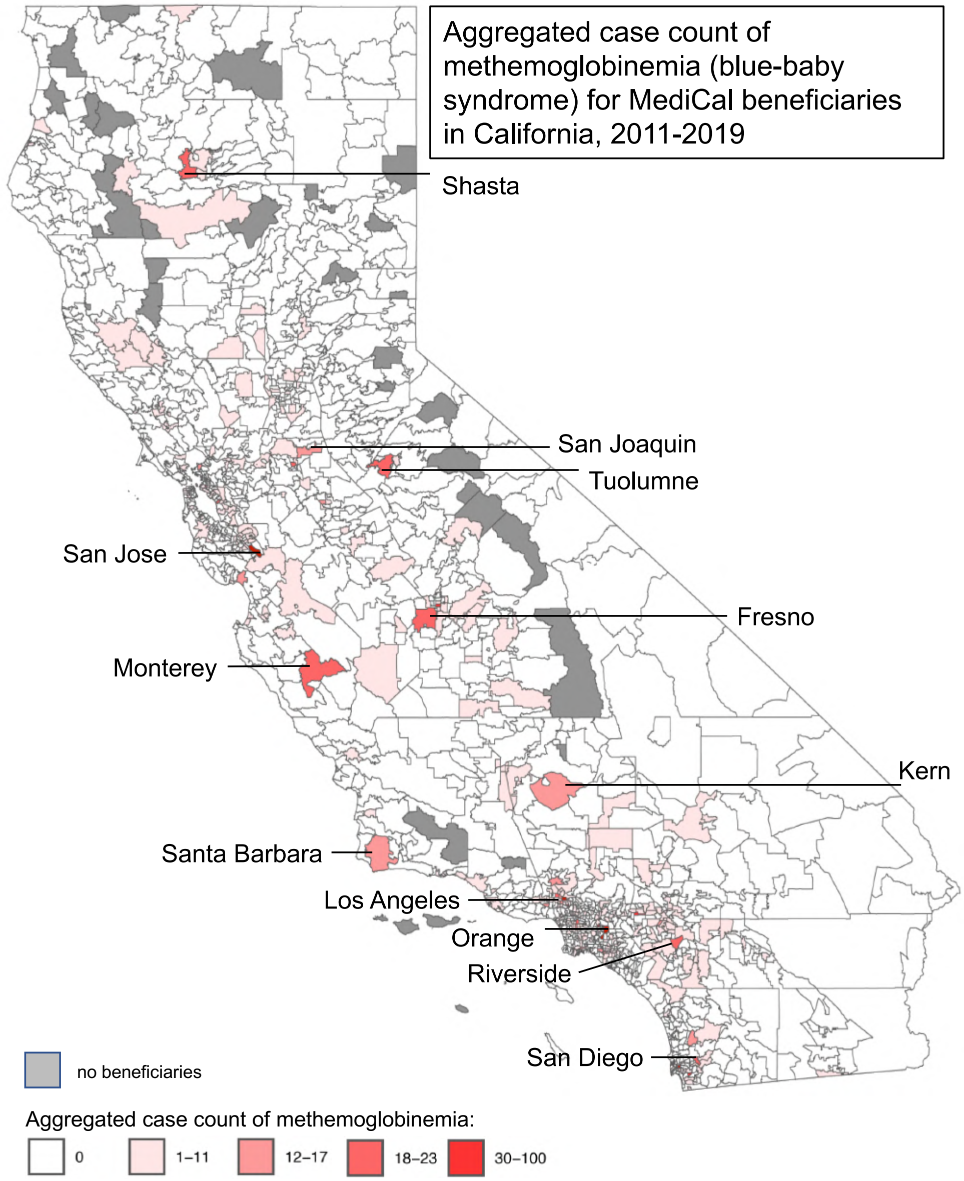


Figure 1: Aggregated case counts of methemeglobinemia (blue-baby syndrome) among MediCal beneficiaries at the ZIP-code level in California, 2011-2019.

centers. If everyone has the same risk of getting sick, more people get sick in areas where more people live. The clusters we identify in agricultural areas are not located in populous ZIP codes.

Among 1,730 cases of methemeglobinemia, 117 cases are babies in the first year of life, 46 cases are babies between the ages of 1 and 2 and 1,529 cases are associated with older ages. There are also 38 cases where age information is missing. These numbers could underestimate the number of newborns affected, because the beneficiary's age is not necessarily identical to the patient's age. Since it takes time for a new beneficiary record to be created when a baby is born, health issues experienced by newborns are sometimes recorded through the parent, in which case the age of the beneficiary would be that of the parent, not that of the newborn.

