HIGH SCHOOL EDITION
Journal of Student Research
Volume 12 Issue 3 (2023)

Minimizing the Consequences of Neonatal Abstinence Syndrome in the American Indian and Alaska Native Populations of California

Michelle Lee[1], Emily Zhou[1] and Rachel Kaci[1#]

[1]Henry M. Gunn High School
[#]Advisor

ABSTRACT

The opioid epidemic has had a consequential impact on the health of the infant population as many are born with neonatal abstinence syndrome (NAS). Babies born with NAS suffer from many developmental and physical consequences following prenatal exposure to opioids. Specifically, the American Indian and Alaska Native (AI/AN) populations are disproportionately affected by this in California with significantly higher cases of NAS compared to other racial groups. This research focuses on the consequences of NAS as well as an assessment of the current programs in place to support the AI/AN population. Using a combination of extensive literature review as well as, evaluating sources for the government programs for aiding the AI/AN population with opioid addiction, it is concluded that the current programs are insufficient in providing culturally relevant approaches. Further implementation of more accessible and culturally centered programs for the AI/AN population to decrease the effects of the opioid epidemic are necessary.

Introduction

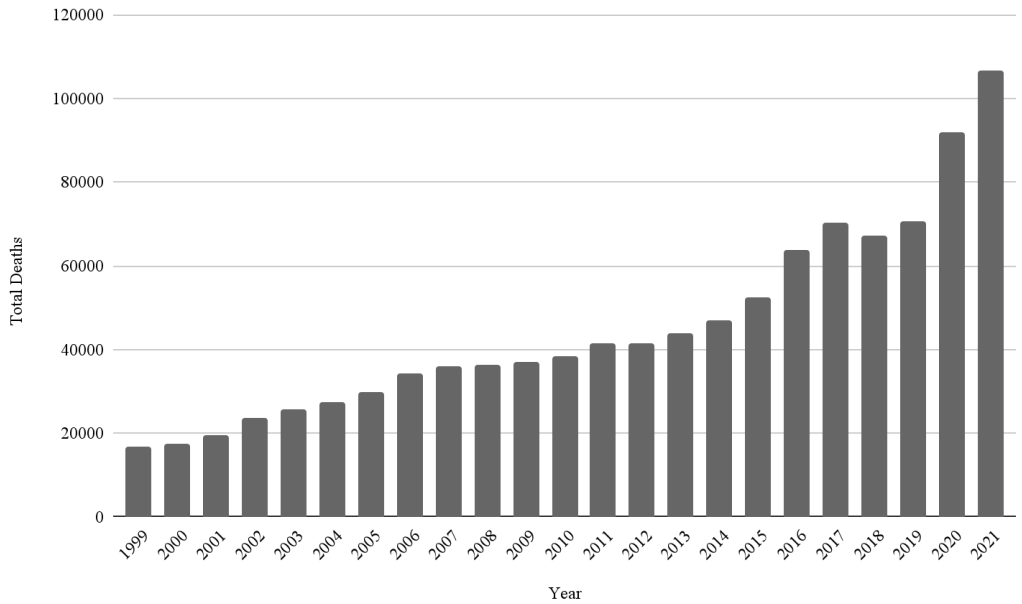

Fig. 1 | National Drug-Involved Overdose Deaths—Number Among All Ages, 1999-2021 [1].

The opioid epidemic is a major public health concern that has taken a toll on 564,000 lives [2]. As overdoses and deaths from opioid usage spiked in recent years, more people are being affected by these addictive and life-threatening drugs (Fig. 1). Opioids are a class of drugs that are generally prescribed by doctors for pain relief, but they come with serious risks and side effects that include addiction and overdose [3]. Of the large population of adults who are becoming more reliant on these addictive drugs, it is important to also examine the effects that the opioid epidemic has had on the prenatal population. Many children with parents addicted to opioids are growing up in turbulent households with increased risks of hospitalization, poverty, and unsanitary living conditions [4]. In addition, there is also a large population of infants who are born with neonatal abstinence syndrome (NAS). The percentage of infants born with opioid-related diseases has increased by 131% between 2010 and 2017. Furthermore, the percentage of infants born with NAS in the US rose by 82% between 2010 to 2017 [5]. Although this data is for NAS, it also applies to neonatal opioid withdrawal syndrome (NOWS); between 2004 and 2014, NOWS cases increased by 433% [6]. Clearly, the impact of opioids goes much further than the overdose rates in adults as infants born with NAS have lasting impacts on their physical and emotional development.

