Baltimore City Health Department
1001 E. Fayette Street • Baltimore, Maryland 21202
Stephanie Rawlings-Blake, Mayor
Leana Wen, M.D., Commissioner of Health

America's Heroin and Opioid Abuse Epidemic
Testimony of Dr. Leana Wen, Baltimore City Health Commissioner
March 22, 2016

Baltimore City Health Department's "3-Pillars" of Combating Opioid Addiction

1. Prevent deaths from overdose and save lives. I have declared opioid overdose a public health emergency in Baltimore City and led the charge in one of the most aggressive opioid overdose prevention campaigns across the country. We have trained over 8,000 people how to use naloxone. Through a "Standing Order" approved by the Maryland State Legislature, I have written a blanket prescription for naloxone to 620,000 residents, and have started the first-of-its-kind online naloxone training.

2. Increasing access to on-demand treatment and long-term recovery support. Baltimore City has taken several actions to improve access to on-demand treatment, including a 24/7 crisis, information and referral phone line (with approximately 1,000 calls/week); securing $3.6M to build a sobering center; hiring of community-based peer recovery specialists; and universal screening for addiction in our hospitals. We strive to establish a 24/7 "Urgent Care" for addiction and mental health disorders and for increased evidence-based programs including diversion from incarceration and wrap-around services such as housing.

3. Provide education to reduce stigma and prevent addiction. We must change the dialogue around substance use disorder. We are leading a citywide effort to educate the public and providers on the nature of addiction: that it is a disease, recovery is possible, and we all must play a role in preventing addiction and saving lives. We have launched a public education campaigns-- "DontDie.org". We have brought together hospitals and ER leaders and have implemented citywide best practices to reduce opioid prescribing.

Working with the Federal Government

While we have made significant progress, there are areas where we face continued challenges. We have four specific areas that should be more comprehensively addressed by the federal government:

1. **Expand funding for and availability of on-demand and wrap-around addiction treatment services**
    a. Allow funding to establish 24/7 treatment centers for addiction and mental health
    b. Ensure equitable insurance coverage for evidence-based addiction services
    c. Expanded funding for wrap-around services (including housing) and diversion programs
2. **Directly fund local jurisdictions with highest need**
    a. Allow innovations with new care delivery models
    b. Encourage community resources for recovery including peer recovery specialists
3. **Improve federal regulations around addiction and overdose treatment**
    a. Monitor and regulate the price of naloxone
    b. Require co-prescription of naloxone to every individual receiving opioid medications
    c. Require "black box warning" on opioids and benzodiazepines
    d. Remove barriers to prescribing Buprenorphine
4. **Fund a national stigma-reduction and opioid-awareness campaign**

CITY OF BALTIMORE
STEPHANIE RAWLINGS-BLAKE, Mayor

HEALTH DEPARTMENT
Leana S. Wen, M.D., M.Sc., FAAEM
Commissioner of Health
1001 E. Fayette St.
Baltimore, MD 21202
health.commissioner@baltimorecity.gov
Tel: 410-396-4387

March 22, 2016

TO: Members of the House Oversight Committee

FROM: Dr. Leana Wen, Baltimore City Health Commissioner

RE: Testimony: America's Heroin and Opioid Abuse Epidemic

Chairman Chaffetz, Ranking Member Cummings and Members of the Committee:

Thank you for inviting me to testify on the epidemic of opioid abuse that is sweeping across our country. Opioid abuse is a public health emergency that is claiming the lives, the livelihoods, and the souls of our citizens.

As an emergency room (ER) doctor, I have witnessed firsthand the effects of substance addiction on individuals and families, including treating hundreds of patients who have overdosed on opioids. I remember well my patient, a 24-year old mother of two who came to the ER nearly every week requesting addiction treatment. She would be told there was nowhere for her to go that day or the next, and would be offered an appointment in three weeks time. Because she lacked housing and other supportive services, she would relapse. One day, her family found her unresponsive and not breathing. By the time she arrived in the ER, it was too late for us to save her, and she died.

I always think back to my patient now: she had come to us requesting help, not once, not twice, but over and over again, dozens of times. Because we do not have the treatment capacity, people looking to us for help fall through the cracks, overdose, and die. Why has our system failed her, just as it is failing so many others who wish to get help for their addictions?

My colleagues and I frequently felt frustrated by the limitations of clinical practice; by the time patients made their way to us, society had missed significant opportunities to intervene farther upstream in that individual's life. We treat addiction differently than we treat any other illness. Would we ever tell someone who has had a heart attack to wait three weeks to get treatment? Despite scientific studies showing that addiction is a disease and that recovery is possible, many still question why people "choose" a lifestyle of using drugs. Would we impose such stigma on any other disease? These are the experiences that drove me to public health: a desire to tackle the epidemic of addiction at a community level, and, in doing so, save lives while also redefining our societal approach to the treatment of addiction.

As the Health Commissioner of Baltimore City, I work every day with my dedicated staff at the Health Department and partners across our city, to prevent overdose and stem the tide of addiction. I am encouraged that the approach to the opioid epidemic is shifting away from the

rhetoric of the "war on drugs" and instead focusing on treating addiction as a disease. But while our rhetoric is changing, funding for treatment lags behind. Of the more than 20 million people who abuse some form of drug, only about 1 in 10 is able to receive treatment. In Baltimore and around the country, our patients come requesting assistance, but are forced to wait weeks, even months, to access needed care.

This struggle is not unique to Baltimore; millions of Americans struggle to find treatment when they are ready to seek it. Ensuring those struggling with addiction can access treatment on-demand requires systems change. We can learn from cities that have taken the lead across the country using innovative approaches to address this national issue; Baltimore is one such city that is at the cutting edge of addiction prevention and treatment.

The Opioid Problem in Baltimore

With over 20,000 active heroin users in Baltimore and far more who misuse and abuse prescription opioid medications, opioid addiction and overdose is a critical health priority in our city. In 2014, 303 people died from drug and alcohol overdose, which is more than the number of people who died from homicide. Drug addiction impacts our entire community and ties into nearly every issue facing our city including crime, unemployment, poverty, and poor health. It claims lives every day and affects those closest to us—our neighbors, our friends, and our family. (For more information about the state of health of the city, please see Appendix A)

Since my appointment in January 2015, I have made overdose prevention and addiction treatment my top priority. I worked closely with Mayor Stephanie Rawlings-Blake to guide the work of the Mayor's Heroin Treatment and Prevention Task Force that released ten bold and progressive recommendations in July 2015. These ambitious recommendations form the framework and guide the roadmap of our efforts, which are led by the Baltimore City Health Department and Behavioral Health System Baltimore, a nonprofit that is the designated behavioral health authority of the city (of which I serve as Chair of the Board), in close coordination with our public and private partners across the city.

Baltimore's Response to Addiction and Overdose

Our work in Baltimore is built on three pillars:

- First, we have to prevent deaths from overdose and save the lives of people suffering from addiction.
- Second, we must increase access to quality and effective on-demand treatment and provide long-term recovery support.
- Third, we need to increase addiction education and awareness for the public and for providers in order to reduce stigma and encourage prevention and treatment.

Our work in each of these areas is multifaceted because addressing a disease like addiction requires a comprehensive approach. We are working tirelessly to change the conversation, and our efforts serve as a model nationally and for other local and state jurisdictions. We know what works for combating addiction but we need help to make sure all who seek treatment are able to

get it. We are all in this together, and Baltimore is happy to share our innovations and lessons learned.

1. Preventing deaths from overdose

In Baltimore, I have declared opioid overdose a public health emergency and led the charge in one of the most aggressive opioid overdose prevention campaigns across the country.

a. The most critical part of the opioid overdose prevention campaign is expanding access to naloxone – the lifesaving drug that reverses the effect of an opioid drug overdose. Naloxone is safe, easily administered, not addictive, and nearly 100% effective at reversing an overdose. In my clinical practice as an emergency physician, I have administered naloxone to hundreds of patients and have seen how someone who is unresponsive and about to die will be walking and talking within seconds.

   Since 2003, Baltimore City has been training drug users on using naloxone through our Staying Alive Program. Last year, we successfully advocated for change in State law so that we can train not only individuals who use drugs, but also their family and friends, and anyone who wishes to learn how to save a life. This is critical because someone who is overdosing will be unresponsive and friends and family members are most likely to save their life.

   Our naloxone education efforts are extensive. In 2015, we trained over 8,000 people to use naloxone: in jails, public housing, bus shelters, street corners, and markets.

   We were one of the first jurisdictions to require naloxone training as part of court-mandated time in Drug Treatment Court. We have trained federal, state and city legislators so that they can not only save lives, but also serve as ambassadors and champions to their constituents.

b. We use up-to-date epidemiological data to target our training to "hotspots", taking naloxone directly into the most at risk communities and putting it in the hands of those most in need. This was put into effect in 2015, when we saw that 39 people died from overdose to the opioid Fentanyl between January and March of 2015. Fentanyl is many times stronger than heroin, and individuals using heroin were not aware that the heroin had been laced with Fentanyl. These data led us to target our messaging so that we could save the lives of those who were at immediate risk. We coordinate our data with agencies across the city including the police department, fire department, and hospitals, so as to ensure our information is complete and our efforts are unified.

c. As of October 1, 2015, I have the authority to write blanket prescriptions for naloxone for the roughly 620,000 residents in Baltimore City under a "Standing Order" approved by the Maryland State Legislature. This is one of the single largest efforts in the country to achieve citywide naloxone distribution. A Standing Order means that someone can receive a short training (which can be done in less than five minutes) and immediately

receive a prescription for naloxone, in my name, without having seen me personally as their doctor.

In order to train even more people in the use of naloxone, we have launched an online platform that now allows residents to get trained online and immediately receive a prescription for naloxone. This online platform, which is the first-of-its-kind around the country and the world, is the next step to reduce barriers to naloxone. In Baltimore, we believe that naloxone should be part of everyone's medicine cabinet and everyone's First Aid kit.

d. Already, our naloxone outreach and trainings are changing the way our frontline officials approach addiction treatment, with a focus on assessment and action. In addition to training paramedics, we have also started to train police officers. The initial trainings were met with resistance from the officers who were hesitant to apply medical interventions that some did not see as part of their job description. However, in the first month of carrying naloxone, four police officers used naloxone to save the lives of four citizens. Recently, I attended a training where I asked the officers what they would look for if they were called to the scene for an overdose. In the past, I would have received answers about looking for drug paraphernalia and other evidence. This time, officers answered that their job was to find out what drugs the person might have taken, to call 911 and administer naloxone, because their duty is to save a life. By no means is naloxone training the panacea for repairing police and community relations. However, it is one step in the right direction as we make clear that addiction is a disease and overdose can be deadly. We are changing the conversation so that all of our partners can join in encouraging prevention, education, and treatment.

e. We successfully advocated for Good Samaritan legislation, which expanded protections for those who assist in the event of an overdose, and malpractice protection for doctors who prescribe naloxone.

f. Our state Medicaid program has agreed to set the co-pay for naloxone at $1. While we still struggle with the pricing for naloxone (see below), this has allowed us to provide prescriptions to patients and others at a greatly reduced cost. We have to get naloxone into the hands of everyone who can save a life—which we believe is each and every one of us.

Some people have the misconception that providing naloxone will only encourage a drug user by providing a safety net. This dangerous myth is not based on science but on stigma. Would we ever say to someone whose throat is closing from an allergic reaction, that they shouldn't get epinephrine because it might encourage them to eat peanuts or shellfish? An Epi-Pen saves lives; so does naloxone, and it should be just as readily available. Our mantra is that we must save a life today in order for there to be a better tomorrow.

2. Increasing access to on-demand treatment and long-term recovery support

Stopping overdose is only the first step in addressing addiction. To treat people with substance addiction, we must ensure there is adequate access to on-demand treatment. Nationwide, only 11% of patients with addiction get the treatment they need. There is no physical ailment for which this would be acceptable—imagine if only 11% of cancer patients or 11% of patients with diabetes were being treated. If we do not increase access to quality treatment options we are merely treading water, waiting for the person who has overdosed to use drugs and overdose again.

The evidence is clear: addiction treatment requires a combination of medication-assisted treatment, psychosocial support, and wrap-around services including supportive housing. All of these must be in place for individuals suffering from addiction to recover, and they must be available at the time the individual is seeking these services—the same as for any medical condition.

a. In Baltimore, we have started a 24/7 "crisis, information, and referral" phone hotline that connects people in need to a variety of services including: immediate consultation with a social worker or addiction counselor; connection with outreach workers who provide emergency services and will visit people in crisis at homes; information about any question relating to mental health and substance addiction; and scheduling of treatment services and information. This hotline is not just for addiction but for mental health issues, since these issues in behavioral health are so closely related and there is a high degree of co-occurrence. Those who are seeking treatment for behavioral health should be able to easily access the services they need, at any time of day. This 24/7 line has been operational since October 2015; already, there are approximately 1,000 phone calls every week. It is being used not only by individuals seeking assistance, but by family members seeking resources, and police and providers looking to connect their patients to treatment.

b. We have implemented the Screening, Brief Intervention, and Referral to Treatment (SBIRT) approach, which provides universal screening of patients presenting to ERs and primary care offices. Three of our hospitals are early pioneers in SBIRT; we are looking to expand it to all hospitals and clinics in the city to ensure delivery of early intervention and treatment services for those with or at risk for substance use disorders.

c. We are developing a real-time treatment dashboard to obtain data on the number of people with substance use disorders, near-fatal and fatal overdoses, and capacity for treatment. This will enable us to map the availability of our inpatient and outpatient treatment slots and ensure that treatment availability meets the demand. The dashboard will be connected to our 24/7 hotline that will immediately connect people to the level of treatment that they require—on demand, at the time that they need it.

d. We have secured $3.6 million in capital funds to build a "stabilization center"—also known as a sobering center—for those in need of temporary service related to intoxication. This is the first step in our efforts to start a 24/7 "Urgent Care" for addiction and mental health disorders—a comprehensive, community-based "ER" dedicated to

patients presenting with substance abuse and mental health complaints. Just as a patient with a physical complaint can go into an ER any time of the day for treatment, a person suffering from addiction must be able to seek treatment on-demand. This center will enable patients to self-refer or be brought by families, police, or EMS—a "no wrong door" policy ensures that nobody would be turned away. The center would provide full capacity treatment in both intensive inpatient and low-intensity outpatient settings, and connect patients to case management and other necessary services such as housing and job training.

e. We are expanding and promoting medication-assisted treatment, which is evidence-based and a highly effective method to help people with opioid addiction recover. This combines behavioral therapy with medication, such as methadone or buprenorphine, along with other support. Taking medication for opioid addiction is like taking medication to control heart disease or diabetes. When prescribed properly, medication does not create a new addiction, but rather manages a patient's addiction so that they can successfully achieve recovery. Baltimore has been at the leading edge of innovation for incorporating medication-assisted treatment, including providing medications in structured clinical settings through the Baltimore Buprenorphine Initiative. This year, we expanded access to buprenorphine treatment by offering services in low-barrier settings, such as recovery centers, emergency shelters, and mental health facilities. Providing access to buprenorphine services in these settings allows us to engage people who are more transient or unstably-housed into much needed treatment.

f. We are expanding our capacity to treat overdose in the community by hiring community-based peer recovery specialists. To build trust, these individuals will be recruited from the same neighborhoods as individuals with addiction, and will be trained as overdose interrupters who can administer overdose treatment and connect patients to treatment and other necessary services.

g. We are working to expand case management and diversion programs across the city so that those who need help get the medical treatment they need. In our city of 620,000, 73,000 people are arrested each year. The majority of these arrests are due to drug offenses. Of the individuals in our jails and prisons, 8 out of 10 use illegal substances and 4 out of 10 have a diagnosed mental illness. Addiction and mental illness are diseases, and we should be providing medical treatment rather than incarcerating those who have an affliction.

