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I. INTRODUCTION

Newborn Screening Programs (NBS) have proven to be a successful model of public health intervention. Shortly after birth, a blood sample is taken from the heel of newborn babies and tested for certain conditions.[1] Analysis of the newborn's genome is used at the present time only for confirmation of a positive test from a newborn screen.[2] Whole Genome Sequencing (WGS) of newborns as a routine procedure, however, is the next progression in the development of newborn screening programs. The reason for this progression to a whole genome approach, according to the President's Commission on Bioethics, is "because the logic of personalized medicine and of technological progress will inexorably demand it."[3] Further, the interest among parents exists for such a program to develop.[4] This article examines the history of current newborn screening programs and looks beyond into the potential for expansion into WGS as a newborn screening method. Benefits from WGS of newborns could reap enormous benefits for public health research for disease prevention and health promotion. Expansion into new scientific areas is never easy and will require a consideration of ethical and legal constructs and changes in state statutory law. This article looks at policy considerations that will necessarily be examined and addressed for a shift from the current blood spot program to a WGS approach.

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1. PRESIDENT'S COUNCIL ON BIOETHICS, THE CHANGING MORAL FOCUS ON NEWBORN SCREENING: AN ETHICAL ANALYSIS BY THE PRESIDENT'S COUNCIL ON BIOETHICS 6-7 (2008), *available at* https://repository.library.georgetown.edu/bitstream/handle/10822/548394/newborn_screening.pdf?sequence=1.

2. *See id.* at 9.

3. *Id.* at 56.

4. *See* Aaron J. Goldenberg et al., *Parents' Interest in Whole-Genome Sequencing of Newborns*, 16 GENETIC IN MED. 78, 80 (2014). A recent study done of parents throughout the U.S. found that over seventy percent of parents surveyed would be definitely or somewhat interested in utilizing WGS if offered through a state's newborn screening program. *Id.*

II. NEWBORN SCREENING PROGRAMS

Newborn Screening Programs are essential to public health practice in the United States. Through NBS programs, early identification and treatment of disease can reduce childhood morbidity and mortality rates by providing an opportunity for early intervention and treatment.[5] The Centers for Disease Control and Prevention (CDC) have recognized NBS as playing an important role in public health achievements in the first ten years of the twenty-first century.[6]

While programs vary between states, newborn screenings generally involve a blood test and a hearing test.[7] The first heel stick blood sample is performed between twenty-four and forty-eight hours of the newborn's birth, preferably before the newborn leaves the hospital.[8] A second screening is sometimes conducted between ten days and two weeks following birth, traditionally at the newborn's health care provider's office.[9] In some states, pulse oximetry is performed to test for critical congenital heart disease.[10] Today, state health labs throughout the United States screen approximately four-million babies annually as part of NBS programs.[11] Of these four-million newborns, close to 12,500 are diagnosed with one of the twenty-nine conditions that are universally tested for in every state through NBS programs.[12]

State NBS programs date back to the early 1960s, when newborn screening was created to test infants for phenylketonuria (PKU).[13] PKU is caused by a gene mutation that that interrupts the enzyme which breaks down phenylalanine, and the subsequent buildup of the substance in the body can

5. Ctrs. for Disease Control & Prevention, *CDC Grand Rounds: Newborn Screening and Improved Outcomes*, 61 MORBIDITY & MORTALITY WKLY. REP. 390, 390 (2012), *available at* http://www.cdc.gov/mmwr/pdf/wk/mm6121.pdf.

6. Ctrs. for Disease Control & Prevention, *Ten Great Public Health Achievements - United States, 2001-2010*, 60 MORBIDITY & MORTALITY WKLY. REP. 619, 620 (2011), *available at* http://www.cdc.gov/mmwr/pdf/wk/mm6019.pdf.

7. Nat'l Insts. of Health, *How are newborn screening tests done?* (reviewed Apr. 12, 2013), http://www.nichd.nih.gov/health/topics/newborn/conditioninfo/Pages/how-done.aspx.

8. *Id.*

9. *Id.*

10. Nat'l Newborn Screening & Genetics Res. Ctr., *National Newborn Screening Status Report* (updated Jan. 6, 2013), http://genes-r-us.uthscsa.edu/sites/genes-r-us/files/nbsdisorders.pdf; *How are newborn screening tests done?*, *supra* note 7.

11. Bill Malone, *Newborn Screening at a Crossroads: What Happens if Congress Waits to Act?*, CLINICAL LABORATORY NEWS (2013), http://www.aacc.org/publications/cln/2013/august/Pages/Newborn-Screening.aspx. The four-million babies screened account for more than ninety-eight percent of the babies born in the U.S. *CDC Grand Rounds: Newborn Screening and Improved Outcomes*, *supra* note 5.

12. *CDC Grand Rounds: Newborn Screening and Improved Outcomes*, *supra* note 5.

13. PRESIDENT'S COUNCIL ON BIOETHICS, *supra* note 1, at 1; Malone, *supra* note 11.

cause serious defects including permanent severe retardation.[14] Notably, a special diet absent of this substance allows affected children to entirely avoid these consequences and live a healthy life.[15] Early detection is the key to their health and quality of life. Dr. Robert Guthrie thus developed a screening test for PKU that involved pricking the foot of a newborn and collecting and transporting the blood samples on filter paper.[16]

Massachusetts was the first to launch a voluntary newborn screening program for PKU in 1962, and its program demonstrated the feasibility of mass screening.[17] Multifarious advocacy campaigns led most states to pass laws mandating PKU screening soon thereafter.[18] Forty-three states had programs in place by 1973, with panels expanding to include other actionable conditions, and state health departments generally assumed the central role in the laws' implementation.[19] The programs' federal support grew with the passing of federal legislation to support screening in 1976, the establishment of the CDC's Newborn Screening Quality Assurance Program (NSQAP) in 1978, and the award of federal funding to thirty-four state genetic service programs between 1979 and 1980.[20] Federal involvement in the development of newborn screening programs has continued, with the NSQAP steadily adding disorders to its program, which is devoted to quality assurance and state public health assistance.[21]

