DAY 3

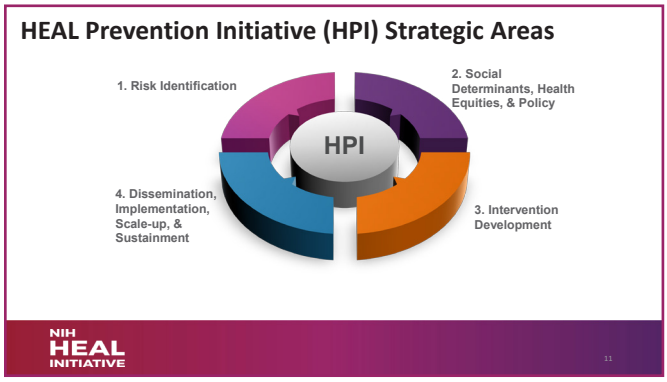
Helping to End Addiction Long-Term (HEAL)
HEAL Prevention Initiative (HPI)
Year 3 Meeting

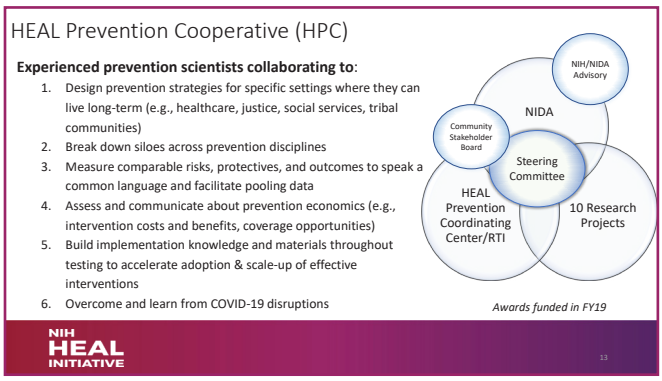
Wednesday, November 10, 2020
1:00 p.m.–5:30 p.m. ET / 10:00 a.m.–2:30 p.m. PT

HEAL Prevention Initiative: Overview of Vision and Four Strategic Areas of Opportunity for Prevention Research

Prevention is an essential component of addressing the opioid crisis. Effective prevention will decrease demand for treatment; save lives; reduce personal and societal costs; and promote positive outcomes, including reducing risk for opioid and other substance misuse. A major focus on prevention is warranted given the number of people who would benefit from services to prevent opioid use disorder. In 2020, according to the National Survey on Drug Use and Health, 3.4% or 9.5 million people ages 12 and older had misused opioids in the past year—that is, they could have benefited from services to prevent misuse, and the now need services to prevent disorder. In comparison, 1.0% or 2.7 million people had an opioid use disorder.

The HPI vision is that health care organizations and public systems will be able to make evidence-based preventive intervention services available and accessible to all persons at risk for opioid and other substance misuse or disorder. The HPI specifically addresses challenges in community capacity and in funding, focusing on four strategic areas: risk identification; social determinants, health equities, and policy; intervention development; and dissemination, implementation, scale-up, and sustainment.





Through the HEAL Prevention Cooperative (HPC), it is developing and testing 10 interventions to prevent opioid misuse and OUD in at-risk young people ages 15–30. The transition from adolescence into young adulthood is a key developmental period for preventing substance use. In 2020, according to the National Survey on Drug Use and Health, 1.6% of adolescents ages 12–17 misused opioids, but among young adults ages 18–25, about 4.1% misused opioids. Further, we don't know whether the evidence-based interventions to prevent other substances also prevent opioid misuse among vulnerable adolescents and young adults.

HPI Strategic Area 1: Identifying Risk for Opioid Use

3:10–3:40 p.m.

Key Takeaways

- Cannabis use and tobacco use in early adolescence may be risk factors for opioid use in young adulthood among African Americans living in urban areas, highlighting the need for early prevention intervention efforts to reduce risk of opioid misuse later in life.
- Policy makers who look to legalize cannabis use to combat the opioid epidemic must note the possible unintended harm that increased legal access to cannabis may cause to adolescents.
- Policies are needed to address cannabis/tobacco co-use in early adolescence to reduce risk of negative health outcomes like opioid misuse in young adulthood.
- Assessments like implicit association tests are useful to identify perceptions regarding substances such as marijuana and opioids among youth; the results can be used to tailor targeted prevention efforts.
- Next Steps: Future research may consider validation of opioid misuse study findings in older or clinical populations that report higher percentages of opioid use without a medical prescription. (Researchers have not studied elderly populations enough in this regard.)

Summary

The research teams from Johns Hopkins University (JHU) and the University of Washington (UW) presented their work. The JHU team looked at substance use trajectories from adolescence through adulthood, with particular focus on urban areas and minorities. Research found that adolescent-onset of cannabis use (regardless of whether it continues into young adulthood) increases vulnerability for opioid misuse in young adulthood (highlighting the need for early prevention). This could be a notable point of note for policy makers looking to legalize cannabis to combat the opioid epidemic, in that potential unintended consequences may arise for adolescents.

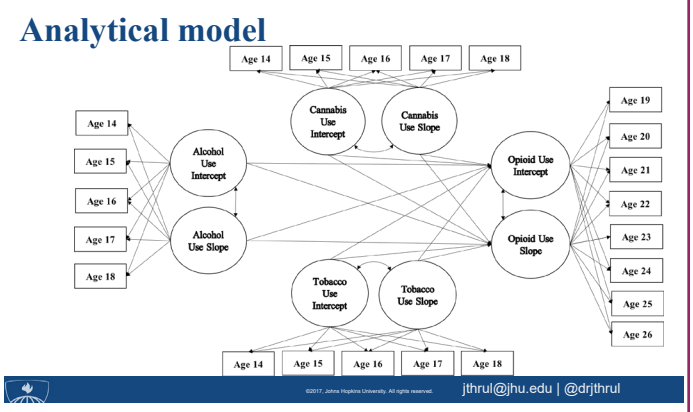
Researchers from UW presented their development of an implicit association test (IAT) looking at opioids and risk perceptions among late adolescents in the Seattle area who are at higher risk for current or future opioid misuse. They found that youth were more likely to associate opioids with risk and statistically weakly associated with self-reported opioid risk perceptions. Future research may consider validation of the research in older or clinical populations who report more opioid use without medical prescriptions.

