

Childhood trauma and chronic disease in Alaska:

New ways to visualize brain health, engage patients, and encourage treatment uptake

Tim Collins, MPH, MS, MA

April 14, 2023



Aanii, I'm Tim...



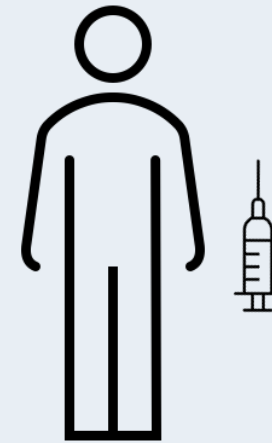
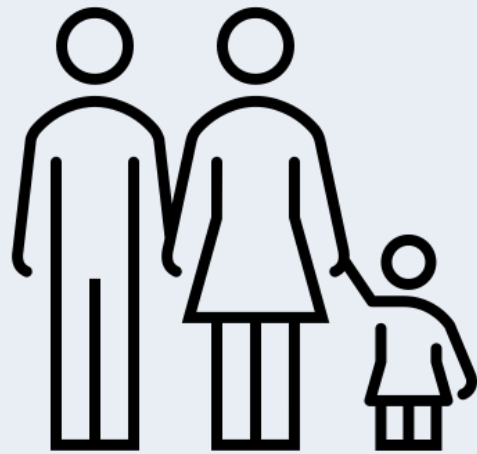
Summary

- Background
- Surveillance: Childhood trauma in Alaska ED data
- Brain health, behavior, and chronic disease
- A case for interactive Augmented Reality

Background

Inspiration from tribal health experiences

Two cases



87% in Alaska with OUD did not get evidence-based treatment (2019).

About **18,000** individuals in Alaska with OUD (2019).

3% of the population - opioid misuse prevalence in Alaska (people age 12 and over, 2019).

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Research Paper
Has the treatment gap for opioid use disorder narrowed in the U.S.? A yearly assessment from 2010 to 2019^a
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ARTICLE INFO
Keywords: Medications for opioid use disorder; Treatment gap; Opioid use disorder; Methadone; Buprenorphine; Overdose

ABSTRACT
Background: The United States overdose crisis continues unabated. Despite efforts to increase capacity for treating opioid use disorder (OUD) in the U.S., how actual treatment receipt compares to need remains unclear. In this cross-sectional study, we estimate progress in addressing the gap between OUD prevalence and OUD treatment receipt at the national and state levels from 2010 to 2019.
Methods: We estimated past-year OUD prevalence rates based on the U.S. National Survey on Drug Use and Health (NSDUH), using adjustment methods that attempt to account for OUD underestimation in national household surveys. We used data from specialty substance use treatment records and outpatient pharmacy claims to estimate the gap between OUD prevalence and number of persons receiving medications for opioid use disorder (MOUD) during the past decade.
Results: Adjusted estimates suggest past-year OUD affected 7,631,804 individuals in the U.S. (in 2,773 per 100,000 adults 12+), relative to only 1,023,959 individuals who received MOUD (365 per 100,000 adults 12+). This implies approximately 86.6% of individuals with OUD nationwide who may benefit from MOUD treatment do not receive it. MOUD receipt increased across states over the past decade, but most regions still experience wide gaps between OUD prevalence and MOUD receipt.
Conclusions: Despite some progress in expanding access to MOUD, a substantial gap between OUD prevalence and treatment receipt highlights the critical need to increase access to evidence-based services.

Introduction
Two decades after initial reports of rising overdose deaths, the U.S. overdose epidemic continues to accelerate. The COVID-19 pandemic has exacerbated this crisis, leading to historically high overdose deaths in 2020, with provisional data indicating continued increases in 2021 (Ahmed *et al.*, 2022). Opioids continue to be the central driver of overdose deaths, involved in three quarters of past-year deaths, with unregulated fentanyl – a potent synthetic illicit opioid – being the primary driver (O’Donnell *et al.*, 2021). Despite numerous federal and state initiatives to address overdose deaths (Grogan *et al.*, 2020), such efforts have been slow to keep pace with the escalation of the crisis.

Particularly challenging to the overdose response has been expanding access to evidence-based treatment for opioid use disorder (OUD). Methadone, buprenorphine, and extended-release naltrexone are three FDA-approved medications for OUD (MOUD) that are consistently associated with improved health outcomes, including reduced opioid use, transmission of HIV and Hepatitis-C, and overdose risk (Lesher *& Mander*, 2019). Population-based studies have found that compared to no-treatment or treatments not involving medications, MOUD decreases overdose risk by over 50% (Santo *et al.*, 2021). While methadone can only be dispensed by certified opioid treatment programs (OTPs), buprenorphine can be prescribed by providers waived under the Drug Addiction Treatment Act of 2000 (DATA 2000). Naltrexone can be

Abbreviations: OUD, Opioid use disorder; MOUD, Medications for opioid use disorder; OTP, Opioid treatment program; FDA, Food and Drug Administration; DEA, Drug Enforcement Administration; NSDUH, National Survey on Drug Use and Health; NSSATS, National Survey of Substance Abuse Treatment Services.
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0955-9899/© 2022 Published by Elsevier B.V.

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CRIME AND COURTS

Successful opioid addiction treatment slow to catch on in South Dakota

“...physicians in the state are reluctant to prescribe the drugs that have shown great promise in overcoming opioid abuse.”

News > Medscape Medical News > Psychiatry News

PCPs Don't Back 'Gold Standard' Treatment for Opioid Addiction

“...one third of US primary care physicians do not believe medications used to treat OUD are more effective than nonpharmacologic treatment or that they are safe for long-term use.”

There's a highly successful treatment for opioid addiction. But stigma is holding it back.

Medication-assisted treatment is often called the gold standard of addiction care. But much of the country has resisted it.

By German Lopez | @germanlopez | german.lopez@vox.com | Updated Nov 15, 2017, 2:25pm EST

Many Residential Addiction Tx Centers Don't Offer MAT, at a Deadly Cost

— Abstinence-only models aren't for everyone

by Elizabeth Hlavinka, Staff Writer, MedPage Today September 29, 2020

“When Quincie Berry was discharged from a rehabilitation facility on June 26, his caretakers weaned him off Suboxone... no halfway houses would accept him if he was on opioid agonist treatment... Berry...died from an overdose on July 23.”

In the midst of opioid crisis, Harrisburg dismisses evidence on treatment | Editorial

At the heart of the bill is the false notion that treating addiction with medication only replaces one drug with another.

Surveillance

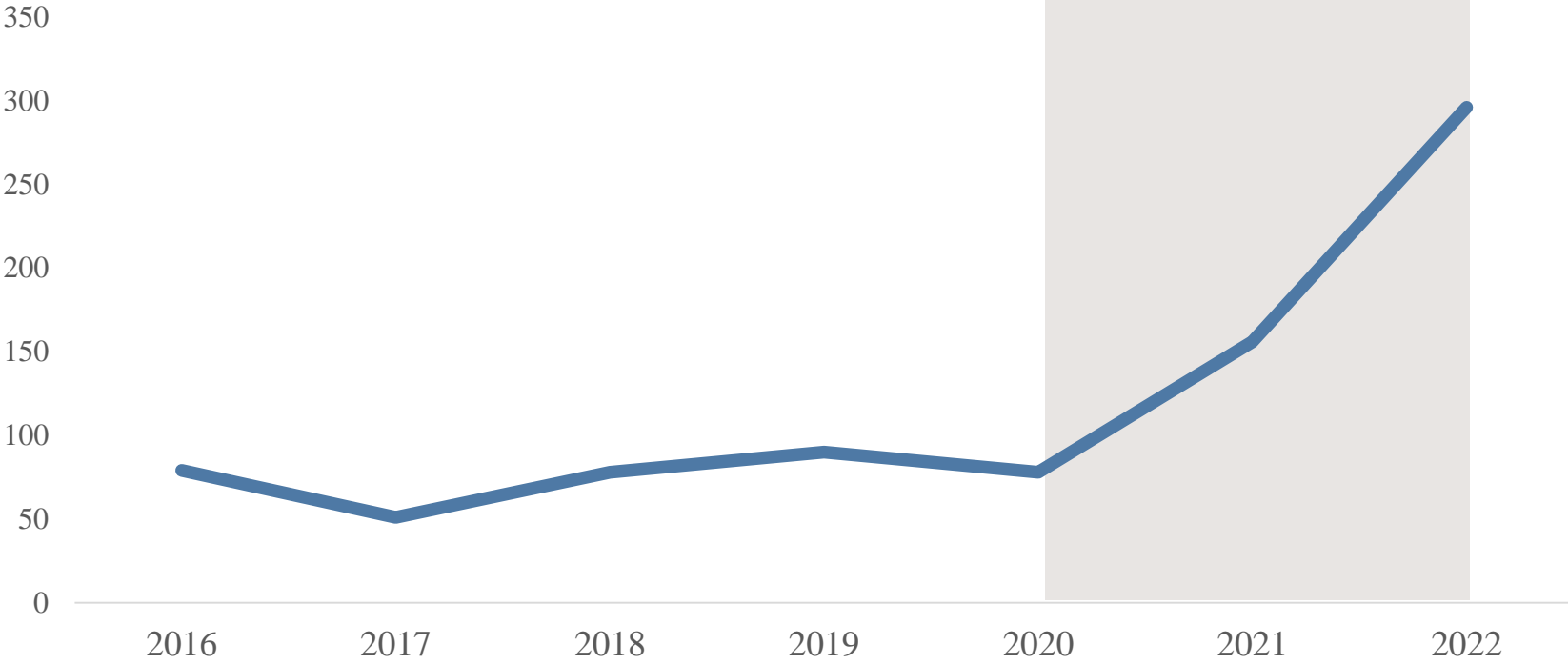
Alaska hospital data

‘Problems related to upbringing’ (Z62 in any diagnosis field)

Z62	Problems related to upbringing
Z62.0	Inadequate parental supervision and control
Z62.1	Parental overprotection
Z62.2	Upbringing away from parents
Z62.21	Child in welfare custody
Z62.22	Institutional upbringing
Z62.29	Other upbringing away from parents
Z62.3	Hostility towards and scapegoating of child
Z62.6	Inappropriate (excessive) parental pressure
Z62.8	Other specified problems related to upbringing
Z62.81	Personal history of abuse in childhood
Z62.810	Personal history of physical and sexual abuse in childhood
Z62.811	Personal history of psychol abuse in childhood

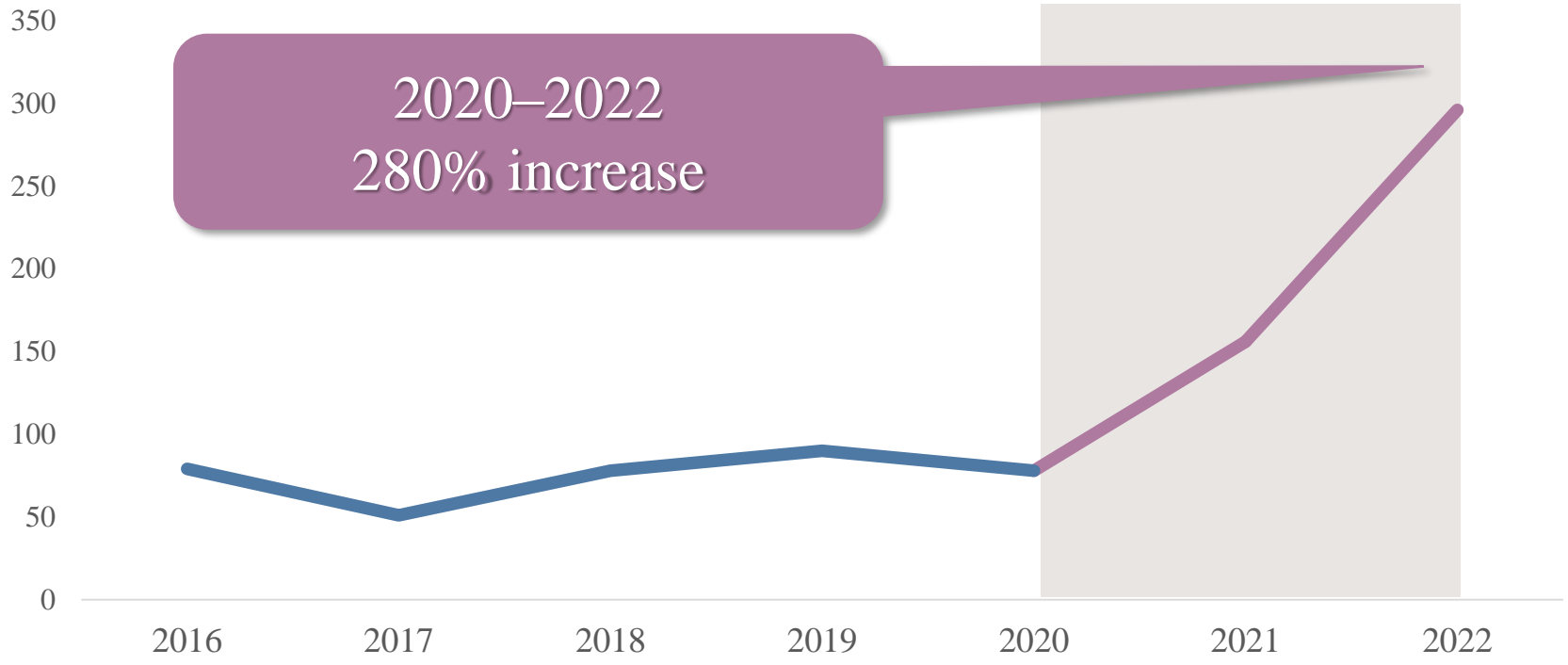
Z62.812	Personal history of neglect in childhood
Z62.813	Personal history of forced labor or sexual exploitation in childhood
Z62.819	Personal history of unspec abuse in childhood
Z62.82	Parent-child conflict
Z62.820	Parent-biological child conflict
Z62.821	Parent-adopted child conflict
Z62.822	Parent-foster child conflict
Z62.89	Other specified problems related to upbringing
Z62.890	Parent-child estrangement NEC
Z62.891	Sibling rivalry
Z62.898	Other specified problems related to upbringing
Z62.9	Problem related to upbringing, unspecified