Though testing for PKU caught on quickly, the expansion of testing for additional conditions through NBS programs grew slowly. In 2002, the Maternal and Child Health Bureau and the Health Resources Services Administration (HRSA) of the U.S. Department of Health and Human Services commissioned a report from the American College of Medical Genetics (ACMG) to analyze the effectiveness of newborn screening, develop recommendations for a uniform list of conditions that should be included, and

14. Mayo Clinic, *Phenylketonuria (PKU) – Definition* (Nov. 17, 2011), http://www.mayoclinic.org/diseases-conditions/phenylketonuria/basics/definition/con-20026275; Mayo Clinic, *Phenylketonuria (PKU) – Symptoms* (Nov. 17, 2011), http://www.mayoclinic.org/diseases-conditions/phenylketonuria/basics/symptoms/con-20026275.

15. Univ. of Wash., *See What is the Diet for PKU?*, http://depts.washington.edu/pku/about/diet.html (last visited May 22, 2014).

16. LORI B. ANDREWS ET AL., GENETICS: ETHICS, LAW & POLICY 381 (3d ed. 2010). The "Guthrie test" was the prominent method of newborn screening for decades until its recent widespread replacement with tandem mass spectrometry. *Id.*

17. *Id.*

18. *Id.* at 382.

19. *Id.*

20. *Id.*

21. U.S. DEP'T OF HEALTH & HUMAN SERVS. ET AL., *Newborn Screening Laboratory Bulletin* (Oct. 2008), http://www.cdc.gov/nbslabbulletin/bulletin.html. The NSQAP program included one disorder at its inception in 1978, eight disorders in 1988, seventeen disorders in 1998, and forty-eight disorders by 2008. *Id.*

consider other critical components of achieving positive outcomes for screened children.[22] The report, issued in 2005, recommended the use of the new technology to expand screening capabilities and include more conditions in newborn panels.[23] The most influential part of the ACMG's report was its "core panel" of twenty-nine conditions, identified as primary screening targets, and its additional twenty-five "secondary targets."[24]

The Federal Newborn Screening Saves Lives Act (NSSLA) was passed in 2008, three years after the ACMG's statement. At the time of its passage, state-mandated NBS panels still included as few as nine conditions, despite the ACMG's recommended minimum of twenty-nine.[25] The NSSLA expanded the duties of HRSA to take the lead in developing uniform recommendations for screening and to assist states in satisfying these goals.[26] Meeting the HRSA's guidelines was made a prerequisite for receiving certain grant funding to states, made available by the Act for education and training, development of screening programs, genetic counseling, and post-diagnostic treatment.[27] Finally, the Act assigned the Secretary's Advisory Committee on Heritable Disorders in Newborns & Children (SACHDNC) the role of creating a "Recommended Uniform Screening Panel" and a decision-matrix to apply to future disorders in question, and it created an inter-agency committee to provide guidelines for how the samples and information are handled.[28] The Act is currently up for reauthorization.[29] As of late May 2014, the Newborn Screening Saves Lives Reauthorization Act of 2013 had passed the U.S. Senate and was referred to the U.S. House Committee on Energy and Commerce.[30]

The SACHDNC's Recommended Uniform Screening Panel consists of thirty-one disorders.[31] Traditionally, testing has only been done for actiona-

22. Am. Coll. of Med. Genetics, *Newborn Screening: Toward A Uniform Screening Panel and System* 7 (2005), http://www.hrsa.gov/advisorycommittees/mchbadvisory/heritabledisorders/uniformscreening.pdf; *see* Michael S. Watson et al., *Newborn Screening Panel and System*, 8 GENETICS IN MED. 12S, 12S (2006), *available at* https://www.acmg.net/resources/policies/NBS/NBS_Main_Report_00.pdf.

23. *Newborn Screening: Toward A Uniform Screening Panel and System*, *supra* note 22, at 84.

24. Watson, *supra* note 22, at 14S.

25. Malone, *supra* note 11. Based on the minimal increase in panel size in the three years following ACMG's statement, federal action appears to be a potentially more effective catalyst for expansions than the recommendation of persuasive scientific authorities.

26. *See* Newborn Screening Saves Lives Act of 2007, Pub. L. 110-204, 122 Stat. 705 (2008).

27. § 2, 122 Stat. at 705-6.

28. § 4, 122 Stat. at 707.

29. Newborn Screening Saves Lives Reauthorization Act of 2013, S. 1417, 113th Cong. (referred to House Committee on Energy and Commerce Subcommittee on Health, Feb. 7, 2014).

30. *Id.*

31. Baby's First Test, *About Newborn Screening: Conditions Screened by State*,

ble conditions, such as PKU or hypothyroidism.[32] However, there has been a notable shift in recent years, turning away from screening only if testing may bring immediate benefit to the child, to an approach of testing for non-actionable conditions. This shift is demonstrated by the inclusion of Cystic Fibrosis,[33] a non-treatable condition that the Cystic Fibrosis Foundation explicitly recommended against including in NBS panels in 1983.[34] Though only six states mandated testing for Cystic Fibrosis just five years ago, all fifty states now do so.[35] While uniformity of newborn screening programs has increased overall with federal efforts, state laws surrounding newborn screening implementation still differ significantly.[36]

All fifty states conduct screening of newborns shortly after birth.[37] In 2013, state NBS panels ranged from testing for thirty-one to fifty-five conditions, with every U.S. state testing for at least all twenty-nine of the ACMG's core panel disorders.[38] Minnesota and New Jersey mandate the largest NBS panel, requiring fifty-five conditions to be tested.[39] These large panels are a huge and rapid leap from the small six-condition panel used by forty-six states as recently as ten years ago.[40] The adoption of new technologies, such as tandem mass spectrometry (MS/MS), which allows multiple conditions to be tested rapidly from the same sample, have been instrumental in the rapid growth of NBS programs.[41]

Other than panel size, one key variance among states is the cost to par-

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http://www.babysfirsttest.org/newborn-screening/states (last visited May 22, 2014).