HPI Strategic Area 1: Identifying Risk for Opioid Use

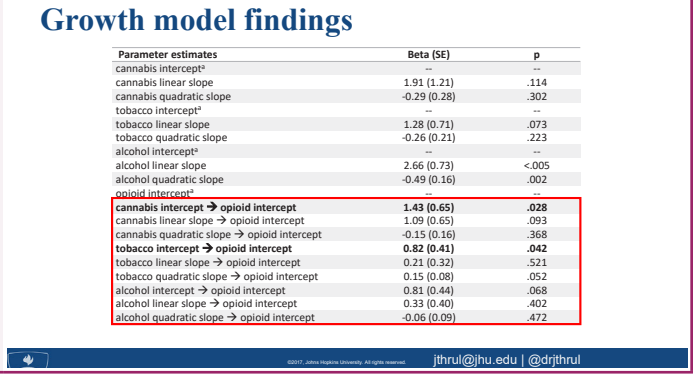
RECAP

Dr. Nicholas Ialongo introduced a presentation by Drs. Johannes Thrul and Jill Rabinowitz, of Johns Hopkins University, and Dr. Beth Reboussin, of Wake Forest University. Their project is based on data from Hopkins Second Generation Universal Preventive Intervention Trial. Fielded in 1993 in 27 first-grade classrooms in nine Baltimore City public elementary schools, the trial aimed to test whether greater intervention impact could be achieved by (1) combining the Good Behavior Game with an academic instruction intervention and (2) involving parents in supporting child behavioral and academic success. The proximal targets of the intervention were early aggressive course of behavior or low academic performance. The distal targets were antisocial behaviors and substance and mental health disorders. Students were randomly assigned to one of three first-grade classrooms in each of the nine schools. One classroom combined the Good Behavior Game with an academic instruction intervention; one had an intervention that included a social learning-based care component, along with parent-teacher components; one was a control.

As an update to the 1993 trial, Johannes presented an analytical model published in *Addiction* in March of this year [2021]. The current team's goal was to investigate the association between developmental trajectories of cannabis, tobacco, and alcohol use in adolescence and opioid use in young adulthood in an urban cohort over the span of 12 years. This study included 583 participants—87% of whom were African American and 55% male—who were originally recruited as first-grade students in nine elementary schools in Baltimore. The team assessed cannabis, alcohol, and tobacco use annually from ages 14 to 18 and opioid use from ages 19 to 26. Sociodemographic status was assessed at age 6, and intervention status was also randomly assigned at age 6. Gender, race, free or reduced-price lunch, and intervention status were covariates in this inddividual and sequential growth models.

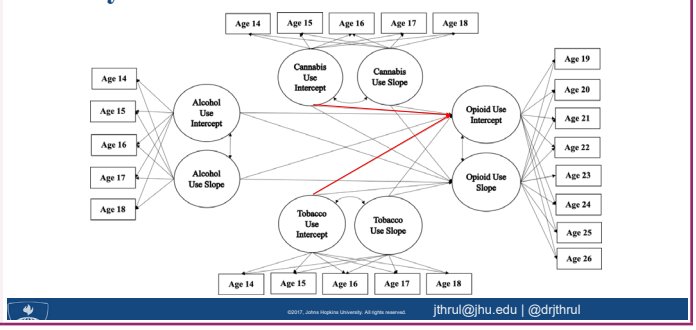


Johannes and colleagues found significant positive association between cannabis use intercept at age 14 and opioid use intercept at age 19, as well as a significant association between tobacco use intercept at age 14 and opioid use intercept at age 19.



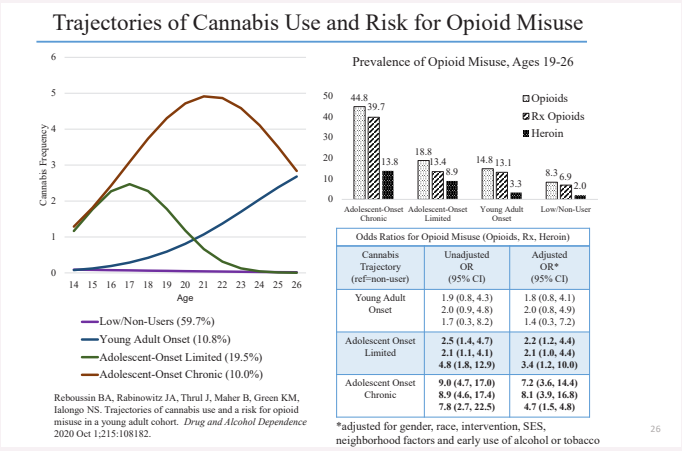
Parameter estimates	Beta (SE)	p
cannabis intercept[a]	--	--
cannabis linear slope	1.91 (1.21)	.114
cannabis quadratic slope	-0.29 (0.28)	.302
tobacco intercept[a]	--	--
tobacco linear slope	1.28 (0.71)	.073
tobacco quadratic slope	-0.26 (0.21)	.223
alcohol intercept[a]	--	--
alcohol linear slope	2.66 (0.73)	<.005
alcohol quadratic slope	-0.49 (0.16)	.002
opioid intercept[a]	--	--
cannabis intercept → opioid intercept	**1.43 (0.65)**	**.028**
cannabis linear slope → opioid intercept	1.09 (0.65)	.093
cannabis quadratic slope → opioid intercept	-0.15 (0.16)	.368
tobacco intercept → opioid intercept	**0.82 (0.41)**	**.042**
tobacco linear slope → opioid intercept	0.21 (0.32)	.521
tobacco quadratic slope → opioid intercept	0.15 (0.08)	.052
alcohol intercept → opioid intercept	0.81 (0.44)	.068
alcohol linear slope → opioid intercept	0.33 (0.40)	.402
alcohol quadratic slope → opioid intercept	-0.06 (0.09)	.472

More frequent use of cannabis and tobacco at age 14 was associated with more frequent use of opioids at age 19. So, cannabis and tobacco use in early adolescence may be risk factors for opioid use in young adulthood among African Americans living in urban areas.

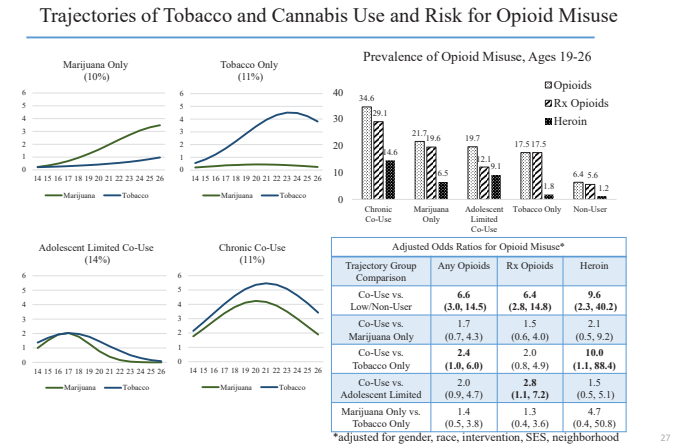


HPI Strategic Area 1: Identifying Risk for Opioid Use

Beth built on Johannes' analysis, focusing on identifying subgroups of substance use trajectories from adolescence to young adulthood. There is likely a great deal of heterogeneity in the longitudinal patterns of use that might reflect different etiological pathways and susceptibilities to opioid misuse. First, she and her team examined cannabis use and identified four trajectories: no use, young adult onset, and two adolescent onset trajectories (limited and chronic). They examined the prevalence of opioid misuse in young adulthood, both overall and specific to prescription opioids and heroin, by these trajectory subgroups. The trajectories for opioid misuse were highest for those who started using cannabis in adolescence and continued using into young adulthood. Even adjusting for other risk factors, adolescent cannabis use—whether it continues into young adulthood or declines—increases vulnerability to opioid misuse. Beth notes that these findings highlight the importance of early prevention and should raise a note of caution to policy makers who perceive cannabis legalization as a means to combatting the opioid crisis, given the potential for unintended consequences for adolescents.



