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MPH Culminating Experience

Hypertension in Premature Infants in the Pediatric Office *Follow Up* Study
Pediatric Practice Research Group
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Background: The American Academy of Pediatrics (AAP) Bright Futures clinical practice guidelines promote screening for elevated Blood Pressure (BP) in children 0 - 2 years of age who were born prematurely (< 37 weeks of gestational age). An updated guideline was released in August 2017 that recommended screening BP in infants that were born premature (< 32 weeks of gestational age). In 2016, Dr. Kornfeld led a Pediatric Practice Research Group (PPRG) study, Hypertension in Premature Infants in the Pediatric Office (HyPInPO), assessing provider reported routines for obtaining BP measurements and conducted a medical record review to evaluate medical record documentation of BP measurements and factors that prompt screening. Findings from the 2016 HyPInPO study showed most children < 3 years of age with history of prematurity are not screened for hypertension. Data from the medical record review indicated that a history of kidney disease and/or hypertension increased BP screening rates among children with a history of prematurity while a history of umbilical lines did not.

Hypothesis/Question: The objectives of the *follow up* study were to assess the effects of distributing HyPInPO study reports to PPRG practices, specifically to assess changes in care and understand clinician's perceptions on following blood pressure guidelines for infants that were born premature. A literature review was conducted in parallel to understand what factors influence the progression of hypertension in premature infants and how elevated BP may potentially track into adulthood.

Data/Findings: 10 providers were invited to participate in in depth interviews. The findings showed that 8/10 of providers reported being more aware of the importance of measuring BP in premature infants after HyPInPO. 8 providers reported identifying a child that was born premature in the EHR was fairly easy if it was documented in the problem list. When asked about their perception of the importance of adhering to the guideline all providers reported that it

was very important, while 6/10 reported being familiar with the guideline. 8/10 providers believe that BP should be measured at every well-child visit for infants born premature. Further, 8/10 providers reported prematurity, umbilical lines and a history of kidney disease as patient characteristics that prompt BP screening in children < 3 years of age. The literature review findings indicated the etiology of HTN in premature infants could be explained by impaired intrauterine kidney growth which is associated with a reduction in the number of nephronic units. A lower number of nephronic units is a characteristic of kidneys of patients with hypertension(1). The presence of HTN in children born prematurely has been shown to persist into adulthood (1-8). The studies reviewed indicated that all children with an infantile diagnosis of HTN had full resolution of hypertension with time, whereas only 31% of children with a childhood diagnosis (after the age of 4) of HTN had resolution of HTN(9). It appears that early identification and treatment can impact the clinical course of HTN.

Conclusions: The findings from the *follow* up study suggested that dissemination of HyPInPO study reports increased awareness among providers on the importance of measuring BP in prematurely born infants. There seems to be associated changes in BP related care. There seems to be a discrepancy between provider reported patient characteristics (prematurity, umbilical lines and kidney disease) and what is found in the medical record as the reason to prompt screening. Provider experience and lit review findings coincide on the importance of routine BP screening for infants born premature.

Significance: Findings of this pilot help shed light on the potential disconnect between what is suggested in the blood pressure management guideline and what is feasible in clinical care. It also informs the PPRG –Practice Based Research SEED Grants and their impact on clinical care. Details have also been collected on how to effectively disseminate the results of these studies.

Introduction:

Prematurity is defined as being born <37 weeks of gestational age (GA). Being born premature is associated with several risk factors that can impact health and health outcomes for these children (1). As technology has advanced over the last decade, more infants born preterm are able to survive into adulthood and emerging evidence has pointed to the development of chronic health conditions, like hypertension (HTN), among this population (10). Guidelines have historically emphasized the importance of routinely screening for hypertension in children after 3 years of age or if they have specific risk factors like being born premature (<37 weeks of GA) or being small for gestational age (11).

The American Academy of Pediatrics (AAP) released an updated guideline in August 2017 on blood pressure (BP) screening in children and adolescence. The guideline recommends beginning screening BP for those <3 years of age if they present any of the following risk factors; history of prematurity <32 week's gestation or small for gestational age, very low birth weight (VLBW), other neonatal complications requiring intensive care, umbilical artery line, as well as other specific conditions that may impact the development of comorbidities such as kidney disease or heart conditions (11). Prematurity (<32 weeks of GA) is listed as one of the top factors to prompt screening from a developmental perspective.

Epidemiologic studies have determined that individuals born premature have higher risk for cardiovascular disease (CVD) than individuals born at term. This differential in risk is likely a result of differences in vascular, renal, neural and cardiac underdevelopment (1). As these factors progress into adulthood, this population of children could be contributing to CVD mortality, the leading cause of death in the U.S. (12). Over the last decade, several studies have

been conducted to better understand the relationship between being born prematurely and developing hypertension in infancy and its progression into adulthood (2-9, 13). Development of hypertension in the preterm population has been attributed mostly to perinatal risk factors while those born at term mostly develop HTN related to secondary causes of HTN (kidney malformations, congenital health defects…etc) (9). It has been shown that high BP in infants born premature progresses into adulthood, but early identification and treatment for high blood pressure for this population can lead to full resolution of HTN and overall improved health outcomes (9). Ensuring that these guidelines are adhered to by physicians is thus relevant to public health as it targets primary and secondary prevention of elevated BP and HTN in premature infants. Proper adherence and awareness about the importance of screening BP in this high risk, premature population can effectively reduce the disease burden that this vulnerable population may experience.