Number of ‘problems related to upbringing’-related (any Z62) ED visits, Alaska statewide data, 2016-2022 (n=828)



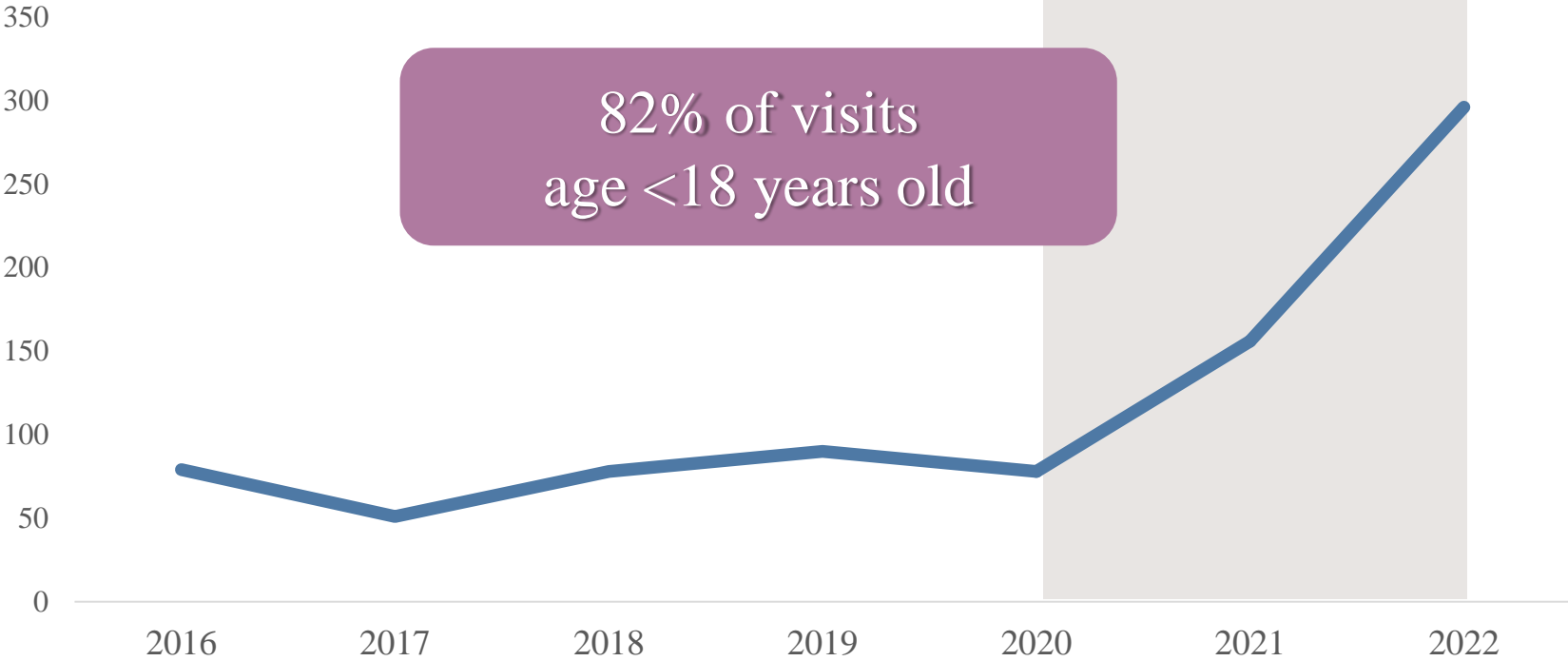
Source: Alaska Emergency Department Database. (2016, 2017, 2018, 2019, 2020, 2021, 2022). Alaska Health Facilities Data Reporting Program. Alaska Department of Health and Social Services, Division of Public Health.

Number of ‘problems related to upbringing’ (any Z62) ED visits, Alaska statewide data, 2016-2022



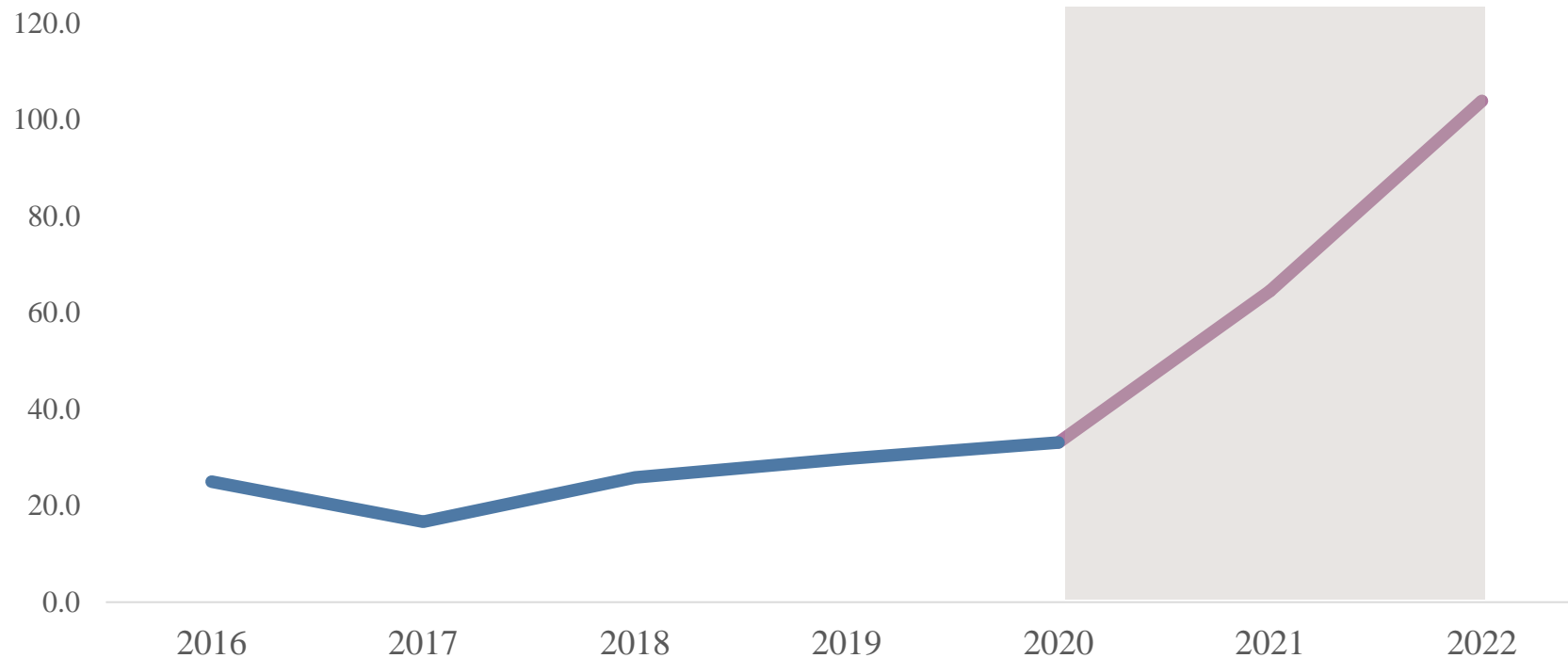
Source: Alaska Emergency Department Database. (2016, 2017, 2018, 2019, 2020, 2021, 2022). Alaska Health Facilities Data Reporting Program. Alaska Department of Health and Social Services, Division of Public Health.

Number of ‘problems related to upbringing’ (any Z62) ED visits, Alaska statewide data, 2016-2022



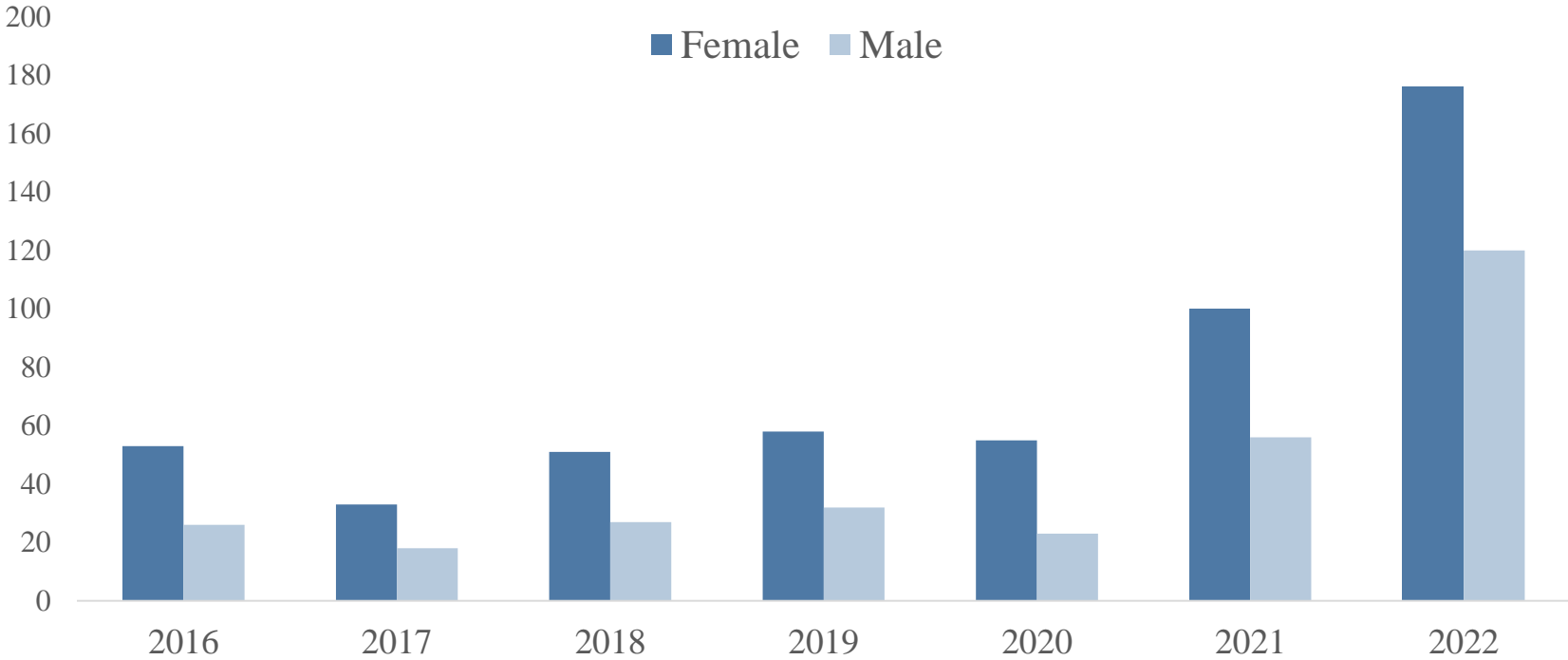
Source: Alaska Emergency Department Database. (2016, 2017, 2018, 2019, 2020, 2021, 2022). Alaska Health Facilities Data Reporting Program. Alaska Department of Health and Social Services, Division of Public Health.

Proportion of ‘problems related to upbringing’ (any Z62) ED visits to total ED visits, Alaska statewide data, 2016-2022



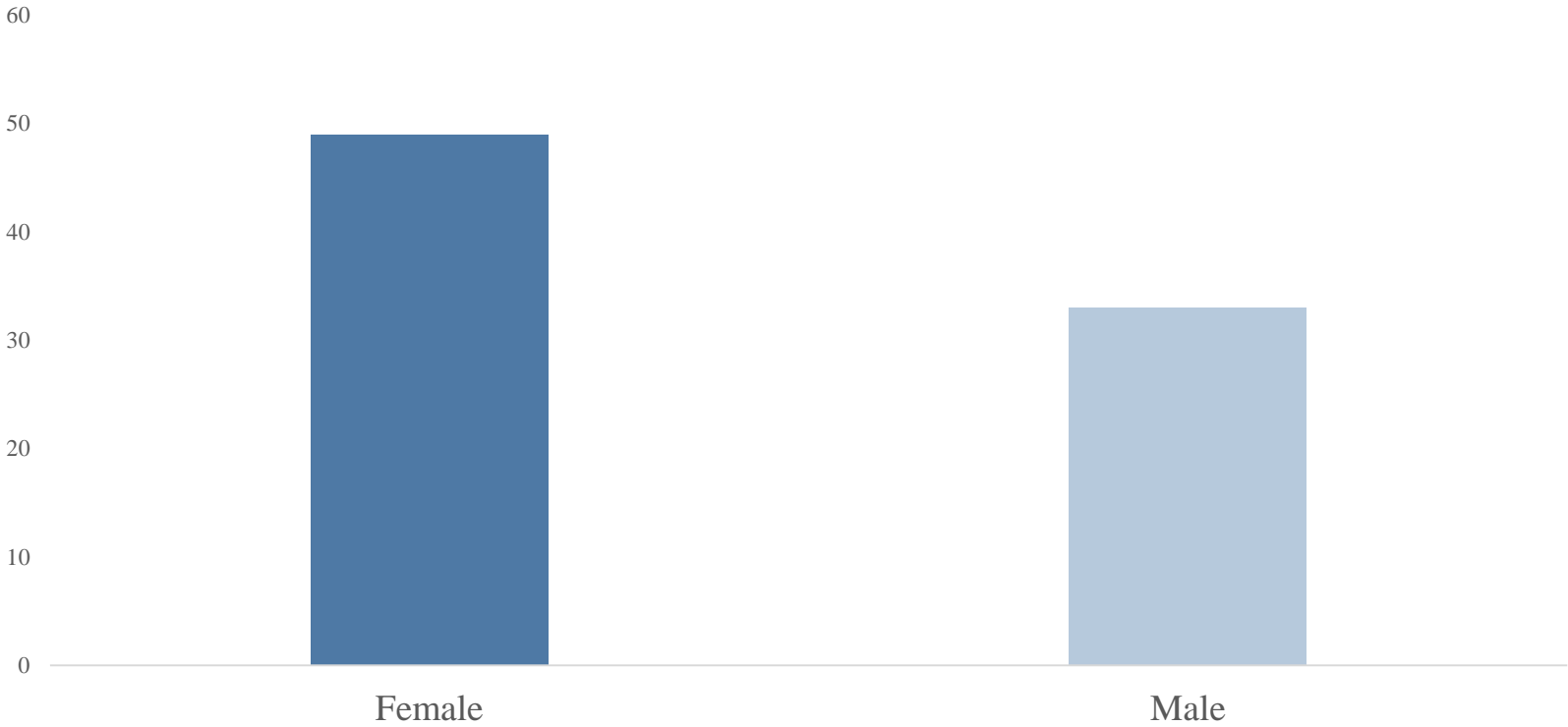
Source: Alaska Emergency Department Database. (2016, 2017, 2018, 2019, 2020, 2021, 2022). Alaska Health Facilities Data Reporting Program. Alaska Department of Health and Social Services, Division of Public Health.