Similarly, because of the high rates of co-use of cannabis and tobacco, Beth and colleagues examined dual trajectories of cannabis and tobacco use and found four use trajectories representing adolescent onset: chronic co-use, adolescent limited co-use, marijuana only, and tobacco only. They found that the risk for opioid misuse was greatest for adolescent onset chronic co-users of cannabis and tobacco, consistent with many other studies that have shown poorer outcomes associated with co-use of these products. Beth remarks that as cannabis becomes more widely available, and alternative modes of tobacco use that facilitate co-use are increasing among youth and young adults, these data highlight the need for the development of early interventions that address co-use of these substances.



Jill's study sought to examine whether the associations between alcohol and cannabis with opioid misuse were partially genetically driven and whether sex differences existed in these associations. Her team leveraged summary results from large-scale Genome-Wide Association Studies (GWAS) on alcohol and cannabis use and examined whether polygenic risk scores (PRS) for these phenotypes were associated with lifetime opioid use in the sample under study.

In the whole sample, Jill and colleagues found that alcohol and cannabis use PRS were associated with opioid misuse when adjusting for participant sex, intervention status, cohort, and genetic ancestry principal components.

Higher lifetime cannabis use PRS, higher maximum drinking PRS, and higher alcohol consumption PRS were all associated with greater risk for misusing opioids in one's lifetime.

Study Findings

Higher polygenic risk scores for cannabis and alcohol use are associated with greater risk for misusing opioids.

Table 2. Cannabis and alcohol consumption PRS associations with likelihood of ever opioid misuse in the whole sample (N = 1,103)

	Opioid Misuse				
PRS	**aOR (95% CI)**	***p***	**AUC**	**S80**	**Δ R^2 (%)**
Lifetime cannabis use PRS	1.33 (1.05, 1.69)	0.017	0.64	0.32	1.2%
Heavy drinking PRS	1.31 (1.06, 1.62)	0.013	0.63	0.41	1.3%
Alcohol consumption PRS	1.30 (1.04, 1.64)	0.023	0.62	0.41	1.1%

Note. Participant sex, intervention status, cohort, and 10 ancestry-specific principal components were included as covariates.
AUC = area under the curve; S80 = sensitivity corresponding to 80% specificity.

HPI Strategic Area 1: Identifying Risk for Opioid Use

Jill noted that when participants were stratified by sex, cannabis and alcohol use PRS were specifically associated with opioid misuse among males but not females. Overall, consistent with the common liability hypothesis of addiction development, findings suggest an overlap between the genetics of alcohol/cannabis and those of opioid misuse. Explanations for the sex difference observed include that different environmental factors may influence opioid misuse differently by sex. For example, some work suggests that greater exposure to poverty and lower socioeconomic status was associated with prescription opioid misuse among females but not males. Moreover, women seeking treatment for opioid use disorder are more likely than men to have experienced trauma and to have greater psychiatric comorbidities; it is thought that environmental stressors might account for greater variance in opioid misuse in women relative to men.

Study Findings

Findings from sex-stratified analyses indicate that higher polygenic risk scores for cannabis and alcohol use are associated with greater risk for misusing opioids among males, but not females.

Table 3. Sex-stratified analyses involving associations between the cannabis and alcohol consumption PRS with likelihood of ever opioid misuse

	Opioid Misuse				
PRS	**aOR (95% CI)**	***p***	**AUC**	**S80**	**Δ R^2 (%)**
Males					
Lifetime cannabis use PRS	1.56 (1.10, 2.21)	0.013	0.67	0.38	2.9%
Heavy drinking PRS	1.59 (1.17, 2.17)	0.003	0.67	0.40	3.9%
Alcohol consumption PRS	1.68 (1.18, 2.39)	0.004	0.67	0.40	4.1%
Females[b]					
Lifetime cannabis use PRS	1.21 (0.87, 1.67)	0.261	0.64	0.38	0.50%
Heavy drinking PRS	1.08 (0.79, 1.47)	0.627	0.63	0.38	0.09%
Alcohol consumption PRS	1.06 (0.77, 1.45)	0.718	0.63	0.38	0.05%

Note. Intervention status, cohort, and 10 ancestry-specific principal components were included as covariates. AUC = area under the curve; S80 = sensitivity corresponding to 80% specificity.

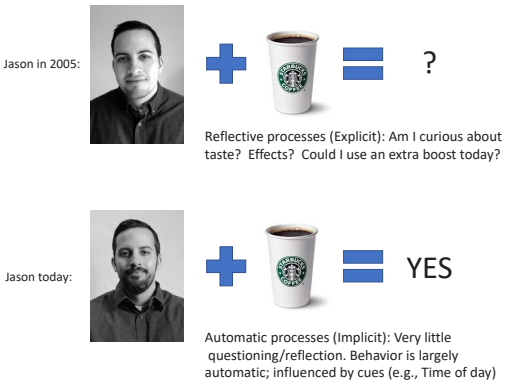
Dr. Jason Ramirez introduced himself as a research assistant professor at the University of Washington. He said that he would be talking about the development of an Implicit Association Test (IAT) to measure implicit associations between opioids and risk perceptions among late adolescents. He also would discuss the Teen Identity Project (TIP) Supplement, an R21 brief longitudinal study that recruited late adolescents (ages 15–18_ in the Seattle area; over three-quarters of them were recent marijuana users. Jason believed there was a unique opportunity to develop a new implicit measure assessing opioid and risk among a sample of adolescents at higher risk for opioid misuse. The aims of this supplement were to (1) develop the novel Opioid-Risk IAT to measure associations between opioids and risk among late adolescents), (2) examine descriptive statistics and psychometric properties of the Opioid-Risk IAT, and (3) examine the concurrent validity of the Opioid-Risk IAT.

When considering important risk factors for prevention and screening, it is important to recognize implicit cognitive processes that can act as risk factors for misuse. These implicit cognitive processes are recognized by dual-process models of substance misuse—models that distinguish between explicit and implicit cognitions.

Explicit cognitions are those that are slower and more reflective, such as reasoning; implicit cognitions are faster, reflexive, and automatic. Dual-process models recognize that both types of processes are risk factors for substance use.

Some theories posit that the influence of implicit processes strengthens as substance use becomes habitual and escalates over time. Implicit (or indirect) measures attempt to assess implicit cognitions and are less prone to self-awareness—substance users may lack insight into cognitive processes underlying their own behaviors.

As an example to illustrate the influence of explicit and implicit cognitive processes, Jason referred to his own life in 2005, when he began drinking coffee. Whether or not he would drink coffee on a given day was an open question. The decision was generally guided by explicit or reflective processes. He may have been curious about the taste or the effects. Now, whether or not to drink coffee on a given day is an automatic "yes." He has built associations, potentially implicit associations, between coffee and his morning routine and being alert.