Adherence to the AAP guidelines for measuring BP in premature infants in the Chicago metropolitan area was investigated by Dr. Benjamin Kornfeld in collaboration with the Pediatric Practice Research Group (PPRG). The PPRG resides at the Mary Ann and J. Milburn Smith Child Health Research Outreach and Advocacy (SCHROA) Center, one of programs at the Stanley Manne Children's Research Institute. The PPRG is a network of primary care practitioners interested in research related to children's health care. With leadership at Lurie Children's Hospital, PPRG community-based studies have involved hundreds of community clinicians and thousands of their patients since 1984. The PPRG is one of the oldest practice-based research networks in the country. It has 55 member practices and 405 pediatric providers in Illinois, most of them in the Chicagoland. PPRG practices serve a very diverse pediatric patient clientele and has a long history of successful community research. Some PPRG practices

are part of networks such as Community Connect Health Exchange Network, Alliance Chicago, and the Peoria, IL, OSF Healthcare and UnityPoint Health. Frequently topics of study in PPRG practices include studies on health care delivery, natural history of illnesses and behaviors, epidemiology, child behaviors, parental perceptions and experiences with care provided at their practice.

Dr. Kornfeld's pilot study assessed provider reported routines for obtaining BP measurements and conducted a medical record review to evaluate documentation of BP measurements and factors that prompt screening (14). The pilot study was entitled, Hypertension in Premature Infants in the Pediatric Office (HyPInPO), determined that most pediatric providers did not routinely check BP prior to age 3 in patients born prematurely, despite most of the providers reporting of having the proper equipment (Figure A1)(14). The study also determined that most practices (96%) did not have a protocol in place for measuring BP in infants that were born prematurely and the decision to perform this screen is usually left to the provider's discretion at the visit (14). According to the medical record review, among children born premature, BP screening was more often performed on children with a history of kidney disease and/or hypertension compared to those with a history of umbilical lines. From this study, it was evident that new systems are needed to identify and prompt BP screening at primary care visits of children with a history of prematurity (14). These findings were disseminated to the PPRG practices through electronic reports. Following the report dissemination, it was important for PPRG leadership to understand the impact of the HyPInPO study activities on current screening for hypertension in infants with a history of prematurity. Currently, no study has been conducted to evaluate the effects of disseminating study results to practices using electronic reports.

The objectives of the *follow up* study were to assess the effects of distributing HyPInPO study reports to PPRG practices, specifically to assess changes in care and understand clinician's perceptions on following blood pressure guidelines for infants that were born premature. The HyPInPO study findings showed that basic understanding of prematurity as a risk factor for developing HTN is known by providers, yet it is not entirely understood and implemented in practice (14). We planned to conduct a literature review in parallel to explain what factors influence the progression of hypertension in premature infants and how elevated BP may potentially track into adulthood.

Methods:

The HyPInPO *follow up* study was conducted using a mixed methods approach using two distinct components; qualitative research and a literature review.

The qualitative research component was used to conduct interviews. A semi-structured, open-ended interview questionnaire was designed based on the HyPInPO study interview questionnaire. The questions aimed to assess changes in awareness about measuring BP in premature infants, practice level changes in measuring BP in these infants and key factors that prompt BP screening for children < 3 years old. The design of the interview questionnaire was an iterative process that underwent several phases of review by all PPRG staff. The final version of the interview questionnaire tool consisted of 11 open ended questions.

The HyPInPO study sample consisted of 32 practices. A convenience sample of 10 practices from the HyPInPO study was approached for this *follow-up* study. This sample of practices was selected based on those that had completed both the practice level interview and the provider survey in the first phase of the study (14). The sample of providers from these

practices were recruited through email. All ten practices agreed to participate in the in-depth interviews. All interviews were conducted with the lead clinician from each practice. One interview was conducted in person and 9 were conducted over the phone. Detailed notes were taken during the interview by the interviewee and a PPRG staff member. Interview notes were combined and compared after each interview. The notes were used to create codes and develop themes. The analysis was conducted by assessing response frequency. The findings were reported through a poster presentation at the Association for Teaching Prevention and Research conference in April of 2018. PPRG practice characteristics were used to the describe practices that participated (Table A1). Responses to the interview were used to decide on a medical record review assessing documentation of BP measurements. The study was approved by the Lurie Children's IRB, protocol number 2016-192 with PI Benjamin Kornfeld.

A brief literature review was conducted in parallel to the study. Northwestern University Galter Library and ProQuest online databases were used to find supporting evidence for the relationship between premature birth and the development of hypertension. Key words and phrases such as "hypertension in infants", "prematurity", "preterm", "high blood pressure in infants", "preterm birth risk factors", "HTN in those born premature" and "comorbidities in preterm birth" were used to identify all relevant sources. Each study was objectively selected based on relevance in explaining the etiology of HTN and the progression and persistence of HTN in those born premature.