Number of ‘problems related to upbringing’ (any Z62) ED visits, Alaska statewide data, by year and sex, 2016 through 2022



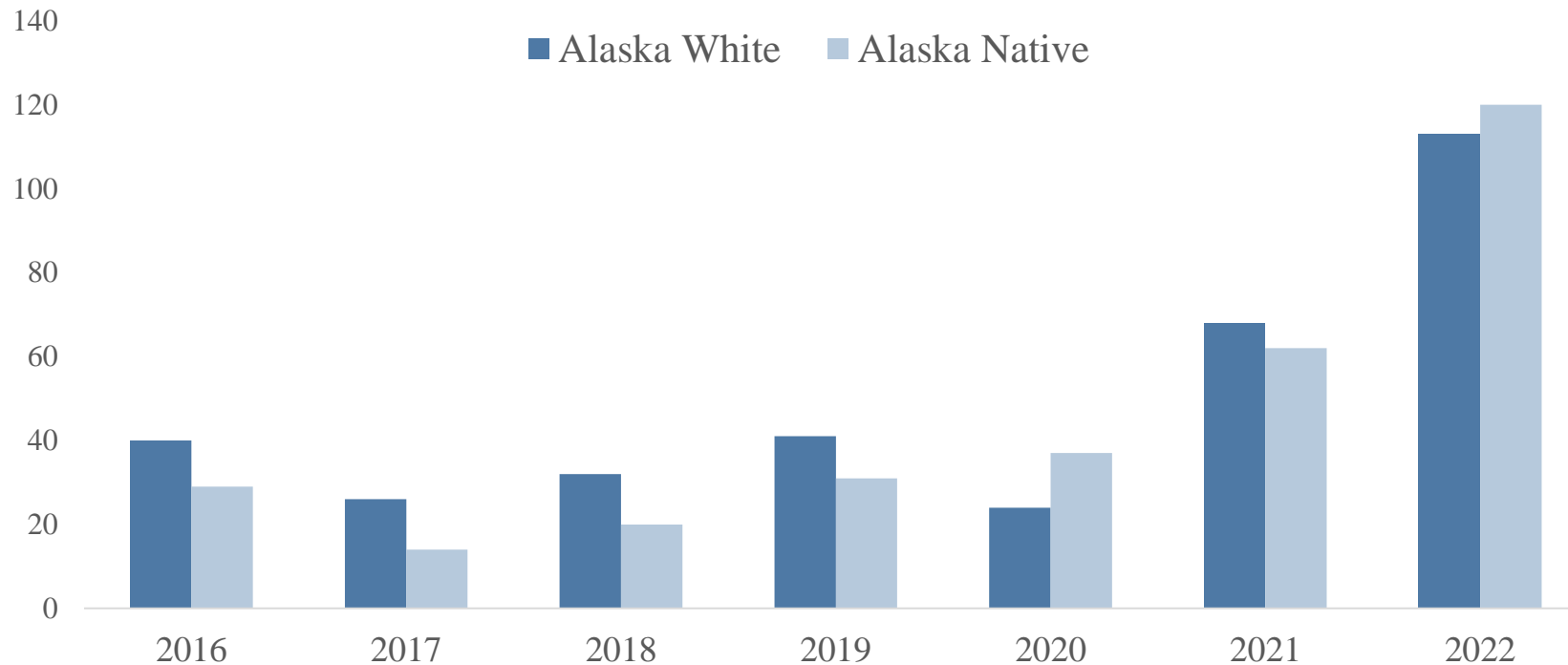
Source: Alaska Emergency Department Database. (2016, 2017, 2018, 2019, 2020, 2021, 2022). Alaska Health Facilities Data Reporting Program. Alaska Department of Health and Social Services, Division of Public Health.

Proportion of ‘problems related to upbringing’ (any Z62) to number of visits, Alaska statewide data, by sex, 2016-2022 (combined)



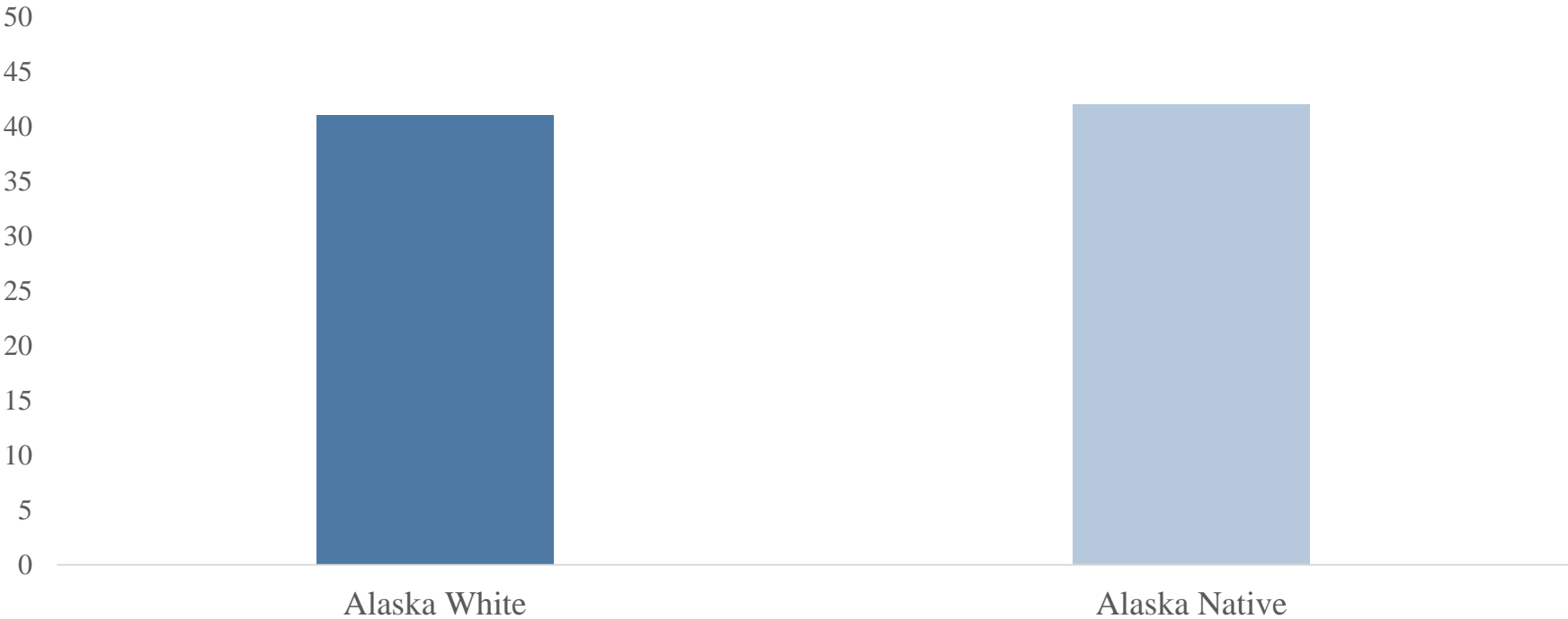
Source: Alaska Emergency Department Database. (2016, 2017, 2018, 2019, 2020, 2021, 2022). Alaska Health Facilities Data Reporting Program. Alaska Department of Health and Social Services, Division of Public Health.

Number of ‘problems related to upbringing’ (any Z62) ED visits to total ED visits, Alaska statewide data, Alaska Native and Alaska White, by year, 2016 through 2022



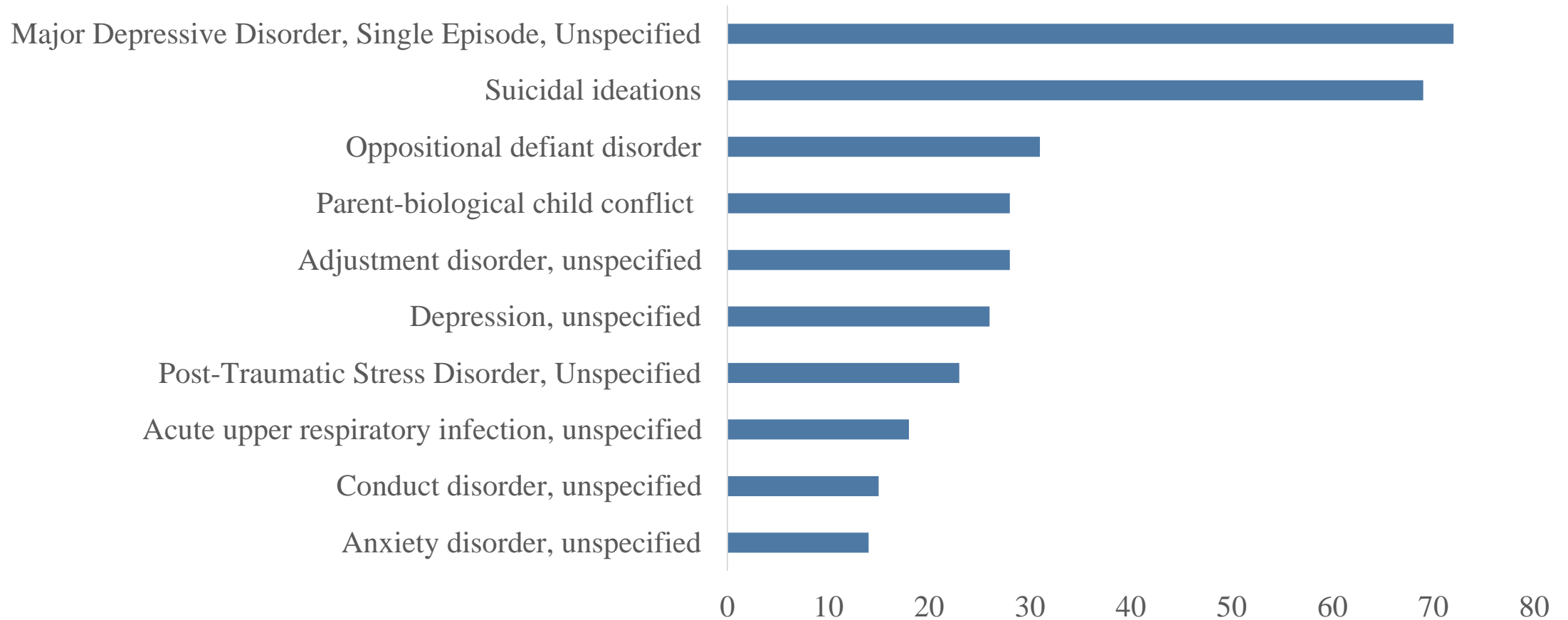
Source: Alaska Emergency Department Database. (2016, 2017, 2018, 2019, 2020, 2021, 2022). Alaska Health Facilities Data Reporting Program. Alaska Department of Health and Social Services, Division of Public Health.

Proportion of ‘problems related to upbringing’ (any Z62) per visits, Alaska statewide data, Alaska Native and Alaska White, 2016 through 2022 (combined)



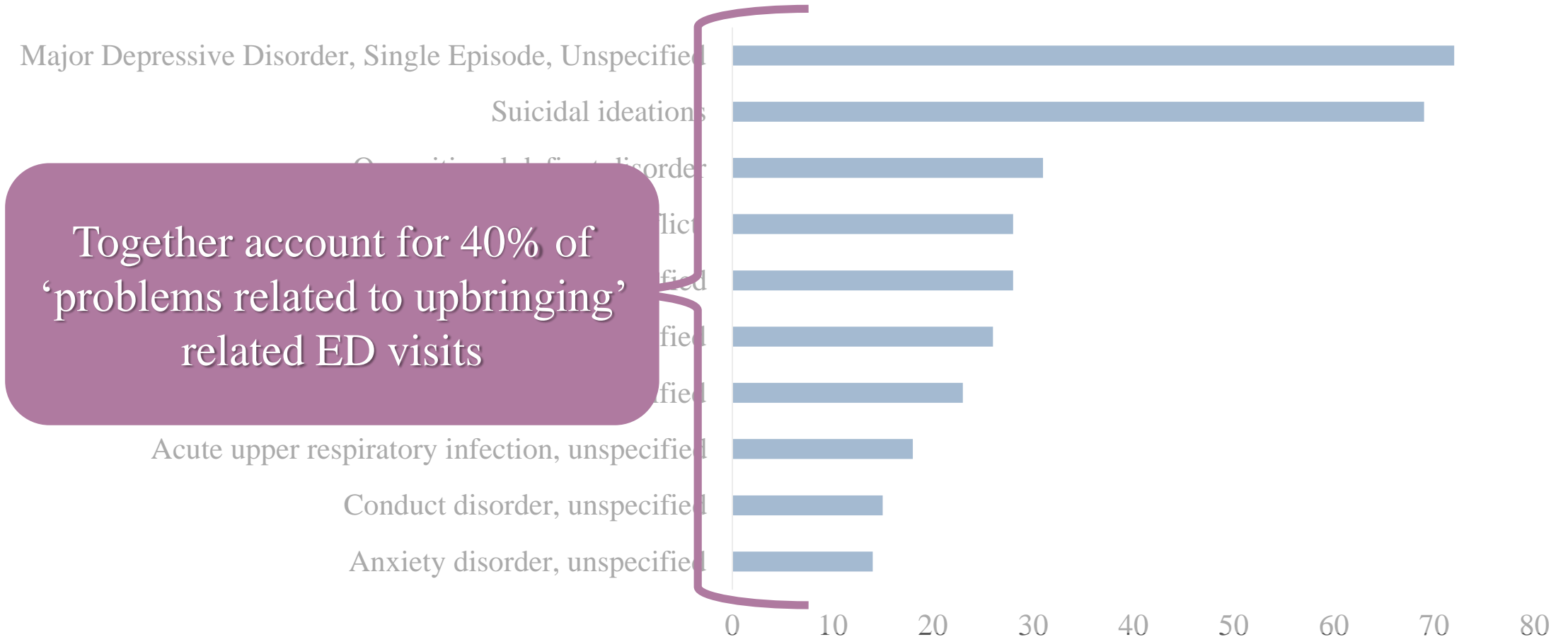
Source: Alaska Emergency Department Database. (2016, 2017, 2018, 2019, 2020, 2021, 2022). Alaska Health Facilities Data Reporting Program. Alaska Department of Health and Social Services, Division of Public Health.