32. *See* Ctrs. for Disease Control & Prevention, *Newborn Screening* (updated May 13, 2013), http://www.cdc.gov/ncbddd/pediatricgenetics/newborn_screening.html. While PKU is mitigated with a special diet, the effects of slowed growth and brain damage that accompany hypothyroidism can be avoided by early use of hormone treatment through medication. *Id.* Other conditions that are not as easily treated early, but are included in panels, have secondary benefits from early identification, such as increased protections to compensate for vulnerability to infection that occurs with sickle cell anemia. *Id.*

33. *See* Cystic Fibrosis Found., *Why are Newborns Screened for CF?* (updated Jan. 31, 2014), http://www.cff.org/AboutCF/Testing/NewbornScreening/ScreeningforCF/.

34. Lynn M. Taussig et al., *Committee Report: Neonatal Screening for Cystic Fibrosis*, 72 PEDIATRICS 741, 744 (1983).

35. *Why are Newborns Screened for CF?*, *supra* note 33.

36. *About Newborn Screening: Conditions Screened by State*, *supra* note 31.

37. Suzanne T. Kotkin-Jaszi & John E. Sherwin, *Newborn Screening: The Tandem Mass Spectrometry Revolution*, CLINICAL LABORATORY NEWS (2011), http://www.aacc.org/publications/cln/2011/June/Pages/NewbornScreening.aspx.

38. Malone, *supra* note 11; *see National Newborn Screening Status Report*, *supra* note 10; *About Newborn Screening: Conditions Screened by State*, *supra* note 31.

39. *See National Newborn Screening Status Report*, *supra* note 10.

40. Jeffrey R. Botkin, *Whole Genome Sequencing in Newborn Screening: What are we testing for?*, NAT'L HUMAN GENOME RESEARCH INST. (Apr. 25, 2013), www.genome.gov/Multimedia/Slides/HGP10Symposium/06_Botkin.pdf.

41. Kotkin-Jaszi & Sherwin, *supra* note 37. As early as 2011, all forty-nine states that used MS/MS technology required testing for no fewer than 30 medical conditions. *Id.* at Fig. 1.

ents. Currently, fees to newborns' parents range from zero to over $150, with some states requiring repeat tests or charging by the specimen.[42] These charges do not reflect the full cost of running the panels, which is largely subsidized by the state and other funding sources.[43]

Another key difference between states is the parental requirement to either opt-in or opt-out of newborn screenings. A majority of states allow parents to opt-out of screenings.[44] In seven states, parents can opt-out for any reason, while in all but four states the parents may opt-out on religious grounds.[45] The requirement for informed consent also varies, as only eleven states require parents to be informed of the screening before it occurs, and only two require consent to be given before testing may commence.[46] Additionally, requirements for the storage and use of residual blood samples acquired through newborn screening vary tremendously.[47] Three states permit the destruction of a child's blood sample if requested by that child upon reaching adulthood.[48] Twenty states have laws that address the retention or use of residual dried blood samples from newborn screening.[49] In four of those states, the blood samples remain the property of the state.[50] On the other hand, in ten states, the laws provide specific purposes for which dried blood sample information may be utilized, including for public health purposes or research.[51]

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42. *See* Nat'l Newborn Screening & Global Res. Ctr., *Newborn Screening* (updated Oct. 4, 2013), http://genes-r-us.uthscsa.edu/resources/consumer/statemap.htm (click links for individual states). Kansas, Pennsylvania, New York and the District of Columbia offer NBS free of charge, while Rhode Island charges the highest amount at $157.54. *Id.* Texas charges parents per each mandated specimen ($29.50). *Id.* Arizona, requires two rounds of testing. *Id.*

43. *See id.*

44. Michele Caggana et al., *Newborn Screening: From Guthrie to Whole Genome Sequencing*, 128 PUB. HEALTH REPS. (SUPPLEMENT 2) 14, 16 (2013).

45. Michelle H. Lewis et al., *State Laws Regarding the Retention and Use of Residual Newborn Screening Blood Samples*, 127 PEDIATRICS 703, 707 (2011); PRESIDENT'S COUNCIL ON BIOETHICS, *supra* note 1, at 88.

46. Maryland, Wyoming, and the District of Columbia require informed consent. PRESIDENT'S COUNCIL ON BIOETHICS, *supra* note 1, at 89. However, the manner in which these three states require informed consent differs. Maryland requires informed consent through regulation, while Wyoming and the District of Columbia both require parental consent through statute. *Id.* at 89-90, n.10.

47. A small amount of blood remains on the paper card following a newborn screening, and this card with the residual blood spot is sometimes stored for future laboratory use. Caggana, *supra* note 44, at 17.

48. Michelle H. Lewis et al., *State Laws Regarding the Retention and Use of Residual Newborn Screening Blood Samples*, 127 PEDIATRICS 703, 707 tbl. 1 (2011).

49. *Id.* at 706 tbl. 1.