Qualitative Study Findings:

10 providers from 10 practices were invited to participate in in depth interviews. All of the invited providers agreed to participate. The participating practices were located in the

Chicagoland area. Two practices were located in a suburban area, five were located in an urban area and three were located in both an urban and suburban area. Most practices had between 15-27 providers working within the clinic. 6 of the practices use Lurie Children's Community Connect, a shared electronic health record (EHR). 6 practices serve mostly private insurance and 4 practices serve mostly Medicaid or uninsured patients. There were 9 female providers interviewed and 1 male. The practice level characteristics are summarized in Table A1.

The first interview question assessed general changes in practice regarding measuring blood pressure in children under 3 years of age since the dissemination of the HyPInPO study reports. 8 out of 10 practices reported experiencing some kind of change. 5 providers reported an increase in awareness and 3 reported practice level changes. Practice level changes included the implementation of a new BP measurement protocol for children under 3 years of age, implementation of new procedures regarding measuring BP and flagging charts of those with elevated BP. Flagging charts allows for the provider to be aware of elevated BP and ensure that these patients return in two weeks to get repeat measurements. This process has also allowed this practice to improve compliance with guidelines and take BP at appropriate times.

When asked about procedural changes for measuring BP in infants born premature only one practice reported a change. This change was associated with the implementation of a new protocol for BP measurement in children <3 years of age. This protocol included detailed instructions, based on the guideline and recommendation, on how and when to measure BP. This site specifically expressed interest in improving compliance to the guideline after the HyPInPO study.

Overall, there was a provider reported change in BP measurement frequency in 7 of the 10 practices. This frequency was either associated with a decrease frequency of BP measurements due to better compliance with guidelines and measuring BP at appropriate times or with increased frequency due to improved awareness about the importance of measuring BP. One practice reported having a practice wide provider meeting to discuss the HyPInPO study reports. The provider reported that the meeting helped facilitate adherence to the guideline and the importance of doing so.

In regards to equipment, according to the HyPInPO pilot study, 9 of the 10 practices already had the necessary blood pressure equipment for infants under 3 years of age (14). One practice reported purchasing new cuffs after the HyPInPO study. Two practices reported changes in their EHR that helps them better comply with blood pressure measurement guidelines. One practice reported that a recent EPIC update allows for BP vitals to be easily viewed with percentiles in medical records. Another practice reported the existence of a provider charting template within the EHR that can be used when BP is flagged as a concern within the record. When prompted about the ease of finding prematurity within the EHR all providers reported that it was easy to find if it was previously entered in the problem list.

All 10 providers reported that it was important for them to comply with the guideline and measure BP in prematurely born children and 6 of the providers reported being familiar with the guideline (Figure A2). 8 out of 10 providers reported that the ideal frequency for measuring BP in infants born premature is at every well-child visit. 2 providers reported being unsure of the best frequency for BP measurement. When asked about the factors that prompt BP screening the three most reported patient characteristics were prematurity, a history of umbilical lines and a

history of kidney disease. These and the frequency of the other patient characteristics reported by providers are further outlined in Figure A3.

Literature Review Findings:

11 articles were chosen for the literature review. These articles were objectively selected based on their ability to explain what factors influence the progression of hypertension in premature infants and how elevated BP may potentially track into adulthood for this population. One meta-analysis, two systemic reviews and eight cohort studies were reviewed. The studies took place within a variety of settings including tertiary pediatric clinics and hospitals (8, 9). Some studies were conducted using previously developed cohorts such as the Project on Preterms and Small for Gestational Age Infants (POPS) cohort and the Preterm Birth and Early Life Programming of Adult Health and Disease (ESTER) cohort (3, 5).

Major findings from the literature show that hypertension occurs in higher prevalence among infants that are born premature compared to matched at-term controls (1-7, 9, 13). It is evident that HTN at birth, in those born premature, persists and can be successfully resolved if identified early (9, 13). Several cohort studies have also showed that those born premature typically experience elevated systolic BP (SBP) at all ages. Studies assessing BP in infants, children, adolescents and adults have all seen consistently seen statistically significant elevated SBP for those born premature (1-7, 9, 13).

The Extremely Preterm Infants in Sweden Study was interested investigating if BP is elevated at 2.5 years of age after an extremely preterm birth (EXPT) (13). 68 survivors of EXPT (gestational age: 23.6–26.9 weeks) and 65 matched controls born at term were assessed for systolic BP and diastolic BP. The findings showed that EXPT children had significantly higher

BP than the controls born at term (13). At a corrected age of 2.5 years, children in this study born extremely preterm had elevated office SBP and DBP. The study concluded being born premature has clear implications for cardiovascular health as elevated BP is persistent from birth to 2.5 years (13).

One study examined the effect of early identification and diagnosis of HTN in children that were born premature. This study was conducted in a tertiary pediatric hypertension clinic. Through a retrospective chart review, 36 preterm (<37 weeks GA) hypertensive children were included in the sample, 23 of which were diagnosed in the NICU (infantile) and 13 diagnosed at an older age (childhood after age 4) (9). All those diagnosed in the NICU were treated with antihypertensive drugs either upon diagnosis or at clinical visits, those diagnosed as children were treated with lifestyle changes and medication or both. All children diagnosed with infantile hypertension had full resolution within 1.5 years after diagnosis and no treatment required after 6 months. Only 31% had resolution in childhood and most had persistent HTN. Infantile hypertension was associated with perinatal risk factors; low GA, longer NICU stay, higher incidence of intubation, chronic lung disease, and abnormal renal ultrasounds (9). Childhood hypertension was associated with more traditional risk factors such as ethnicity and obesity, showing that environmental factors play a larger role in childhood diagnosis than infantile. Thus, infantile and childhood diagnosis of systemic HTN in premature children each have unique risk factors and clinical course and early identification and treatment of HTN in infancy can lead to full resolution of HTN (9).