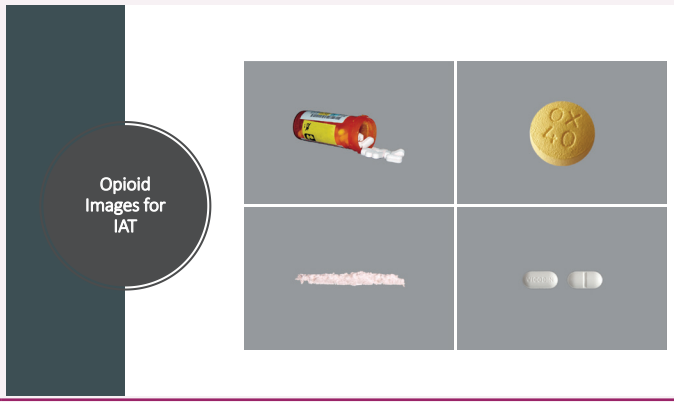


HPI Strategic Area 1: Identifying Risk for Opioid Use

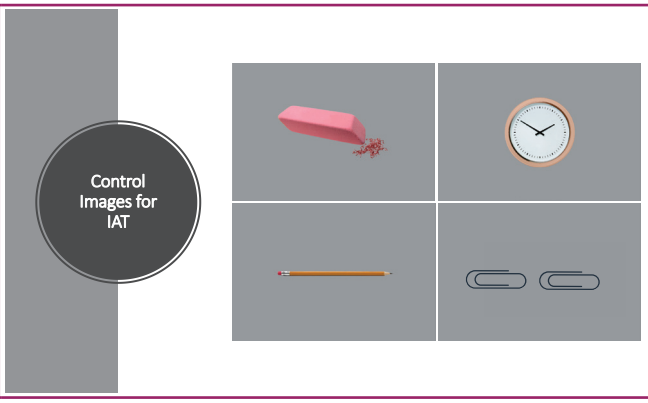
IATs, which seek to measure these implicit cognitive processes, were originally developed to assess implicit bias and racism and are very much used today in that domain. IATs have been adapted to the substance use field, and evidence supports the utility of IAT scores as predictors of problematic alcohol and tobacco use. Participants in Jason's study were presented with stimuli from four categories. Each stimulus was presented individually on a computer screen, and the participant was asked to categorize it by pressing one of two keys. For example, in some trials, participants were asked to categorize opioid images and "risk" words with the left key, and office images and "safe" words with the right key. After a number of trials, those contingencies were switched and participants were asked to categorize opioid images and "safe" words with the left key and office images and "risk" words with the right key. The researchers then calculated the D-score, which measures the extent to which one was faster categorizing opioids with risk words relative to categorizing opioids with safe words. There has been very little work with IATs with regard to opioids and prescription drugs. Some evidence suggests that stronger implicit associations between heroin and pleasure are associated with greater frequency of heroin use.

In the TIP Supplement, Jason's team ran three focus groups to inform stimuli selection for Opioid-Risk IAT. From those focus groups, they came up with stimuli to represent the categories "Dangerous," "Safe," "Opioid," and "Neutral." They used the following words as stimuli to represent the *"Dangerous" and "Safe" categories: Dangerous, Harmful, Risky, Toxic and Safe, Gentle, Innocent, Peaceful*.

The four opioid images selected from focus groups are easily recognizable and adolescents perceive them to be a good fit for their perception of prescription opioids.



The four control images selected are ideally images of things that adolescents would have very little association with regard to risk and safety. They were selected to roughly match the shape, size, and orientation of the opioid images.



HPI Strategic Area 1: Identifying Risk for Opioid Use

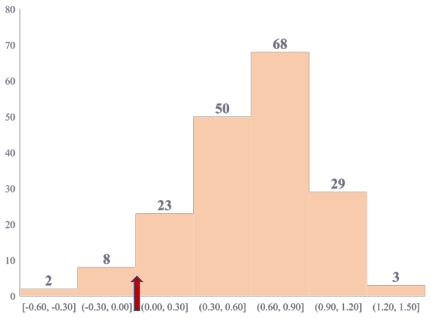
Jason and colleagues implemented the Opioid-Risk IAT into their larger study and it, along with opioid self-report measures, was completed by 138 participants ages 15–18. To increase the sample size, they recruited 50 additional marijuana-using teens in the same age range. Thus, the combined sample consisted of 188 participants: 53% were female, 82% White, 66% in high school, 21% in college, with a mean age of 16.9 years (SD = 0.9). Nonmedical use of prescription opioids in their lifetime was reported by 15.6%, a much higher percentage than would be expected for this age range in a completely random sample, but this limited their ability to examine the predictive validity of the IAT with regard to use itself.

Jason presented the distribution of scores on the IAT. The mean score was 0.61 (SD = 0.34). The main takeaway is that the vast majority of scores (178 of 188) were positive. A positive score on this IAT means that participants were faster in categorizing opioids with risk and danger words than in categorizing opioids with safe words.

Many of these scores were quite positive by the standards of the IAT, reflecting strong associations between opioid and risk. Internal consistency (i.e., split-half reliability) was r = 0.45, certainly lower than what is seen in self-report measures but in line with substance-related IATs.

Descriptive Statistics

- The mean opioid-risk IAT score was 0.61 (*SD* = 0.34).
- Internal consistency (i.e., split-half reliability) was *r* = 0.45.



Jason and his team found acceptable psychometric properties and descriptive statistics. Scores on the Opioid-Risk IAT were associated with self-reported risk perceptions of opioids and opioid misuse willingness in expected directions (column 3 of the table on the slide). However, they were weakly associated with self-report measures and significantly so only for opioid misuse willingness.

Zero-order correlations

- N = 188, Gender coded male = 0, female = 1,
- Higher scores on Opioid-Risk IAT indicate faster reaction times when opioids were paired with dangerous.
- * p < .05, *** p < .001

Correlations among primary study variables

Variable	1.	2.	3.	4.	5
1. Gender	--	--	--	--	--
2. Age	-0.18*	--	--	--	--
3. Opioid-Risk IAT	-0.14	0.08	--	--	--
4. Opioid Risk Perceptions	0.09	-0.01	0.15	--	--
5. Opioid Misuse Willingness	0.13	-0.14	-0.10	0.44***	--

Note. N = 188. Gender coded male = 0, female = 1. Higher scores on Opioid-Risk IAT indicate faster reaction times when opioid paired with dangerous; higher scores for opioid risk perceptions indicate greater perceived risk; higher scores for opioid misuse willingness indicate greater willingness to misuse. * $p < .05$, *** $p < .001$

Jason summarized that they developed an IAT that does its job and is validated by psychometrics and descriptive statistics. They found that the group of late adolescents were demonstrating the stronger associations between opioid and risk that they hoped to see. In this study, they were limited in their ability to assess the IAT's potential to act as a screening tool and establish predictive validity. He noted it would be useful to see the IAT included in a future study, potentially for a longer longitudinal study, where there would be more an opportunity to see whether scores on the IAT may predict initiation of use that potentially occurs over a longer time frame.