In this review paper, a focus will be placed on opioids; specifically, heroin, morphine, and codeine; and methadone, a medication used to treat Opioid Use Disorder (OUD). Opioids are both synthetic and natural substances that are commonly prescribed for pain relief while opiates refer to the natural version of opioids that are derived from plants. Prenatal exposure to these drugs causes NAS, a syndrome resulting from the sudden discontinuation of opioid exposure with withdrawal symptoms [7]. More specifically, prenatal exposure to opioids causes NOWS [6]. It is assumed that there are immediate and long-term effects of prenatal exposure to opioids that are caused by both paternal and maternal use.

Methods

The inquiry approach for this project is a combination of descriptive and content analysis with a focus on evaluation research. An analysis was done on the current programs that address the opioid epidemic in the AI/AN community with an emphasis on the prenatal impacts of opioid usage. The data was collected from databases of the California State Department, papers addressing the opioid epidemic in the AI/AN population, and evaluative papers on the current approaches in the AI/AN population. Published research on the immediate and long-term effects of fetal exposure to opioids was also heavily referenced. To understand the data, the main effects of fetal exposure to opioids were categorized into behavioral and physical changes. There are many previously published papers that go in-depth into NAS, NOWS, and the long-term behavioral effects of opioid exposure. Using the data for the cases of NAS in the state of California from the California databases showed that the AI/AN population is disproportionately affected. From there, the impact of the opioid epidemic on the AI/AN populations, as well as the programs in place to support the AI/AN populations, was explored. Therefore, a combination of primary research papers and secondary evaluative sources was used. There is currently a lot of raw data on NAS cases and a lot of research done on the effects of fetal exposure to opioids. These primary sources were helpful in understanding the science behind NAS and NOWS as well as the statistics behind the opioid epidemic. A few evaluative secondary sources that looked at the effectiveness of programs currently in place to support the AI/AN population with opioid usage were also included in the research. These sources brought nuance into the research and provided a second opinion on how the AI/AN population should be supported. Finally, the goal of this process was to identify the efficacy of current programs to decrease the disproportional impact of the opioid epidemic, and thus decrease the high rates of NAS on the AI/AN population.