In a review article on prematurity-related HTN in children and adolescence, 15 clinical trials where BP values were measured for different groups of children were analyzed. The sample consisted of ex-preterm children either very low birth weight (VLBW), premature or

children that experienced intrauterine growth restriction (IUGR). The current age of the sample was split into three groups; school age children (6-12), adolescence (13-18) and adults (18-27). The findings showed that children (6-12) had the highest prevalence of HTN compared to other age groups (1). It was also evident that HTN diagnosis in pediatric patients is more precise, as BP measurement techniques have improved over the years. The study showed that less over-diagnosis occurs in children compared to the adult populations due to the use of ambulatory BP monitoring (ABPM) and casual measurements in combination (1). Systolic blood pressure (SBP) in 10 of the 15 studies was also significantly higher for former preterm newborns compared to term controls. There was also a greater number of HTN diagnosis in the preterm born group (1).

A systematic review of 27 observational studies that compared the resting or ambulatory systolic blood pressure or diagnosis of hypertension among children, adolescents, and adults born preterm or very low birth weight with those born at term was also reviewed (4). A meta-analysis was conducted within the review using a subset of 10 studies that reported the resting systolic blood pressure. The 10 studies were composed of 1342 preterm or very low birth weight and 1738 term participants from 8 countries. Findings from this study showed that former preterm or very low birth weight infants had higher systolic blood pressure than term infants. The study concluded that infants who are born preterm or very low birth weight have higher systolic blood pressure later in life and may be at increased risk for developing hypertension (4). This study suggested that prematurely born infants have prenatal and postnatal factors that impact their development and there is a clear link between being born prematurely and experiencing elevated SBP. This meta-analysis helps shed light on the relevance of prematurity and how it not only impacts infants but persists as they age into adulthood (4). A few cohort studies were analyzed independently to examine this relationship further.

A cohort study done through Hacettepe University Faculty of Medicine obstetrics department database aimed to understand the progression of elevated BP in those born preterm to matched at term controls (7). The patients were on average 8.9 years old at the time of the study and ABPM was used to measure BP. The study found that the preterm born group had a significant nocturnal elevation of SBP and 28% had been identified as dippers compared to 60% in the controls (7). The study indicated that the prevalence of non-dipping in this patient group is important as non-dipping is an important independent risk factor for cardiac and cerebrovascular morbidity in adults. The results indicate that those born preterm have higher risks for cardiovascular disease as they age compared to their matched at term controls (10).

In another cohort study, the POPS cohort included all live-born individuals born in the Netherlands with GA <32 weeks and a group of controls. These two groups were used to compare ABPM measures over a 24-hour period and undergo a renal function test and renal ultrasonography (5). The baseline SBP in the premature population was higher than controls and renal ultrasonography reveled subclinical renal abnormalities in 8 prematurely born individuals. The matched controls did not exemplify any of these risk abnormalities (5). The study concluded that those born premature have increased SBP at a young adult age and IUGR does not attenuate this effect. The study found that prematurity alone is an import risk factor for developing elevated BP (5).

In Helsinki, a cohort of 118, 18 to 27-year old's that were born premature and very low birth weight (mean 1.1 kg compared to 3.6 kg at term controls) and their matched controls were assessed for 24-hour ambulatory blood pressure (6). VLBW subjects had systolic BP that was on average 2.4 mm Hg higher than the controls (6). This study also found 11 VLBW subjects and 3 term-born subjects to have HTN. This study concluded that HTN is found in higher rates

amongst those born VLBW, and so, VLBW may also be considered a risk factor for adverse cardiovascular health outcomes (6).

Likewise, in another study, in order to better understand the rates of cardiovascular risks factors among pre-term born infants in comparison to small size at birth, a cohort of 30-year-olds were recruited for a follow up assessment from a previously conducted clinical trial (2). The study found that preterm birth was associated with a significantly increased SBP and insulin resistance at age 30. The study found that preterm birth and not poor fetal growth, defined by birth weight, is the major determinant of this association (2).

Several cohort studies have also been conducted to examine the progression of HTN and elevated BP in those born preterm. The Preterm Birth and Early Life Programming of Adult Health and Disease (ESTER) Study is a population-based cohort study of individuals born between 1985-1989 in Northern Finland (3). Within this study a clinical examination of 134 early preterm (<34 weeks of GA), 242 late preterm (<37 weeks GA) and 344 controls was conducted to explain the relationship between being born at different levels of prematurity and having elevated blood pressure. It was found that the preterm group had higher body fat percentages, waist circumference, blood pressure, alanine aminotransferase levels, aspartate transaminase levels and was more likely to have metabolic syndrome compared to the term controls (3). Elevated levels of conventional and emerging risk factors suggest a higher risk for cardiometabolic disease later in life. The early preterm group had HTN 2 to 3 times more than the adult control group, which was not seen in the late preterm group (3). The study indicated that there may be a dose response relationship between shorter gestation and elevated SBP in adulthood (3).