Take Home

- **Most scores (94%) on the opioid-risk IAT were positive, indicating faster reaction times when opioid images were paired with "dangerous" words compared to when paired with "safe" words.**
- **Participants' IAT scores were not associated with willingness to misuse opioids, and were only weakly, positively associated with self-reported opioid risk perceptions. However, only 15.6% of the sample reported NMPO in their lifetime, and it is possible that our ability to examine the IAT's concurrent validity was limited in this sample.**
- **Future research may consider validation in older and/or clinical populations that report more NMPO. Further, the IAT may be examined in longer longitudinal studies for which rates of use may be expected to increase over time.**

HPI Strategic Area 1: Identifying Risk for Opioid Use

Barbara read a question from the chat: Early upstream prevention efforts to reduce cannabis, alcohol, and tobacco use are critical to opioid prevention in early adulthood – is this correct? Nicholas asked Jill, who wrote a paper in which she predicted opioid use from first-grade baseline characteristics, what the best predictors were at age 6. Jill responded that early childhood aggression was the most robust predictor for opioid misuse at age 30. Phillip Graham asked if this is across all youth or certain subpopulations, and Jill confirmed it is the same sample from Nicholas' study—low-income African American students in Baltimore. Nicholas clarified that all interventions were universal, meaning the participants were in mainstream classrooms and not selected for being at higher risk.

Barbara read a question from the chat: Prevention principles have previously discouraged drug-specific prevention; do you feel we are moving toward reversing this? Beth noted that her findings argue for drug-specific prevention. There are associations with cannabis, tobacco, and alcohol use predicting opioid use. With co-use that risk is higher. Johannes agreed that drug use should be looked at more generally; co-use has a different impact on treatment outcomes and has specific triggers for relapse.

Barbara read another chat question: Is there space for prevention among young people who have already begun using specific drugs but have not advanced to problematic opioid use? Beth answered that if the root of their substance use is environmental, there is space for intervention (e.g., density of alcohol outlets in neighborhoods, policy efforts). Jason noted that in his study, the sample was largely teens who had used marijuana; most would probably self-report that they do not view marijuana as being very risky and IATs would reflect that.

Nicholas pointed out that evidence shows these preventive interventions work. The father of modern-day prevention, Shep Kellam, has talked about nested universal selective indicated interventions and treatment services across the lifespan. It is important to examine effects across the lifespan.

Barbara introduced Dr. Amy Goldstein to lead the next section.

HPI Strategic Area 2: Social Determinants, Health Equities, and Policy

3:40–4:10 p.m.

Key Takeaways

- Theme: Social determinants of health must be considered and factored into substance use prevention work.
- Evidence shows that risk factors at each stage of life further expand the inequities over the life course and lead to issues for future generations as well.
- Long-lasting protective interventions (e.g., smoking cessation interventions), changing the context where individuals live, and socioeconomic factors matter much more to population impact than treatment interventions.
- Recommendations for policy makers and medical leaders based on a study done on West Virginia prescribing laws include
  - wider stakeholder involvement in law and policy development,
  - improved anticipation of related harms to law enforcement,
  - fail-safes to avoid patient abandonment, and
  - improved knowledge of and access to non-opioid treatments for pain in rural communities.

Summary

This session focused on social determinants of health and how they must consider a wide spectrum of factors such as economic stability, social and community context, neighborhood and environment, health care, and education. Discussion noted that inequities in those areas—even before conception (inequities faced by the parents)—will affect birth outcomes and early childhood development, as well as later life stages. Risk factors present at each stage of life further expand the inequities over the life course and hence the need for early preventive work. Long-lasting preventive interventions that target social factors have a major effect on population impact. The presentation focused on the reasons for doing prevention work and the various prevention framework "buckets," from the traditional to the innovative to the total community or population. Examples were, respectively, increasing the use of evidence-based services in clinical settings, providing services outside the clinical setting, and implementing interventions that reach whole areas.

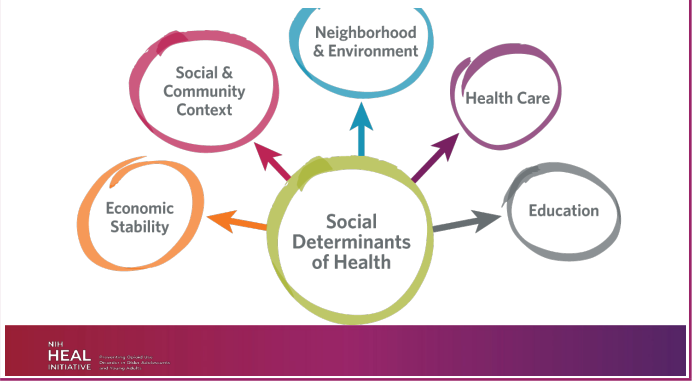
An impact study of recent restrictive opioid prescribing laws in West Virginia, which limit ongoing opioid prescriptions to 30 day supplies and first-time prescriptions to 7-day supplies, identified the effects that policy can have on treatment. The main recommendation based on this study was that lawmakers and medical leaders need to anticipate the ramifications of policy changes and be ready for the fallout with more resources available across the board. This approach includes wider stakeholder involvement in the development of those laws, improvement of knowledge of and access to non-opioid treatments for pain in rural communities, and fail-safes for patients to prevent their falling out of treatment because they lack access to care.

HPI Strategic Area 2: Social Determinants, Health Equities, and Policy

RECAP

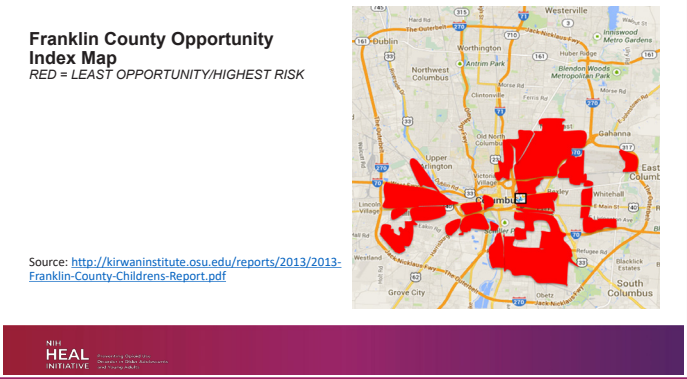
Amy noted that increasing attention is being paid to the role of social determinants in opioid and other substance misuse. There has been a lot of attention on individual-level risk, but researchers are noticing community- and society-level risks that go beyond the individual. HPC is evaluating the role of context and structural factors in the prevention of opioid misuse, and that could be intervening directly on social determinants or looking at policy research. Amy introduced Dr. Kelly Kelleher as the first speaker.

Kelly showed a picture of his 1-year-old grandson and said that he hopes everyone recognizes in their work that they are discussing the futures of individual children. He then presented a graphic of the social determinants of health. He noted that he will focus less on a review of his study and more on why he does this work. The whole idea that the economy, social and community context, neighborhood and environment, health care, and education can play into drug abuse and addiction is grossly underexplored.



Kelly noted that for every phase of the escalation of risk—from drug initiation to active drug use to addiction to nonfatal and even fatal overdoses—there are papers demonstrating the association of these with social determinants. These are all [aspects] of risks well within the boundaries of individual risk for whole groups of children and communities.

