

Preterm Birth

A Growing Human Healthcare Crisis

An Opportunity to Prevent Global-Scale Human Tragedy & Mounting Socioeconomic Loss



November 13, 2009
(Rev: 05232011)

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1. Introduction

Numerous independent studies agree that Preterm Birth (“PB”), which means less than 37 weeks gestation, is the leading cause of infant death and morbidity in the first month of life, and a contributing factor to more than a third of all infant deaths worldwide.

There are various causes of PB, including Incompetent Cervix (IC), other known cases of organ and / or tissue compromise which may contribute to accelerated effacement and dilation, pregnancies involving multiple fetuses, and a growing number of women having children later in life.

Tragically, those infants surviving an early birth, for whatever cause, face the risk of serious health problems including autism, cerebral palsy, spina bifida, cardiovascular defects, blindness and various other lifelong crippling disabilities. In fact, independent studies show that the leading cause-factor to each of these disabilities is indeed PB.

Internet bulletin boards are full of heart-wrenching posts from mothers and families who have tragically lost their children late in pregnancy – but these reports and statistics are from developed countries and “privileged” populations and do not take into mind the even more overwhelming circumstances to the condition and outcomes for the underprivileged and those from underdeveloped and developing countries which constitute nearly 80% of all cases.

After more than 23 years of research and development, and with the launch of its parent company TechDyne, ViaTechMD is at the threshold of bringing to life a device-based preventative treatment for various conditions leading to PB. By working with major universities, institutions, and bioengineering experts, TechDyne / ViaTechMD is forging a pathway toward resolving disjointed and confusing data and the development of advanced and highly accessible prevention treatments. Our patent pending biomedical device-based technologies are in development now and promise to significantly reduce the occurrence of preterm births in the near future.

TechDyne LLC / ViaTechMD has brought together an experienced team including seasoned business development and operations managers, technology and product developers, a Medical Advisory Panel consisting of prominent Doctors of Maternal Fetal Medicine and Obstetricians / Gynecologist, industry-veteran CEO and CFO advisors, and a Yale bioengineer.

We have also been successful in establishing strategic relationships with a global medical device manufacturer and a prominent life sciences industry clinical research organization, and we are now into our third generation of prototypes and have our initial human trials designed and ready to implement.

We hope that you will be interested to learn more about this endeavor and to assist by helping to advance the remaining research and development necessary to put this

technology in the hands of physicians and world health organizations that can help millions of families avoid these tragic outcomes.

2. Preterm Birth – A Growing Global Healthcare Crisis

Preterm Birth (“PB”) is the leading cause of death in the first month of life and a contributing factor in more than a third of all infant deaths. Moreover, infants who survive an early birth face the risk of serious lifelong health problems. Even late preterm infants have a greater risk of respiratory problems, feeding difficulties, temperature instability, delayed brain development and an increased risk of autism, cerebral palsy and mental retardation. In fact, according to a very recent analysis of nearly 7 million U.S. live births, preterm infants are more than twice as likely to have major birth defects as full term infants.

In a report on the topic of child health, from the Institute of Medicine of the National Academies, it is stated that in 2005, 12.5 percent of births in the U.S. were preterm (less than 37 weeks gestation). The high rate of premature births in the U.S. alone constitutes a public health concern that costs society at least \$26 billion a year. The heartbreaking toll in terms of human and family suffering cannot be calculated. For the underprivileged and those in underdeveloped and developing countries, additional tens of millions are even more devastated – as the families and children struggling with this condition and suffering these outcomes are unable to obtain medical assistance and are also often outcast by their societies.

The report, “Preterm Birth: Causes, Consequences, and Prevention”, notes that despite great strides in improving the survival of infants born preterm, little is known about how preterm births can be prevented (a primary focus to the research and development underway at TechDyne / ViaTechMD). Nevertheless, survival very often comes at the great cost of serious lifelong health problems. The report goes on to recommend a multidisciplinary research agenda aimed at improving the prediction and prevention of preterm labor and better understanding the health and developmental problems to which preterm infants are more vulnerable. With layer upon layer of bureaucracy complicating matters, little is being accomplished.