50. *Id.*

51. *Id.*

III. LEGAL CHALLENGES TO NBS PROGRAMS

The constitutionality of mandating NBS against parents' objections has been challenged and upheld by the courts.[52] In 2005, Nebraska's Supreme Court upheld the state's newborn testing program when challenged by parents who claimed that mandatory testing violated their constitutional rights based on their religious objections.[53] In the county's action to compel the parents' compliance, the court, held that the State's interest in infant screening as a means to protect the health and welfare of all children satisfied the compelling interest standard and was thus constitutional.[54]

A lawsuit filed in 2009 by twenty-one families against the Minnesota Department of Health alleged that the collection, use, storage, and dissemination of residual blood spots and test results violated the Minnesota State Genetic Information Act of 2006 due to a lack of parental consent.[55] The Minnesota Supreme Court held that use of residual blood spots and test results beyond the initial screening was not authorized by statute.[56] In 2012, the Minnesota legislature passed a bill requiring all negative test results be maintained for seventy-one days and then destroyed, unless parental consent to retain the blood spot for a longer period was received.[57] In January 2014, Minnesota settled the lawsuit over its storage and use of newborn screening residual dried blood spots.[58] As a result of the settlement, the state began the process of destroying 1.1 million archived blood spots and test results that had been collected prior to the November 2011 ruling by the Minnesota Supreme Court.[59] However, in May 2014, the Minnesota legislature passed a bill, repealing the 2012 law, allowing the Department of Health to keep samples and negative test results indefinitely for certain newborn screening activities, unless parents provide informed consent revoking authority.[60]

A lawsuit filed in Texas challenged the collection of blood spots.[61] Five

52. *See, e.g.*, Douglas Cnty. v. Anaya, 694 N.W.2d 601, 608 (Neb. 2005), *cert. denied*, 546 U.S. 826 (2005).

53. *Id.*

54. *Id.*

55. Bearder v. Minn., 806 N.W.2d 766, 769 (Minn. 2011).

56. *Id.* at 776. The court remanded the case to the district court for further fact finding in order to determine the appropriate remedy. *Id.* at 777.

57. 2012 Minn. Sess. Law Serv. Ch. 292 (H.F. 2967) (West, WestlawNext).

58. Press Release, Minn. Dep't of Health, Lawsuit settlement allows newborn screening program to move forward (Jan. 13, 2014), http://www.health.state.mn.us/news/pressrel/2014/newbornscreening011314.html.

59. *Id.*

60. 2014 Minn. Sess. Law Serv. Ch. 203 (S.F. 2047) (West, WestlawNext). The new law becomes effective August 1, 2014. *Id.*

61. First Amended Complaint, Beleno v. Tex. Dep't. of State Health Servs., No. SA-09-CA-188-FB (W.D. Tex. Sept. 29, 2009), ECF No. 45; Press Release, Parents Sue Texas

families sued the Texas Department of Health Services and Texas A & M University System, asserting the collection and storage of newborn blood samples for research purposes, without parental consent, was an unreasonable search and seizure and violated constitutional principles.[62] The Texas legislature later enacted a statute requiring that parents be made aware that their newborn's genetic information may be retained by the Department of Health Services for research purposes unless the parent, in written form, requests otherwise.[63] The state agreed as part of settling the *Beleno* case to destroy approximately five-million blood samples obtained prior to the settlement of the lawsuit.[64]

IV. WHOLE GENOME SEQUENCING

Whole Genome Sequencing, the ability to acquire an individual's entire set of genetic information with one test, is anticipated to be a "game changer" in medical research and clinical treatment, creating profound implications for science, public health, and law.[65] In 2004, the federal government set a $1000 goal for sequencing a complete human genome, and that goal was met even more quickly than the challenge anticipated.[66] The technology push continues to drive down the time and cost of WGS and bring it closer to affordable commercial use.[67] In particular, for applications that currently use genetic testing (such as NBS), sequencing technology will soon be more efficient and cost-effective than a slew of individual tests that range in cost from several hundred to several thousand dollars each.

Health Dept. and Texas A&M over Infant Blood Databank (Mar. 18, 2009), http://www.texascivilrightsproject.org/1096/parents-sue-texas-health-dept-and-texas-am-over-infant-blood-databank.

62. Amended Complaint, *supra* note 61 at ¶ 23; Ann Waldo, *The Texas Newborn Bloodspot Saga has Reached a Sad – and Preventable – Conclusion,* GENOMICS LAW REPORT (Mar. 26, 2010), http://www.genomicslawreport.com/index.php/2010/03/16/the-texas-newborn-bloodspot-saga-has-reached-a-sad-and-preventable-conclusion.

63. TEX. HEALTH & SAFETY CODE ANN. §§ 33.0111, 33.018 (West, WestlawNext through 2013 Third Called Session of the 83rd Legislature).

64. Jay Root, *Texas officials agree to destroy babies' blood samples after settling lawsuit,* DALLAS NEWS (Feb. 14, 2010), http://www.dallasnews.com/news/state/headlines/20091223-Texas-officials-agree-to-destroy-babies-1751.ece.

65. *See* Gary E. Marchant & Rachel A. Lindor, *The Game Changer: Whole Genome Sequencing*, BIOTECH BRIEFING, Fall 2011, at 3-4, http://www.americanbar.org/content/dam/aba/publications/emerging_news/biotech_briefing_fall2011.authcheckdam.pdf.

66. *Id.* at 1-2; Andrew Pollack, *The Race to Read Genomes on a Shoestring, Relatively Speaking*, N.Y. TIMES, Feb. 9, 2008, at C1. In 2012, LifeTechnologies introduced a sequencer that can sequence a whole genome in less than twenty-four hours, for less than $1000. Press Release, LifeTechnologies, Life Technologies Introduces the Benchtop Ion Proton Sequencer; Designed to Decode a Human Genome in One Day for $1,000 (Jan. 10, 2014), http://www.lifetechnologies.com/us/en/home/about-us/news-gallery/press-releases/2012/life-techologies-itroduces-the-bechtop-io-proto.html.html.