Number of ‘problems related to upbringing’ (any Z62) ED visits, Alaska statewide data, by leading 10 primary diagnoses, 2016 through 2022 (combined)



Source: Alaska Emergency Department Database. (2016, 2017, 2018, 2019, 2020, 2021, 2022). Alaska Health Facilities Data Reporting Program. Alaska Department of Health and Social Services, Division of Public Health.

Number of ‘problems related to upbringing’ (any Z62) ED visits, Alaska statewide data, by leading 10 primary diagnoses, 2016 through 2022 (combined)



Together account for 40% of ‘problems related to upbringing’ related ED visits

Source: Alaska Emergency Department Database. (2016, 2017, 2018, 2019, 2020, 2021, 2022). Alaska Health Facilities Data Reporting Program. Alaska Department of Health and Social Services, Division of Public Health.

‘Childhood trauma’ (any Z62.81)

Z62.81 Personal history of abuse in childhood

Z62.810 Personal history of physical and sexual abuse in childhood

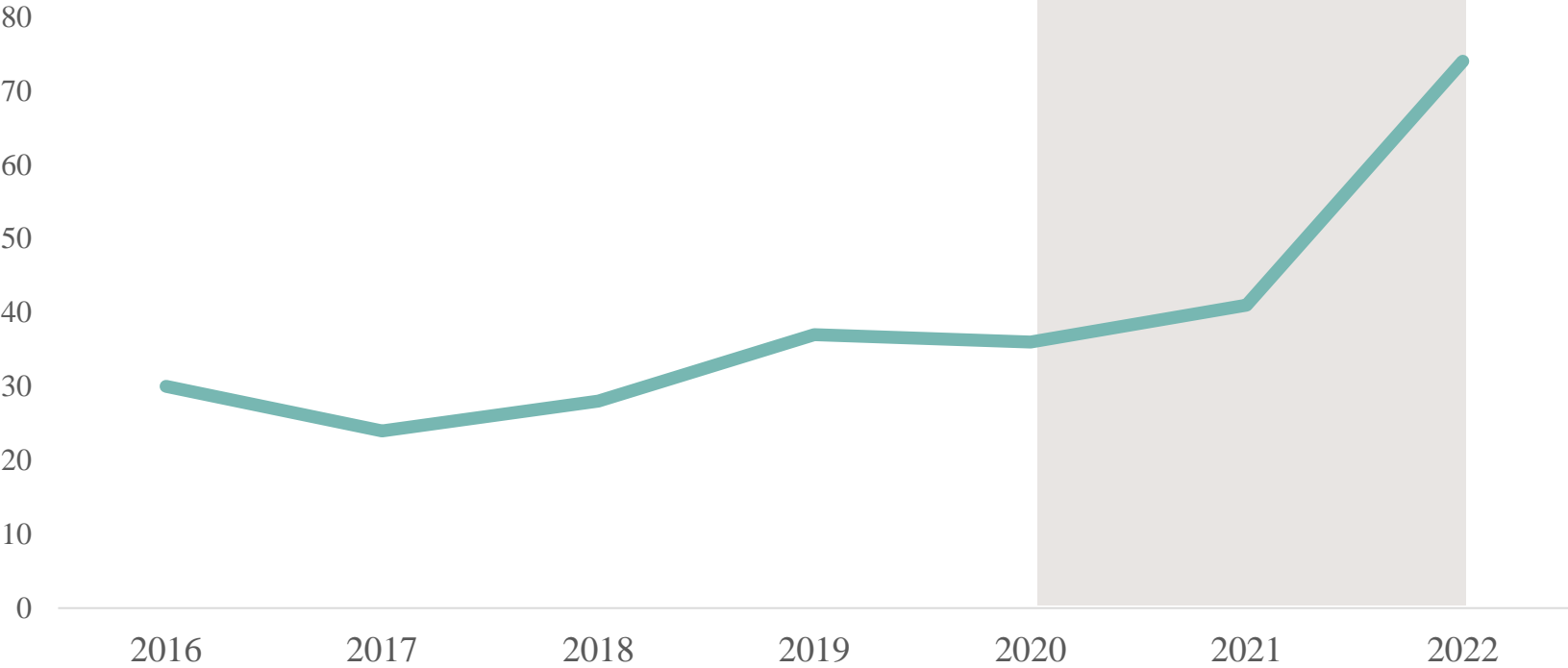
Z62.811 Personal history of psychological abuse in childhood

Z62.812 Personal history of neglect in childhood

Z62.813 Z62.813 Personal history of forced labor or sexual exploitation in childhood

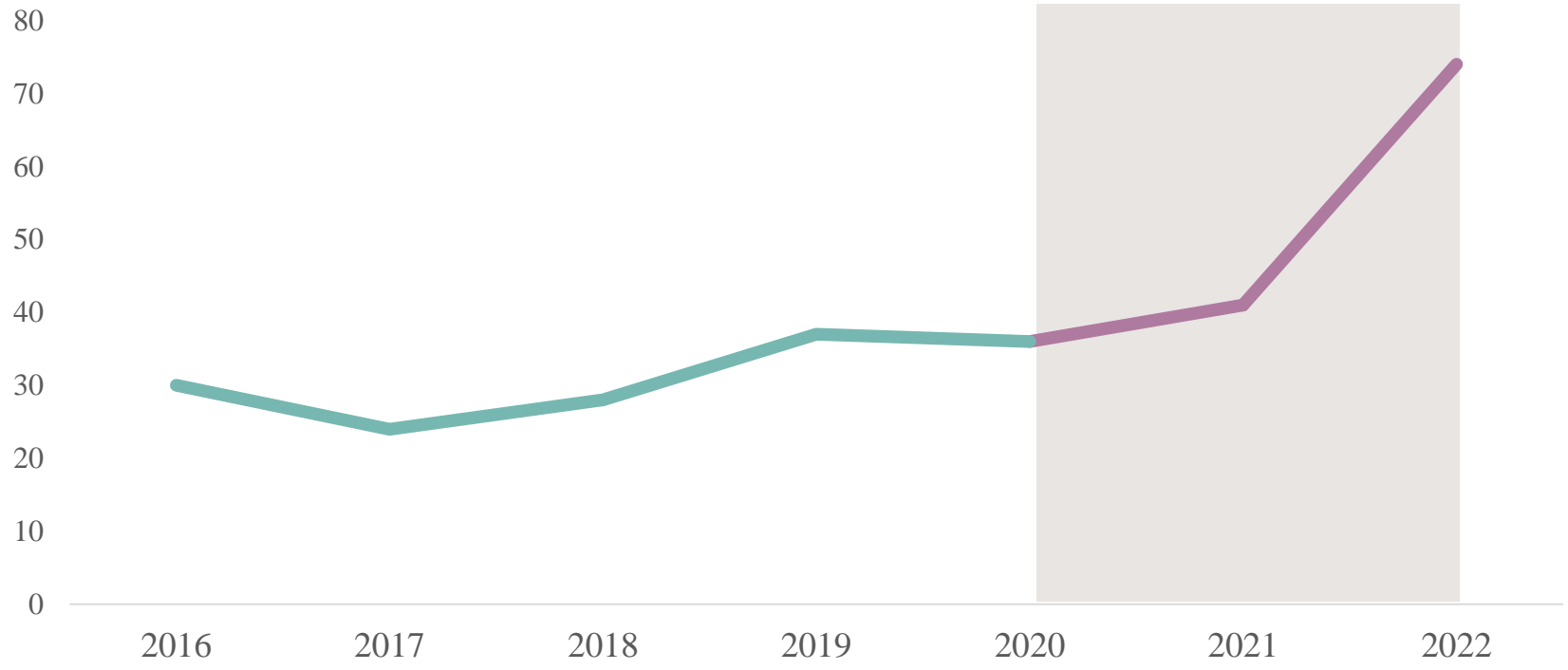
Z62.819 Personal history of unspecified abuse in childhood

Number of 'childhood trauma'-related ED visits (any Z62.81), Alaska statewide data, 2016-2022 (n=270)



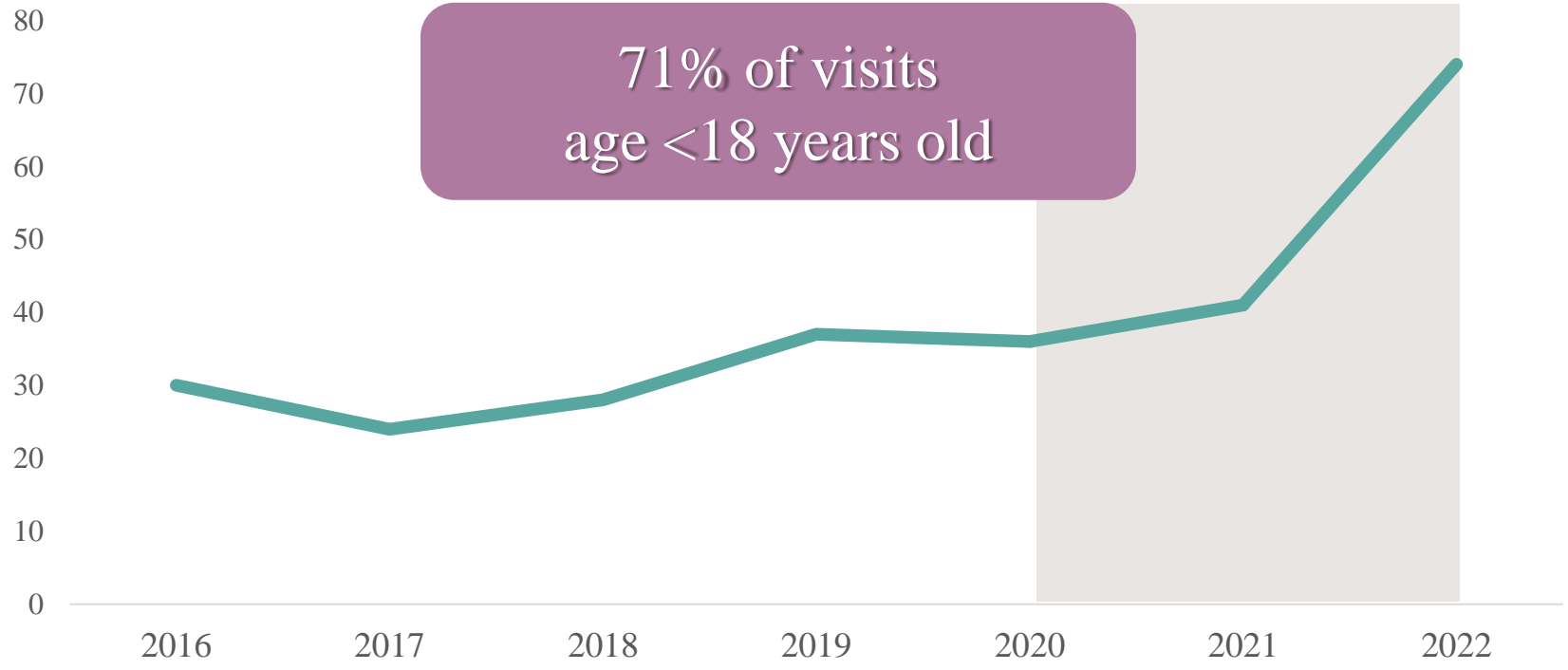
Source: Alaska Emergency Department Database. (2016, 2017, 2018, 2019, 2020, 2021, 2022). Alaska Health Facilities Data Reporting Program. Alaska Department of Health and Social Services, Division of Public Health.

