EXAMINING PUBLIC HEALTH LEGISLATION: H.R. 2820, H.R. 1344, AND H.R. 1462

HEARING

BEFORE THE

SUBCOMMITTEE ON HEALTH

OF THE

COMMITTEE ON ENERGY AND COMMERCE

HOUSE OF REPRESENTATIVES

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EXAMINING PUBLIC HEALTH LEGISLATION: H.R. 2820, H.R. 1344, AND H.R. 1462

THURSDAY, JUNE 25, 2015

HOUSE OF REPRESENTATIVES,
SUBCOMMITTEE ON HEALTH,
COMMITTEE ON ENERGY AND COMMERCE,
Washington, DC.

The subcommittee met, pursuant to call, at 10:13 a.m., in room 2322 of the Rayburn House Office Building, Hon. Joseph R. Pitts (chairman of the subcommittee) presiding.

Members present: Representatives Pitts, Guthrie, Barton, Murphy, Lance, Griffith, Bilirakis, Ellmers, Bucshon, Brooks, Collins, Green, Capps, Butterfield, Castor, Matsui, Schrader, Kennedy, and Pallone (ex officio).

Staff present: Clay Alspach, Chief Counsel, Health; Noelle Clemente, Press Secretary; Katie Novaria, Professional Staff Member, Health; Graham Pittman, Legislative Clerk; Chris Santini, Policy Coordinator, Oversight and Investigations; Adrianna Simonelli, Legislative Associate, Health; Heidi Stirrup, Policy Coordinator, Health; Traci Vitek, Detailee, Health; Gregory Watson, Staff Assistant; Christine Brennan, Democratic Press Secretary; Jeff Carroll, Democratic Staff Director; Waverly Gordon, Democratic Professional Staff Member; Tiffany Guarascio, Democratic Deputy Staff Director and Chief Health Advisor; Meredith Jones, Democratic Director of Communications, Member Services, and Outreach; Una Lee, Democratic Chief Oversight Counsel; and Samantha Satchell, Democratic Policy Analyst.

Mr. PITTS. Our guests can take their seats. We are voting on the floor right now, so we are going to try to expedite this a little bit, get through our opening statements on the panel. I would ask the Members to abbreviate their opening statements so that we can go to the floor and came back after the votes to hear the testimony and do the Q&A.

I have a UC request. I would like to submit the following documents for the record: a statement from Representative David Jolly, Florida 13; a letter of support from American Academy of Pediatrics, American Congress of Obstetricians and Gynecologists, March of Dimes, and Society of Maternal-Fetal Medicine. Without objection, those will be entered into the record.

[The information appears at the conclusion of the hearing.]

Mr. PITTS. The chairman will now call the subcommittee to order and recognize himself for an opening statement.

OPENING STATEMENT OF HON. JOSEPH R. PITTS, A REPRESENTATIVE IN CONGRESS FROM THE COMMONWEALTH OF PENNSYLVANIA

Today's hearing will examine three bipartisan public health bills to improve health care for newborns, infants and children. As many of you know, one of this subcommittee's top priorities has been helping and protecting children and families. These bipartisan bills that are the subject of today's hearing represent our ongoing effort to work together to strengthen public health and solve problems in our Nation's health care system.

H.R. 2820, the Stem Cell Therapeutic and Research Reauthorization Act, introduced by Representative Chris Smith of New Jersey and Doris Matsui of California, reauthorizes the Stem Cell Therapeutic and Research Act of 2005, which provides Federal support for cord blood donation and research essential to increasing patient access to transplant.

H.R. 1462, the Protecting Our Infants Act of 2015, authored by Representatives Katherine Clark of Massachusetts and Steve Stivers of Ohio, will combat the rise of prenatal opioid abuse and neonatal abstinence syndrome. The bill will address the growing problem of overdose deaths involving heroin and help protect newborns and infants. Additionally, this bill has a Senate companion bill, S. 799, sponsored by the Senate Majority Leader, Mitch McConnell.

Finally, H.R. 1344, the Early Hearing Detection and Intervention Act of 2015, authored by Health Subcommittee Vice Chairman Brett Guthrie and Representative Lois Capps, amends the Public Health Service Act to reauthorize a program for early detection, diagnosis, and treatment regarding deaf and hard-of-hearing newborns, infants, and young children.

I would like to welcome all of our witnesses here today. We look forward to your testimony.

[The prepared statement of Mr. Pitts follows:]

PREPARED STATEMENT OF HON. JOSEPH R. PITTS

Today's hearing will examine three bipartisan public health bills to improve health care for newborns, infants and children. As many of you know, one of this subcommittee's top priorities has been helping and protecting children and families. These bipartisan bills that are the subject of today's hearing, represent our ongoing effort to work together to strengthen public health and solve problems in our Nation's health care system.

H.R. 2820, the Stem Cell Therapeutic and Research Reauthorization Act, introduced by Reps. Chris Smith (NJ) and Doris Matsui (CA), reauthorizes the Stem Cell Therapeutic and Research Act of 2005, which provides Federal support for cord blood donation and research essential to increasing patient access to transplant.

The purpose of the National Marrow Donor Program is to help save lives of patients with blood cancers, like leukemia, lymphoma, and other life-threatening diseases through adult stem cell transplants. Every 4 minutes, someone is diagnosed with blood cancer. In most cases, a bone marrow, cord blood, and peripheral blood stem cell transplant is the only option for a cure. 70 percent of patients do not have a donor in their family and rely upon the national registry to find a match.

The National Marrow Donor Program in my home State of Pennsylvania has already conducted 2,159 transplants as of 2014. The Transplant Centers in PA include:

- Thomas Jefferson University Hospital in Philadelphia
- Hahnemann University Hospital in Philadelphia
- University of Pennsylvania Medical Center in Philadelphia
- Temple University Hospital in Philadelphia
- Western Pennsylvania Cancer Institute in Homeacre

• UPMC Hillman Cancer Center in Pittsburgh
• Penn State Hershey Medical Center in Hershey
• Children's Hospital of Philadelphia
• And Children's Hospital of Pittsburgh

There are 930 donors in PA. Since 1987, more than 61,000 transplants nationwide have occurred through this program.

H.R. 1462, the Protecting Our Infants Act of 2015, authored by Reps. Katherine Clark (MA) and Steve Stivers (OH), will combat the rise of prenatal opioid abuse and neonatal abstinence syndrome. In recent years, sadly, there has been a steady rise in the number of overdose deaths involving heroin. According to the Centers for Disease Control and Prevention, the death rate for heroin overdose doubled from 2010 to 2012. The bill will address the growing problem and help protect newborns and infants. Additionally, this bill has a Senate companion bill, S. 79 sponsored by the Senate Majority Leader Mitch McConnell (KY).

Finally, H.R. 1344, the Early Hearing Detection and Intervention Act of 2015, authored by Health Subcommittee Vice Chairman Brett Guthrie (KY) and Rep. Lois Capps (CA), amends the Public Health Service Act to reauthorize a program for early detection, diagnosis and treatment regarding deaf and hard-of-hearing newborns, infants, and young children.

I would like to welcome all of our witnesses for being here today. I look forward to your testimony.

Mr. PITTS. I now recognize the ranking member, Mr. Green, for his opening statement.

Mr. GREEN. Thank you, Mr. Chairman. I have a statement I would like to put in the record.

I want to welcome our panels.

These bills are all very bipartisan, and I appreciate the Chair and the majority setting them for today, but I would like to ask unanimous consent to place my statement into the record and yield——

Mr. PITTS. Without objection, so ordered.

Mr. GREEN [continuing]. My time to my colleague from California.

[The prepared statement of Mr. Green follows:]

PREPARED STATEMENT OF HON. GENE GREEN

Good morning and thank you all for being here today.

This hearing was called to examine three bills that will strengthen public health, each of which is the product of bipartisan effort.

H.R. 2820, the Stem Cell Therapeutic and Research Reauthorization Act, is led by Representatives Doris Matsui and Chris Smith. According to the Health Resources and Service Administration, nearly 20,000 patients in the United States need a bone marrow, peripheral, or cord blood transplant each year.

H.R. 2820 will reauthorize Federal programs that support cord blood donation, a national bone marrow registry, and related research, all of which expand access to transplants for patients in need.

H.R. 1344, the Early Hearing Detection and Intervention Act, is championed by Representatives Lois Capps and Brett Guthrie. Beginning in 2000, Congress took steps to facilitate the development of newborn and infant screening, and intervention programs.

H.R. 1344 reauthorizes and makes further improvements to the Early Hearing Detection and Intervention program. Early identification of a child's hearing loss increases the likelihood that intervention and treatment services can successfully prevent or limit development delays.

Finally, we are considering H.R. 1462, the Protecting Our Infants Act. The CDC has found drug overdose to be the leading cause of injury death in the U.S., and according to a recent study in the New England Journal of Medicine, the incidence rate of neonatal abstinence syndrome (N.A.S.) quadrupled between 2004 and 2013.

H.R. 1462, led by Representatives Katherine Clarke and Steve Stivers, is an important step to combat the rise of N.A.S. and prenatal opioid abuse. It will require the Agency for Healthcare Research and Quality to develop recommendations for

preventing and treating prenatal opioid abuse and N.A.S., provide for better coordination of Federal efforts, and improve data collection.

I thank all of my colleagues from both sides of the aisle for putting forward these thoughtful and worthy proposals, and for their commitment to improving access to and delivery of health care. I look forward to continuing to work in a bipartisan manner on the many issues before our subcommittee.

I yield the balance of my time to my colleague from California.

Mrs. CAPPS. Thank you, Mr. Chairman, and thank you, Mr. Green for yielding time, and I appreciate the hearing on these important bills.

I am particularly pleased that H.R. 1344, the Early Hearing Detection and Intervention Act, will be discussed here today. As a co-author of that bill along with my colleague, Representative Guthrie, I thank you for including this reauthorization in today's hearing.

Since the program received its authorization in 2000, we have seen how vital it is for babies and their families. As a school nurse, this hits home for me too. Back in 2000, only 44 percent of newborns were being screened for hearing loss. Now we are screening newborns at a rate of over 98 percent before they leave the hospital and linking them to follow-up care, which is the critical piece, and we know that early intervention is key in helping children with hearing loss achieve academically and developing in line with their peers.

Our work isn't done. As a school nurse, I had a lot of interaction with students who were already behind lagging from their classmates due to undiagnosed and/or untreated hearing loss. We can prevent more children from suffering in the classroom through better investment in follow-up and intervention as part of a successful hearing screening program for newborns and infants. We need to ensure that every newborn is screened, every family has access to follow-up care. Early identification and intervention are key to a child's well-being, and that is what this bill would support.

I am hopeful we continue to work in a bipartisan way to move this and other bills that we are examining today and bring them all to the floor this year.

So thank you, witnesses, for being here, and I yield back.

Mr. PITTS. The Chair thanks the gentlelady.

Chairman Upton has asked to yield his time to Representative Guthrie, so the Chair recognizes Representative Guthrie at this time.

OPENING STATEMENT OF HON. BRETT GUTHRIE, A REPRESENTATIVE IN CONGRESS FROM THE COMMONWEALTH OF KENTUCKY

Mr. GUTHRIE. Thank you very much. In the interests of time, Congresswoman Capps had a lot of statements that I was going to make, so I am pleased to be here to support 1344 that I am pleased to have co-authored with Congresswoman Capps. And I have been interested in this issue, early detection and screening, since I was in the State legislature. I did research when a bill was going through the legislature and learned if a newborn—at the early stages if you have hearing loss and you don't have the opportunity to hear correctly, you can never gain that back, even if you learn

it as a young adult or a teenager or whatever. You can never gain it back. So it's important to do it early, through early detection.

The current law is set to expire September of 2015, a mere 3 months from now, and these services will go away and we will lose the opportunity to catch these early screenings. So I am pleased that Chairman Pitts has put this on the agenda for today. This bill appears to be moving forward, and I appreciate working with Congresswoman Capps, and I appreciate your time, Mr. Chairman, and I yield back.

Mr. PITTS. The Chair thanks the gentleman. I thank him for expediting as well.

The Chair now recognizes the ranking member of the full committee, Mr. Pallone, for his opening statement.

Mr. PALLONE. Thank you, Mr. Chairman.

Did you have a statement on the other side?

Mr. PITTS. Yes, we did.

Mr. PALLONE. OK. I know you are trying to get it done fast here.

OPENING STATEMENT OF HON. FRANK PALLONE, JR., A REPRESENTATIVE IN CONGRESS FROM THE STATE OF NEW JERSEY

Let me thank Chairman Pitts and Ranking Member Green for holding this hearing on important pieces of legislation that will surely improve the health of our Nation. I am pleased that all three bills have robust bipartisan support and continue this committee's tradition of a thoughtful, collaborative approach to public health legislation.

I am not going to read all the bills. I mean, obviously H.R. 2820, the Stem Cell Therapeutic and Research Reauthorization Act, it continues the highly successful Be The Match Registry for bone marrow, and this bill ensures that this critically important program continues to operate.

As far as H.R. 1344, the Early Hearing Detection and Intervention Act of 2015 introduced by Representatives Capps and Guthrie, obviously this is important for newborns who now are regularly screened for hearing loss, and so this is something that we support.

And finally, H.R. 1462, the Protecting Our Infants Act of 2015, is a greatly needed piece of legislation to address a sad reality of our country's opioid epidemic. This bill rightly recognizes the immediate need for a comprehensive national strategy to address prenatal opioid abuse. So I also thank Representative Clark. She has talked to me about this in the past. I look forward to working with you and our colleagues on these important public health bills.

I yield the remainder of my time to Representative Capps—she already spoke.

I yield back. Thank you.

[The prepared statement of Mr. Pallone follows:]

PREPARED STATEMENT OF HON. FRANK PALLONE, JR.

Thank you Chairman Pitts and Ranking Member Green for holding this hearing on important pieces of legislation that will surely improve the health of our Nation. I am pleased that all three bills have robust bipartisan support and continue this committee's tradition of a thoughtful, collaborative approach to public health legislation.

H.R. 2820, the Stem Cell Therapeutic and Research Reauthorization Act, continues our highly successful Be the Match Registry for bone marrow and umbilical cord blood transplantation. I'd especially like to thank Representative Matsui for her continued leadership on this issue. For nearly 20,000 patients each year, such transplants are lifesaving. Of those patients, 70 percent will not find a match within their family member and will require a non-relative donor. That is why the Be the Match Registry and its nearly 12.5 million registered bone marrow donors and the collection of more than 209,000 cord blood units is so important. This bill ensures that this critically important program continues to operate.

We will also hear about H.R. 1344, the Early Hearing Detection and Intervention Act of 2015 which was introduced by Representatives Capps and Guthrie. Prior to the authorization of the Early Hearing Detection and Intervention Program, less than half of all newborns were regularly screened for hearing loss. We're proud to say that now approximately 97 percent of newborns receive hearing screening. This gives hearing impaired children early access to the interventions and treatments they desperately need. The evidence tells us that these early treatments are critical in minimizing a hearing-impaired child's risk of developmental delays, especially communication, social skills and cognition. This bill would ensure that we continue to support a public health program that has a proven track record of success as well as continue our obligation to protect the health of our children.

Finally, H.R. 1462, the Protecting Our Infants Act of 2015is a greatly needed piece of legislation to address a sad reality of our country's opioid epidemic: prenatal opioid abuse and the steep increase in the incidence of neonatal abstinence syndrome or NAS. According to a recent study the incidence of NAS quadrupled between 2004 and 2013. NAS occurs in newborns who were exposed to opiates while in their mother's womb and is associated with negative health outcomes including preterm births, low birthweight, and complications such as respiratory distress.

This bill rightly recognizes our imminent need for a comprehensive national strategy to address prenatal opioid abuse and NAS. H.R. 1462 would require HHS to develop recommendations for the treatment and prevention of prenatal opiate abuse and neonatal abstinence syndrome, it would require the CDC to assist States in collecting data to monitor the problem and would direct HHS to develop a coordinated research and programming strategy to address the public health challenge of NAS. I want to also thank Rep. Katherine Clark for her leadership on this critical and timely issue.

Mr. Chairman, I look forward to working with you and our colleagues on these important public health bills.

Mr. PITTS. The Chair thanks the gentleman, and the Chair recognizes Mr. Green for a UC request.

Mr. GREEN. Mr. Chairman, I ask unanimous consent to place into the record a statement by our colleague Doris Matsui in support of the bills.

Mr. PITTS. Without objection, so ordered.

I have someone monitoring the floor with the number of minutes and Members not voting, so I will keep you updated on that.

At this time I will introduce our panel. We have one panel today, and thank you all for coming. I will introduce you in the order of your presentations and ask if you can abbreviate them somewhat. At some point if we don't get through them, we will have to go to the floor and return to hear the rest.

But first Dr. Jeff Chell, Chief Executive Officer, National Marrow Donor Program; Dr. Joanne Kurtzberg, President of the Cord Blood Association; Dr. Patti Freemyer Martin, Ph.D., Director of Audiology and Speech and Language Pathology, Arkansas Children's Hospital; Dr. Stephen Patrick, Assistant Professor of Pediatrics and Health Policy, Department of Pediatrics, Vanderbilt University School of Medicine; and finally, Dr. Mishka Terplan, Medical Director of Behavior Health Systems of Baltimore.

Thank you for coming today. Your written opening statements will be made a part of the record as will all Members' written open-

ing statements as usual. You will be given 5 minutes to make your summary. If you can abbreviate that, we would appreciate it.

So at this point, the Chair recognizes Dr. Chell for 5 minutes.

STATEMENTS OF JEFFREY W. CHELL, M.D., CHIEF EXECUTIVE OFFICER. NATIONAL MARROW DONOR PROGRAM; JOANNE KURTZBERG, M.D., PRESIDENT, CORD BLOOD ASSOCIATION; PATTI FREEMYER MARTIN, PH.D., DIRECTOR, AUDIOLOGY/ SPEECH-LANGUAGE PATHOLOGY DEPARTMENT, ARKANSAS CHILDREN'S HOSPITAL; STEPHEN W. PATRICK, M.D., ASSISTANT PROFESSOR OF PEDIATRICS AND HEALTH POLICY, DIVISION OF NEONATOLOGY, VANDERBILT UNIVERSITY SCHOOL OF MEDICINE; AND MISHKA TERPLAN, M.D., MEDICAL DIRECTOR, BEHAVIOR HEALTH SYSTEM BALTIMORE

STATEMENT OF JEFFREY W. CHELL

Dr. CHELL. Good morning, Mr. Chairman and other distinguished members of the committee. Thank you so much for inviting us today.

As you have heard, I serve as the CEO of the National Marrow Donor Program and Be The Match. We have operated the C.W. Bill Young Cell Transplantation Program since its inception, and that includes a single point of access, the Office of Patient Advocacy, the Bone Marrow Coordinating Center, as well as the Cord Blood Coordinating Center, and with the Medical College of Wisconsin, we hold a contract for the Stem Cell Therapeutics Outcome Database through our research entity, the CIBMTR. I serve as Executive Director of that entity.

I would like to thank you all and members of the subcommittee for inviting us to speak on behalf of our 565 network partners all over the world, and at the NMDP, we deeply appreciate your support of helping us fight blood cancers through transplantation, often, the only potential cure for these deadly diseases. I would also like to thank Representatives Chris Smith, Doris Matsui, David Jolly, and Chaka Fattah for their leadership in introducing H.R. 2820.

As I testify before you today, I am reminded of a hearing in 1987. On that day, the late Congressman Bill Young called on Congress to establish the national registry where children and adults with leukemia and other fatal blood disorders could find a donor. Congress heard that call at that point and established the national registry.

Congressman Young's vision was inspired by a child, 11-year-old Brandy Bly, who was fighting leukemia. No one in her family was a suitable match, and without access to a transplant, she would not survive. At that time there was no registry available, and it was the simple statement from her physician that really stimulated Congressman Young to take action, and he said, "Wouldn't it be great if there was a registry of donors that we could tap in to help save a life like this this?" And that really became the basis of our national registry.

Since that hearing in 1987, we have made great progress. The NMDP is now the global leader in providing cellular therapy, which is often the only treatment available that can cure some of

these life-threatening blood disorders and other significant diseases like sickle cell disease. We also educate healthcare professionals, conduct research, and offer support and education in multiple languages to help patients lead healthy lives after transplant. Today, children like Brandy have a much better chance for a lifesaving transplant.

We have been honored to serve as the steward of this critical resource for the last 28 years. During that time, the growth of transplant has increased significantly, and even since 2005, transplants overall have grown 200 percent, and for minorities it has grown 250 percent. We now have over 12 million donors in our registry and over 200,000 cord blood units, but we partnered with 66 registries all over the world to provide a total of 25 million donors and over 600,000 units of cord blood, and it is as easy to find a donor and make that transplant happen if that donor was halfway across the world or across the street.

Outcomes for transplant for have also improved as well as the number of transplants, so your survival has gone from 40 percent to over 70 percent in the last 10 years. But we are especially proud—if we could show the first slide—of our work fighting diseases afflicting children.

[Slide.]

In 2014, we facilitated 1,200 unrelated transplants for patients 18 years and older, and the first slide shows how important the source, not only bone marrow but also umbilical cord blood, is in fighting transplants. Dr. Kurtzberg and other pioneers in this field introduced cord blood in the late 1990s, and those truly are helping patients that we would have otherwise not been able to help.

But your ongoing commitment has made these advances possible and turned the tragic loss of Brandy into hopes for tens of thousands of Americans. One of those is Hadley Mercer. She was just 6 months old when she was diagnosed with acute myeloid leukemia. After two rounds of chemotherapy, her parents and physicians agreed that a bone marrow transplant was likely her only chance as well as her best chance of survival. We found a perfect match for her, a young man in his 20s. Now almost 2 years old, she is going to have a normal and healthy life because of her donor angel. She is also alive because of your continued support for the C.W. Bill Young Cell Transplantation Program.

The NMDP has never forgotten the importance of that physician's simple statement that inspired Congressman Young, and every day we are inspired by people who we meet, young and old, who are seeking to find that match. If we could show the next slide?

[Slide.]

It shows us that, even though we have made tremendous progress, we are meeting less than half the need of the pediatric population, and in this slide you can see the lighter-colored areas are areas where we are only meeting 25 percent or more of the total need, and as we get darker colors, you can see that there is more and more. So there are many, many more children we can help. So thank you very much for your time and attention.

[The prepared statement of Dr. Chell follows:]

Written Testimony of Dr. Jeffrey W. Chell
before the House Committee on Energy and Commerce
Hearing on "Examining Public Health Legislation:
H.R. 2820, H.R. 1344, and H.R. 1462"
June 25, 2015

Summary of Key Points

- The NMDP/Be The Match appreciates the continuing bipartisan support to reauthorize the C.W. Bill Young Cell Transplantation Program and the National Cord Blood Inventory. It is critically important to reauthorize these programs before their authorizations expire at the end of September 2015.

- Since the late Congressman Bill Young was first inspired by 11-year-old Brandy Bly who did not survive her battle with leukemia and he testified before the Commerce Committee in 1987, significant progress has been made to provide access to transplant for all Americans in need of a life-saving bone marrow or cord blood transplant.

- Today, the NMDP/Be The Match is the global leader in helping patients seeking a cure for one of the more than 70 different diseases or conditions, including blood cancers and sickle cell disease. Cellular therapy is their best hope for a cure.

- The Be The Match Registry has grown to include nearly 12.5 million donors and more than 209,000 cord blood units and through international relationships, we have access to more than 24.5 million potential donors and 622,000 cord blood units worldwide.

- Between 1988 and 2005, the one-year survival rate for these patients has increased from just over 40 percent to 70 percent. Access to multiple cell sources allows us to find the best match possible for patients.

- In 2014, we facilitated more than 1,200 unrelated transplants for patients 18 or younger using bone marrow or cord blood. Current pediatric research focuses not only on malignancies, but also on curing non-malignant diseases such certain metabolic diseases and hemaglobanopathies like sickle cell disease and thalassemia.

- The calculated need for unrelated transplant has increased by 25 percent since 2005. Much of the reason is due to the expansion in the number of indications for transplant.

- The number of transplants for minority patients has increased from 253 in 2000 to 990 in 2014.

- The non-match barriers to access and care have a profound affect on our ability to make transplant therapies accessible to all.

Good morning Mr. Chairman, and other distinguished members of the Subcommittee. My name is Dr. Jeffrey Chell and I am the Chief Executive Office of the National Marrow Donor Program (NMDP)/Be The Match. We operate the C.W. Bill Young Cell Transplantation Program (Program) through four competitively bid contracts with the Health Resources and Services Administration (HRSA). These contracts include the Single Point of Access and Office of Patient Advocacy, the Bone Marrow Coordinating Center, and the Cord Blood Coordinating Center. Collectively, these contracts allow NMDP/Be The Match to operate the national Be The Match Registry and provide life-saving blood and marrow transplants using individual adult donors and umbilical cord blood units. And with the Medical College of Wisconsin, NMDP/Be The Match also holds the contract for the Stem Cell Therapeutic Outcomes Database, known as the Center for International Blood and Marrow Transplant Research (CIBMTR) of which I am the executive director.

To begin, I would like to thank Chairman Pitts, Ranking Member Green, and all of the Members of the Health Subcommittee for inviting me to speak with you today. On behalf of 565 Network partner organizations and everyone at the NMDP/Be The Match, we also want to thank you for maintaining the Congressional commitment to patients fighting blood cancers and other disorders whose only hope for a cure is a bone marrow or cord blood transplant.

I would also like to thank Congressman Chris Smith, Congresswoman Doris Matsui, Congressman David Jolly, and Congressman Chaka Fattah for their leadership in introducing H.R. 2820 to reauthorize the Program, as well as the National Cord Blood Inventory (NCBI) grant program. These programs are examples of how the Congress can inspire innovation to bring cures to patients across America.

Who We Are

As I testify before you today, I cannot help but be reminded of another hearing that took place in 1987. On that day, the late Congressman Bill Young called on the Congress to establish a national registry where men, women, and children with leukemia and other fatal blood disorders could find an unrelated donor to save their lives. He was joined by Dr. Robert Graves, whose daughter received the first unrelated bone marrow transplant for leukemia, and Navy Admiral Bud Zumwalt. The Congress heard that call and established the national registry. First housed in the Department of the Navy, it found its permanent home as one of the nation's premier public health programs at HRSA.

Congressman Young's quest was inspired by a child, 11-year-old Brandy Bly, and her family racing to save her life. Unfortunately, no one in her family was a suitable match and she did not survive. It was the simple statement from her physician – "Wouldn't it be great if there were a way that doctors could search for adults willing to donate their bone marrow?" – that led to the national registry.

Since that first hearing in 1987, we have made great progress. Today, the NMDP/Be The Match is the global leader in providing a cure to patients with life-threatening blood and marrow cancers such as leukemia and lymphoma, as well as other diseases. Through the contract with HRSA, we manage the world's largest registry—the Be The Match Registry—of potential marrow donors and umbilical cord blood units, connect patients to their donor match for a life-saving marrow or umbilical cord blood transplant, educate health care professionals, and conduct research so more lives can be saved. Today, children like Brandy have a much better chance to find that life-saving match and ultimately a cure.

But, the C.W. Bill Young Program as it has come to be known, is more than the national registry. Through the Program, the NMDP/Be The Match also operates the Office of Patient Advocacy. The Office of Patient Advocacy assists patients and their families in navigating the complexities of health insurance and helps them overcome logistical, psychosocial and informational barriers throughout the transplant continuum. We also work closely with donor and collection centers through the Bone Marrow Coordinating Center contract to recruit and retain volunteer potential donors, produce a comprehensive plan for donor retention, and plan for increasing operational efficiencies. We similarly provide financial and educational support to public cord blood banks as the manager of the Cord Blood Coordinating Center and provide guidance to HRSA in the administration of the National Cord Blood Inventory program to determine optimal composition of cord blood inventory. And, we partner with the Medical College of Wisconsin to operate the Stem Cell

Therapeutic Outcomes Database, which facilitates research to improve patient outcomes and find new and exciting ways bone marrow and umbilical cord blood can be used to save lives.

The Success of the Program

During the past 28 years, the NMDP/Be The Match has been honored to serve as the steward of this critical national resource. Today, the Be The Match Registry serves as the single point of access for both umbilical cord blood units and adult volunteer donors. This single point of access assures that these physicians will have access to any potential donor or umbilical cord blood unit regardless of where located across the globe in order to perform adult stem cell transplants that can cure more than 70 different diseases or conditions, including blood cancers and sickle cell disease. The Be The Match Registry has grown to include nearly 12.5 million donors and more than 209,000 cord blood units. Through international relationships, the NMDP/Be The Match has access to more than 24.5 million potential donors and 622,000 cord blood units worldwide.

For patients battling these fatal cancers and other blood disorders, the NMDP/Be The Match offers support and education to help them live healthy lives after transplant. We provide patient services, caregiver support, and financial support through the Be The Match Foundation. We also work closely with transplant physicians throughout the country by developing and improving upon post-transplant guidelines to improve survival rates.

Our focus is on patients for whom cellular therapy is the best hope for cure of their diseases and is often the only therapy available with an intent to cure. Today, we are able to treat patients with cancers and pre-cancers, such as leukemia, Myelodysplasia, and lymphomas; bone marrow failure disorders, such as aplastic anemia and immunodeficiency syndromes; and genetic diseases, such as sickle cell disease. To treat these diseases, we infuse bone marrow, peripheral blood stem cells, or cord blood cells into a patient after having eliminated his/her current bone marrow. These new cells restore the patient's ability to make blood cells or provide a new immune system to attack cancer cells. Finding the best match possible is important because if donor stem cells are not the same HLA type as the recipient they will recognize the recipient as being different and attack, leading to rejection.

Because we collect data on all transplants, we have been able to improve patient outcomes and reduce rejection. Between 1988 and 2005, the one-year survival rate for these patients has increased from just over 40 percent to 70 percent. Access to multiple cell sources allows us to find the best match possible for patients. Initially focused only on bone marrow, the Program today also allows physicians to select peripheral blood stem cells and cord blood, as well as bone marrow, as the source of the adult stem cells used in transplant.

We are especially proud of the work we have done to help children in need of a transplant. In 2014, the NMDP/Be The Match facilitated more than 1,200 unrelated

transplants for patients 18 or younger using bone marrow or cord blood. Our current research focuses not only on malignancies, but also on curing non-malignant diseases such certain metabolic diseases and hemaglobinopathies like sickle cell disease and thalassemia. These blood disorders can be fatal if left untreated. Prior to transplantation therapy, children with these diseases would often die prematurely.

We are also learning more about how to improve outcomes for children fighting blood cancers. By having access to all three sources of adult stem cells, physicians can select the best source to meet their young patients' needs. For example, most physicians prefer a fully matched bone marrow graft if available for all patients, including children. In certain instances, umbilical cord blood is used, especially if there is no fully matched adult donor. In this way, umbilical cord blood has significantly extended the opportunity for all patients who otherwise would not have found an acceptable adult match. Through the CIBMTR, researchers throughout the world are finding new and exciting ways that bone marrow and cord blood transplants can help children fight life-threatening diseases.

More Needs To Be Done

However, more needs to be done. The need for transplants is increasing, especially among older Americans. The calculated need for unrelated transplant has increased by 25 percent since 2005. Much of the reason is due to the expansion in the number of indications for transplant, as well as advances that allow older Americans to be

candidates for transplants. Transplants for patients 51-64 years old are growing faster than other age groups. NMDP/Be The Match facilitated transplants have grown by 200 percent overall and 250 percent for minorities since 2006.

While we have made significant improvements in transplants for racial and ethnic minority patients, there too more work is needed. The number of transplants for minority patients has increased from 253 in 2000 to 990 in 2014. We continue our efforts to expand the diversity of the national adult volunteer donor registry and 46 percent of cord blood units on the registry are from a minority donor. During the last 5 years cord blood has been the product source for about 21 percent of all transplants and 37 percent of minority patients who received a transplant relied upon cord blood.