67. Marchant & Lindor, *supra* note 65, at 2.

Recognizing these changes, in 2013 the National Institutes of Health (NIH) granted $5 million each to four recipients to research genomic sequencing and newborn screening disorders."[68] As of September 2013, the four grant recipients were researching methods for making newborn information available as a resource for parents and medical providers,[69] the benefits of using larger and faster sequencing in Neonatal Instensive Care Units,[70] the value of additional information gained by exome sequencing of currently screened disorders,[71] and the ethical, legal, and social implications for informed consent and the return of results to parents.[72] The NIH's large investment in these grants demonstrates that an expansion of newborn screening is an influential current consideration, but that issues with such a proposal have been anticipated and warrant careful research and consideration. Certain organizations, such as the American Academy of Pediatrics (AAP), have voiced support in favor of mandatory genetic screening of all newborns.[73]

V. HEALTH APPLICATIONS OF WHOLE GENOME SEQUENCING FOR NEWBORN SCREENING

A. Benefits for Individual Health

The WGS of newborns has the potential to revolutionize disease detection, prevention, and treatment, resulting in radical changes to public health practice and research. With the use of WGS on newborns, "[p]ersonalized genomic medicine will then start from the moment of birth, as the [child's health care provider] will be in possession of a complete map of each young patient's known genetic defects, vulnerabilities, and susceptibilities."[74] Rare

68. Nat'l Insts. of Health, *News & Events: NIH program explores the use of genomic sequencing in newborn healthcare* (Sept. 4, 2013), http://www.nih.gov/news/health/sep2013/nhgri-04.htm.

69. *Id.* (discussing Brigham and Women's Hospital in Boston, Massachusetts).

70. *Id.* (discussing Children's Mercy Hospital in Kansas City, Missouri).

71. *Id.* (discussing University of California, San Francisco). Exome sequencing selectively examines only the functionally important sequences of DNA that are translated into proteins (as opposed to the entire sequence of DNA, of which only 1.5% is actually expressed). *See* Leah Eisenstadt, *What is Exome Sequencing?* (Oct. 15, 2010), http://www.broadinstitute.org/blog/what-exome-sequencing.

72. *News & Events: NIH program explores the use of genomic sequencing in newborn healthcare*, *supra* note 68 (discussing University of North Carolina at Chapel Hill).

73. *See, e.g.*, AM. ACAD. OF PEDIATRICS, *AAP Issues New Guidance on Genetic Testing of Children* (Feb. 21, 2013), http://www.aap.org/en-us/about-the-aap/aap-press-room/pages/AAP-Issues-New-Guidance-on-Genetic-Testing-of-Children.aspx.

74. PRESIDENT'S COUNCIL ON BIOETHICS, *supra* note 1, at 55. Personalized medicine is an emerging field engendering the concept that medical care can and should be tailored to the genetic and molecular profile of the individual, and it aims to shift medical practices to proactive health management and customized care. *See generally* Edward Abrahams, Geoffrey S. Ginsburg & Mike Silver, *The Personalized Medicine Coalition*, 5 AM. J.

genetic disorders that in the past could have led to years of unnecessary testing and treatment due to misdiagnoses could now be discovered shortly following a child's birth.[75] Parents may also learn if their child is at an increased risk for certain childhood diseases and implement necessary prevention programs at an early age.

WGS on newborns could impact the individual and population's health in terms of disease treatment. One significant public health concern – pediatric adverse drug events (ADEs) – would be greatly impacted by a WGS on newborns.[76] Children are three times more likely to suffer from an ADE than adults, and over half a million children seek outpatient care for ADEs annually.[77] The field of pharmacogenomics offers the potential to reduce ADEs and to enhance the efficacy of pharmaceutical drugs by identifying gene variants that could affect a person's response to a drug.[78] With a whole genome in hand at a child's birth, such information may potentially reduce the number of dangerous pediatric ADEs by providing a personalized roadmap to how a child may respond to a medication prior to the medication's administration. This is especially important for pediatric cancer patients. Twenty-two percent of all hospital admissions for pediatric cancer patients are due to an ADE.[79] The consequences of an ADE in a pediatric cancer patient can be life-threatening or leave the patient with long-lasting disease or disabilities.[80] Gene variant identification can improve treatment outcomes for pediatric cancer patients by identifying which patients are at an increased risk for adverse reactions and manipulating the treatment plan

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PHARMACOGENOMICS 345 (2005). Public health genomics is an emerging field that seeks to utilize genetic variation and gene-environment interaction data to design and implement mechanisms to prevent disease and improve overall health status. M.J. Khoury et al., *A Decade of Public Health Genomics in the United States: Centers for Disease Control and Prevention 1997–2007*, 12 PUB. HEALTH GENOMICS 20, 21 (2009).

75. *See* PRESIDENT'S COUNCIL ON BIOETHICS, *supra* note 1, at 14; *see also* B.D. Solomon et al., *Applying Genomic Analysis to Newborn Screening,* 3 MOLECULAR SYNDROMOLOGY 59, 66 (2012). While positive movement in research and surveillance may occur, it is also important to note that negative repercussions may result from the WGS of newborns. PRESIDENT'S COUNCIL ON BIOETHICS, *supra* note 1, at 70. For example, there is potential for immense stress and anxiety from false positives or from positive tests for conditions that may never manifest. *See id.*

76. *See* Dennis J. O'Kane et al., *Pharmacogenomics and reducing the frequency of adverse drug events*, 4 PHARMACOGENOMICS 1, 3 (2003).

77. Florence T. Bourgeois et al., *Pediatric Adverse Drug Events in the Outpatient Setting: An 11-Year National Analysis,* 124 PEDIATRICS e744, e747-48 (2009); Donna Woods et al., *Adverse Events and Preventable Adverse Events in Children*, 115 PEDIATRICS 155, 158 (2005).

78. *See* Colin J.D. Ross et al., *Pharmacogenomics of Serious Adverse Drug Reactions in Pediatric Oncology*, 18 J. POPULATION THERAPEUTICS & CLINICAL PHARMACOLOGY e134, e144 (2011); Dennis J. O'Kane et al., *Pharmacogenomics and Reducing the Frequency of Adverse Drug Events,* 4 PHARMACOGENOMICS 1, 1 (2003).