The increasing prevalence of PB, related mortality, and lifelong disability is a complex public health issue that requires multifaceted solutions. Currently, the subject of PB is described by a confused cluster of datum, with a complex set of overlapping factors of influence. Its causes may include individual-level behavioral and psychosocial factors, sociodemographic and neighborhood characteristics, environmental exposure, medical conditions, infertility treatments, and biological factors. Many of these factors co-occur, particularly in those who are socioeconomically disadvantaged or who are members of racial and ethnic minority groups, further complicating the equation.

While advances in perinatal and neonatal care have improved survival for preterm infants, those infants who do survive have a greater risk than infants born at full term for developmental disabilities, health problems, and poor growth. The birth of a preterm

infant can also bring considerable emotional and economic costs to families and have implications for public sector services, such as health insurance, educational, and other social support systems.

It is important that something more is done now. According to Science Daily (Jan. 10, 2009), new government statistics confirm that the decades long rise in the incidence of PB in U.S. is putting more infants than ever at increased risk of death and disability.

In the U.S. alone, nearly 543,000 infants were born preterm in 2006, according to the National Center for Health Statistics, in the recently released “Births: Final data for 2006,” National Vital Statistics Reports; Vol. 57, No. 7. The nation's PB rate rose to 12.8 percent in 2006 – that's a 36 percent increase since the early 1980s. Global statistics, including the underprivileged and those from underdeveloped and developing countries are sure to more than quadruple these values.

The report attributed much of the increase to the growing number of late preterm infants (34 to 36 weeks gestation), which increased 25 percent since 1990. The report also noted an increase in preterm births to Hispanic women, while rates were unchanged for non-Hispanic, whites and blacks. However, black women continue to have the highest PB rate, at 18.5 percent. Unfortunately, a great portion of the world's population, including in underdeveloped and developing countries is not factored – nor do those populations have any current hope for consideration or treatment solutions (TechDyne / ViaTechMD aims to change that).

Moreover, the PB rate continued to rise despite the fact that multiple births, a known risk factor for PB, have begun to stabilize. The rate of twin births was unchanged in 2005 and 2006, and triplets and higher order multiples declined 5 percent in 2006. Early this year, the March of Dimes issued its first ever Premature Birth Report Card (comparing 2005 PB rates to the national Healthy People 2010 objective of 7.6 percent), which gave the U.S. a “D” (not a single “A” to any state). If the U.S. report card scored only a “D”, how do underprivileged and unconsidered populations rate?

PB is a serious and growing global healthcare issue with respect to both its causes and outcomes. The health and economic consequences of premature birth require refined and targeted approaches from healthcare professionals, public health officials, policy makers, professional associations and clinical, basic, behavioral, and social science researchers. Furthermore, as statistics clearly demonstrate, the increasing practice of modern diagnostic procedures such as cone biopsy is exposing even greater numbers of the youngest generations within the child bearing population (as doctors face dealing with an out of control legal system, and are unable to arrest such consequential and tragic patient trends).

To date, only cerclage, practiced in various forms for more than 100 years, and a few more recent and highly controversial pharmaceutical treatments, which Payers are now rejecting, exist to address this crisis. However, cerclage is a costly and invasive surgical procedure (available only to an “elite” few), which offers treatment for only one of the

conditions leading to PB, IC, and then, only for a very narrow period of time during pregnancy (amounting to rescue and emergency treatments).

Like the controversial pharmaceutical treatments, cerclage has no proof of efficacy. Moreover cerclage, on average, costs Payers \$20,000 per patient and is not a treatment option for most of the world's population.

In 2010 the March of Dimes and World Healthcare Organization reported that premature birth costs Payers an average of \$79,000 per child, and can sometimes top \$1,000,000. Beyond the immeasurable human tragedy, in total global economic consequences of PB are estimated to exceed \$52 billion annually. This paper addresses the need to better organize and correlate these efforts and focus on direct approaches to preventative treatments.