Federal funding remains critical to continuing to provide access to transplantation. We need to continue to recruit new potential donors both to improve access for minority patients and to renew the current list of donors with younger donors. Grafts from younger donors have shown improved clinical outcomes. For every one million dollars allocated by the Congress, the Program can add 10,000 adult volunteer donors or 750 cord blood units to the national registry. Preserving these funds through the reauthorization of the Program allows it to continue to improve the chances of every American needing a transplant to find a match and provides the critical infrastructure that allows NCBI cord blood units to be used to save lives.

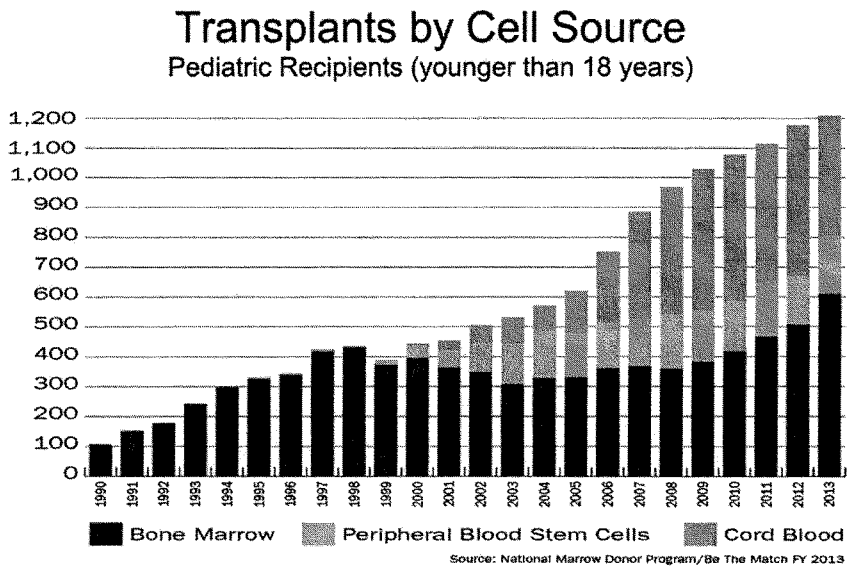
Even though the NMDP/Be The Match has improved the ability of those needing a transplant to find a match, there are other barriers that continue to make access difficult. These non-match barriers to access and care have a profound affect on our ability to make transplant therapies accessible to all. Language, literacy, finances, insurance, geography, lack of knowledge, and predisposition by general hematologists and oncologists towards non-transplant therapies all have an impact. The NMDP/Be The Match continues to work with patients, physicians, community leaders, and others to address these problems as well.

Conclusion

The ongoing Congressional commitment has made these advances possible and turned the tragic loss of 11-year-old Brandy Bly into hope for tens of thousands of Americans. One of those Americans is Hadley Mercer. When she was just six months old, Hadley was diagnosed with acute myeloid leukemia (AML). After two rounds of chemotherapy, her parents began to consider a bone marrow transplant as an alternative treatment option for Hadley. They consulted various physicians, who all agreed that having a bone marrow transplant would be her best chance of survival. The family held a bone marrow drive and registered more than 1,000 people in five hours. A few months later, Hadley was matched with a young man in his twenties. Now almost two, Hadley is alive because of her "donor angel". She is also alive because of your continued support for the C.W. Bill Young Cell Transplantation Program.

The NMDP/Be The Match has never forgotten the importance of the physician's simple statement that inspired Congressman Young and every day we are inspired by the people we meet, young and old, who are seeking to find a match and undergo a transplant.

Appendix: Statistical Charts and Graphs



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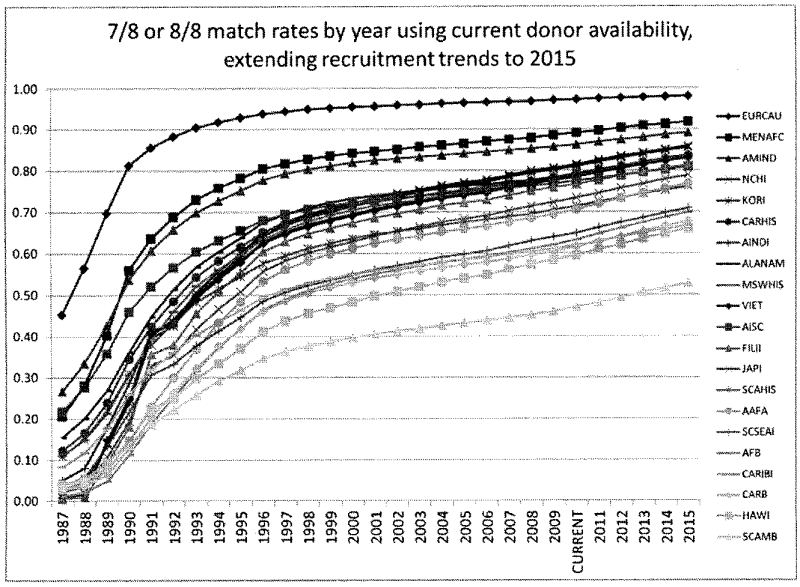

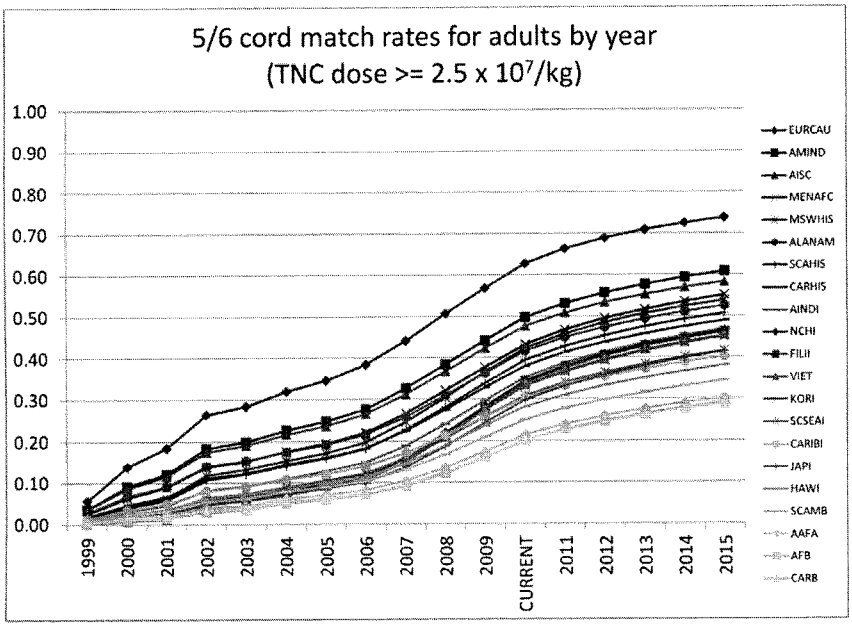
5/6 cord match rates for adults by year
(TNC dose >= 2.5 x 10^7/kg)
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SCAHIS
CARHIS
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NCHI
FILII
VIET
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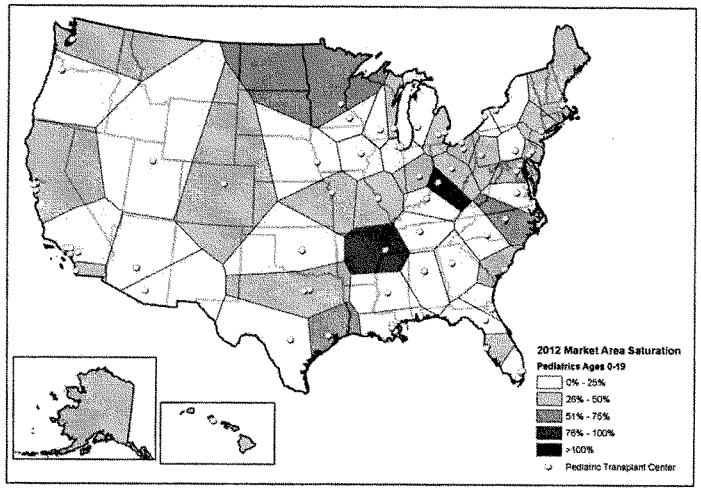
SCAMB
AAFA
AFB
CARB

Percent Market Saturation, 0-19 years
(Actual / Calculated Demand)



Mr. PITTS. The Chair thanks the gentleman, and we are out of time on votes for the floor. At this point the Chair recognizes Dr. Kurtzberg.

STATEMENT OF JOANNE KURTZBERG

Dr. KURTZBERG. Mr. Chairman, Ranking Member Green, and members of the subcommittee, thank you for inviting me to discuss H.R. 2820, the Stem Cell Therapeutics and Research Reauthorization Act of 2015. My name is Joanne Kurtzberg, and I am the President of the Cord Blood Association of Pediatric Transplant and I am the founder and Director of the Carolinas Cord Blood Bank, which is a public cord blood bank at Duke.

I want to thank both Congressman Chris Smith and Congresswoman Doris Matsui for their leadership and the introduction of this legislation. I also want to acknowledge the subcommittee's bipartisan commitment to the creation and support of the NCBI, or National Cord Blood Inventory, a public cord blood banking network which began when this bill was introduced in 2005.

I am talking about a network of banks that save cord blood, which is the baby's blood remaining in the placenta, or afterbirth, after the baby is born. In the past, this cord blood was discarded as medical waste, so it has never been a controversial source of stem cells. Cord blood contains stem and progenitor cells of the blood and other tissues, and it can be collected without harming the mother or the baby and banked for future use, and I put a picture up there of what the bag looks like that we save cord blood in.

[Slide.]

We save it in less than an ounce of fluid in two compartments with little pigtails so we can test it later and make sure it is appropriate for a patient for transplant.

If I could have the next slide, it shows you a picture of the very first recipient of cord blood transplant in the world, who is a little boy from North Carolina with a fatal disease called Fanconi anemia.

[Slide.]

His sister was a match and not affected, and when he was 5 years old he went to France for this transplant, and you can see him 27 years later doing well, a happy, healthy, working, married adult with me. He reached the benchmark of being taller than me, which is what many of my patients like to do post-transplant. But most importantly, he is fully engrafted with his baby sister's cells, and that proved that cord blood contains stem cells of the blood.

Next slide.

[Slide.]

Briefly, after that transplant, unrelated donor cord blood banks were established, first at the New York Blood Center, later through support from Congress to establish at NHLBI the COBLT program at Duke and two other sites, and as you know, the first legislation was passed in 2005 establishing the National Cord Blood Inventory as part of the C.W. Bill Young Cell Transplantation program. This stem cell source is unique because FDA has issued guidance to license cord blood, and there are now five licensed cord blood banks in the United States. In 2014, we also created the Cord Blood Asso-

ciation to represent both public and private cord blood banks and the cord blood community.

Next slide, you can see just the milestones in cord blood transplantation.

[Slide.]

It has been pioneered in children with inherited metabolic diseases. It has been used with two cord blood or double cord blood transplantation at the University of Minnesota, and there have been over 35,000 cord blood transplants performed worldwide and 160 banks established worldwide since it started.

[Slide.]

This just shows you—next slide—some of the research that is going on, so we now have ways to expand cord blood in the red line, so that the patient is in graft in 6 to 10 days instead of 20 to 30 days, and if you would go to the next slide, you will see some just facts about the NCBI.

[Slide.]

There are 13 members, 5 licensed banks, and not all the money appropriated has actually been—authorized has been appropriated over the past 10 years, but with the funding we have had, 90,000 high-quality, diverse cord blood units have been stored.

The next slide shows you a kit that we can send out to moms who want to donate anywhere in the country so the cord blood can be stored in the national inventory.

[Slide.]

The next slide shows you just an example of a little boy with Hurler syndrome.

[Slide.]

This is a fatal disease where children die by age 5. With a cord blood transplant, you can see on the right, this child is a healthy adolescent with normal intelligence, and many children with these kind of diseases have been helped.

The next slide lists some of the exciting regenerative medicine trials that are emerging for uses of cord blood beyond treating patients with leukemia and other diseases, and that includes autism, hearing loss, stroke, and cerebral palsy.

[Slide.]

The next slide shows you some data showing that babies with birth asphyxia have had their outcomes improved when they receive a cord blood infusion in the first 2 days of life.

[Slide.]

The next slide shows you our data from Duke showing that a cord blood infusion can actually help children with cerebral palsy regain function and regain normal performance.

[Slide.]

And the next slide shows you just how the brain can, in the lower left, actually re-form connections after a cord blood infusion.

[Slide.]

So I thank you for your attention and for your support, and we will be able to entertain questions later.

[The prepared statement of Dr. Kurtzberg follows:]

Statement of Joanne Kurtzberg, M.D.

President of the Cord Blood Association
Jerome Harris Distinguished Professor of Pediatrics and Pathology
Chief Scientific Officer and Medical Director, Robertson Clinical and Translational Cell Therapy Program
Director, Pediatric Blood and Marrow Transplant Program
Director, Carolinas Cord Blood Bank
Co-Director, Stem Cell Laboratory
Duke University School of Medicine

Testimony Before the U.S. House of Representatives
House Energy and Commerce Committee
Health Subcommittee

"Examining Public Health Legislation: H.R. 2820, H.R. 1344, and H.R. 1462"

June 25, 2015

Introduction:

Mr. Chairman, Ranking Member Green, and members of the Subcommittee, thank you for inviting me to discuss H.R. 2820, the Stem Cell Therapeutic and Research Reauthorization Act of 2015.

My name is Joanne Kurtzberg and I currently serve as the President of the newly-created Cord Blood Association (CBA). The CBA is an international, non-profit organization that promotes both public and family cord blood banking, with the objectives of saving lives, improving health and changing medicine. Our priorities are advocacy, quality products and services, market expansion, research and development, and public and professional education. CBA members include public and family cord blood banks as well as health care providers in the cord blood community and their patients.

In addition to serving as the President of CBA, I also serve in multiple roles at Duke University. I am a Distinguished Professor of Pediatrics and Pathology in the School of Medicine's Department of Pediatrics; Chief Scientific Officer and Medical Director of the Robertson Clinical and Translational Cell Therapy Program; Director, Pediatric Blood and Marrow Transplant Program; and Co-Director of the Stem Cell Laboratory. Finally, I am also the Director of the Carolinas Cord Blood Bank, which is a public cord blood bank. I have dedicated my professional career to cord blood research, banking and transplantation.

Both the CBA and Duke University Medical Center strongly support passage of H.R. 2820. I want to thank both Congressman Chris Smith and Congresswoman Doris Matsui (a member of this Subcommittee) for their leadership on the introduction of the Stem Cell Therapeutic and Research Reauthorization Act of 2015.

I also want to acknowledge this Committee's unwavering bipartisan commitment to the creation and support of public cord blood banks, which began when the bill was first introduced in 2005. The original Stem Cell Therapeutic and Research Act of 2005 reflected a compromise between Congress and the key stakeholder groups deeply interested in establishing cord blood banks for public use. This legislation not only reauthorized the National Marrow Donor Program (NMDP) but also created a national network of public cord blood banks. The law also provides health care professionals the ability to search for bone marrow and cord blood units through a single electronic point of access, which is operated by NMDP.

All of us working on the 2005 bill had one goal in mind – to expand patient access to the best therapies possible. We worked together to get this legislation approved by Congress and signed into law by the President. The 2005 bill and the 2010 bill were approved by both the House and the Senate with overwhelming support.

In the House, the late Congressman Bill Young, Congressman Chris Smith and Congresswoman Doris Matsui played important roles – without their leadership, we would not be where we are today. All of us who have worked on this program for the last 10 years are so grateful for your long-standing dedication and we look forward to working with all of you again this year.

The bill that we are discussing today reauthorizes both the National Cord Blood Inventory (NCBI) Program and the C.W. Bill Young Cell Transplantation Program from Fiscal Year 2016 through Fiscal Year 2020. NCBI would be reauthorized at $23 million each year and the C.W. Bill Young Cell Transplantation Program would be reauthorized at $30 million each year. Both programs have made a tremendous difference in the lives of thousands of patients, as I will discuss in greater detail, beginning first with a description of the National Cord Blood Inventory.

The National Cord Blood Inventory:

The National Cord Blood Inventory (NCBI) was created in 2006 as part of the C.W. Bill Young Cell transplantation Program after passage of the Stem Cell Therapeutic and Research Act of 2005. The original and over-riding goal of the C.W. Bill Young Program was to increase unrelated donor blood stem cell transplants. This goal was approached through a series of contracts from HRSA to the National Marrow Donor Program (NMDP). The goals of the NCBI were to create a network of cord blood banks and make available high-quality, diverse umbilical cord blood units, to add at least 150,000 new cord blood units, and to make cord blood units available for research. The CW Bill Young Program's additional cord blood priorities also included the establishment of the Cord Blood Coordinating Center (CBCC), to provide financial support to NCBI banks to make cord blood units more rapidly available through the Program. Contracts for NCBI are awarded through and negotiated by the Health Resources and Services Administration (HRSA). The contract for the CBCC is competed through a Request for Proposal (RFP) process from HRSA and is currently and historically awarded to the NMDP.

Cord blood, or the baby's blood remaining in the placenta or afterbirth, can be collected after the birth of the baby without risk to the mother or baby. In fact, in the past, cord blood was routinely discarded as medical waste. With the discovery that cord blood contained important stem cells of the blood and other organs, collection of cord blood for banking and later use in medical therapies is now common practice. Cord blood can be collected after a vaginal or cesarean section delivery. Generally collections are performed within 10 minutes of the birth of the baby. After collection, cord blood is transported to a processing laboratory where it is qualified, volume and red blood cell reduced, and frozen at ultra cold temperatures for long-term storage. Today, we know that cord blood units can be stored for over 20 years and successfully used for transplantation of patients with blood cancers and certain genetic diseases. Each cord blood unit is tested to ensure that the proper numbers of cells were collected, that the cells are alive, that the cells are sterile and that the cells are potent (capable of restoring the blood forming system in a patient whose system was destroyed by treatment and or disease). Mothers donating their baby's cord blood are screened to be sure they do not have any infectious or genetic diseases that can be transmitted through the blood. Public cord blood banks recruit and educate mothers to donate their baby's cord blood so that it can be distributed to patients in need of a donor for blood stem cell transplantation. Qualified cord blood units are listed on the NMDP "Be the Match" registry and distributed through the NMDP from banks to transplant centers for use in patients.

A goal of adding 150,000 high quality unrelated donor cord blood units to the national registry was established by the original legislation. This number was based on assumptions about HLA-matching that would allow for 50% of patients to identify a 5/6 matched donor, and 90% to identify a 4/6 matched donor. To support accrual of cord blood units towards this goal, the NCBI was authorized to receive approximately $90 million during the first 5-year authorization cycle. However, due to many factors, only about $40 million was appropriated. The legislation was reauthorized in 2010 and approximately 60 million was appropriated over the next 5 years. The total appropriation to the NCBI to date is approximately $105 million. Since November of 2006, 13 banks have been gradually added to the NCBI network. As of May 31, 2015, the program has funded the banking of 86,921 cord blood units with 75,000 realized to date. A significant proportion of these units represent non-Caucasian donors—14% African American, 12% multi-race, and 5% Asian. Over 3,800 cord blood units collected for the NCBI have been released for transplant as of April 30, 2015.

Cord Blood Licensure:

The original legislation also called for the establishment of guidelines for licensure of unrelated donor cord blood banks by the FDA. Multiple hearings occurred and draft guidance for licensure was issued and finalized. To date, five of the NCBI banks have been granted licenses from the FDA. The process of obtaining and maintaining licensure has been challenging for the public banks to date. Many of the regulations, created for drug manufacturing, are not easily applied to manufacturing of cord blood units, particularly when each cord blood unit represents a 'batch' or a lot of one. Requirements for an expiration date, for requalification of materials FDA approved for cord blood manufacturing, timelines for approvals of manufacturing changes and other aspects of the current FDA regulations are seen by some as stifling innovation and progress in the field. Furthermore, licensure has greatly increased the costs associated with public cord blood banking diverting limited resources from the recruitment and collection of cord blood donors and banking of new cord blood units.

Brief history of cord blood banking and transplantation:

In the mid 1980's, it was shown by Hal Broxmeyer and other scientists that cord blood contained high numbers of young blood stem cells. In fact, cell for cell, cord blood was highly enriched for these blood forming stem cells as compared to bone marrow, the traditional source of these types of cells. Shortly after these observations were reported, a cord blood transplant was planned for a 5 year old boy with Fanconi Anemia (a genetic disease affecting the blood and leading to bone marrow failure, or leukemia and death in the first decade of life), under my care at Duke whose mother conceived a healthy child who was a full match to her brother. A team of physicians and scientists in New York City and at Duke arranged for the cord blood to be collected at the time of the baby's birth and later, for the transplant to be performed by Dr. Eliane Gluckman at L'Hospital St. Louis, in Paris, France. The transplant performed in 1988 was a success and paved the way for the field. The patient, named Matthew, is now nearly 33 years of age, married, working and living a healthy productive life. Importantly, he is fully engrafted with his baby sister's cord blood cells and as such, is living proof that cord blood contains blood stem cells that can repopulate the bone marrow (blood factory) and immune system for life.

After that transplant, others were performed between siblings, confirming the findings of the first transplant. In addition, these transplants, using cord blood, caused significantly less of a complication of transplantation called graft-versus-host disease (GVHD) which is a serious condition in which the donor cells attack the recipient. GVHD is a major barrier to the success of blood stem cell transplantation overall. Given that cord blood causes less GVHD, it was hypothesized that cord blood could be used in the unrelated setting and also that cord blood might not have to match as closely as bone marrow. This is important because there are many patients in need of a donor for transplantation who cannot find a fully matched donor.

In 1992, the first unrelated cord blood bank was created at the New York Blood Center by Dr. Pablo Rubinstein and with the support of the National Heart, Lung, and Blood Institute (NHLBI) of the National Institutes of Health (NIH). I established a pediatric blood and marrow transplant program at Duke in 1990 and collaborated with Dr. Rubinstein, agreeing to use cord blood units from his bank for transplantation. In 1993, we performed the first unrelated donor cord blood transplant in the world at Duke in a young child with refractory leukemia. The transplant engrafted, (grew in the bone marrow), in spite of the fact that the cord blood unit and the patient matched at only four of six required locations. Over the next few years, additional transplants were performed at Duke and in other transplant centers, establishing the benefits of cord blood for use in blood stem cell transplantation to treat patients with blood cancers, bone marrow failure, congenital immune deficiencies, certain inherited metabolic diseases and hemoglobinopathies (sickle cell anemia and thalassemias).

In 1996, the NHLBI was funded through Congress to establish additional public cord blood banks and to study the applications of cord blood donors in blood stem cell transplantation. They established and issued RFPs for the COBLT (Cord Blood Transplantation Program), a program which funded the establishment of three additional public banks in the United States and five multicenter prospective clinical trials designed to test the potential benefits of cord blood as a donor for unrelated transplantation. I, on behalf of Duke, applied for and was awarded one of the three banking contracts and established the Carolinas Cord Blood Bank in 1997. I was also one of the principle investigators (PIs) for the COBLT clinical transplantation studies and served on

the steering committee for both the banking and transplantation projects. This steering committee established standards for cord blood banking and the initial guidelines for the use of cord blood in blood stem cell transplantation. Over time, innovative models for kit donations, automation of processing techniques, assays for cord blood viability and potency have been developed.

Early experiences with cord blood transplantation demonstrated that not all cord blood units contained enough cells to transplant a single adult. Establishment of a minimal effective cell dose based on the weight of the recipient was determined for transplantation of patients receiving preparative therapy that destroyed their bone marrow and immune systems (myeloablative conditioning). It was also recognized that the amount of cord blood that could possibly be collected from a single placenta was limited and that the majority of collected units were too small for the transplantation of larger children and adults. This led investigators at the University of Minnesota, Drs. John Wagner and Juliet Barker, to pilot the use of two cord blood units for a single transplant in adults in 2005. This approach was successful and increased access to cord blood transplantation for larger children and adults. However, it also increased the costs of cord blood transplantation because two cord blood units had to be utilized for one transplant.

Between 2005 and 2010, the double cord blood transplant approach was tested in a multicenter, phase III trial in pediatric patients with acute leukemia conducted by the Blood and Marrow Transplant Clinical Trials Network (BMT-CTN). John Wagner and I were the PIs of this study which showed that in children, one cord blood unit was sufficient for transplantation when the unit contained enough cells. In fact, children receiving two cord blood units had more GVHD than those receiving one unit. In adults, however, the practice of double cord blood transplantation continues, with increased GVDH and increased costs of transplantation.

Strategies to increase the numbers of cells provided by a single cord blood unit are the subject of active and ongoing scientific investigation. Ex vivo expansion (or expanding stem cells in the laboratory) before infusion to the patient is showing great progress. At least five promising technologies are currently undergoing testing in the clinic. These modified cord blood products engraft (or grow back) more rapidly after transplant as compared to unmodified cord blood. For example, average times to engraftment after a standard cord blood transplant range from 20-27 days. With ex vivo expansion, engraftment times have decreased to 9-15 days. Additional technologies that improve homing of cord blood cells to the bone marrow are also being tested.

Today, cord blood is a standard graft source for unrelated donor blood stem cell transplantation, providing access to transplantation for patients who lack a matched related donor in their family or unrelated adult donor. The program has particularly met the needs of patients of minority ancestry, as they are less likely to find a fully matched donor. The lower incidence of GVHD is another advantage of this unique stem cell product. Emerging evidence also suggests that when a cord blood donor is used to transplant a patient with acute leukemia, relapse post transplant is lower than when other types of donor cells are utilized. Cord blood is also an important graft source for patients with sickle cell anemia, a disease which can be cured with blood stem cell transplantation.

However, there are challenges to the success of cord blood transplantation. Cord blood engrafts more slowly than bone marrow or adult cells leading to longer hospitalizations for recipients of cord blood units. The immune system, which comes from a newborn baby, also recovers more

slowly after a cord blood transplant compared to other sources. These obstacles can in part be addressed with transplantation of larger cord blood units. However, these units must also be racially diverse. Thus, there is a great need for larger, racially diverse units in the NCBI. Biological properties of blood stem cells vary by race. Specifically, blood from African American donors has fewer cells per volume than blood from Caucasian donors. Thus, to increase the size of cord blood units in the inventory while preserving ethnic and racial diversity, increased collections of cord blood units, particularly from minority births units must be supported. Furthermore, the 150,000 unit target may be outdated today. Rather than targeting a specific number for the inventory, the largest and most diverse units should be targeted. As such, funding strategies should be readjusted to enable increased collections and banking of the largest, racially diverse units.

The potential of cord blood in cellular therapies and regenerative medicine:

In addition to use in patients with malignant and genetic diseases, cord blood is showing enormous potential for use in the emerging fields of cellular therapies and regenerative medicine. Cord blood derived vaccines against viruses and certain types of cancers are currently under development and in early phase clinical trials. Cells, manufactured from cord blood units, are being developed to boost recovery of the immune system. Cells regulating autoimmunity (Regulatory T cells) are also in early clinical trials. These approaches, which often utilize cord blood banked in family banks, may help patients with Type I Diabetes, as well as other diseases.

We, and others, are developing uses for cord blood to treat acquired brain disorders. Over the past six years, we have initiated trials of autologous (the patient's own) cord blood in babies with birth asphyxia (hypoxic ischemic encephalopathy), cerebral palsy, hearing loss, and autism. These studies are showing promising results in conditions for which few treatments are available. We now realize that it will never be possible for all patients who might benefit from cord blood therapies to have access to their own cord blood. For this reason, we are exploring the use of donor cord blood to treat adults with acute stroke. If this proves to be safe, we plan to also test the safety and efficacy of donor cord blood infusions in children with cerebral palsy, autism and other brain injuries.

Summary:

In summary, I have testified that cord blood holds enormous potential for use as a donor for blood stem cell transplantation, providing increased access to transplantation for patients unable to find a fully matching related or unrelated adult donor. Cord blood cells are extremely important for the emerging fields of cellular therapies and regenerative medicine. Cord blood must be harvested in a fashion that maintains sterility, protects against disease transmission and promotes collection of large numbers of cells. Techniques for cord blood banking are well established, but there is a need to explore methods to recover more cells from each collection. Exciting advances in cord blood expansion technology are likely to reduce the risk of a cord blood transplant, extending its use to patients with chronic but serious diseases like Sickle Cell Anemia. Cord blood and derivative therapies can be utilized to treat children with brain injuries and show great promise for treatment of adults with stroke, and other chronic and debilitating diseases.

The NCBI program has created a large inventory of high quality, racially diverse, unrelated donor cord blood units for use in patients needing a donor for blood stem cell transplantation. Continuation and refunding of the program is essential to continue to increase the number of units listed in the NCBI and also to increase the size and diversity of units banked. The potential for cord blood to treat additional serious and life-threatening diseases is just beginning to be realized. With these new applications, it is likely that the NCBI will enable patients to have access to these new and emerging therapies.

Conclusion:

On behalf of our patients, we urge Congress to reauthorize both NCBI and the C.W. Bill Young Cell Transplantation Program by approving the Stem Cell Therapeutic and Research Reauthorization Act of 2015. We look forward to working with you and key stakeholders of the cord blood banking community—patients, physicians, transplanters, researchers and cord blood banks—to ensure that this important bill is signed into law this year.

Mr. Chairman, Ranking Member Green, and members of the Subcommittee, thank you for the opportunity to testify today and I look forward to answering your questions.

Mr. PITTS. The Chair thanks the gentlelady, and I apologize for the interruption here but we must now go to the floor to vote. We are going to vote for three bills and then we will recess for that and come back immediately for the rest of the hearing.

So without objection, the subcommittee stands in recess.

[Recess.]

Mr. PITTS. The time for our recess having expired, we will reconvene the subcommittee, and we are now ready for Dr. Martin. You are recognized for 5 minutes for your opening statement.

STATEMENT OF PATTI FREEMYER MARTIN

Dr. MARTIN. Good morning, Mr. Chairman and members of the committee. I want to express ACH's and my appreciation to Congressman Guthrie and Congresswoman Capps for their leadership in introducing H.R. 1344, the Reauthorization of the Early Hearing and Detection Intervention Act for Children.

This important bill provides assistance to States in identifying hearing loss in infants and young children and places an emphasis on ensuring that those identified with hearing loss receive appropriate intervention.

Hearing loss is the most commonly occurring condition that newborns are screened for. Three babies per thousand are born with hearing loss, and this number almost triples by the time children enter kindergarten.

When hearing loss is detected early, children can learn sign language, be fit with hearing aids for cochlear implants and/or receive early intervention services that enable them to achieve on par with their hearing peers. If it is not detected early, it can be devastating to children's academic and psychosexual development. There is now abundant scientific evidence that the brain develops in response to early visual and/or auditory stimulation, which is critical for children with hearing loss. Almost 30 years ago, a report commissioned by Congress showed that the average deaf child at that time had a 4th-grade reading level when they were old enough to graduate from high school, in large part due to the fact that these children were not identified until they were 2 ½ years to 3 years old. Since newborn hearing screening has been implemented, we have seen the average age of identification drop to 2 to 3 months. More importantly, deaf children who are diagnosed early and receive appropriate early intervention often achieve on the same level with their hearing peers by the time they reach 1st grade.

H.R. 1344 is the reauthorization of a very successful program, which has been in place for 15 years. Because of this initiative called EHDI, 98 percent of babies are now screened for hearing loss before they are discharged from the hospital. Most of these babies go home to families where it never even occurred to their parents to wonder if they could hear them sing or whisper or cool mommy loves you or daddy's big boy. Early screening allows those infants who do not need assistance to be connected with services—who need assistance to be connected with services, to learn to communicate with their families using sign language and/or hearing technology and start on the path to prepare them for school readiness. Of babies who need follow-up, we know that 95 percent of those are born to hearing parents, often with little or no exposure to individ-

uals who are deaf or hard of hearing. They find themselves in a situation that was unanticipated and for which their roadmap on parenting and all their how-to guides may not really apply. A great resource for many of these parents is having access to adults who are deaf or hard of hearing or other forms of parent-to-parent support and family-to-family support as stipulated in this bill.