79. Ross et al., *supra* note 78, at e134.

80. *Id.*

accordingly.[81]

Similarly, WGS results would be beneficial in relation to toxicogenomics. Toxicogenomics is an emerging technology that would allow scientists to predict whether certain people would be vulnerable to the effects of certain chemicals.[82] From birth, with information from a whole genome sequence, doctors and parents could ensure children were protected from exposure if vulnerability was found and modify a child's environment in response. This protection could continue from birth into adulthood to prevent unnecessary exposure and risk of potential deleterious health complications. For example, asbestos exposure led to a dramatic spike in cancerous mesothelioma, but this exposure only affected a fraction of individuals. It was later discovered that certain genetic traits were linked to development of the disease, and had that subpopulation been identifiable, avoiding exposure to the substance could have significantly reduced the cancer incidence.[83]

Not only could information improve a child's health, but certain results could also provide needed health information for a child's parent. For example, a child may have inherited a late-onset disorder from a parent, and the parent may not yet exhibit symptoms at the time of the child's birth.[84] Such information may aid in the parent's diagnosis and further treatment of the disorder.[85] This would be most relevant in the early years of a whole genome newborn program, when adults may not have yet had a whole genome sequence of their own DNA.

The results of WGS may also improve individual disease prevention. By knowing in advance the diseases a person may be most susceptible to, prevention programs can be targeted to prevent disease development or severity.[86] For example, in cardiovascular disease, genomics plays a role in dis-

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81. *Id.* at e144.

82. *See* NAT'L RESEARCH COUNCIL COMM. ON APPLICATIONS OF TOXICOGENOMIC TECHS. TO PREDICTIVE TOXICOLOGY, APPLICATIONS OF TOXICOGENOMIC TECHNOLOGIES TO PREDICTIVE TOXICOLOGY AND RISK ASSESSMENT 1 (2007), *available at* http://www.ncbi.nlm.nih.gov/books/NBK10209. Toxicogenomics is defined "as the application of genomic technologies (for example, genetics, genome sequence analysis, gene expression profiling, proteomics, metabolomics, and related approaches) to study the adverse effects of environmental and pharmaceutical chemicals on human health and the environment." *Id.* at Box 1-1.

83. *See, e.g.*, Amy Powers & Michele Carbone, *The Role of Environmental Carcinogens, Viruses and Genetic Predisposition in the Pathogenesis of Mesothelioma,* 1 CANCER BIOLOGY & THERAPY 348 (2002); Michele Carbone & Haining Yang, *Molecular Pathways: Targeting Mechanisms of Asbestos and Erionite Carcinogenesis in Mesothelioma*, 18 CLINICAL CANCER RESEARCH 598 (2012).

84. O. M. Vanakker & A. De Paepe, *Pharmacogenomics in Children: Advantages and Challenges of Next Generation Sequencing Applications,* 2013 INT'L J. PEDIATRICS 1, 7 (2013).

85. *Id.*

86. *See* Bonnie Rochman, *Will my son develop cancer? Sequencing your kids' genomes* (updated Oct. 22, 2012, 10:05 AM), http://www.cnn.com/2012/10/22/health/sequence-children-genomes/index.html. While such testing may have the potential to provide predic-

ease prediction and identification of therapeutic targets.[87] Identification of certain genetic markers has already been associated with cardiovascular disease, and whole genomic sequencing could identify genes with previously unknown roles in the development of cardiovascular disease.[88] Additionally, genetic variant identification indicating an increased risk of cancer is now being utilized to influence disease screening, disease risk counseling, and preventive treatments.[89] In addition to disease prevention, WGS can be used to predict prognosis and treatment response in certain cancers.[90]

A reduction of risk from a common disease, such as cardiovascular disease, could affect many millions of individuals throughout the population.[91] In addition to the traditional focus on the risk of developing common diseases, the field of public health genomics could find dramatic success by expanding the focus to rare diseases.[92] This expansion could potentially identify millions of individuals who unknowingly carry mutations that predispose them to preventable disease.[93] One such example is Lynch syndrome.[94] Approximately 0.2% of individuals in the U.S. carry deleterious genetic mutations in any one of the four genes associated with Lynch syndrome.[95] These individuals are at a greater than 80% risk for colon cancer.[96] Knowing such cumulative information at a child's birth could lead to dramatic increases in disease prevention.

B. Benefits to Population Health

Besides benefits to the individual child or his parents, WGS of newborns could lead to advances in population health. The population's health as a

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tive results, some evidence has shown that current genomic profiling for disease risk may not be as effective as previously anticipated. *See* Glenn E. Palomaki et al., *Use of Genomic Panels to Determine Risk of Developing Type 2 Diabetes in the General Population: a Targeted Evidence-Based Review*, 15 GENETICS MED. 600, 609 (2013). This may improve, however, as research continues to evaluate combinations of genomic markers. *See, e.g.*, Glenn E. Palomaki et al., *Use of genomic profiling to assess risk for cardiovascular disease and identify individualized prevention strategies—A targeted evidence-based review*, 12 GENETICS MED. 772, 782 (2010).

87. Santhi K. Ganesh et al., *Genetics and Genomics for the Prevention and Treatment of Cardiovascular Disease: Update: A Scientific Statement from the American Heart Association*, 128 CIRCULATION 2813, 2813 (2013).

88. *Id.*

89. Cinnamon S. Bloss et al., *Genomics for Disease Treatment and Prevention*, 34 PSYCHIATRIC CLINICS N. AM. 147, 154-55 (2011).

90. *Id.* at 157.

91. James Evans et al., *We screen newborns, don't we?: realizing the promise of public health genomics*, 15 GENETICS MED. 332, 332 (2013); *see* Ganesh, *supra* note 87, at 2814-17.