3. Incompetent Cervix – A Significant Factor to Preterm Birth Rates

Cervical Insufficiency, commonly referred to as Incompetent Cervix (“IC”), is a significantly growing, yet widely unrecognized factor to the increased incidence of PB and its consequences worldwide. As many as ten percent of all pregnancies end in preterm delivery (prior to 37 weeks), with approximately half of those preterm deliveries being problematic, as a result of IC and various other related conditions.

IC, a condition that affects from one to two percent of all pregnancies, refers to a deficiency in the structure or function of the cervix that can lead to PB (which is often mischaracterized as a miscarriage or stillborn).

Obstetrically, IC refers to a uterine cervix that becomes dilated before term and without labor often resulting in miscarriage or premature birth. Unfortunately, the condition remains largely unrecognized as a primary factor to the growing number of preterm births (resulting in the loss of millions of infants and lifelong suffering of a number many times the death rate), and little has been done to improve treatment of the disorder.

The cervix is the narrow, tubular, lower end of the uterus that extends into the vagina. Prior to pregnancy, the cervical canal remains open a tiny bit to allow sperm to enter the uterus and menstrual blood to flow out. During pregnancy however, secretions fill the canal and form a protective barrier called the mucous plug. During a normal pregnancy, the cervix remains firm, long, and closed until late in the third trimester. At that point it usually starts to soften, efface (grow shorter), and dilate (open up) as the woman's body prepares for labor.

IC is a condition whereby the cervix is softer and weaker than normal or is abnormally short or otherwise compromised by “nature”, general health, and/or previous surgical procedure. Therefore, it may efface and dilate without contractions in the second or early third trimester, as the weight of the growing baby adds increasing pressure which can

result in second trimester miscarriage; preterm premature rupture of the membranes ('PPROM' – in which the water breaks before full term and before labor); or preterm delivery (before 37 weeks). IC particularly increases the risk for early preterm delivery, which means giving birth before 32 weeks (again, very often “written off” as simple miscarriage).

Historically, the diagnosis of the condition became obvious only after multiple second-trimester miscarriages or early preterm births from no other known cause. Now, the risk can be detected by regular transvaginal ultrasounds beginning at 16 to 20 weeks to measure the length of the cervix and to check for signs of early effacement (shortening). Nevertheless, these procedures have yet to become widely recognized by practitioners or insurance companies as necessary to improving prenatal infant healthcare, and those in underdeveloped and developing countries have no access to these diagnostic tools.

When examinations expose significant effacement progression, there is a much higher risk for PB (and the shorter the cervix, the greater the risk). Nevertheless, diagnosing the condition remains “tricky” and controversial with regard to treatment strategies. One benefit of having early warning that the cervix is changing and preterm delivery is likely, is the opportunity to utilize corticosteroids, which helps minimize health problems in premature babies. But this does not remedy the condition or reduce the risk of un-survivable PB.

Unfortunately, existing treatment for IC is not well refined, has questionable effectiveness (for those fortunate to be diagnosed in sufficient time), and has numerous possible complications. In most all cases, extended bed confinement (as much as four months or more) is necessary to assure the best possible outcome. Even with the procedural treatments, bed confinement and extended hospitalization can be necessary.

The single currently available surgical treatment for IC, known as cerclage (“Cerclage”), involves a spinal or epidural anesthetic and strong post procedural medication to prevent miscarriage related directly to the procedure (all adding to the unborn infant’s health risks). During this most primitive of procedures, the very fragile tissue of the cervix is literally stitched closed with a strong thread. If the procedure itself does not act as a catalyst to spontaneous preterm delivery, at about the ninth month of pregnancy (or sooner if labor begins), the stitches are removed to prepare for vaginal delivery. The entire procedure and outcome is highly problematic and, ultimately (after all the risk and complication), most infants are delivered by caesarian procedure.