Number of 'childhood trauma'-related ED visits (any Z62.81), Alaska statewide data, 2016-2022



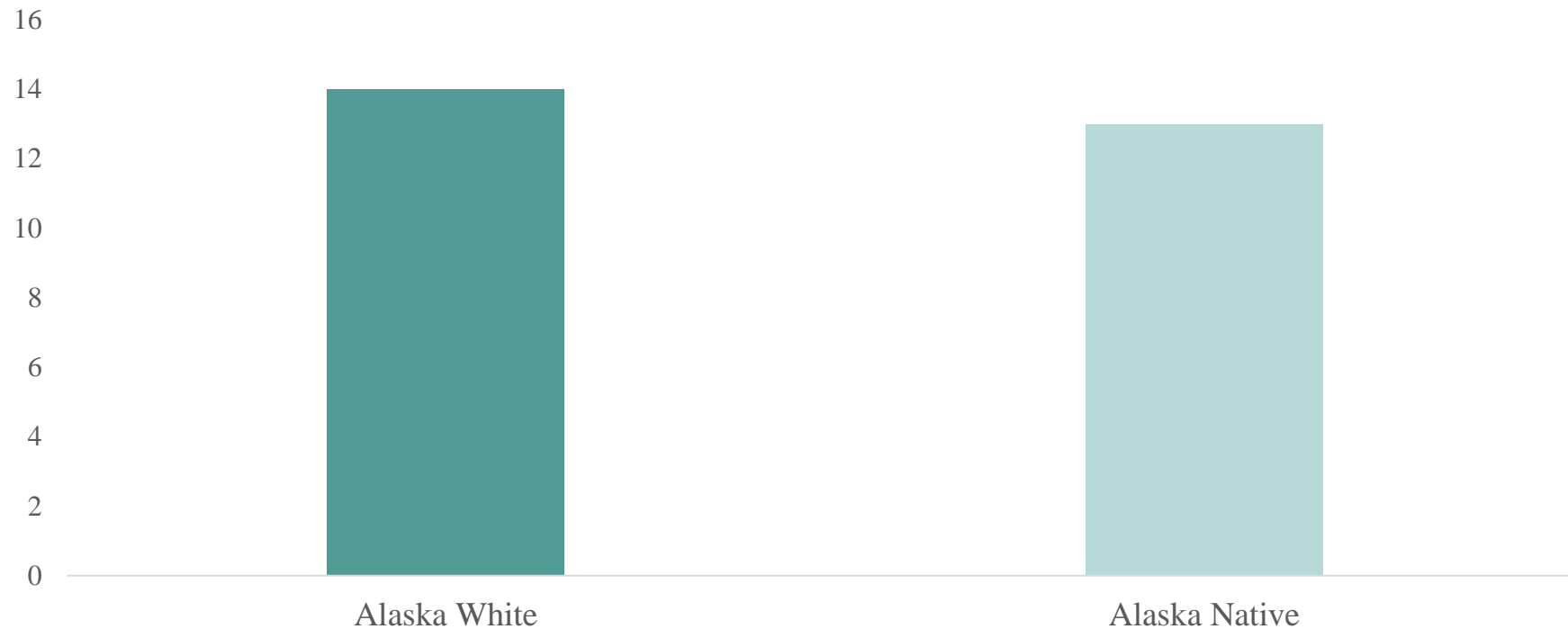
Source: Alaska Emergency Department Database. (2016, 2017, 2018, 2019, 2020, 2021, 2022). Alaska Health Facilities Data Reporting Program. Alaska Department of Health and Social Services, Division of Public Health.

Number of 'childhood trauma'-related ED visits (any Z62.81), Alaska statewide data, 2016-2022



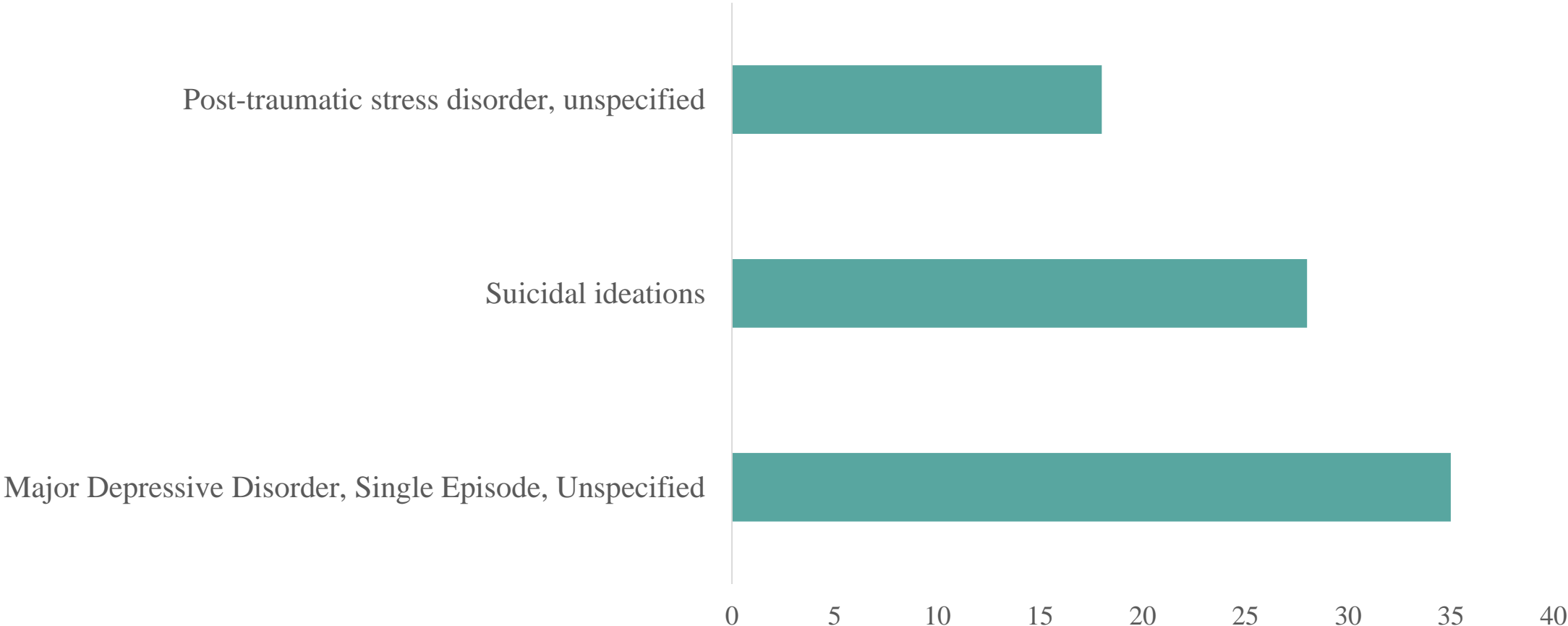
Source: Alaska Emergency Department Database. (2016, 2017, 2018, 2019, 2020, 2021, 2022). Alaska Health Facilities Data Reporting Program. Alaska Department of Health and Social Services, Division of Public Health.

Proportion of ‘childhood trauma’-related (any Z62) visits to total ED visits, Alaska statewide data, Alaska Native and Alaska White, 2016 through 2022 (combined)



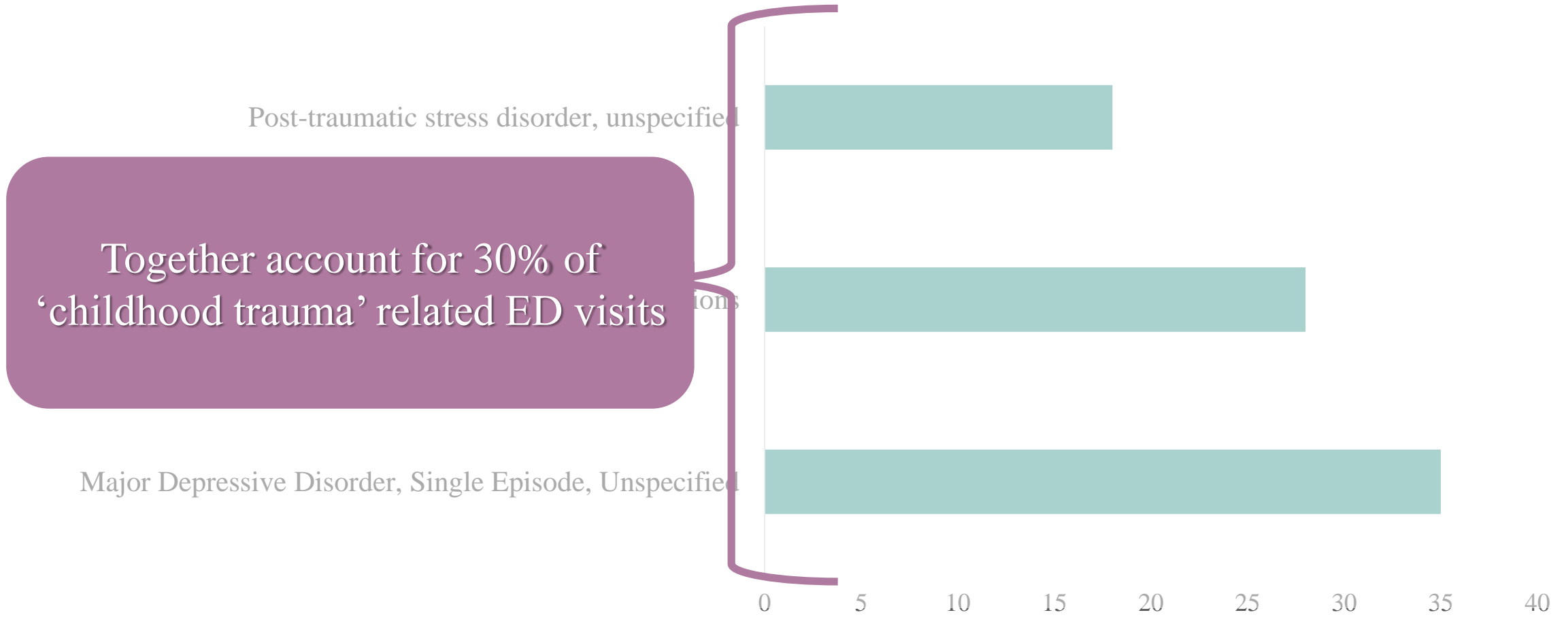
Source: Alaska Emergency Department Database. (2016, 2017, 2018, 2019, 2020, 2021, 2022). Alaska Health Facilities Data Reporting Program. Alaska Department of Health and Social Services, Division of Public Health.

Number of 'childhood trauma'-related (any Z62.81) ED visits, Alaska statewide data, by leading 3 primary diagnoses, 2016 through 2022 (combined)



Source: Alaska Emergency Department Database. (2016, 2017, 2018, 2019, 2020, 2021, 2022). Alaska Health Facilities Data Reporting Program. Alaska Department of Health and Social Services, Division of Public Health.

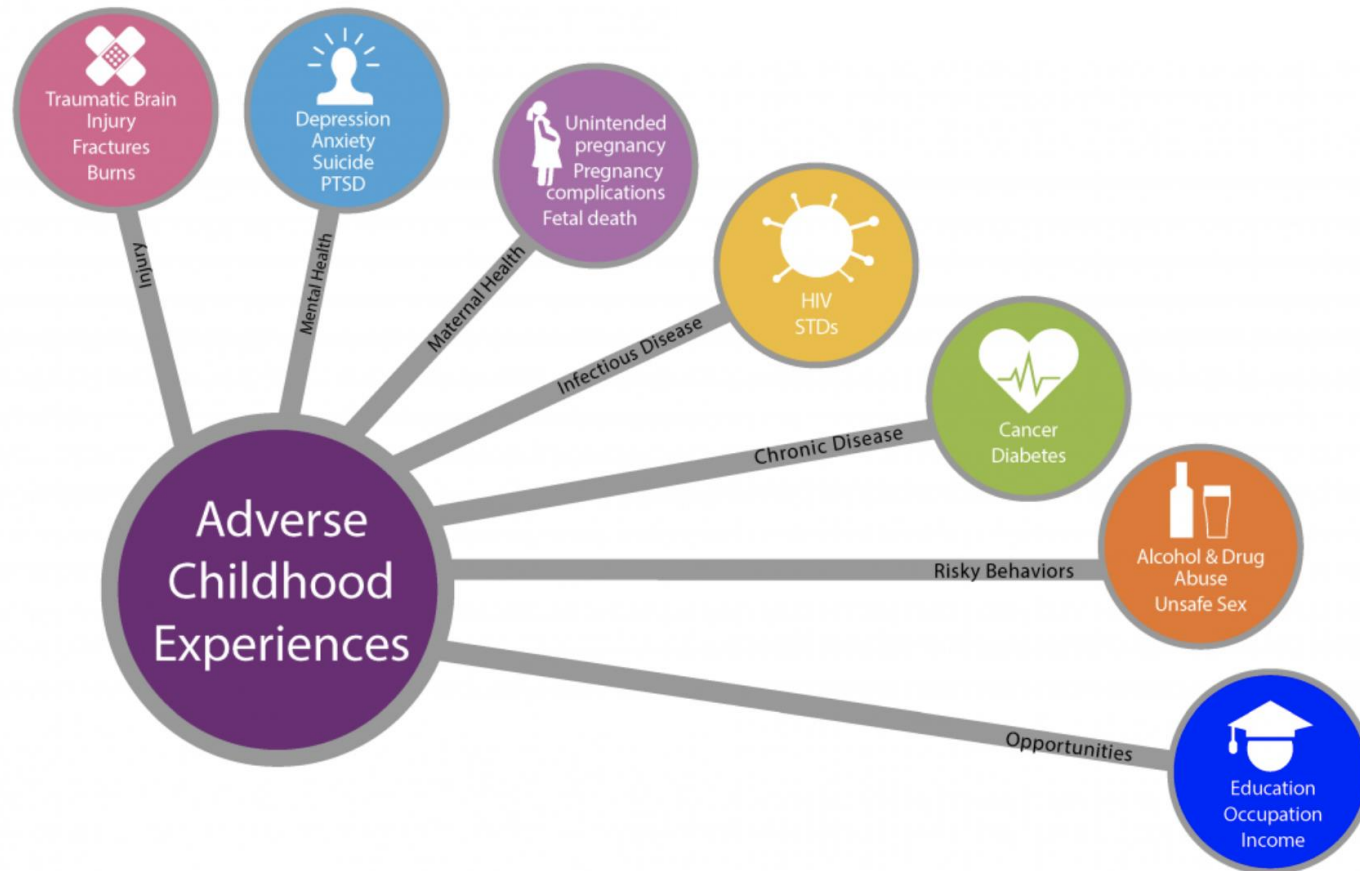
Number of 'childhood trauma'-related (any Z62.81) ED visits, Alaska statewide data, by leading 3 primary diagnoses, 2016 through 2022 (combined)



Source: Alaska Emergency Department Database. (2016, 2017, 2018, 2019, 2020, 2021, 2022). Alaska Health Facilities Data Reporting Program. Alaska Department of Health and Social Services, Division of Public Health.

