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CENTER FOR
SUBSTANCE
ABUSE
RESEARCH

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**Drs. Kathleen Reeves and Ellen Unterwald's testimony to the joint
House Republican, House Democratic, and Senate Democratic Policy Committees;
Hearing on the opioid abuse epidemic, August 16, 2016**

Dear Members of the Committee:

Thank you for the opportunity to participate in this very important hearing. My name is Kathy Reeves. I am a pediatrician and the Senior Associate Dean of Health Equity, Diversity and Inclusion at the Lewis Katz school of Medicine. I am here with Dr. Ellen Unterwald who is a Pharmacologist and the Director of the Center for Substance Abuse Research here at the medical school. As a clinician and a basic scientist we appreciate the chance to share with you what we think is the best way to address the problem of opioid addiction.

I am sure you all know a lot about the significance of the current epidemic of opioid and heroin use in the United States today, so we are not going to spend time sharing those statistics. We would like to move on to what we believe needs to be done to address the problem of opioid abuse and dependence.

As with any disease that is as prevalent as this and that is growing at such an exponential rate as this, a comprehensive public health approach much be implemented. This requires a three pronged approach: an evidence based prevention strategy; better access to already proven-treatment plans; and a strong translational research effort that starts with understanding the biology of the disease and progresses through applying newly acquired knowledge to new prevention and treatment modalities especially for patients who do not respond to traditional treatment programs.

1. Improve Prevention Approaches:

Temple Health is uniquely positioned to build and evaluate this public health approach. First and foremost, we must concentrate on prevention. Prevention, more than anything else, results in the best health outcomes and causes the largest reduction in cost associated with addiction. Most prevention strategies have focused on education at a community level. Few if any resources have been committed to preventing opioid addiction *when* people are being exposed to the drug for medical indications. There is good evidence regarding which populations of patients are most susceptible to becoming addicted to opioids and heroin. We know that exposure to adverse experiences in childhood, genetic changes that result from exposure to trauma, and our family histories all greatly impact our likelihood to become addicted. We are implementing programs to study a new prevention strategy that screens patients for their susceptibility to addiction prior to them ever receiving an opioid medication. Based on these screening results we will develop and implement a treatment plan at the time when the patient is needing pain control and taking an opioid analgesic. This will include maximizing other methods of pain reduction, close monitoring of opioid use, and ongoing behavioral health individual and group counseling. We have also noted opioid addiction to be an educational priority in our medical school. We are developing curricula for medical students, residents and attending physicians regarding more responsible treatment and follow up plans when prescribing any opioids to any patient.

2. Enhance Access to Treatment:

Next we must concentrate on better access to already proven treatment programs. We are all very appreciative of what you have already done regarding this; the newly announced centers of excellence will fill a much needed hole regarding access for many of our communities. However, there are still large gaps in access. SAMSHA has reported that there are huge needs in both rural and urban areas regarding access, but the needs differ. For example, there is a difference in how people are referred to treatment centers. In rural areas people are often referred to rehabilitation programs through the criminal justice system. The patients are much more willing to take part in therapy when referred in this way and they also realize that their access to the substance will be limited going forward. In urban centers, hardly anyone is referred through criminal justice; self referral is more common which makes it much more difficult to successfully enroll people into therapy. We have a specific community engagement core centered on the strengths and challenges of an urban, distressed community and believe we have the expertise to engage this community in a way to improve awareness and access to treatment. We are developing, implementing and evaluating innovative ways to work with our local communities and neighborhoods to find other avenues to help people get into available treatment programs without suffering terrible legal and social consequences.

3. Expand Research on Addiction:

Finally and maybe even most importantly, we need to research better ways to prevent and treat addiction. That is what we would do with any disease that is afflicting so many people. And that is something we excel in locally, nationally and internationally. There are so many new and innovative ways to use science to prescribe less opioids but still achieve pain relief, to treat individuals with different drugs and different strategies especially when traditional treatment methods have not been successful. We are so very fortunate to have Dr. Ellen Unterwald as a leader in the field here at Temple. She directs the Center for Substance Abuse Research and, together with her colleagues have been bringing science to bear on the addiction crisis.