In a brief review of current literature, the link between preterm birth and HTN risk were found to be independent from birth weight (10). The studies found that there is a significant inverse correlation between SBP and GA at birth which has been observed consistently within several cohort studies – some of these have been outlined above (1, 5). The etiology and pathophysiology of hypertension were also examined within the literature review. The findings suggest that there are clear morphological and physiological differences within organ system of those born extremely premature (<32 weeks of GA) compared to those born at term (1-3, 5, 7, 8, 10). This review suggests that premature infants have a multifactorial risk for developing elevated BP due to alterations to renal, cardiac and vascular development and function that relate to gestational age.

In one study the etiology of hypertension in ex-preterm children was examined through radial glomerular counts in order to measure preterm infants glomerulogenesis (1). The study found that preterm infants glomerular counts were markedly decreased compared to term controls. Further analysis identified that preterm infants have a different kidney structure and usually have impaired kidney development till their second year of life (1). In another study an analysis on nephrogenesis and kidney function was conducted on ex-preterm infants compared to controls. According to ultrasound results, fetal weight is inversely related to kidney volume. This study suggests that postnatal nephrogenesis in low birth weight, preterm infants is impaired. The reduced number of nephrons in this population is most likely due to the morphological adaption of the nephrons to maintain glomerular function as normal as possible – which has been observed in animal models (8). Adult autopsy of those with primary HTN have shown a reduced number of nephrons. One study explained the possible mechanism of impaired nephrogenesis due to accelerated renal maturation in preterm infants. Nephrogenesis is triggered upon birth and

so preterm born infants don't have the same maturation time as those born at term. This may result in the diminished endowment of functional nephrons at the beginning of life which later on impairs the glomerular filtration rate and kidney function (10). All studies showed that in some cases those born preterm have morphological and pathophysiological differences within their kidneys.

In regards to cardiac development, one review found that HTN is unrelated to cardiac structure and function after preterm birth, but it can be particularly susceptible to effects of elevated BP (10). Cardiac dysfunction can be detected in preterm infants through increased left ventricular dimensions in first month of life and then smaller left ventricular cavity with increased left ventricular mass compared to controls at age 5 and in adults born preterm (10). The study concluded that these factors play a role in the persistence of HTN in prematurely born children. Prematurity may also disrupt or arrest development of the vascular tree resulting in stiffer arteries, restricted vascular bed and relatively narrowed blood vessels – predisposing to endothelial dysfunction and arterial HTN (10). This review observed an increased aortic stiffness in children 7-14 years old that were born premature. It was also found that adolescence born premature have smaller aortic, carotid, and branchial artery diameters compared to those born at term (10). These factors suggest that prematurity alone plays a huge role in the development and function of organ systems.

One review also discussed the oxidative stress paradigm that may play a role in organ damage and health risks experienced by prematurely born infants. Hyperoxia exposure and oxidative stress are related to HTN susceptibility in premature infants (10). Exposure to free radicals while premature infants may still have an immature antioxidant defense system at birth can lead to apoptosis and result in organ development damage. This may also damage oxygen

sensing pathways which may impact postnatal organ and vascular development in preterm neonates (10, 15). Other studies have seen age related increase in blood pressure characterized by oxygen-related damage. It is possible that accelerated cellular aging may be triggered by oxidative exposure in early development (10).

Besides organ underdevelopment, pathogenic mechanisms for inducing elevated BP in prematurely born infants have been suggested – such as, increased tubular sodium channel expression, dysregulation of the intrarenal renin-angiotensin system, oxidative stress, and decreased NO production (1). These mechanisms and the clear differences within kidney morphology suggest that premature infants are inherently at greater risk for elevated BP (1).

A study done from the Hospital de Cruces neonatal records of children born between July 1989 and December 1995, school age children at the time of the study, are affected by their birth history (8). 40 infants that weighed less than 1000 g at birth and 43 matched by race, age and demographic healthy comparison group were selected for the study. Those born at a low birthweight were significantly smaller and thinner than controls. Although renal sonography showed no statistically significant difference and no significant difference in BP measurements, renal function, plasma creatine and urea concentrations were significantly higher in study subjects. This led to the conclusion that there is a defect in tubular transport of phosphate. The study also concluded that glomerular filtration rate (GFR) in school age children born premature was significantly lower in comparison to controls (8). These findings show that there are distinct differences between those born premature and those born at term.

Discussion:

Screening premature (<32 weeks GA) infants for hypertension is an evidence based best practice guideline supported by the American Academy of Pediatrics Guidelines and the U.S. Preventive Services Task Force (11). These two entities have important influence over preventive services for infants, children and adolescents (11). The guidelines and recommendations are put together using evidence-based studies that have shown important implications about screening and diagnosing HTN in infants. Over the last decade, extensive studies have been conducted to examine how being born premature correlates with high blood pressure in childhood and later on in adulthood. Prospective cohort studies examining this relationship have been conducted worldwide with varying population characteristics. These studies provide insight into individual level case examples of the progression of high blood pressure (5-11). Meta-analysis and systemic reviews regarding the relationship between being born premature and high blood pressure have also been compiled throughout the years to further describe this relationship. These studies have provided evidence to support the guidelines and recommendations published by the AAP and the Preventive Service Task Force. The findings from the compiled review of the literature in this paper enhance the HyPInPO *follow up* study findings by strengthening the rationale for measuring BP in infants born prematurely.