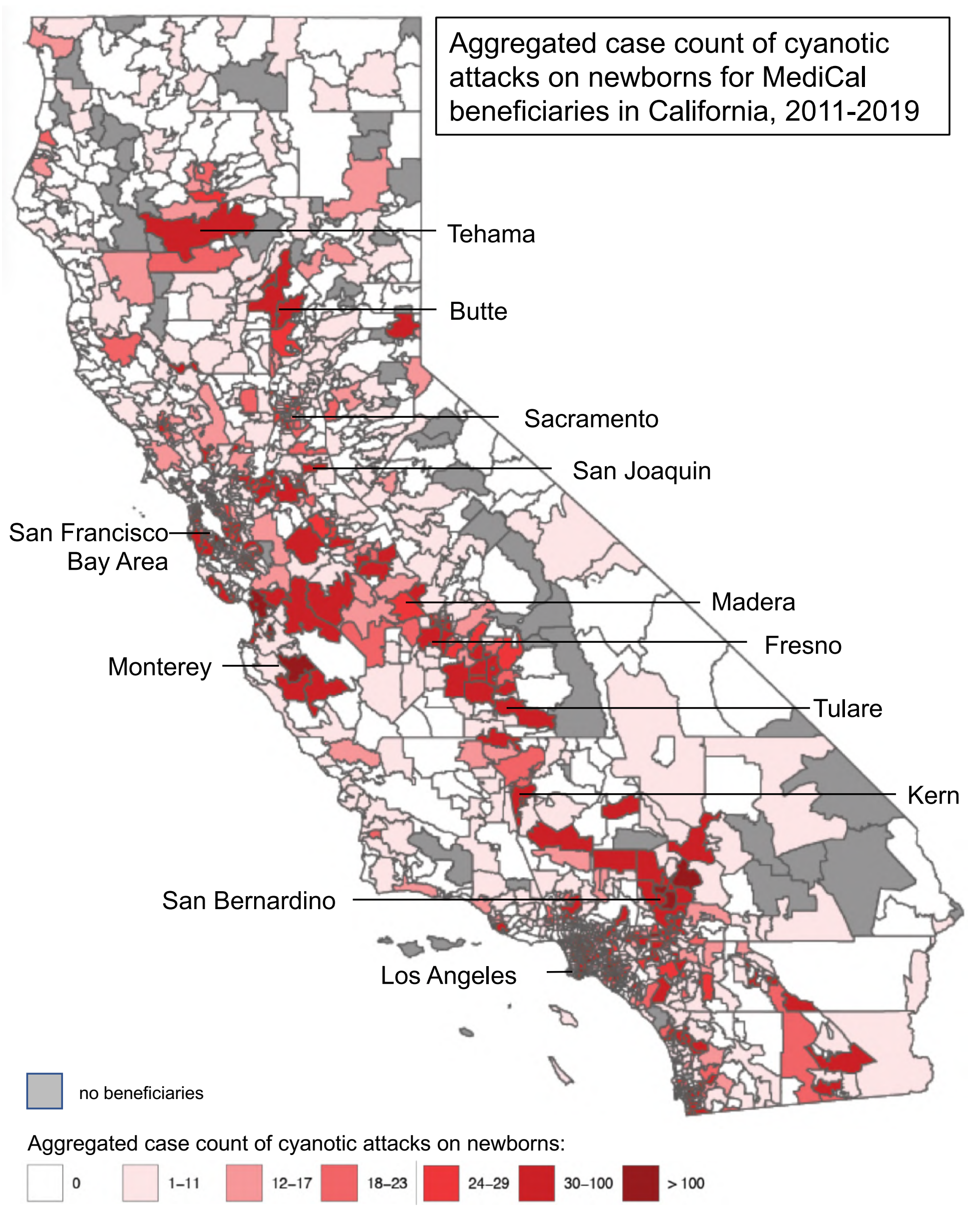


Figure 2: Aggregated case counts of cyanotic attacks on newborns among MediCal beneficiaries at the ZIP-code level in California, 2011-2019.