We would like to propose to you that a critical missing piece in the effort to solve the opioid abuse problem is in the area of research. High quality basic, translational and clinical research is needed to establish the best practices in the areas of prevention and treatment of addiction. Evidence-based approaches that are built upon rigorous scientific findings are essential to successfully prevent and treat addiction in our communities. The National Institutes of Health recognizes addiction as a brain disease. Like all other diseases, understanding the biological basis of the disease is essential to effectively prevent and treat it. Basic science research has been the cornerstone for improving health in our country and around the world. Through research discoveries, effective prevention and treatment approaches have been put into practice for many illnesses. Addiction should be no different.

There are two areas of basic and translational research that could have a major impact on the opioid abuse epidemic; these include research focused on 1) reducing the reliance on opioids for the treatment of pain and 2) the addiction process itself. New knowledge gained from these areas of investigation would help prevent opioid abuse and provide support for novel treatment approaches. Here at the Lewis Katz School of Medicine at Temple University, there are faculty in the Center for Substance Abuse Research who are dedicated to such important goals. For example, on-going basic science research studies are discovering promising approaches to eliminate or decrease the amount of opioid needed to alleviate pain. One of these approaches includes the use of combination therapies with clinically approved non-addicting drugs which results in greatly reduced doses of opioids while being efficacious in relieving even severe pain. Other basic science studies are testing novel treatments for pain that will eliminate the need for opioid drugs entirely. It is well appreciated that one of the main causes of the current opioid abuse epidemic is the drastic increase in the prescribing of opioids for pain that has occurred over the past 15 years. Hence, reduced reliance on opioids for the treatment of pain should be a primary goal, and basic research such as that going on at Temple is needed to achieve this goal.

The second area of research that is needed is in the understanding of the addiction process. What are the changes that occur in the brain that drive the compulsion to continue to engage in drug-taking activities despite the known harm to oneself and one's family? Our faculty are using state-of-the-art rodent models to discover alterations in

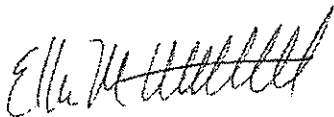
brain function produced by opioids that drives this compulsion and perpetuates addiction. As brain changes are identified, so too are methods to reverse them as a way to treat addiction and prevent relapse to drug use.

Findings such as those described above must be translated into clinical use in order for them to impact the current opioid abuse epidemic. Support for translational research to rigorously test new discoveries for the relief of pain and the treatment of addiction in clinical populations is needed to implement research advancements. Likewise, clinical research is required to evaluate the efficacy of current prevention and treatment approaches. Research on the needs of specific populations should be undertaken given what we know about differences in, for example, urban and rural populations and access to treatment, in order to use our resources in the most efficient and effective manner.

Addiction is a chronic disease. As such, we need to approach its prevention, treatment and cure as we have for other diseases. We need to implement proven evidence-based approaches while continuing to research new and better treatments. In order to be successful, financial support for research is essential. What can be achieved with the proper support is highlighted by the progress made in the treatment of HIV/AIDS. Twenty years ago, an AIDS diagnosis was a death sentence. Through aggressive funding of HIV research by our government, extraordinary progress has been made in areas of education, prevention, and treatment of this disease. AIDS has been transformed to a chronic illness with hopes of a cure on the horizon. Addiction deserves the same attention and support.

Thank you for this opportunity to provide testimony on this important issue.

Respectfully submitted, August 16, 2016,



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Appendix: please see attached document "Temple Health Institute for Research on Education, Prevention and Treatment of Addiction"

Temple Health Institute for Research on Education, Prevention and Treatment of Addiction

Deaths from drug overdose have been increasing at alarming rates, and Pennsylvania has one of the highest overdose rates in the country. Prescription opiates, being second only to marijuana as the first illicit substance individuals try, have led to a rise in opiate use disorders with significant morbidity and mortality. Not surprisingly, opiates are significant contributors to escalating death rate from drugs as well as substantial morbidity, decreased work productivity and soaring medical expenditures. In addition to the clear commitment that Pennsylvania has made to expanding opportunities for community based treatment, a substantial investment is required in research to develop new, cutting edge treatment and prevention strategies including enhanced education for healthcare professionals. Addressing this public health crisis has intrinsic challenges given limited scientific evidence on best practices for the prevention and treatment of those struggling. Temple Health has always acknowledged our responsibility and commitment to improving the health of the people who live in North Philadelphia. As with any epidemic, we are moving to find the best and most innovative ways to address this health crisis. As a result, Temple Health is creating the Temple Health Institute for Research on Education, Prevention and Treatment of Addiction, described herein, to provide these answers.