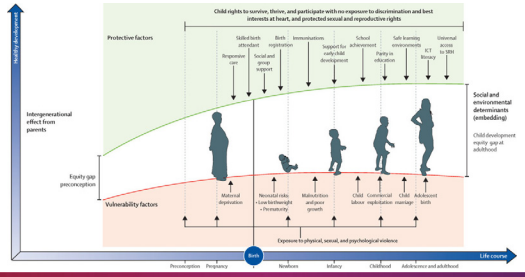
Kelly used Franklin County as an example of how this plays out. He showed the Opportunity Index Map for the county in which previously redlined communities are colored red. These communities account for about 30% of the population in Columbus, but they account for 60% of overdose episodes, 65–70% of gunshot injuries reported in emergency rooms, and 70% of the infant mortality. Furthermore, these risks are so severe that distances as small as 1 mile separate neighborhoods with a 30-year gap in life expectancies.



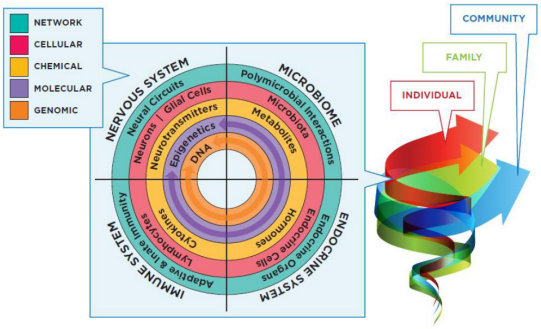
HPI Strategic Area 2: Social Determinants, Health Equities, and Policy

Kelly showed the UNICEF Life Course model, which demonstrates that inequities occur before conception. It is known that the health of the mother and father before conception influences birth outcomes, and each stage further expands the risk factors through the life course. That explains why there are generational life expectancy differences. These risks accrue through very basic processes.

UNICEF Lifecourse

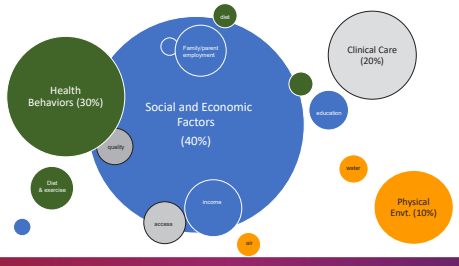


These processes have been described well by the National Academy of Medicine, as shown in the slide. They affect telomeres and epigenetics (the expression of genes) as well as interaction with the environment in complex systems. They alter the immune and nervous systems, the microbiome, and the endocrine system—and not just in the individual; these changes are contagious in families. There are community and neighborhood differentials—for example, neighborhoods can transmit obesity and depression and other risk factors for poor outcomes, especially for addiction and substance use.



Studies suggest that the clinical care we provide is limited to 20% of population outcomes in health, and even less in children (15%). What really drives health outcomes are health behavior and social and economic factors.

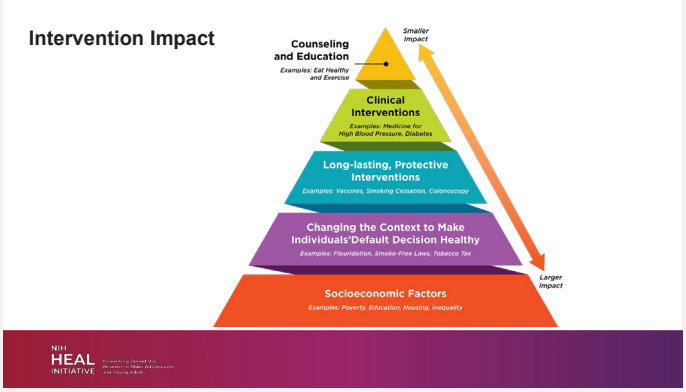
Population Health – Social Determinants



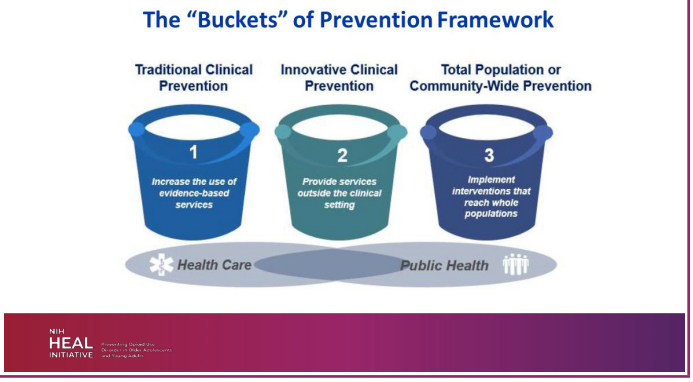
HPI Strategic Area 2: Social Determinants, Health Equities, and Policy

The CDC has come up with an Intervention Impact pyramid. The very top (with the smallest impact) is the counseling and education provided to individuals. Under that are clinical interventions such as medicine for high blood pressure. These top two buckets account for 92% of health care dollars.

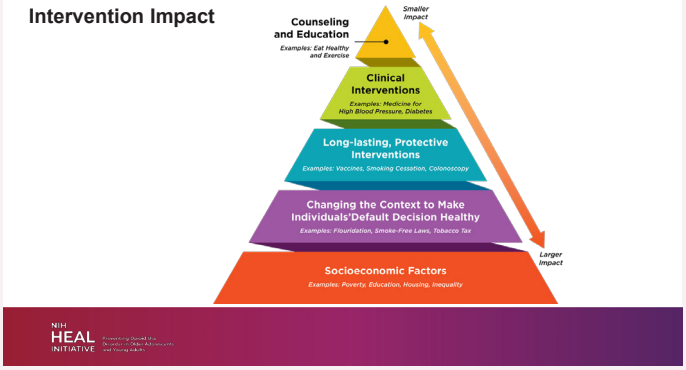
But according to the CDC, long-lasting, protective interventions; changing the context to make individuals' default decision healthy; and socioeconomic factors matter much more in population impact. Long-lasting interventions include vaccines, smoking cessation interventions, and colonoscopies. Changing the context can include fluoridating water, passing smoke-free laws, and implementing a tobacco tax—changes that make it easy for people to change the way they behave in a community. And last, socioeconomic factors, such as poverty and education, are the most important in influencing population health outcomes.



Kelly presented the "buckets" of prevention. Most health care money goes into the first bucket: "Traditional Clinical Prevention"—how an individual prevention specialist going provides a prevention intervention for an individual child or adult. The second bucket, "Innovative Clinical Prevention," is delivered outside a health care setting. The third bucket is "Total Population or Community-Wide Prevention." How do we deliver community-wide prevention that includes social factors? It is important to acknowledge that delivering interventions comes second to having a place to sleep and food to eat.