Figure 2 shows the spatial distribution of the case counts for cyanotic attacks on newborns at the ZIP-code level, aggregated over the time period 2011-2019. In all of California, there are 23,330 total cases of cyanotic attacks on newborns associated with 9,411 unique beneficiaries. Among these 9,411 beneficiaries, 56% experienced only one cyanotic attack, while 44% experienced cyanotic attacks repeatedly. Of the 23,330 total cases, 844 cases lack information about the beneficiary ZIP code. We remove these cases for plotting purposes. The remaining 22,486 cases are distributed heterogeneously. Most of the 1,721 ZIP codes in California have 10 or fewer cases. Of the 22,485 cases shown in Fig. 2, 90 % occurred in 539 ZIP codes located primarily in large urban areas such as the San Francisco Bay Area and the Los Angeles area and in agricultural areas including the Central Valley, the area east of Monterey, and the Inland Empire region.

Given that case counts cluster in areas with more beneficiaries, it is valuable to compare

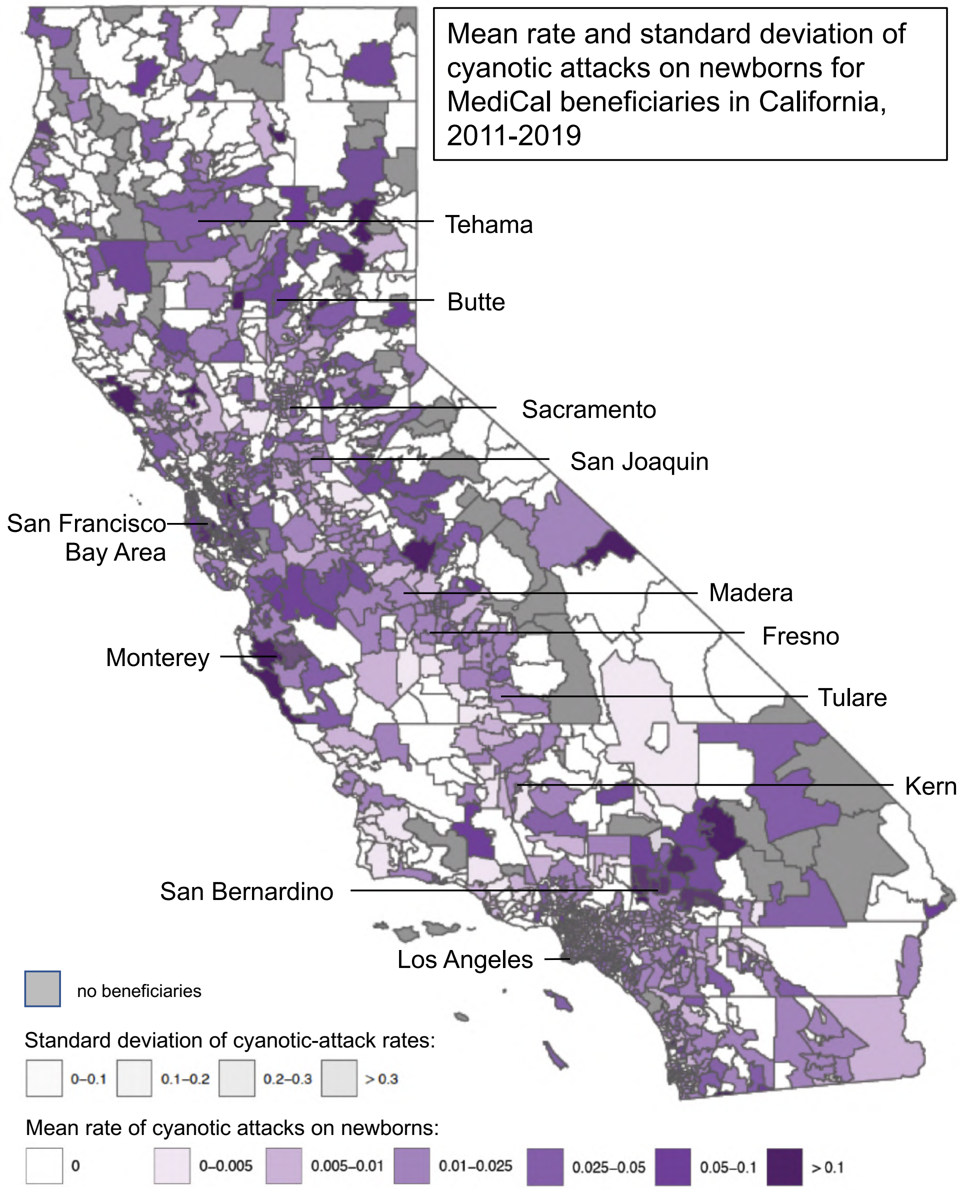


Figure 3: Mean rate and weighted standard deviation of cyanotic attacks on newborns by ZIP code in California, 2011-2019, in comparison to the mean nitrate concentration in domestic wells listed in the GAMA data set.