Temple University Lewis Katz School of Medicine is one of the premier research institutions in the Commonwealth and has the advantage of housing the internationally recognized Center for Substance Abuse Research (CSAR) headed by Dr. Ellen Unterwald, coupled with a network of community based treatment, education and prevention programs. The following mission statement outlines our integrated Temple Research Institute leveraging the unique strengths of our basic science research program with the clinical populations required to test and implement clinically relevant advancements, in addition to enhancing educational programming. Once tested and perfected, these innovations will be widely implemented thus transforming care of patients with substance use disorders across the Commonwealth of Pennsylvania. The proposed Temple Health Institute for Research on Education, Prevention and Treatment of Addiction would make Pennsylvania a leader in identifying, through research, new and innovative strategies to prevent and treat substance abuse disorders.

The Specific Aim of the new Temple Research Institute is to provide an infrastructure for engaging Temple experts from multiple disciplines in collaborative research to determine the best practices to combat the opioid abuse epidemic. This aim will be achieved using the following multimodal approaches:

1. Evaluate and identify the most effective education programs for health care professionals.
2. Expand the preclinical research of the existing Temple Center for Substance Abuse Research in understanding the biological basis of addiction and the development of new approaches to prevent and treat opioid abuse and dependence.
3. Provide a mechanism for translational research, in order to convert preclinical findings into clinical studies to more effectively prevent and treat opioid use disorders.
4. Use evidence-based findings to develop and implement enhanced prevention strategies particularly in populations at high risk for development of substance abuse, such as persons who have experienced trauma during childhood, patients with chronic pain, and persons exposed in utero to opioids.
5. Engage the North Philadelphia community in health needs assessments in order to develop and study optimal patient treatment strategies for Pennsylvanians who suffer from opiate addiction.
6. Disseminate research findings throughout Pennsylvania.

Temple is uniquely positioned to develop this Institute as it has core, essential components already in place:

1. The Center for Substance Abuse Research (CSAR) is a nationally recognized basic science research center, established in 1998, dedicated to discovering new knowledge on the molecular, biochemical, anatomical and physiologic basis of drug addiction and dependence. CSAR has been recognized as a premier research group by the National Institute on Drug Abuse (NIDA/NIH) with the award of a major

Center of Excellence grant establishing a “Center on Intersystem Regulation by Drugs of Abuse” (continuous funding since 2000-2020).

2. Lewis Katz School of Medicine is a national leader in medical education and has the tools needed to develop, implement and study new educational models that can be used to better train health care providers to use proven tools to help prevent and treat substance abuse.
3. Temple Health Department of Psychiatry provides comprehensive high quality mental health services to the communities in Philadelphia and has the expertise to oversee a clinical research arm for the treatment and prevention of substance abuse.
4. Temple Health Department of Obstetrics/Shriner’s Pediatric Research Institute has applied to the Commonwealth of Pennsylvania to develop a Clinical Center of Excellence to expand opportunities for treatment of opioid use disorder (OUD) in pregnancy, specifically to provide more ready access to buprenorphine based regimens which are associated with improved perinatal outcomes. The Temple/Wedge Medical Center OUD Program provides the ideal venue for research that could potentially lead to the development of an optimal treatment program for addicted mothers while reducing enhance vulnerability to substance abuse in their offspring.
5. Our Center for Bioethics, Urban Health and Policy (CBUHP) has a strong community engagement core that will be essential to engaging communities in a research effort that will help us better understand addiction and current treatment strategies. CBUHP also is currently studying the effects of childhood and unresolved trauma on health and believes this is an area that is under-studied in the treatment of addiction.

Leveraging relationships from existing community partnerships with Saint Joseph’s Hospital Detox and Rehabilitation Services, Wedge Medical Center, and Outpatient Services at the Girard Medical Center, the Institute will draw on Temple’s vibrant community engagement core to layer community health needs assessments in caring for patients struggling with substance misuse onto newly studied prevention and treatment strategies. The integration of new scientific data on substance abuse prevention and management as well as the community health needs assessments can be utilized to transform existing infrastructures, such as Saint Joseph’s Hospital Detox and Rehabilitation Services, into treatment centers that also are excellent research centers to study new, evidence based and innovative modalities to prevent addiction and more effectively treat people who already are suffering from substance abuse disorders. The Institute will be able to develop and validate improved educational curricula that will allow us to foster a more educated and prepared group of health care professionals. This new infrastructure will further the educational mission of the Institute in serving as a location where students and other trainees across health care disciplines can learn evidence-based prevention and treatment modalities to combat substance misuse.