Childhood trauma and chronic disease

Brain health and behavioral outcomes



Source: National Center for Injury Prevention and Control, Division of Violence Prevention: <https://www.cdc.gov/violenceprevention/aces/about.html>

Childhood trauma is associated with increased risk of opioid and substance misuse in adulthood

- “Compared to participants with no ACEs, participants with ≥ 4 ACEs and 0–3 ACEs were 2.93... and 1.96... times more likely to be at risk for opioid misuse, respectively.”¹
- “...the ACE score was inversely associated with age of initiating opioid use... positively associated with recent injection drug use... and the likelihood of experiencing an overdose... in a graded dose response manner.”²
- “ACEs was positively associated with prescription opioid misuse across both samples. Respondents reporting three or more ACEs had increased odds of taking opioids more than prescribed, without a prescription, and for the feeling they cause. Our results support a strong link between ACEs and prescription opioid misuse.”³

1. Fortson, K., Rajbhandari-Thapa, J., Ingels, J., Thapa, K. & Dube, S.R. (2021) Adverse childhood experiences, risk of opioid misuse and its pathway among students at a public university, Journal of American College Health, DOI: 10.1080/07448481.2021.2002336

2. Stein MD, Conti MT, Kenney S, et al. Adverse childhood experience effects on opioid use initiation, injection drug use, and overdose among persons with opioid use disorder. Drug Alcohol Depend. 2017;179:325-329. doi:10.1016/j.drugalcdep.2017.07.007

3. Merrick MT, Ford DC, Haegerich TM, Simon T. Adverse Childhood Experiences Increase Risk for Prescription Opioid Misuse. J Prim Prev. 2020 Apr;41(2):139-152. doi: 10.1007/s10935-020-00578-0. PMID: 31989435.

Childhood trauma has been associated with external locus-of-control

- “...the children/youths that had been victims of maltreatment showed little confidence in the possibility that they could have an impact on their own experiences.¹
- “Our findings suggest bullying by peers in childhood as a major risk factor for poor self-esteem and external locus of control in adulthood.”²
- “Harsh discipline, a proxy measure of physical abuse... was found associated with low parenting self-efficacy”³

1. Roazzi, A., Attili, G., Di Pentima, L. *et al.* Locus of control in maltreated children: the impact of attachment and cumulative trauma. *Psicol. Refl. Crít.* **29**, 8 (2016).

2. Fosse, G. K. & Holen, A. (2007). Reported Maltreatment in Childhood in Relation to the Personality Features of Norwegian Adult Psychiatric Outpatients. *The Journal of Nervous and Mental Disease*, *195* (1), 79-82. doi: 10.1097/01.nmd.0000252312.98109.d4.

3. Oosterman, M., Schuengel, C., Forrer, M., & De Moor, M. (2019). The impact of childhood trauma and psychophysiological reactivity on at-risk women's adjustment to parenthood. *Development and Psychopathology*, *31*(1), 127-141. doi:10.1017/S0954579418001591 as abstracted by in Beaulieu, M. C., & Normandeau, S. (2012). Predictors of parents: Parental social cognitions and behavior of children with ADHD. *Canadian Journal of Behavioural Science*, *44*, 59–69. doi:10.1037/a0023844

Childhood trauma is associated with adult impaired spatial learning and cognition

- “We observed a significant effect of (childhood) trauma history on spatial/pattern learning.”¹
- “Physical neglect correlated with impaired spatial working memory and pattern recognition memory.”²
- “Decreased white matter FA in the prefrontal and temporal cortex was associated with decrements in performance on a spatial planning task and a visual learning and memory task in children who suffered early neglect.”³

1. Syal S, Ipser J, Phillips N, Thomas KG, van der Honk J, Stein DJ. (2014). The effect of childhood trauma on spatial cognition in adults: a possible role of sex. *Metab Brain Dis*. 2014 Jun;29(2):301-10. doi: 10.1007/s11011-014-9497-4. Epub 2014 Feb 21. PMID: 24553877.
2. Majer, M., Nater, U.M., Lin, JM.S. *et al.* (2010). Association of childhood trauma with cognitive function in healthy adults: a pilot study. *BMC Neurol* **10**, 61 (2010).
3. De Bellis, M. D. et al. (2009). Neuropsychological Findings in Childhood Neglect and Their Relationships to Pediatric PTSD.” *J Int Neuropsychological Soc* 15.6: 868–878.

Childhood trauma can change structures and functions of threat, memory, and reward systems

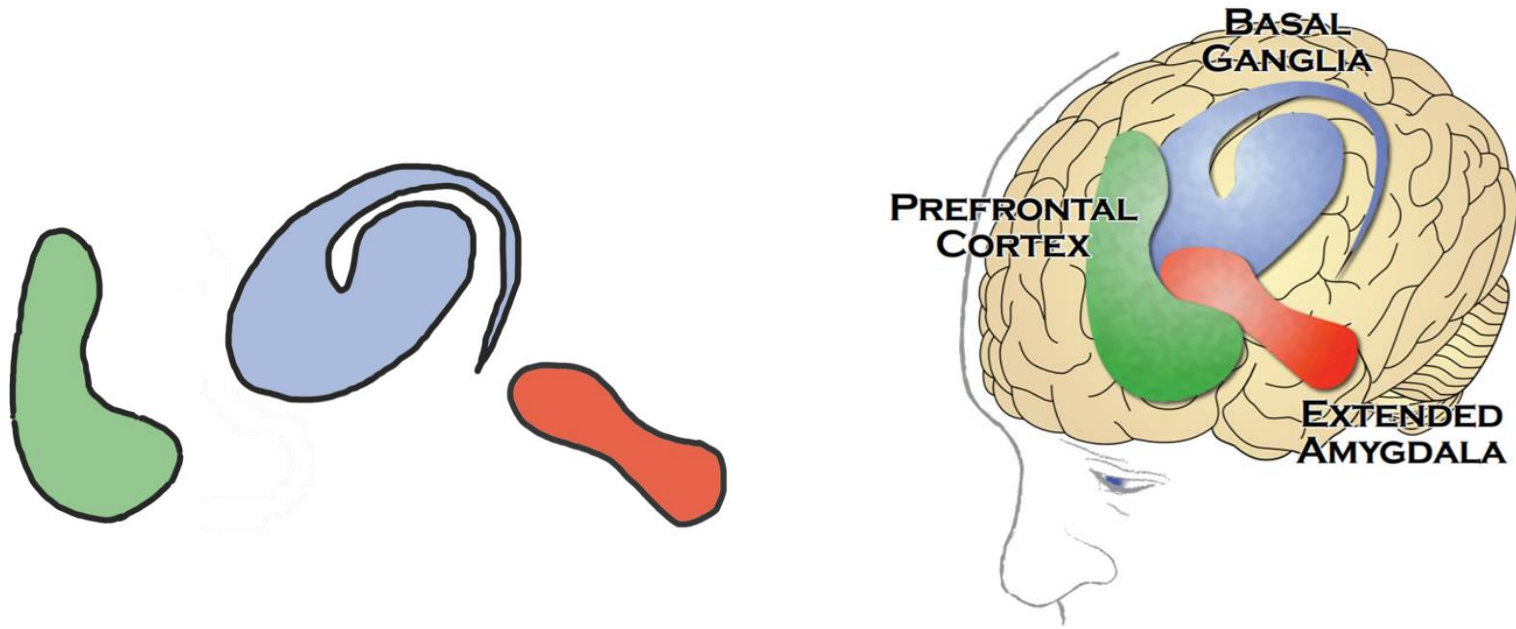
Brain structures affected by childhood trauma and related behavioral health conditions/outcomes

	PFC -	AMG -/+	HPC -	ACC -	VS +	HT -
1. Emotional regulation	■	■	■	■		
2. Depression	■	■	■		■	
3. Social relationships	■	■	■	■		
4. Hypervigilance	■	■				■
5. Alcohol use disorder	■	■	■			
6. Opioid use disorder	■	■				■
7. Nicotine dependence	■	■		■	■	
8. Diabetes	■	■				■
9. Learning	■	■	■			
10. Incarceration	■	■	■	■		

A case for interactive Augmented Reality

Informed patients can make better decisions about care

Traditional informational media may not be as accessible to some patients

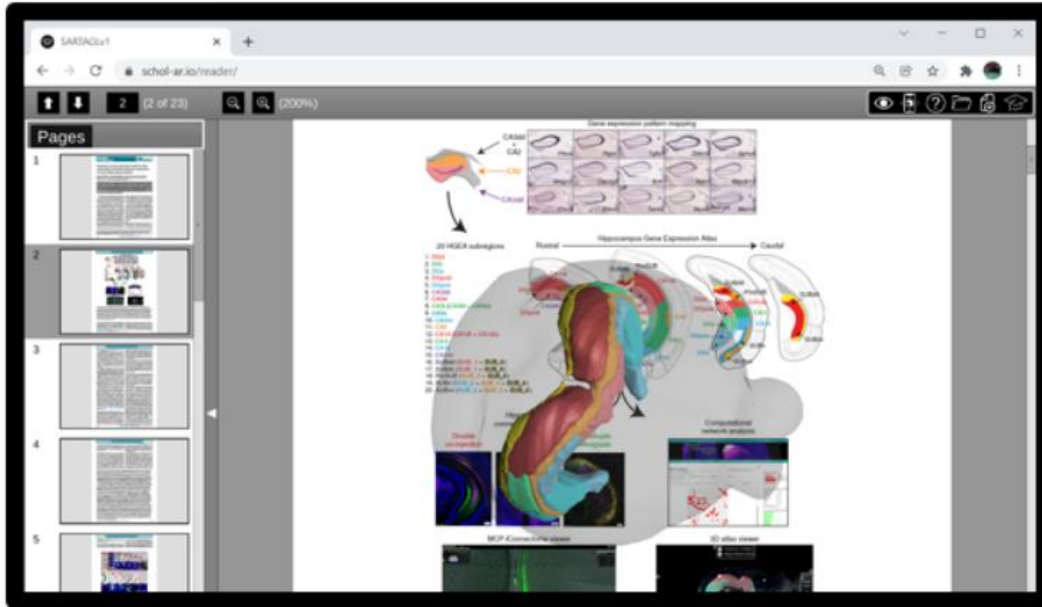


Augmented Reality makes neuro models easy to understand

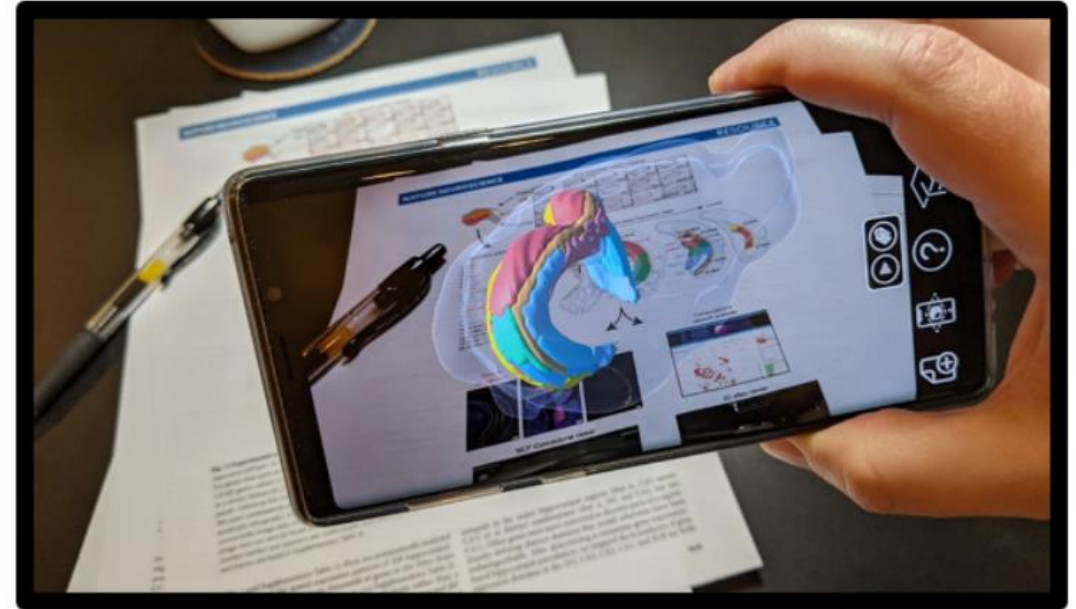




PDF
Reader



Augmented
Reality

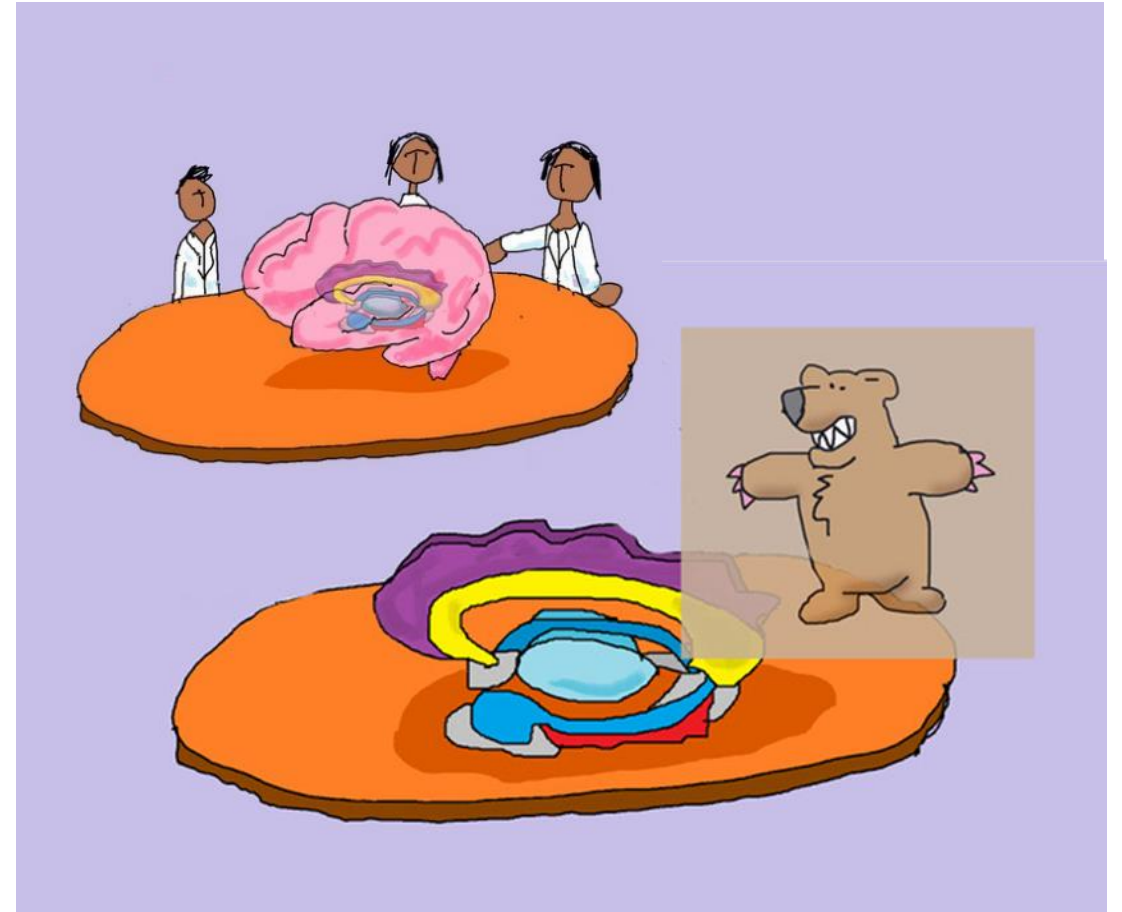


<https://hscnews.usc.edu/usc-institute-launches-pioneering-augmented-reality-smartphone-application>