Results

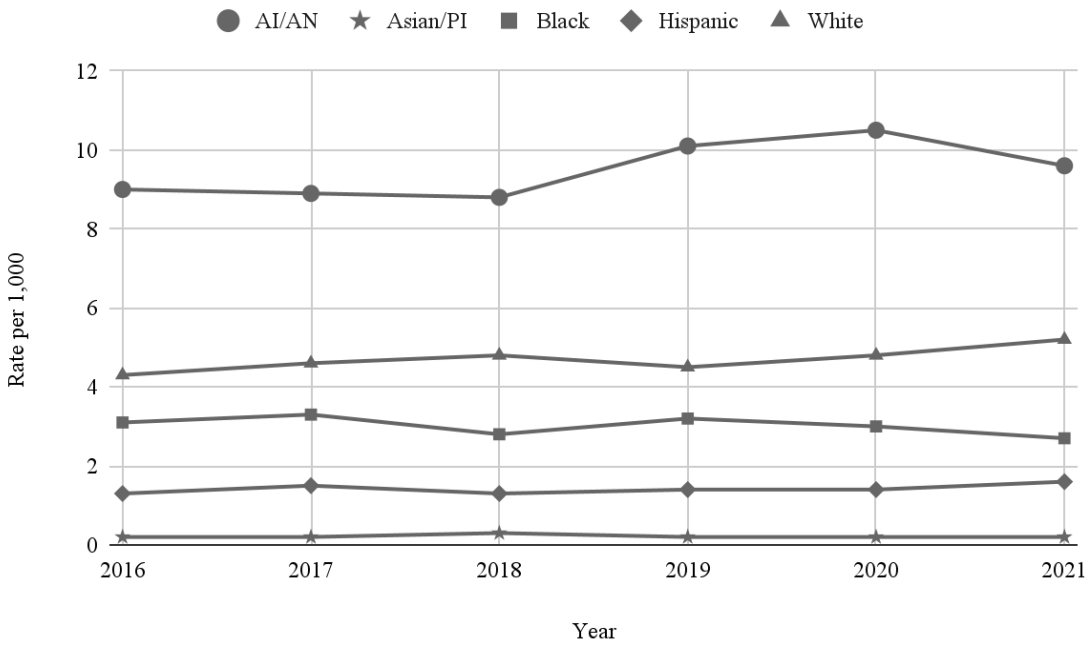

Fig. 2 | Cases of NAS by Race/Ethnicity in California, 2016-2021. Note that the cases of NAS in the AI/AN population are substantially higher than in other populations, almost doubling the next leading population in NAS cases [8].

Currently, the American Indian and Alaska Native (AI/AN) populations are disproportionately affected by the opioid epidemic with the highest rates of NAS in California (Fig. 2). In addition, the rates of drug overdose deaths involving opioids in the AI/AN population are higher than the national average [9]. Current programs and approaches that are currently in place to decrease the effects of the opioid epidemic on the AI/AN population will be focused on. Much of the current legislation and work on the national level to address the opioid epidemic have neglected the need for culturally relevant methods to address opioid addiction in AI/AN populations. Addressing the opioid crisis in the AI/AN population requires a holistic approach that takes into consideration the intergenerational trauma, the spiritual culture, and the societal factors of this group [10].

The American Indian and Alaska Native populations are referred to as AI/AN in accordance with the US census data. AI/AN is an acronym used by the Census Bureau to count the population of people living in federally recognized tribes. This paper recognizes that there are many indigenous people and many non-recognized tribes that are not included in this data so the effects of the opioid epidemic on the AI/AN population are likely higher than reported.

Infant exposure to opioids as fetuses from their parents is a very complex field of research that examines the physical and behavioral consequences of opioid exposure. Physically, it is commonly accepted that prenatal opioid exposure will lead to smaller gestational sizes of infants, weights, and birth head circumference (Fig. 3). The reason why various organs were smaller than their supposed gestational size is usually attributed to a subnormal number of cells in various organs [12]. When talking about opium exposure, there are generally two stages of prenatal exposure to opioids. The first stage consists of NAS and increased central nervous system arousal. This causes hyperactivity, disturbed sleep and usually lasts for about 12 weeks. This stage is relatively long because it takes a long time to clear the drugs from neonatal tissue. The second stage is lesser known but it is generally accepted that heroin exposure can result in impaired organizational and perceptual abilities as well as heightened activity [13]. Furthermore, when scientists modeled four generations of rat populations with the father being exposed to heroin, a kind of opioid, this

showed smaller litter sizes which will manifest itself in smaller infants in humans. In addition, it has been shown that paternal exposure to heroin does make a difference in their offspring [14]. Adolescent male rats who were exposed to morphine were found to experience delayed puberty and inhibited sexual maturation [15]. Overall, prenatal exposure to opioids can result in detrimental physical effects.