There is much to be proud about this previous legislation that has captured in the reauthorization. The EHDI program has enabled unprecedented collaboration between public and private agencies and across all levels of Government. The EHDI program is often cited as a model of how Government at different levels and private and public entities should and can work together. The reauthorization continues to emphasize the partnerships among HRSA, CDC and the NIH, and includes language for those agencies for further collaboration.

I want to call your attention to a couple of sections in the bill. First, it focuses on continuing to provide limited Federal support to programs already in place for infants. In the previous version of the bill, the focus was exclusively on babies. This bill reauthorizes services for babies and extends it to young children. This is critical because now we know that by the time children are 5 years of age, we will almost triple the number of children who have hearing loss, and we need to intervene with this group early so that they are ready to learn when they hit school age.

Another important aspect is the focus on families being involved and empowered in the process for their children in a timely way. So engaging and enabling these families is not just desirable but critical. Family involvement is described as the tipping point for children having full access to language, whether it is visual, spoken or a combination of both, and involvement with families is described as family-to-family support and from a variety of professionals including deaf and hard-of-hearing consumers in this bill.

It is about more than just screening for hearing loss. We do screening really well but there is work to be done on getting appropriate services for many infants and young children. We have the basis in place but systems to ensure that infants with hearing loss receive the appropriate follow-up for diagnosis, for medical care, and early intervention services from providers that have the knowledge and skills to help them communicate with their families needs to be refined and improved.

Because of previous funding for the EHDI programs, loss to follow-up has been reduced by half over the last 10 years, but there is much more work to be done.

Thank you.

[The prepared statement of Dr. Martin follows:]

Testimony

Before the House Energy and Commerce Committee Subcommittee on Health

Regarding H.R. 1344, Reauthorization of the Early Hearing Detection and Intervention Act

June 25, 2015

Good morning Mr. Chairman and Members of the Committee, my name is Dr. Patti Martin, I am the Director of Audiology and Speech-Language-Pathology Services for the Arkansas Children's Hospital, and am here today as an expert on the EHDI program and a member of the American Speech-Language Hearing Association.

ASHA is the national professional, scientific, and credentialing association for 182,000 members and affiliates who are audiologists; speech-language pathologists; speech, language, and hearing scientists; audiology and speech-language pathology support personnel; and students

I want to express ASHA's and my appreciation to Chairman Guthrie and Congresswoman Capps for their leadership in introducing and sponsoring H.R. 1344, the reauthorization of the Early Hearing Detection and Intervention Act. This important bill provides assistance to states in identifying hearing loss in new infants and young children, and places an emphasis on ensuring those identified with hearing loss receive appropriate intervention.

Hearing loss is the most frequently occurring condition for which newborns are typically screened. Three babies per thousand are born with hearing loss and this number triples by the time children enter Kindergarten. When hearing loss is detected early, children can learn sign language, be fit hearing aids or cochlear implants, and/or receive early intervention services that enable them to achieve on par with their typically hearing peers. If hearing loss is not detected early it can be devastating to children's academic and psychosocial development. There is now abundant scientific evidence showing that the brain develops in response to early visual and/or auditory stimulation—which is critical for children with

hearing loss. Almost 30 years ago a report commissioned by Congress (Toward Equality, 1988) showed that the average deaf child at that time had a 4th grade reading level when they were old enough to graduate from high school – in large part because the average age of identification at that time was 2 ½ to 3 years of age. Now that newborn hearing screening has been implemented throughout the United States, we have seen the average age of identification drop to 2-3 months of age. More importantly, deaf children who are diagnosed early and receive appropriate early intervention services, often achieve on the same level with their hearing peers by the time they reach first grade. Examples of children who are flourishing using sign language or listening and spoken language can be viewed at http://infanthearing.org/2015EHDIReauthorize/.

Investing in early intervention results in positive long term outcomes regardless of the way a family chooses to communicate with their child. It can result in tens of thousands of dollars either saved once a child enters school or allows for resources that can be redirected towards children requiring more specialized services. Research has demonstrated that important language skills are learned before the age of 3. This is a very critical time period during which infants can acquire language. Brain development of the auditory pathways and language cortex is occurring in young children as they respond to auditory and visual language. In families that are part of the deaf culture, these parents automatically sign from day one, so the baby is learning visual (sign) language, and the appropriate brain development is occurring. However, if a child's hearing loss is undiagnosed and the parents are unaware, the child will not receive the needed language stimulation — and the hoped-for development won't take place. The more age-appropriate sensory input a child receives, the greater the development of complex brain connections and language skills. The most important reason for early detection is so we can understand how to help a child's language and communication growth. Such stimulation needs to happen during the first few months of life in order to prevent language delays and the child's resulting frustrations with communication and social-emotional growth.

HR 1344, the Early Hearing Detection and Intervention Act of 2015 that you are considering, is a reauthorization of a very successful program which has been in existence for fifteen years. Because of this initiative, called EHDI or E-H-D-I for short, 98% of babies are now screened for hearing loss before they are discharged from the hospital. Most of these babies go home to families where it never even occurred to their parents to wonder if their babies were hearing them sing, coo or whisper, "Mommy loves you or "you're Daddy's big boy". Early screening allows those infants who do need assistance to be connected with services, learn to communicate with their families using sign language and/or hearing technology and start on the path to prepare them for school readiness. Of those babies needing additional follow-up, we know that approximately 95% of them are born to hearing parents, often with little or no previous exposure to individuals who are deaf or hard of hearing. They suddenly find themselves in a situation that was unanticipated and for which their road map on parenting, their guide books full of "how-tos' and the advice of friends and families may not apply. A great resource for many of these parents is having access to adults who are deaf or hard of hearing, or other forms of family-to-family support as stipulated in this bill.

There is much to be proud of about the impact of the previous legislation that is captured in this reauthorization. The Early Hearing Detection and Intervention program has enabled unprecedented collaboration between public and private agencies and across all levels of government. The EHDI program is often cited as a model of how government at different levels and public and private agencies should and can work together. The reauthorization continues to emphasize the partnership among HRSA, CDC and NIH and includes language for these agencies to collaborate with additional public and private entities that will further strengthen EHDI programs. As stipulated by HR 1344 HRSA will be responsible for developing and monitoring the efficacy of state-wide hearing screening programs and systems, the prompt evaluation and diagnosis of children referred from screening programs; and appropriate educational, audiological, and medical interventions for children confirmed to be deaf or

hard of hearing. CDC will take the lead on the development, maintenance, and improvement of data tracking and surveillance systems on newborn, infant and young childhood hearing screens, audiologic and medical examinations, and early intervention services. And the National Institutes of Health (NIH) will continue a program of research and development related to development of technologies and clinical studies of screening methods, efficacy of interventions, and related research.

Collaboration among staff from HRSA, CDC, and NIH has been an important element in the success of EHDI programs and will be strengthened by this bill. For example, staff from all three agencies participate in the National EHDI meeting (along with people from many other professional and advocacy groups such as the American Academy of Pediatrics, the American Speech Language Hearing Association, the National Association of the Deaf, the Joint Committee on Infant Hearing, and others) which brings together approximately 1,000 EHDI stake holders each year to participate discuss how EHDI programs can be improved. HRSA and CDC staff are routinely invited to each others' grantee meetings, and CDC recently worked with HRSA and ASHA to develop on online locator system for pediatric audiologists (http://www.ehdi-pals.org/).

I'd like to call your attention to several sections in this bill that offer examples of the wonderful benefits that the reauthorization of this bill will have for children and families.

First, HR 1344 is focused on continuing to provide limited federal support to programs already in place to improve hearing screening for newborn infants and young children. In the previous version of the bill, the focus was exclusively on infants. This bill reauthorizes services for babies and extends services to young children. This is critical because the incidence of hearing loss triples between birth and five years of age and this bill allows us to identify this group of children as well, and intervene so that they enter our schools ready to learn. Although federal money is a small part of the total resources

being devoted to EHDI programs, it is the "glue money" that holds the programs together and enables them to be successful. (Sec 3, Lines 23-26)

Another important aspect of this bill is the focus on the importance of families being involved in the process and empowered to make decisions for their child in a timely way. Research tells us that engaging and enabling families is not just desirable, but critical. Family Involvement can be described as the tipping point for children who are deaf or hard of hearing in having full access to language, whether visual, spoken, or a combination. Involvement of families is described as family-to-family support and support from a variety of professionals, including deaf/hard of hearing consumers. (Sec 4; Lines 16-20)

Because of previous funding for the EHDI program, loss to follow-up has been reduced by half over the last ten years, but more work is needed. Federal money from the current EHDI program has enabled states to work on Quality Improvement initiatives that are focused on reducing loss to follow-up and these efforts have resulted in significant progress. Of the 3.4 million reported by the CDC as being screened for hearing loss in 2013, only 10,118, -- less than 3 per 1,000 were actually lost to follow up after failing the hearing screening test. So the newborn hearing screening system is working like it should for more than 99.5% of newborns. (Section 5; Lines 6-9)

This EHDI bill is about more than just screening babies at birth for hearing loss. We "do" screening very well in all our states, but there is work to be done on getting appropriate services for many infants and young children. We have the basics in place, but systems to ensure that infants with hearing loss receive the appropriate follow up for diagnosis, medical care and early intervention services from providers that have the knowledge and skills to help them communicate with their families must be refined and improved.

When I was about ten years old, my parents took a detour on our vacation to see Ivy Green, the home where Helen Keller was raised. I was awed and amazed as I stood by the water pump where Annie

Sullivan reached into Helen's dark and silent world and opened the door to communication for her. Helen Keller has been my hero since that time. But for Helen's parents, Annie Sullivan was the true hero...she shepherded them down a path they did not choose, that was new and frightening and impacted their basic understanding of what it means to be human—to be able to communicate . EHDI is not a person, but this system of Early Hearing Detection and Intervention can continue to be a hero, much like Annie was to Helen's family, to countless families in the United States. In the words that Helen Keller herself spoke, "Alone we can do so little; together we can do so much".

Mr. PITTS. The Chair thanks the gentlelady and now recognizes Dr. Patrick, 5 minutes for your opening statement.

STATEMENT OF STEPHEN W. PATRICK

Dr. PATRICK. Chairman Pitts, Ranking Member Green, and honorable members of the committee, my name is Stephen Patrick. I am a Neonatologist and Researcher at Vanderbilt University School of Medicine.

It is a privilege to speak with you today about the rising number of infants being born diagnosed with drug withdrawal in the United States. The bill before you, H.R. 1462, the Protecting Our Infants Act of 2015, makes positive steps to improve the health of women and infants impacted by opioid use and misuse.

A few months ago, I was caring for a 2-day-old baby in the neonatal intensive care unit at Vanderbilt Children's Hospital. At just 48 hours of life, the infant became fussy and jittery. Over the next 24 hours, the infant continued to worsen with diarrhea, sneezing and increased fussiness. Each of these signs are classic for drug withdrawal. However, as mother denied use of any drugs that may cause withdrawal, until the baby's drug screen came back positive for prescription opioids. Once I informed the mother of the baby's drug screen, she reluctantly admitted that she had been using pain pills without a prescription. The baby remained in the hospital for a bit undergoing treatment.

And as I reflected on this case, I began to wonder, what if the infant had been discharged to home at the typical 24 hours of life only to have drug withdrawal at home. Would he have been brought back to the hospital critically ill, and with systems may help his mother be more knowledgeable and forthcoming about her drug use, and how do we connect her with drug treatment, particularly during pregnancy. This situation unfortunately is increasingly common.

Neonatal abstinence syndrome is a drug withdrawal syndrome that infants exposed to opioids experience shortly after birth. Opioids pass from the mother through the placenta to the fetus. At the time of birth when the supply is stopped, the infant is at risk of developing drug withdrawal within the first few days of life. Infants with neonatal abstinence syndrome have difficulty feeding and are more likely to have breathing problems, tremors, increased muscle tone, fever, difficulty sleeping, and inconsolability. Severe neonatal abstinence syndrome requires treatment with an opioid like morphine or methadone and an average hospital stay of about 3 weeks. Watching an infant have drug withdrawal is distressing for doctors, nurses, and for parents.

According to the Centers for Disease Control and Prevention, the number of prescription opioids used in the United States quadrupled over the last decade, and by 2012, there were 259 million prescriptions written for an opioid, more than one for every American adult. This rapid increase in opioid use and misuse impacted nearly every population in the United States including women of childbearing age and pregnant women, and a study our group published in May using data from the Tennessee Medicaid program, we found that of 110,000 pregnancies in a 3-year period, nearly 30

percent filled a prescription for an opioid pain reliever during pregnancy.

Throughout the country, as prescription opioid use grew, so did the incidence of neonatal abstinence syndrome. Using billing data from the Nation's hospitals, our research team conducted a series of studies to determine national rates of neonatal abstinence syndrome. From 2000 to 2012, the number of infants diagnosed with the syndrome grew nearly fivefold. By 2012, one infant was born every 25 minutes on average in the United States with neonatal abstinence syndrome, accounting for an estimated $1.5 billion in healthcare expenditures, 80 percent of which are paid for by Medicaid.

The scope of the problem is staggering in some communities. For example, some areas of my home State, Tennessee, reported one in 20 infants born in their community have neonatal abstinence syndrome, and in some NICUs, nearly 50 percent of their total annual hospital days are dedicated to treating this one condition. This rapid increase has largely caught communities and providers off guard. Today there are no well-researched standard treatment protocols for infants with NAS, and as a result, treatment and clinical outcomes vary widely throughout hospitals in the United States.

Addressing the complexity of perinatal opioid use and neonatal abstinence syndrome requires a thoughtful public health approach. Our goal should be to promote healthy mothers and infants by supporting prevention and recovery, and this must begin with primary prevention—engaging public health measures to prevent opioid misuse even before pregnancy including bolstering prescription drugs monitoring programs, improving access to contraception, ensuring opioid prescribing is necessary and appropriate, especially among pregnant women; and secondary prevention—improving screening for drug use in pregnancy and ensuring that drug treatment is available when it is needed and that it includes medication-assisted treatment when appropriate; treatment should be comprehensive, gender-specific, and inclusive of obstetric care; and tertiary prevention—improving identification and treatment of infants suffering with neonatal abstinence syndrome and working to improve post-discharge outcomes.

Mothers and infants impacted by the prescription of opioid and heroin epidemics are in desperate need of a public health approach to address this problem. We cannot wait any longer to respond, and the status quo is simply unacceptable.

The Protecting Our Infants Act takes the necessary and important steps forward to improving research and service care delivery. For the patient I described in my introduction and for the thousands like him, we need the tools to learn how to treat him better, and perhaps even more importantly to prevent him from being there in the first place.

As a neonatologist and researcher, I applaud the bill's authors and the committee's interest in this critical public health problem and this issue that affects so many vulnerable mothers and infants in the United States today.

Mr. Chairman, I thank you for the opportunity to speak today and I look forward to your questions.

[The prepared statement of Dr. Patrick follows:]

TESTIMONY BEFORE THE UNITED STATES HOUSE OF REPRESENTATIVES
COMMITTEE ON ENERGY AND COMMERCE
SUBCOMMITTEE ON HEALTH

Hearing on H.R. 1462, The Protecting our Infants Act of 2015

Stephen W. Patrick, MD, MPH, MS
Assistant Professor of Pediatrics and Health Policy
Division of Neonatology
Vanderbilt University School of Medicine

June 25, 2015

Summary of Testimony:

The number of infants diagnosed with neonatal abstinence syndrome, a post-natal drug withdrawal syndrome which most commonly occurs after *in utero* exposure to opioids, grew nearly 5-fold from 2000 to 2012. This increase occurred with a concurrent rise in the number of prescription opioids being used throughout the US. By 2012, one infant was born every 25 minutes having drug withdrawal, accounting for an estimated $1.5 billion in healthcare expenditures. Despite the substantial increase in the number of infants being diagnosed with neonatal abstinence syndrome, large gaps remain in our knowledge to prevent, identify and treat the syndrome. Our approach to understanding perinatal opioid use and neonatal abstinence syndrome must be grounded in a public health framework aimed at improving the health of both women and their infants. The Protecting Our Infants Act of 2015 embodies a multidisciplinary, public health approach aimed at understanding the problem and filling knowledge and service gaps.

Chairman Pits, Ranking Member Green and honorable members of the Committee, it is a privilege to speak with you today about the rising numbers of infants being diagnosed with drug withdrawal in the United States. The bill before you, HR 1462 the Protecting Our Infants Act of 2015, makes positive steps to improve the health of women and infants impacted by opioid use and misuse.

A few months ago, I was caring for a two-day-old baby in the neonatal intensive care unit (NICU) at The Monroe Carrel Jr. Vanderbilt Children's Hospital. At just 48 hours of life the infant became fussy and jittery. Over the next 24 hours, the infant continued to worsen with diarrhea, sneezing and increasing fussiness. Each of these signs are classic for drug withdrawal, however, his mother denied use of any drugs that may cause withdrawal until the baby's drug screen came back positive for prescription opioids. Once I informed the mother of the baby's drug screen, she reluctantly admitted that she had been using pain pills without a prescription. This baby remained in the hospital for over a week as we managed his symptoms.

As I reflected on this case I began to wonder, what if the infant had been discharged at the typical time of 24 hours of life only to have drug withdrawal at home? Would he have been brought back to the hospital critically ill? What systems might help his mother be more knowledgeable and forthcoming about her drug use and how could we connect her with drug treatment, particularly during her pregnancy?

This situation, unfortunately, is increasingly common.

Neonatal Abstinence Syndrome

Neonatal abstinence syndrome is a drug withdrawal syndrome that infants exposed to opioids experience shortly after birth. Opioids pass from the mother through the placenta to the fetus. At the

time of birth, when the supply of opioids is stopped, the infant is at risk of developing drug withdrawal within the first few days of life. Infants with neonatal abstinence syndrome have difficulty feeding and are more likely to have breathing problems, tremors, increased muscle tone, fever, difficulty sleeping and inconsolability. Severe neonatal abstinence syndrome requires treatment with an opioid, like morphine or methadone, and an average hospital stay of three weeks. Watching an infant experience drug withdrawal is distressing for doctors, nurses and parents.

A Rising Diagnosis

According to the Centers for Disease Control and Prevention, the number of prescription opioids used in the United States quadrupled over the last decade. By 2012, there were 259 million prescriptions written for an opioid – more than one prescription for every American adult.[1]

The rapid increase in opioid use and misuse has impacted nearly every population in the US, including women of childbearing age[2] and pregnant women.[3] In a study our group published in May using data from the Tennessee Medicaid program, we found that of 110,000 pregnancies in a 3-year period, nearly 30 percent filled a prescription for an opioid pain reliever during their pregnancy.[3]

Throughout the country, as prescription opioid use grew, some women turned to using prescription opioids illegally or to heroin; taken together this led to an increase in the the incidence of neonatal abstinence syndrome. Using billing data from the nation's hospitals, our research team conducted a series of studies to determine national rates of neonatal abstinence syndrome. From 2000 to 2012, the number of infants diagnosed with the syndrome grew nearly 5-fold. By 2012, one infant was born every 25 minutes on average in the United States with the neonatal abstinence syndrome accounting for an estimated $1.5 billion in healthcare expenditures – 80% of which are paid for by Medicaid.[4,5] The scope of the problem is staggering in some communities. For example, some areas of my home state, Tennessee, report that 1 in 20 infants born in their community have neonatal abstinence

syndrome.[6] And in some NICUs, nearly 50% of their total annual hospital days are dedicated to treating this one condition.[7]

This rapid increase has largely caught communities and providers off guard. Today, there is no well-researched standard treatment protocol for infants with NAS and as a result, treatment and clinical outcomes vary widely throughout hospitals in the US.[8] As the Government Accountability Office (GAO) pointed out earlier this spring, there are large gaps in research and service delivery for mothers and infants impacted by opioid use and misuse.[9] These knowledge gaps are present in every facet of an affected infant's care; we have difficulty identifying infants at risk for the syndrome, we diagnose the syndrome based upon a subjective scoring system developed decades ago, and while our research suggests infants with neonatal abstinence syndrome are two and a half times as likely to be readmitted to the hospital within 30 days of discharge,[10] we have no good system to ease their transitions home. As the GAO report noted, the federal government spent only $21.6 million over a seven-year period on research related to perinatal opioid use and neonatal abstinence syndrome – quite small when you consider Medicaid alone was charged nearly $1.2 billion for neonatal abstinence syndrome hospitalizations in 2012.[5]

What We Must Do

Addressing the complexity of perinatal opioid use and neonatal abstinence syndrome requires a thoughtful public health approach targeting the pre-pregnancy, pregnancy and post-pregnancy periods for women and infants. Our goal should be to promote healthy mothers and infants by supporting prevention and recovery:

1. Primary Prevention: Enhancing public health measures to prevent opioid misuse even before pregnancy, including:
    a. Increasing education among the public

b. Bolstering prescription drug monitoring programs

c. Improving access to contraception, including long-acting reversible contraception, because research suggests that women with opioid dependency are nearly twice as likely to have an unplanned pregnancy[11]

d. Ensuring opioid prescribing is necessary and appropriate, especially among pregnant women

2. Secondary Prevention:

a. Improving screening for drug use during pregnancy

b. Ensuring that drug treatment is available when it is needed, and that it includes medication-assisted treatment when appropriate. Treatment should be comprehensive, gender specific and inclusive of obstetric care

3. Tertiary Prevention:

a. Improving identification and treatment (including non-pharmacologic treatment) of infants suffering from neonatal abstinence syndrome

b. Supporting families in the transition from the hospital to home, through care coordination and home visitation programs

c. Providing specific pediatric care for the high-risk substance-exposed infants, including close developmental follow-up

d. Providing acceptable contraceptive services in the postpartum period

Funding for research and care delivery for each of these domains are critically needed.

The Protecting Our Infants Act of 2015

The Protecting Our Infants Act of 2015 takes several positive steps toward a public health approach to perinatal opioid use and neonatal abstinence syndrome. The Act calls on the Department of Health and Human Services to conduct a study and develop recommendations for preventing and treating

prenatal opioid abuse and neonatal abstinence syndrome. It addresses many of the issues we have discussed this morning, including improving our understanding of:

1. Prevention, identification, treatment and long-term outcomes for infants with neonatal abstinence syndrome
2. Risk factors for opioid use among women of reproductive age
3. Barriers to identifying and treating opioid use disorders in pregnancy
4. Medically indicated uses of opioids in pregnancy
5. Improvement in treatment of opioid use disorders in pregnant and postpartum women

The GAO report released this spring also found that federal programs for pregnant women and infants impacted by opioid dependency are not well coordinated, at risk for duplication and fragmented.[9] The Act directs the Department of Health and Human Services to close gaps in research and programming for perinatal opioid use and neonatal abstinence syndrome.

Lastly, the Act directs the Centers for Disease Control and Prevention to coordinate and improve surveillance systems for NAS and to craft a public health response to the syndrome.

Summary

Mothers and infants impacted by the nation's prescription opioid abuse and heroin epidemics are in desperate need of a public health approach in addressing this problem. We cannot wait any longer to respond and the status quo is simply unacceptable. The Protecting Our Infants Act takes necessary and important steps forward to improving research and service delivery. For the patient I described in my introduction and thousands like him, we need the tools to allow us to treat him better, and perhaps even more importantly prevent him from having drug withdrawal in the first place. As a neonatologist and a researcher, I applaud the bill authors and this committee's interest in this critical public health issue that affects so many vulnerable mothers and infants in the US today.

In reference to our research findings, I would like to acknowledge our team's funders, including the Robert Wood Johnson Foundation, the National Institute on Drug Abuse at the NIH and the Tennessee Department of Health.

Mr. Chairman, thank you for the opportunity to speak today. I look forward to your questions.

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Appendix: Relevant Publications

Journal of Perinatology (2015), 1–6

www.nature.com/jp

ORIGINAL ARTICLE

Increasing incidence and geographic distribution of neonatal abstinence syndrome: United States 2009 to 2012

SW Patrick[1,2,3,4], MM Davis[5,6,7], CU Lehman[1,2,8] and WO Cooper[1,3,4]

OBJECTIVE: Neonatal abstinence syndrome (NAS), a postnatal opioid withdrawal syndrome, increased threefold from 2000 to 2009. Since 2009, opioid pain reliever prescriptions and complications increased markedly throughout the United States. Understanding recent changes in NAS and its geographic variability would inform state and local governments in targeting public health responses.

STUDY DESIGN: We utilized diagnostic and demographic data for hospital discharges from 2009 to 2012 from the Kids' Inpatient Database and the Nationwide Inpatient Sample. NAS-associated diagnoses were identified utilizing *International Classification of Diseases, Ninth Revision, Clinical Modification* codes. All analyses were conducted with nationally weighted data. Expenditure data were adjusted to 2012 US dollars. Between-year differences were determined utilizing least squares regression.

RESULTS: From 2009 to 2012, NAS incidence increased nationally from 3.4 (95% confidence interval (CI): 3.2 to 3.6) to 5.8 (95% CI 5.5 to 6.1) per 1000 hospital births, reaching a total of 21 732 infants with the diagnosis. Aggregate hospital charges for NAS increased from $732 million to $1.5 billion ($P < 0.001$), with 81% attributed to state Medicaid programs in 2012. NAS incidence varied by geographic census division, with the highest incidence rate (per 1000 hospital births) of 16.2 (95% CI 12.4 to 18.9) in the East South Central Division (Kentucky, Tennessee, Mississippi and Alabama) and the lowest in West South Central Division Oklahoma, Texas, Arkansas and Louisiana 2.6 (95% CI 2.3 to 2.9).

CONCLUSION: NAS incidence and hospital charges grew substantially during our study period. This costly public health problem merits a public health approach to alleviate harm to women and children. States, particularly, in areas of the country most affected by the syndrome must continue to pursue primary prevention strategies to limit the effects of opioid pain reliever misuse.

Journal of Perinatology advance online publication, 30 April 2015; doi:10.1038/jp.2015.36

INTRODUCTION

Neonatal abstinence syndrome (NAS) is a withdrawal syndrome that occurs in opioid-exposed infants shortly after birth.[1–3] Infants with NAS have longer, more complicated postnatal hospitalizations characterized by a myriad of clinical signs ranging from feeding difficulty to seizures.[1,4,5] Recently, NAS emerged as a significant public health problem, increasing in number and healthcare expenditures.[5] By 2009, one infant was born per hour with the syndrome, accounting for an estimated $720 million in hospital charges.[5] The increase in NAS occurred temporally with an increase in opioid pain reliever (OPR) use[6] among several populations, including pregnant women.[7,8]

Data from the Centers for Disease Control and Prevention suggest that since 2009, when the most recent national estimates of NAS were reported, OPR use continued to increase. In 2012, the total number of OPR prescriptions rose to 259 million, enough for every American adult to have one bottle.[9,10] Recent data also highlight substantial variation in OPR use across different United States geographic regions.[9] To date, however, there are no national studies describing geographic variation in NAS. Understanding recent changes in NAS, including its variability in geographic regions, would inform state and local governments in targeting public health responses.

We sought to determine whether the incidence of NAS increased since 2009 in parallel with the marked increase in OPR use nationally and whether the incidence varied across the United States. Further, we aimed to determine whether healthcare utilization patterns of infants with NAS changed over time.

METHODS

Study design and setting

For this retrospective serial cross-sectional analysis, we used data from the Kids' Inpatient Database (KID) for 2009 and 2012 and from the Nationwide Inpatient Sample (NIS) for 2010 and 2011. Both data sets are compiled by the Agency for Healthcare Research and Quality as part of the Healthcare Utilization Project. The KID is the largest publicly available all-payer database for hospitalized children in the United States. The KID contains 2 to 3 million pediatric inpatient records per year from 2500 to 4100 hospitals and is created through systematic random sampling to select 10% of uncomplicated term births and 80% of other pediatric discharges. This sampling strategy gives the KID statistical power to evaluate rare conditions and provide more precise point estimates for all pediatric conditions.[11] The NIS is the largest publicly available all-payer inpatient database in the United States, containing more than 8 million hospital stays sampled from a 20% stratified sample of 1000 community hospitals.[12] Both the KID and NIS have been used broadly in national

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studies of pediatric[5,13,14] and adult[5,15,16] conditions. As the study used de-identified data, it was considered exempt from human subjects review by the Vanderbilt University School of Medicine.

Identification of sample

Infants with NAS were identified if the *International Classification of Diseases, Ninth Revision, Clinical Modification* (*ICD-9-CM*) code 779.5 (drug withdrawal syndrome in a newborn) appeared in any 1 of 25 diagnostic fields.[17] Infants with presumed iatrogenic NAS from medical treatment were excluded using strategies described previously.[5] KID and NIS provide data for hospital births using *ICD-9-CM* codes (V3000 to V3901 with the last two digits of '00' or '01') if the patient is not transferred from another acute care hospital or healthcare facility. Uncomplicated births are identified using the diagnosis-related group code for 'Normal Newborn' (391, version 24).[11,12]

Descriptive variables

Infants with NAS are more likely to have neonatal respiratory complications, feeding difficulty, seizures and low birthweight.[1] Clinical characteristics of infants were obtained using the following *ICD-9-CM* codes in any one of the diagnostic fields during the birth hospitalization: transient tachypnea of the newborn (770.6), meconium aspiration syndrome (770.11, 770.12), respiratory distress syndrome (769.x), other neonatal respiratory diagnoses (770.x excluding above codes and 770.7), feeding difficulty (779.3x), concern for sepsis (771.81), jaundice (774.x) and seizure (779.0, 780.3). Additional descriptive variables, including primary payer (private, Medicaid, uninsured and other) and sex were provided in the KID and NIS.

Outcome variables

National incidence rates of NAS were estimated by dividing the total number of infants with NAS by the total number of hospital births and expressed as incidence per 1000 births. Beginning in 2012, the KID and NIS samples increased, providing sufficient reliability to create estimates by the United States Census Bureau geographic division. Length of stay (LOS) data were obtained from the KID and NIS; as infants not receiving pharmacotherapy for NAS are unlikely to have LOS >6 days,[1] we evaluated LOS for all infants with NAS and then for infants with NAS who had a LOS >6 days (presumed pharmacologically treated). Throughout the article we will refer to infants presumed to be pharmacologically treated as 'pharmacologically treated'. Hospital charges were obtained from the KID and NIS and adjusted to 2012 US$.[18] Missing charges (<3%) were imputed using a regression approach using the command 'impute' with diagnosis-related groups, LOS, age and NAS as predictors. Mean charges before and after imputation were compared and were not significantly different; data with imputed values are presented.

Data analysis

Statistical analyses were conducted using Stata version 13.1 (StataCorp, College Station, TX, USA). For all analyses, survey weights provided by Healthcare Utilization Project were applied to facilitate nationally representative estimates. For 2012, differences in clinical characteristics and primary payer for infants with NAS versus all other hospital births were assessed. Trends for LOS and hospital charges were evaluated using variance-weighted least squared regression.[5] NAS incidence rates were

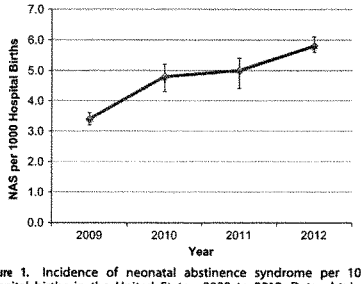
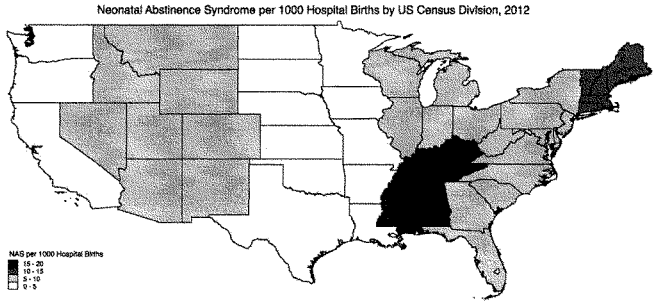


Figure 1. Incidence of neonatal abstinence syndrome per 1000 hospital births in the United States, 2009 to 2012. Data obtained from the Kids' Inpatient Database for 2009 and 2012 and from the Nationwide Inpatient Sample in 2010 and 2011. 2009: 3.4 (95% confidence interval (CI) 3.2 to 3.6); 2010: 4.8 (95% CI 4.3 to 5.2); 2011: 5.0 (95% CI 4.4 to 5.4); 2012: 5.8 (95% CI 5.5 to 6.1).