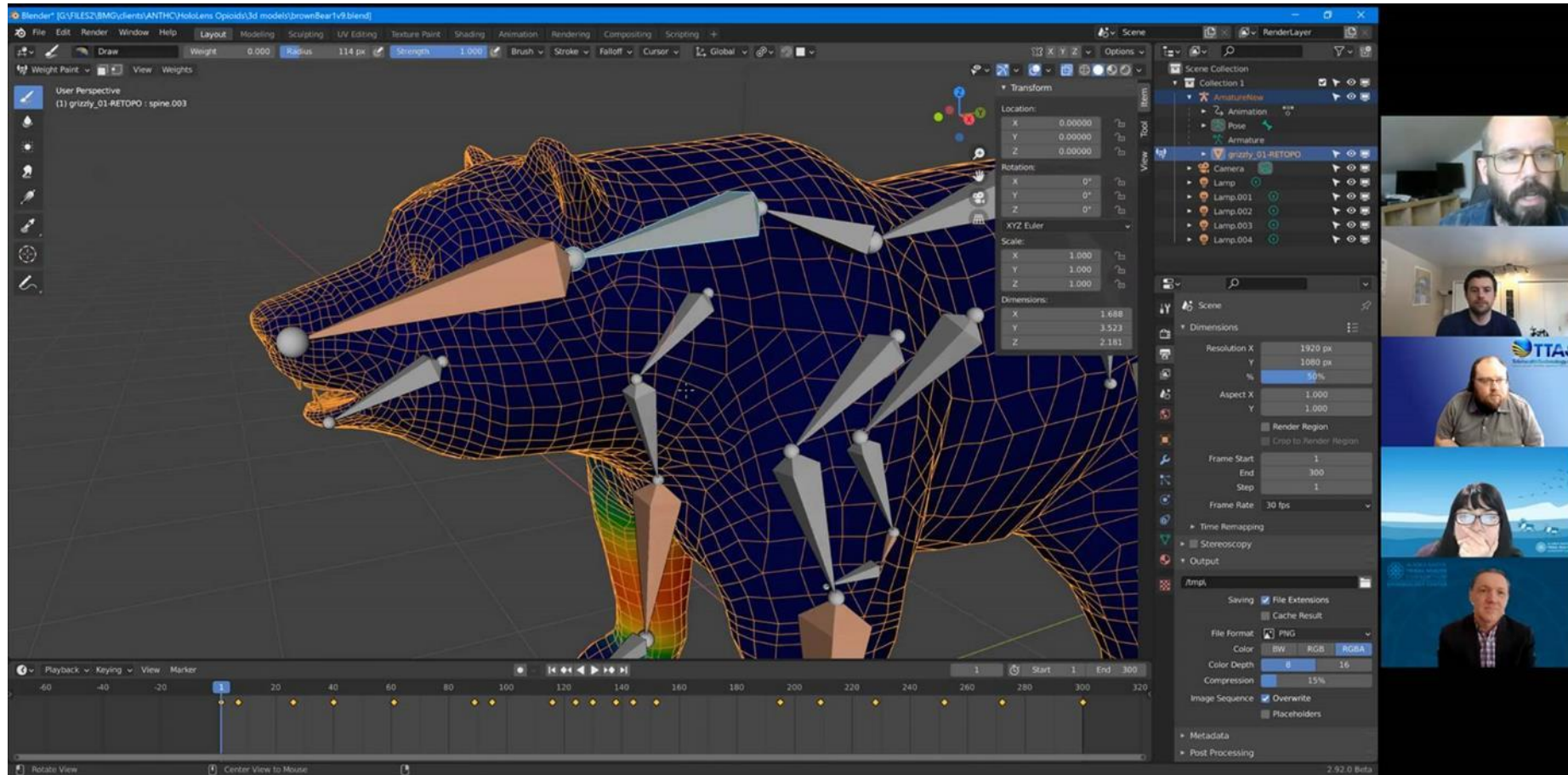
Interactive AR puts users in control



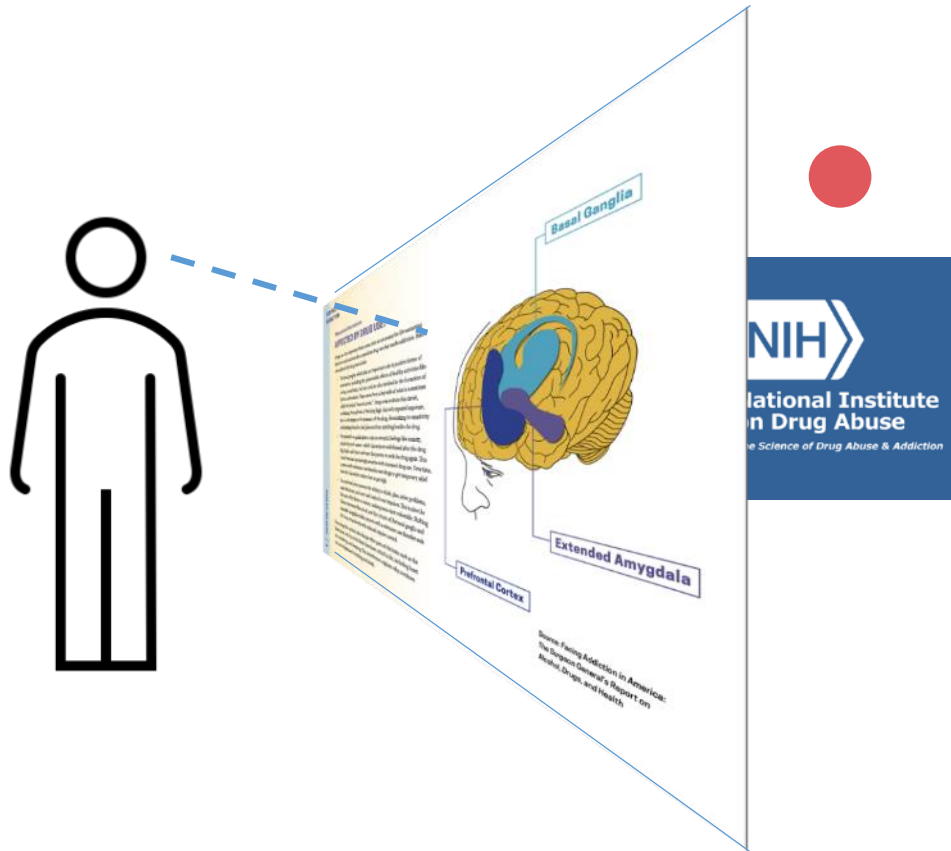
So we made storyboards...



And wrote some programs...



Brochures: External locus of control

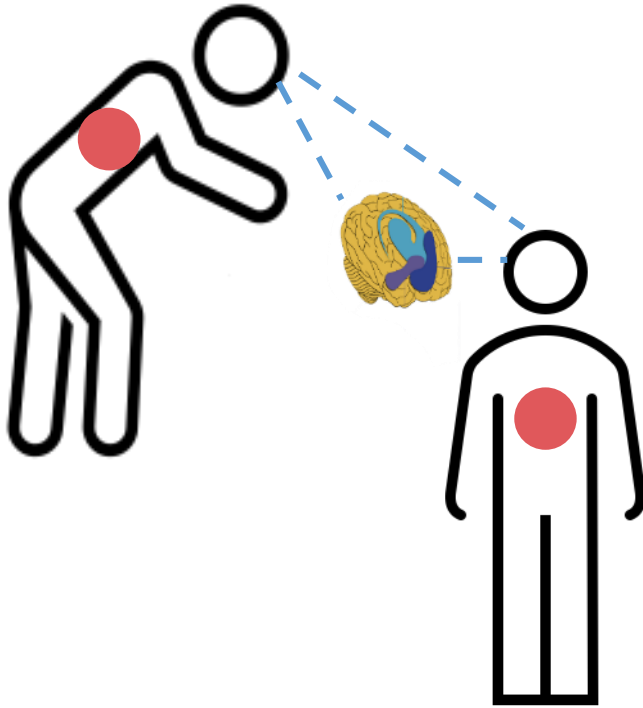


Information comes from an outside authority.

The user passively consumes content.

Spatial and volumetric information are lost.

AR: Internal locus of control



The user and the medical information share the same space.

The user actively controls the content.

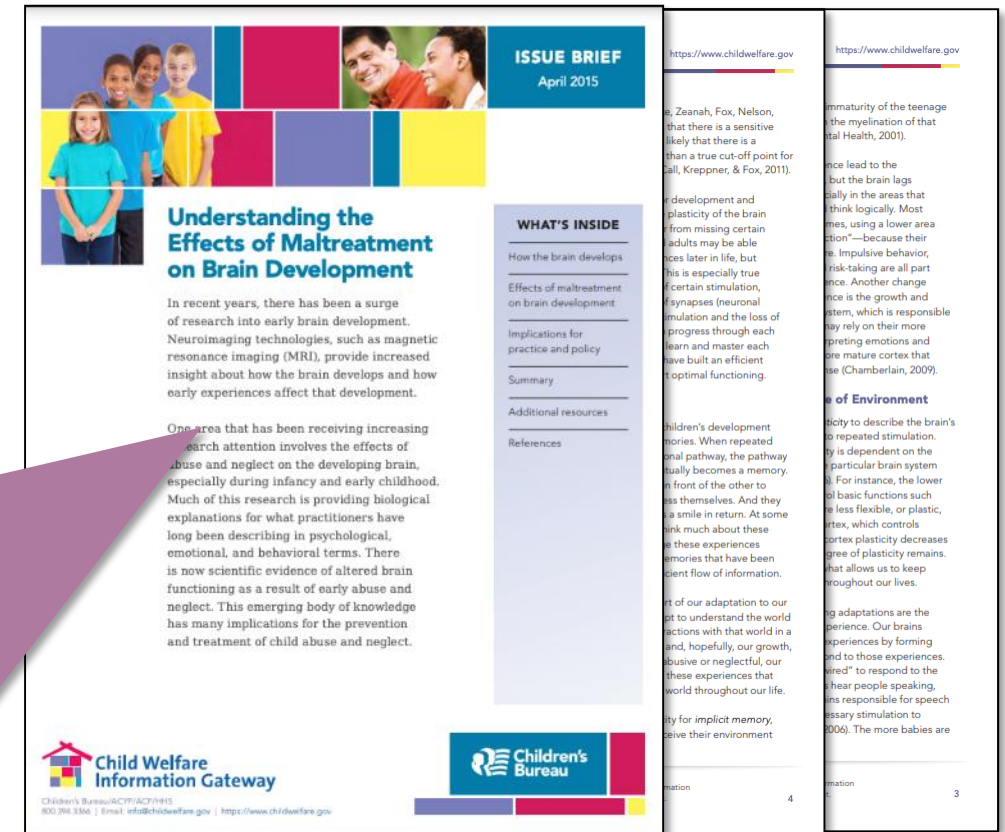
Spatial and volumetric information are preserved.

“In recent years, there has been a surge of research into early brain development. Neuroimaging technologies... provide increased insight about how the brain develops and how early experiences affect that development.

One area that has been receiving increasing research attention involves the effects of abuse and neglect on the developing brain...

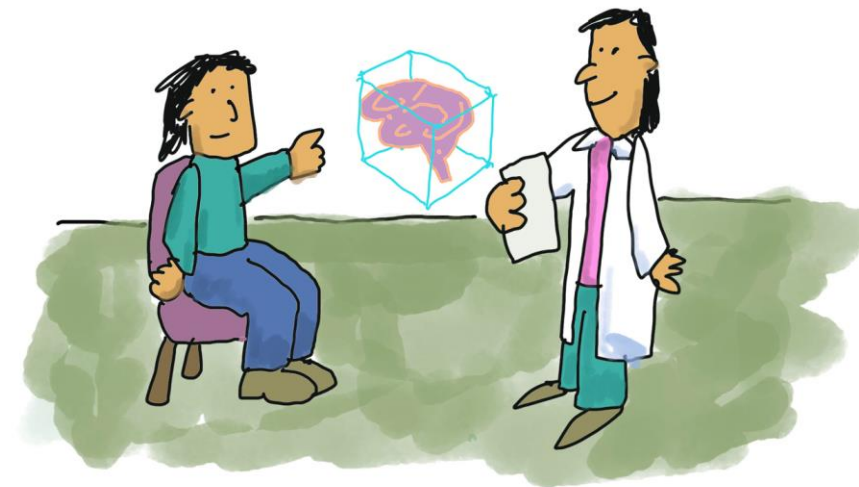
There is now scientific evidence of altered brain functioning as a result of early abuse and neglect.