the rate of cyanotic attacks on newborns rather than the aggregated case count. One challenge in the rate computation is that the number of newborn beneficiaries varies dramatically between ZIP codes. About 30% of the ZIP codes have fewer than 50 newborn beneficiaries for the years 2011 to 2019 of our analysis, while other ZIP codes have tens of thousands of newborn beneficiaries. Also, the number of newborn beneficiaries varies significantly over time as the MediCal program expanded in California.

In Figure 3 we estimate the mean rate of cyanotic attacks on newborns at the ZIP-code level. We first compute an annual rate by dividing the total case count in a given year and ZIP code by the total number of newborn beneficiaries in that year and ZIP code, where newborns are defined as babies within the first 28 days of their life. We then take the mean of these annual rates. ZIP codes without any newborn beneficiaries are colored gray and labeled as "no beneficiaries". In addition to the mean rate, we estimate the standard

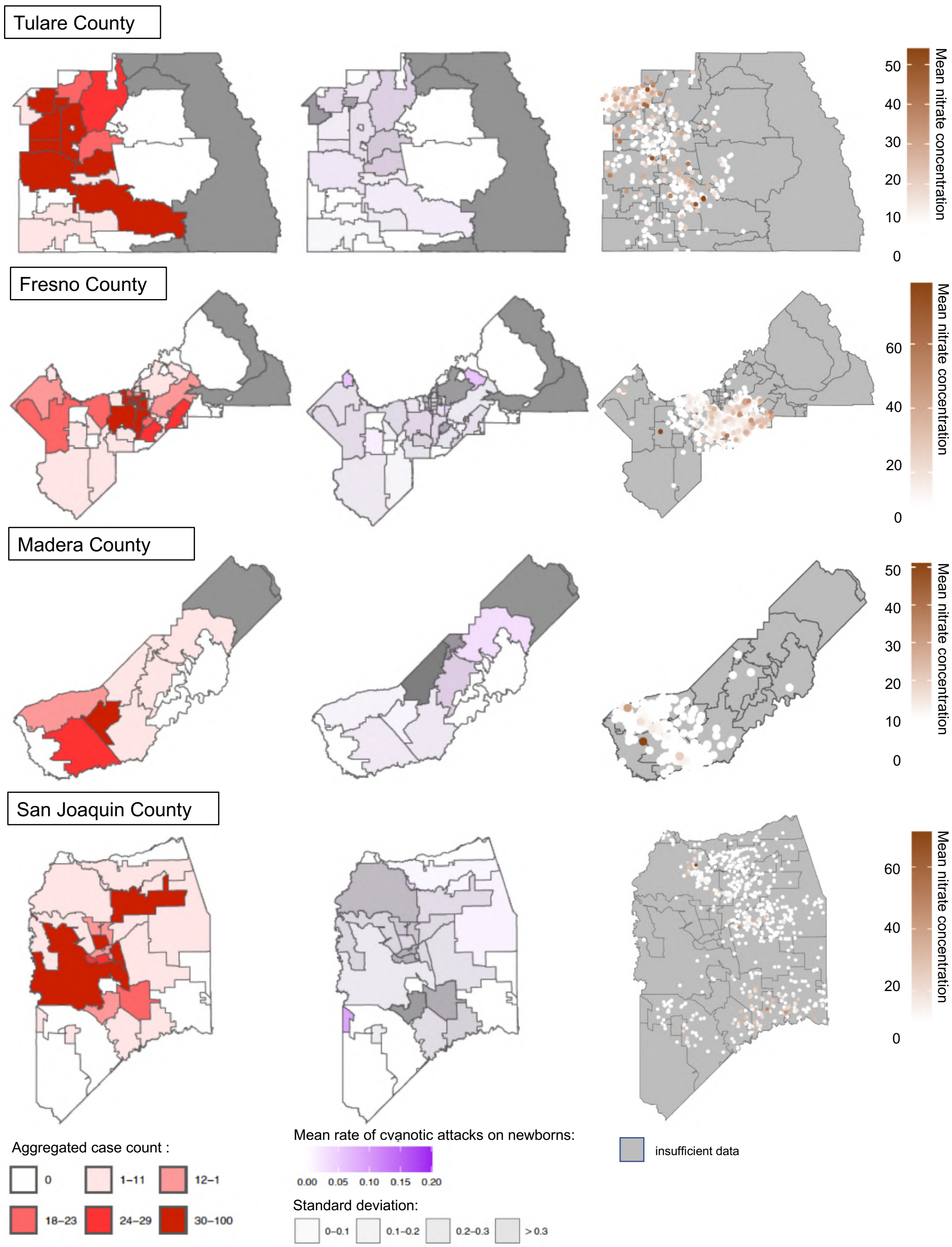


Figure 4: Aggregated case counts (left) and average rates (middle) of cyanotic attacks on newborns by ZIP code for Tulare, Fresno, Madera and San Joaquin County, 2011-2019, as compared to the mean nitrate concentration in domestic wells (right) from the GAMA data set.

deviation of the annual rates. We show the standard deviation in Figure 3 as a gray layer for which the transparency increases as the standard deviation decreases, so that a standard deviation of zero corresponds to an entirely transparent layer. The spatial pattern that emerges is more complex and heterogeneous than for the case count, but similar in the sense that rates are high in many Central Valley counties as well as the Monterey and the Inland Empire region.

To compare the case count and mean rate of cyanotic attacks on newborns with the nitrate concentration in domestic wells, we focus on four Central Valley counties, Tulare, Fresno, Madera, and San Joaquin County, in Figure 4. The left column shows the aggregate case counts, the middle column shows the mean rates with standard deviation superimposed, and the right column shows the mean concentration of nitrate in domestic wells from the GAMA data set. For ZIP codes that overlap with county boundaries, we only show cases that fall both into the shown ZIP codes and into the shown county. In all four counties, there are numerous wells that significantly exceed the maximum contaminant level of 10 mg/L, often by a factor of five or more. Only a subset of wells is available to us through the GAMA data set. There are likely other unmonitored wells.