Table 1. Characteristics of infants with neonatal abstinence syndrome vs all other hospital births, 2012

	Infants with neonatal abstinence syndrome (N = 21 732)		*All other hospital births (N = 3 716 916)*		*P-value*
	N	%	N	%	
Female	9902	45.6	1 817 513	48.9	< 0.001
Clinical characteristics					
Low birthweight	5308	24.4	267 885	7.2	< 0.001
Respiratory diagnoses					
Transient tachypnea	2552	11.7	113 483	3.1	< 0.001
Meconium Aspiration syndrome	613	2.8	13 235	0.4	< 0.001
Respiratory distress syndrome	977	4.5	74 001	2.0	< 0.001
Jaundice	7134	32.8	708 872	19.1	< 0.001
Feeding difficulty	3765	17.3	111 288	3.0	< 0.001
Seizures	309	1.4	4208	0.1	< 0.001
Sepsis	3218	14.8	81 845	2.2	< 0.001
Insurance					< 0.001
Private	2688	12.4	1 717 308	46.2	
Medicaid	17 717	81.5	1 726 432	46.4	
Uninsured	853	3.9	144 137	3.9	
Other	405	1.9	118 918	3.2	

Point estimate (standard error) *N* for NAS = 21 732 (857); unweighted sample *n* = 16 254. Point estimate (standard error) *N* for all other hospital births = 3 716 916 (55 864); unweighted sample *n* = 1 094 748.



US Census Division	NAS Rate per 1000 Births (95% CI)
New England	13.7 (12.5-14.5)
Middle Atlantic	6.8 (5.9-7.6)
East North Central	8.9 (8.0-7.8)
West North Central	3.4 (3.0-3.8)
South Atlantic	6.9 (6.3-7.4)
East South Central	16.2 (12.4-18.9)
West South Central	2.6 (2.3-2.9)
Mountain	5.1 (4.6-5.5)
Pacific	3.0 (2.7-3.3)

Figure 2. Incidence of neonatal abstinence syndrome per 1000 hospital births by US Census Bureau geographic division, 2012. Division 1 (New England): Maine, New Hampshire, Vermont, Massachusetts, Rhode Island and Connecticut. Division 2 (mid-Atlantic): New York, Pennsylvania and New Jersey. Division 3 (East North Central): Wisconsin, Michigan, Illinois, Indiana and Ohio. Division 4 (West North Central): Missouri, North Dakota, South Dakota, Nebraska, Kansas, Minnesota and Iowa. Division 5 (South Atlantic): Delaware, Maryland, District of Columbia, Virginia, West Virginia, North Carolina, South Carolina, Georgia and Florida. Division 6 (East South Central): Kentucky, Tennessee, Mississippi and Alabama. Division 7 (West South Central): Oklahoma, Texas, Arkansas and Louisiana. Division 8 (Mountain): Idaho, Montana, Wyoming, Nevada, Utah, Colorado, Arizona and New Mexico. Division 9 (Pacific): Alaska, Washington, Oregon, California and Hawaii.

calculated by division (nine overall: New England, Mid-Atlantic, East North Central, West North Central, South Atlantic, East South Central, West South Central, Mountain and Pacific) for 2012. Maps were generated to evaluate geographic variation of NAS using the spmap command[19] in Stata, with map data obtained from the National Oceanic and Atmospheric Administration.[20] Throughout our analysis, all tests were two sided, with data reported with standard errors or 95% confidence intervals (CIs).

RESULTS

In 2012, there were an estimated 21 732 (95% CI: 20 052 to 23 413) infants diagnosed with NAS and 3 716 916 (95% CI: 3 607 375 to 3 826 456) other hospital births. Infants with NAS were more likely to have complications than other hospital births, including low birthweight (24.4% vs 7.2%), transient tachypnea of the newborn (11.7% vs 3.1%), meconium aspiration syndrome (2.8% vs 0.4%), respiratory distress syndrome (4.5% vs 2.0%), jaundice (32.8% vs 19.1%), feeding difficulty (17.3% vs 3.0%), seizures (1.4% vs 0.1%) and possible sepsis (14.8% vs 2.2%; $P < 0.001$). Infants with NAS were also more likely than other hospital births to be insured by Medicaid (81.5% vs 46.4%; $P < 0.001$; Table 1).

From 2009 to 2012, incidence (95% CI) of NAS increased from 3.4 (3.2 to 3.6) to 5.8 (5.5 to 6.1) per 1000 hospital births overall (Figure 1). By 2012, approximately one infant was born every 25 minutes in the United States with the syndrome. There was significant geographic variation in NAS diagnoses. In the most recent studyyear, the East South Central division (Kentucky, Tennessee, Mississippi and Alabama) had the highest incidence of NAS at 16.2 (12.4 to 18.9) per 1000 hospital births compared with the West South Central division (Oklahoma, Texas, Arkansas and Louisiana) that had the lowest national incidence rate of 2.6 (2.3 to 2.9) per 1000 hospital births (Figure 2).

From 2009 to 2012, there was no significant change in overall mean LOS for all NAS infants, pharmacologically treated NAS infants and for uncomplicated term infants with mean LOS in 2012 of 16.9 (16.0 to 17.7), 23.0 (22.2 to 23.8) and 2.1 (2.1 to 2.1) days, respectively. Inflation-adjusted mean hospital charges increased for all groups and in 2012 reached $66 700 (61 800 to

Table 2. Mean length of stay and inflation-adjusted hospital charges for all infants with neonatal abstinence syndrome, infants with neonatal abstinence syndrome with a length of hospital stay >6 days and uncomplicated term infants, 2009–2012

Year	*2009* N *(95% CI)*	*2010* N *(95% CI)*	*2011* N *(95% CI)*	*2012* N *(95% CI)*
Neonatal abstinence syndrome				
Mean length of stay (days)	16.5 (15.9–17.2)	17.2 (15.8–18.5)	16.6 (15.1–18.1)	16.9 (16.0–17.7)
Mean hospital charges (2012 US$)	53 800 (49 400–58 300)	59 000 (49 600–68 400)	62 300 (52 900–71 700)	66 700 (61 800–71 600)
Pharmacologically treated neonatal abstinence syndrome				
Mean length of stay (days)	22.7 (21.9–23.4)	22.9 (21.6–24.1)	22.8 (21.5–24.2)	23.0 (22.2–23.8)
Mean hospital charges (2012 US$)	75 700 (69 500–82 000)	80 500 (68 000–93 100)	87 700 (76 300–99 100)	93 400 (86 900–100 000)
Uncomplicated term infant				
Mean length of stay (days)	2.1 (2.1–2.1)	2.1 (2.1–2.1)	2.1 (2.1–2.1)	2.1 (2.1–2.1)
Mean hospital charges (2012 US$)	2800 (2700–2900)	3500 (3300–3800)	3700 (3400–3900)	3500 (3400–3600)

Abbreviation: CI, confidence interval. All US$ inflation adjusted to 2012 and rounded to nearest hundred.

Table 3. Aggregate hospital charges by primary payer for neonatal abstinence syndrome, 2009–2012

Year	*2009*		*2010*		*2011*		*2012*		
	Total charges ($)	*SE ($)*	*Total charges ($)*	*SE ($)*	*Total charges ($)*	*SE ($)*	*Total charges($)*	*SE ($)*	p-for-trend
Private	133 553 300	11 176 700	167 466 500	24 810 000	208 363 300	30 929 400	202 233 600	12 054 400	< 0.001
Medicaid	563 809 300	33 650 300	865 649 700	79 181 000	903 654 700	94 344 100	1 170 206 600	68 789 500	< 0.001
Uninsured	20 079 300	1 603 200	35 995 700	4 906 100	30 842 700	4 735 100	40 370 800	3 004 500	< 0.001
Other	14 248 300	2 628 000	29 379 400	6 807 800	30 117 700	8 011 000	33 395 300	4 890 800	< 0.001
Total	731 841 300	40 290 000	1 098 996 200	98 050 800	1 174 848 900	117 316 500	1 449 389 600	76 698 100	< 0.001

All US$ inflation adjusted to 2012 and rounded to nearest hundred.

71 600) for infants with NAS, $93 400 (86 900 to 100 000) for pharmacologically treated NAS infants and $3500 (3400 to 3600) for uncomplicated term infants (Table 2).

During the study period, the aggregate hospital charges for NAS nearly doubled from an estimated total of $731 841 300 in 2009 to $1 449 389 600 in 2012. Through all study years the majority of hospital charges were attributed to state Medicaid programs, growing from $563 809 300 to $1 170 206 600 (Table 3, $P < 0.001$).

DISCUSSION

The incidence of NAS in the United States nearly doubled during our study period and has grown nearly fivefold since 2000.[5] NAS results in longer, more costly and complicated hospital stays compared with other hospital births. The rapid rise in NAS parallels the increase in OPR use in the United States, suggesting that preventing opioid overuse and misuse, especially before pregnancy, may prevent NAS. NAS is a rapidly increasing public health problem that merits a focused public health approach to mitigate its now far-reaching impact.

We found significant geographic variation in NAS that parallels variations in OPR prescription.[9] We found high rates of NAS in New England (Maine, New Hampshire, Vermont, Massachusetts, Rhode Island and Connecticut; 13.7, 95% CI: 12.5 to 14.5) and the East South Central (Kentucky, Tennessee, Mississippi and Alabama; 16.2, 95% CI: 12.4 to 18.9) divisions. The New England division contains two of the top five prescribing states of long-acting OPR (Maine and New Hampshire) and the East South Central division contains three of the top five prescribing states of short-acting OPR (Alabama, Tennessee and Kentucky),[9] further supporting the association between increased OPR prescription and NAS.

As expected, we found that infants with NAS were more likely to have low birthweight, significant respiratory complications including meconium aspiration and respiratory distress syndrome, feeding difficulties, possible sepsis and seizures—all of which may have contributed to longer LOS compared with other hospital births. More difficult to measure are the associated costs to families affected by the syndrome. Hospitalization for NAS most commonly involves an admission to a neonatal intensive care unit that disrupts maternal and infant bonding. Preventing NAS will prevent the clinical complications of the syndrome and potentially improve the outcomes that are more difficult to measure, including maternal attachment.[21]

Infants with NAS had an overall mean LOS of 16 days and those requiring pharmacologic treatment had a mean LOS of 23 days. We hypothesize that overall mean LOS is positively skewed by some infants who are non-pharmacologically treated or show minimal signs of withdrawal. Interestingly, LOS did not change significantly for either group during the study period. Care for NAS is variable,[4,22] and research suggests that LOS may have decreased with protocol adherence,[23] use of clonidine as an adjunct,[24] breastfeeding when appropriate (for example, when the mother is enrolled in treatment),[25–27] rooming in[28,29] and a site of care outside of the neonatal intensive care unit environment.[30]

Notably, some cases of NAS in our cohort likely occurred in the setting of medication-assisted treatment (MAT) with methadone or buprenorphine. For pregnant women with opioid dependency, current evidence suggests that enrollment in MAT improves pregnancy outcomes including preterm birth.[31,32] However, the literature supporting MAT in pregnancy was developed in the context of heroin use; data supporting optimal management of pregnant women with OPR dependency are limited.[31] With increasing use of OPR in pregnancy,[7] there is an urgent need for research to guide appropriate management of OPR dependency in pregnancy.

Nationally, over 80% of infants with NAS are enrolled in state Medicaid programs, accounting for the majority of the estimated

$1.5 billion in total hospital charges for the syndrome. Given the length of NAS-related hospital care, some states incur substantial expenditures in their Medicaid programs for NAS. For example, the Tennessee Medicaid program estimates that infants with NAS accounted for 1.7% of live births but 13.0% of expenditures on births in 2012.[33] In addition to administering and partially funding Medicaid, states also regulate prescribers and pharmacists. Therefore, states are well positioned to employ public health interventions aimed at preventing OPR misuse. Prescription drug monitoring programs are an intervention employed in every state except Missouri.[34] Prescription drug monitoring programs vary in scope and structure and are a tool to prevent behaviors that increase risk of OPR-related complications (for example, targeting doctor shopping to mitigate risk of overdose death[35]).

Limitations

Our study contains limitations that merit discussion. First, our reliance on administrative data may lead to misclassification bias. There are few studies comparing administrative to clinical data; however, one study noted that administrative data systematically underreported actual NAS.[36] Next, it is possible that the increase in NAS we observed is secondary to observer bias, as the syndrome has received significant attention recently. However, the temporal increases in NAS we observed mirror national increases in OPR use and adverse effects (for example, overdose deaths) attributed to their use. Further, our finding of significant geographic variability in the diagnosis of NAS correlated with geographic variations in use and adverse effects in the United States.[9] In addition, it is important to note that hospital charges do not equal hospital costs and do not include professional fees. In our analysis, we assumed that infants with NAS who had a LOS < 7 days were not pharmacologically treated; however, this may not always be true.

CONCLUSION

NAS has grown nearly fivefold since 2000, accounting for an estimated $1.5 billion in annual hospital expenditures across the United States. This costly public health problem merits a public health approach to alleviate harm to women and children. Federal and state policymakers should be mindful of the impact the OPR epidemic continues to have on pregnant women and their infants, and consider these vulnerable populations in efforts aimed at primary prevention. Finally, efforts aimed at primary prevention and treatment improvements should be targeted at the most affected areas of the country.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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DISCLAIMER

The sponsor had no role in the design and conduct of the study; in the collection, analysis, and interpretation of the data; or in the preparation, review, or approval of the manuscript or the decision to submit.

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Prescription Opioid Epidemic and Infant Outcomes

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abstract

BACKGROUND AND OBJECTIVES: Although opioid pain relievers are commonly prescribed in pregnancy, their association with neonatal outcomes is poorly described. Our objectives were to identify neonatal complications associated with antenatal opioid pain reliever exposure and to establish predictors of neonatal abstinence syndrome (NAS).

METHODS: We used prescription and administrative data linked to vital statistics for mothers and infants enrolled in the Tennessee Medicaid program between 2009 and 2011. A random sample of NAS cases was validated by medical record review. The association of antenatal exposures with NAS was evaluated by using multivariable logistic regression, controlling for maternal and infant characteristics.

RESULTS: Of 112 029 pregnant women, 31 354 (28%) filled ≥1 opioid prescription. Women prescribed opioid pain relievers were more likely than those not prescribed opioids ($P < .001$) to have depression (5.3% vs 2.7%), anxiety disorder (4.3% vs 1.6%) and to smoke tobacco (41.8% vs 25.8%). Infants with NAS and opioid-exposed infants were more likely than unexposed infants to be born at a low birth weight (21.2% vs 11.8% vs 9.9%; $P < .001$). In a multivariable model, higher cumulative opioid exposure for short-acting preparations ($P < .001$), opioid type ($P < .001$), number of daily cigarettes smoked ($P < .001$), and selective serotonin reuptake inhibitor use (odds ratio: 2.08 [95% confidence interval: 1.67–2.60]) were associated with greater risk of developing NAS.

CONCLUSIONS: Prescription opioid use in pregnancy is common and strongly associated with neonatal complications. Antenatal cumulative prescription opioid exposure, opioid type, tobacco use, and selective serotonin reuptake inhibitor use increase the risk of NAS.

WHAT'S KNOWN ON THIS SUBJECT: Although opioid pain relievers are commonly prescribed in pregnancy, their association with neonatal outcomes is not well described. Further, factors associated with development of neonatal abstinence syndrome, a neonatal opioid withdrawal syndrome is inadequately understood.

WHAT THIS STUDY ADDS: Prescription opioid use in pregnancy is common and strongly associated with neonatal complications. Antenatal cumulative prescription opioid exposure, opioid type, tobacco use, and selective serotonin reuptake inhibitor use increase the risk of neonatal abstinence syndrome.

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Recently, sales of opioid pain relievers (OPRs) in the United States have surged.[1] Complications of this increase have affected a wide range of the US population, including pregnant women and their infants.[2,3] Neonatal abstinence syndrome (NAS) is a postnatal withdrawal syndrome, initially described among heroin-exposed infants,[4] that presents with a wide array of clinical signs ranging from feeding difficulties to seizures.[5] From 2000 to 2009, the number of infants in the United States diagnosed with NAS grew nearly threefold, temporally associated with a fourfold increase in OPR prescriptions.[1,6] By 2009, one US infant was born per hour with NAS, accounting for $720 million in national health care expenditures.[6] Despite this temporal association, no large population-based studies have explored the association between OPR use in pregnancy and NAS.

Factors that determine which exposed infants will develop NAS are poorly understood. Rates of NAS among infants exposed to heroin or maintenance medications are reportedly as high as 80%.[5,7] For infants exposed to maintenance medications, risk of NAS seems unrelated to opioid dose[8,9]; however, the association of cumulative opioid exposure for nonmaintenance OPRs and NAS has not been studied. Some reports suggest that the use of tobacco and coprescription of selective serotonin reuptake inhibitors (SSRIs) may also increase the likelihood of developing NAS.[10–12]

Using a large retrospective cohort of pregnant women, our objectives were to identify neonatal complications associated with antenatal OPR exposures and to determine if antenatal cumulative prescription opioid exposure, opioid type, number of cigarettes smoked daily, and SSRI use were associated with a higher likelihood of developing NAS.

METHODS

Study Design and Setting

This retrospective, longitudinal cohort study was conducted by using data from TennCare, Tennessee's Medicaid program; outpatient prescription claims were linked to vital records and hospital and outpatient administrative data. These resources have been used extensively to assess the safety of medications during pregnancy.[13–16] Medicaid serves as an ideal program to study NAS because an estimated 80% of infants with NAS nationwide are enrolled in state Medicaid programs.[6]

The present study was approved with a waiver of informed consent by the Vanderbilt University institutional review board, the State of Tennessee Department of Health, and the Bureau of TennCare.

Cohort Assembly

Maternal and infant dyads were included in the study if: (1) the mother was 15 to 44 years old at the time of delivery; (2) the mother had been enrolled in TennCare at least 30 days before delivery; and (3) the infants were enrolled in TennCare within 30 days after delivery. Last menstrual period and date of delivery were obtained from vital records.[17] Pregnancies were included if the birth occurred between January 1, 2009, and December 31, 2011. Of a total 134 450 births, 112 029 met our inclusion criteria (83.3%).

Exposures

The study's primary exposure of interest was any prescription opioid fill during pregnancy identified from TennCare pharmacy claims data. TennCare pharmacy files contain information on all outpatient prescriptions that are reimbursed by TennCare. Opioid drug types were categorized as short-acting (eg, oxycodone hydrochloride), long-acting (eg, oxymorphone hydrochloride extended release), or maintenance (eg, buprenorphine hydrochloride) medications. Opioid doses were converted to morphine milligram equivalents by using established conversion guidelines to facilitate meaningful comparisons.[18] Duration of opioid use was defined as the period between the prescription start date and the end of the days of supply (allowing up to a 5-day carryover period from previous prescriptions). SSRI prescriptions filled within 30 days before delivery were captured. Information on tobacco use during pregnancy was obtained from birth certificates and from claims by using *International Classification of Diseases, Ninth Revision, Clinical Modification* (ICD-9-CM),[19] diagnostic codes (tobacco: 305.1, V15.82, 989.84, and 649.0x). Data regarding the number of cigarettes smoked per day were obtained from birth certificates, and medication costs were obtained from TennCare pharmacy expenditures. Antenatal exposure to benzodiazepines[20] has been associated with more severe NAS among opioid-exposed infants and was considered in our evaluation; however, the use of these drugs was rare in the study population (167 of 112 029) due to TennCare policies and was not included.

Descriptive Variables, Demographic Characteristics, and Outcomes

Maternal Characteristics

Demographic information was obtained, including maternal age, education (number of years), birth number (parity), and race from birth certificates. Given that the literature describes opioid-using populations to be at increased risk of hepatitis B,[21] hepatitis C,[21,22] HIV,[23] depression,[24–26] and anxiety,[27] data regarding these conditions were obtained from birth certificate data and from outpatient and hospital administrative records by using diagnostic codes (hepatitis B: 070.2x and 070.3x; hepatitis C: 070.41, 070.44, 070.51, 070.54, and 070.7x; HIV: 042, 079.53, and V08;

depression: 296.2x, 296.3x, and 311; and anxiety disorder: 300.x). Acute pain, chronic pain, headache or migraine, and musculoskeletal diseases were identified by using ICD-9-CM codes (acute pain: 338.1x; chronic pain: 338.2x; headache or migraine: 339.x, 346.x, and 784.0; diseases of the musculoskeletal system and connective tissue: 710.x–739.x) as potential OPR indications. Lastly, we identified women with opioid dependency (opioid-type dependence: 304.0x; combinations of opioid type drug with any other drug dependence: 304.7x).

Outcome

Infants with NAS were identified if the ICD-9-CM code 779.5 (drug withdrawal syndrome in newborn) appeared in any diagnostic field during the birth hospitalization. To establish the accuracy of administrative coding for NAS, a chart review was performed of 228 randomly selected cases and noncases. Using a standard definition of NAS as a reference, ICD-9-CM–based identification yielded an 88.1% (95% confidence interval [CI]: 83.3–91.7) sensitivity and a 97.0% (95% CI: 93.8–98.5) specificity (Supplemental Information Appendix A). Infants were further classified as having: (1) no opioid exposure; (2) opioid exposure without NAS; or (3) NAS.

Infant Characteristics

After establishing our cohort, our goal was to describe the clinical characteristics of each infant based a priori on the literature. NAS is characterized by respiratory symptoms, feeding difficulties, and seizures. Opioid-exposed infants and infants with NAS are also more likely to be born preterm or with a low birth weight.[5] Gender, gestational age, and birth weight data were obtained from birth certificates. Clinical signs of NAS, including transient tachypnea of the newborn (770.6), meconium aspiration syndrome (770.11 and 770.12), respiratory distress syndrome (769.x), other neonatal respiratory diagnoses (770.x, excluding the aforementioned codes and 770.7), feeding difficulty (779.3x), and seizure (779.0 and 780.3), were obtained from hospital claims. Infants with NAS might be at greater risk for concerns of sepsis (771.81) considering their clinical presentation (eg, irritability, respiratory distress), and they may also be at an increased risk of jaundice (774.x) due to feeding difficulties. We evaluated for necrotizing enterocolitis (777.5x), given that some authors have reported an association between this condition and NAS.[28] Lastly, we examined the risk of hemolytic disease (773.x) among infants with NAS because of the possibility of previous maternal intravenous drug use.

Data Analysis

The Wilcoxon rank-sum test and χ^2 tests were used where appropriate for bivariate analyses. Candidate predictors of NAS were established a priori from the literature. The level of missing data in our predictors was evaluated; <1% of missing data was found for all variables except number of cigarettes smoked per day, which had 5.6% missing. Birth weights <400 g were deemed unreliable and considered missing. To account for missing data, we used the areglmpute function for multiple imputation by using predictive mean matching[29,30] with 5 imputations. Because of the small numbers of long-acting opioids (n = 177), this group was combined with maintenance opioids for the statistical analyses. Using our entire cohort of 112 029 pregnant women, a logistic regression model was fit with NAS as the outcome and cumulative opioid exposure, opioid type (short-acting, long-acting, or maintenance), number of cigarettes smoked per day, SSRI within 30 days of delivery, infant gender, birth weight, multiple gestations, year of birth, birth number (parity), maternal age, maternal education, and maternal race (white, African American, and other) as predictors. The nonlinear relationship of continuous variables was accounted for by using restricted cubic splines for all variables except morphine milligram equivalents, which were cube root transformed and fit by using a quadratic function to account for skewness.[29] Results for nonlinear predictors are presented graphically (with P values for tests of association) because odds ratios would compare arbitrary data points and may not fully capture their nonlinear relationship with the primary outcome (ie, NAS). Interactions were tested between opioid type × cumulative opioid exposure, number of cigarettes smoked per day × cumulative opioid exposure, opioid type × number of cigarettes smoked per day, and SSRI × cumulative opioid exposure.

Because OPR use early in pregnancy would likely not result in NAS, 2 supplemental analyses restricted to opioid prescriptions were performed that continued through the final 30 and 14 days of pregnancy to determine if restriction to these subsets changed our results. Cost estimates were created by using TennCare pharmacy expenditures and previously published estimates of NAS hospitalization charges.[6] All dollars were adjusted to 2011 US dollars by using the Consumer Price Index.[31] Statistical analyses were completed by using R version 3.1.0. (R Foundation for Statistical Computing, Vienna, Austria)[32] and Stata version 13.0 (StataCorp, College Station, TX).

RESULTS

Among the 112 029 pregnant women in our sample, 31 354 (28.0%) were prescribed at least 1 OPR during pregnancy. Compared with women with no opioid exposure, women taking OPRs were more likely (P < .001) to be white (72.4% vs 65.8%); have depression (5.3% vs 2.7%), anxiety disorder (4.3% vs 1.6%),

headache or migraine (8.3% vs 2.0%), and musculoskeletal disease (23.7% vs 5.8%); use tobacco (41.8% vs 25.8%); and be prescribed an SSRI within 30 days before birth (4.3% vs 1.9%) (Table 1).

Among women prescribed opioids, the majority received short-acting medications (n = 30 192 [96.2%]); fewer received maintenance treatment of opioid use disorder (n = 853 [2.7%]) or long-acting preparations (n = 177 [0.6%]) (Supplemental Table 4). Median (interquartile range) cumulative morphine milligram equivalents were higher among those using maintenance medications (18 480 [8160–37 232]) compared with those using long-acting preparations (4029 [1508–10 800]) or short-acting preparations (150 [75–373]; $P <$ .001). Median (interquartile range) amounts paid for OPRs per individual were $1317 (586–2598) for maintenance treatment, $208 (53–756) for long-acting preparations, and $8 (5–16) for short-acting preparations. Within the last 30 days of pregnancy, 8835 women were prescribed OPRs, 93.6% of whom received a short-acting preparation (Supplemental Table 5). Lastly, 12 896 women received a >7 days' supply of opioids during pregnancy (Supplemental Table 6).

In our cohort, a total of 1086 infants were diagnosed with NAS, 701 (65%) of whom had mothers with at least 1 OPR prescription during pregnancy. Between 2009 and 2011, the quarterly rate of NAS among infants in TennCare rose from 6.0 to 10.7 per 1000 births ($P <$ .001) (Fig 1). NAS occurred more frequently among infants exposed to maintenance opioids (29.3%) and long-acting opioids (14.7%) than in those exposed to short-acting preparations (1.4%) (Supplemental Table 4). Infants with NAS were more likely than other opioid-exposed and nonopioid-exposed infants to be born with a low birth weight (21.2% vs 11.8% vs 9.9%; $P <$ .001) and preterm (16.7% vs 11.6% vs 11.0%; $P <$ .001). Consistent with the characteristics of the syndrome, when comparisons were made between nonopioid and opioid-exposed infants, those with NAS were more likely ($P <$ .001) to have respiratory diagnoses (28.7% vs 10.1% vs 8.8%), feeding difficulties (13.1% vs 2.6% vs 2.3%), and seizures (3.7% vs 0.4% vs 0.3%). Rates of necrotizing enterocolitis were similar among all groups (Table 2). Every $1 spent on short-acting and long-acting opioids (excluding maintenance) was associated with $52 and $12, respectively, in hospital charges for infants with NAS.

After adjusting for maternal age, education, race, infant gender, birth weight, multiple births, birth number (parity), year of birth, the interaction of opioid type × cumulative opioid exposure, opioid type × number of cigarettes smoked per day, and number of cigarettes smoked per day × cumulative opioid exposure, the following factors were independently associated with an increased odds of NAS: cumulative opioid exposure for short-acting OPRs ($P <$ .001), opioid type ($P <$ .001), number of cigarettes smoked per day ($P <$ .001), and SSRI use within 30 days of delivery (odds ratio: 2.08 [95% CI: 1.67–2.60]) (Fig 2). For pregnant women exposed to maintenance/long-acting opioids, the risk of NAS was consistently higher than in other exposure groups, but the risk did not vary with cumulative opioid exposure (P = .16). In supplemental analyses, restricting assessments to women who filled OPR prescriptions through 30 and 14 days before delivery, our results were similar to the findings from our primary analysis (Supplemental Tables 7 and 8, respectively).

TABLE 1 Maternal Characteristics According to Opioid Exposure in Tennessee Medicaid, 2009–2011

Characteristic	No Opioid (n = 80 675)		Any Opioid (n = 31 354)		P
	Median	IQR	Median	IQR	
Age, y	23	20–27	24	21–27	<.001
Education, y	12	12-13	12	11–13	<.001
Birth number	1	1–2	1	1–2	<.001
	N	%	*N*	%	
Race					<.001
Black	25 986	32.2	8362	26.7	
White	53 074	65.8	22 699	72.4	
Other	1298	1.6	188	0.6	
Maternal comorbidities					
Pain					
Musculoskeletal disease	4430	5.8	7439	23.7	<.001
Headache or migraine	1636	2.0	2593	8.3	<.001
Chronic pain	40	0.0	187	0.6	<.001
Acute pain	72	0.1	132	0.4	<.001
Infectious					
Hepatitis C	328	0.4	358	1.1	<.001
Hepatitis B	91	0.1	39	0.1	.61
HIV	144	0.2	43	0.1	0.13
Psychiatric					
Depression	2185	2.7	1672	5.3	<.001
Anxiety disorder	1279	1.6	1361	4.3	<.001
Opioid dependency	154	0.2	262	0.8	<.001
Additional substances used					
Tobacco	20 785	25.8	13 097	41.8	<.001
SSRI (last 30 d of pregnancy)	1529	1.9	1335	4.3	<.001

Percentages may not add to 100% because of rounding.
IQR, interquartile range.

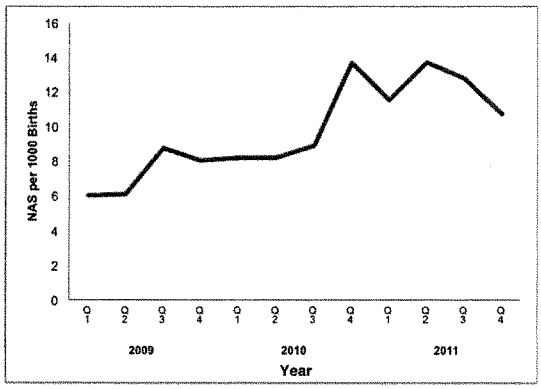

FIGURE 1
Rate of NAS in Tennessee Medicaid according to quarter, 2009 through 2011. $P < .001$.

Based on our regression model, the predicted probability of NAS among mothers who received OPRs during pregnancy varied greatly depending on drug type, cumulative opioid exposure, and number of cigarettes smoked per day. As an example, a woman who took oxycodone hydrochloride 10 mg every 6 hours for 5 weeks with no tobacco or SSRI use had a probability of delivering an infant with NAS of 0.011 (95% CI: 0.008–0.016). In contrast, a woman prescribed buprenorphine hydrochloride 24 mg daily for 25 weeks, who smoked 20 cigarettes (ie, 1 pack) per day and took an SSRI, had a 0.366 (95% CI: 0.270–0.474) probability of her infant having NAS (Table 3).