   Baltimore already has highly-effective diversion efforts such as Drug Treatment Courts and Mental Health Treatment Courts. We are starting to implement a Law Enforcement Assisted Diversion Program (LEAD), a pilot model that has been adopted by a select group of cities, which establishes criteria for police officers to identify eligible users and take them to an intake facility that connects them to necessary services such as drug treatment, peer supports, and housing – rather than to central booking for arrest. Cross agency partnerships will be key in making these programs successful. LEAD implementation in Baltimore involves not only the Health Department and our behavioral health providers but the Police Department, State's Attorney's Office, Public Defender's

Office, and many more entities that together recognize the importance of addiction treatment.

h. We are increasing our capability for case management services for every individual leaving jails and prisons. These individuals are in a highly vulnerable state, and must be linked to appropriate physical and behavioral health care, social and supportive services, employment, mentoring and housing. Our outreach workers already target a subset of this population; we need to expand capacity to every one of these individuals. Additionally, we are deploying community health workers who are individuals in recovery themselves in order to reach people where they are in the community as well as provide a credible messenger. In deploying this tactic, we are also excited to bring jobs and opportunities to vulnerable individuals and neighborhoods that otherwise have limited employment opportunities.

3. Providing education to reduce stigma and prevent addiction

In addition to treating patients, we must also change the dialogue around the nature of substance use disorders. The Baltimore City Health Department is leading a citywide effort to educate the public and providers on the nature of substance addiction: that it is a disease, recovery is possible, and we all must play a role in preventing addiction and saving lives.

a. We have been at the forefront of changing public perception of addiction so those in need are not ashamed to seek treatment. We have launched a public education campaign "DontDie.org" to educate citizens that addiction is a chronic disease and to encourage individuals to seek treatment. This was launched with bus ads, billboard ads, a new website, and a targeted door-to-door outreach campaign in churches and with our neighborhood leaders. We are working with restaurants and bar owners to post "Don't Die" posters in their establishments.

b. "DontDie.org" has also become our portal for online trainings and for dispensing of naloxone through the Standing Order mentioned above. Any resident can watch a short (10 minute) video, take a 4-question quiz, and receive a standing order prescription to receive and to use naloxone to save lives.

c. We have also launched a concerted effort to target prevention among our teens and youth. This involves a campaign called "BMore in Control," and we are also incorporating prevention into the public school curriculum.

d. We have established permanent prescription drug drop boxes at all nine of the city's police stations and have conducted educational awareness campaigns around not using prescriptions that were given to anyone else. This means that anyone can drop-off their unused, unwanted, or unnecessary prescription drugs—no questions asked. Drugs left in the home can end up in the wrong hands—spouses, elderly family members, or even our children. I have treated 2-year olds who were dying from opioid overdose, again underscoring that all of us can be at risk and must play a role.

e. We are targeting our educational efforts to physicians and other prescribers of opioid medications. Nationwide, over-prescribing and inconsistent monitoring of opioid pain medications is a major contributing factor to the overdose epidemic. According to the Centers for Disease Control and Prevention (CDC), there were 259 million prescriptions written for opioids in 2014. That is enough for one opioid bottle for every adult American. Every day, people overdose or become addicted to their prescription opioids.

To address this, I have sent "best practice" letters to every doctor in the city. The letter addressed the importance of the Prescription Drug Monitoring Program and judicious prescribing of opioids, including not using narcotics as the first line medication for acute pain and emphasizing the risk of addiction and overdose with opioids. Importantly, this best practice requires co-prescribing of naloxone for any individual taking opioids or at risk for opioid overdose. Hospitals keep naloxone on hand if patients receive too much intravenous morphine or fentanyl. Patients must also receive a prescription for naloxone if they are to be discharged with opioid medications that can result in overdose.

These best practices were developed through convening ER doctors, hospital CEOs, and other medical professionals in the city. To reach practicing doctors, we have been presenting at Grand Rounds, medical society conferences, and have also launched physician "detailing", where we deploy teams of public health outreach workers and people in recovery to visit doctors to talk about best practices for opioid prescribing. We are working on a convening for pharmacists to set pharmacy best practices, and have supported statewide legislation to require the use of Prescription Drug Monitoring Programs by physicians and pharmacists. All of us—as providers, patients, and family members—must play our part to prevent addiction and overdose.

f. As part of our "best practices" recommendations, we are leading efforts to warn patients and prescribers against combining opioids and benzodiazepines. Nationwide, one in three fatal overdoses is due to this combination—a little known but extremely dangerous phenomenon. Physicians routinely prescribe these two medications together, yet because they both result in respiratory depression and sedation, overdoses are common and fatal.

In February, I co-led a group of over 40 City Health Commissioners and State Health Directors across the country urging the U.S. Food and Drug Administration (FDA) to require a "black box warning" on opioids and benzodiazepines that states that concurrent use of the medications increases the risk of fatal overdose. Black box warnings appear on the labels of prescription drugs and call attention to serious or life-threatening risks. We started a public petition and have over 3,000 signatures from people showing their support for this public warning. This is a first-of-its kind petition delivered to the FDA by frontline health officials. (See Appendix B)

While we wait for the FDA to require a "black box warning," we are also calling on prescribers to warn patients about the risks of combined opioid and benzodiazepine use. Patients with chronic pain are often prescribed opioids to treat their pain and benzodiazepines to treat their associated symptoms, such as anxiety and sleep disorders.

Educating patients about this potentially lethal drug interaction is an important step to reduce the toll of addiction and fatal overdose in communities across the country.

Working with the Federal Government

The Baltimore City Health Department, together with our partners across the city and state, has made significant progress in tackling the opioid epidemic. However, there are some areas where we face continued challenges. Though there is much that can be done on the city and state levels, the federal government plays a critical role in combating America's heroin and opioid abuse epidemic.

Recently, the Senate passed the Comprehensive Addiction and Recovery Act (CARA) which focuses on prevention and treatment efforts. I urge the House to pass this critical legislation. This is a great first step towards promoting prevention, treatment, and more inclusive communities. Although the bill provides for additional funding, far more resources are needed. We have four specific areas that should be more comprehensively addressed:

1. **Congress can expand funding for and availability of on-demand and wrap-around addiction treatment services**

We must treat addiction as a disease and not a crime or a moral failing. In order to successfully treat the disease, we need to ensure there are sufficient high-quality treatment options available to those in need, at the time that they need it. The science is unambiguous and unequivocal: addiction treatment requires medication-assisted treatment, psychosocial support, and wrap-around services. The problem is that we are nowhere near capacity to get everyone treatment at the time they need it.

a. Federal funding could expand treatment on-demand. There is often a small window of opportunity to get an individual with substance abuse or mental health issues into treatment. Additional money should be made available to establish 24/7 treatment centers dedicated to substance addiction and mental health. These centers will provide a one stop shop for those in need at the time they need it, and will also alleviate pressure from emergency rooms and jails, both of which are ill-equipped to handle these patients.

b. Congress can push for equitable insurance coverage for evidence-based addiction services. Medicare pays for pain medications that can lead to addiction, yet many states do not cover medication-assisted treatment and other evidence-based interventions for addiction recovery. Congress can ensure that Medicaid, Medicare, and private payers cover on-demand treatment for acute care (such as sobering, urgent care, and residential services), as well as ongoing treatment and services like medication-assisted treatment and case management. These rates should also be equivalent to mental health and physical health care rates (which they are not currently, leading to a dearth of providers and inadequate care). Services that are not science- and evidence-based—including rapid detoxification or sobriety-only programs—should not be federally funded.

c. Congress can expand funding for wrap-around services. Access to social needs like housing and employment is just as crucial to a person's recovery as medical treatment. These wrap-around services are especially important for those re-entering society after incarceration. Funding for case managers and care coordinators to help those in recovery access services is necessary for those with addiction to have a path to recovery. Housing remains a major challenge. In Baltimore, it is estimated that there are over 18,000 turn-away's each year for individuals seeking recovery housing. Providing stable housing will help to break the cycle of addiction, homelessness, and incarceration, and is critical for supporting those with addiction.

d. Congress can expand funding to diversion programs and ensure that individuals with substance use disorders receive addiction treatment. With the recognition that incarceration is not the solution to addiction, Congress can increase funding to diversion programs such as LEAD and Drug Treatment Courts. Individuals who are incarcerated should also receive evidence-based treatments. Those who enter prison being treated with buprenorphine are often switched to methadone due to its lower cost—a consideration that would not occur for other diseases. Patients should be allowed to continue treatments that work for them upon entering prison, and all who have addictions should be directed to evidence-based treatment options.

2. Congress can directly fund local jurisdictions with highest need

While States have traditionally received block grants from the federal government, local jurisdictions are the closest to the ground in service delivery, and understand the needs of residents the best. We urge Congress to consider direct support for local jurisdictions, particularly those in areas of greatest need, and providing cities and counties with the autonomy to innovate and provide real-time care for our residents. These services include innovative models that are not covered by Medicaid, Medicare, or private insurance, such as:

a. New care delivery models. There is research on new treatment options such as starting buprenorphine from ERs, mobile buprenorphine induction, or telemedicine treatment that would not be eligible for existing reimbursement yet offer much promise. These are examples of delivery models that local and state agencies should have the option of providing grant funding for, with the option of being included in Medicaid formulary after sufficient time and evidence.

b. Peer recovery specialists. In Baltimore, we are aiming to provide a peer recovery specialist for every individual who presents for overdose or addiction-related condition to our ERs and other facilities. However, we are limited by the lack of funding for these individuals. There should be opportunities for expanded funding and reimbursement for services rendered by these trained community health workers; grant funding to local and state agencies can be one way to pursue this.

c. Case management services. Individuals leaving incarceration or inpatient stays are at very high risk; they must receive wrap-around services that connect them immediately to needed medical and psychiatric assistance. These case management services have

inconsistent reimbursement; innovative programs including with telemedicine and use of peer recovery specialists should be encouraged.

d. Community resources for recovery. Recovery from addiction involves more than clinical treatment but also support and long-term care. Local jurisdictions can also innovate with interventions such as recovery housing and reentry support; federal funding can assist in these necessary steps.

e. Prevention. Grant support for tailored and targeted prevention support including public education and provider education must also be a critical component.

3. Congress can change critical federal regulations around addiction and overdose treatment

a. Congress can monitor and regulate the price of naloxone. Naloxone, the opioid overdose antidote, is part of the World Health Organization's (WHO) list of essential medications. Over the last two years, the price of naloxone has dramatically increased. The cost of naloxone skyrocketing means that we can only save a fraction of the lives we were able to before. This is particularly problematic for cities and counties that must purchase naloxone for use by paramedics, police officers, and other front-line workers.

Manufacturers have claimed that this price increase is related to increased demand. However, it is unclear why the cost of a generic medication that is available for much lower costs in other countries will be suddenly so expensive. Congress can join efforts by Senator Sanders and Congressman Cummings to call for investigation into the price increase of naloxone, which would otherwise prohibit us from saving lives at a time that we need to the most.

b. Naloxone should be co-prescribed to every individual receiving opioid medications. This is part of Baltimore's best practices, and we urge this standard to be implemented nationwide. This could be implemented through policy recommendation through the CDC, regulation through the FDA, or through federal legislation. However, we urge federal legislation requiring co-prescribing of naloxone given the escalating rate of opioid overdose deaths.

c. Congress can join local and state health officials to call for a prompt decision by the FDA for "black box warning" labels on opioids and benzodiazepines. This is a rapidly escalating dangerous trend that is fueling the overdose epidemic. (See Appendix B)

d. Congress can remove barriers to prescribing Buprenorphine. Buprenorphine is a medication-assisted treatment option with a much lower chance of overdose than methadone. Importantly, it can be administered by a primary care provider rather than in a designated drug-treatment clinic. This helps to increase the accurate perception that substance use disorder is a medical condition. Unfortunately, at the moment, only medical doctors can prescribe buprenorphine, and a doctor can only provide buprenorphine to a maximum of 100 patients**.** This barrier does not exist for any other medication, and significantly limits the ability of patients to access a life-saving treatment

option and leaves many patients with methadone as their only option for medication-assisted treatment. Methadone requires administration in a designated treatment clinic, which often becomes a point of contention within the communities in which they operate due to the stigma associated with drug addiction.

We strongly support current efforts underway at the Department of Health and Human Services to eliminate the limits on buprenorphine prescription, and urge further support of broadened access to this proven treatment including for Congress to consider broadening prescription authority of buprenorphine to Nurse Practitioners and other providers.

4. Congress can fund a national stigma-reduction and opioid-awareness campaign

Many local jurisdictions like Baltimore have launched public education campaigns. There is much more education that must be done in order to encourage people with addiction into care and to disband stigmas that are leading many communities to avoid providing treatment altogether. Local jurisdictions are limited by funding constraints. Congress can push for the launch of a national campaign to reduce stigma and to increase awareness of opioid addiction. This national campaign will provide the spotlight this critical issue requires. Such national public health campaigns have had dramatic success in the past, including with reducing drunk driving.

Conclusion

While some of the challenges facing Baltimore are unique, we join our counterparts around the country in addressing the epidemic of opioid abuse and addiction. According to the CDC, the number of people dying from overdose has quadrupled from 15 years ago. In many states, there are more people dying from overdose than from car accidents or suicide.