Clearly, the underprivileged and those from underdeveloped and many developing countries have no chance of obtaining the medical assistance necessary to cope with the complications of IC. Unfortunately, the loss of a child in these cases is all too often ignored as the commercialization of science and technology tends to empowered populations, never missing a step or considering the human tragedy at such a level. The approach and technology of TechDyne / ViaTechMD is different.

3a. Incompetent Cervix – Data Notation

Disjointed studies and research noted summarily by this paper further complicate the vast accumulations of blurred statistical data cloaking IC's contribution to this serious healthcare issue. It is therefore necessary that research be directed at singling out areas of primary influence to PB (such as IC), and toward affecting immediate solutions to abate the human suffering and significant socioeconomic factors to this overwhelming and growing global healthcare problem. Additional layers of bureaucracy will not get the job done!

The research and development, subject of this paper and efforts underway at TechDyne / ViaTechMD, is aimed squarely at refining statistical data, early recognition of specific risk factors (specifically IC), development of advanced treatment for IC, and early intervention – all promising to significantly reduce infant mortality and the serious complications facing a growing number of infants surviving PB.

It is of prominent concern that data remains a “confused cluster”, hiding the significance of individual factors such as IC which overlap a number of other individual conditions and thereby posing challenges toward understanding and improving global neonatal healthcare. For example, interpolations are complicated by the data commonality of low birth weight (“LBW”) which can also be associated with social and cultural risk factors (that influence overall prevalence and severity of these conditions).

The prevalence of LBW (birth weight of less than 2500 grams), as estimated by data from the World Health Organization (“WHO”) for 1995-1999, indicate that 20.4 million LBW infants were born each year and that LBW affects 17 percent of neonates in developing countries and 6 percent in developed countries (Save the Children, 2001). An infant may be LBW as a result of either intrauterine growth restriction or preterm delivery. However, no data is available to determine the cause rate of preterm delivery specific to individual factors such as IC and therefore, diagnosis and treatment remains insufficient and underdeveloped.

4. Consequences of Survived Preterm Birth – Largely Preventable by Improved Device-Based Treatment

Infants surviving PB all too often face lifelong debilitating diseases including autism, cerebral palsy, blindness and various other crippling disabilities. Moreover, very preterm infants (those born between 24 and 31 weeks) are five times as likely as full term infants to have a serious birth defect. The most common birth defects for this group were central nervous system defects, such as spina bifida, and cardiovascular defects, such as a hole in the heart.

The human toll is heartbreaking; the socioeconomic cost is measured in many tens of millions of dollars annually. Research is necessary to extrapolate more exacting datum and to develop targeted treatment (as is the focus of this paper as it relates specifically to

IC). To this point, due to overshadowing attention and funding for specific ‘headline diseases’ (rather than contributing causes such as IC), funding from private, institutional, and governmental resources in this specific area of critical research and development is nearly unrecognizable.

4a. Autism – Directly Related to Preterm Birth

Autism is a brain development disorder characterized by impaired social interaction and communication, and by restricted and repetitive behavior. According to the most recent fact-finding, compiled from sources including the National Institutes of Health, the Centers for Disease Control and Prevention, the U.S. Department of Education, and the Autism Society of America, autism is the fastest growing developmental disease (which correlates with the growing incidence of PB birth due specifically to IC).

While research in this critical area is limited at this time, a very recent U.S. study (released by the Journal of Pediatrics on 01/28/09) focused on children born more than three months prematurely provided fresh evidence supporting the thesis of this paper – including the link between PB birth and autism. Those children were found to be two to three times more likely to show signs of autism at age 2 (as measured in a standard screening tool compared to other children).

Autism refers to a group of developmental problems known as autism spectrum disorders that appear in early childhood and impair the ability to communicate and interact with others. Early research suggesting a link between PB and Autism followed 988 U.S. children born very prematurely, at least three months before their due date. At age 2, the children were evaluated using a screening method in which they are rated on a checklist of 23 behaviors for signs of autism. This tool flags children who may have autism but is not considered a definitive diagnosis. While more typically, a formal diagnosis of autism does not occur until around age 3, in this study, less than 6 percent of infants born full term screened positive for possible autism, while 21 percent of infants born preterm scored positive.