The Temple Research Institute will concentrate on opioid abuse, and all activities will be evaluated and translated into education, prevention and treatment strategies for dissemination across Pennsylvania. Examples of some of the innovative new approaches that will be studied are described.

Prevention.

1. The Center for Substance Abuse Research (CSAR) has been investigating new therapeutic strategies to aid in the treatment of pain and prevention of addiction. Reduced reliance on opioid analgesics to treat pain would have a significant impact on opioid abuse and dependence. Using preclinical pain models, investigators in CSAR have demonstrated several promising approaches to eliminate or decrease the total amount of narcotic needed to alleviate pain. These approaches include the use of combination therapies with clinically approved non-addicting drugs such as ceftriaxone, clavulanic acid, and plerixafor, or the use of non-psychoactive phyto-cannabinoids such as cannabidiol. For example, CSAR investigators have discovered that the antibiotic ceftriaxone reduces synaptic glutamate levels in brain regions important for opioid actions, and through this mechanism can reduce opioid analgesic tolerance and dependence. The Temple Health Institute would support continued basic science research aimed at

discovery of novel non-opioid treatments for pain and facilitate translating these findings into clinical studies.

2. Current studies of adults who have experienced unpredictable, repeated traumatic events during childhood have shown a strong relationship between these adverse experiences and later development of substance abuse disorders. The Centers for Disease Control recognizes this connection and has reported that adults who score above 4 on the 10 question Adverse Childhood Experiences (ACE's) study are 7 times more likely to suffer from substance abuse. Despite these data, current risk assessment tools used by physicians do not include ACE scores and therefore the new Temple Research Institute through the work of Dr. Kathleen Reeves, Director of CBUHP, will develop a validated risk assessment tool that appropriately addresses this risk factor. Using tools like the ACE survey to identify the most at risk populations will allow us to tailor preventative strategies before prescribing narcotics for the treatment of pain and help us develop ongoing treatment plans to prevent their high rates of substance abuse. Clinical studies will be informed and augmented by basic research in CSAR on the cause of the association between adverse childhood experiences and substance use disorders. CSAR investigators will utilize preclinical models of early life trauma which will allow the investigation of gene and brain changes that may underlie increased susceptibility to addiction in this population.
3. In an effort to prepare medical students, residents and fellows to address the current opioid epidemic and to contribute to the reduction in opioid abuse, the Lewis Katz School of Medicine has established core competencies for the diagnosis and management of pain, use and misuse of prescription medicines, and prevention and treatment of drug addiction. The core competencies include, but are not limited to, the ability to evaluate a patient in pain and to identify potential pharmacological and non-pharmacological treatment options, ability to evaluate a patient's risk for substance abuse along with skills needed for patient counseling in the prevention of opioid abuse, ability to recognize the symptoms of substance abuse and the treatment options, and to overcome societal biases against individuals with substance abuse disorders. The curriculum will be longitudinal, with aspects to include students from our other health professions schools (eg, physician assistant, pharmacy, nursing and dental). Through the new Temple Research Institute, the effectiveness of different teaching modalities will be assessed to determine best practices for educating health professionals about prevention and treatment of opioid use disorders.
4. The Temple Research Institute would engage with other experts including those in Temple University's Department of Criminal Justice to evaluate current policies in criminal justice settings that not only neglect efforts aimed at preventing substance abuse but may at times contribute to the societal problem of substance abuse.

Treatment

1. Investigators in the Center for Substance Abuse Research are performing preclinical research directed at the discovery of novel strategies to treat opioid dependence and prevent relapse, as well as to understand the biological basis of opioid tolerance and dependence. Using rodent models of heroin, oxycodone, and morphine self-administration, progress has been made in identifying brain pathways and genes involved in opioid dependence. Importantly, several promising leads have been discovered that may prove useful in the treatment of dependence and prevention of relapse. The Institute will support continued basic science research on new treatments and facilitate bringing this knowledge into clinical testing.
2. In 2014 almost 2000 infants were born into PA Medicaid with Neonatal Abstinence Syndrome and 817 infants were removed from their home due to parental substance abuse. Pregnancy is an ideal window of opportunity to identify and treat opioid use disorder (OUD): drug screening occurs in a high proportion of patients, and women have a high level of medical visits and are profoundly motivated to seek treatment due to concerns for fetal effects. An application submitted to the Commonwealth proposes the formation of The Temple/Wedge Opioid Use Disorder Pregnancy Center of Excellence which will collaborate with the Temple Research Institute to identify and validate optimal treatment programs for pregnant women. Above and beyond adequate treatment, there is a growing concern