There are some who say the opioid problem is too big and too complicated—that it cannot be solved. It is true that treating the opioid epidemic requires many approaches. However, this is an issue that requires our attention. According to the WHO, treating opioid addiction saves society $12 for every $1 spent on treatment. Treatment also impacts communities by reducing excess healthcare utilization, increasing productivity and employment rates, and decreasing poverty and unnecessary cost to the criminal justice system. Furthermore, treating addiction is a moral imperative and a matter of life and death.

Baltimore has been fighting the heroin and opioid epidemic for decades and we continue to make progress with bold ideas and innovative strategies. Our efforts to address opioid addiction seek to change the face of Baltimore from the "heroin capital" to the center of addiction recovery. Our goal is to make sure all those who suffer from addiction get the services they need to recover.

We are glad to share our lessons with our counterparts around the country and with our national leaders. With dedicated partners like you in Congress, we can fight the epidemic, save lives and reclaim people and their families.

I want to thank you for calling this important hearing. I look forward to working with you to stop the epidemic of heroin and opioid addiction in the United States.

APPENDIX A

CITY OF BALTIMORE

STEPHANIE RAWLINGS-BLAKE, Mayor

Baltimore City Health Department
Leana S. Wen, M.D., M.Sc.
Commissioner of Health
1001 E. Fayette St.
Baltimore, MD 21202
health.baltimorecity.gov
Tel: 410-396-4398

Baltimore City Health Department
-White Paper-
State of Health in Baltimore:
Summary of Key Issues, Services and Policies
Winter 2016

State of Health in Baltimore: It is impossible to discuss the health and well-being of Baltimore City's residents without applying the lens of health equity and systemic disparities. While the overall mortality rate in Baltimore City has declined over the past decade, the City still has a mortality rate 30% higher than the rest of the state, and ranks last on key health outcomes compared to other jurisdictions in Maryland.

This reality is compounded by a series of complicated systemic social, political, economic, and environmental obstacles. With more than 1 in 3 of Baltimore's children living below the federal poverty line and more than 30% of Baltimore households earning less than $25,000/year, income, poverty, and race have enormous impact on health outcomes.

This state of health is especially urgent when we consider that Baltimore houses some of the best healthcare institutions in the country. We know that healthcare alone cannot drive health: while 97% of healthcare costs are spent on medical care delivered in hospitals, only 10% of what determines life-expectancy takes place within the four walls of a clinic. Where we live, work, and play each day drives our health and well-being.

As the local health authority, the Baltimore City Health Department (BCHD)'s mission is to serve Baltimore by promoting health and advocating for every individual's well-being, in order to achieve health equity for all residents. We work every day to improve the health of our community and address the disparities we face.

A current snapshot of health in the City includes:

- The leading causes of death are heart disease, cancer, and stroke, HIV/AIDS, and chronic lower respiratory disease;
- Across the City, there exists as much as a 20 year difference in life expectancy between neighborhoods;
- Although HIV rates in the City have declined over the past decade, Baltimore consistently ranks in the top five cities world-wide for infections. About 13,400 residents are estimated to be living with HIV; and while African Americans constitute 62% of the population, they account for more than 85% of those living with HIV;
- One in three youths is either obese or overweight. One in four children drinks a regular soda every day, and less than one in five eats recommended servings of fruits and vegetables;
- 19% of adult residents in Baltimore City have been diagnosed with asthma, compared to a statewide average of 14%;
- 12.3% of babies born in the City are low birthweight, compared to a national average of 6%;
- 30% of children in Baltimore have Adverse Childhood Experience (ACE) scores of 2 or more, meaning that they have experienced more than two incidences of events such as domestic violence, living with someone with an alcohol/drug problem, the death of a parent, or being a victim/witness of neighborhood violence.
- 25% of adults living in Baltimore are regular smokers, compared to a national average of 17%.
- Baltimore has one of the highest rates of heroin use and overdose in the country – in 2014, 192 deaths were heroin-related. Over 60,000 people in the City are estimated to have a drug or alcohol addiction.

About BCHD

Founded in 1793, BCHD is the oldest, continuously-operating health department in the country, with more than 1,000 employees and an annual budget of $130 million. BCHD aims to promote health and improve well-being through education, policy/advocacy, and direct service delivery for the residents of Baltimore City. BCHD's wide-ranging responsibilities include maternal and child health, youth wellness, school health, senior services, animal control, restaurant inspections, violence prevention, emergency preparedness, STI/HIV treatment, and acute and chronic disease prevention.

Over the past year, under the leadership of Health Commissioner Dr. Leana Wen, BCHD has made major strides in addressing the public health challenges facing Baltimore City. Several programs have moved the needle on health outcomes in the City and are serving as national models for public health innovation. This white paper captures those accomplishments and is intended to serve as an overview of the City's priority public health issues and how the health department addresses these challenges.

Principles

BCHD's work is driven by three principle tenets:

1) *We go to where people are.* We believe that services and public health information should be delivered directly to community members. BCHD delivers health services in schools to ensure children don't miss class, deploys home-visiting services to ensure people receive critical maternal and child health care, and sends Safe Streets outreach workers into the neighborhoods where conflicts occur in our community.

2) *We engage the community in setting goals.* Our long-term goals are based on scientific best practices, but our short-term metrics are developed and shaped by the community. We adopt a robust community engagement approach to all of our work, partnering with neighborhood associations, faith-based organizations, and issue-specific stakeholders to ensure that the work we do is informed by –and responsive to-- the needs of Baltimore's citizens.

3) *We go "upstream" and tackle the root causes of poor health.* Public health is a powerful tool to fight injustice, and we embrace every opportunity to level the playing field of inequality. We know that health impacts every issue, from education to crime to unemployment – if our youth and adults are not healthy, they cannot learn or work productively. By investing in public health, we can ensure that Baltimore reaches its maximum potential.

Baltimore's Public Health Priorities

Issue 1: Addressing the Opioid Epidemic

Background: With approximately 19,000 active heroin users in Baltimore and far more who misuse and abuse prescription opioid medications, our city cannot be healthy without addressing opioid addiction and overdose. In 2014, 303 people died from drug and alcohol overdose, which is more than the number of people who died from homicide. Drug addiction impacts our entire community and ties into nearly every issue facing our city including crime, unemployment, poverty, and poor health.

Victories: BCHD has developed a comprehensive, 3-pillar strategy to combat opioid addiction that led the way in Maryland and that serves as a national model of innovation:

- **Prevent deaths from overdose and save lives.** In 2015, Commissioner Wen declared opioid overdose a public health emergency and the most critical part of BCHD's opioid overdose prevention campaign has been expanding access to naloxone – the lifesaving drug that reverses the effect of an opioid drug overdose. In October 2015, a new law went into effect that allowed Dr. Wen to issue a "standing order" and prescribe naloxone to the City's 620,000 residents. Baltimore City became the first jurisdiction in Maryland to expand access to naloxone using a standing order.

In 2015, BCHD and partner organizations trained over 8,000 people at street markets, metro stops, jails, and neighborhood meetings on how to administer naloxone. BCHD assisted the Baltimore Police Department to incorporate naloxone training into the police academy and within the first month of carrying this remedy, officers used naloxone to save the lives of four of our citizens. Baltimore City was also one of the first jurisdictions to require naloxone training as part of court-mandated time in Drug Treatment Court. We have trained federal, state and city legislators so that they can not only save lives, but also serve as ambassadors and champions to their constituents.

We use up-to-date epidemiological data to target our training to "hotspots", taking naloxone directly into the most at-risk communities and putting it in the hands of those most in need. This was put into effect in 2015, when we saw that 39 people died from overdose to the opioid Fentanyl between January and March of 2015. Fentanyl is many times stronger than heroin, and individuals using heroin were not aware that the heroin had been laced with Fentanyl. Unfortunately, Fentanyl continues to be an issue and an additional spike in Fentanyl deaths occurred in October 2015, where there were 14 deaths related to fentanyl—a 133 percent increase over last year. To address this spike in Fentanyl related deaths, BCHD launched aggressive outreach efforts in "hotspot" areas and announced a new platform that will allow Baltimore City residents to be trained online in how to use naloxone and receive the "standing order" prescription.

- **Increasing access to on-demand treatment and long-term recovery support.** Stopping overdose is only the first step in addressing addiction. To adequately treat people with substance use disorders, we must ensure there is adequate access to on-demand treatment. Nationwide, only 11% of patients with addiction get the treatment they need. In collaboration with Behavioral Health System Baltimore, the local behavioral health authority, BCHD has already taken several actions to ensure access to treatment, including:

    - Created a 24/7 Crisis, Information and Referral phone line for anyone with addiction and mental health concerns that receives nearly 1,000 calls every week for crisis services and referral to appointments;
    - Secured $3.6M in capital funds to build a stabilization center which will be the first step towards creating a 24/7 "Urgent Care" for behavioral health
    - Hired community-based peer recovery specialists and piloted universal addiction screening in our hospitals;
    - Implementing the Law Enforcement Assisted Diversion Program (LEAD) with City partners, to establish criteria for police officers to identify and connect individuals to services such as drug treatment and housing, rather than to central booking for arrest.

- **Provide education to reduce stigma and prevent addiction.** In addition to treating patients, the dialogue around substance use disorder must also change and BCHD has been at the forefront of changing public perception of addiction so those in need are not ashamed to seek treatment. BCHD is leading a city-wide effort to educate the public and providers on the nature of addiction: that it is a disease, recovery is possible, and we all must play a role in preventing addiction and saving lives.

Key activities include:

- A public education campaign, "DontDie.org", that educates citizens that addiction is a chronic disease and to encourage individuals to seek treatment;
- Conversations with emergency doctors across the City to create awareness about best approaches to prescribing opioid medication;
- Educational programs for doctors and providers of all specialties around careful prescribing of opioid medications and need for training in anti-overdose medication naloxone.

Baltimore City was the first jurisdiction in Maryland to take this proactive approach to address addiction and has one of the most ambitious overdose response and addiction treatment programs in the country. The United States Senate and the Centers for Disease Control and Prevention (CDC) have both highlighted BCHD's innovative approaches to address the opioid epidemic, as a best practice for other cities to learn from.

Challenges and Aspirations: While we have made important strides in responding to substance abuse and overdose within the city, there is still urgent imperative to respond to this crisis by:

- *Ensuring naloxone accessibility* by ensuring that the cost of this life-saving antidote, which has quadrupled over the past two years in Baltimore, remains affordable.
- *Increasing access to on-demand treatment* – we must ensure sufficient high-quality treatment options are available to those suffering from opioid addiction. BCHD ultimately intends to establish a 24/7 emergency room dedicated to behavioral health and on-demand access to addiction support, as well as proven intervention models such as LEAD and expanded case management for individuals being released from jail.
- *Additional funding for prevention and stigma reduction* – to stop the cycle of addiction, we must continue to invest in prevention services and anti-stigma education.

Issue 2: Youth Violence Prevention

Background: Addressing violence and public safety are key priorities for Baltimore City, and BCHD strongly believes that preventing violence is an essential function of public health. The hallmark model for violence prevention at BCHD is the Safe Streets program, a program designed to combat shootings and homicides in targeted communities in Baltimore.

Victories: Safe Streets takes a public health approach to violence and maintains that violence is a learned behavior that can be prevented using disease control methods; as violent events often "cluster" similar to an infectious disease outbreak. The program has proven successful in significantly reducing incidences of shootings and homicides. In 2014 alone, the program had 15,000 client interactions and 800 mediated conflicts, more than 80% of which were deemed likely or very likely to have resulted in gun violence. In addition to neighborhood-level impact, the program also prevents the intensive trauma and often costly city-wide ripple effects associated with a major event of violence.

In light of these results, BCHD has developed a strategic framework for youth violence prevention across the City, including:

- **Scaling what works.** Given Safe Streets' success to date, BCHD believes it is essential to continue supporting and developing the program's current operations as well as investing in expansion to additional sites. We are currently pursuing multiple sources of funding to sustain and potentially expand this program and ensure that we can continue to prevent incidents of violence across the City.

- **Leveraging additional entry points.** To reach people where they are and prevent additional violence, we must identify additional entry points by working with partners throughout the City, including the:
    - Healthcare System– building off of the Safe Streets model, we seek to deploy "hospital interrupters" when youth come into the emergency room as a result of a violent incident. Additionally, we will pilot implementation of Maryland Shock Trauma's Violence Intervention Program, a youth violence prevention model that uses the hospital as an entry point for intervention conversations and services.
    - Justice System – the B'MORE FOR YOUTH Collaborative, drives the City of Baltimore's comprehensive plan to prevent violence affecting youth and reduce the number of people going into the criminal justice system. It is the product of collaboration among local, state, and federal partners, and identifies root causes and recommends a coordinated, multi-sector, multi-tiered approach.

- **Violence as a public health issue.** We know violence is a generational challenge impacted by the social determinants that shape people's lives. BCHD's approach to violence prevention starts as far "upstream" as possible. One such example is ensuring that Baltimore's youth have access to appropriate eye care and equipment – if a child cannot see, then they are unlikely to be motivated to come to school and may turn to other activities within their neighborhood that increase their likelihood of becoming involved in a violent incident later in life. Similarly, other studies have shown that home visiting programs for pregnant women and lead poisoning prevention will improve educational outcomes and reduce violence in the child. We have also developed a robust youth health and wellness campaign within BCHD that will ensure that all youth are healthy and engaged.

Challenges and Aspirations:

- *Sustaining the Safe Streets Program* – Safe Streets has historically been funded by grants, including those from the US Department of Justice and Centers for Disease Control and Prevention (CDC), all of which come to a close this year.
- *Support to pilot and scale new violence prevention initiatives* – Safe Streets, while a best-in-class model, is one innovative way to tackle youth violence. We must also invest in programs similar to MD Shock Trauma's Violence Intervention Program, Hospital Interrupters, and other public health initiatives that lead to reductions in violence—including home visiting programs for pregnant women and lead poisoning prevention programs.

Issue 3: Youth Health and Wellness

Background: A decade ago, Baltimore City's infant health outcomes ranked as one of the poorest in the country, with an infant mortality rate nearly twice the national average and huge disparities between black and white birth outcomes. In response, BCHD in partnership with the Family League of Baltimore City and Health Care Access Maryland, developed a city-wide public-private partnership called B'More for Healthy Babies. The goal of the initiative is to ensure that all of Baltimore's babies are born at a healthy weight, full-term, and ready to thrive in healthy families. It is a comprehensive, evidence-based solution that builds cross-sector partnerships for strategic planning and implementation; strengthens systems and streamlines interventions to assure maximum effectiveness, ensures community and client participation in planning and emphasizes proactive monitoring and data-driven decision-making.