	Drug-exposed (n=45)			Non-exposed (n=48)			Significance test of difference	
	Mean	SD	Range	Mean	SD	Range	95% CI	p
Gestation age (weeks)	38.5	2.2	31.0 to 42.0	40.6	1.2	38.0 to 42.5	1.3 to 2.8	<.001
Brithweight (grams)	3142.6	676.7	1160 to 4380	3761.7	461.2	2620 to 4615	381.9 to 856.4	<.001
Head circumference (cm)	34.2	1.8	28 to 37	35.7	1.2	32 to 38	0.8 to 2.1	<.001
Caregiver education	1.6	0.7	0 to 3.0	2.1	0.7	0.5 to 3.0	0.2 to 0.8	0.11
Age at testing (years)	19.4	1.3	17.6 to 21.9	18.4	0.4	17.3 to 18.9	−1.4 to −0.6	<.001

Fig. 3 | Physical differences in drug-exposed and non-exposed youths born to mothers with opioid and poly-substance abuse problems during pregnancy. Notice how consistently, the size and weight of neonates born to mothers exposed to opioid substances are smaller than those of neonates born to non-exposed mothers [11].

Behavioral effects of prenatal opioids	
Aspect of behavior	POE effect
Anxiety	Decreased time in open arms of Elevated Plus Maze; Decreased time in light compartment of Light/Dark Box (Ahmadalipour et al., 2015; Chen et al., 2015; Klausz et al., 2011)
Depression	Longer immobility time in tail suspension and forced swim test (Hung et al., 2013; Klausz et al., 2011; Wu et al., 2014)
Reward seeking	Greater preference for saccharin water (Gagin et al., 1996); Increased morphine self-administration (Hovious & Peters, 1985); Enhanced conditioned place preference (Gagin et al., 1997)
Memory	Longer escape latency in Morris Water Maze (Wang & Han, 2009); Redacted retention in novel object recognition test (Chen et al., 2015); Longer completion time in radial arm maze (Slamberova et al. 2001)

Fig. 4 | Observed effects of prenatal opioid exposure on rodent behavior [16].

Behaviorally, it has been shown that prenatal heroin exposure causes an increased level of anxiety, depression, and reward-seeking attributes. Anxiety tests in rodents, such as the Elevated Plus Maze, Open Field, and Light/Dark Box, have consistently shown higher levels of anxiety in rodents prenatally exposed to opioids (Fig. 4). In the Elevated Plus Maze, rodents are placed in a cross-shaped maze with open and covered arms. The number of times the rat enters/exits the closed/open arms are quantified and shows the level of anxiety in the rodent. Decreased time in the open arms of the Elevated Plus Maze, as shown in Figure 4, correlates to higher anxiety levels in the rodent. Furthermore, in the same study, those rodents also exhibit higher levels of depression shown through the tail suspension test and forced swim test. Also, prenatal exposure to opioids in rodents has also shown that these rodents have a higher need for pleasurable stimuli, as exhibited by a greater preference for saccharine water and increased morphine self-administration (Fig. 4). It has also been shown that prenatal exposure to opioids in rodents results in poorer memory compared to control rodents. Through the Morris Water Maze test, rodents prenatally exposed to opioids took significantly longer to follow visual cues and swim to a previously located platform than control rats which indicates that opioid-exposed rats have deficits in learning and memory.

	Control	Heroin Exposed
Tail swish	1.25	4.12*
Lateral threat	0.63	3.63*
Bite	2.37	9.50*
Clinch/fight	1.50	7.50*

Fig. 5 | The frequency of aggressive behaviors that were observed in rodents exposed to heroin and those who were not. Note the asterisk means a statistically significant difference compared to control rats ($p < 0.05$). In this test, the father was exposed to increasing dosages of heroin throughout a period of 14 consecutive days. [14]

The level of aggression was also observed to increase (Fig. 5). This was tested using the resident intruder (RI) test where an intruder is introduced into a resident rat's cage. The behaviors were observed by their frequency of occurrence. Across the board, heroin-exposed rats had a higher frequency of aggressive behaviors signaling that these rats have a higher level of aggression in general.

	Bivariate		**Controlled for gender**		**Controlled for gender and age at testing**		**Controlled for gender, age at testing and caregiver education**	
	b	***p***	***b***	***p***	***b***	***p***	***b***	***p***
Visual long-term memory (RCFT)	**0.79**	**<.001**	**0.80**	**<.001**	**0.93**	**<.001**	**0.92**	**<.001**
Verbal memory (CVLT)	**0.47**	**.02**	**0.54**	**.01**	**0.56**	**.02**	0.42	.09
Number short-term memory (WAIS)	**0.69**	**.001**	**0.66**	**.001**	**0.79**	**.001**	**0.73**	**.004**

Fig. 6 | Differences in Cognitive and Fine Motor Abilities between Drug-exposed and Non-exposed Youth [11].