TABLE 2 Infant Characteristics for Infants With and Without NAS in Tennessee Medicaid, 2009–2011

Characteristic	No Opioid (No NAS) (n = 80 292)		Opioid (No NAS) (n = 30 651)		NAS (n = 1086)		P
	N	%	*N*	%	*N*	%	
Female	39 064	48.7	14 986	48.9	502	46.2	.2
Preterm (<37 wk)	8868	11.0	3549	11.6	181	16.7	<.001
Low birth weight (<2500 g)	7940	9.9	3615	11.8	230	21.2	<.001
Clinical conditions							
Respiratory diagnoses	7052	8.8	3083	10.1	312	28.7	<.001
Transient tachypnea of the newborn	2192	2.7	964	3.1	146	13.4	<.001
Respiratory distress syndrome	2170	2.7	1045	3.4	76	7.0	<.001
Meconium aspiration syndrome	321	0.4	106	0.3	36	3.3	<.001
Other respiratory diagnoses	4517	5.6	1965	6.4	177	16.3	<.001
Jaundice	13 963	17.4	5503	18.0	393	36.2	<.001
Feeding difficulty	1809	2.3	788	2.6	142	13.1	<.001
Sepsis	1515	1.9	692	2.3	78	7.2	<.001
Seizure	240	0.3	117	0.4	40	3.7	<.001
Hemolytic disease	1051	1.3	342	1.1	28	2.6	<.001
Necrotizing enterocolitis	136	0.2	56	0.2	**	0.1	.7

Comparisons made among mutually exclusive groups of no opioid exposure and no NAS, opioid exposure and no NAS, and NAS. Percentages may not add to 100% because of rounding.
**Value suppressed given n <10 in cell.

DISCUSSION

In this large retrospective cohort study of >100 000 pregnancies, cumulative OPR exposure for short-acting OPRs, opioid type, tobacco, and SSRI use during pregnancy was associated with an increased risk of NAS. In the study cohort, nearly 1 in 3 women used at least 1 OPR during pregnancy; 96% were nonmaintenance prescription opioids. Although NAS has previously been associated with illicit opioid use, we found that 65% of infants with NAS were exposed to legally obtained OPRs in pregnancy. These associations provide compelling evidence that OPRs and other concurrent antenatal exposures have a measurable deleterious impact on infants who are more likely than others to be born with NAS and related complications.

Maintenance medications were categorized separately, given that women using maintenance medications have different risks and different reasons for using opioids. For women with heroin dependency especially, maintenance medications have been shown to improve both maternal and neonatal outcomes, including improved fetal growth and decreased preterm birth.[33,34]

Neonatal Complications

Rates of NAS nearly doubled in TennCare during our 3-year study period, reaching 10.7 per 1000 births, exceeding previously reported rates of 3.4 per 1000 births.[6] Compared with nonopioid-exposed infants, those with NAS were more likely to have neonatal complications. Opioid-exposed infants and those with NAS were more likely than nonopioid-exposed infants to be born preterm and have low birth weight. Preterm birth imparts risk to the infant for clinical comorbidities, including respiratory distress syndrome, feeding difficulties, and jaundice (as we have shown).

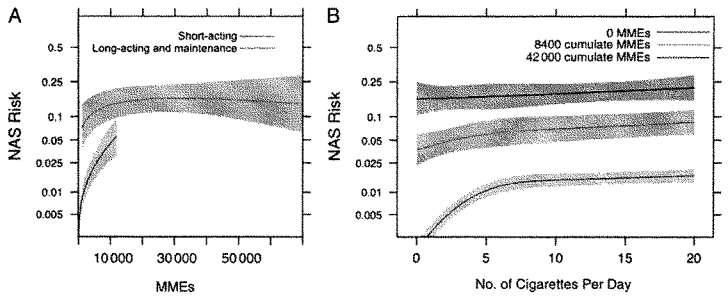

FIGURE 2

Probability of NAS. A, Opioid type and cumulative morphine milligram equivalents (MMEs). B, Number of cigarettes smoked per day and cumulative MMEs after adjusting for maternal characteristics, infant characteristics, and birth characteristics. Graph A: Cumulative MMEs and risk of NAS for short-acting opioid preparations ($P < .001$) and long-acting/maintenance opioid preparations ($P = .16$). Graph B: An increasing number of cigarettes raised the risk of NAS among women with 0 cumulative MME (ie, receiving no legal opioids; $P < .001$) receiving a cumulative total of 8400 MMEs, which equals oxycodone 10 mg q6h × 20 weeks ($P < .001$), and 42 000 MMEs, which equals buprenorphine 24 mg daily × 25 weeks ($P < .001$). The absolute risk and 95% CIs of NAS have been adjusted for cumulative opioid dose in MMEs, maternal age, maternal education, birth number, infant birth weight, year of birth, maternal race, infant gender, multiple gestations, and interaction effects of drug type × cumulative opioid dose ($P = .002$), number of cigarettes smoked per day × cumulative opioid dose ($P < .001$), and drug type × number of cigarettes smoked per day. Total sample = 112 029 mother–infant dyads, 30 651 mothers with OPR use, and 1086 infants with NAS.

In this study cohort, opioid dose for short-acting opioids, tobacco use, and SSRI use were strongly associated with NAS. Similar to previous smaller studies, we found that dose of maintenance opioids did not modify the risk of NAS.[8,9] Furthermore, our findings provide important information that builds on previous studies of OPR use in pregnancy[3,35,36] and several publications describing tobacco and SSRI use in the context of opioid maintenance.[10–12] Both tobacco and SSRIs have been described in the literature as having individual withdrawal syndromes and unique toxidromes.[5] Nevertheless, these exposures could also be associated with a constellation of other risk factors that may be difficult to measure directly (eg, substance abuse) and account for in our analyses. Polysubstance exposure is common among infants with NAS, raising the possibility that observable clinical signs (eg, hypertonia) may not be solely attributable to opioids. In many instances, clinical signs compatible with NAS may be due to multiple withdrawal syndromes and toxidromes occurring simultaneously.

State Policies

The association of increasing use of OPR, overdose deaths, and NAS garnered the attention of many state and federal policymakers.[37] States license and regulate prescribers and pharmacists, and they are financially responsible for the care received by ~80% of infants with NAS through Medicaid programs.[6,38] Nearly all states have implemented prescription drug monitoring programs[39] that aim to reduce diversion and misuse of OPR by identifying high users and high-risk behavior (eg, "doctor and pharmacy shopping"). Tennessee's program began in 2006 as an optional resource for providers and pharmacists. In 2013, the state instituted a requirement that the program must be queried before prescribing most controlled substances.[40] Our study found that ~30% of pregnant women in TennCare were prescribed at least 1 opioid before these policy changes. It will be important moving forward to evaluate the impact of new state policies on reducing opioid use in pregnancy and the incidence of NAS. Furthermore, innovative strategies to enhance prescription drug monitoring databases by including risk predictions of adverse outcomes such as NAS and overdose deaths[41] should be piloted and evaluated.

Variable Risk

The American Academy of Pediatrics recommends that all opioid-exposed infants be observed in the hospital for 4 to 7 days after birth.[5] However, our data suggest there was a wide variability in an infant's risk of drug withdrawal based on opioid type, dose, SSRI use, and number of cigarettes smoked per day by the mother (Fig 2, Table 3). Future studies should evaluate new care models for opioid-exposed infants at different risk levels of developing NAS. For instance, some low-risk infants may be safely discharged from the hospital sooner, whereas high-risk infants may require longer hospital observation.

Limitations

Our study does have several important limitations to consider, similar to other studies that rely on accurate coding of

TABLE 3 Probability of NAS According to Varying Exposures of Short-Acting Opioids and Maintenance Opioids, Tobacco, and SSRI Use

Variable	Short-Acting (eg, Oxycodone Hydrochloride) 10 mg q6h	Maintenance (eg, Buprenorphine Hydrochloride Tablet) 24 mg q24h
	Probability (95% CI)	Probability (95% CI)
5-wk duration	0.011 (0.008–0.016)	0.132 (0.085–0.199)
No cigarette use, SSRI use	0.023 (0.016–0.034)	0.241 (0.157–0.351)
5 cigarettes/d, no SSRI	0.026 (0.020–0.033)	0.165 (0.123–0.219)
5 cigarettes/d, SSRI	0.053 (0.039–0.071)	0.293 (0.217–0.383)
20 cigarettes/d, no SSRI	0.037 (0.029–0.047)	0.179 (0.137–0.231)
20 cigarettes/d and SSRI use	0.074 (0.056–0.098)	0.314 (0.239–0.399)
25-wk duration	0.048 (0.028–0.081)	0.163 (0.103–0.247)
No cigarette use, SSRI use	0.085 (0.055–0.158)	0.289 (0.188–0.416)
5 cigarettes/d, no SSRI	0.073 (0.045–0.115)	0.172 (0.123–0.236)
5 cigarettes/d, SSRI	0.141 (0.088–0.220)	0.303 (0.218–0.404)
20 cigarettes/d, no SSRI	0.104 (0.068–0.156)	0.216 (0.156–0.291)
20 cigarettes/d and SSRI use	0.196 (0.129–0.285)	0.366 (0.270–0.474)

Results shown after adjustment for maternal age, education, race, infant gender, birth weight, year of birth, interaction drug type and cumulative opioid exposure (0.0002), interaction of number of cigarettes smoked per day and cumulative opioid exposure ($P < .001$), and interaction of drug type and number of cigarettes smoked per day.
Probability can be interpreted as 1 = 100% certainty that an event will occur; and 0 = 0% certainty that an event will occur. As an example, a probability of an outcome equal to 0.37 can be interpreted as among a sample of 100 patients, 37 will have the predicted outcome.
As an example, a woman taking oxycodone hydrochloride 10 mg every 6 hours for 5 weeks with no tobacco or SSRI use had a probability of delivering an infant with NAS of 0.011 (95% CI: 0.008–0.016). In contrast, a woman prescribed buprenorphine hydrochloride 24 mg daily for 25 weeks smoking 20 cigarettes (ie, 1 pack) per day and taking SSRIs had a 0.366 (95% CI: 0.270–0.474) probability of delivering an infant with NAS.

hospital administrative and vital statistics data. Both errors of omission and commission are possible, leading to misclassification bias; however, our medical record review suggested that potential misclassification of outcomes was likely to be small. Next, we did not directly observe women in our cohort taking the prescribed OPR. It is possible that OPR medications were not taken as prescribed, resulting in a bias toward the null hypothesis. Next, we were unable to capture other exposures (eg, illicit drugs) that may have influenced our primary outcome (NAS). Opioids obtained by other legal sources not paid for by TennCare (ie, cash payments) were not captured in our sample, which could bias our results toward the null hypothesis. Conversion to morphine milligram equivalents, although the accepted standard, may not create perfect comparisons of various OPRs. Finally, it is possible that opioid prescribing is a surrogate for other unmeasured risk factors for NAS; residual confounding cannot be completely ruled out.

CONCLUSIONS

The use of commonly prescribed, nonmaintenance OPRs in pregnancy increased the infant's risk of developing NAS. Nearly 27% of our cohort of pregnant women was prescribed at least 1 short-acting OPR. Furthermore, NAS risk varied widely based on antenatal cumulative opioid exposure, opioid type, number of cigarettes smoked per day, and SSRI use. Public health efforts should focus on limiting inappropriate OPR and tobacco use in pregnancy. Prescribing opioids in pregnancy should be done with caution because it can lead to significant complications for the neonate.

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THE HIGH COST OF WORKING: *My daughter has begun the search for a summer job or internship. Last year, she was quite fortunate as she found a paid internship in a city only 5 hours from where we live. The company, a provider of wellness packages, seemed a great fit given my daughter's interest in athletics and communication. That she was actually paid to rotate through the different departments and assist in a variety of functions made the experience all the more remarkable. One of my sons, looking for a position overseas, has not been so fortunate.*

As he has found out, and as reported in The New York Times *(Education Life: February 5, 2015), few paid overseas internships exist. Students either volunteer or pay someone else for the opportunity to do an internship. The demand for overseas positions is high. During the 2012-13 year, approximately 40,000 Americans participated in for-credit internships or interned, worked, or volunteered abroad for no credit. Given the demand for positions, companies have sprung up to arrange for internships in a wide array of industries across the globe. While the experiences can be quite gratifying and many students report that the experience helped them find a job back home in the US, the costs of obtaining the internship can be high. Students may have to pay between $8,000 and $15,000 for a six to eight week experience. The cost of the flight and food are additional. While I am supportive of overseas learning experiences, I am having a bit of trouble digesting the concept of paying so much money for the opportunity. I am hoping that my children find summer internships close to home.*

Noted by WVR, MD

Prescription Opioid Epidemic and Infant Outcomes

Stephen W. Patrick, Judith Dudley, Peter R. Martin, Frank E. Harrell, Michael D. Warren, Katherine E. Hartmann, E. Wesley Ely, Carlos G. Grijalva and William O. Cooper

Pediatrics; originally published online April 13, 2015;
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Mr. PITTS. The Chair thanks the gentleman and now recognizes Dr. Terplan for 5 minutes for an opening statement.

STATEMENT OF MISHKA TERPLAN

Dr. TERPLAN. Good morning, Chairman Pitts, Ranking Member Green, and distinguished members of the subcommittee, and thank you for having me here today.

My name is Mishka Terplan, and I am an OB/GYN and Addiction Medicine Specialist and the Medical Director of Behavioral Health System Baltimore. I am pleased to testify on behalf of the American Congress of Obstetricians and Gynecologists in support of H.R. 1462, the Protecting Our Infants Act. I would like to thank Representatives Katherine Clark and Steve Stivers for their leadership in introducing this legislation and the eight cosponsors on the Health Subcommittee, and I urge the committee to act swiftly in reporting out this bill.

H.R. 1462 represents a bipartisan, bicameral effort to address the critical problem of opioid addiction and neonatal abstinence syndrome facing pregnant women from all socioeconomic backgrounds. NAS refers to medical issues associated with drug withdrawal in newborns following prenatal opioid exposure and is expected and treatable with no long-term negative outcomes documented in the literature.

While I want to stress the importance of the mother-infant dyad, my testimony will focus primarily on the woman and how passage and implementation of this bill would improve access to quality treatment and care for this population.

Specifically, the bill would commence three important initiatives that address the following: One, prevention and treatment of prenatal opioid use disorders. Preventing inappropriate opioid use among pregnant women and women of childbearing age is crucial. Quality preconception care and family planning optimize a woman's health and knowledge before conceiving a pregnancy, improving the likelihood of having a healthy pregnancy and a healthy baby. Among women with opioid addiction, almost 90 percent of their pregnancies are unplanned. All pregnant women are concerned for the health of their baby-to-be and are motivated to change unhealthy behaviors. Most pregnant women who use substances including opioids quit or cut back. Those who cannot stop using by definition meet criteria for having a substance use disorder. In other words, continued use in pregnancy is pathognomonic for addiction, which is a chronic relapsing brain disease.

When treating pregnant women with opioid addiction, withdrawal or detoxification are rarely clinically appropriate. Detox results in relapse, and any abrupt discontinuation of opioids can result in preterm labor, fetal distress, or fetal demise. Safe prescribing during pregnancy includes opioid-based medications such as methadone or buprenorphine, which are standard of care for pregnant women with opioid addiction. However, pregnant women continue to face access issues and most do not receive opioid agonist therapy. Denying pregnant women evidence-based treatment in order to prevent NAS is discriminatory.

Additionally, opioid medication should be accurately labeled to ensure appropriate access to medication for women who are addicted and for whom the alternatives such as heroin or withdrawal during pregnancy are much more dangerous. Specifically, the FDA boxed warning related to pregnancy should be removed or updated to remove the inaccurate information linking opioid use during pregnancy with "life-threatening neonatal opioid withdrawal syndrome," a claim with no scientific evidence.

Number two: Gaps in research and programming. Additional research is needed on effective and non-addictive pain treatment, and any such research should include women of childbearing age and pregnant women. However, it is important to note that medically appropriate opioid use in pregnancy is not uncommon, and opioids are often the safest and most appropriate treatment for a variety of medical conditions and severe pain during pregnancy. Pregnant women with substance use disorders need access to comprehensive services including prenatal care, drug treatment, and social support. Punishing pregnant women with substance use disorders by targeting them for criminal prosecution or forced treatment is inappropriate and will drive women away from care. Innovative treatment models are needed and should be tailored to pregnant or parenting women and should provide priority access.

Number three: Improved data collection and surveillance. Opioid addiction has become more widespread geographically and demographically. In communities with high opioid prescription and addiction rates, there will be higher rates of pregnant women with opioid addiction and subsequent NAS. Access to national and State-specific NAS data would enable trend analysis and foster greater sharing of best practices and treatment strategies. Improved data collection would also help us better track and understand the long-term outcomes of infants with NAS. For those purposes, data endpoints need to be of both clinical and sociological significance.

Thank you for the opportunity to testify at today's hearing. The committee's attention to and interest in reducing maternal opioid addiction and NAS are crucial, and the Protecting Our Infants Act represents a positive step forward in addressing this growing issue I welcome your questions. Thank you.

[The prepared statement of Dr. Terplan follows:]

Written Testimony

Of

Dr. Mishka Terplan, MD, MPH, FACOG, Diplomate ABAM

Before the

House Energy and Commerce Subcommittee on Health

Regarding

Examining Public Health Legislation: H.R. 2820, H.R. 1344, and H.R. 1462

June 25, 2015

Summary of Testimony

The testimony of Dr. Mishka Terplan will seek to summarize how passage and implementation of H.R. 1462, the Protecting Our Infants Act, will improve access to quality treatment and care for pregnant women with opioid addiction and their infants.

1. Prevention and treatment of prenatal opioid use disorders
    - Among women with opioid addiction, 86% of pregnancies are unplanned
    - Safe prescribing during pregnancy includes opioid-based medications, such as methadone or buprenorphine. In most instances, withdrawal or detoxification is not clinically appropriate.
    - Screening, brief intervention, and referral to treatment can facilitate early detection and referral.
    - Provider education and public awareness efforts can enrich the patient-provider discussion on the risks and benefits of various medications, including opioids, and potential risks to the fetus.

2. Gaps in research and programming
    - Medically-appropriate opioid use in pregnancy is not uncommon and opioids are often the safest and most appropriate treatment for a variety of medical conditions and severe pain during pregnancy. Additional research is needed on effective and non-addictive pain treatment.
    - Punishing pregnant women with substance use disorders by targeting them for criminal prosecution or forced treatment is inappropriate and will drive women away from seeking prenatal care and other drug treatment.
    - Innovative treatment models are needed and should be tailored to pregnant or parenting women.

3. Improved data collection and surveillance
    - Opioid addiction has become more widespread geographically and demographically. In communities with high opioid prescription and addiction rates, there will be higher rates of pregnant women with opioid addiction and subsequent NAS.
    - Access to national and state-specific NAS data would enable trend analyses and foster greater sharing of best practices and treatment strategies.
    - Improved data will help us better track and understand long-term outcomes of infants with NAS. Data end points need to be long term.

Good morning Chairman Pitts, Ranking Member Green, and distinguished members of the Subcommittee on Health of the Energy & Commerce Committee and thank you for having me here today. My name is Dr. Mishka Terplan and I am double boarded in obstetrics and gynecology and addiction medicine and currently serve as the Medical Director of Behavioral Health System Baltimore.

As a specialist in both women's health and addiction, I have devoted my career to treating women with psychosocial risk including substance use disorders and improving prescribing practices. As a Fellow of the American College of Obstetricians and Gynecologists (ACOG) and member of the American Society of Addiction Medicine (ASAM), I was an author of the joint Committee Opinion "Opioid Abuse, Dependence, and Addiction in Pregnancy." In addition I represent ACOG on the American Medical Association's (AMA) Federation Task Force to Reduce Opioid Abuse and am a member of ASAM's Women and Substance Use Disorders Action Group. I have also participated in expert panels for the Centers for Disease Control and Prevention (CDC), the Substance Abuse and Mental Health Services Administration (SAMHSA), and the Office of National Drug Control Policy (ONDCP) on screening tools for substance use among pregnant women, maternal addiction and neonatal abstinence syndrome (NAS).

I am pleased to testify on behalf of the American Congress of Obstetricians and Gynecologists (ACOG) in support of H.R. 1462, the Protecting Our Infants Act. I would like to thank Representatives Katherine Clark (D-MA) and Steve Stivers (R-OH) for their leadership in introducing this legislation, and the 8 cosponsors on the Health Subcommittee: Representatives

Susan Brooks (R-IN), Kathy Castor (D-FL), Chris Collins (R-NY), Brett Guthrie (R-KY), Joseph Kennedy (D-MA), Leonard Lance (R-NJ), Jan Schakowsky (D-IL) and Ed Whitfield (R-KY). I urge the Committee to act swiftly in reporting out this legislation.

H.R. 1462 represents a bipartisan effort to address the critical problem of opioid addiction and (NAS) facing pregnant women from all socioeconomic backgrounds. NAS refers to medical issues associated with drug withdrawal in newborns following prenatal exposure to opioids and is expected and treatable with no long term negative outcomes documented in the literature. Specifically, H.R. 1462 would commence three important initiatives:

1. Direct HHS to conduct a study and develop recommendations for the **prevention and treatment of prenatal opioid use disorders** and neonatal abstinence syndrome, soliciting input from stakeholders like ACOG.
2. Task the Secretary of HHS with leading a review of planning and coordination within HHS to **close the gaps in research and programming** identified by GAO in their February 2015 report.
3. Encourage **improved data collection and surveillance** by the states and promote an increased public health response to reducing NAS.

This bipartisan, bicameral legislation provides a badly needed public health approach to addressing maternal addiction and NAS and moves us away from punitive proposals that we have seen in many states. In fact, so far in 2015 at least 8 states have considered criminal penalties or immediate revocation of child custody for women who use opioids or other

substances during pregnancy. These efforts are harmful to families and drive women away from accessing prenatal care and addiction services.

I have seen firsthand the recent increase in opioid use and its impact on women and their babies. And I can say with confidence that passing the Protecting Our Infants Act would be a good thing for families. While I want to stress the importance of the mother-infant dyad, my testimony will focus primarily on the woman and how passage and implementation of H.R. 1462 would improve access to quality treatment and care for this population.

1. Prevention and treatment of prenatal opioid use disorders

Preventing inappropriate opioid use among pregnant women and women of childbearing age is crucial. Addressing this issue requires a focus on women of childbearing age, pregnant women, and infants from preconception through early childhood. **For pregnant women, it is most appropriate to treat and manage maternal substance use in a non-punitive manner through family-centered medical treatment.**

For women of childbearing age, quality preconception care and family planning optimize a woman's health and knowledge before planning and conceiving a pregnancy, improving the likelihood of having a healthy pregnancy and a healthy baby.[i] Unplanned pregnancies are at greater risk for a range of negative birth outcomes, such as low birthweight and preterm birth. Among women with opioid addiction, about 86% of pregnancies are unplanned, compared with 46% of pregnancies in the overall population.[ii]

All pregnant women are concerned for the health of their baby-to-be and all are motivated to change unhealthy behaviors. From population level data, we know the natural history of substance use during pregnancy – most women who use substances including opioids quit or cut back. Those who cannot stop using, by definition, meet criteria for having a substance use disorder. In other words, continued substance use in pregnancy is pathognomonic for addiction, a chronic, relapsing brain disease.

When treating pregnant women with opioid addiction, in most instances withdrawal or detoxification it is not clinically appropriate. Medically supervised tapered doses of opioids during pregnancy often result in relapse to former use within a short period of time, adding increased risk to the fetus and increasing the mother's risk for overdose postpartum. Abrupt discontinuation of opioids in an opioid-addicted pregnant woman can result in preterm labor, fetal distress, or fetal demise.[iii]

Safe prescribing during pregnancy includes opioid-based medications, known as opioid agonist therapy (OAT). OAT, such as methadone or buprenorphine, is the medical standard of care for pregnant women with opioid addiction. Physician prescribed and supervised use of OAT improves outcomes for both mom and baby when compared to no treatment or to medication-assisted withdrawal. However, pregnant women continue to face access issues. In fact most pregnant women with opioid addiction in the U.S. do not receive OAT.[iv] It is important to note that denying pregnant women evidence-based treatment, such as OAT, out of concern for NAS, is not only discriminatory, but is counter to the standard of care and will result in worse outcomes for mom and baby.

Screening, brief intervention, and referral to treatment (SBIRT) can facilitate early detection and referral and should be expanded to diverse settings where at-risk women can be reached. If biological testing for drugs is utilized, the woman should be informed of the test and how the results of the test will be managed.

Additionally, provider education and public awareness efforts can enrich the patient-provider discussion on the risks and benefits of various medications, including opioids, and potential risks to the fetus. Providers should be educated on the most current substance use screening tools and universal screening should be the standard of care for all obstetrics patients. Opioid medication should be accurately and precisely labeled to ensure appropriate access to medication and therapy for women who are addicted and for whom the alternatives – such as heroin or withdrawal during pregnancy – are much more dangerous. Specifically, the FDA boxed warning related to pregnancy should be removed or updated to remove the inaccurate and imprecise information linking opioid use during pregnancy with "life-threatening neonatal opioid withdrawal syndrome," a claim with no scientific evidence.

There are a number of provider education efforts currently underway. For example, as a member of AMA's Task Force to Reduce Opioid Abuse, I am assisting in the development of a CME course on safe prescribing, I will be representing ACOG at AMA's Pain Management Expert Panel in Chicago next month, and am on an expert panel to develop a "guide to the management of opioid-dependent pregnant and parenting women and their children" through SAMHSA.

2. Gaps in research and programming

Additional research is needed on effective and non-addictive pain treatment, and any such research should include women of childbearing age and pregnant women. However it is important to note that medically-appropriate opioid use in pregnancy is not uncommon and opioids are often the safest and most appropriate treatment for a variety of medical conditions and severe pain during pregnancy.

Pregnant women with substance use disorders need access to comprehensive services, including prenatal care, drug treatment, and social support services. Women with substance use disorders often have other psychosocial risk factors that need to be addressed in order to ensure they successfully discontinue using drugs. **Punishing pregnant women with substance use disorders by targeting them for criminal prosecution or forced treatment is inappropriate and will drive women away from seeking prenatal care and other drug treatment.**

Innovative treatment models are needed and should be tailored to pregnant or parenting women, taking into account the woman's family and professional obligations, and should provide priority access for pregnant women.

3. Improved data collection and surveillance

Opioid addiction has become more widespread geographically and demographically, crossing into unexpected affluent suburban and rural communities. In fact, according to the CDC, in some states there are as many as 96-143 prescriptions for opioids per 100 adults per year.[v] In

communities with high opioid prescription and addiction rates, there will be higher rates of pregnant women with opioid addiction and subsequent NAS.

While we have general state-by-state data for prescribing rates, similar information is absent for rates of NAS. Access to national and state-specific NAS data would enable trend analyses and foster greater sharing of best practices and treatment strategies. For instance, select states with active maternity and perinatal quality collaboratives have enacted programs to address NAS, and many of these programs have partnerships with hospitals and a data collection component.

Improved data collection will also help us to better track and understand the long-term outcomes of infants with NAS. For those purposes, data end points need to be long term, not just short term, and be of both clinical and sociological significance.

Thank you for the opportunity to testify at today's hearing. The Committee's attention to and interest in reducing maternal opioid addiction and NAS is crucial and the Protecting Our Infants Act represents a positive step forward in addressing this growing issue. I welcome your questions.

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[i] American College of Obstetricians and Gynecologists Committee on Gynecologic Practice, *Committee Opinion No. 313 The Importance of Preconception Care in the Continuum of Women's Health Care*, September 2005 (Reaffirmed 2012).

[ii] Heil S, Jones H, Arria A, et al. "Unintended pregnancy in opioid-abusing women." J Subst Abuse Treat. 2011 Mar, 40(2): 199-202.

[iii] ACOG. *Committee Opinion No. 524. Opioid Abuse, Dependence, and Addiction in Pregnancy (Reaffirmed 2014).*

[iv] Martin C, Longinaker N, Terplan, M. "Recent trends in treatment admissions for prescription opioid abuse during pregnancy." J Subst Abuse Treat. 2015 Jan, 48 (1): 37-42

[v] Paulozzi L, Mack K, Hockenberry, J. "Vital Signs: Variation Among States in Prescribing of Opioid Pain Relievers and Benzodiazepines – United States, 2012." CDC MMWR. 2014. 63(26); 563-568.

Mr. PITTS. The Chair thanks the gentleman. That concludes the opening statements of our panel. We will now begin questioning. I will recognize myself for 5 minutes for that purpose.

Dr. Chell, we will start with you. In what patient population do you see the number of transplants rising the fastest, if you can give us sort of a——

Dr. CHELL. Yes. The group that is rising the most quickly is the elderly population, the senior population, and that is growing by double digits every year, and the reason for that is, the medical conditions for which transplant is often the only cure tend to occur in older populations, diseases like acute myeloid leukemia, myelodysplastic syndrome, myelofibrosis, and others.

Mr. PITTS. Dr. Kurtzberg, while the cord blood and the bone marrow donor programs have enjoyed great success over the past 10 years, what, if any, are the barriers you face to realizing the full potential of these programs?

Dr. KURTZBERG. There are two major barriers I would cite. The first is that cord blood grows slower than bone marrow when you first give it for a transplant, and so there is a big need for more research to develop ways to expand cord blood in the laboratory before it is infused, and I showed one slide showing that there is promising work being done in that area.

The second is that the cost of a cord blood transplant, and that is for procuring the donor and also taking care of the patient, is higher than some other types of transplantation, and part of that is due to the fact that with licensure of cord blood, the costs of manufacturing have gone up while the market-bearing price for reimbursement cannot change because really, it is already too expensive to have a transplant. So we are really struggling for cord blood to be able to be subsidized through programs like this so that the patient can afford to use the donor.

Mr. PITTS. Thank you.

Dr. Martin, can you elaborate on the importance of medical intervention for and follow-up with medical services for deaf individuals? Why is a public health-based approach important at this time?

Dr. MARTIN. Children with hearing loss need follow-up for medical intervention because sometimes hearing loss will be coexisting with other conditions. We want these children to be evaluated for what other coexisting morbidities might occur with hearing loss. What we do know is about a third of children with hearing loss also have another disability as well, and so that medical pace is really critical for them. It makes it a very important public health program. The American Speech and Hearing Association, the National Center for Hearing Assessment and Management, the American Academy of Pediatrics, and American Academy of Otolaryngology have all worked really well on this to ensure that these children get the type of medical care that they need to assist them in having improved outcomes.

Mr. PITTS. Thank you.

Dr. Patrick, you have performed extensive research on neonatal abstinence syndrome. In your written testimony, you state that Medicaid spent $1.2 billion for NAS hospitalizations in 2012. In February of 2015, the GAO released a report that showed gaps in

research funded by the Federal Government in this area. Where should future research focus to close those gaps?

Dr. PATRICK. Well, we have research gaps throughout the continuum of neonatal abstinence syndrome. We need better measures to identify patients at risk of drug withdrawal. We need better systems to diagnose drug withdrawal. The current way we diagnose drug withdrawal is if we have an infant that we know has been exposed to an opioid, so we have to know that first, and then we score them on a system that can be pretty subjective. Basically it's an observation of the infant, and we go through a checklist of what they look like. That was developed decades ago. We need better systems that are more objective and perhaps use technology to aid in that, and we also don't have great mechanisms to understand what is the most effective way to treat these infants, how can we be most efficient, how can we ensure that we can keep mom and baby together when we can. There is a lot that we have to learn, and I think there are gaps throughout the continuum of our treatment of infants.

Mr. PITTS. Thank you.

Dr. Terplan, can you provide more background on the statement in your testimony that the FDA boxed warning related to pregnancy is incorrect and is not validated with scientific evidence? What problems has this caused? To your knowledge, is the FDA in the process of addressing this?

Dr. TERPLAN. So the statement on the box is that use of methadone can cause life-threatening neonatal opioid withdrawal syndrome. The likelihood of death from NAS is no different from the likelihood of death for other infants born at matched gestational age. So it does not contribute in excess mortality risk to newborns, neonatal abstinence syndrome. So that is scientifically inaccurate.

The FDA has convened a panel to discuss the labeling of this medication that both ACOG and the American Society of Addiction Medication testified at a couple weeks ago, so they are working towards that.

Mr. PITTS. All right. Thank you. My time is expired.

The Chair recognizes the ranking member, Mr. Green, 5 minutes for his questions.