Victories:

- **B'More for Healthy Babies** Since its inception, B'More for Healthy Babies has experienced extraordinary success in:
  - Reducing the infant mortality by an astonishing 28%, bringing it to its lowest point in Baltimore's history;
  - Closing the disparity between black and white infant deaths by almost 40% between 2009 and 2012;
  - Decreasing the teen birth rate in the City by an unprecedented 36%.
  - Reducing sleep-related infant deaths by 50%

  The program's success has been widely recognized and was recently awarded the Academy for Excellence in Local Governance County Best Practices Award, presented by Governor Larry Hogan at the 2015 Winter Maryland Association of Counties Conference, in addition to receiving the 2015 Spirit of Service Award from the Healthy Teen Network.

  Building upon the success of B'More for Healthy Babies, BCHD seeks to take a comprehensive approach to youth health and wellness through:

- **Youth Health and Wellness Plan** BCHD has developed a comprehensive youth health and wellness plan that applies the same principles that have made the B'More for Healthy Babies program so successful, to the full youth life course of 0-19 years old. This plan will focus on three categories of long-term outcomes:
  - **Healthy Minds**- including improved social and emotional development as well as improved behavioral health;
  - **Healthy Bodies**-including continuation of reduced teen births and improved physical health outcomes including immunizations and oral health;
  - **Healthy Connections**-including improved peer relationships, community connectedness, and connections with trusted adults.

- **School Health** The Bureau of School Health at BCHD provides health services in all Baltimore City Public Schools. We have helped children better achieve their potential by

supporting mental health services to 119 schools, providing students with access to health suite services, with nearly 300,000 annual visits in 180 schools**.** However, capacity is severely limited: several school-based health centers must share one nurse practitioner or provide care via the school health suites, which do not have nurse practitioners or physicians readily available to provide diagnosis, treatment, and preventative services.

Telemedicine is an innovative and effective way to address this gap in capacity and expand the level of care offered across schools without having to staff each with a full-time primary care provider. BCHD seeks to launch a telemedicine pilot to improve care coordination by virtually connecting community physician providers to over 1,500 school children, allowing them to stay in class and keep their parents at work. This will enable regular evaluation and treatment of both acute and chronic illnesses, as well as enhance availability of key behavioral and mental health services.

- **Reproductive Health** BCHD and a broad coalition of partners in the City, including Baltimore City Public Schools, were awarded an $8.5 million grant from the U.S. Department of Health and Human Services that will be used to ensure comprehensive sex education in middle schools and high schools, with the aim of reducing the teen birth rates as well as provide accurate, evidence-based reproductive health education.

Challenges and Aspirations:

- *B'More for Healthy Babies Sustainability* - With state and federal budgets steadily decreasing, this critical program faces a $1.5 million deficit in the upcoming fiscal year. To ensure that all of Baltimore's babies are born healthy, we must fill this gap by pursuing multiple funding streams, including philanthropic, government, and billable services.
- *School Health Telemedicine Pilot* – Deploying telemedicine will significantly expand the capacity of the school health program and ensure the improved health of hundreds of schoolchildren. We are pursuing grant and other funding opportunities to support this initiative.

Issue 4: Behavioral Health

Background: Baltimore City faces significant behavioral health challenges and disparities. Baltimore City residents, despite making up only 11% of Maryland's total population, have consistently represented 30% of all statewide inpatient hospital discharges for individuals with mental illness. In 2013, 28% of Baltimore City students reported symptoms of mental illness, compared to 23% of Maryland students. Over 60,000 residents are estimated to have a drug or alcohol addiction.

Victories:

- **Establishment of a stabilization center** BCHD has secured $3.6 million in capital funds to build a "stabilization center" – also known as a sobering center – for those in need of temporary service related to intoxication. This is the first step in our efforts to start a 24/7 "Urgent Care" for addiction and mental health disorders – a comprehensive, community-

based "ER" dedicated to patients presenting with substance abuse and mental health complaints. Just as a patient with a physical complaint can go into an ER any time of the day for treatment, a person suffering from addiction must be able to seek treatment on-demand. This center will enable patients to self-refer or be brought by families, police, or EMS – a "no wrong door" policy ensures that nobody would be turned away. The center would provide full capacity treatment in both intensive inpatient and low-intensity outpatient settings, and connect patients to case management and other necessary services such as housing and job training.

- **Increased focus on treatment and case management** Three hospitals in Baltimore City participate in the Screening, Brief Intervention, and Referral to Treatment (SBIRT) project, an evidence-based public health approach to providing early intervention and treatment services to at-risk of substance use and mental health disorders. BCHD is leading a city-wide effort to expand use of SBIRT to all healthcare institutions in the city to delivery of early intervention and treatment services for those with or at risk for behavioral health and substance use disorders.

  BCHD seeks to increase case management capability for every individual leaving jails and prisons. These individuals are at a highly vulnerable state, and must be connected to medical treatment, psychiatric and substance abuse treatments if appropriate, housing and employment support, and more. We know that deploying community health workers in order to reach people where they are in the community as well as provide a credible messenger works: in deploying this tactic, BCHD also aspires to bring jobs and opportunities to vulnerable individuals and neighborhoods that otherwise have limited employment opportunities.

- **Trauma-Informed Care** There is growing recognition in Baltimore City that generations of exposure to poverty, racism, violent crime and domestic violence has resulted in extremely high levels of traumatic stress for individuals, families and communities across the City. Recognizing that trauma is a major underlying factor of behavioral health issues and violence, BCHD has launched a trauma-informed care training initiative across city government, which has already reached more than 1,200 city employees including police officers and other front-line city workers. The goal of this initiative is to educate all front-line city workers educated in trauma-informed approaches, including:

  - Understanding trauma
  - Understanding the impact of traumatic stress on brain development
  - Integrating trauma-informed practices into work with City residents

Challenges and Aspirations:

- *Operational budget for the stabilization center* – While we have secured capital funding, the stabilization center requires $2.5M in operating dollars to successfully launch and begin providing services to potential attendees.
- *Increased investment in trauma-informed care* – Trauma is prevalent in Baltimore, and a driving factor of many other obstacles and systemic issues in the City. To ensure city-wide resilience, it is imperative that we invest further in this approach and provide trauma and resilience training for all city employees and partners.

- ***24/7 Substance Abuse and Mental Health Center*** – Building upon the idea of the stabilization center, this facility would be a one step closer to on-demand treatment for addiction and mental health services, which are significant unmet needs in Baltimore. The center will also alleviate pressure from emergency rooms and jails, which are ill-equipped to address these patients' needs.

Issue 5: Chronic Disease Prevention

Background: BCHD is committed to fighting one of the most pervasive challenges and leading cause of death and poor health in Baltimore City: chronic disease. We take a multi-pronged approach to addressing chronic disease that encompasses direct services, education and policy actions. Our chronic disease efforts encompass the following:

- **Cardiovascular Disease/Tobacco Cessation** Smoking is the number one preventable contributor to early death from heart disease, stroke, and cancer. BCHD provides smoking cessation services, community education, school-based projects, and enforcement of retailer compliance with tobacco control ordinances. Programs are community-based and deploy health educators and youth educators to engage community members in cessation campaigns, in recognition that 90% of adult smokers started smoking before age 18.

    - Related to this tobacco work is ongoing education and awareness for chronic disease including projects such as a cancer awareness education and cross-city hypertension initiative to provide screening for high blood pressure in vulnerable communities.

- **Food Access** *Baltimarket* is a suite of community-based food access and food justice programs through BCHD. The program envisions a Baltimore with communities that have equitable access to healthy, affordable, and culturally-specific foods every day. The mission of the program is to improve the health and wellness of Baltimore City residents by using food access and food justice as strategies for community transformation. The three programs that make up Baltimarket include:

    - Virtual Supermarket – a grocery delivery service that serves over 600 customers at 6 sites and manages over $200,000 in orders, which are handled by 21 trained community-based advocates.
    - Healthy Corner Stores – 10 stores located in Upton/Druid Heights, Harlem Park, and Franklin Square communities that engage in promotion of healthy eating via community nutrition education, PSAs about healthy snacking, and more.
    - Neighborhood Health Advocates and Food Justice Forum – This summer, the Food Justice Community Conversation Guide will launch with the goal of 25 community-run conversations about food justice in the next year. These conversations are facilitated by BCHD-trained Neighborhood Health Advocates—members of the community who work to help others to get access to healthy, affordable and fresh food through BCHD.

- **Lead Prevention** BCHD seeks to reduce lead poisoning in the City through primary prevention and aggressive enforcement of the city's lead laws. More than 56,000 children under age 6 are at risk for lead poisoning in Baltimore. Lead poisoning can cause permanent brain damage and no amount of lead in children is safe. BCHD educates and encourages families and providers to test children ages 1 and 2 for lead levels, outreach to pregnant women to evaluate potential lead hazards, and with other partners, including Baltimore Housing, conducts home visits and develops strategies to reduce lead paint hazards in homes.

- **Asthma** 12.4 % of Baltimore City adults currently have asthma, compared to 8.4% statewide and 8.6 % nationally. The hospitalization rate for adult asthmatics in the City was 3.3 times higher than the state rate (42.9 vs. 13.2 per 10,000 people). BCHD's asthma programs focus on disease management and access to key resources for patients struggling with asthma. BCHD conducts home visits for children with asthma to educate caregivers about preventing asthma triggers and reducing ER visits for children.

Victories: We have made significant progress in tackling chronic disease through public health campaigns and advocating for policy changes at all levels of government:

- **Lead prevention reforms:** Childhood lead poisoning has decreased significantly and are currently at the lowest levels since Maryland's lead law was implemented in 1994 and enhanced enforcement began at the City level in 2000. Since then, the number of lead poisoning cases has decreased by 98%. Additionally, a BCHD-led pilot to test children's' jewelry revealed extreme levels of lead in many readily available products at local stores. Based on the results of this testing, BCHD implemented regulatory action against lead in children's jewelry which prohibits the sale of such jewelry if measuring over 600ppm of lead.

- **Sugar-sweetened beverages:** one in three children in Baltimore are overweight or obese, and a major contributor is sugar-sweetened beverages (SSBs). With the support of BCHD, legislation has been introduced to the City Council that would require retailers to post warning labels stating the fact that sugar-sweetened beverages lead to tooth decay, obesity, and diabetes. The legislation is based on scientific evidence that warning labels influence consumer behavior and ensures that consumers can make informed choices about their purchase. This is particularly important in Baltimore City with rising rates of obesity among children and with beverage companies' practices of disproportionate marketing in communities of color and low-income communities.

- **Alcohol and tobacco regulation:** BCHD has advocated for several policy initiatives to address the harmful effects of tobacco and alcohol. These include regulation of hookah establishments, a state-wide tobacco tax to be used for medical care, a ban on indoor smoking, including e-cigarettes, buffer zones around schools, and increased enforcement funding and capacity. In the last year, BCHD's advocacy has resulted in a statewide ban of powdered alcohol and a citywide ban of the sales of the dangerous compounds known as synthetic drugs.

Challenges and Aspirations:

- ***Lead prevention*** – Despite significant progress, our work is far from done: over 5% of children test positive for lead. Building upon current lead prevention efforts, additional funding is necessary at the local, state and federal levels in order to implement universal screening and provide primary prevention services. Most importantly, additional efforts are needed to support lead abatement in homes, as lead paint hazard is the leading cause of childhood lead poisoning.
- ***Sugar-sweetened beverages labels*** – As mentioned above, legislation has been introduced to the City Council that would require retailers to post warning labels noting the connection between sugar-sweetened beverages and health conditions such as obesity. We have experienced pushback from the American Beverage Association and similar special interests, despite the scientific foundation on which this legislation was developed. We are continuing to work with community partners on this and other efforts to reduce the scourge of childhood obesity and reduce disparities in Baltimore.
- ***Local tobacco authority*** – Due to a previous ruling, Baltimore City is unable to successfully enforce tobacco violations locally. We are currently pursuing legislation in the Maryland General Assembly that would permit local jurisdictions to enact and enforce measures regulating the sale and distribution of tobacco products, with measures at least as stringent as those enacted in state law.

Issue 6: Senior Health and Wellness

Background: As with youth health and wellness, BCHD is committed to providing health education and services for our city's older adults. The Division of Aging and Care Services serves as the local Area Agency on Aging and coordinates funds from the federal Older Americans Act to ensure an adequate service delivery system. Additionally, the Division ensures essential services for seniors, including health evaluation, personal care, transportation, and volunteer opportunities.

Victories: BCHD has piloted several innovative approaches to ensure improved health outcomes amongst the elderly, including:

- **Falls** The Robert Wood Johnson Foundation recently awarded a $200,000 grant to a BCHD-led partnership with local hospitals and community partners such as the American Association of Retired Persons (AARP) that will use predictive data to track patients and reduce falls by one-third over three years. This project involves interventions in senior housing buildings and through hospitals and ERs to educate about falls prevention and provide services to reduce the risk of falls.

- **Community Resources** A growing concern among many Baby Boomers is taking on the role of caregiver for their parents. BCHD has teamed up with the city's libraries to offer a "Caregiver Corner" for anyone looking to find information on aging. This project was designed to provide caregivers with information and resources through several different initiatives by BCHD. The goal is to broaden outreach and support to family caregivers. Caregiver Corner is one initiative under the "Project Taking Care

of Mom and Dad" designed to provide caregivers and older adults who visit the library with relevant resources and information.

- **Advocacy and Planning** BCHD has lead advocacy efforts to oppose cuts to State funding for Baltimore City; including funding for senior centers. We will develop a strategic plan for care for older adults in Baltimore, in a similar vein as the Youth Health and Wellness Plan, that will tie together efforts across the city and present a blueprint for ensuring that our most vulnerable seniors have access to the comprehensive care and community they need.

Challenges and Aspirations:

- *Senior Center Funding* – currently, the state distribution model for senior center funding is based on total unemployment and income rates rather than total population. We have pursued legislation in the Maryland General Assembly to change the formula so that it is based off of a population's total elderly population, *as well as* the elderly population living 150% below the federal poverty line. We are also proposing that a state task force be created to examine the state funding distribution for seniors.
- *Older Americans Act* - The Older Americans Act was created to ensure that preference is given to providing services to older persons with the greatest economic and social need, particularly low-income minority persons. Funding has not kept up with the aging impoverished population, and it is essential that those dollars are aligned with those who have the greatest economic need and that the right balance is struck among need and costs. The current intrastate funding formula does not adequately target this vulnerable population and we have proposed revisions so that it is more responsive to the need of Baltimore City seniors.