These developmental and physical changes continue to be present in adolescence and adulthood. Long-term memory and short-term memory were observed to worsen in adolescents and adults ranging in age between 17 and 22 (Fig. 6). The short-term and long-term consequences of drug exposure suggest that prenatal exposure to opioids produces detrimental effects on children, and thus is an issue that needs to be addressed alongside the opioid epidemic.

In California, the main effort to help decrease the opioid epidemic falls under the California MAT Expansion Project. The California MAT Expansion Project aims to increase access to Medication-assisted Treatment to reduce opioid-related deaths through increased funding and investments [17]. Within this, the California MAT Expansion Project has a complete project dedicated to tribal communities, titled Tribal MAT Project (TMAT). This paper will be focusing on three programs under TMAT: California Consortium for Urban Indian Health (CCUIH), California Rural Indian Health Board (CRIHB), and Two Feathers Native American Family Services (NAFS).

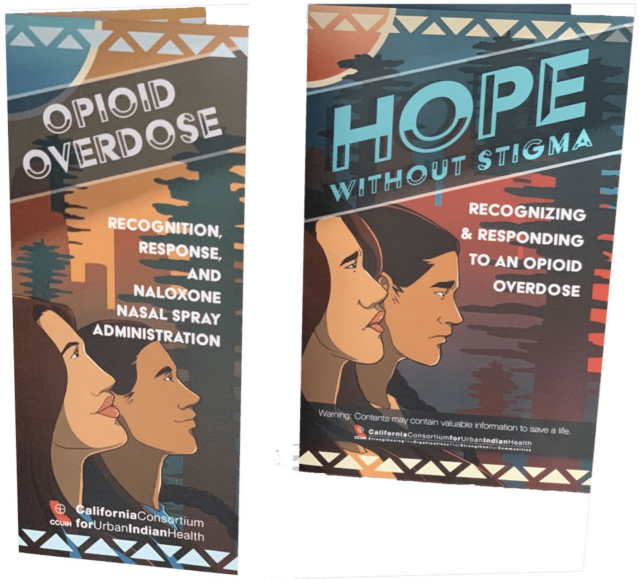

Fig. 7 | An example of the culturally relevant resources CCUIH has available to address the opioid epidemic in American Indian communities [18].

The CUCIH and the CRIHB are both statewide organizations dedicated to the health and wellness of indigenous communities in urban and rural areas [19, 20]. To reduce opioid overdose cases, a major aspect of the CUCIH and CRIHB is the distribution of NARCAN® (naloxone) Nasal Spray. Narcan is a nasal spray that rapidly reverses opioid overdoses and is a very effective way of reversing an opioid overdose [21]. In addition to providing Narcan to indigenous groups, both CRIHB and CUCIH provide resources to address the opioid epidemic in indigenous groups through pamphlets and flyers (Fig. 7). Specifically, CUCIH focuses on aiding the American Indians living in urban cities who may be separated from their indigenous tribe and any health services that they don't have access for [22]. The CRIHB is a network of many tribal health programs dedicated to individual tribal communities' health services. CRIHB streamlines the services and training for these tribal communities to ensure each of these communities working with CRIHB has access to the same resources. Something to consider is that CRIHB does not include every single health tribal health program so some tribal communities are not included in CRIHB.