that in-utero exposure to opioids affects fetal brain chemistry in ways that may predispose exposed children to adverse behavioral outcomes and increased susceptibility to subsequent addiction disorders. Novel methods developed in Dr. Laura Goetzl's laboratory include ways to interrogate fetal and neonatal brain development through a simple maternal or pediatric blood test. This testing is based on the discovery that small packets of information are released by fetal and infant neurons which can be obtained from maternal or pediatric blood samples. This permits monitoring fetal brain levels of important drug receptors during pregnancy and childhood. Using this novel testing strategy we plan to translate basic science discoveries from animal models pioneered in Dr. Unterwald's Center for Substance Abuse Research to pregnant women in North Philadelphia. We plan to investigate whether buprenorphine based treatments used in weaning mothers to an opioid-free state improves or restores normal fetal brain chemistry. The premise of this potentially high impact project is that children born to Pennsylvania women with OUD would have available interventions to decrease next generation opioid abuse and adverse behavioral effects, preventing the creation of a vulnerable second generation of citizens.

3. The management of substance use disorders requires a multidisciplinary and multimodal approach. Community health needs assessments that draw on information from individuals who have already sought and/or received treatment as well as those community members who are not involved in substance use treatment will be critical in identification of appropriate services and partners that need to be part of the medical neighborhood to care for patients with substance use disorders. Drs. Mary Morrison and David O'Gurek and their collaborators in the Temple Research Institute will use this knowledge in the transformation of care sites into comprehensive treatment centers. Newer innovative evidence-based harm reduction strategies will be considered in the community needs assessment such as opioid overdose education, naloxone distribution and supervised injection sites. These programs have facilitated reduction in overdoses related to opioid use in individuals who are not ready for treatment but also have facilitated an entry point into care for substance use disorders.
4. Educational interventions will expose students, residents, and current physicians to innovative research and strategies for the treatment of opioid use disorders. Medication assisted therapy has been a consistent option for the treatment of opioid use disorders. As of the most recent statistics, only about 2% of all US physicians (4% of primary care physicians) have a valid waiver under the Drug Addiction Treatment Act of 2000 (DATA 2000) to prescribe buprenorphine to patients. This certainly falls short of the national needs. Even if all these actively waived physicians prescribed medication assisted therapy to the fullest extent possible, only 1.4 million patients would have access to treatment. Educational curriculum, particularly that targeted at resident physicians, will be studied for its effects on potential access to medication assisted therapy for communities.

Summary: Substance abuse is a disease that is currently at epidemic proportions, especially opioid use and abuse. The only chance at a substantial positive impact on any disease is to invest in developing new and proven prevention and treatment strategies. Dedicated research expenditures have allowed us to prevent, treat and cure many types of cancer that were death sentences just decades ago. HIV disease has transformed from a terminal illness to a chronic disease. We must mount a strong effort to begin to counteract and hopefully solve the opioid abuse epidemic. In 2014, over 2500 Pennsylvanian's lost their lives to opioids. Countless more lost jobs, saw their families ruptured, and were incarcerated. Pennsylvania spends over 870 million dollars on health care associated with the consequences of the opioid abuse epidemic. If incarceration and other societal costs are included, the cost escalates to over 2 billion dollars. Temple Health is committed to treating opioid misuse and addiction as the health epidemic it is by creating the Temple Health Institute for Research on Education, Prevention and Treatment of Addiction. *Research focused on education, treatment and prevention is a sensible and cost effective investment.* If we spend even a small fraction of this amount on truly preventing and treating this disease rather than trying to arrest our way to a cure or remaining trapped in an endless cycle paying the associated health care and societal costs, we could not only save lives but save money. The causes of this epidemic are based in science and thus the answers are there as well. Not only is a research approach most

appropriate for the well-being of Pennsylvanians but it is also the most fiscally responsible way to improve outcomes and decrease cost. The Temple Health Institute for Research on Education, Prevention and Treatment of Addiction will reframe the approach by providing proven, practical strategies to combat this epidemic.

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