Issue 7: Acute Communicable Disease and Public Health Preparedness

Background: BCHD provides several essential functions for the City, including: communicable disease tracking, education and prevention, emergency preparedness and response, restaurant inspections, and animal control. Our field staff, from animal control officers; to sanitarians; to outbreak investigators, have tackled emergencies ranging from Legionnaire's, measles, and Ebola investigations to transporting patients to life-saving treatment during severe weather. These activities are core to Baltimore City's safety and preparedness response.

Victories:

- **HIV Prevention and Education.** In the fall of 2015, BCHD secured two grants totaling $22 million to bring HIV prevention, prophylaxis and treatment to underserved populations while creating 70 new jobs in the City. The White House has acknowledged Baltimore's leadership in this area, and Baltimore was one of a handful of cities to join the Fast Track Cities coalition to end AIDS by 2030. Our HIV team will continue to partner directly with community and provider groups, provide education and treatment, in one of the largest collaborations to combat HIV.

BCHD has a long history of providing innovative services to prevent and treat HIV/AIDS. As one of the first jurisdictions in the country to implement a Needle Exchange Program (NEP), the program has exchanged over one million syringes annually with a 75% return rate. The NEP program is credited with significantly moving the needle on HIV transmission with injecting drug users in Baltimore since its inception. The NEP is also the test bed for the Staying Alive Program, naloxone training, and directly observed therapy for non-compliant patients on HIV medications. In 2015, almost 3,000 individuals received naloxone training by NEP staff.

While the Affordable Care Act has improved access to health insurance and Medicaid, many of our residents with HIV/AIDS need additional support. BCHD provides clinical and support services for people living with HIV/AIDS and their contacts through programs like Linkage to Care and the Ryan White Program. Linkage to Care staff members identify patients who test HIV positive and patients are then taken directly to a participating physician to educate the patient and initiate the appropriate therapy. This program has linked over 1200 patients to primary care, an important step in stopping the transmission of HIV. In 2015, the Maryland Department of Health and Mental Hygiene recognized this program by awarding them with two state-wide awards, "Most Encounters with HIV Positive Clients" and "Most Referrals to HIV Primary Care". The Ryan White Program receives approximately $17 million annually to provide HIV-related medical and support services to over 10,000 individuals living in Baltimore City and the five surrounding counties.

The Baltimore City Health Department has hosted the "Get Yourself Tested" Ball, annually for the last 6 years. This event is aimed at the "House and Ball community", which is made up of gay and transgender individuals. Each year, approximately 600 individuals attend the event, with hundreds of people volunteering for HIV testing. These events have yield between 4%-6% new HIV diagnoses. At all other venues where testing occurs in Baltimore – emergency departments, CBOs, clinics, our outreach testing and STD clinics – the new diagnoses rate is 1% or less. Because of this extremely high rate infection found at this event, we have identified the Ball as a key event that reaches both a viable high risk population group of undiagnosed individuals and useful arm into the community to address HIV. All individuals with new diagnoses are able to be linked to care through our Linkage to Care Program.

- **Vaccines** In the aftermath of the Disneyland measles outbreak last spring, BCHD took the lead in coordinating the Baltimore Statement on Childhood Vaccinations through a coalition of pediatric chiefs and chairs in the City, as well as the Maryland Chapter of the American Academy of Pediatrics. The statement highlighted BCHDs unequivocal message regarding the safeness and effectiveness of childhood vaccines.

- **Public Health Preparedness** BCHD's Office of Public Health Preparedness and Response (OPHPR) is equipped to steward the City through any major public health emergency. This program trains staff and during times of emergency convenes and communicates with the City's healthcare infrastructure. In the aftermath of the unrest following Freddie Gray's death, BCHD lead the public health response; setting up a

prescription access line to assist seniors whose pharmacies were closed and arranged shuttles to and from senior buildings for food and banking needs.

Recently, in response to record-breaking blizzard that hit Baltimore City, BCHD led a city-wide response to ensure that patients were able to access life-saving medical treatments, including dialysis and chemotherapy. Working in tandem with the Baltimore City Fire Department, the Office of Emergency Management and the National Guard, BCHD was able to deploy resources to safely and successfully transport 300+ patients in the midst of snow-covered roads and hazardous driving conditions. Baltimore City was recognized as the only jurisdiction state-wide that provided medical transports immediately post-blizzard.

Other ongoing efforts include BCHD's response to emerging diseases like the Zika virus; and the essential core public health activities that include investigation and surveillance of foodborne illness, animal bites/rabies and other infectious diseases such as Legionnaire's disease; and tracking of HIV, syphilis, gonorrhea, chlamydia and other sexually-transmitted diseases. In 2015, Acute Communicable Disease Program investigated over 50 outbreaks and hundreds of potential rabies exposures. Outbreaks occur in many settings, including restaurants, hospitals, schools and daycares and often the health impact of a reportable disease is significant. Large outbreaks, like a foodborne outbreak that occurred at the City's Convention Center a few years ago required the Department to reassign staff to interview as many 5,000 conference attendees and collect samples from all of those with symptoms.

Challenges and Aspirations:

- *Funding for emergency preparedness* – We can and should be prepared for all severe emergencies, particularly unanticipated ones. We advocate for continued funding to prepare for emergencies and outbreaks, particularly in anticipation of an upcoming Zika virus outbreak. After 9/11 and the Anthrax Attack, the federal government made available significant grant funding to build public health capacity to train staff, plan for emergencies and respond. In 2012, the BCHD OPHPR had a staff of 12. In 2016, OPHPR is staffed by 4, severely impacting the department's capacity to respond to any sustained emergency. As the federal funding decreases, the program's capacity decreases leaving the City vulnerable.
- *Funding for clinic safety net* - The decrease in State and Federal funding is not limited to just the emergency preparedness program, but also many of the safety net programs our vulnerable citizens depend on. As mentioned previously, the Affordable Care Act was intended to provide all citizens access to health insurance and healthcare. While there have been some successes, many of our very low income, vulnerable citizens rely on our grant funded safety net programs, such as tuberculosis control, syphilis and gonorrhea testing and family planning clinics. Failure to support essential public health services will dramatically impact very visible public health measures and the lives of all of our citizens.

Issue 8: Population Health and Health in All Policies

Background: We know that medical care accounts for only 20% of a patient's health outcomes: social, behavioral, and environmental factors comprise the remaining 80%. Where we live, work, and play is the major driver of health outcomes, and as the public health authority for the City, BCHD is leading the way on initiatives that address the "upstream" factors of health—the social determinants—from housing to food to transportation to education.

We view health as foundational to every issue – unhealthy children cannot learn in school, and unhealthy adults cannot be a productive part of the workforce. As we examine critical issues across the City – the economy, public safety, education— health is an essential driver that cuts across all of them.

This is particularly significant in Maryland, where we are already leading the way on public health due to the establishment of global budgeting. Global budgeting shifts virtually all of the hospital revenue from a "fee-for-service" model to a global payment model, incentivizing hospitals to work in partnership with other providers and the community to prevent unnecessary hospitalizations and readmissions. The goal of the model is to promote quality healthcare, better patient health and lower cost, and as a result creates incentives for treatment of the whole person as well as the intersection of health with other policy priorities.

Victories:

Our current initiatives include:

- **Coordination with hospitals**. BCHD works closely with local healthcare providers, including hospitals and federally qualified health centers to identify shared priorities: behavioral health, for example. From creating a stabilization center to tracking patients who are the highest utilizers of care, coordination with our healthcare partners is key to ensuring that patients are receiving essential public health services. As the neutral convener, BCHD is positioned to coordinate citywide initiatives and collaborations that involve competing hospital systems and other health organizations. Department leaders participate in grant planning and visioning sessions with local hospital systems to ensure the City's public health priorities are included. In September 2015, BCHD convened over 100 hospital and healthcare leaders to discuss behavioral health priorities and coordination of case management services for high utilizers. BCHD is engaged with hospitals, clinics, and community groups in a number of other state, federal, and private grants to provide coordinated services to our residents.

- **Social determinants of health**. All of BCHD's programs, from B'More for Healthy Babies, to Safe Streets, to HIV prevention and treatment programs adopt this approach of comprehensive attention to social needs and services ---and as a result have experienced significant success to date. We are in the process of implementing a city-wide initiative to ensure that every patient can get access to the services they need: just as a doctor connects a patient to a pharmacy for medication, there should be simple ways to connect a patient to food to take with that medication.

- **Health in all policies**. Health touches every issue. As a result, BCHD's health perspective must be a consideration in all policies in the City. For example, if the City is considering implementing bike paths, or placing an incinerator into the community, the health impact should be considered. Previously, a cross-agency task force for health existed within the city, with representation from every agency. BCHD proposes re-launching this task force, to be chaired by the Health Commissioner, to ensure an ongoing city-wide dialogue regarding the role of health in all policies.

Challenges and Aspirations:

- *Unified approach to addressing patients' social needs* – While efforts are underway across the City that integrate social needs into clinical care, there is still significant variation in the quality of those programs as well as their ability to sync with one another. We are currently leading a city-wide proposal to the Centers for Medicaid and Medicare Services, the federal agency responsible for overseeing services, payments, and innovations for Medicaid and Medicare patients, in partnership with all of the Baltimore City hospitals and federally qualified health centers, that will unify these efforts and ensure that all patients can benefit from services that address the realities of their daily lives.
- *Coordination and alignment* – Speaking about cross-agency or cross-issue collaboration is easy; actually implementing it from a standard operating perspective is much more complicated. To facilitate this, we propose re-launching a Cross-Agency Taskforce that can systematically bring the Health in All Policies philosophy to bear in conversations taking place within the City.
- *Strategic plan for health* – In addition to the initiatives above, we must also establish our forward-looking vision for health in the City. BCHD has launched Healthy Baltimore 2020, a comprehensive process that will build on the successes listed in this document to establish a five-year blueprint for heath and well-being. This blueprint will pull on data that is produced by our ongoing epidemiology work -- including our Neighborhood Health Profiles, which provide snapshots of key health outcomes in each city neighborhood—as well as input from key community stakeholders that we collect via numerous community conversations.

Conclusion

While Baltimore City faces a number of public health challenges, we also have invaluable assets: one of the strongest healthcare infrastructures in the country, invested community members and partners, and a willingness –borne of necessity—to test and implement new, innovative approaches to keep our citizens healthy. As the City's health authority, BCHD is fortunate to work directly with excellent partners and leaders in every sector: government, business, community advocacy, healthcare, faith-based, and more – all of whom share a deep commitment to ensuring the health of our citizens. We hope that this briefing serves as a valuable tool to you and look forward to answering any questions you may have. Thank you for your partnership in ensuring that all of Baltimore's citizens are healthy.

APPENDIX B

February 22, 2016

Division of Dockets Management
Food and Drug Administration
5630 Fishers Lane
Room 1061, HFA-305
Rockville, MD 20852

CITIZEN PETITION

The undersigned submit this petition pursuant to Title 21, Chapter 9, Subchapter V, Part A of the Federal Food, Drug, and Cosmetic Act and 21 C.F.R. § 10.30 to request that the Commissioner of the U.S. Food and Drug Administration (FDA) place a black box warning on pharmaceuticals in the opioid and benzodiazepine classes warning patients of the potential serious risks with concomitant use of both classes of medications.

ACTION REQUESTED

The Petitioner requests the FDA to:

1. Amend current black box warnings on all opioid analgesic and benzodiazepine class medications to state:

    a. *Labeling for all Opioid Class Medications should read:*

    WARNING: CONCURRENT USE WITH BENZODIAZEPINES REDUCES THE MARGIN OF SAFETY FOR RESPIRATORY DEPRESSION AND CONTRIBUTES TO THE RISK OF FATAL OVERDOSE, PARTICULARLY IN THE SETTING OF MISUSE.

    b. *Labeling for all Benzodiazepine Class Medications should read:*

    WARNING: CONCURRENT USE WITH OPIOIDS REDUCES THE MARGIN OF SAFETY FOR RESPIRATORY DEPRESSION AND CONTRIBUTES TO THE RISK OF FATAL OVERDOSE, PARTICULARLY IN THE SETTING OF MISUSE.

2. Require medication guides for both classes of medications that specifically warn patients of the potential dangers of combined use of opioids and benzodiazepines.

STATEMENT OF GROUNDS

I. OVERVIEW

Concurrent misuse of benzodiazepines and opioids is contributing to the epidemic of fatal overdose in the United States. Biological data indicate that these two drug classes have synergistic effects in producing sedation and respiratory depression. Epidemiological data show polysubstance overdose fatalities involving both opioids and benzodiazepines are common and increasing.

FDA guidance indicates that a black box warning is appropriate in several circumstances, including when:[1]

- "There is an adverse reaction so serious in proportion to the potential benefit from the drug (e.g., a fatal, life-threatening, or permanently disabling adverse reaction) that it is essential that it be considered in assessing the risks and benefits of using the drug;"

OR

- "There is a serious adverse reaction that can be prevented or reduced in severity by appropriate use of the drug (e.g., patient selection, careful monitoring, avoiding certain concomitant therapy, addition of another drug or managing patients in a specific manner, avoiding use in a specific clinical situation)"

Both of these conditions are met in this case. Clinicians should consider the serious adverse reaction of fatal overdose when assessing the risks and benefits of co-prescribing benzodiazepines and opioids. Moreover, clinicians can prevent fatal overdose by reducing rates of co-prescribing these classes of medications.

The labels and medication guides of only a few drugs in these two classes contain specific information on the dangers of concurrent use; none contain black box warnings. Accordingly, we are petitioning the FDA to add black box warnings for all medications in the opioid and benzodiazepine classes that appropriately warn prescribers and patients about a

[1] Food and Drug Administration. "Guidance for Industry: Warnings and Precautions, Contraindications, and Boxed Warning Sections of Labeling for Human Prescription Drug and Biological Products-Content and Format." 6 October 2011. Accessed January 18, 2016 at http://www.fda.gov/downloads/Drugs/.../Guidances/ucm075096.pdf

reduced margin of safety and increased risk of fatal overdose when these classes of medication are used together.

II. BIOLOGY

Benzodiazepines and opioids operate on different receptors and have been long-understood to have synergistic effects on sedation and respiratory depression, such that concurrent use lowers the margin of safety.