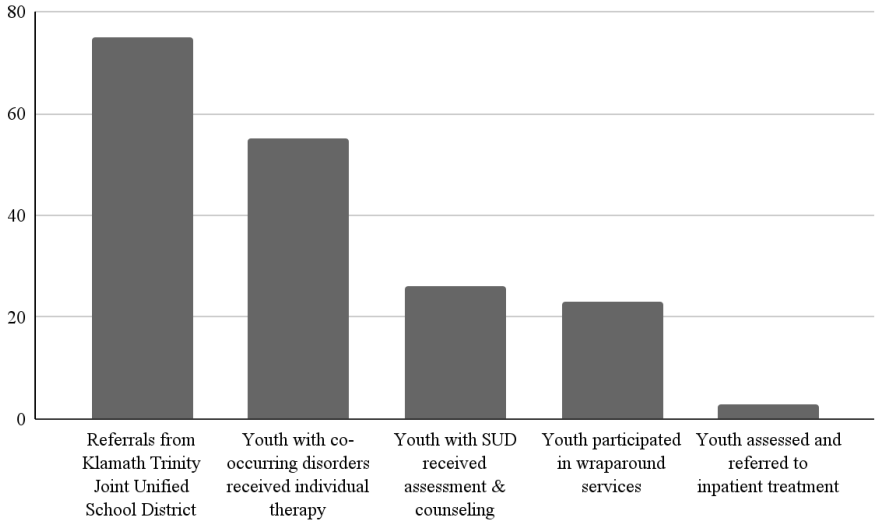

Fig. 8 | An Overview of the MAT Substance Abuse Services offered by NAFS [23].

NAFS is a program that provides children and family-oriented services to Native American families in the Humboldt County area, not just to those who are affiliated with tribal groups [24]. NAFS is effective at forming a support community for the children in Native American communities who may have opioid substance abuse issues. While CRIHB and CUCIH mostly focus on providing support and resources for adults who are already experiencing withdrawal or addiction to opioids, NAFS supports the teenage populations who are primarily susceptible to opioid addiction. NAFS only provides support, however, to the Humboldt County area and the Humboldt school district.

	Non-implementers (N=86)		Implementers (N=53)	
Perception	**N**	**%**	**N**	**%**
Consistent with treatment approach and philosophy	12	14	31	59
Culturally appropriate	3	4	10	19
Existing research base proves its effectiveness	36	42	33	62
Fits with staff expertise and training	6	7	24	45
Billable service	4	5	14	26

Fig. 9 | Respondents' perceptions of medication-assisted treatment (MAT) in 192 substance abuse treatment programs serving AI/AN [25].

These MAT programs can be used to help decrease the incidence of opioid use disorder however, there are many barriers. One issue is that it is not implemented in all clinics; only 28% of the clinics in this study provided MAT for their patients [25]. Additionally, AI/AN reservations are especially concentrated in rural areas where they have less access to public health care resources [26]. Although there are programs that target American Indians living in urban areas, these programs are not very common and still leave a large population of American Indians without access to public health resources. Also, barriers highlighted by participants who were part of an Indian health program or community-based organizations were the distance and lack of transportation to the clinics, lack of insurance coverage, unstable living conditions, privacy, and lack of readiness [27]. The issue of privacy is connected to the stigma present in AI/AN communities about addiction in general and more specifically, the use of MAT as treatment [28]. Another issue that prevents people from seeking out these supports is that these treatments are not culturally centered, meaning they do not take into account AI/AN traditional healing methods. Participants also perceived MAT treatments as not culturally appropriate (Fig. 9). Although outreach and publicity have culturally centered graphics, the actual treatment methods do not include traditional healing methods. Adding to this, there is a disconnect between native and non-native providers who are not aware of the cultural practices that are used. Many providers do not integrate traditional practices into the currently used Western treatments for opioid abuse and addiction [27, 28].

Conclusion

The opioid epidemic has had a significant impact on the neonatal population, both long-term and short term and in California, the AI/AN population is the most impacted by this epidemic. This research on the neonatal effects of opioid exposure emphasizes the detrimental effects of the opioid epidemic on children and infants, placing the AI/AN population most at risk with their high rates of NAS. This research also shows how there are programs in place to help support the AI/AN population to help them overcome their addiction.