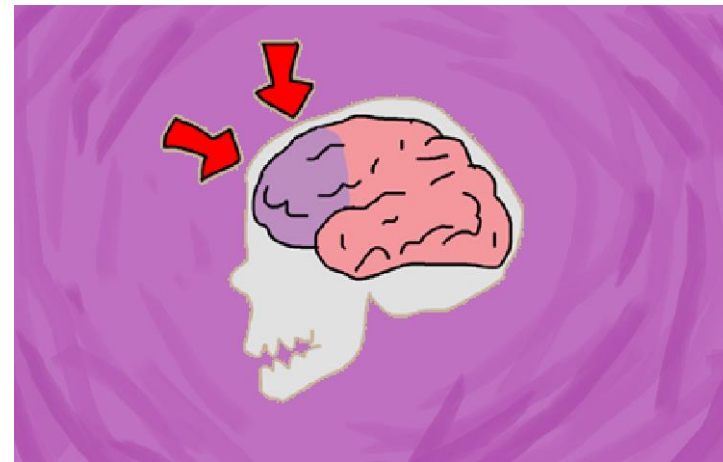
This emerging body of knowledge has many implications for the prevention and treatment of child abuse and neglect.”

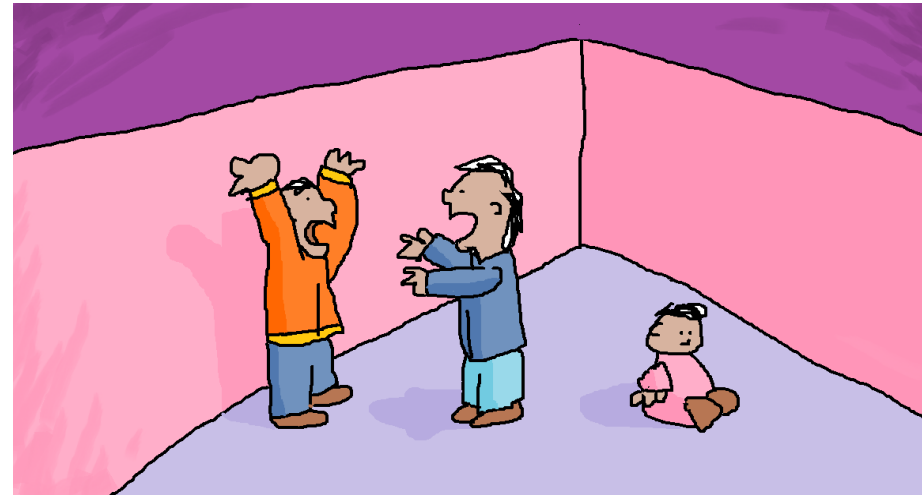
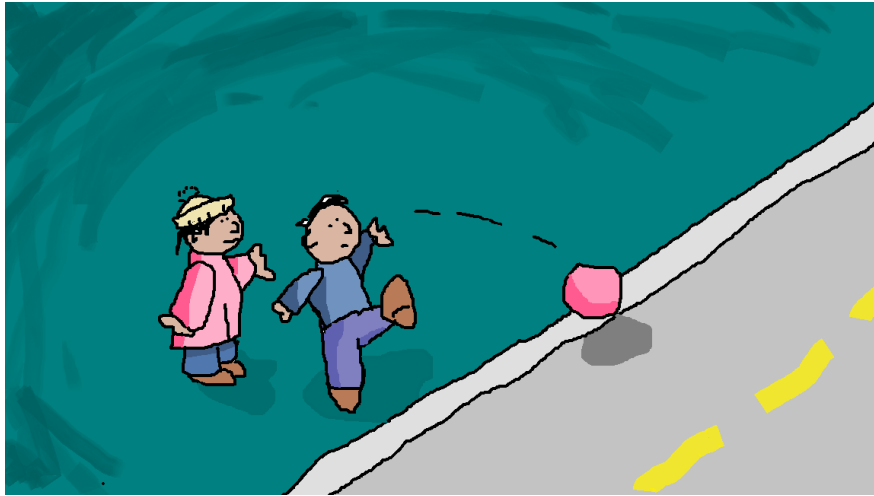
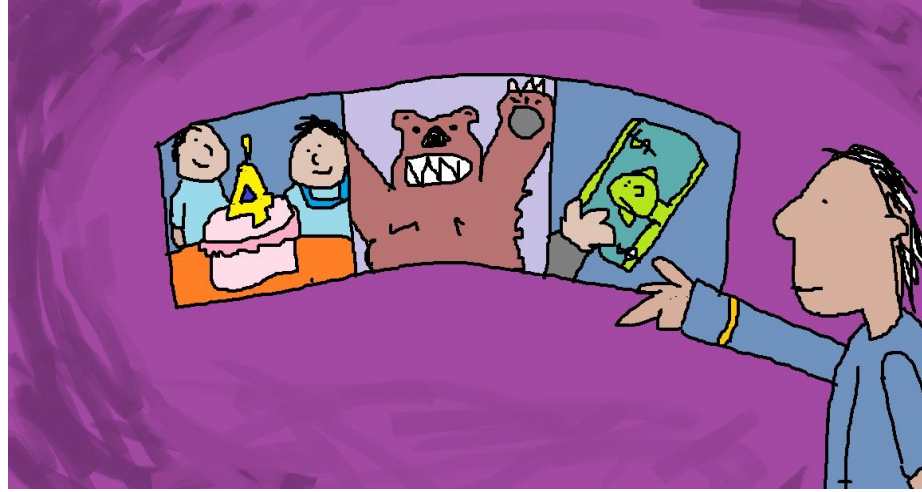
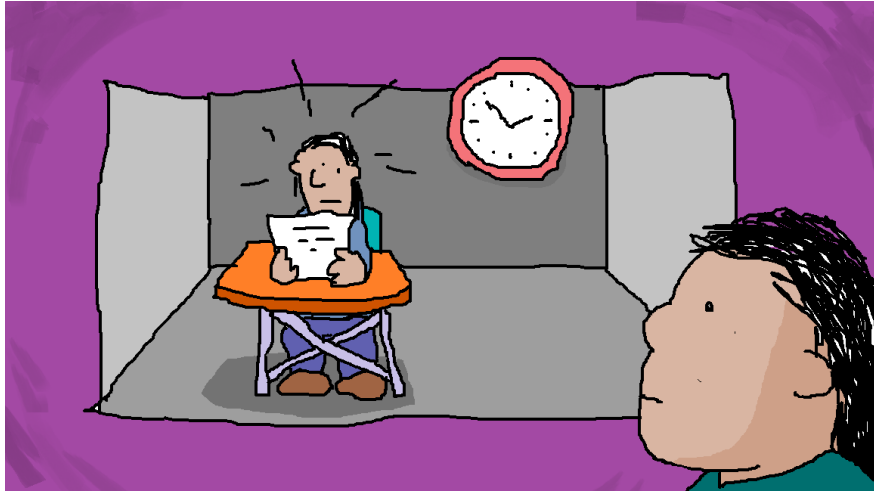


Source: Understanding the effects of maltreatment on early brain development, Child Welfare Information Gateway (October, 2001). Department of Health and Human Services, Administration for Children and Families, Administration on Children, Youth and Families Children's Bureau, Washington, DC.

Childhood trauma facilitated discussion app







Why brain health literacy?

1. Informed patients can make better decisions about their care.
2. Reduce anxiety.
3. Reduce social stigma.
4. Increase uptake of treatment.
5. Help communities plan and respond to public health needs.
6. If we don't give patients information, they'll get it themselves from other sources, and that information may be wrong, incomplete, or harmful.
7. New technology makes patient education affordable, more engaging than ever.

Discussion

Questions and feedback

References

- Gorzelańczyk, E., Walecki, P., Błaszczyszyn, M., Laskowska, E., Kawala-Sterniuk, A. (2021). Evaluation of risk behavior in gambling addicted and opioid addicted individuals. *Frontiers in Neuroscience*, 14, 1311. DOI: 10.3389/fnins.2020.597524
- Gorzelańczyk, E. J., Fareed, A., Walecki, P., Feit, J., & Kunc, M. (2014). Risk behavior in opioid-dependent individuals after the administration of a therapeutic dose of methadone. *The American journal on addictions*, 23(6), 608–612. <https://doi.org/10.1111/j.1521-0391.2014.12154.x>
- Huang, A. S., Mitchell, J. A., Haber, S. N., Alia-Klein, N., & Goldstein, R. Z. (2018). The thalamus in drug addiction: from rodents to humans. *Philosophical Transactions of the Royal Society of London. Series B, Biological Sciences*, 373(1742), 20170028. <https://doi.org/10.1098/rstb.2017.002>
- Kalia, V., Knauff, K., & Hayatbini, N. (2021). Adverse childhood experiences (ACEs) associated with reduced cognitive flexibility in both college and community samples. *PloS one*, 16(12), e0260822 <https://doi.org/10.1371/journal.pone.0260822>
- Koenigs, M. & Grafman, J. 2009. Posttraumatic stress disorder: the role of medial prefrontal cortex and amygdala. *Neuroscientist*, 15, 540-8.
- Lin, J. C., Chu, L. F., Stringer, E. A., Baker, K. S., Sayyid, Z. N., Sun, J., Campbell, K. A., & Younger, J. W. (2016). One month of oral morphine decreases gray matter volume in the right amygdala of individuals with low back pain: Confirmation of previously reported magnetic resonance imaging results. *Pain Medicine*, 17(8), 1497–1504.
- Luby, J. L., Barch, D., Whalen, D., Tillman, R., & Belden, A. (2017). Association between early life adversity and risk for poor emotional and physical health in adolescence: A putative mechanistic neurodevelopmental pathway. *JAMA pediatrics*, 171(12), 1168–1175. Kutlu, M. G., & Gould, T. J. (2016). Effects of drugs of abuse on hippocampal plasticity and hippocampus-dependent learning and memory: contributions to development and maintenance of addiction. *Learning & Memory* (Cold Spring Harbor, N.Y.), 23(10), 515–533. <https://doi.org/10.1101/lm.042192.116>
- Milgram, Paul & Kishino, Fumio. (1994). A Taxonomy of mixed reality visual displays. *IEICE Trans. Information Systems*. vol. E77-D, no. 12. 1321-1329
- National Institute on Drug Abuse (29 What are the long-term effects of methamphetamine misuse? <https://www.drugabuse.gov/publications/research-reports/methamphetamine/what-are-long-term-effects-methamphetamine-misuse>

References

National Institute on Drug Abuse (2007, June). Brain Power: Module 1: An introduction to the brain and nervous system. NIDA, Washington, D.C. <https://www.drugabuse.gov/publications/brain-power/grades-6-9/introduction-to-brain-nervous-system-module-1>

Schoolcraft, H.R. (1851). *Historical and statistical information respecting the history, condition, and prospects of the Indian tribes of the United States (pt. 1)*. Philadelphia: Lippincott, Grambo & Company (successors to Grigg, Eliot & Co.). Retrieved from <https://doi.org/10.5479/sil.131145.39088002742823>

Sirakaya, Mustafa & Alsancak Sirakaya, Didem. (2018). Trends in educational Augmented Reality studies: A systematic review. *Malaysian Online Journal of Educational Technology*. 6. 60-74. 10.17220/mojet.2018.02.005.

Stoet, G. (2010). PsyToolkit: A software package for programming psychological experiments using Linux. *Behavior Research Methods*, 42(4), 1096-1104

Stoet, G. (2017). PsyToolkit: A novel web-based method for running online questionnaires and reaction-time experiments. *Teaching of Psychology*, 44(1), 24-31

Stojanovska, M., Tingle, G., Tan, L. et al. Mixed Reality anatomy using Microsoft HoloLens and cadaveric dissection: A comparative effectiveness study. *Med.Sci.Educ.* 30, 173–178 (2020). <https://doi.org/10.1007/s40670-019-00834-x>

Upadhyay, J., Maleki, N., Potter, J., Elman, I., Rudrauf, et al (2010). Alterations in brain structure and functional connectivity in prescription opioid-dependent patients. *Brain: A Journal of Neurology*, 133(Pt 7), 2098–2114. <https://doi.org/10.1093/brain/awq138>

U.S. Department of Health and Human Services (HHS), Office of the Surgeon General, Facing addiction in America: The Surgeon General’s spotlight on opioids. Washington, DC: HHS, November 2016. https://addiction.surgeongeneral.gov/sites/default/files/OC_SpotlightOnOpioids.pdf

Yang, J. Z., Kang, C. Y., Yuan, J., Zhang, Y., Wei, Y. J., Xu, L., Zhou, F., & Fan, X. (2021). Effect of adverse childhood experiences on hypothalamic-pituitary-adrenal (HPA) axis function and antidepressant efficacy in untreated first episode patients with major depressive disorder. *Psychoneuroendocrinology*, 134, 105432. Advance online publication. <https://doi.org/10.1016/j.psyneuen.2021.105432>

Zou F, Wu X, Zhai T, Lei Y, Shao Y, Jin X, Tan S, Wu B, Wang L, Yang Z. Abnormal resting-state functional connectivity of the nucleus accumbens in multi-year abstinent heroin addicts. *J Neurosci Res*. 2015 Nov;93(11):1693-702. doi: 10.1002/jnr.23608. Epub 2015 Aug 17. PMID: 26280556. <https://pubmed.ncbi.nlm.nih.gov/26280556>

Thank You

qagaasakung baasee' tsin'aen quyanaq
dogedinh quyanaa igamsiqanaghalek
'awa'ahdah gunalchéesh chin'an mahsi'
miigwech tsin'e e way dankoo háw'aa quyana

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Miigwech bizindawiyeg! (Thanks for listening!)

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