Benzodiazepines. The primary allosteric mechanism of action for benzodiazepines is through binding to gamma-amino-butyric acid (GABA) receptors. This increases the activity of GABA, the principal, endogenous, inhibitory neurotransmitter in the central nervous system.[2] Benzodiazepines are known to decrease oropharyngeal muscle tone and blunt the arousal response to hypoxia and hypercapnia during sleep and thus increase risk of sleep apnea, even among healthy individuals.[3,4] In addition to their other properties, such as anti-seizure activity, benzodiazepines are known to enhance the sedating effects of other medications and substances, including: full-agonist opioids, partial agonist opioids such as buprenorphine, alcohol, barbiturates, and sedating antihistamines.[5]

Opioids. Opioids, in addition to acting as potent analgesics, cause sedation up to and including complete loss of consciousness and respiratory arrest. Opioids function primarily through stimulation of the Mu (μ), Kappa (ϰ), and Delta (δ) receptors that are normally activated in response to noxious stimuli by endogenous molecules (endorphins, enkephalins, and dynorphins). In addition to analgesia, stimulation of Mu receptors in the brainstem and medial thalamus causes respiratory depression and sedation, particularly in non-tolerant individuals. Kappa receptors (found in limbic and other diencephalic areas of the brain, the brainstem, and spinal cord) mediate spinal analgesia, sedation, dyspnea, and respiratory depression.[6]

---

[2] Mehdi, T. Benzodiazepines Revisited. *BJMP*. 2012; 5(1):a501.

[3] Hedemark LL, Kronenberg RS. Flurazepam attenuates the arousal response to CO2 during sleep in normal subjects. *Am Rev Respir Dis.* 1983 Dec;128(6):980-3.

[4] Drummond, GB. Comparison of sedation with midazolam and ketamine: effects on airway muscle activity. *British Journal of Anaesthesia*. 1996; 76:663-667.

[5] Olsen, Y, Adams, J, Alvanzo, A, et al. Clinical Guidelines for the Use of Benzodiazepines Among Patients Receiving Medication-Assisted Treatment for Opioid Dependence." *Baltimore Substance Abuse Systems, Inc.* May 2013. Accessed January 18, 2016 at http://www.bhsbaltimore.org/site/wp-content/uploads/2013/02/Benzo-Guidelines-FINAL-May-2013.pdf.

[6] Trescot, AM, Datta, S, Lee, M, Hansen, H. Opioid Pharmacology. *Pain Physician: Opioid Special Issue.* 2008; (11): S133-S153.

Laboratory and Human Subject Studies on Concurrent Use. Receptors for both opioids and benzodiazepines are highly concentrated in the respiratory centers of the medulla.[7] Multiple laboratory studies in animals and humans have indicated that co-administration of these drugs decreases the margin of safety with respect to respiratory depression.

For example, a study in rats demonstrated that while high doses of an opioid (buprenorphine) and a benzodiazepine (midazolam) alone both resulted in mild, but significant increases in PaCO2, the combined administration of these two drugs resulted in rapid, substantial and prolonged respiratory depression and hypoxia.[8]

Studies of human subjects have found synergistic effects in combining opioids with benzodiazepines:

- An experimental study on the effects of administering sedative doses of fentanyl, midazolam, or fentanyl plus midazolam, in 12 healthy adult males found fentanyl alone produced hypoxemia in 50% of subjects and apnea in none; the combination produced hypoxemia in 11 of 12 participants and apnea in half of the subjects.[9]

- An experimental study on the effects of co-administering high dose diazepam (40mg) with high dose methadone among patients maintained on regular opioid therapy (buprenorphine or methadone) found decreased SpO2 levels in the methadone group at 150% of normal dose, demonstrating a synergistic effect on respiratory depression.[10] (This effect was not seen with buprenorphine in this study.)

- Utah researchers conducted diagnostic polysomnographies on 140 patients with chronic pain who had been maintained on daily opioid therapy for at least 6 months, with a stable dose for at least 4 weeks. The patients were taking a variety of medication regimens, including benzodiazepines, muscle relaxants, and others. Of assessed combinations, the only medication usage pattern that had a statistically significant impact on the central apnea index was the combined used of methadone and

[7] White JM, Irvine RJ. Mechanisms of fatal opioid overdose. *Addiction.* 1999; 94(7):961–972.

[8] Gueye, PN, Borron, SW, Risede, P, et al. Buprenorphine and Midazolam Act in Combination to Depress Respiration in Rats. *Toxicol. Sci.* 2002; 65(1):107-114. doi: 10.1093/toxsci/65.1.107.

[9] Bailey, PL, Pace, NL, Ashburn, MA, Moll, JWB, East, KA, Stanley, TH. Frequent Hypoxemia and Apnea after Sedation with Midazolam and Fentanyl. Anesthesiology. 1990; 73:826-830.

[10] Lintzeris N, Mitchell T, Bond A, Nestor L, Strang J. Pharmacodynamics of diazepam co-administered with methadone or buprenorphine under high dose conditions in opioid dependent patients. *Drug Alcohol Depend.* 2007;91(2-3):187- 94.

benzodiazepines. The authors reported that "...benzodiazepines appeared to have an additive effect to the prevalence of methadone-related central sleep apnea."[11]

Of note, the danger of combining benzodiazepines and opioids has not always been observed at therapeutic doses of both medication classes. For example, in one study, therapeutic doses of diazepam in 16 patients on stable methadone or buprenorphine regimens caused sedation and subtle performance deficits in reaction time, but not physiologic changes in pulse, blood pressure, respiratory rate, or SpO2.[12]

Investigators have proposed potential mechanisms to explain the synergistic impact of opioids and benzodiazepines. It is generally thought that buprenorphine, a partial opioid agonist that is normally rarely associated with overdose death due to its natural ceiling effect for respiratory depression, loses this ceiling effect when taken in combination with benzodiazepines, resulting in risk of respiratory depression and death.[13,14] Other potential mechanisms include: (1) benzodiazepines may alter the pharmacokinetics of opioids through noncompetitive inhibition of opioid metabolism, (2) the analgesic, hyperphagic/hyperdipsic, anxiolytic, and rewarding effects of benzodiazepines may be partially mediated via opioidergic mechanisms, and (3) benzodiazepines may amplify the Mu agonist effects of opioids.[15]

[11] Webster, LR, Choi, Y, Desai, H, Webster, L, Grant, BJB. Sleep-Disordered Breathing and Chronic Opioid Therapy. *Pain Medicine.* 2008;9(4): 425-32.

[12] Lintzeris N, Mitchell T, Bond A, Nestor L, Strang J. Interactions on mixing diazepam with methadone or buprenorphine in maintenance patients. *J Clin Psychopharmacol*. 2006;26(3):274- 83.

[13] Lintzeris N, Nielsen S. Benzodiazepines, methadone and buprenorphine: interactions and clinical management. *Am J Addict.* 2010; 19(1):59-72.

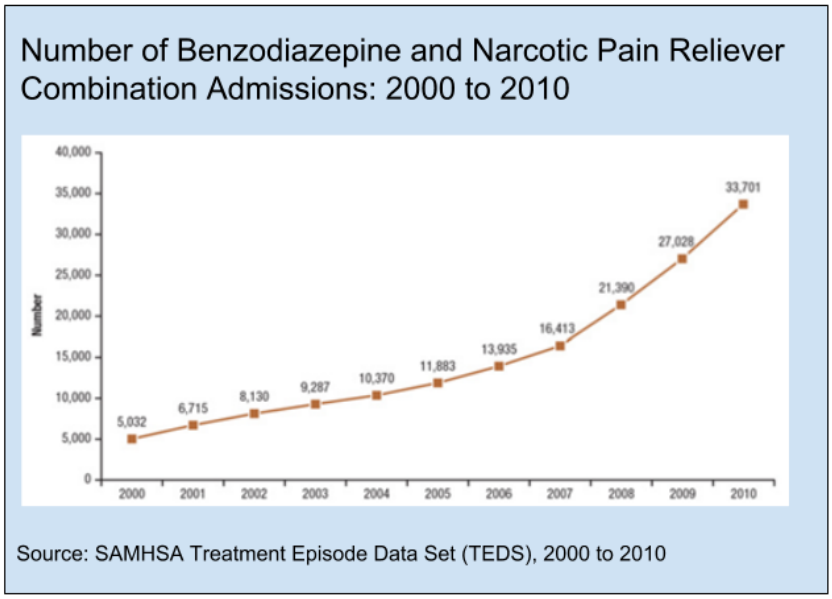
[14] DiPaula, B, Love, R. Lethal Mixtures-Benzodiazepines and Opioids, including Buprenoprhine. University of Maryland-School of Pharmacy. June 2014. Accessed January 18, 2016 at http://bha.dhmh.maryland.gov/OVERDOSE_PREVENTION/Documents/2014.06.11%20-%20Letter%20to%20Boards%20re%20Benzos%20and%20Opioids.pdf.

[15] Jones JD, Mogali S, Corner SD. Polydrug abuse: A review of opioid and benzodiazepine combination use. *Drug Alcohol Depend.* 2012; 125(1-2): 8–18.

III. EPIDEMIOLOGY

Complementing the biological evidence, data from multiple sources indicate that concurrent use and misuse of benzodiazepines and opioids is associated with addiction and overdose.

Data from Treatment Admissions. Studies of patient perception have shown that benzodiazepines potentiate the intensity and duration of the analgesic, euphoric, and sedative effects of opioids in a dose-response pattern, indicating potential for misuse and addiction.[16] Indeed, substance use disorders involving both opioids and benzodiazepines appear to be sharply increasing. According to the Substance Abuse Mental Health Services Administration, treatment admissions due to co-occurring addiction to benzodiazepines and opioids increased 569.7% from 2000 to 2010, while admissions due to all other substance use disorders decreased by 9.6% in the same time period.[17] (see Figure). During the month prior to treatment admission, of patients admitted for co-use of opioids and benzodiazepines, 57.1% and 45.5% reported daily use of opioids and benzodiazepines, respectively.[18]



Data from Death Certificates and Autopsies. The combination of benzodiazepines and opioids is becoming increasingly common in overdose deaths. Moreover, there is epidemiological evidence of a synergistic effect of the combination on the risk of death.

---

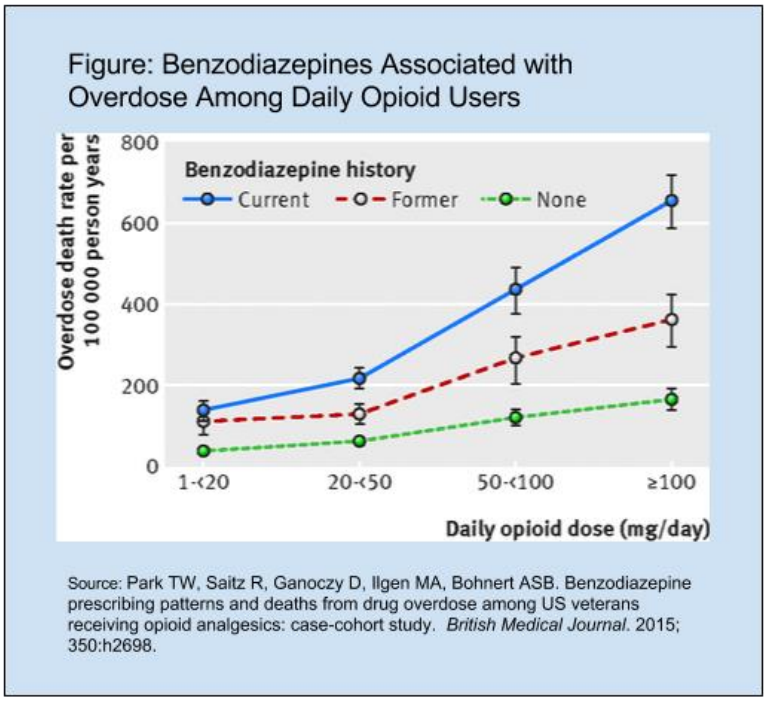
[16] *Ibid.*

[17] Substance Abuse and Mental Health Services Administration (SAMHSA), Center for Behavioral Health Statistics and Quality. *The TEDS Report: Admissions Reporting Benzodiazepine and Narcotic Pain Reliever Abuse at Treatment Entry.* 13 December 2012. Accessed January 18, 2016 at http://archive.samhsa.gov/data/2k12/TEDS-064/TEDS-Short-Report-064-Benzodiazepines-2012.htm.

[18] *Ibid.*

A recently published six-year case-cohort study of U.S. veterans nation-wide analyzed the relationship between history of benzodiazepine prescription, dose, type, and schedule and the associated risk of death from a drug overdose among patients who received treatment with opioid analgesics from the Veterans Health Administration. Study groups included veterans who died of a drug overdose and received opioids (n=2400) and a random sample of veterans who received opioid analgesics and services (n=420,386) from 2004 to 2009. During this study period, "...about half of the deaths from drug overdose (n=1185) occurred when veterans were concurrently prescribed benzodiazepines and opioids."

Significantly, the risk of death from drug overdose increased in a synergistic, dose-response fashion as daily benzodiazepine dose increased, as shown in the Figure. This risk was independent of dosing schedule.



The authors also found risk of death from overdose increased with history of benzodiazepine prescription, with the greatest risk associated with a current prescription.[19]

Epidemiological data show a high rate of involvement of benzodiazepines in opioid-related overdose deaths. For example:

- According to data from the National Vital Statistics System, 17% of the 13,800 opioid analgesic related deaths in 2006 involved concurrent use of benzodiazepines.[20] This rate of benzodiazepine involvement increased to 30% by 2010.[21]

[19] Park TW, Saitz R, Ganoczy D, Ilgen MA, Bohnert ASB. Benzodiazepine prescribing patterns and deaths from drug overdose among US veterans receiving opioid analgesics: case-cohort study. *British Medical Journal*. 2015;350:h2698.

[20] Warner M, Chen LH, Makuc DM. Increase in fatal poisonings involving opioid analgesics in the United States, 1999–2006. NCHS data brief, no 22. Hyattsville, MD: National Center for Health Statistics. 2009.

[21] Jones CM, Mack KA, Paulozzi LJ. Pharmaceutical overdose deaths, United States, 2010. *Journal of the American Medical Association* 2013 Feb 20;309(7):657-9.