During the HyPInPO *follow up* study interviews, all providers reported that it was important to comply to the guidelines and recommendations for screening BP in infants born premature, yet not very many were familiar with the guidelines. Some physicians expressed that premature birth is often forgotten as the child ages and no longer considered a concern during their well-child checks as it gets removed from the problem list and becomes more difficult to find within the EHR. Understanding the general risks associated with being born preterm can

give insight into the importance of keeping prematurity in the problem list as the child ages and would aid in improving adherence to the guidelines and recommendations set out by the AAP.

The literature review findings showed that prematurely born infants, children, adolescents and adults have elevated BP compared to at-term born controls (1-7, 13). This finding was consistent over many clinical studies and meta-analyses. Preterm infants also experience HTN diagnosis more often than those born at term. This increase in prevalence of HTN and elevated BP among those born premature suggests that this population is intrinsically more at risk compared to those born at term. While this is potentially due to the fact that premature and low birth weight infant survival has improved over the years and thus there is potential for increased number of diagnoses, it's important to note that with increasing survival there is also a potential for increasing rates of long-term complications that need to be further examined. The relationship between preterm birth and elevated BP remains to be significant. Knowing this, it is clear that prematurity should continue to be included within the problem list as the child ages as they are at risk for elevated BP and HTN. As mentioned previously, the HyPInPO *follow up* study findings showed that providers often did not keep prematurity in mind as the child ages, in context of the literature review findings, it is clear that this needs to be reconsidered. Adjusting the EHR system to include prematurity in areas where it can be found more easily may be a potential avenue to improving providers adherence. Understanding the persistence and risk of developing HTN for this population enhances the importance of following the guidelines and recommendations set out by the AAP.

Many cohort studies reported a significant elevated SBP in those born premature compared to those born at term (1-7, 13). While the difference between BP readings ranged from 2 – 3 mm Hg, a difference of 2 mm Hg of SBP is associated with a 15% reduction in the risk of

stroke (9). Thus, monitoring BP measurements in this population is incredibly important as it is directly related to cardiovascular health outcomes. Ensuring that physicians understand that even small differences in BP measures are significant, can potentially help improve compliance to the guidelines and recommendations. The literature review findings also show that early identification and treatment of elevated BP in infants born premature can lead to full resolution within the infants first year of life (9). Although providers reported improved compliance with the guideline and a change in practice after dissemination of the HyPInPO study reports, there still seems to be a gap in what is recommended and what is done in practice. By improving providers adherence to the guideline, these infants can be identified early which could decrease the burden of disease that they may experience in their lives.

Evidently, as seen in the literature review, there are many factors that put prematurely born infants at greater risk for the development of comorbidities. Their increased susceptibility to impaired cardiac, renal and vascular development and function suggests that this population should be carefully monitored from birth and into adulthood as developmental issues are known to persist (1-3, 5, 7, 8, 10). The interview findings from the HyPInPO *follow up* study showed that the providers recognized prematurity, kidney disease and a history of umbilical lines to be the top factors that prompt blood pressure screening. These factors are clearly impacted upon premature birth (10). It is apparent that physicians have a good understanding of the risks that are associated with premature birth and that they coincide with the literature findings, yet, there is some disconnect between what providers report and what is actually done in practice. The medical record review conducted during the HyPInPO pilot study suggested that provider report and what is actually done in practice, in regards to BP measurement in this population, does not coincide (14). For example, while a history of umbilical lines was the most reported

characteristic to prompt BP screening, medical records with a history of umbilical lines seldom had BP measured (14). It appears as though providers recognize the importance of BP measurement and the risks associated with premature birth, but don't necessarily comply with the guidelines in practice.

One study made the distinction that those born extremely preterm (<32 weeks of GA) experience greater comorbidities associated with kidney development and function as well as an increase diagnosis of HTN (3). This dose response relationship with preterm birth and GA is incredibly important as the gestational age for considering preterm birth a risk factor that should prompt BP screening according to guidelines and recommendations has been reduced from 37 weeks of gestational age to 32 weeks within the last year (3). From the HyPInPO findings, even though 80% of providers have improved awareness within their practice, only 30% made significant changes in regards to compliance with the guideline. This finding further supports the need for improved early screening and diagnosis of elevated BP in the premature population for all practices.

There are some limitations within this study that must be considered. The impact of disseminating the study reports is not totally clear as we only interviewed 10 providers. This sample is relatively small and has limitations with generalizability. The sample was also a convenience sample and may not be entirely representative of the PPRG network. This study also did not objectively evaluate frequency of BP measurement documentation through a medical record review. The small sample of interviews and responses did not prompt the necessity of a chart review. Without a medical record review, we cannot confirm the change in frequency of BP measurements in children born premature as reported by providers. Findings from the pilot

study were used to draw conclusions within the *follow up*. Future studies should consider conducting a medical record review to strengthen the findings.