Mr. GREEN. Thank you, Mr. Chairman. Again, I would like to thank our witnesses for being here today and also for your understanding of our unusual schedules to run and vote on the floor.

I would like to ask about the treatment that is available to women with opioid use disorders during pregnancy. The GAO report released earlier this year cited numerous gaps in the treatment of NAS as well as into the treatment of women with opioid use disorders. One of the major barriers the GAO identified was the stigma and criminalization of pregnant women who struggle with substance use during pregnancy. For instance, some State laws require healthcare providers to report substance use during pregnancy to State or local law enforcement officials. One State, Tennessee, defines drug use during pregnancy as criminal assault. According to Guttmacher Institute, 18 other States treat substance abuse during pregnancy as child abuse under civil child welfare statutes.

Dr. Terplan, what is the impact of such laws on the incentive for pregnant women to seek treatment for addiction as well as prenatal care?

Dr. TERPLAN. Thank you very much for asking that question. Criminalizing or punishing pregnant women for substance use during pregnancy is a disincentive for them to seek prenatal care or seek substance treatment services or to continue with them. I know anecdotally from colleagues of mine who practice in Tennessee, which is the only State that has explicitly criminalized substance use during pregnancy that they are seeing women who are entering prenatal care late, going across State lines to deliver, delivering at home. One colleague of mine had a patient who delivered at home out of concern for being reported. She started bleeding, and the infant had something going on. They went to the emergency room, and that point in time she was arrested, so her concern, her actual concern with avoiding healthcare because of a fear of being caught up in the criminal system was realized.

Mr. GREEN. How do these—Dr. Patrick, how do these laws impact the diagnosis of treatment of NAS?

Dr. PATRICK. Well, I think in part, beginning with women avoid care, they are more likely to not seek care in a hospital, and that alone is a disincentive. It creates a barrier to improving infant outcomes. The other piece is that we have to know about the exposure. If there aren't systems that allow women to be forthcoming about their drug use and seek treatment, then we don't know about the exposure. So the infant that I described in my introduction, if we didn't know about it and that infant didn't have a rapid weight loss within the first 2 days of life, that infant would have been discharged home because we wouldn't have known about it, having to withdraw at home and potentially having complications at home including severe dehydration.

So I think that is why these systems, public health systems and public health approach, is much preferred to a criminal justice approach.

Mr. GREEN. Well, and I understand the legislature and people are being shocked by a mother having a child that is a user. What would you recommend as effective alternatives to address the issue of the prenatal drug use and improve health outcomes for both the mother and the child?

Dr. PATRICK. Well, I think it begins with a lot of what the bill is doing, to begin to get people at the table, to understand what are the knowledge gaps, how do we coordinate things better. It begins with a public health approach to improving access to treatments and to understanding how we curb opioid use and misuse overall, even before pregnancy. I think the easiest way to prevent an infant having drug withdrawal in my unit is to prevent opioid misuse even before pregnancy. So I think those public health measures are critical.

Mr. GREEN. Dr. Terplan, you had identified a number of additional treatment gaps for pregnant women with substance use disorders. You mentioned, for instance, a lack of access to medication-assisted therapy for pregnant women.

Dr. Terplan, is medication-assisted treatment the standard of care for pregnant women with opioid use disorders?

Dr. TERPLAN. Yes, and not just for pregnant women. It would be for men and non-pregnant women. Medication-assisted treatment would be the standard of care for opioid use disorders.

Mr. GREEN. What are the barriers to women accessing medication-assisted therapy and what can the Federal Government do to address these barriers?

Dr. TERPLAN. There seems to be—we did some research on this. Only 40 percent of pregnant women who are admitted into drug treatment for an opioid use disorder receive medication-assisted treatment in the United States. Some of that has to do with context of treatment. There are many abstinence-only treatment modalities and treatment programs so they are not getting access to it in the treatment context. I know in my State of Maryland, I hear a lot of questions from providers throughout the State. There are large counties in Maryland where there is not a single buprenorphine provider who will take pregnant women. So I am in the process of going around the State and educating the substance treatment providers on how to care for the pregnant women, and one of the concerns that people have is that misperception and perhaps a medical legal liability, lack of knowledge in how to care for the pregnant woman, and oftentimes a lack of good, integrated care between the prenatal care providers and the addiction treatment providers.

Mr. GREEN. OK. Thank you, Mr. Chairman. I know I am out of time.

Mr. PITTS. The Chair thanks the gentleman and now recognizes the vice chairman of the subcommittee, Mr. Guthrie, 5 minutes for questions.

Mr. GUTHRIE. Thank you very much

Before I get to my questions, Dr. Patrick, I am from Bowling Green, Kentucky, so a lot of people have been to the NICU at Vanderbilt, and it has been a blessing to have such a world-class facility that close. We do have a NICU in our area, and my cousin, Scott Guthrie—I am not sure if you have ever practiced with him—he is from Jackson, Tennessee, but does cover the NICU in Bowling Green.

Dr. PATRICK. Yes.

Mr. GUTHRIE. So thanks for what you do.

So I want to talk to Dr. Martin. I am the sponsor of the early detection hearing bill, so I want to focus on that. Universal newborn screenings work very well, the newborn side. Could you help the committee understand why it is important to expand to early childhood screening? You know, I can see where a parent would not understand if their newborn wasn't listening, particularly if it is your first one and you are not sure exactly what they are supposed to communicate, but wouldn't a parent know if a child was 3 or 4 and they couldn't hear?

Dr. MARTIN. Well, one of the things that we see is that children who have what is called light-onset hearing loss like that that were born with normal hearing and acquired hearing loss in the first 3 to 5 years of life, that really they are pretty good at hiding out from their parents. So they read lots of visual cues that go on in their environment. There is lots of redundancy in how we tell kids to do things at that age, and parents want their kids to be typically de-

veloping, so it really flies under the radar a lot with that age child. We know from the statistics that we will almost triple the number of kids who are identified. So if it is three per thousand at birth, we are going to have two to three times that number of kids who enter kindergarten, and even a mild, moderate to severe hearing loss in a child can be missed until they enter school age, and we want to intervene with them early. We have got great programs in place that can help them be ready to learn when they enter school. So it is important to expand it.

Mr. GUTHRIE. OK. Thank you. Also, there seems to be a sense of urgency about deciding how to communicate with your child once they are diagnosed with a hearing issue and some strong opinions about whether families should use American Sign Language or spoken language. How does the early detection bill address this issue?

Dr. MARTIN. One of the important decisions that families have to make when their child is diagnosed with hearing loss is how they want to communicate with them, so they are making decisions about technology use, they are making decisions about the best way to communicate with their child or not. One of the stipulations in this bill is that families be given all the information about all the options that are available to them. So we want for families is for them to have the opportunity of informed choice, so we want to give them the information and help them weigh that in their family situation with their family dynamics, what their desired outcomes long term are for their child, with their culture and traditions and beliefs and their family and make a decision about what sort of communication mode they choose. So it might be ASL, American Sign Language. It might be listening and spoken language. It might be some combination of both.

The good news is that there is not a right choice. The right choice is the choice that a family makes for their child, and we know that the EHDI bill has provisions in it that help us engage and equip families to make those decisions and to follow through with whatever decision that the make.

Mr. GUTHRIE. Well, thanks, and I was involved in creating and expanding the Governor's initiative, involved in getting it passed when I was in the State legislature, and so a lot of States are doing this. What is important for Federal funding? What is the role of the Federal Government in this?

Dr. MARTIN. Well, the Federal funding really primes the pump for this. It is a great example of the Federal Government seeing something that could take place and really be beneficial to families and to children, and stepping in and setting that program up, and so basically it is money that primes the pump for States to do what needs to be done to identify these children and get them enrolled in services and helps them continue that process. So the States are all implementing it in different ways, in lots of different successful ways. The Federal money helps us be able to share information back and forth and to be able to move towards best practice and evidence-based practice as we move forward in helping these kids attain their full potential.

Mr. GUTHRIE. Well, thank you very much. When I was involved, I did research on the bill, and I remember talking to a researcher at Vanderbilt—that is where I went down to really understand

what was moving forward and whether to move forward or not, how much Government do you get involved in—and they told me that if a newborn child, even if it is healthy, put them in a room where they couldn't hear, by the time they were 3, they would never be able to develop the proper speech patterns. So what if a child could be corrected or get on the right path in the earliest stages?

The other thing they did was eye screening, and the only reason I bring that up, because this is a hearing, is they said the normal pediatric screening would catch you going into kindergarten almost all the time except for about 1 or 2 percent, and so do you increase this program for 1 or 2 percent? Well, if you are one of those parents, you do, and it turned out when we passed the bill, my child had to go to an optometrist before kindergarten at 5, and he was one of the 1 or 2 percent. So these are important programs, and I am pleased to be involved and pleased to work with Congresswoman Capps on this, and thank you for coming from Arkansas.

Dr. MARTIN. Thank you very much.

Mr. GUTHRIE. I yield back.

Mr. PITTS. The Chair thanks the gentleman and now recognizes the gentlemen from Oregon, Mr. Schrader, 5 minutes for questions.

Mr. SCHRADER. No questions, Mr. Chairman.

Mr. PITTS. All right. We will go to Mr. Kennedy.

Mr. KENNEDY. Thank you, Mr. Chairman. I want to thank the witnesses for attending today and your testimony, and I really want to recognize the chairman for calling a very important hearing.

I am going to focus my comments a bit on the opioid epidemic, which has been devastating for parts of Massachusetts and for expanding communities across our country. One thing that I know the entire group can agree on is with regards to the opioid crisis that is devastating in its reach, as we have heard from your testimony so far this morning. It does not discriminate, not by race, gender, age, demographics, income, or any other metric. The breadth and depth of this epidemic is particularly painful when it comes to its youngest victims—newborns—and the rise of neonatal abstinence syndrome, NAS.

In the United States, the rate of opiate-dependent births has nearly tripled since 2009. In my home State of Massachusetts, the Department of Children and Families received 2,376 reports of substance use-exposed newborns between March of 2014 and March of 2015. In Tennessee, a recent study of the State's Medicaid program found that over a quarter of all women in the program were prescribed opioid pain relievers during pregnancy. Of the infants born there with NAS, 65 percent were born to mothers who were legally prescribed opioids. These statistics make it clear: We are falling far short in our efforts to protect the youngest among us from an epidemic and we are failing to provide reliable, appropriate care to pregnant women. We need to start researching today to protect our children tomorrow.

I want to recognize and congratulate and celebrate the efforts of Congresswoman Katherine Clark from Massachusetts and Congressman Steve Stivers, whose efforts will help address this dan-

gerous failure to grasp the reach of NAS, and I thank them both for their leadership on this critical issue.

With that said, I wanted to focus my first question to both Dr. Patrick and Dr. Terplan. Can you expand on the gaps in research in NAS, particularly around prevention and treatment, and what evidence-based medical guidance is currently available to doctors and nurses who treat mothers and newborns? I know you both touched on it a little bit in some of the questions but I would like to flesh it out a little bit more.

Dr. PATRICK. Well, I think the gaps—we talked a little bit about some of the issues with diagnosis. We can go on throughout the spectrum in understanding how we send these kids home safely. We have—infants with neonatal abstinence syndrome are about two and a half times as likely to be readmitted to the hospital within 30 days after discharge. We really need systems, both service care delivery as well as research into the best mechanisms to ease that transition home. It is a complicated time for families, and you can think about an infant who is already a bit more fussy than usual and how this can be a challenging time for families. And so part of it is supporting families in that transition, perhaps using things that we know work well with the evidence that exists for childhood like home visitation programs. There really needs to be more targeted evidence towards this population and perhaps using evidence that we have garnered from other places.

And as far as prevention, I think the committee's work that the committee has been working on more broadly on the heroin and prescription drugs epidemics, I think bolstering programs like prescription drugs monitoring programs and targeting special populations is really important, and ensuring that they are well funded at the State level and perhaps even targeted towards special populations such as women of childbearing age.

Mr. KENNEDY. Thank you.

Doctor?

Dr. TERPLAN. So I am going to focus my comments more on women. Identifying women with substance use disorders at the time of labor and delivery is 9 months too late. So we need to be doing universal screening for substance use during prenatal care, and that should be done not just with toxicology testing, which is the most common way we test for things with a urine test, which is not a test for a behavioral disorder that addiction is but with an instrument, a validated instrument, and we actually need to have more good comparison between what is the right set of questions to ask. There is a CDC-funded study that just—I don't know if it started yet but it just got approved—to compare different screening instruments during pregnancy. So we will have better data for that in the future.

Really, for me, the research question is one about implementation. We know what treatment modalities work. The issue is that women aren't getting access to them, and so it becomes not a hypothesis question of what is, you know, best practice per se but how to deliver what we know to a population.

Mr. KENNEDY. I have got 25 seconds, Doctor. I want to push a little bit. What are the barriers to access? What can we do to alleviate those?

Dr. TERPLAN. I think there is a knowledge deficit. I think that also criminalizing of pregnant women for substance use disorders discourages adherence with treatment or access and care, and so they are showing up on labor and delivery rather than during treatment or during pregnancy, and I think there is also some Federal barriers in terms of dissemination of methadone and also we don't have enough prescribers for buprenorphine in the United States.

Mr. KENNEDY. Thank you both. I yield back. I thank the chairman.

Mr. PITTS. The Chair thanks the gentleman and now recognizes the gentleman from Pennsylvania, Dr. Murphy, 5 minutes for questions.

Mr. MURPHY. Thank you. I will try and rush through these.

First, Dr. Kurtzberg, as an experienced cord blood banker and cord blood transplanter, what is your definition of a high-quality cord blood unit?

Dr. KURTZBERG. That is a great question. So a high-quality cord blood unit needs to be sterile. It needs to be checked incapable of transmitting genetic or infectious diseases, and most importantly, it needs to be potent, and potency can be measured by the number of cells that are in the unit, and we know now that we need a certain dose of cells to transplant individual patients and that many of the units that are collected are too small and don't contain that number of cells.

Mr. MURPHY. So do you think the current HRSA contracting policies optimize the collection of high-quality cord blood units?

Dr. KURTZBERG. No, I think HRSA needs to help the banks to be incentivized to collect bigger units with more cells, and right now their policy does not do that.

Mr. MURPHY. And you mentioned that among the potential uses for cord blood are in regenerative medicine. You have initiated trials using cord blood to treat brain disorders including autism. Could you please explain for the committee the current status of that project and insight you have about the future of that research?

Dr. KURTZBERG. Sure. So we think this research has enormous potential in autism, cerebral palsy and other brain disorders in children that are probably acquired and not genetic, and in these cases, we have initiated studies predominantly funded through the Marcus Foundation or the Robertson Foundation where we are looking at the role of cord blood infusions in those children.

In autism, we have completed a 25-patient study for children ages 2 to 6 where we are looking at endpoints at 6 months and changes in symptoms of ASD, and we have shown that children who get a higher dose of cord blood cells similar to the dose we would give a patient with leukemia or another malignant diagnosis benefit and have improvement in the symptoms with decrease in autistic symptoms. We think and we have evidence on MRI that this is due to a normalization of the connectivity in the brain that is coming from signaling of the cord blood cells to cells in the child's brain, which helps repair these conduction pathways.

Mr. MURPHY. That is fascinating. I want to follow up with you in the future.

But let me ask Dr. Terplan and Dr. Patrick, I used to work in an NICU as a psychologist and would follow up children with developmental disorders, and I would be correct in saying that maternal opiate use has increased risk for developmental problems in a child either directly or also related to such things as low birthweight, prematurity, decreased head circumference? Am I correct in that continuing to be a concern?

Dr. PATRICK. I am happy to address that. I think the literature is difficult. There have been several studies demonstrating some issues with behavior, particularly some other issues, lazy eye, strabismus has also been described. But one of the things that we need is more research to follow these infants long term.

Mr. MURPHY. Well, let me ask this too, and also concern for increased risk for mortality if a physician is not aware of some of these problems during pregnancy and increased risk for fetal demise. Am I correct with those?

I am going to ask this question. I believe, Dr. Terplan, you mentioned one of the issues is information. I also chair the Oversight and Investigations Subcommittee here, and many of my colleagues have been part of that. We have looked at the issue of the concern for if someone is in treatment, those medical records are not there, so you can't find out, an OB/GYN cannot find out because it is not in the record, and we have tried to address it, should it be wholly within the record, should it be under the patient's approval. This was based on 1970s law and regulations. Should the patient say, well, put a 1-year waiver in to allow that information in there? We had testimony just a week ago where one of our former colleagues had said, you know, it is in the chart if he has an allergy to penicillin, why can't it be in the chart that he has a reaction to opiates, please don't prescribe it, or if I am on there, to know those things. I wonder if you can comment on this 42 C.F.R. part 2, the thing that we tried to deal with. Do you want access to those records?

Dr. TERPLAN. So the reason for that legislation was just because individuals with substance use disorders are prejudiced against in our society and to protect them——

Mr. MURPHY. But I understand, but we have already established it is the neonates that suffer.

Mr. TERPLAN. Yes, and so I think that the law which had a reason in the past actually does serve as a barrier to effective communication between parties. What I stressed when I talk about this is that there needs to be close collaboration between prenatal care providers and drug treatment providers and that consent forms need to be signed to get around that so that information can be easily shared.

Mr. MURPHY. I just want to make sure we are not making behavioral medicine and physical medicine separate but equal.

Dr. TERPLAN. Correct.

Mr. MURPHY. And if these are—you can have toxic and higher mortality rates. We know the mortality rate has skyrocketed to 42,000 deaths from drug overdose last year. We know there is a huge problem with neonatal abstinence syndrome. I hope you will respond more to this committee with your insights. I am fascinated by them and I want to hear more, because we want to make sure

that you as providers have the information you need to know when you are dealing with a baby so you can deal with it effectively.

I thank you very much. I yield back.

Mr. PITTS. The Chair thanks the gentleman and now recognizes the Ranking Member of the full committee, Mr. Pallone, 5 minutes for questions.

Mr. PALLONE. Thank you, Mr. Chairman.

I think it is important to understand neonatal abstinence syndrome, or NAS, in the context of the public health challenge of the overprescribing of opioid painkillers in the United States. Between 2000 and 2010, there was a fourfold increase in the use of prescribed opioids for the treatment of pain. In 2012, healthcare providers wrote 259 million prescriptions for opioid painkillers, enough for every adult American to have a bottle of pills.

So my questions. Dr. Patrick, first, can you describe what has happened with the incidence of NAS in the past decade? In your opinion, is this phenomenon tied to the issue of the overprescribing of opioid painkillers for pain?

Dr. PATRICK. Well, over the last decade, we know that neonatal abstinence syndrome has grown fivefold, and by 2012, one infant was born every 25 minutes on average with the syndrome. When we look at specific studies, there have been several studies looking at what is happening in generally prescribing, as you described, it has increased, but it has also increased among women of childbearing age as well as pregnant women over time. In a recent study we conducted in Tennessee, we looked specifically at opioid prescribing in pregnancy, and we found that nearly a third of pregnant woman had an opioid pain reliever prescribed in pregnancy, and most of those, 96 percent, were short-acting opioids. So yes, I think there is compelling evidence that what we have seen in our neonatal intensive care units and in labor and delivery is a result of the broader prescription opioid epidemic and it is the downstream effect that we are seeing negatively impact both women and infants.

Mr. PALLONE. I think I was going to ask some questions about the Tennessee Medicaid program but I think you just answered them, so let me move on.

I was surprised by the prevalence of opioid prescribing in pregnant woman. It is eye-opening, to say the least, and I think most of us associate NAS with illicit opioid use including heroin. While it is certainly important to ensure that pregnant women have access to treatment for pain, it is also important for patients and providers to understand that medical use of opioids during pregnancy presents a risk of NAS.

So do you think there needs to be more research conducted to inform us on when it is indicated to prescribe opioid painkillers during pregnancy?

Dr. PATRICK. So from my perspective as a neonatologist, yes, I think guidelines would be helpful. I think the nuance here is that we have in one population perhaps overprescribing but we also have difficulty accessing medication-assisted treatment. So one thing that is important to know is that neonatal abstinence syndrome is not the worst complication of pregnancy; preterm birth is.

And in some women with substance use disorder, accessing medication-assisted treatment is vital.

So we have this group of patients who have difficulty accessing medication-assisted treatment and we have another group of patients who are likely being overprescribed opioid pain relievers and another group of patients who are now using heroin, and so we need more research to understand this diverse population and how we improve outcomes based upon all of them, and I think that is why the goal needs to be overall to improve health for moms and babies because they are tied so closely together.

Mr. PALLONE. Thanks. In your paper, you conclude, and I quote, "Prescription opioid use in pregnancy is common and strongly associated with neonatal complications." Could you just elaborate on that statement? In other words, what are the neonatal complications associate with NAS and how are they linked to prescription opioid use during pregnancy?

Dr. PATRICK. Well, in that study, we looked at two different groups of people. We looked at—or three, actually—where there were no opioids prescribed, where there were opioids prescribed but neonatal abstinence syndrome did not occur, and when neonatal abstinence syndrome occurred. For infants that were exposed to opioids and for infants with neonatal abstinence syndrome, they are more likely to be born preterm and low birthweight, more likely to have respiratory complications, have things like jaundice and feeding difficulty. That was much more common among those infants, and I think, again, that is why primary prevention aimed at both moms and babies is really where we should target.

Mr. PALLONE. All right. I want to thank you for your good work on this issue and for bringing much-needed public attention to the issue of NAS. I also want to thank Representatives Clark and Stivers for their work on Protecting Our Infants Act of 2015, which will hopefully focus our efforts to address NAS at the Federal level.

You were pretty fast in answering those questions so we can get it within our 5 minutes. Thanks again.

Dr. PATRICK. I am a fast talker. Thank you.

Mr. PITTS. The Chair thanks the gentleman and now recognizes the gentleman from New Jersey, Mr. Lance, 5 minutes for questions.

Mr. LANCE. Thank you very much, Mr. Chairman, and good morning to the distinguished panel.

To Dr. Patrick, opiate abuse is a growing problem across the country obviously including in New Jersey. As a result, about 5 years ago, the Children's Specialized Hospital in New Jersey developed a neonatal withdrawal and rehabilitation program. When a baby is admitted, the hospital evaluates the child's symptoms using a 21-point checklist to determine how much medicine needs to be administered as the baby is weaned from its opiate, and a course of therapies designed to address many of the symptoms associated with neonatal abstinence syndrome, NAS, which has been discussed here this morning.

For example, the hospital uses a special stimulation device on the baby's throat to teach the infant how to swallow, and the hospital also teaches the mother massage and calming techniques. Can you discuss the role that these types of rehabilitative therapies

play in a child's recovery and how will H.R. 1462 help to ensure that more children receive the comprehensive care that they receive at a wonderful hospital in New Jersey, the Children's Specialized Hospital?

Dr. PATRICK. Well, one of the things that we need to learn are more innovation such as the things that you have described where the literature may not be as robust, and so I think that is one thing that this bill provides. It outlines potential gaps. You know, I think that is one of the targets and one of the potential ways that this bill helps. What was the second part of your question?

Mr. LANCE. I think you have answered it. We want to make sure that the bill is effective in developing techniques that will save the child's life.

Are there similar programs—I am sure that our program in New Jersey is not the only program that is trying to develop techniques in this area. Are there other programs across the Nation, and what are some of the methods used in other programs?

Dr. PATRICK. Well, one of the most important things that we have seen grown up over the last several years are States building perinatal collaboratives focused on improving care to moms and babies, and nationally, a group called the Vermont Oxford Network that we have been involved in that——

Mr. LANCE. The Vermont Oxford——

Dr. PATRICK. Network, yes, sir.

Mr. LANCE. That is Oxford in England or——

Dr. PATRICK. It initially started that way. But this program involves at the start 200 NICUs, mostly in the United States but in a couple other countries, focused on improving the care to infants with neonatal abstinence syndrome. One of the first things that we needed to do was just standardize the care that occurred because there's great variability from place to place, and hospitals like the hospital that you described where they have a standard approach, were focused on this one population and we know that we treat this population the same way every time, that alone is associated with improved outcomes. And so that is part of where we have been working over the last several years. There are a few hospitals that have popped up specifically focused—West Virginia is one specifically called Lily's Place just to treat infants with neonatal abstinence syndrome, and those innovations, to be able to allow rooming in where moms and babies stay together—because the NICU environment can be a chaotic environment where we have ventilators and all kinds of machinery—places where there can be a dark, quiet environment where healing can occur as you have described.

Mr. LANCE. Thank you. Is there anyone else on the panel who would like to comment?

Very good. Mr. Chairman, I yield back 1 ½ minutes.

Mr. PITTS. Excellent. Thank you, Mr. Lance.

The Chair now recognizes Mr. Butterfield, 5 minutes for questions.

Mr. BUTTERFIELD. Thank you very much, Mr. Chairman, and I thank all of the panelists for their willingness to testify today.

I will start off by apologizing for being late for the hearing. I have been trying to watch some of it on television while I have been trying to read the Supreme Court decision in the Burwell case

a few moments ago, the 6–3 decision that for the second time affirms the Affordable Care Act, which was the historic law that we debated in this committee some years ago, and I was part of that debate, and our committee passed it, it passed the Congress, and now it is the law of the land and it is working, and I just wanted to make that statement for the record. I realize that is not the subject of today's hearing but I could not go back to my office without saying it. I am not gloating, Mr. Chairman. I am not gloating. I am not. I am not. I am not gloating. I just wanted to reach across the aisle and say to my colleagues that the law is working and let us make it work and let us get healthcare to all Americans because they deserve it.

I welcome the witnesses and I am happy to recognize Dr. Joanne Kurtzberg, who is testifying today in her capacity as President of the Cord Blood Association. She is a Professor of Pediatrics and Pathology at Duke University School of Medicine. Duke is one of the world's premier healthcare providers. That is undisputed. It educates and employs the world's top doctors and nurses and researchers, and I am proud to represent Duke Med here in the Congress.

Mr. Chairman, I support these three bills that we are discussing today. I encourage their expeditious consideration. As chairman of the Congressional Black Caucus, I know that many of the conditions which can be treated using cells from cord blood like sickle cell anemia disproportionately impact African Americans, and also as a member of Gallaudet University Board of Trustees, I care deeply about preventing hearing loss and supporting the deaf and hard-of-hearing community.

Equally concerning is the marked increase in prescription opiate abuse among pregnant women and its impact on infants.

Mr. Chairman, H.R. 1462 addresses this important issue and will identify ways to reduce neonatal abstinence syndrome, and so I appreciate the opportunity to discuss these very important topics.

Now, Dr. Kurtzberg, it is no surprise that I am going to go to you first with the time that I have. What are some of the diseases which impact African Americans disproportionately and are treatable by using cells from cord blood?

Dr. KURTZBERG. So the first disease we all think of is sickle cell anemia, which can be cured with hematopoietic stem cell transplant, and children and adults with sickle cell often have a hard time finding a match donor in their family or in the registry. Cord blood has the advantage of not having to be completely matched and therefore it has become one of the optimal donor sources for patients with sickle cell disease.

Mr. BUTTERFIELD. Can you elaborate on the need for racially diverse units in the NCBI?

Dr. KURTZBERG. Yes. So, you know, it is kind of a debate because we need big units, and biologically, patients with sickle cell—I am sorry—patients who are African American have sticky cells and their cells stick to the walls of their blood vessels. So when you do a blood test or a cord blood collection, you actually get a fewer number of cells per volume of blood than you would from a Caucasian, and so it makes it more challenging to collect high-quality units from African American patients because you have to collect more to get big enough ones.

Having said that, the match, which is somewhat related to ancestry, will be better often if a patient receives a unit from someone of their own race. So really, the program is challenged to collect probably twice as many units from African American patients and donors in order to have a high-quality inventory for those patients.

All in all, we need more African American donations and collections, and they will provide better matches to African American patients, but they have to also be targeted to be big enough to serve those patients well.

Mr. BUTTERFIELD. I am also interested in the potential for new applications using cord blood and some of the cutting-edge breakthroughs that are being made in your field. Can you describe how your discovery of using unrelated cord blood for transplant benefits patients and how it could lead to future breakthroughs?

Dr. KURTZBERG. So we have specifically studied at Duke the use of unrelated cord blood in children with certain genetic diseases that affect the brain. These are leukodystrophies like adrenal leukodystrophy, Krabbe disease, and diseases like Hurler syndrome and many others, and from that work, we have also learned that cord blood cells go to the brain and facilitate repair of various abnormalities in the brain like demyelination or abnormal connections, and we are now using that observation to treat children with birth asphyxia, cerebral palsy, autism, and then adults with stroke, and I think we are just at the beginning of seeing the opportunity for cord blood to also treat patients with adult demyelinating diseases like M.S. or others.

Mr. BUTTERFIELD. Thank you very much. I yield back.

Mr. PITTS. The Chair thanks the gentleman and now recognizes the gentlelady from North Carolina, Mrs. Ellmers, 5 minutes for questions.

Mrs. ELLMERS. Thank you, Mr. Chairman, and thank you to our panel for being here today discussing this very important issue.

Dr. Martin, I am going to start with you. Can you talk about the early hearing detection and intervention program that has led to unprecedented collaboration between the public and private agencies across all levels of Government and what has made this model so successful?

Dr. MARTIN. I think that the previous legislation—and this is carried on in the reauthorization—really outlines the role of HRSA, the role of CDC, the role of NIH, and we have just had great success in working together to improve outcomes for children. We have also partnered at the State level across departments of health, departments of education. We have accessed resources in the private sector as well, and this seems to be an issue that people have been able to come together around and really show how that has been done, so that has been an excellent outcome for us.

Mrs. ELLMERS. That is great. That is a great model for us to use into the future.

And Dr. Terplan, I know this question was posed to Dr. Patrick a little earlier in the subcommittee hearing, but I would like to get your take on the type of innovative treatment models that are needed to close the gaps in research and programming for pregnant women who are addicted to opioids.

Dr. TERPLAN. So I think we know a lot of the pieces that work: medication-assisted treatment for opioid-dependent women, which is methadone or buprenorphine. We need to think about there is a third medication that exists. Vivitrol is the brand name, and that has not really been studied in the United States in pregnant women, and having options is key. I think we get a little hung up one versus the other as if having a choice is an impediment rather than actually something that is great and liberating clinically and allows us to actually be able to individualize therapies.

I think we also have to work on, it is not just the medication, it is also the other associated services. Pregnant women with substance use disorders are a unique population in addiction medicine and come with a whole host of needs—psychosocial needs, transportation needs, childcare needs and things like that—and we have to find ways to integrate those into treatment and find ways to reimburse for some of those things, which aren't traditional medical services.

Mrs. ELLMERS. Thank you, Dr. Terplan.

And Dr. Kurtzberg, again, thank you for being here representing Duke Medicine and the Core Blood Bank. Now, with the Cord Blood Bank at Duke and the Carolina Cord Blood Bank and the licensing that the FDA put forward in 2012, can you tell us what the impact of that licensure has made on the Cord Blood Bank?

Dr. KURTZBERG. Yes. The licensure process has been challenging, in large part because this is the first hematopoietic stem cell source that has been licensed, and it has been a learning process on both sides of the fence. But the bottom line is that licensure has increased costs of running a bank, and because of that, banks are using more of their limited resources to comply with some of these regulations as opposed to put more cord blood units in the bank and collect more units from donors. So we are hoping there could be some conversation with the FDA to help optimize the guidelines to apply to cells since most of these guidelines are really written for drugs, and to both keep the high quality of cord blood units but enable more resources to go into collection and storage.

Mrs. ELLMERS. Again, I just truly appreciate you being here testifying with our subcommittee here today on H.R. 2820. Can you just talk a little bit about the difference between the cord blood stem cells and the embryonic stem cells, and what that means to the future of research and the role that you are playing?

Dr. KURTZBERG. Well, cord blood cells are not embryonic cells. That is the first important thing to say. And cord blood cells can be collected without any risk to the mother or the baby, and in fact, they used to be discarded as medical waste. So we are literally recycling something that used to be thrown in the trash to save lives, so there is no real common or similarity between the two cells. Cord blood cells cannot give rise to every cell in the body. Cord blood cells are blood stem cells and progenitors, and they help reconstitute bone marrow after a transplant.