- In 2012 in New York State, of 883 opioid analgesic-related deaths, 308 (34%) involved benzodiazepines.[22]

- According to data from the Rhode Island Department of Health, benzodiazepines were involved in 33% of prescription opioid fatalities from 2014 to 2015.[23]

- Maryland found benzodiazepines to be associated with 17.4% of prescription opioid deaths in 2012, 15.8% in 2013 and 18.5% in 2014.[24,25]

These data complement older data showing high rates of concurrent use of benzodiazepines in opioid overdose:

- A study reviewing death certificate data from 1999 to 2009 using the CDC Wide-Ranging Online Data for Epidemiologic Research database found benzodiazepines with opioids to be the most common polysubstance overdose fatality among 15 to 64 year olds.[26]

- A review of 493 methadone-associated deaths in New York City from 2003 found 32% involved benzodiazepines,[27] a review of 139 methadone-associated deaths in Palm Beach from 1998 to 2002 found 33% involved benzodiazepines,[28] and a review of 84

[22] Sharp MJ, Melnik TA; Centers for Disease Control and Prevention (CDC). Poisoning deaths involving opioid analgesics – New York State, 2003–2012. *MMWR*. 2015; 64:377–380

[23] Rhode Island Governor's Overdose Prevention and Intervention Task Force. Rhode Island's Strategic Plan on Addiction and Overdose Four Strategies to Alter the Course of an Epidemic. 4 November 2015. Accessed January 18, 2016 at http://www.health.ri.gov/news/temp/RhodeIslandsStrategicPlanOnAddictionAndOverdose.pdf.

[24] Maryland Department of Health and Mental Hygiene. Drug and Alcohol-Related Intoxication Deaths in Maryland, 2013. June 2014. Accessed January 10, 2016 at http://bha.dhmh.maryland.gov/OVERDOSE_PREVENTION/Documents/2014.07.07%20-%202013%20final%20intoxication%20report_updated.pdf.

[25] Maryland Department of Health and Mental Hygiene. Drug and Alcohol-Related Intoxication Deaths in Maryland, 2013. May 2015. Accessed January 10, 2016 at http://bha.dhmh.maryland.gov/OVERDOSE_PREVENTION/Documents/2015.05.19%20-%20Annual%20OD%20Report%202014_merged%20file%20final.pdf

[26] Calcaterra S, Glanz J, Binswanger IA. National trends in pharmaceutical opioid related overdose deaths compared to other substance related overdose deaths: 1999–2009. *Drug Alcohol Depend.* 2013; 131(3): 263-270.

[27] Chan G, Stajic M, Marker E, Hoffman R, Nelson L. Testing Positive for Methadone and Either a Tricyclic Antidepressant or a Benzodiazepine Is Associated with an Accidental Overdose Death: Analysis of Medical Examiner Data. *Acad Emerg Med.* 2006;13(5).

[28] Wolf BC, Lavezzi WA, Sullivan LM, Flannagan LM. Methadone-related deaths in Palm Beach County. *J Forensic Sci.* 2004;49(2):375–378.

methadone-associated deaths in Australia from 1993 to 1999 found 74% involved benzodiazepines.[29]

- In a comprehensive assessment of 117 fatalities from 1996 to 2000 involving high-dose buprenorphine in France, benzodiazepines were involved in at least 91 (78%).[30]

- A 1999 study of 82 opioid-related deaths in Ireland found benzodiazepines identified in 52 (61%) of the deaths.[31]

While most studies and attention have focused on the involvement of benzodiazepines in opioid-related deaths, the converse is also true: There is an extraordinarily high rate of opioid involvement in benzodiazepine associated deaths. For example, in Maryland, 74.0% of benzodiazepine associated deaths in 2012, 72.5% in 2013, and 59.2% in 2014 involved prescription opioids.[32,33]

IV. CLINICAL EDUCATION

Prescribers need to consider the serious adverse reaction of fatal overdose when assessing the risks and benefits of co-prescribing benzodiazepines and opioids. However, existing educational measures have not been sufficient for this purpose. As a result, a black box warning would provide significant benefit.

Prescribing Trends. The CDC's 2014 Vital Signs brief reported that prescribers wrote 82.5 opioid prescriptions and 37.6 benzodiazepine prescriptions per 100 persons in the United States in 2012.[34] Evidence indicates rates of co-prescription are rising. According to a study based on a database of 3.1 billion primary care visits, from 2002 to 2009, concurrent prescription of benzodiazepines with opioids increased by 12.0% per year, and benzodiazepine

[29] Ernst E, Bartu A, Popescu A, Ilett K, Hansson R, Plumley N. Methadone-related deaths in Western Australia 1993–99. *Aust Nz J Publ Heal.* 2002;26(4):364–370.

[30] Kintz P. Deaths involving buprenorphine: a compendium of French cases. *Forensic Sci Int*. 2001;121(1–2):65–69.

[31] Ward M, Barry J. Opiate-related deaths in Dublin. *Irish Journal of Medical Science*. 2001; 170 (1):35-37.

[32] Maryland Department of Health and Mental Hygiene 2014, *op. cit.*

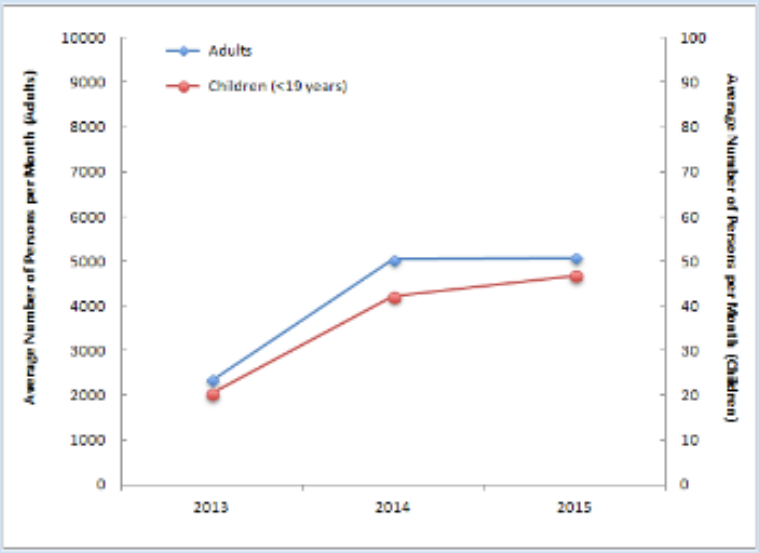
[33] Maryland Department of Health and Mental Hygiene 2015, *op. cit.*

[34] Paulozzim LJ, Mack KA, Hockenberry JM, Centers for Disease Control and Prevention. Vital Signs: Variation among states in prescribing of opioid pain relievers and benzodiazepines — United States, 2012.Morbidity and Mortality Weekly Report (MMWR). 2014: 63(26);563-568.

prescriptions increased by 12.5% per year. During this time, 12.6% of all primary care visits involved benzodiazepine or opioid prescriptions.[35]

Rhode Island has also seen increasing numbers of patients receiving both benzodiazepines and opioids, as shown in the figure below.

Figure: Average number of people dispensed both a benzodiazepine and an opioid medication within 30 days in Rhode Island



Source: Rhode Island Governor's Overdose Prevention and Intervention Task Force. Rhode Island's Strategic Plan on Addiction and Overdose Four Strategies to Alter the Course of an Epidemic.

Data from the Rhode Island Department of Health illustrate the frequency of co-prescription. Among all patients dispensed an opioid in the state in 2015, 27% also were dispensed a benzodiazepine at least once within 30 days of receiving an opioid. Of those dispensed a benzodiazepine, 59% were also dispensed an opioid at least once within 30 days of receiving a benzodiazepine.[36]

Based on such data, Rhode Island has set a priority of reducing co-prescription of benzodiazepines with opioids as a key component of their state's strategy to reduce prescription drug-related deaths.[37] As part of its citywide overdose prevention and response plan, the Baltimore City Health Department issued best

[35] American Academy of Pain Medicine (AAPM). Prescriptions for benzodiazepines rising and risky when combined with opioids, researchers warn. *ScienceDaily.* 6 March 2014. Accessed January 18, 2016 at www.sciencedaily.com/releases/2014/03/140306211040.htm.

[36] Rhode Island Governor's Overdose Prevention and Intervention Task Force, *op. cit.*

[37] Rhode Island Governor's Overdose Prevention and Intervention Task Force, *op. cit.*

practice letters to clinicians that emphasize the necessity of judicious prescribing of these two classes of medications.[38]

A common clinical scenario for co-prescription of opioids and benzodiazepines is the patient with chronic pain. Patients who receive opioids for chronic pain are often also prescribed benzodiazepines for associated symptoms including muscle spasms, anxiety and sleep disorder despite little evidence for therapeutic benefit in this clinical situation. In a national sample of chronic non cancer pain patients prescribed opioids, approximately one-third were current users of benzodiazepines.[39]

Yet there are hazards to this clinical practice. Concurrent benzodiazepine use in opioid users is not associated with improved symptoms; instead daily benzodiazepine users have reported higher pain severity and less coping with their pain.[40] While benzodiazepines are primarily indicated for sleep and anxiety disorders, Lintzeris and Nielsen of the University of Sydney have written that the evidence for these clinical recommendations is primarily, "...confined to short-term controlled trials of up to several months duration in non-opioid-dependent populations, and long-term observational studies of [benzodiazepine] treatment for these indications are difficult to interpret due to imprecision in the differentiation of relapse, rebound, and withdrawal phenomena."[41] A clinical guideline from the American College of Physicians and the American Pain Society in 2007 highlighted that benzodiazepines are not FDA-approved for treating low back pain and highlighted the risk for addiction and misuse if used for more than short-term relief for acute or chronic back pain. The guideline recommended benzodiazepines should only be used for a time-limited course of therapy.[42]

A second common clinical scenario is co-prescribing in the setting of co-existing psychiatric illness. Chronic pain patients using benzodiazepines frequently have comorbid mental health conditions. One study found that active benzodiazepine users were 50% more likely to have used antidepressants and three times more likely to have taken antipsychotic

---

[38] Committee Hearing: Opioid Abuse in America: Facing the Epidemic and Examining Solutions, 114th Cong. (2015) (testimony of Dr. Leana Wen). Accessed February 23, 2016 at http://www.help.senate.gov/imo/media/doc/Wen1.pdf.

[39] Nielsen, S., Lintzeris, N., Bruno, R., et al. Benzodiazepine use among chronic pain patients prescribed opioids: Associations with pain, physical and mental health, and health service utilization. *Pain Medicine* 2015; 16(2), 356-366.

[40] *Ibid.*

[41] Lintzeris N, Nielsen S. 2010, *op. cit.*

[42] Chou R, Qaseem A, Snow V, Casey D, Cross JT, Shekelle P, et al. Diagnosis and Treatment of Low Back Pain: A Joint Clinical Practice Guideline from the American College of Physicians and the American Pain Society. *Ann Intern Med.* 2007;147(7):478-491.

medication in the past month.[43] According to the Treatment Episode Dataset, a national data system that captures all admissions to addiction treatment centers in the U.S., almost half (45.7 percent) of all patients admitted for combined opioid and benzodiazepine use in 2010 reported having a co-occurring psychiatric disorder.[44] A black box warning will draw greater attention to the risks of combined use in this population.

Alternative approaches to combined use of opioid analgesic and benzodiazepines include nonpharmacologic treatment modalities for pain such as manipulation therapy, physical therapy, and massage. Similarly, use of other medication classes, meditation, and cognitive behavioral therapy for anxiety and sleep disorders may reduce concurrent use of benzodiazepines in patients with chronic pain.[45] A black box warning would help clinicians to consider alternatives to combined prescribing of opioids and benzodiazepines.

A black box warning would also lead specialty societies and others to focus on the risks of co-prescribing in their guidelines and educational programs to clinicians, supplementing existing measures to improve appropriate prescribing. In recent years, several clinical guidelines have been released advising providers and patients of the dangers of concurrent use. A CDC Brief assessing commonalities in recently-issued provider guidelines about opioids in chronic pain found the Utah State Clinical Guidelines on Prescribing Opioids for Treatment of Pain, the Washington State Agency Medical Directors Group Interagency Guideline on Opioid Dosing for Chronic Noncancer Pain, the Canadian Guideline for Safe and Effective Use of Opioids for Chronic Noncancer Pain, the New York City Department of Health and Mental Hygiene Opioid Prescribing Guidelines, and the American Society of Interventional Pain Physicians Guidelines for Responsible Opioid Prescribing in Chronic Noncancer Pain all recommended against co-prescription of benzodiazepines and opioids or urged caution or tapering one medication class.[46] The December 2015 draft of draft guidelines from the CDC on opioids for chronic pain

[43] Nielsen S, Lintzeris N, Bruno R., et al. 2015, *op. cit.*

[44] Substance Abuse and Mental Health Services Administration (SAMHSA), Center for Behavioral Health Statistics and Quality. *The TEDS Report: Admissions Reporting Benzodiazepine and Narcotic Pain Reliever Abuse at Treatment Entry.* 13 December 2012. Accessed January 18, 2016 at http://archive.samhsa.gov/data/2k12/TEDS-064/TEDS-Short-Report-064-Benzodiazepines-2012.htm.

[45] Gudin, JA, Mogali, S, Jones, JD, Comer, SD. Risks, Management, and Monitoring of Combination Opioid, Benzodiazepines, and/or Alcohol Use. Postgrad Med. 2013;125(4): 115–130.

[46] CDC: National Center for Injury Prevention and Control. Common Elements in Guidelines for Prescribing Opioids for Chronic Pain. 2016 January. Accessed February 7, 2016 at: http://www.cdc.gov/drugoverdose/pdf/common_elements_in_guidelines_for_prescribing_opioids-20160125-a.pdf

recommend against co-prescription whenever possible because "[c]oncurrent use is likely to put patients at greater risk for potentially fatal overdose."[47]

In January 2014, Institutes for Clinical Systems Improvement released an Acute Pain Assessment and Opioid Prescribing Protocol document for providers that specifically included benzodiazepine use in their ABCDPQRS Opioid risk assessment due to the increased risk of sedation and overdose with concurrent use leading to their clinical recommendation that "…patients using [benzodiazepines] and opioids should be counseled not to combine these medications…"[48]

With these guidelines buttressed by a black box warning, clinicians will be more likely to review their patients' medication lists, including medications prescribed by others, to avoid this potential hazard. A few examples of current risk assessment and mitigation tools include: the use of Prescription Drug Monitoring Programs, integration of appropriate urine drug tests into practice, increased consideration for non-opioid and non-pharmacological alternatives for pain management, and educational initiatives to increase provider awareness of Screening, Brief Intervention, and Referral to Treatment (SBIRT) initiatives and other referral resources.