Conclusion:

Disseminating the study reports was an effective way to engage practices within the PPRG in order to evaluate the impact of the reports and how the reports may prompt changes within the clinical setting. The HyPInPO *follow up* study found that the dissemination of HyPInPO study reports seemed to have increased awareness among providers on the importance of measuring BP in prematurely born infants. Providers also reported changes in BP related care within their practices. There seems to be greater care coordination between doctors, medical assistants and clinical staff. Providers reported that prematurity, umbilical lines and kidney disease were the top three patient characteristics that prompt BP screening in infants under the age of 3. This finding was not supported by the medical record documentation from the pilot study. This discrepancy suggests that there is some disconnect between provider report and what happens within the clinical setting. Future studies should delve deeper into the feasibility of obtaining infant blood pressure during well child visits. Studies should examine the best method, documentation and technology in order to make this task run as smoothly as possible. This can be done through evaluating the success of implementation of new BP measurement protocols within practices and working on a more user-friendly system within the EHR.

Overall, providers experience and literature review findings coincide on the importance of screening for BP in all infants born premature. It is evident that prematurely born infant experience a greater risk for several developmental issues that have to do with cardiac, renal and vascular function. These factors play a role in the development of elevated BP and its

progression into HTN. Studies have also shown that being premature is a risk factor for developing HTN in childhood, adolescents and adulthood and that HTN in infancy can track into adulthood (5-11). These findings clearly support the guidelines and recommendations for measuring BP in infants born premature. One of the most important findings is that early identification and treatment of HTN in these infants can lead to 100% resolution within the first year of life (9).

The HyPInPO *follow up* study showed that providers need ways to help improve adherence to guidelines within their practice in order to decrease the burned of elevated BP and HTN, the leading risk factor for cardiovascular disease. Improving prematurely born infant health by screening early and monitoring BP can potentially aid in decreasing the cost and burden of CVD (16). Disseminating the findings of the pilot study was an effective way to change providers adherence to the guidelines and recommendations and improve their awareness about the relationship between being born premature and developing HTN. Understanding the evidence behind what is stated in guidelines and recommendations and what actually happens in the primary care setting has important implications for public health. This study has identified the gap between policy and clinical care and has put forth recommendations that could potentially improve compliance to the guideline. Future studies should consider this effectiveness of disseminating study reports to induce practice level changes and improve adherence to guidelines and recommendations.

This *follow up* study has been instrumental in informing the PPRG – Practice Based Research SEED Grants and their impact on clinical care. Evaluating pilot studies is an effective way to understand the impact and inform future directions. We have also collected details as to

how to effectively disseminate the results of these studies and can use them for future work to better reach the PPRG practices and effectively promote better care for all patients.

Appendix:

Table 1.

Practice Characteristics of Participating Providers (N=10)	
Location	
Urban	5
Suburban	2
Urban and Suburban	3
# of Physicians (MD/DO) at Each Practice	
0-5	3
6-14	3
15-30	4
Shared EHR (Lurie Community Connect)	
Yes	6
No	4
Practice Payer Mix	
Mostly Private	6
Mostly Medicaid/Uninsured	4

Table 1 summarizes the practice level characteristics of the sample.

Figure 1.

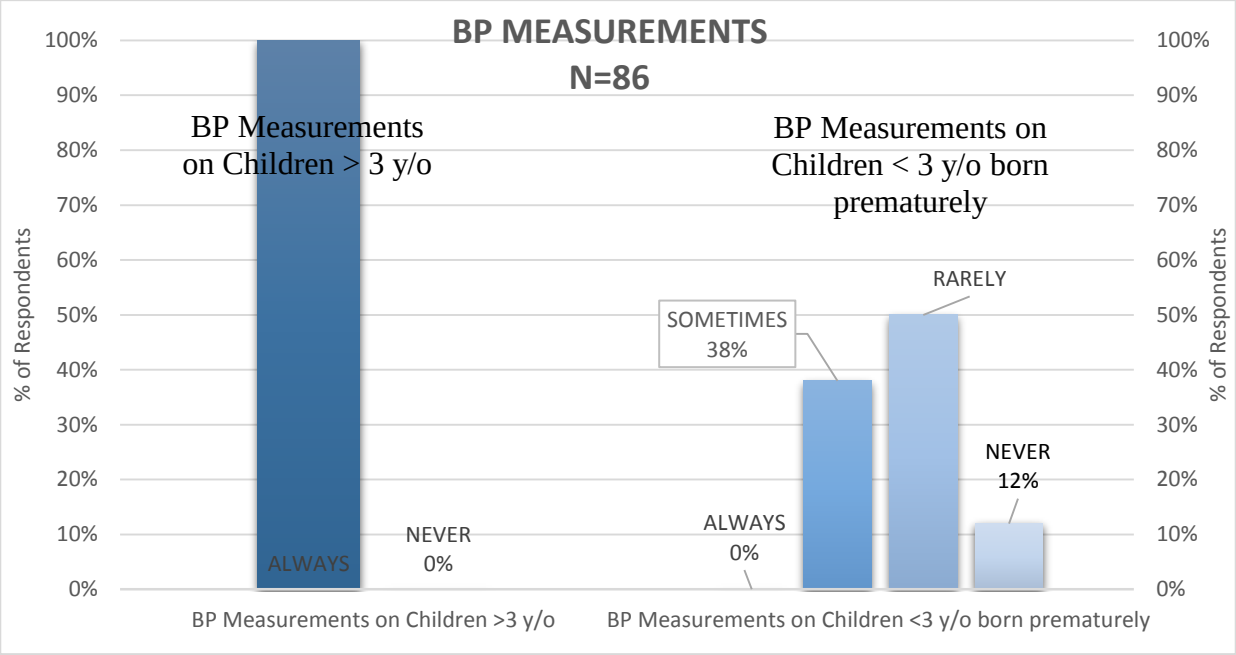

Figure 1 shows the findings from the HyPInPO pilot study. Most providers rarely measure BP on infants <3 years of age who were born prematurely while they always measure BP on children >3 years of age.