Kelly presented the CDC's HI-5 pyramid of effective, well-documented interventions that create positive health outcomes in the community. Changing the context includes evidence-based activities like pricing strategies for alcohol products, tobacco control interventions, safe routes to school, etc. Many of these are known to the drug addiction and use field. Kelly's team is investing locally in school-based programs to increase physical activity, school health care settings, and school prevention programs. Changing the context is changing where and how care is delivered. Social determinants are where the real investment comes in. Early childhood education expansion is one of the major investments he works with. His team has also partnered with the city and county for several million dollars' worth of home improvement loans and grants. They have set up tax clinics for low-income working families to help them use the earned income tax credit. This past year, they returned more than a million dollars to families through these clinics. They are enrolling 10,000 children in Supplemental Social Security Income. And as part of the HEAL initiative, in a randomized trial with 240 youth experiencing homelessness, they are testing whether housing first initiatives can improve health outcomes and prevent drug use and addiction.



HPI Strategic Area 2: Social Determinants, Health Equities, and Policy

Why might hospitals invest in these kinds of programs? First, it is the ethical thing to do; science has shown that social settings matter. Hospitals also benefit in many ways. Kelly noted that his hospital's grant receipts from local, state, and federal sources have increased dramatically since the hospital began working with social determinants of health. Philanthropy has also increased; there have been new donors. The hospital has an accountable care program in which it is paid a fixed fee per child; reducing costs by making children's health outcomes better saves health care dollars. Finally, a hospital investing in its communities wins many political battles, especially when looking for tax abatements and partnerships with the city and state.

Kelly showed his grandson again and acknowledged that he had many exposures to risk factors in the health care system. However, Kelly noted that the local health care system takes a distant second place to the community collaboratives and partnerships in improving the health care of the schools they serve.

Amy thanked Kevin for his presentation and introduced Cara Sedney to present "Assessing the Impact of a Restrictive Opioid Prescribing Law in West Virginia."

Cara noted that West Virginia was one of many states that enacted restrictive opioid prescribing laws; West Virginia's, Senate Bill 273, limits ongoing chronic opioid prescriptions to 30 days' supply and first-time opioid prescriptions to 7 days' supply for surgeons and 3-4 days' supply for emergency rooms and dentists. It requires counseling on the risk of opioids and that one uses the lowest possible dose of opioids. The bill does not apply to some patients, such as cancer patients and those in palliative care. Patients receiving chronic ongoing opioid treatment as of January 1, 2018—3 months before the bill was enacted—are also excluded.

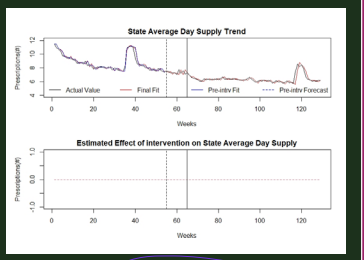
Cara is a spine-focused neurosurgeon, so she was interested in the impact of this law on patients in West Virginia. She and her research team designed a sequential, explanatory, mixed-methods study using interrupted time series quasi-experimental analysis of prescription data from the West Virginia PDMP [prescription drug monitoring program] and an explanatory qualitative explanation that included interviewing stakeholders (prescribers, dispensers, and patients) and conducting a thematic analysis.

They used an ARIMA [autoregressive integrated moving average] methodology and looked at all opioid prescriptions and compared them to benzodiazepines as a control. For both opioids and the control, they calculated the number of unique first-time opioid prescriptions, the number of unique overall opioid prescriptions, the daily MME [morphine milligram equivalents], and days' supply, using a 128-week sequence of data for all variables.

When assessing the average days' supply, they found that it did decrease across the study period; the initial average days' supply was around 11.5 days and the final value was 6.2 days. However, the change was not associated with the law. Taking into account the pre-intervention trend, the law had zero impact on average days' supply. Cara noted that this lack of effect may be because, at the time of legislation implementation, the average days' supply was already at 6.8 days, which is in line with the prescription limitation of 7 days. There was no effect of the law on the control substance.

Results

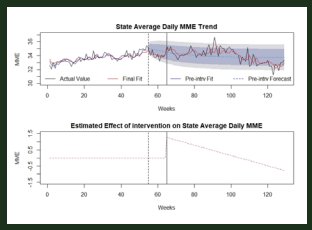
1. Average Days' Supply:
   - Supply decreased across the pre and post-intervention periods
   - The initial average days' supply was 11.5 days and the final value was 6.2 days.



They looked at the daily MME because the law required lowest possible dose; the average daily MME ranged from 31.2 mg to 36.7 mg throughout the study period. There was a notable increase after law enactment, followed by a decrease of less than 1 MME (1.1% change overall).

Results

2. Daily MME
   - The average daily MME ranged from 31.2 mg to 36.7 mg throughout the time period under study

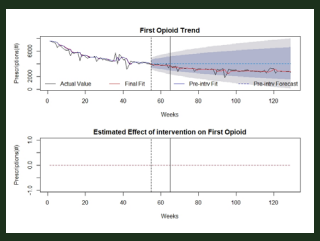


HPI Strategic Area 2: Social Determinants, Health Equities, and Policy

Just over half a million first-time opioid prescriptions were filled in the time period of the study, with most being from family medicine or general practice. Although the number decreased over time, the team did not see any impact of the law on first-time opioid prescriptions. There was no effect of the law on the control substance.

Results

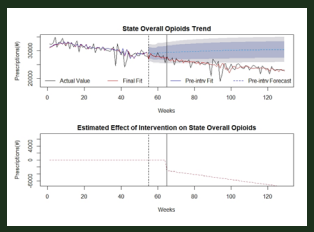
3. First-Time Opioid Prescriptions:
   - 509,233 first-time prescriptions for opioid medications were filled
   - Decreased throughout the entire study period
   - Family medicine/General practice (122,838)



West Virginia filled over 3.5 million overall opioid prescriptions during the entire study period; again, family medicine and general practice were the highest prescribers. This number also decreased substantially, and researchers did see a relationship between the law and prescription that was significant. Cara estimated that there was a 22% decrease in overall opioid prescriptions associated with law implementation. There was no effect of the law on the control substance.

Results

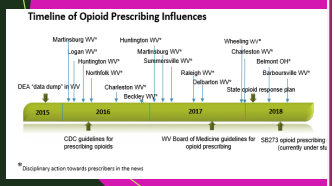
4. Overall Opioid Prescriptions:
   - 3,523,959 overall opioid prescriptions filled through entire period
   - Number decreased throughout the study period
   - Family medicine/General practice (1,285,746)



Overall opioid prescriptions decreased in association with the law without a corresponding decrease in first time opioid prescriptions or days' supply, which were the specific targets of the legislation.
Cara noted that a different methodology is needed to understand why this occurred. She and her team interviewed 20 prescribers, 10 dispensers, and 20 patients, including people with acute or chronic pain who were prescribed opioids and people who use illicit substances. A predominant theme that appeared in many interviews was fear of disciplinary action. Physicians noted that this fear was present before SB273 and provided examples of physicians in their own community who were investigated for opioid prescriptions and lost their practices despite never doing anything wrong.

Prescribers: Fear of disciplinary action

- "the fear of having your license taken away or the fear of imprisonment, or you've been burned by the DEA as someone who has been negligent, that will take over."
- "[It] really started to scare a lot … of providers into feeling that it wasn't worth the risk to continue to prescribe for fear of being labeled as an over prescriber or being outside of the norm or, you know, the potential liability that goes along with it."
- "They were coming in and busting a lot of docs and then making it so… that we didn't need that law to be afraid."