A black box warning would enhance educational efforts by public health officials. In June 2014, the Maryland Department of Health and Mental Hygiene sent a letter to all licensed physicians warning of the "potentially lethal combination of benzodiazepines and opioids."[49] Other states and localities are planning similar efforts.

---

[47] Dowell, D, Haegerich, TM, Chou, R. CDC Guideline for Prescribing Opioids for Chronic Pain — United States, 2016 [Draft]. 15 December 2015.

[48] Thorson D, Biewen P, Bonte B, Epstein H, Haake B, Hansen C, Hooten M, Hora J, Johnson C, Keeling F, Kokayeff A, Krebs E, Myers C, Nelson B, Noonan MP, Reznikoff C, Thiel M, Trujillo A, Van Pelt S, Wainio J. Institute for Clinical Systems Improvement. Acute Pain Assessment and Opioid Prescribing Protocol. January 2014. Accessed February 7, 2016 at: https://www.icsi.org/_asset/dyp5wm/Opioids.pdf.

[49] Sharfstein J, Jordan-Randolph G, Gahunia M, Hadley L. Maryland Department of Health and Mental Hygiene Public Letter. 11 June 2014. Accessed January 18, 2016 at http://bha.dhmh.maryland.gov/OVERDOSE_PREVENTION/Documents/2014.06.11%20-%20Cover%20Letter%20to%20Boards%20re%20Benzos%20and%20Opioids.pdf

V. EXISTING LABELING

Only a few labels and medication guides contain specific information on the dangers of concurrent use of these two classes of medications; none contain black box warnings.

Opioids. The labels or guides for buprenorphine, fentanyl, and methadone specifically mention the risk of concurrent use with benzodiazepines. For example, the buprenorphine label, in warnings, states, "A number of deaths have occurred when addicts have intravenously misused buprenorphine, usually with benzodiazepines concomitantly." Suboxone (buprenorphine) also has a medication guide that informs patients about the risk of benzodiazepines, stating: "You have a higher risk of death and coma if you take Suboxone with other medications, such as benzodiazepines." The label for methadone states, "Deaths associated with illicit use of methadone frequently have involved concomitant benzodiazepine abuse." The medication guide for methadone, however, does not mention this risk. The labels and medication guides for other commonly prescribed opioids, including oxycodone, hydrocodone, and codeine, only make general and inconsistent mention of interactions with Central Nervous System (CNS) depressants and sedatives.

Benzodiazepines. There is scattered and inconsistent mention of potential problems with concurrent use of opioids on the labels of some benzodiazepine medications. For example, the label for midazolam states, in the interaction section, "the sedative effective….is accentuated by any concomitantly administered medication which depresses the central nervous system, particularly narcotics (e.g., morphine, meperidine and fentanyl)…" The label of diazepam states, in the precautions section, "If diazepam is to be combined with other psychotropic agents…careful consideration should be given to the pharmacology of the agents to be employed, particularly with known compounds which may potentiate the action of diazepam, such as….narcotics." The medication guide for diazepam generically cautions against simultaneous use with alcohol and other CNS-depressant drugs.

Existing warnings on concurrent use of benzodiazepines and opioids are inconsistent, infrequent, and insufficient. They fail to reflect the strong biologic and epidemiological data on risks to patients of respiratory depression and fatal overdose from combining these classes of medications.

VI. PUBLIC EDUCATION

A black box warning would help patients recognize the risks of concurrent use of benzodiazepines and opioids and would emphasize the need to discard old or expired medications that could be otherwise combined with new prescriptions for dangerous effects. It

would support education efforts aimed at informing the general public about the epidemic of fatal overdose and the importance of judicious prescribing.

VII. POTENTIAL OBJECTIONS

Some may object to class warnings when all possible combinations between opioids and benzodiazepines have not been fully studied. However, it is our view that the basic science and epidemiology support class effects that obviate the need for additional research. Moreover, clinicians and patients should generally be aware of the dangers; a strong black box warning will provide a clear general message to improve care and save lives.

VIII. FDA AUTHORITY

The Food and Drug Administration Amendments Act of 2007 ("FDAAA"), Section 901(a) of the FDAAA added Section 505(o)(4) to the FDCA, granted FDA authority to mandate post-approval safety-related labeling changes for both individual drugs and classes of drugs.[50]

IX. CONCLUSION

FDA guidance[51] supports the use of black box warnings in several circumstances, including when:

- "There is an adverse reaction so serious in proportion to the potential benefit from (e.g., a fatal, life-threatening or permanently disabling adverse reaction) that it be considered in assessing the risks and benefits of using the drug;"
  or
- "There is a serious adverse reaction that can be prevented or reduced in severity by appropriate use of the drug (e.g., patient selection, careful monitoring, avoiding certain concomitant therapy, addition of another drug or managing patients in a specific manner, avoiding use in a specific clinical situation)"

Both of these conditions are met for the risk of fatal overdose from co-prescribing of benzodiazepines and opioids. Biological and epidemiological data support the urgency of action to warn prescribers and the public about this risk.

Based on this scientific record, we petition that the FDA:

1. Create and mandate black box warnings for all opioids and benzodiazepine class medications to read as follows:

   Labeling for all Opioid Class Medications should read:

[50] Danzis, SD, Pitlyk, SE. FDAAA's Safety Labeling Provisions. *Update Magazine.* 2009; 10-13. Accessed February 7, 2016 at https://www.cov.com/~/media/files/corporate/publications/2009/01/fdaaas-safety-labeling--provisions.pdf

[51] Food and Drug Administration 2011, *op. cit.*

WARNING: CONCURRENT USE WITH BENZODIAZEPINES REDUCES THE MARGIN OF SAFETY FOR RESPIRATORY DEPRESSION AND CONTRIBUTES TO THE RISK OF FATAL OVERDOSE, PARTICULARLY IN THE SETTING OF MISUSE.

Labeling for all Benzodiazepine Class Medications should read:

WARNING: CONCURRENT USE WITH OPIOIDS REDUCES THE MARGIN OF SAFETY FOR RESPIRATORY DEPRESSION AND CONTRIBUTES TO THE RISK OF FATAL OVERDOSE, PARTICULARLY IN THE SETTING OF MISUSE.

2. Require medication guides for both classes of medications that specifically warn patients of the potential dangers of combined use of opioids and benzodiazepines.

As physicians, public health officials, and researchers who have both analyzed the evidence and seen the impact of opioid overdose first-hand in our patients and loved ones, we urge the FDA to promptly consider these changes.

ENVIRONMENTAL IMPACT

According 1921 CPR Sec. 25.31(a), this Petition qualifies for a categorical exclusion from the requirement that an environmental impact statement be submitted.

ECONOMIC IMPACT

According to 21 CPR See 10.30(b)~ an economic impact statement is to be submitted only when requested by the Commissioner following reviewing of this Petition.

CERTIFICATION

The undersigned certifies that, to the best knowledge and belief of the undersigned, this petition includes all information and views on which the petition relies, and that it includes representative data and information known to the petition that are unfavorable to the petition.

Respectfully submitted,

Leana Wen, M.D. M.Sc
Commissioner of Health,
Baltimore City Department of Health

Nicole Alexander-Scott, M.D., M.P.H.
Director, Rhode Island Department of Health

Elizabeth Fracica,
M.D., M.P.H candidate,
Johns Hopkins Bloomberg School of Public Health, Mayo Medical School

Abdul El-Sayed, M.D., DPhil
Executive Director & Health Officer,
City of Detroit

Harry Chen M.D.,
Commissioner, Vermont Department of Health

Asha Isable, M.D.,
M.P.H. candidate,
Johns Hopkins Bloomberg School of Public Health

Mary T. Bassett, M.D., M.P.H.
Commissioner,
New York City Department of Health

Edward P. Ehlinger, M.D., MSPH
Commissioner,
Minnesota Department of Health

Traci Green, MSc, PhD, Assistant Professor of Emergency Medicine and Epidemiology at Brown University

Julie Morita, M.D.,
Commissioner,
Chicago Department of Public Health and Mental Hygiene

Howard M. Haft, M.D.,
Deputy Secretary for Public Health Services, Maryland Department of Health and Hygiene

Elinore F. McCance-Katz, M.D., PhD
Chief Medical Officer,
Rhode Island Department of Behavioral Health, Developmental Disabilities, and Hospitals

Gretchen Musicant,
Commissioner of Health,
Minneapolis Health Department

Raul Pino M.D., M.P.H.,
Acting Commissioner,
Connecticut Department of Public Health

G. Caleb Alexander, M.D., FACP
Co-Director, Johns Hopkins Center for Drug Safety and Effectiveness

Monica Valdes Lupi, J.D., M.P.H.
Executive Director,
Boston Public Health Commission

Karen M. Murphy, PhD R.N.
Secretary of Health,
Pennsylvania Department of Health

Sidney Wolfe, M.D.,
Founder and Senior Adviser, Health Research Group, Public Citizen

Huy Nguyen, M.D.
Medical Director,
Boston Public Health Commission

Karyl Thomas Rattay M.D., M.S.
Director, Delaware Division of Public Health

Josiah D. Rich, M.D., M.P.H.
Director of the Center for Prisoner Health and Human Rights

Caroline C. Johnson, M.D.
Acting Medical Director,

Monica Bharel, M.D., M.P.H.
Commissioner,

Wayne Nicholson, M.D., Pharm.D.
Assistant Professor of

Philadelphia Department of Public Health

Robert McDonald
Executive Director, Public Health Administrator,
Denver Department of Environmental Health

Stephen L. Williams, M.Ed., M.P.A.
Director,
Houston Health Department

Tomás J. Aragón, M.D., DrPH
Director, Population Health Division (PHD) San Francisco Department of Public Health

Zachary Thompson
Director, Dallas County Health and Human Services

Olivia Kasirye, M.D., M.S.
County Public Health Officer
Sacramento County

Kelly Colopy
Director, Long Beach Department of Health and Human Services

Massachusetts Department of Public Health

Esther Muna, M.H.A, C.P.C.
Acting Secretary for Hospital Administration, Northern Mariana Islands Department of Public Health

James W. Gillan
Director, Guam Department
of Public Health and Social Services

Kenneth Albert R.N., Esq.
Director and Chief Operating Officer
Maine Center for Disease Control & Prevention

Catherine Heigel,
Director (SHO), South Carolina Department of Health and Environmental Control

Richard H. Opper,
State Health Officer and Director,
Montana Department of Public Health and Human Services

Rahul Gupta, M.D., M.P.H., FACP
Commissioner, State Health Officer
Bureau of Public Health
West Virginia Department of Health and Human Resources

Jay C. Butler, M.D.
Chief Medical Officer, and Director,
Division of Public Health
Alaska Department of Health
And Social Services

Cara Christ, M.D., M.S.
State Health Official, Arizona
Director, Arizona Department of Health Services

Nathaniel Smith, M.D., M.P.H.
Director and State Health Officer,
Arkansas Department of Health

Anesthesiology and Pharmacology
Mayo Clinic College of Medicine

Tae Woo (Ted) Park, M.D., M.S.
Assistant Professor, Depts. of Medicine and Psychiatry and Human Behavior, Warren Alpert Medical School of Brown Univ.

Yngvild Olsen, M.D., M.P.H.
Medical Director, Institutes for Behavior Resources, Inc./ REACH Health Services

CITY OF BALTIMORE

STEPHANIE RAWLINGS-BLAKE, Mayor

HEALTH DEPARTMENT
Leana S. Wen, M.D., M.Sc., FAAEM
Commissioner of Health
1001 E. Fayette St.
Baltimore, MD 21202
health.commissioner@baltimorecity.gov
Tel: 410-396-4387

Biography for Leana S. Wen, M.D. M.Sc. FAAEM

Dr. Leana Wen is the Health Commissioner of Baltimore City. She leads the Baltimore City Health Department (BCHD), the oldest continuously-operating health department in the United States, formed in 1793. BCHD is an agency with a $130 million annual budget and 1,000 employees that aims to promote health and improve well-being through education, policy/advocacy, and direct service delivery. BCHD's wide-ranging responsibilities include maternal and child health, school health, senior services, animal control, restaurant inspections, emergency preparedness, STI/HIV treatment, and acute and chronic disease prevention. Dr. Wen also serves as Chair of the Board of Behavioral Health System Baltimore, a $75-million nonprofit that is the City's designated behavioral health authority.

Since her appointment in January 2015, Dr. Wen has led the implementation of the citywide opioid overdose prevention and response plan, which includes "hotspotting" and street outreach teams to target individuals most at risk, training police officers and lay people on naloxone use, issuing a "blanket prescription" for all 620,000 residents in the city, and launching a new public education campaign (www.dontdie.org) that includes a first-of-its-kind online naloxone training. In the wake of the civil unrest in April, she directed the city's public health recovery efforts, including ensuring prescription medication access to seniors after the closure of 13 pharmacies and developing the Mental Health/Trauma Recovery Plan, with 24/7 crisis counseling and healing circles and group counseling in schools, community groups, and churches.

Dr. Wen is a board-certified emergency physician. She received her medical training from Washington University School of Medicine in St. Louis and Brigham & Women's Hospital/Massachusetts General Hospital in Boston, where she was a Clinical Fellow at Harvard Medical School. A Rhodes Scholar, she received her Master's degrees at the University of Oxford. She has served as a consultant with the World Health Organization, Brookings Institution, and China Medical Board; an advisor to the Patient-Centered Outcomes Research Institute and the Lown Institute; as national president of the American Medical Student Association and American Academy of Emergency Medicine-Resident & Student Association; as a member of the Council on Graduate Medical Education, an advisory commission to Congress. Prior to her appointment in Baltimore, she was a professor of Emergency Medicine and Health Policy at The George Washington University, where she co-directed the Residency Fellowship in Health Policy and co-led a new national collaboration on health policy and social mission with Kaiser Permanente.

An expert on public health policy, patient safety, and U.S. and international health systems reform, Dr. Wen has published over 100 articles including in *The Lancet*, *The Journal of the American Medical Association*, *Health Affairs*, *American Journal of Public Health*, *Journal of Health Security*, *Annals of Internal Medicine*, and *British Medical Journal*. Author of the critically-acclaimed book *When Doctors Don't Listen: How to Avoid Misdiagnoses and Unnecessary Tests*, Dr. Wen has been featured on NPR, CNN, Fox, and MSNBC, and in *The Atlantic*, *The New York Times*, and *The Washington Post*. Her TED talk on transparency in medicine has been viewed over 1.4 million times.