Figure 2.

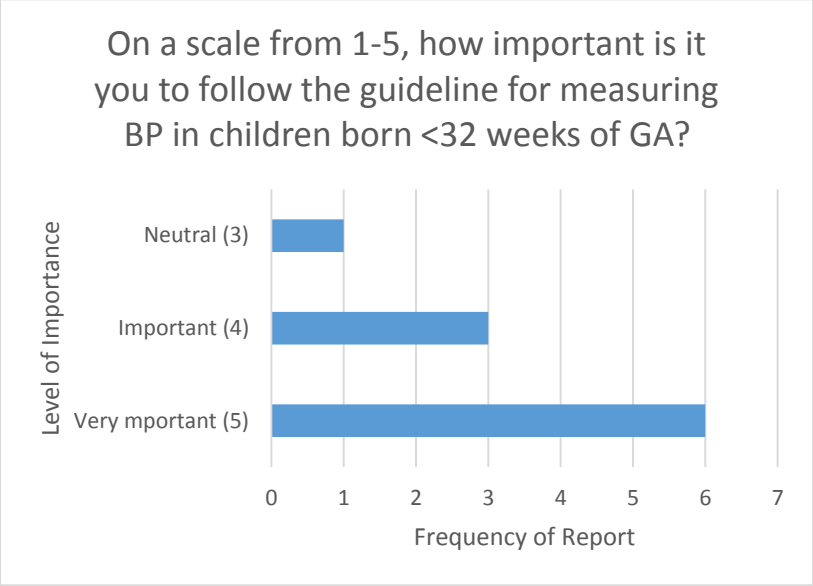

Figure 2 shows the response frequency for the importance of adhering to the guideline for measuring BP in infants born <32 weeks of GA.

Figure 3.

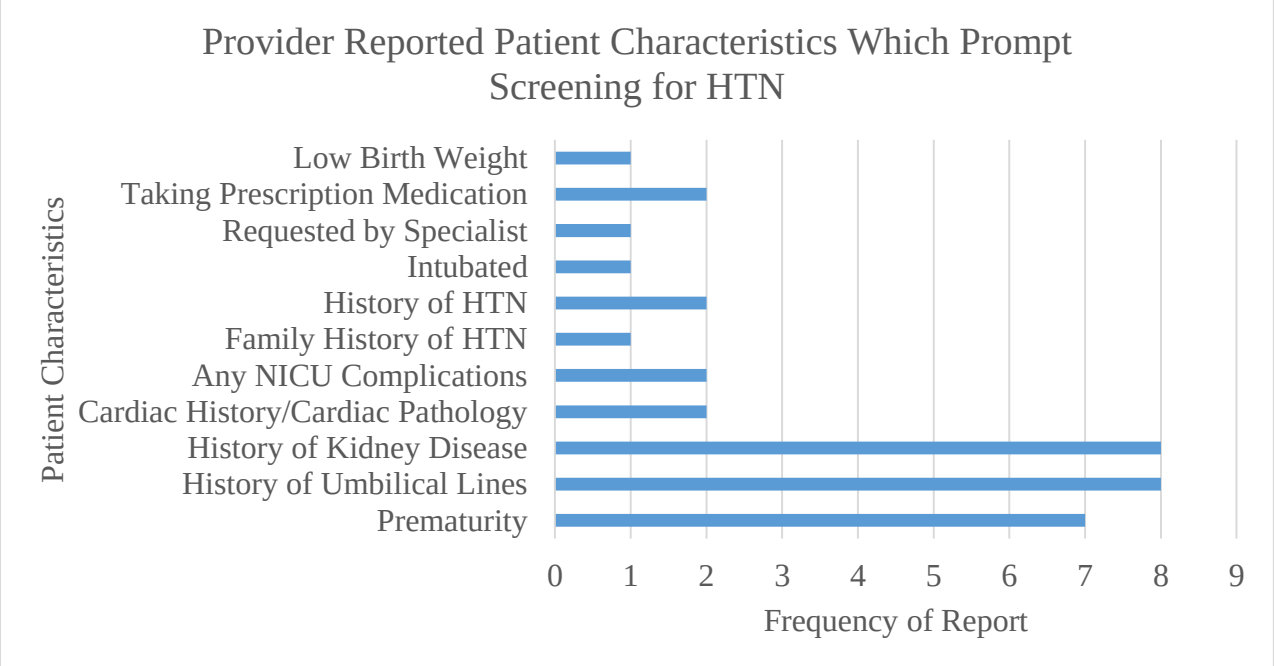

Figure 3 shows the various patient characteristics and their frequency that providers reported prompt BP screening in the clinical setting for children <3 years of age.

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