Even with this dramatic evidence, researchers remain confused, partially because preterm infants may also demonstrate certain developmental problems unrelated to autism that could trigger a positive score. For example, researchers typically excluded children with motor, vision and hearing impairments. Even after doing that, 16 percent of the preterm infants scored positive for possible autism. Moreover, after also excluding infants with cognitive impairment on the premise that it may not be autism related, about 10 percent of the preterm children still had a positive screening score. What researchers are likely missing is the fact that multiple disorders are possible as a result of PB (just as multiple injuries to an individual are possible as a result of a single automobile accident). Confused research or not, it is very clear that PB is associated with a long list of health risks for infants.

About 1 in 150 U.S. children has an autism spectrum disorder, according to U.S. government figures. The socioeconomic consequences of autism, all told exceed \$90 billion annually (U.S. only).

4b. Cerebral Palsy – Directly Related to Preterm Birth

Healthcare organizations and researchers agree that the strongest predictor of cerebral palsy is PB. Cerebral palsy (CP) is an umbrella term encompassing a group of nonprogressive, noncontagious conditions that cause physical disability in human development. Cerebral refers to the cerebrum, which is the affected area of the brain (although the disorder most likely involves connections between the cortex and other parts of the brain such as the cerebellum), and palsy refers to disorder of movement. CP is caused by damage to the motor control centers of the developing brain and most often occurs during pregnancy and childbirth.

CP is a nonprogressive disorder, meaning the brain damage does not worsen, but secondary orthopedic difficulties are common. For example, onset of arthritis and osteoporosis can occur much sooner in adults with cerebral palsy. In addition, motor disorder(s) may be accompanied by disturbances of sensation, cognition, communication, perception, and/or behavior, and/or by a seizure disorder.

An infant can develop cerebral palsy for many reasons; however, the leading cause of cerebral palsy is brain injury from premature birth. Because preterm infants are born with less developed lungs, specifically including those cases related to IC, they are at higher risk for brain injury from lack of oxygen. In fact, preterm infants are 8 times more likely to develop cerebral palsy than are full term infants. The most common cause of brain injury in preterm infants is an infection or lack of oxygen causing periventricular leukomalacia (PVL), which is characterized by the softening death of the white matter of the brain. PVL is caused by a lack of oxygen or blood flow to the periventricular area of the brain, which results in the death or loss of brain tissue. This increases the risk of asphyxia and other injury to the brain, which in turn increases the incidence of cerebral palsy. Approximately 60-100 percent of infants with PVL later develop signs of CP.

There is no known cure for CP and medical intervention is limited to the treatment and prevention of complications arising from its effects. A 2003 study put the economic cost for CP sufferers in the U.S. alone at \$921,000 per case – over \$9 billion annually. For the unattended underprivileged and those from underdeveloped and developing countries the condition leads to lifelong human tragedy!

4c. Other Disabilities – Directly Related to Preterm Birth

PB is also known to lead to other developmental disabilities (DD); chronic conditions that initially manifest in persons less than 18 years of age and result in impairment of physical health, mental health, cognition, speech, language, and self-care. The majority of persons with DD require long-term supportive care or services. In 2003, the Centers for

Disease Control, along with Research Triangle Park, North Carolina analyzed data from multiple surveys and reports to estimate the direct and indirect economic costs associated with DD in the U.S. On the basis of that analysis, estimated lifetime costs in 2003 dollars are expected to total \$51.2 billion for persons born in 2000 with mental retardation, \$11.5 billion for persons with cerebral palsy, \$2.1 billion for persons with hearing loss, and \$2.5 billion for persons with vision impairment.