When SB273 was enacted, many physicians noted that it was the last straw for them; either they or other prescribers would not prescribe opioids at all. This coincides with the team's quantitative data, explaining why there was a decrease in overall opioid prescriptions but no change in the metrics measured in the law; it was more of an emotive decision.

Prescribers: Opioid legislation exacerbated prescriber fear → refusal to prescribe

"[SB273] ended up affecting mostly the responsible prescribers of opioids. The people who were already doing due diligence ended up being the ones who were concerned about the law because all the irresponsible prescribers I think were already getting obliterated."

"Almost all prescribers in West Virginia have cut it back, a few that still do it, really do so at great risk to themselves. I think the law that occurred in 2018, really, if anything shifted us to a place where there's not enough opioid prescribing for many painful conditions that aren't treatable with other means."

HPI Strategic Area 2: Social Determinants, Health Equities, and Policy

Physician participants also noted subsequent care shifts and treatment gaps as a result of these changes. Patients were abandoned when physicians refused to prescribe opioids and turned to other physicians who were forced to shoulder that responsibility and possible liability. Frequently, the local infrastructure was not able to accommodate this influx; prescribers wanted to know where these patients went after leaving their offices.

Prescribers: Care shifts and treatment gaps resulted from disciplinary actions and legislation

- "Every time a physician is raided or arrested, we get several hundred referrals of those patients who are, either appropriately or inappropriately on opioids, that we have to sort out."
- "When these prescribers were shut down by the, either Board of Medicine or the DEA, we had to pick up the pieces as other local physicians-- well, we would get an influx of patients from these doctors each time"

Compounding these shifts was a lack of good alternatives for chronic pain, especially in rural communities. Pain clinics were characterized as inaccessible, and alternative treatments were frequently not covered by insurance.

Prescribers: Lack of available and efficacious alternatives for opioids for chronic pain

- *"…but instead of making me take drug diversion training [required for state licensure] and learn how many people are OD-ing on heroin, why don't you make me take a three-hour course on how to treat pain without a narcotic?"*
- *"But you know what, there's no alternative. The alternative issues come from insurance issues. For example, we know that aqua therapy, pain clinics with their interventions and even acupuncture and so forth, they help, but insurances will not cover."*

The physicians' general hypothesis about where these patients went after they left the physician's office was that the patients transitioned to using illicit substances.

Prescribers: Transition to illicit substances

- "[T]hey show up at my door a year later, using heroin for a year… saying, 'I need help.' And I said, 'Well, what happened?' 'Well, I was getting a legitimate prescription, and then they stopped…' And it's definitely, honestly, it's a lot more now than what it was before this legislation."
- "That was a big problem and a big oversight on behalf of law enforcement and the physician community… We didn't have a good plan when we got these doctors down. We didn't- we didn't go in and find all these patients and… pick up the pieces from these patients. So that we could appropriately taper them and in a way that managed … their withdrawal symptoms and their dependency without them turning to the illicit market. And I think that's a big source of a lot of our problems."

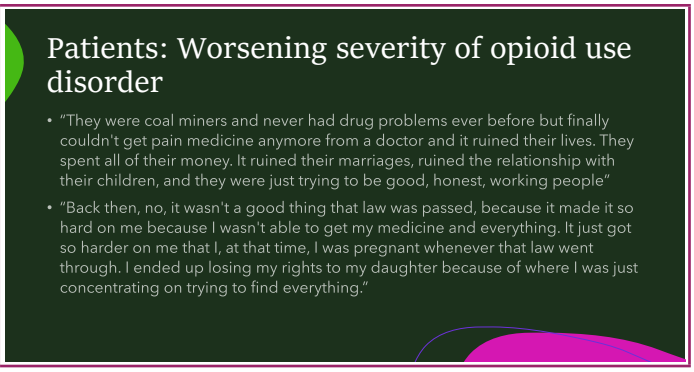
The patient interviewees confirmed that they did use illicit substances when their physicians stopped prescribing opioid medications. Patients who were transitioned to buprenorphine reported being satisfied with the pain control afforded by the medication and avoided the secondary harms associated by others who were not transitioned.

Patients: Transition to illicit substances

- "They were cracking down on all of that. There was no doctors taking new patients to prescribe opiates. Nobody would do anything and I couldn't go to the ER, I couldn't do anything because then you'd be a drug-seeker. I had to come back to the street and pretty much supply all my needs that way."
- "I wanted to stay doing the painkillers, but I just couldn't find them anywhere, so I took some Valium that the doctor had prescribed me. I traded the Valium for some heroin"

HPI Strategic Area 2: Social Determinants, Health Equities, and Policy

Nearly all the patients interviewed who used illicit substances started with chronic pain. Even if they wanted to self-treat pain, they often ended up with synthetic opioids, and for many participants, this resulted in severe opioid use disorder.



In conclusion, SB273 was associated with opioid prescribing changes, but not in the way intended by the law. Opioid prescribing was already declining significantly before the law's implementation. The law may have exacerbated this and its related harms. Cara inquired what we can learn from this. She encourages policy makers and medical leaders to incorporate some of the following: wider stakeholder involvement in law development, improved anticipation of related harms, fail-safes to avoid patient abandonment, and improvement of knowledge of and access to non-opioid treatments for pain in rural communities.

Amy read a question for Cara: Were there any educational outreach/academic detailing programs (or related initiatives) in place during the study period that could have potentially influenced your results? Cara answered that while many things occurred in 2018, the strength of their modeling was that it can really target effects around one date.

Amy read another question about how the use of Z codes in epidemiological surveillance can be improved. Kelly commented that geospatial is very important when looking at outbreaks, as evidenced by COVID-19 and flu real-time emergency room data. He notes we should be doing this for opioid surveillance as well, but Z codes are not used widely and improving the coding is important. He suggested looking at other indicators in electronic health records and exchanges that are sensitive besides Z codes; there are also good public databases that can look at geospatial risk and are being indexed.

Someone asked whether social determinants have been standardized and have a place in health records. Kelly noted that CMS has a large national trial to this, although it is not yet standardized.

Someone asked Cara whether she examined inappropriate curtailing of opioids in her study. Cara noted that the PDMP data she used did not have that information, but she is interested in obtaining it to verify qualitative data. In discussing how to do more evidence-informed policy decision making, she pushes for the use of qualitative research and story sharing, because her local lawmakers make decisions based on constituents, not just quantitative evidence.

Aria Crump noted that NIDA remains interested in research regarding social determinants of health. NIDA released this non-binding notice last summer: https://grants.nih.gov/grants/guide/notice-files/NOT-DA-21-050.html. They are interested in multilevel interventions that address social determinants.

In response to a question on community health assessments and programs, Kelly said that community hospitals are required to do needs assessments to maintain their not-for-profit status. However, in his work in Appalachia, he saw that community needs around addiction were ignored by most of the hospitals because they did not have the expertise and there is stigma associated with these interventions. He commented that stigma and expertise must be addressed to properly integrate community needs.