92. Evans, *supra* note 91, at 332.

93. *Id.*

94. *Id.*

95. *Id.*

96. *Id.*

whole could benefit through research of disease trends through surveillance from data collected as a result of WGS of newborns.[97] Public health researchers could not only survey the current status of disease patterns, but also be able to research future population health needs.[98] Funding could be allocated to research diseases for which large groups of the population are known to be at risk. Instead of retrospective research of disease, studies could be done prospectively to advance further disease treatment.

Standardizing newborn WGS also has the potential to reduce health disparities throughout the population by improving and equalizing care. In particular, though all states are required to meet a federal minimum panel, most states have added additional conditions to their screenings. Thus, currently, children born in particular states receive more information than children located in a state testing for a smaller number of conditions. If WGS is implemented as the standard for population-wide newborn screening, its benefits would not be limited to certain residents in particular states or to those that can afford genomic testing.[99]

VI. POLICY CONSIDERATIONS FOR FUTURE IMPLEMENTATION OF A WGS APPROACH

All fifty states maintain a newborn screening program and statutory and regulatory laws govern how the programs operate. An overhaul of state law will therefore be necessary for a WGS newborn screening approach to exist. For certain disorders, such as PKU, current newborn screening testing may be more accurate than a DNA-based testing.[100] Therefore, WGS may be implemented alongside current newborn bloodspot screening, rather than replace it.[101] It may also be implemented in a manner allowing parents to select the WGS of their newborn child, in addition to the traditional heel stick exam.[102]

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97. Public health surveillance allows the public health community to monitor infectious and noninfectious diseases, birth defects, injuries, illicit drug use, mental illness, and occupational and environmental exposures. James W. Buehler, *Introduction*, 61 MORBIDITY & MORTALITY WKLY. REP. (SUPPLEMENT) 1, 1 (2012), *available at* http://www.cdc.gov/mmwr/pdf/other/su6103.pdf.

98. *See* Lawrence O. Gostin & James G. Hodge, Jr., *Genetic Privacy and the Law: An End to Genetics Exceptionalism*, 40 JURIMETRICS 21, 39 (1999) ("Carefully planned surveillance or epidemiological activities facilitate rapid identification of health needs.").

99. *See, e.g.*, Mark A. Rothstein, *The Case Against Precipitous, Population Wide, Whole-Genome Sequencing,* 40 J. L. MED. & ETHICS 682, 685 (2012) (explaining the concern for a lack of equitable access to genetic services when implementing population-wide whole genome sequencing).

100. Beth A. Tarini & Aaron J. Goldenberg, *Ethical Issues with Newborn Screening in the Genomics Era*, 13 ANN. REV. GENOMICS & HUM. GENETICS 381, 389 (2012).

101. *Id.*

102. *See* Yuval E. Landau et al., *Genomics in Newborn Screening*, 164 J. PEDIATRICS 14, 18 (2014); *see also How are newborn screening tests done?*, *supra* note 7 (explaining the

Lessons from the legal challenges and constraints from current newborn screening programs can guide policymakers in the development of necessary statutory changes in order to implement a WGS approach to newborn screening. Some of the issues that will need to be studied and considered include informed consent, the reporting of results, the storage, ownership, and use of genetic samples and data, privacy, and the constitutionality of a WGS mandate.

A. Informed Consent

While all states mandate newborn screening, a majority of states allow parents to opt-out of screenings if they object on religious or philosophical grounds.[103] Although the AAP supports mandatory genetic screening for all newborns, the AAP recommends parents be given the right to refuse newborn screening following information on benefits and risk of genetic testing and screening.[104] Most states do not currently require informed consent prior to the screening, and only approximately half of states require parents be given educational materials pertaining to the screening.[105] With the shift to WGS, more states may need to structure mandatory newborn screening programs to include an informed consent requirement and education regarding the results.[106] Information may include the risks to the actual testing, the WGS process, and the potential results in terms of genomic disorders and determination of disease risk.

B. Reporting of Results

One overarching legal and ethical issue when dealing with newborn health information includes deciding what information to provide to the newborn's parents and how specifically to deliver the information to the parents, especially if such information provides negative health consequences. Policymakers would need to consider whether results would include late or adult onset disorders, or only disorders for which a childhood onset manifests. The AAP currently discourages the practice of reporting late-onset disorders discovered through whole genome newborn screening.[107] In the ACMG's recommendations for reporting of incidental findings, however, the ACMG felt that the ethical concerns about providing the clinicians of children with genetic risk information about adult-onset dis-

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traditional process used for screening).

103. Botkin, *Whole Genome Sequencing in Newborn Screening*, *supra* note 40.

104. AM. ACAD. OF PEDIATRICS, *supra* note 73.

105. PRESIDENT'S COUNCIL ON BIOETHICS, *supra* note 1, at 89; Tarini & Goldenberg, *supra* note 100, at 385.

106. *See* O. M. Vanakker & A. De Paepe, *supra* note 84, at 6.

107. AM. ACAD. OF PEDIATRICS, *supra* note 73.

eases were outweighed by the potential benefit to the future health of the child and the child's parent of discovering an incidental finding for which intervention might be possible.[108] Thus, the ACMG recommended the reporting of incidental findings "not be limited by the age of the person being sequenced."[109]

C. Storage, Ownership, and Use

Another crucial consideration will be the issue of storage, ownership, and use of the samples and increased amount of genetic data gained from WGS.[110] The storage and use of residual blood spots are of prevailing debate and litigation, and the use of WGS will add an advanced dimension to the controversy, especially considering the increased amount of personal information that will be contained in the results. Policymakers would need to examine such issues as whether the state should retain genetic data generated from WGS for use in future research, and if so, whether an opt-in or opt-out approach for parents to decide if their newborn's data could be utilized for future research would be most appropriate.[111] Further considerations include who shall gain ownership over the samples and resulting data (possibly the state itself); the type and number of entities that will be granted access to the data for research purposes; how long the data should be maintained; and who should maintain oversight of the data.[112]

D. Privacy

Privacy of health information is of preeminent concern. Genetic information has the potential for abuse, and information about a newborn's health could negatively follow the child throughout their lifetime.[113] This concern for the protection of the privacy of genetic information has been reviewed and studied extensively.[114] While privacy should be an issue to be taken into thorough consideration in the development of a WGS approach to newborn screening, the authors would like to focus on one aspect of the

108. Robert Green et al., *ACMG recommendations for reporting of incidental findings in clinical exome and genome sequencing*, 15 GENETICS MED. 565, 568 (2013).