Mrs. ELLMERS. Well, thank you very much, and I yield back the remainder of my time.

Mr. PITTS. The Chair thanks the gentlelady and now recognizes the gentlelady from California, Mrs. Capps, 5 minutes for questions.

Mrs. CAPPS. Thank you, Mr. Chairman, and thank you to each of our witnesses for your testimony. I appreciate this opportunity that we have to come together to talk about these important public health bills. I want to especially focus, as I did earlier in my remarks, on a program near and dear to my heart, the Early Detection Hearing and Intervention Act, to reauthorize this important program. It is one as a school nurse I have worked on for over 15 years.

Each year, more than 12,000 infants are born with a hearing loss, and since the first authorization of this bill in 2000, we have seen a tremendous increase in the number of newborns who are now being screened for hearing loss. Back in 2000, only 44 percent of newborns were being screened for hearing loss and now it is over 89 percent before they leave the hospital. That is pretty astounding.

We have also seen an increase in the surveillance and tracking of hearing screens and examination. The reauthorization bill I have introduced with Representative Guthrie would not only ensure this program is there for the children who need it in the future but it would also strengthen the program based on lessons we have learned over this time.

Once such area where reauthorization would improve the program is the way in which it clarifies CDC's role in conducting surveillance on early hearing detection and interventions. I want to focus three questions on our audiologist on the panel, Dr. Martin. You are the Audiologist at Arkansas Children's Hospital, and I am going to ask you three questions, and if you could be fairly brief so we can hopefully get these in.

What is an example of the surveillance conducted by CDC in which we have now seen gaps in addressing hearing loss? What has come out that reveals areas that we need to work on?

Dr. MARTIN. So one of the things that the CDC is helps us set benchmarks of what we want to try to track among States and then compare those, and so one of the most important numbers that we have seen come out of that work has been the loss to follow-up rates, and we have made really tremendous strides in the last few years because there has been funding available to help States look at loss to follow-up. We have reduced that number by 50 percent. There are still babies who are lost to follow-up and we are continuing to work on that.

Some of those lost-to-follow-up babies are not actually lost to follow-up. The EHDI program coordinators know those babies. They know where they are and their families have opted not to follow up for some reason, either financial or access.

Mrs. CAPPS. Let me push that a little further just to entice you to talk a bit more about it. While we are screening babies at a higher rate and we are doing better at follow-up, there still is a challenge, as you say, so follow-up care for newborns diagnosed with a hearing loss, this is such a critical time to get that intervention. How does this bill increase the likelihood that they are going to receive the appropriate follow-up care?

Dr. MARTIN. One of the things that it does is, it expands the way that we can share information among States and among providers, and it guarantees that we—ensures that we really make access for

families easier to find. We have had some programs put in place that have been collaborative between American Speech and Hearing Association, the American Academy of Pediatrics that helps primary care physicians and parents find audiologists so that they can get good follow-up and be connected to services more quickly.

Mrs. CAPPS. And maybe you said this sufficiently, but if you could, there is a minute and a half left to elaborate on the importance of these programs, focusing now on the parents, because many of the parents are hearing parents and so this is all totally new territory to them.

Dr. MARTIN. Absolutely brand-new territory to them. Ninety-five percent of children who are born with hearing loss are born to hearing parents, and so they have really little or no contact prior to that time with anyone who has been deaf or hard of hearing, and so the great thing about the reauthorization is, it really recognizes the role of the family. So we figure that the family is the expert about their child. It puts the family in the driver's seat to make decisions. It sets up programs and systems where we provide information to these families so that they can make informed choice, and it helps engage them in the process. So it helps them be their child's first teacher, the expert on their child, and really help them partner with the different agencies in ensuring that their desired outcome for their child is the one that they get.

Mrs. CAPPS. Well, if that isn't reason enough for us all to support this legislation and the reauthorization. I appreciate your answering these questions.

I do, Mr. Chairman, wish to submit for the record a letter from the American Academy of Pediatrics supporting the reauthorization of the Early Hearing Detection and Intervention Act. I will submit that for the record.

And I will yield back my time.

Mr. PITTS. Without objection, so ordered.

[The information appears at the conclusion of the hearing.]

Mr. PITTS. The Chair now recognizes the gentlelady from Indiana, Mrs. Brooks, 5 minutes for questions.

Mrs. BROOKS. Thank you, Mr. Chairman, and thank you for calling this important hearing on public health issues.

The Indianapolis Star—and I represent Indianapolis and to the north—a columnist by the name of Matt Tully has been doing quite a bit of series on the opioid and heroin addiction plaguing our country, and a recent article cited some startling statistics the epidemic is having on hospitals in Indiana, so I am very, very pleased that you are here.

At Eskenazi Health, a hospital in downtown Indianapolis, officials say the hospital is on track to see a 22 percent increase this year in the number of newborns experiencing narcotic withdrawal. A doctor at St. Vincent's, a north side Indianapolis hospital, said between 20 and 30 percent of the babies admitted to the NICU suffer from drug dependency—20 to 30 percent. And obviously, and as Matt Tully has written, wrote of a 5-day-old at Franciscan St. Health on the south side of Indianapolis—so this knows no geographic boundaries in our community or in our districts—who was receiving morphine treatments because his body was shaking so bad and he was wracked with diarrhea so bad that it was affecting

his skin and it was just horrible watching the withdrawal, which actually this columnist was seeing, but I think what I learned today, Dr. Terplan, you indicated the babies can stay in the hospital for an average of 3 weeks when they are going through this type of withdrawal, and I must say that Representative Kennedy and I just recently introduced a companion bill to the Senate to Senators Donnelly and Ayotte of the Heroin and Prescription Opioid Abuse Prevention, Education and Enforcement Act, and it is a multipronged approach, and it focuses on a number of things including interagency task forces to try to get better prescribing practices specifically, focusing on prescription drug monitoring programs, but I have to tell you one thing. I am a former U.S. Attorney. I have been involved in the criminal justice system most of my career, and I appreciate that punitive approaches aren't appropriate, as you say. However, many of these women are in the criminal justice system or find themselves in the criminal justice system, and I am curious what you think our approaches should be with those who are in the criminal justice system. They are in there, in all likelihood, for other crimes they are committing during this time or maybe for being arrested for dealing or for possession, and so what approach do you think should work specifically for our children in our jails and our prisons with respect—because there are a lot of them, and so this is the hospitals, but I think if we talk to our sheriffs around the country, they are experiencing these issues too. What is the best approach that we should have for the so many pregnant women in our jails and prisons?

Dr. TERPLAN. That is a great question, and our jails and prisons are the largest behavioral healthcare systems in the United States, unfortunately, and there are—I mean, I have spoken of barriers to access to medication-assisted treatment amongst pregnant women in general. Those barriers are far higher in prisons. So some of it has to do with how prisons are financed and the cost of medications, even though cheap, methadone across a huge population of prisoners who need it is a costly thing. So I think what we really need is access to prisoners and people in detention need access to behavioral healthcare in general and for opioid use disorders to medication-assisted treatment in particular.

In addition, we need better linkages from release into the community. So right now in the State of Maryland, only individuals who are arrested and are on methadone receive methadone in the jail. People who have an opioid use disorder come to jail and they withdraw. We know withdrawal for pregnant women is dangerous to the fetus, and we need to find ways to provide medication and other counseling services and then linkage upon release into the community.

Mrs. BROOKS. Dr. Patrick, do you have any thoughts on our jail and prison issues with pregnant women?

Dr. PATRICK. I would just echo the access to medication-assisted treatment when it is needed for pregnant women. It is really the standard of care and improves infant outcomes as well.

Mrs. BROOKS. Have you done any work with our drug treatment courts? Because a lot of times those judges who are presiding in the drug treatment courts see the same women. They may or may not be in jail or prisons, people who are in the drug treatment courts,

and I know that we have struggled with learning whether or not—some believe in abstinence as the best method, but certainly have you done any work in following drug treatment courts or advising drug treatment courts?

Dr. TERPLAN. A little bit in Baltimore City, and mostly around educating, not just the staff but especially the judges and also the judges who aren't drug court but might be subbing for somebody else around the importance of the evidence base for treatment for substance use disorders.

Mrs. BROOKS. Thank you. I yield back.

Mr. PITTS. The Chair thanks the gentlelady. We are about to see another vote series, so we will try to move this along.

The Chair recognizes Ms. Matsui of California, 5 minutes for questions.

Ms. MATSUI. Thank you, Mr. Chairman, and thank you to the witnesses for being here today and a special thank you to Dr. Chell and Dr. Kurtzberg for testifying today about the importance of the National Marrow Donor Program and cord blood banking.

Every 4 minutes, someone is diagnosed with blood cancer or another blood disorder. Often, the only cure for these fatal diseases is a bone marrow or a cord blood transplant. Congress has recognized the national need for bone marrow transplant since 1987, and 10 years ago formally added the National Cord Blood Inventory to the C.W. Bill Young Cell Transplantation Program.

A big part of the Stem Cell Therapeutic and Research Act is the national registry known as Be The Match, which matches as many patients as possible to bone marrow or cord blood donations that they need, and during the last 30 years, the registry has grown to include over 12 million adult volunteer donors and over 200,000 cord blood units donated by moms after the birth of their children.

The growth of the registry over the last decade is promising but we know we must continue our efforts to encourage donors.

Dr. Chell, as you mention in your testimony, some of the roles that the National Marrow Donor Program plays in addition to running the national registry. Can you elaborate a bit on all the work that Be The Match and NMDP does?

Dr. CHELL. So we are responsible for a network of centers all over the world that help recruit donors and recruit moms to donate their cord blood, to create that inventory, and yet that inventory, despite having 25 million donors worldwide and over 600,000 cord blood units, is really only meeting less than half the need in the United States and only 5 percent of the need worldwide, and that is because the population of the United States as well as the world becomes more diverse, and so that diversity requires us to continue to add more donors to the registry.

But we also advocate for patients from the time of diagnosis through survivorship through multiple languages so they can get the education and the information they need. Through the SCTOD portion of the contract, we create the infrastructure and the reporting mechanism so that we can collect data on every single transplant done in the United States and 60 percent of the transplants done worldwide so that researchers from all over the world can enter that database and help us define new ways of using these therapies and rapidly turn those discoveries into use throughout

the world. We also work with a cord blood coordinating center to manage the relationships with the cord blood banks as well as multiple centers that recruit adult donors.

Ms. MATSUI. OK. Thank you.

Dr. Kurtzberg, as you know, the goals in creating the NCBI were to create a network of high-quality, diverse cord blood units and to make cord blood units available for research. Can you elaborate on the work that you do to meet these goals?

Dr. KURTZBERG. Sure. I have run a public cord blood bank named the Carolinas Cord Blood Bank at Duke and work every day to collect cord blood units from moms who donate their baby's cord blood after a healthy pregnancy and delivery. We also work to develop new models to increase the opportunity for cord blood donation from moms of minority backgrounds. We have opened a program recently at Grady Hospital to do that. We are looking at ways to decrease cost of cord blood donation and banking, which is always an issue in the field, and we are looking at ways to apply cord blood transplantation to new diagnoses.

Ms. MATSUI. OK. Thank you.

Dr. Chell, you mentioned that the number of transplants for racial and ethnic minority patients has increased substantially from the year 2000 to today, and I just want to follow up on what my colleague, Mr. Butterfield, was talking about because he mentioned the African American population. I know that the Asian American population is feeling a great need, and you see the individual-type activities more forward trying to find a match. What efforts can Be The Match make to continue to increase the diversity of the registry to ensure that minority patients can find matches, understanding that this country itself is such a diverse country that we need to figure out a system. There is a lot going on, but what do you think you can do to help increase the diversity of this?

Dr. CHELL. I think it is important also to raise awareness. If we were to take a Caucasian patient as well as an Asian American patient, if they are in the right healthcare system and get access to a search, the likelihood to move on to transplant is equal. The challenge is, many Asian Americans don't have access to that first initial step of doing a search, being in a healthcare system to do that search. But with that, we need to across all ethnic groups significantly increase the diversity of the registries. For Asian Americans, we also benefit from having partnerships with China, Japan, Korea, Hong Kong, and other countries to allow us to increase the diversity. For African Americans, we don't have partners in African companies that help us with diversity.

Ms. MATSUI. Well, I know my time is up, so thank you very much.

Mr. PITTS. The Chair thanks the gentlelady.

We have less than 10 minutes left. We are going to try to conclude the hearing.

The Chair recognizes Mr. Bilirakis, 5 minutes for questions.

Mr. BILIRAKIS. Thank you, Mr. Chairman. I appreciate you very much holding this very important hearing on some really good bills.

Dr. Martin, in the interests of time, I really have a lot of questions but we will start with the hearing loss screening. You stated

that the number of individuals who have lacked follow-up care from their initial screening has been reduced by half over the past 10 years. H.R. 1344 states that one purpose for which States can use funds is to develop models that will ensure babies identified as needing follow-up care receive those services.

My first question is, what are the challenges for a child who does not receive follow-up care with an early intervention provider and how is it harmful to the child?

Dr. MARTIN. There is this critical period for children to acquire communication that really, birth to 3 is the most critical time period, and so we have seen rapid improvements in the outcomes for children when they enter the educational system and their long-term outcomes if they have been identified early within the first year of life as compared to children who are identified after that. So kids who are lost to follow-up fail their newborn screen and then show up at a pediatrician's office at 3 or 4 or fail a kindergarten screening, they are already significantly behind their typically hearing peers and are really going to have a difficult, if not impossible, time catching up with a language linguistics sort of base and from a psychosocial base as well.

Mr. BILIRAKIS. Thank you.

A question for Dr. Patrick and Dr. Terplan. Counties within my district were found to be suffering from some of the highest numbers of babies born with neonatal abstinence syndrome. What practices have been successful at addressing this issue in other regions? How would this legislation help those at-risk populations?

Dr. PATRICK. Well, as far as treating infants with neonatal abstinence syndrome, the practices that have been most effective have really been around standardizing care and working together through networks of hospitals and neonatal intensive care units. That has really been effective in making sure that we are treating these infants the same collectively. I mean, the bill brings together data and evidence. It also brings together a multidisciplinary group of people who think about how we attack every part of the problem including before pregnancy, in pregnancy and in the treatment period for the infant. So I think we will see a positive effect in communities like yours and mine as well.

Mr. BILIRAKIS. Thank you, and Mr. Chairman, I will submit the questions for the record because I want everyone to have an opportunity. Thank you.

Mr. PITTS. The Chair thanks the gentleman and now recognizes Ms. Castor, 5 minutes for questions.

Ms. CASTOR. Thank you, and I thank Mr. Bilirakis as well, and I want to thank our witnesses for being here today to testify on these important public health bills. I want to thank Representatives Clark and Stivers for their work on H.R. 1462 especially, Protecting Our Infants Act of 2015. I am a cosponsor of the bill, and I think it is clear that we need additional efforts and resources to address the challenges of neonatal abstinence syndrome, and the bill before us does that in many critical ways. Mr. Bilirakis and I share the counties, and I just want to get this on the record. In 2007, our counties had 67 reported cases; 2008, 108; and by just 2011, about 280 reported cases. So we have got to do more.

These are the questions I would like you to answer for the record. According to the GAO report, there are a number of existing research gaps relating to best practices in the screening, diagnosis and treatment of NAS. You have discussed them, and if you would also discuss them in more detail in written testimony.

Dr. Patrick, what do we know about the best practices and screening and diagnosis and treatment, and what are the most pressing research gaps? How does the Protecting Our Infants Act help to address the gaps? And then if you could also share in written response, are we underinvesting in research related to NAS, given the significant public health burden that it presents?

Thank you all again for being here today, and I look forward to your written response.

Dr. PATRICK. Well, your first question was about best practices, and I think it begins with identifying the infants, so it begins with that transition from pregnancy to the infant being cared for. We have to know the infant has been exposed, and so screening, universal screening through both standardized verbal screenings as well as diagnostic screenings, using the same scoring system to identify and be consistent with that. Treatment—it is clear from the evidence that using an opioid like methadone or morphine is the most effective though we see some hospitals using other drugs like phenobarbital that may actually have some long-term harm. And——

Ms. CASTOR. I am going to cut you short so Mr. Collins can do it, but I do want to express my gratitude to All Children's Hospital and St. Joseph's Children's Hospital and all of the medical professionals across the country who are tackling this issue, and I yield back the balance of my time.

Mr. PITTS. The Chair thanks the gentlelady, and you can respond more fully in writing to that question. We will provide the questions to you in writing. Thank you.

Dr. PATRICK. Thank you.

Mr. PITTS. Mr. Collins, you are recognized. We have 2 minutes left on the floor.

Mr. COLLINS. Well, I will be quick. Luckily they always hold votes over, and also if you could, I will direct this to Dr. Patrick perhaps answer in more detail.

I am one of the cosponsors on H.R. 1462. Your testimony here has done a great job in showing the importance of reauthorizing these. What I would like you to perhaps respond in writing is, some of the differences between NAS and fetal alcohol syndrome. We know about those. If you could maybe compare and contrast what is going on in those two fields, I think that would be helpful to truly show the importance on the opioid abuse, which we have had several Oversight hearings on, and maybe simply—also, could you just confirm verbally now, is a child born with NAS impaired for life or are the treatments in fact moving them into what could be a normal life?

Dr. PATRICK. There is no evidence that the infants are impaired for life. There has been some subtle evidence of some behavioral issues. It is definitely an area that needs to be more well studied but I think it would be very unfair to say that the infant is affected significantly for life.

Mr. COLLINS. Well, and that is what I would hope you were saying so the treatments in fact are life-changing, and that is what we are all about here.

So Mr. Chairman, I yield back, and I guess we will go down and vote.

Mr. PITTS. The Chair thanks the gentleman.

We will provide questions in writing from those of us who were here and those who were in other hearings. We would ask that you please respond promptly.

We thank you very much for your patience, for all the interruptions, really a very interesting, very important hearing.

I have a unanimous consent request. I would like to submit for the record statements of Doris Matsui, Gene Green, and the American Academy of Pediatrics. Without objection, so ordered.

Mr. PITTS. I remind Members they have 10 business days to submit questions for the record. I ask the witnesses to respond promptly. Members should submit their questions by the close of business Thursday, July 9th.

Thank you very much for this very important testimony today. Without objection, this hearing is adjourned.

[Whereupon, at 12:26 p.m., the subcommittee was adjourned.]

[Material submitted for inclusion in the record follows:]

[DISCUSSION DRAFT]

114TH CONGRESS
1ST SESSION

H. R. _____

To reauthorize the Stem Cell Therapeutic and Research Act of 2005, and for other purposes

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IN THE HOUSE OF REPRESENTATIVES

Mr. SMITH of New Jersey introduced the following bill; which was referred to the Committee on _____

A BILL

To reauthorize the Stem Cell Therapeutic and Research Act of 2005, and for other purposes

Be it enacted by the Senate and House of Representatives of the United States of America in Congress assembled,

SECTION 1. SHORT TITLE.

This Act may be cited as the "Stem Cell Therapeutic and Research Reauthorization Act of 2015".

SEC. 2. AMENDMENTS TO THE STEM CELL THERAPEUTIC AND RESEARCH ACT OF 2005.

(a) CORD BLOOD INVENTORY.—Section 2 of the Stem Cell Therapeutic and Research Act of 2005 (42 U.S.C. 274k note) is amended in subsection (h)—

(1) in paragraph (1)—

(A) by striking "$23,000,000 for each of fiscal years 2011 through 2014 and"; and

(B) by inserting before the period at the end the following: "and $23,000,000 for each of fiscal years 2016 through 2020"; and

(2) in paragraph (2), by striking "2011 through 2015" and inserting "2015 through 2020".

(b) NATIONAL PROGRAM.—Section 379B of the Public Health Service Act (42 U.S.C. 274m) is amended by striking "2011 through 2014" and inserting "2016 through 2020".

I

114TH CONGRESS
1ST SESSION

H. R. 1344

To amend the Public Health Service Act to reauthorize a program for early detection, diagnosis, and treatment regarding deaf and hard-of-hearing newborns, infants, and young children.

IN THE HOUSE OF REPRESENTATIVES

MARCH 10, 2015

Mr. GUTHRIE (for himself and Mrs. CAPPS) introduced the following bill; which was referred to the Committee on Energy and Commerce

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A BILL

To amend the Public Health Service Act to reauthorize a program for early detection, diagnosis, and treatment regarding deaf and hard-of-hearing newborns, infants, and young children.

Be it enacted by the Senate and House of Representatives of the United States of America in Congress assembled,

SECTION 1. SHORT TITLE.

This Act may cited as the "Early Hearing Detection and Intervention Act of 2015".

SEC. 2. FINDINGS.

The Congress finds as follows:

(1) Deaf and hard-of-hearing newborns, infants, toddlers, and young children require access to specialized early intervention providers and programs in order to help them meet their linguistic and cognitive potential.

(2) Families of deaf and hard-of-hearing newborns, infants, toddlers, and young children benefit from comprehensive early intervention programs that assist them in supporting their child's development in all domains.

(3) Best practices principles for early intervention for deaf and hard-of-hearing newborns, infants, toddlers, and young children have been identified in a range of areas including listening and spoken language and visual and signed language acquisition, family-to-family support, support from individuals who are deaf or hard-of-hearing, progress monitoring, and others.

(4) Effective hearing screening and early intervention programs must be in place to identify hearing levels in deaf and hard-of-hearing newborns, infants, toddlers, and young children so that they may access appropriate early intervention programs in a timely manner.

SEC. 3. REAUTHORIZATION OF PROGRAM FOR EARLY DETECTION, DIAGNOSIS, AND TREATMENT REGARDING DEAF AND HARD-OF-HEARING NEWBORNS, INFANTS, AND YOUNG CHILDREN.

Section 399M of the Public Health Service Act (42 U.S.C. 280g–1) is amended to read as follows:

"SEC. 399M. EARLY DETECTION, DIAGNOSIS, AND TREATMENT REGARDING DEAF AND HARD-OF-HEARING NEWBORNS, INFANTS, AND YOUNG CHILDREN.

"(a) HEALTH RESOURCES AND SERVICES ADMINISTRATION.—The Secretary, acting through the Administrator of the Health Resources and Services Administration, shall make awards of grants or cooperative agreements to develop statewide newborn, infant, and young childhood hearing screening, diagnosis, evaluation, and intervention programs and systems, and to assist in the recruitment, retention, education, and training of qualified personnel and health care providers for the following purposes:

"(1) To develop and monitor the efficacy of statewide programs and systems for hearing screening of newborns, infants, and young children, prompt evaluation and diagnosis of children referred from screening programs, and appropriate edu-

cational, audiological, and medical interventions for children confirmed to be deaf or hard-of-hearing, consistent with the following:

"(A) Early intervention includes referral to and delivery of information and services by organizations such as schools and agencies (including community, consumer, and parent-based agencies), pediatric medical homes, and other programs mandated by part C of the Individuals with Disabilities Education Act, which offer programs specifically designed to meet the unique language and communication needs of deaf and hard-of-hearing newborns, infants, and young children.

"(B) Information provided to parents must be accurate, comprehensive, and, where appropriate, evidence-based, allowing families to make important decisions for their child in a timely way, including decisions relating to all possible assistive hearing technologies (such as hearing aids, cochlear implants, and osseointegrated devices) and communication options (such as visual and sign language, listening and spoken language, or both).

"(C) Programs and systems under this paragraph shall offer mechanisms that foster family-to-family and deaf and hard-of-hearing consumer-to-family supports.

"(2) To develop efficient models (both educational and medical) to ensure that newborns, infants, and young children who are identified through hearing screening receive follow-up by qualified early intervention providers, qualified health care providers, or pediatric medical homes (including by encouraging State agencies to adopt such models).

"(3) To provide for a technical resource center in conjunction with the Maternal and Child Health Bureau of the Health Resources and Services Administration—

"(A) to provide technical support and education for States; and

"(B) to continue development and enhancement of State early hearing detection and intervention programs.

"(b) TECHNICAL ASSISTANCE, DATA MANAGEMENT, AND APPLIED RESEARCH.—

"(1) CENTERS FOR DISEASE CONTROL AND PREVENTION.—The Secretary, acting through the Director of the Centers for Disease Control and Pre-

vention, shall make awards of grants or cooperative agreements to State agencies or their designated entities for development, maintenance, and improvement of data tracking and surveillance systems on newborn, infant, and young childhood hearing screenings, audiologic evaluations, medical evaluations, and intervention services; to conduct applied research related to services and outcomes, and provide technical assistance related to newborn, infant, and young childhood hearing screening, evaluation, and intervention programs, and information systems; to ensure high-quality monitoring of hearing screening, evaluation, and intervention programs and systems for newborns, infants, and young children; and to coordinate developing standardized procedures for data management and assessing program and cost effectiveness. The awards under the preceding sentence may be used—

"(A) to provide technical assistance on data collection and management;

"(B) to study and report on the costs and effectiveness of newborn, infant, and young childhood hearing screening, evaluation, diagnosis, intervention programs, and systems;

"(C) to collect data and report on newborn, infant, and young childhood hearing screening, evaluation, diagnosis, and intervention programs and systems that can be used—

"(i) for applied research, program evaluation, and policy development; and

"(ii) to answer issues of importance to State and national policymakers;

"(D) to identify the causes and risk factors for congenital hearing loss;

"(E) to study the effectiveness of newborn, infant, and young childhood hearing screening, audiologic evaluations, medical evaluations, and intervention programs and systems by assessing the health, intellectual and social developmental, cognitive, and hearing status of these children at school age; and

"(F) to promote the integration, linkage, and interoperability of data regarding early hearing loss and multiple sources to increase information exchanges between clinical care and public health including the ability of States and territories to exchange and share data.

"(2) NATIONAL INSTITUTES OF HEALTH.—The Director of the National Institutes of Health, acting

through the Director of the National Institute on Deafness and Other Communication Disorders, shall for purposes of this section, continue a program of research and development related to early hearing detection and intervention, including development of technologies and clinical studies of screening methods, efficacy of interventions, and related research.

"(e) COORDINATION AND COLLABORATION.—

"(1) IN GENERAL.—In carrying out programs under this section, the Administrator of the Health Resources and Services Administration, the Director of the Centers for Disease Control and Prevention, and the Director of the National Institutes of Health shall collaborate and consult with—

"(A) other Federal agencies;

"(B) State and local agencies, including those responsible for early intervention services pursuant to title XIX of the Social Security Act (42 U.S.C. 1396 et seq.) (Medicaid Early and Periodic Screening, Diagnosis and Treatment Program); title XXI of the Social Security Act (42 U.S.C. 1397aa et seq.) (State Children's Health Insurance Program); title V of the Social Security Act (42 U.S.C. 701 et seq.) (Maternal and Child Health Block Grant Program);

and part C of the Individuals with Disabilities Education Act (20 U.S.C. 1431 et seq.);

"(C) consumer groups of and that serve individuals who are deaf and hard-of-hearing and their families;

"(D) appropriate national medical and other health and education specialty organizations;

"(E) persons who are deaf and hard-of-hearing and their families;

"(F) other qualified professional personnel who are proficient in deaf or hard-of-hearing children's language and who possess the specialized knowledge, skills, and attributes needed to serve deaf and hard-of-hearing newborns, infants, toddlers, children, and their families;

"(G) third-party payers and managed-care organizations; and

"(H) related commercial industries.

"(2) POLICY DEVELOPMENT.—The Administrator of the Health Resources and Services Administration, the Director of the Centers for Disease Control and Prevention, and the Director of the National Institutes of Health shall coordinate and collaborate on recommendations for policy development

at the Federal and State levels and with the private sector, including consumer, medical, and other health and education professional-based organizations, with respect to newborn, infant, and young childhood hearing screening, evaluation, diagnosis, and intervention programs and systems.

"(3) STATE EARLY DETECTION, DIAGNOSIS, AND INTERVENTION PROGRAMS AND SYSTEMS; DATA COLLECTION.—The Administrator of the Health Resources and Services Administration and the Director of the Centers for Disease Control and Prevention shall coordinate and collaborate in assisting States—

"(A) to establish newborn, infant, and young childhood hearing screening, evaluation, diagnosis, and intervention programs and systems under subsection (a); and

"(B) to develop a data collection system under subsection (b).

"(d) RULE OF CONSTRUCTION; RELIGIOUS ACCOMMODATION.—Nothing in this section shall be construed to preempt or prohibit any State law, including State laws which do not require the screening for hearing loss of newborns, infants, or young children of parents who object

to the screening on the grounds that such screening conflicts with the parents' religious beliefs.

"(e) DEFINITIONS.—For purposes of this section:

"(1) The term 'audiologic', in connection with evaluation—

"(A) refers to procedures to assess the status of the auditory system;

"(B) to establish the site of the auditory disorder, the type and degree of hearing loss, and the potential effects of hearing loss on communication; and

"(C) to identify appropriate treatment and referral options, including—

"(i) linkage to State coordinating agencies under part C of the Individuals with Disabilities Education Act (20 U.S.C. 1431 et seq.) or other appropriate agencies;

"(ii) medical evaluation;

"(iii) hearing aid/sensory aid assessment;

"(iv) audiologic rehabilitation treatment; and

"(v) referral to national and local consumer, self-help, parent, and education or-

ganizations, and other family-centered services.

"(2) The term 'early intervention' refers to—

"(A) providing appropriate services for the child who is deaf or hard of hearing, including nonmedical services; and

"(B) ensuring the family of the child is—

"(i) provided comprehensive, consumer-oriented information about the full range of family support, training, information services, and language and communication options; and

"(ii) given the opportunity to consider and obtain the full range of such appropriate services, educational and program placements, and other options for their child from highly qualified providers.

"(3) The term 'medical evaluation' refers to key components performed by a physician, including history, examination, and medical decisionmaking focused on symptomatic and related body systems for the purpose of diagnosing the etiology of hearing loss and related physical conditions, and for identifying appropriate treatment and referral options.

"(4) The term 'medical intervention' refers to the process by which a physician provides medical diagnosis and direction for medical or surgical treatment options for hearing loss or related medical disorders.

"(5) The term 'newborn, infant, and young childhood hearing screening' refers to objective physiologic procedures to detect possible hearing loss and to identify newborns, infants, and young children who require further audiologic evaluations and medical evaluations.

"(f) AUTHORIZATION OF APPROPRIATIONS.—

"(1) STATEWIDE NEWBORN, INFANT, AND YOUNG CHILDHOOD HEARING SCREENING, EVALUATION AND INTERVENTION PROGRAMS AND SYSTEMS.—For the purpose of carrying out subsection (a), there is authorized to be appropriated to the Health Resources and Services Administration $17,800,000 for each of fiscal years 2017 through 2022.

"(2) TECHNICAL ASSISTANCE, DATA MANAGEMENT, AND APPLIED RESEARCH; CENTERS FOR DISEASE CONTROL AND PREVENTION.—For the purpose of carrying out subsection (b)(1), there is authorized to be appropriated to the Centers for Disease Con-

trol and Prevention $10,800,000 for each of fiscal years 2017 through 2022.

"(3) TECHNICAL ASSISTANCE, DATA MANAGEMENT, AND APPLIED RESEARCH; NATIONAL INSTITUTE ON DEAFNESS AND OTHER COMMUNICATION DISORDERS.—No additional funds are authorized to be appropriated for the purpose of carrying out subsection (b)(2). Such subsection shall be carried out using funds which are otherwise authorized (under section 402A or other provisions of law) to be appropriated for such purpose.".

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114TH CONGRESS
1ST SESSION

H. R. 1462

To combat the rise of prenatal opioid abuse and neonatal abstinence syndrome.

IN THE HOUSE OF REPRESENTATIVES

MARCH 19, 2015

Ms. CLARK of Massachusetts (for herself and Mr. STIVERS) introduced the following bill; which was referred to the Committee on Energy and Commerce

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A BILL

To combat the rise of prenatal opioid abuse and neonatal abstinence syndrome.