## 4 Conclusions

Our analysis reveals concerning spatial patterns in how reported cases of both methemeglobinemia and cyanotic attacks on newborns are distributed throughout California for the years 2011 to 2019. We find that the reported cases of methemeglobinemia cluster in population centers and agricultural areas, including several ZIP codes in the Central Valley (Figure 1). Clusters in population centers are expected because more people get sick where more people live. Clusters in less populous agricultural areas could indicate that newborns in these regions are at increased risk.

We emphasize that we cannot determine whether the mapped cases were caused by nitrate exposure on the basis of the data we have. A definitive diagnosis as presented in the medical literature would require an interview with caregivers and a test of the water source[13]. Not all healthcare centers might have the personnel or resources to support these diagnostic steps. As a consequence, methemeglobinemia may be underdiagnosed, particularly in areas with limited access to healthcare.

[13] Hunter H Comly. Cyanosis in infants caused by nitrates in well water. *Journal of the American Medical Association*, 129(2):112–116, 1945

Although ICD-10 code D74 and ICD-9 code 289.7 are the more precise and preferable measure for identifying methemeglobinemia (blue baby syndrome), we also analyze spatial patterns in the prevalence of cyanotic attacks. We emphasize that cyanotic attacks on newborns, sometimes referred to as blue spells, are a much more common condition than blue-baby syndrome (methemeglobinemia) and are not necessarily related to nitrate pollution. We look at them here, because they are symptomatically similar to blue-baby syndrome. A newborn with bluish skin discoloration could be encoded in our database in both ways. We find clusters of cyanotic attacks in several counties of the Central Valley where domestic wells exhibit high nitrate concentration (Figure 4).

Our result that case counts of both methemeglobinemia and cyanotic attacks on newborns tend to cluster in Central Valley counties suggests that newborns in these areas could have elevated risk. We suggest monitoring water quality in areas with high prevalence rates, ensuring the availability of safe drinking water, and increasing awareness among communities is an immediate priority, particularly among pregnant women who could be at risk for other adverse reproductive and developmental problems related to exposure to nitrate[14].

[14] Deana M Manassaram, Lorraine C Backer, and Deborah M Moll. A review of nitrates in drinking water: maternal exposure and adverse reproductive and developmental outcomes. *Environmental health perspectives*, 114(3):320–327, 2006

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