Next Steps

However, more work is needed to support the unique AI/AN community as there are still many barriers present that prevent them from being able to access this treatment. Specifically, the increased influence of the programs is extremely important. Many programs serve only one community and the programs that serve a larger community do not have the same level of cultural, personalized care. While this study is an important step toward decreasing the influence of opioid addiction on the AI/AN neonatal population, much more research still needs to be done. In terms of the consequences of prenatal exposure to opioids, further research and data are needed that take into consideration the socioeconomic situations of the participants. The socioeconomic background of a parent with a child diagnosed with NAS is a crucial aspect that needs to be considered when prescribing a treatment plan or drafting new programs to help support these populations. Additionally, the standardization of prenatal exposure to opioids is necessary to provide clearer evidence for the connections between exposure and the consequences that were observed. Factors such as the level of addiction of the parent and the environment the child is born into can have major effects on the behavioral and physical attributes observed in the child. In the future, research should be streamlined on the effects of prenatal exposure to opioids and take into account the environment in which the children are raised as well as the severity of the parent's reliance on opioids during pregnancy as a major component of the research. Future programs aimed to support the AI/AN community should be even more culturally centered, with an emphasis on merging cultural medicine with Western medicine. In addition, these programs should also aim to increase the stretch of their resources so that AI/AN communities in different areas can have access to MAT and other opioid-related resources.

Works Cited

1. "Drug Overdose Death Rates." *NIH*, nida.nih.gov/research-topics/trends-statistics/overdose-death-rates.
2. "Understanding the Opioid Overdose Epidemic." *CDC*, www.cdc.gov/opioids/basics/epidemic.html.
3. "Opioid Basics." Center for Disease Control and Prevention, 23 May 2022, www.cdc.gov/opioids/basics/index.html. Accessed 4 May 2023.
4. Winstanley, Erin L., and Amanda N. Stover. "The Impact of the Opioid Epidemic on Children and Adolescents." Clinical Therapeutics, vol. 41, no. 9, Sept. 2019, pp. 1655-62, https://doi.org/10.1016/j.clinthera.2019.06.003.
5. "Data and Statistics About Opioid Use During Pregnancy." CDC, www.cdc.gov/pregnancy/opioids/data.html#:~:text=Neonatal%20Abstinence%20Syndrome&text=That%20is%20approximately%20one%20baby,59%20newborns%20diagnosed%20every%20day.
6. Weller, Andrew E., et al. "Neonatal Opioid Withdrawal Syndrome (NOWS): A Transgenerational Echo of the Opioid Crisis." Cold Spring H*arbor Perspectives in Medicine*, vol. 11, no. 3, 30 Mar. 2020, p. a039669, https://doi.org/10.1101/cshperspect.a039669.
7. "Neonatal Abstinence Syndrome." *Stanford Medicine Children's Health*, www.stanfordchildrens.org/en/topic/default?id=neonatal-abstinence-syndrome-90-P0238
8. "Neonatal Abstinence Syndrome." *California Department of Public Health*, www.cdph.ca.gov/Programs/CFH/DMCAH/surveillance/Pages/Neonatal-Abstinence-Syndrome.aspx. Accessed 6 May 2023.
9. "Drug Overdose Prevention in Tribal Communities." Centers for Disease Control and Prevention, 5 May 2022, www.cdc.gov/injury/budget/opioidoverdosepolicy/TribalCommunities.html. Accessed 4 May 2023.
10. "'To Walk in the Beauty Way': Treating Opioid Use Disorder in Native Communities." National Institutes of Health, 23 Feb. 2023, heal.nih.gov/news/stories/native-cultures. Accessed 4 May 2023.
11. Nygaard, Egil, et al. "Cognitive Function of Youths Born to Mothers with Opioid and Poly-substance Abuse Problems during Pregnancy." Child Neuropsychology, vol. 23, no. 2, 16 Oct. 2015, pp. 159-87, https://doi.org/10.1080/09297049.2015.1092509.
12. Naeye, Richard L., et al. "Fetal Complications of Maternal Heroin Addiction: Abnormal Growth, Infections, and Episodes of Stress." *The Journal of Pediatrics*, vol. 83, no. 6, Dec. 1973, pp. 1055-61, https://doi.org/10.1016/s0022-3476(73)80550-5.
13. Hutchings, D E. "Methadone and heroin during pregnancy: a review of behavioral effects in human and animal offspring." *Neurobehavioral toxicology and teratology* vol. 4,4 (1982): 429-34.
14. Farah Naquiah, Mohd Zaki, et al. "Transgenerational Effects of Paternal Heroin Addiction on Anxiety and Aggression Behavior in Male Offspring." Behavioral and Brain Functions, vol. 12, no. 1, 31 Aug. 2016, https://doi.org/10.1186/s12993-016-0107-y.
15. Cicero, T J et al. "Influence of morphine exposure during adolescence on the sexual maturation of male rats and the development of their offspring." The Journal of pharmacology and experimental therapeutics vol. 256,3 (1991): 1086-93.
16. Boggess, Taylor, and W. Christopher Risher. "Clinical and Basic Research Investigations into the Long-term Effects of Prenatal Opioid Exposure on Brain Development." *Journal of Neuroscience Research*, vol. 100, no. 1, 27 May 2020, pp. 396-409, https://doi.org/10.1002/jnr.24642.
17. "The California MAT Expansion Project Overview." *Department of Health Care Services*, www.dhcs.ca.gov/individuals/Pages/MAT-Expansion-Project.aspx#:~:text=The%20California%20MAT%20Expansion%20Project%20aims%20to%20increase%20access%20to,%2C%20treatment%2C%20and%20recovery%20activities. Accessed 6 May 2023.
18. "Medicine Assisted Treatment." *California Consortium of Urban Indian Health*, ccuih.org/medication-assisted-treatment-project/. Accessed 4 May 2023.
19. "About." *California Consortium for Urban Indian Health*, ccuih.org/about/. Accessed 4 May 2023.