Be it enacted by the Senate and House of Representatives of the United States of America in Congress assembled,

SECTION 1. SHORT TITLE.

This Act may be cited as the "Protecting Our Infants Act of 2015".

SEC. 2. FINDINGS.

Congress finds as follows:

(1) Opioid prescription rates have risen dramatically over the past several years. According to the Centers for Disease Control and Prevention, in

some States, there are as many as 96 to 143 prescriptions for opioids per 100 adults per year.

(2) In recent years, there has been a steady rise in the number of overdose deaths involving heroin. According to the Centers for Disease Control and Prevention, the death rate for heroin overdose doubled from 2010 to 2012.

(3) At the same time, there has been an increase in cases of neonatal abstinence syndrome (referred to in this section as "NAS"). In the United States, the incidence of NAS has risen from 1.20 per 1,000 hospital births in 2000 to 3.39 per 1,000 hospital births in 2009.

(4) NAS refers to medical issues associated with drug withdrawal in newborns due to exposure to opioids or other drugs in utero.

(5) The average cost of treatment in a hospital for NAS increased from $39,400 in 2000 to $53,400 in 2009. Most of these costs are born by the Medicaid program.

(6) Preventing opioid abuse among pregnant women and women of childbearing age is crucial.

(7) Medically appropriate opioid use in pregnancy is not uncommon, and opioids are often the

safest and most appropriate treatment for moderate to severe pain for pregnant women.

(8) Addressing NAS effectively requires a focus on women of childbearing age, pregnant women, and infants from preconception through early childhood.

(9) NAS can result from the use of prescription drugs as prescribed for medical reasons, from the abuse of prescription drugs, or from the use of illegal opioids like heroin.

(10) For pregnant women who are abusing opioids, it is most appropriate to treat and manage maternal substance use in a non-punitive manner.

(11) According to a report of the Government Accountability Office (referred to in this section as the "GAO report"), more research is needed to optimize the identification and treatment of babies with NAS and to better understand long-term impacts on children.

(12) According to the GAO report, the Department of Health and Human Services does not have a focal point to lead planning and coordinating efforts to address prenatal opioid use and NAS across the department.

(13) According to the GAO report, "given the increasing use of heroin and abuse of opioids pre-

scribed for pain management, as well as the increased rate of NAS in the United States, it is important to improve the efficiency and effectiveness of planning and coordination of Federal efforts on prenatal opioid use and NAS".

SEC. 3. DEVELOPING RECOMMENDATIONS FOR PREVENTING AND TREATING PRENATAL OPIOID ABUSE AND NEONATAL ABSTINENCE SYNDROME.

(a) IN GENERAL.—The Secretary of Health and Human Services (referred to in this Act as the "Secretary"), acting through the Director of the Agency for Healthcare Research and Quality (referred to in this section as the "Director"), shall conduct a study and develop recommendations for preventing and treating prenatal opioid abuse and neonatal abstinence syndrome, soliciting input from nongovernmental entities, including organizations representing patients, health care providers, hospitals, other treatment facilities, and other entities, as appropriate.

(b) REPORT.—Not later than 1 year after the date of enactment of this Act, the Director shall publish on the Internet Web site of the Agency for Healthcare Research and Quality a report on the study and recommendations under subsection (a). Such report shall address each of

the issues described in paragraphs (1) through (3) of subsection (c).

(c) CONTENTS.—The study described in subsection (a) and the report under subsection (b) shall include—

(1) a comprehensive assessment of existing research with respect to the prevention, identification, treatment, and long-term outcomes of neonatal abstinence syndrome, including the identification and treatment of pregnant women or women who may become pregnant who use opioids or other drugs;

(2) an evaluation of—

(A) the causes of and risk factors for opioid use disorders among women of reproductive age, including pregnant women;

(B) the barriers to identifying and treating opioid use disorders among women of reproductive age, including pregnant and postpartum women and women with young children;

(C) current practices in the health care system to respond to and treat pregnant women with opioid use disorders and infants born with neonatal abstinence syndrome;

(D) medically indicated use of opioids during pregnancy;

(E) access to treatment for opioid use disorders in pregnant and postpartum women; and

(F) access to treatment for infants with neonatal abstinence syndrome; and

(3) recommendations on—

(A) preventing, identifying, and treating neonatal abstinence syndrome in infants;

(B) treating pregnant women who are dependent on opioids; and

(C) preventing opioid dependence among women of reproductive age, including pregnant women, who may be at risk of developing opioid dependence.

SEC. 4. IMPROVING PREVENTION AND TREATMENT FOR PRENATAL OPIOID ABUSE AND NEONATAL ABSTINENCE SYNDROME.

(a) REVIEW OF PROGRAMS.—The Secretary shall lead a review of planning and coordination within the Department of Health and Human Services related to prenatal opioid use and neonatal abstinence syndrome.

(b) STRATEGY TO CLOSE GAPS IN RESEARCH AND PROGRAMMING.—In carrying out subsection (a), the Secretary shall develop a strategy to address research and program gaps, including such gaps identified in findings

made by reports of the Government Accountability Office. Such strategy shall address—

(1) gaps in research, including with respect to—

(A) the most appropriate treatment of pregnant women with opioid use disorders;

(B) the most appropriate treatment and management of infants with neonatal abstinence syndrome; and

(C) the long-term effects of prenatal opioid exposure on children; and

(2) gaps in programs, including—

(A) the availability of treatment programs for pregnant and postpartum women and for newborns with neonatal abstinence syndrome; and

(B) guidance and coordination in Federal efforts to address prenatal opioid use or neonatal abstinence syndrome.

(c) REPORT.—Not later than 1 year after the date of enactment of this Act, the Secretary shall submit to the Committee on Health, Education, Labor, and Pensions of the Senate and the Committee on Energy and Commerce of the House of Representatives a report on

the findings of the review described in subsection (a) and the strategy developed under subsection (b).

SEC. 5. IMPROVING DATA ON AND PUBLIC HEALTH RESPONSE TO NEONATAL ABSTINENCE SYNDROME.

(a) DATA AND SURVEILLANCE.—The Director of the Centers for Disease Control and Prevention shall, as appropriate—

(1) provide technical assistance to States to improve the availability and quality of data collection and surveillance activities regarding neonatal abstinence syndrome, including—

(A) the incidence and prevalence of neonatal abstinence syndrome;

(B) the identification of causes for neonatal abstinence syndrome, including new and emerging trends; and

(C) the demographics and other relevant information associated with neonatal abstinence syndrome;

(2) collect available surveillance data described in paragraph (1) from States, as applicable; and

(3) make surveillance data collected pursuant to paragraph (2) publically available on an appropriate Internet Web site.

(b) PUBLIC HEALTH RESPONSE.—The Director of the Centers for Disease Control and Prevention shall encourage increased utilization of effective public health measures to reduce neonatal abstinence syndrome.

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House Energy and Commerce subcommittee on Health
June 25, 2015 Hearing on Public Health legislation: H.R. 2820, H.R. 1344, and H.R. 1462
Congressman David W. Jolly statement for the record

Mr. Chairman, I want to thank you and the members of the committee for expediting this hearing on H.R. 2820, the Stem Cell Therapeutic and Research Act of 2015, legislation of which I am a proud original cosponsor.

As you know, this is the legislation that authorizes the miraculous, life-saving work of the C.W. Bill Young Cell Transplantation Program, which this committee in a previous authorization bill named for my predecessor. It holds a special place in my heart and the heart of so many people in the 13th Congressional District of Florida I represent. It was there almost 30 years ago that this program had its birth when a young 11-year-old girl named Brandy Bly befriended Bill and Beverly Young. Brandy was a patient at All Children's Hospital where she was admitted with a form of leukemia for which the only treatment was a bone marrow transplant. The only problem was that Brandy had no siblings and thus no chance for finding a matched donor. You see, there was no National Marrow Donor Program at the time.

Brandy died from leukemia before she could turn 12 and it was in the hallway the night she died that Bill Young asked her doctors what could have been done to save her life. The answer was a bone marrow transplant from an unrelated donor. By some divine providence, All Children's Hospital was home to the research work being done by Dr. Bob Good, the doctor credited with pioneering the procedure known as unrelated marrow transplantation. He proved that the success rate of bone marrow transplants between perfectly matched family members could be virtually the same as those between perfectly matched complete strangers.

The challenge was being able to match perfect strangers, because on average, the chance of any two unrelated individuals being perfect matches is one in 20,000. Thus began the work of Bill Young, to learn everything he could about the science of bone marrow transplantation and the mechanics of establishing a national registry to match volunteer donors with terminally ill patients whose only hope was a bone marrow transplant.

Many doors were slammed in his face along the way and the National Institutes of Health, in a hearing of this very subcommittee, even told him early on that a national registry would never work and he would never recruit more than 50,000 potential donors.

Along the way, Bill Young's path eventually crossed that of Admiral Elmo Zumwalt, the legendary former Chief of U.S. Naval Operations, whose own sign died of leukemia because he could not find a matched donor. Together they joined forces along with a few other early pioneers to establish a national registry. Their search led them to the United States Navy, which had an interest in marrow transplantation, and with an infusion of $1,500,000 by Congressman Young into a Navy medical research account in 1986, the national registry was born.

It was on December 16, 1987, Bill Young's birthday, that the National Marrow Donor Program matched its first donor and patient, harvested its first bone marrow donation, and shipped it from Milwaukee in a driving snowstorm to a waiting patient in North Carolina.

From there the program has grown and flourished. Bill Young would travel the country to promote the national registry, picking up families of searching patients along the way. He even recruited his colleagues and staff in the House and Senate. The registry grew slowly to 100,000 potential donors then to 250,000. Congressman Young had the idea in 1990 to fund a special program at the Department of Defense to recruit service members, the ultimate volunteers, to join the national registry. He knew from the Navy that bone marrow transplantation was the preferred method of treatment of our troops who might be exposed to a chemical weapons attack during Operation Desert Storm.

Today, I am proud to report, that the national registry has more than 12,500,000 potential donors in our national registry and with its linkage to national registries across the world, searching patients have access to more than 24,500,000 potential donors.

Bone marrow and cord blood transplantation is a preferred method of treatment for many forms of leukemia and blood cancers with the number of diseases totaling more than 70. In addition, as Bill Young predicted many years ago, bone marrow transplantation would be a cure for many other diseases, including today sickle cell anemia. Since 1987, more than 68,000 patients have received the living gift of life from a donor on the national registry. Last year alone, 6,300 patients received a transplant. These are children, mothers and fathers, brothers and sisters all of whom are alive today or at least received a few extra years of life from the gift of bone marrow or a cord blood transplant from a complete stranger.

Mr. Chairman, our colleagues in the House and Senate, past and present, can take great pride in what we have done together to establish this program, to fund this program, to authorize this program, and to grow and support this program that has saved enough lives to fill one of our nation's largest stadiums.

We are here today, though, because our work is not done. We need to authorize the work of the National Marrow Donor Program for another five years to continue saving lives and to continue to give hope for patients searching for that matched stranger that will give them that chance at life. You see, we still need to recruit more donors, especially among minority populations, because genetically, patients will most likely find a matched donor from a similar ethnic background. Donor recruiters all around the country are working hard to increase minority participation, as close to half of all new donors are minorities. As Bill Young used to say though, our job is not done until every one of the searching patients can find a donor. For the 14,000 patients who need an unrelated transplant annually, that is their only hope for a cure.

Your colleague Doris Matsui and I are proud co-chairmen of the bipartisan Congressional Caucus to Cure Blood Cancers and Other Blood Disorders. The members of our caucus look

forward to working with you and the members of your committee to carry on the legacy of Bill Young and the work he began 30 years ago this year to establish, fund, and support the National Marrow Donor Program and its dedicated network of transplant centers, donors centers, donor recruitments organizations, and individuals who simply want to save a life.

Mr. Chairman, thank you for your time today, your longtime support of this program, and your commitment to move this authorization legislation through this Congress as soon as possible. I can think of no more important legislative effort to our colleagues as it is a program that touches virtually every district across our nation.

June 25, 2015

The Honorable Joe Pitts
Chairman
House Energy and Commerce
Subcommittee on Health
2125 Rayburn House Office Building
Washington, DC 20515

The Honorable Gene Green
Ranking Member
House Energy and Commerce
Subcommittee on Health
2125 Rayburn House Office Building
Washington, DC 20515

Dear Chairman Pitts and Ranking Member Green:

As organizations representing the nation's pediatricians, obstetricians and gynecologists and members of the public who care about pregnant women and children, the American Academy of Pediatrics (AAP), American Congress of Obstetricians and Gynecologists (ACOG), March of Dimes, and the Society for Maternal-Fetal Medicine endorse the bipartisan *Protecting Our Infants Act of 2015* (H.R. 1462), introduced by Representatives Katherine Clark (D-Mass.) and Steve Stivers (R-Ohio). The legislation takes proactive steps to help reduce the number of newborns born exposed to drugs, such as opioids, and to improve their care, and we thank the Subcommittee on Health for scheduling a hearing to discuss this important issue.

Reports show the significant rise of opiate use and abuse has led to an alarming increase of babies born with neonatal abstinence syndrome (NAS). NAS refers to medical complications associated with drug withdrawal in newborns due to exposure to opioids or other drugs in utero. Babies born with NAS often need to be hospitalized for weeks, are difficult to console, and can suffer from seizures and other complications. There are no standardized guidelines for diagnosis and treatment for these newborns, and there is an urgent need for more research to optimize the identification and treatment of babies with NAS to determine any long-term health impacts.

A 2012 study published in the Journal of the American Medical Association found that the average hospital costs for newborns suffering from NAS were five times greater than other hospital births. The report also found that Medicaid was the primary insurance provider for more than 75 percent of these babies.

Addressing NAS requires a focus on women of childbearing age, and infants from preconception through early childhood. It is also important to note that medically-appropriate use of opioids during pregnancy is not uncommon. Preventing inappropriate opioid use and abuse among pregnant women and women of child-bearing age is imperative. Education is needed for both physicians and patients regarding the appropriate prescription and use of opioids for women who are or could become pregnant. For pregnant women who are abusing opioids, it is most appropriate to treat and manage maternal substance use in a non-punitive manner through family-centered medical treatment.

The bipartisan *Protecting Our Infants Act* directs the U.S. Department of Health and Human Services (HHS) to identify and make available recommendations for the diagnosis and treatment of NAS, evaluate and coordinate federal efforts to research and respond to NAS, and assist state health agencies with their data collection efforts. The legislation will encourage the development of a needed agenda to promote additional research on and standardize best practices for babies with NAS.

We thank you for your strong commitment to the health and well-being of women, children, infants, and newborns and we look forward to working with you as you consider this legislation.

Sincerely,

American Academy of Pediatrics
American Congress of Obstetricians and Gynecologists
March of Dimes
Society for Maternal-Fetal Medicine

CC The Honorable Katherine Clark (D-Mass.)
The Honorable Steve Stivers (R-Ohio)

American Academy of Pediatrics
DEDICATED TO THE HEALTH OF ALL CHILDREN™

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March 26, 2015

The Honorable Brett Guthrie
U.S. House of Representatives
2434 Rayburn House Office Building
Washington, DC 20515

The Honorable Lois Capps
U.S. House of Representatives
2231 Rayburn House Office Building
Washington, DC 20515

Dear Representatives Guthrie and Capps:

On behalf of the American Academy of Pediatrics (AAP), an organization of 62,000 primary care pediatricians, pediatric medical sub-specialists, and pediatric surgical specialists dedicated to the health, safety, and well-being of infants, children, adolescents, and young adults, I write to express our strong support for continued provision of early hearing screening and interventions to all newborns, infants and young children through reauthorization of the *Early Hearing Detection and Intervention Act.*

The prevalence of newborn hearing screening has grown dramatically since the passage of the hearing screening provisions in the Child Health Act of 2000. At that time, only 40 percent of newborns were being screened. Today, approximately 96 percent of newborns receive audiologic screening. This is extremely important for the 33 children born every day with hearing impairment, making it the most common congenital condition in the United States. Studies have shown that important language skills are learned before the age of 3 because hearing and learning language are closely tied together. However, if a child has an undiagnosed hearing impairment and the parents are unaware, the child will not receive the needed language stimulation, which can have a detrimental effect on development. That is why early interventions facilitated through the *Early Hearing Detection and Intervention Act* are so important.

While the increased prevalence of children receiving initial newborn hearing screenings is very positive, there are still many infants who do not receive timely follow-up and treatment. We also still need to train more health care providers to care for infants with hearing loss. We are pleased that this reauthorization includes provisions to improve follow-up and continues to support better training of medical providers to screen and treat children who need intervention.

Thank you for introducing the *Early Hearing Detection and Intervention Act of 2015*. We appreciate your efforts in this important area in children's health. We look forward to working with you on this issue and others important to our nation's children.

Sincerely,

Sandra G. Hassink, MD, FAAP

Sandra G. Hassink, MD, FAAP
President

SMG/pmj

FRED UPTON, MICHIGAN
CHAIRMAN

FRANK PALLONE, JR., NEW JERSEY
RANKING MEMBER

ONE HUNDRED FOURTEENTH CONGRESS

Congress of the United States

House of Representatives

COMMITTEE ON ENERGY AND COMMERCE

2125 RAYBURN HOUSE OFFICE BUILDING
WASHINGTON, DC 20515–6115
Majority (202) 225–2927
Minority (202) 225–3641

July 21, 2015

Dr. Jeffrey W. Chell
Chief Executive Officer
National Marrow Donor Program
3001 Broadway Street, N.E.
Minneapolis, MN 55413

Dear Dr. Chell:

Thank you for appearing before the Subcommittee on Health on June 25, 2015, to testify at the hearing entitled "Examining Public Health Legislation: H.R. 2820, H.R. 1344, and H.R. 1462."

Pursuant to the Rules of the Committee on Energy and Commerce, the hearing record remains open for ten business days to permit Members to submit additional questions for the record, which are attached. The format of your responses to these questions should be as follows: (1) the name of the Member whose question you are addressing, (2) the complete text of the question you are addressing in bold, and (3) your answer to that question in plain text.

To facilitate the printing of the hearing record, please respond to these questions with a transmittal letter by the close of business on August 4, 2015. Your responses should be mailed to Graham Pittman, Legislative Clerk, Committee on Energy and Commerce, 2125 Rayburn House Office Building, Washington, D.C. 20515 and e-mailed in Word format to graham.pittman@mail.house.gov.

Thank you again for your time and effort preparing and delivering testimony before the Subcommittee.

Sincerely,

Joseph R. Pitts
Chairman
Subcommittee on Health

cc: The Honorable Gene Green, Ranking Member, Subcommittee on Health

Attachment

The National Marrow Donor Program (NMDP) appreciates the opportunity to respond to the questions presented to Dr. Jeffrey Chell by the Committee. Please do not hesitate to contact us if you would like further clarification or have additional questions.

1) *You mentioned in your testimony some of the roles that the National Marrow Donor Program plays in addition to running the national registry. Can you elaborate a bit on all the work that Be The Match – NMDP does?*

Operating the National Registry (Be The Match) consists of recruiting potential donors, making them available to searching patients through their transplant physician, and managing the donors safely through the donation process followed by delivering the collected stem cells or cord blood unit to the patient. Although operating the National Registry is the principal role of the NMDP, there are a number of other programs the NMDP has initiated to reduce barriers to transplantation. The National Registry is the Single Point of Access authorized by the Congress.

Assistance to Patients and Families

We know that some populations have extraordinary barriers to accessing transplantation. Family finances, health insurance, delays in diagnosis, treatment or referral, language and literacy all conspire to make it difficult for patients to complete the transplant journey from diagnosis to survivorship. As a tireless patient advocate, NMDP has developed programs to address each of these issues. Our Foundation raises money to help cover expenses that are not covered by insurance. We advocate on behalf of patients with their insurance companies if they are denied coverage. We provide the evidence to payers regarding the effectiveness of transplant therapy. We provide information in multiple languages and have multilingual patient advocacy staff that can provide information and education to patients and families. NMDP provides information and education to non-transplant physicians to help them understand, by diagnosis, the optimal time to refer their patients to a transplant center for assessment. Much of this assistance is provided through the Office of Patient Advocacy authorized by the Congress.

Emergency Preparedness

In addition to our advocacy work, the NMDP operates a multi-organization and multi-agency program called the Radiation Injury Treatment Network (RITN). RITN is prepared to respond to a nuclear accident or act of terror that may cause radiation exposure and bone marrow suppression or failure syndrome. Our contingency planning is robust and tested on a regular basis. These activities are consistent with the requirements of operating the Bone Marrow and Cord Blood Coordinating Centers, which are authorized by the Congress.

Research

Through our Bioinformatics Department and our research organization, the Center for International Blood and Marrow Transplant Research (CIBMTR), the NMDP leads the world in defining the criteria for the best matching donor so that we can continually provide the best source of cells and the best outcomes for our patients. We also conduct research on improving the outcomes of transplant by reducing the complications. This work relates to the operation of the Stem Cell Therapeutic Outcomes Database (SCTOD), which is also authorized by the statute.

2) *Can you elaborate on the way that Be The Match – NMDP coordinates internationally and the differences that makes for the possibility of a patient finding a match?*

NMDP is the largest registry in the world with more than 12.5 million adult donors and 209,000 units of cord blood. But there are another 13 million donors and 400,000 cord blood units listed with the other 65 registries and cord blood banks worldwide. Because matching is so critical to a good patient outcome, having access to the inventory of all of the registries and cord blood banks around the world increase the likelihood that we will find a match for a United States patient. And in fact this is the case, with 25% of the donors or cord blood units that best match U.S. patients have come from donors or cord blood units that are found outside the United States.

Through secure electronic connectivity, NMDP can search our Registry in a few minutes and the rest of the world's registries within one business day. If the best donor is an international donor, we can facilitate the collection of that donor's cells or cord blood much like we do for domestic donors and cord bloods so we can meet the needs of the patient on a timely basis.

3) *What about research – how has data collection through the registry and other activities led to improved patient outcomes?*

NMDP, through its research affiliate, the Center for International Blood and Marrow Transplant Research (CIBMTR), contract with the federal government to operate the Stem Cell Transplantation Outcomes Database, which collects research quality outcomes data for virtually every allogeneic transplant in the United States. It makes that database available to researchers and support that research with research consultation and design services, biostatistical expertise and other support. But research supported by NMDP is not limited to just he database and CIBMTR has supported more than 900 peer review publications since our inception in the following areas:

Observational Research
Through the SCTOD contract and other means, CIBMTR has compiled the results of nearly all transplants performed in the United States and about 50% of the transplants performed abroad. We provide access to researchers to this database so they can retrospectively review the outcomes of transplant and query the database to determine if changes in treatment approaches have an impact on outcomes. With this large database of over 300,000 transplants, we can learn more effective therapies for even the rarest of diseases.

Clinical Trials
With our research colleagues at transplant centers, we conduct prospective clinical trials that are designed to answer a critical question in improving outcomes of transplant. We work with multiple transplant centers at the same time in each trial so that we can accrue patients to a trial more rapidly. This gives us the answer to the research question earlier so we can communicate the results to the transplant and patient community to allow more rapid dissemination and acceptance of the new approach to improve outcomes.

Health Services Research
Our Health Services Research Department focuses on issues of access to transplant by identifying barriers to access and studying ways to remove them effectively and efficiently. Health Services Research also enables the NMDP to ensure that diverse populations can benefit from our research findings.

Immunobiology Research
This area of research encompasses the science of matching donor to recipient. We have learned that there are multiple genetic and non-genetic factors that impact the identification of the best donor or cord blood for a patient. This department identifies those factors and incorporates them into our searching algorithm and communicate them to the transplant community.

4) *You mentioned that current pediatric research focuses not only on malignancies, but also on non-cancer diseases that can still be fatal if untreated, like sickle cell disease. How does Be The Match – NMDP help children with both cancer and non-cancerous diseases?*

Historically, transplant has been used to treat malignant disease. However, there are a number of diseases that are non-malignant in nature that could benefit from a transplant. The first two are Sickle Cell Disease and Thalassemia. Both are diseases of red blood cells which make them less effective at carrying oxygen to our tissues and can cause chronic illnesses and early death. A transplant replaces the dysfunctional red blood cell production system in the bone marrow with that of a healthy normal donor production system thereby curing the disease. Both Sickle Cell Disease and Thalassemia disproportionately impact African Americans and Asians in the United States and cause significant public health issues. These diseases

can be cured early in life and allow these children a healthy life and a brighter future.

There are other non-malignant diseases of childhood generally called Glycogen Storage Diseases. In these diseases children are missing a vital enzyme to aid in eliminating toxins that can build up in the bloodstream. By choosing a donor that is genetically matched and capable of producing the enzyme, we can restore the function of this enzyme in the child's system and restore its natural function. Without this treatment, these children do no develop normally and succumb to their disease early in life.

There is also exciting research using cord blood to potentially treat Autism, brain injuries and autoimmune diseases. It is too early to tell if these treatments will be effective but the future of these treatments is exciting and many, many more patients may benefit from cellular therapy.

5) *As you mentioned, the number of transplant for racial and ethnic minority patients has increased substantially form the year 2000 to today. What efforts is the Be The Match – NMDP making to continue to expand the diversity of the registry to ensure that minority patients can find matches?*

NMDP actively recruits potential donors every year to expand the size of the registry and replace those who no longer qualify as potential donors. Annually, NMDP's direct efforts add approximately 400,000 new registry members and it works to ensure that half of those recruits are from racial and ethnic minorities. In addition, other organizations including the C. W. Bill Young program at the Department of Naval Research add another 250,000 – 300,000 new members, many of whom represent minority populations. NMDP also works with member cord blood banks to support targeted recruitment of cord blood units in minority populations by providing marketing and education materials and grants to support these efforts. We also partner with minority institutions like Historically Black Colleges and Universities, local churches, tech schools. In addition, we identify leaders in the local community, as well as community members that have donated or received stem cells to share their story.

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July 21, 2015

Dr. Joanne Kurtzberg
President
Cord Blood Association
DUMC Box 3850
Durham, NC 27710

Dear Dr. Kurtzberg:

Thank you for appearing before the Subcommittee on Health on June 25, 2015, to testify at the hearing entitled "Examining Public Health Legislation: H.R. 2820, H.R. 1344, and H.R. 1462."

Pursuant to the Rules of the Committee on Energy and Commerce, the hearing record remains open for ten business days to permit Members to submit additional questions for the record, which are attached. The format of your responses to these questions should be as follows: (1) the name of the Member whose question you are addressing, (2) the complete text of the question you are addressing in bold, and (3) your answer to that question in plain text.

To facilitate the printing of the hearing record, please respond to these questions with a transmittal letter by the close of business on August 4, 2015. Your responses should be mailed to Graham Pittman, Legislative Clerk, Committee on Energy and Commerce, 2125 Rayburn House Office Building, Washington, D.C. 20515 and e-mailed in Word format to graham.pittman@mail.house.gov.

Thank you again for your time and effort preparing and delivering testimony before the Subcommittee.

Sincerely,

Joseph R. Pitts
Chairman
Subcommittee on Health

cc: The Honorable Gene Green, Ranking Member, Subcommittee on Health

Attachment

The Honorable Representative Matsui:

1. *As you know, the goals in creating the NCBI were to create a network of high-quality, diverse cord blood units, and to make cord blood units available for research. Can you elaborate on the work that you do to meet those goals?*

In 1997, I established, with the support of the National Heart Lung and Blood Institute, through the COBLT (Cord Blood Transplantation program), the Carolinas Cord Blood Bank, (CCBB) a public cord blood bank at Duke University Medical Center. Over the years, the bank established standard operating procedures for donor recruitment and screening, cord blood collection, processing, testing, cryopreservation, storage, release, thaw and wash and administration for transplantation; created an electronic-web based cord blood database which interfaces with the NMDP Be the Match Donor Registry, established multiple regional staffed collection sites, established a remote kit donation program, became a member of the National Cord Blood Inventory (NCBI) program, became FACT accredited, CAP accredited and CLIA certified, and obtained a BLA from the FDA. The CCBB has banked over 35,000 high quality unrelated donor cord blood units which are available on the NMDP registry. Over 2500 units have been distributed to patients in need of a donor for hematopoietic stem cell transplantation. In addition, over 6,000 units have been distributed to academic and industry researchers for use in their research. The CCBB has explored innovative and novel approaches to cord blood banking and has developed staffed, hybrid and kit donor collection models. Currently they are exploring an "all collect" model at selected hospitals which aims to change the culture about cord blood collection and increase numbers of units collected for consideration for banking.

What is your definition of a high quality cord blood unit?

A high quality cord blood unit is a unit that is collected, processed, cryopreserved, stored and tested using controlled and validated processes and that meets specifications for donor screening, hemoglobinopathy testing, total nucleated cell count (TNCC), viability, viable CD34, colony forming unit (CFU) growth, sterility, and potency testing of an attached segment before release from the bank to the transplant center. The specifications I would propose are listed in the table below.

Specifications of a High Quality Cord Blood Unit

Donor Screening	Negative
Donor Testing	Negative
Hemoglobinopathy Testing	No homozygous
Pre-TNCC x 10^9	≥ 1.5
Viability	≥ 90%
Post-TNCC x 10^9	
Viable CD34 x 10^6	≥ 1.25
CFU Growth	Present
Sterility	Negative
Segment Potency	
ALDH bright cells	≥ 0.1%
CD45 Viability	≥ 40%
CFU	Growth
Segment HLA	Confirmed

In addition, cord blood inventories should represent a diverse spectrum of races and ethnicities of their donors to meet the objective to find the best HLA match and cell dose for each patient in need of a donor for transplantation. As there is an ongoing need for more African American donors, in particular, collection strategies should focus on recruitment of these donors. However, there are some inherent biological challenges in meeting this goal because African American's have lower numbers of circulating cells per volume of blood as compared to Caucasians. In practical terms this means that many more units must be collected from African American donors to obtain a high quality cord blood unit, compared to Caucasian donors. Specifically, 1 in 9 Caucasian units will qualify compared to 1 in 20 African American units. To this end, collection strategies and banking processes should target increased numbers of African American units to maintain diversity of the NCBI inventory. The funding strategies from HRSA should also appropriately fund and enable initiatives to increase African American donors.

2. *What about research – how has data collection through the registry and other activities' led to improved patient outcomes?*

The Stem Cell Transplant Outcomes Database (SCTOD), contracted to the Center for International Blood and Marrow Transplant Research (CIBMTR), collects outcomes data from all patients undergoing hematopoietic stem cell transplantation (HSCT) in the USA and selected international centers on an ongoing basis. This data is utilized to assess the overall success of HSCT measured as overall and disease-free survival, as well as success of various graft sources and the impact of conditioning regimens, patient age and diagnosis, and other variables commonly used by the transplant community. Information obtained from the CIBMTR is invaluable and essential to assess impacts in change in practice, on patient outcomes. The information from the CIBMTR is also used to model future clinical trials, to benchmark success of new innovations (both academic and industry sponsored) and as data for control groups for phase I/II clinical trials.

In addition to the outstanding work performed by the CIBMTR, there is exciting clinical research emerging in the past 5 years using cord blood as a cellular/regenerative therapy for patients with injures or degenerative diseases. In our program, we are testing whether cord blood can be used to treat children with hypoxic brain injury at birth, cerebral palsy, congenital hydrocephalus, autism and in adults with acute ischemic stroke. Others are examining whether cord blood infusions can help children with Type I Diabetes, congenital hearing loss, certain congenital eye diseases, and adults after myocardial infarction or with chronic limb ischemia. Our work at Duke has demonstrated a beneficial effect infusing cord blood in children with hypoxic ischemic encephalopathy, cerebral palsy and autism. Results of ongoing studies in children and adults with the conditions mentioned above, are pending. In addition, cord blood expansion technologies are becoming more robust and derivation of specialized cells from cord blood (e.g. induced pluripotent stem cells) and cord tissues (e.g. mesenchymal stromal cells) may provide unique cellular products in the future.

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