5. Socioeconomic Costs Related to Preterm Birth and its Consequences

The March of Dimes reports that in order to cope with this growing crisis, families, health plans and employers in the U.S. pay out more than \$11 billion annually. Therefore, in addition to the increases in diagnosed chronic diseases, employers now need to be concerned about the rise in preterm labor deliveries and number of infants born at very low birth weights.

Further driving the mounting costs related to PB are lengthy hospitalizations in neonatal intensive care units, which account for 75 percent of charges for pregnancy management. These occur ordinarily when infants are born with LBW of 2,500 grams or less, and in the extreme, when born with very LBW of 1,500 grams or less.

Based on a report by the U.S. Agency for Healthcare Research and Quality, while the cost per discharge of a normal newborn is just over \$1,000, the medical costs related to very LBW infants average more than \$79,000.

According to the Emory Center on Health Outcomes and Quality, hospitalization costs for women with high-risk pregnancies amount to \$36 million annually in the U.S., with that patient base then leading to an estimated \$5 billion spent to hospitalize newborn infants in neonatal intensive care units.

Even more alarming is the fact that some babies can cost a family, company, or health plan (Payers) millions of dollars if they are born extremely premature. A baby born just a few weeks shy of the ideal gestation period of 37 weeks could cost as little as \$4,733 while an infant born eight weeks early could increase that cost to \$49,540.

In the case of a birth a few weeks earlier, critical infant care could bring the total to over \$1 million (and that does not include the 25 percent of the youngest and smallest babies who suffer from long-term health problems after they are released from the hospital).

6. The Promise of Improved Diagnosis and Device-Based Preventative Treatment offered by TechDyne / ViaTechMD

Our patent pending medical device technologies promises to save the lives of more than 15 million children who otherwise die each year from complications related to PB -- and

to reduce new cases of autism, cerebral palsy, blindness and other crippling disease by up to 20% each year. Again, before considering the human / family emotion and suffering, this growing health problem, in socioeconomic terms, exceeds \$50 billion in losses each year.

Clearly, as conditions exist today, the underprivileged and those from underdeveloped and many developing countries have no chance of obtaining the medical assistance necessary to cope with conditions leading to PB or to treat surviving infants suffering related consequences. Unfortunately, the loss of a child's life or a lifetime of suffering, in these cases is all too often ignored as the commercialization of science and technology tends to empowered populations, never missing a step or considering the human tragedy at such a level. The approach and technology of TechDyne / ViaTechMD is different.

With timely funding necessary to finalize research and development necessary to fully perfect the advanced preventative treatment options in development at TechDyne / ViaTechMD now, very near term solutions are expected; promising to lift significant socioeconomic burdens and provide relief to extreme human suffering. Moreover, the advanced treatment solutions being developed by TechDyne / ViaTechMD are designed to be highly accessible (in terms of cost and distribution) and to require minimal professional supervision (so that the existing presence of world healthcare organizations will be able to reach deeply into underprivileged communities to offer this new hope for a better life).

Therefore, ongoing efforts at TechDyne / ViaTechMD are threefold; focusing not only on refining statistical data while extrapolating individual cause factors to unravel the confused cluster of existing datum, but also on improved diagnosis along with early intervention, as well as technological innovation toward immediate biophysical-based solutions to advanced preventative treatment. This work is directed toward mechanisms of birth and various physical factors they contribute to PB and its consequences. This focus on the "physical realm", aimed at significantly improving treatment and outcome, is well-founded direction, as biochemical knowledge in this area is lopsidedly well-defined; even as primitive procedural treatments available today are ineffective and further disruptive to normal birthing (often contributing to, rather than preventing, PB and its consequences) – while also being unavailable to most of the world's population.

This is an opportunity for far reaching and near term success, in overcoming significant challenges to the wellbeing of tens of millions of infants and families in the U.S. and abroad, while lifting enormous and mounting socioeconomic burdens and further establishing U.S. technology and industry at the forefront of medical science and innovation in this field.

Respectfully submitted on behalf of TechDyne / ViaTechMD et al,

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