20. "About Us." *California Rural Indian Health Board Inc.*, crihb.org/about/. Accessed 4 May 2023.
21. "Naloxone DrugFacts." *NIH*, nida.nih.gov/publications/drugfacts/naloxone. Accessed 6 May 2023.
22. "About Urban Indians." *California Consortium for Urban Indian Health*, ccuih.org/about/about-urban-indians/. Accessed 4 May 2023.
23. "Tribal Response to the Opioid Epidemic in California." *Institute for Health Promotion & Disease Prevention Research (IPR)*, Keck School of Medicine of USC, ipr.usc.edu/wp-content/uploads/2020/11/TMAT-Community-Report-FINAL-2020.10.30.pdf. Accessed 4 May 2023.
24. *Two Feathers Native American Family Services*. twofeathers-nafs.org/about-us/. Accessed 4 May 2023.
25. Rieckmann, Traci, et al. "National Overview of Medication-Assisted Treatment for American Indians and Alaska Natives with Substance Use Disorders." Psychiatric Services, vol. 68, no. 11, Nov. 2017, pp. 1136-43, https://doi.org/10.1176/appi.ps.201600397. Accessed 4 May 2023.
26. Komro, Kelli A., et al. "Culturally Responsive Opioid and Other Drug Prevention for American Indian/Alaska Native People: A Comparison of Reservation- and Urban-Based Approaches." Prevention Science, 24 June 2022, https://doi.org/10.1007/s11121-022-01396-y. Accessed 4 May 2023.
27. Zeledon, Ingrid, et al. "Statewide Collaborative Partnerships among American Indian and Alaska Native (AI/AN) Communities in California to Target the Opioid Epidemic: Preliminary Results of the Tribal Medication Assisted Treatment (MAT) Key Informant Needs Assessment." Journal of Substance Abuse Treatment, vol. 108, Jan. 2020, pp. 9-19, https://doi.org/10.1016/J.jsat.2019.04.003.
28. Venner, Kamilla L., et al. "Future Directions for Medication Assisted Treatment for Opioid Use Disorder with American Indian/Alaska Natives." Addictive Behaviors, vol. 86, Nov. 2018, pp. 111-17, https://doi.org/10.1016/J.addbeh.2018.05.017.