109. *Id.* The ethical and legal issues pertaining to the return of results from newborn screenings are included in one of the aforementioned NIH funded grant projects.

110. *See* Jeffrey R. Botkin et al., *Retention and Research Use of Residual Newborn Screening Bloodspots*, 131 PEDIATRICS 120, 122-25 (2013); John A. Robertson, *The $1000 Genome: Ethical and Legal Issues in Whole Genome Sequencing of Individuals*, 3 AM. J. BIOETHICS W35, W37 (2003).

111. *Id.*

112. *Id.*

113. *See, e.g.*, Yuval E. Landau et al., *supra* note 102, at 18.

114. *See, e.g.*, Gostin & Hodge, Jr., *supra* note 98; PRESIDENTIAL COMM. FOR THE STUDY OF BIOETHICAL ISSUES, PRIVACY AND PROGRESS IN WHOLE GENOME SEQUENCING (2012), *available at* http://bioethics.gov/sites/default/files/PrivacyProgress508_1.pdf.

discussion: de-identification. While a recent survey found that a majority of parents would be interested in utilizing WGS for newborns, interest dropped when parents were presented with the potential for de-identified data generated from the WGS to be stored and used for research in the future.[115] De-identification, used often for use in future research, separates any linkable identifiable information from the data. A usable standard for the de-identification of health information comes from the Health Insurance Portability and Accountability Act of 1996 (HIPAA) Privacy Rule, which finds that de-identification occurs when "there is no reasonable basis to believe that the information can be used to identify an individual."[116] Along with the consideration for the storage of genetic data, policymakers will need to consider policies to ensure privacy is maintained and, specifically, whether any stored data should be maintained in an identified or de-identified manner.[117]

E. Constitutionality of Mandate

Lastly, newborn screening programs are lawfully mandated under states' *parens patriae* power, which provides the states with power to protect the well-being of children or other groups of a diminished capacity, based on the fact that they cannot adequately protect themselves.[118] In addition, public health measures can survive scrutiny based on constitutional challenges, such as alleged Fourth Amendment violations of unreasonable search and seizure in the context of blood draws, if the government interest justifies the intrusion on the right. Since the seminal *Jacobson v. Massachusetts,* when the government can demonstrate a public health interest, it may take action that is proportional to the benefits and minimizes harm to others.[119] The

115. Aaron J. Goldenberg et al., *Parents' interest in whole-genome sequencing of newborns*, 16 GENETICS MED. 78, 82 (2014).

116. In addition, the HIPAA Privacy Rule allows covered entities to disclose protected health information to public health authorities, without authorization, for general public health activities, including conducting public health surveillance. *See* 45 C.F.R. §§ 164.514(e)(1)(i), 164.512(b)(1)(i) (West, through May 15, 2014; 79 Fed. Reg. 27,771); U.S. Dep't of Health & Human Servs., *Health Information Privacy: Pub. Health* (revised Apr. 3, 2003), http://www.hhs.gov/ocr/privacy/hipaa/understanding/special/publichealth/index.html (stating that covered entities include health care providers, health care clearinghouses, and health plans); U.S. Dep't of Health & Human Servs., *For Covered Entities and Business Associates,* http://www.hhs.gov/ocr/privacy/hipaa/understanding/coveredentities/index.html (last visited May 22, 2014).

117. *See* Botkin, *Retention and Research Use of Residual Newborn Screening Bloodspots*, *supra* note 110.

118. *See* JAMES G. HODGE, JR., PUBLIC HEALTH LAW IN A NUTSHELL 35 (2014) ("[A] state may serve as guardian of, or provide protections for, persons who may otherwise lack capacity to look after their own interests or welfare."); Tarini & Goldenberg, *supra* note 100, at 384; Jennifer Kraszewski et al., *Legal Issues in Newborn Screening: Implications for Public Health Practice and Policy*, 121 PUB. HEALTH REP. 92, 93 (2006).

119. Jacobson v. Mass., 197 U.S. 11, 25-27 (1905).

government's interest in public health and welfare has long since been recognized as justifying invasive measures that proportionally benefit the population's health.[120] Thus, expanding newborn screening to include the whole genome would be constitutionally valid so long as the expansive cumulative benefits of such an expansion are deemed greater.

VII. CONCLUSION

It is easy to postulate about the revolutionary changes a WGS newborn screening approach could have on future research and individual and population health outcomes. Such changes could include early diagnoses of genetic disorders prior to the child becoming symptomatic. Research programs and research funding could prospectively be targeted to certain disorders for which a large percentage of the population is at risk. If a WGS approach to newborn screening is to co-exist or replace the traditional heel stick blood spot newborn screening programs currently in existence, numerous legal changes will need to examined and implemented. Statutory and regulatory codes will need to be amended and adjusted for the inclusion of routine gathering of genetic information through newborn screening. Policymakers can use prior legal challenges to existing newborn screening programs as a model for developing sound legal and ethical policies for future realization of a WGS approach to newborn screening

120. *See id. See also* LAWRENCE O. GOSTIN, PUBLIC HEALTH LAW: POWER, DUTY, RESTRAINT 126-28 (2nd ed. 2008) (stating that public health powers are constitutionally permissible if exercised in agreement with the following five standards: public health necessity, reasonable means, proportionality, harm avoidance, and fairness).