

Evaluating the “Sensitivity and Specificity” of the Newborn Screening Debate:  
How Tradeoffs between Population and Individual Benefit are shaping the Conversation between Public  
Health and Genetic Advocates

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**Abstract**

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Newborn screening (NBS) is a national program that identifies and treats newborns with rare congenital conditions before the onset of symptoms, preventing premature death and serious disability in thousands of newborns each year in the U.S. Recent advances in analytic technology have exponentially expanded the scope and number of candidate disorders that could be screened for at birth, contributing to the currently recommended panel of 31 core conditions. Yet, the potential to expand the panel of NBS conditions continues to increase as we enter the genomic era. This has led to a debate over the criteria that should be used to evaluate a potential NBS test; at stake are the trade-offs for different stakeholders inherent in balancing competing values. In the debate, one side supports maintaining a limited panel using traditional public health criteria, while the other side challenges this rationale and instead supports expanded screening criteria. Therefore, the purpose of this analysis is to identify areas of agreement and disagreement between the two sides of the NBS criteria debate to elucidate the underlying issues and offer potential recommendations to enhance collaboration. To do this, I conducted a discourse analysis of 61 texts representing different perspectives in this debate to elucidate the underlying motives, values, and perspectives. I reviewed all of the texts using a set of structured questions to systematically identify the facts and moral arguments used to support different inclusion criteria. I specifically coded for phrases that

implicitly or explicitly discussed the different types of benefits associated with NBS tests, the role of technology, and the distributions of social goods within NBS. I found that the two sides have more areas of agreement than disagreement, including a shared primary value of the life-saving and other health benefits of NBS, but that the underlying values, motives, and perspectives of each side of the debate was shaped by differing foci of attention that extended to formulate different senses of normative moral duty. For the public health side of the debate, duty extended to balance benefit and harms at the population level, contributing to emphasis on clinical utility to justify NBS, technology to be limited within the scope of traditional public health criteria, and social goods that are more broadly distributed to balance competing societal goals. Conversely, genetic advocates' duty extended to provide benefit and minimize harms for individuals. These values translated into support for a broader definition of benefit warranting NBS, a maximization of technology's potential, and increased social goods directed to NBS. Since we cannot expect or desire that either side will change their sense of moral obligation, practical steps forward must address other routes. For example, it may be acknowledged that value differences require "winners" and "losers" and that the most compelling argument will be chosen to lead policy decisions. Or, a consequentialist framework could be adopted, whereby mutually agreed upon outcomes would likely dictate characteristics of the criteria. Regardless, clarifying the issues on which each side of the debate agrees and disagrees is valuable in promoting mutual moral "recognition" of the other's values and perspectives. Ultimately, public health and genetic advocates have more areas of agreement concerning NBS criteria, which reinforces the two stakeholders as partners in their shared mission to improve health.

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## I. Introduction

### A. Background

#### History of Newborn Screening in the United States

The year 2013 marked a 50-year celebration of newborn screening (NBS) in the United States. As the public health program that identifies and treats newborns with rare congenital conditions before the onset of symptoms, NBS is attributed to saving the lives of more than 12,000 infants each year<sup>1</sup>. Yet, such a lifesaving program only became possible in the recent past following the widespread use of antibiotics and vaccines, as well as adoption of improved sanitary practices and nutrition. Once these advances subdued the threat of the most common dangers to infants like influenza or diarrheal disease, rare diseases were finally able to be addressed as a cause of infant mortality<sup>2</sup>.

One such rare disease that launched the development of screening programs for newborns, is phenylketonuria, or PKU<sup>1</sup>. Plaguing approximately 1 in every 19,000 infants, the disease was first described in 1934 by the Norwegian biochemist and physician, Asbjorn Folling and is characterized by severe cognitive impairment, microcephaly, motor impairment and skin abnormalities. These symptoms manifest due to a malfunctioning phenylalanine hydroxylase enzyme and results in the inability to metabolize the amino acid, phenylalanine, which is prevalent in the human diet, including breast milk<sup>3</sup>. Thus, the resulting treatment for PKU was a strict diet that limited the intake of phenylalanine, which if initiated early in life and before widespread symptoms, can prevent neurological damage. While the treatment cannot reverse neurological damage that had already occurred, it was considered a breakthrough in reducing morbidity and mortality in PKU patients<sup>3</sup>. However, the need for early detection fostered a related need to develop a method to detect PKU in individuals prior to the onset of symptoms or accumulation of neurological damage<sup>2</sup>.

To that end, Robert Guthrie, an American microbiologist successfully developed an assay to detect PKU in asymptomatic individuals in the early 1960's<sup>2</sup>. The assay utilizes a small sample of the individual's blood, which is placed on a culture of *Bacillus subtilis*. An excess of bacterial growth in culture indicates the individual has PKU, prior to the onset of symptoms<sup>2</sup>.

Following development of the PKU bacterial assay, immense pressure to implement NBS for the disease was applied by various sources<sup>4</sup>. For example, the National Association for Retarded Children (NARC) urged Robert Guthrie to quickly publish his screening assay in a letter to the editor, rather than waiting for publication through peer-review<sup>4</sup>. In addition, the media channeled the excitement of the screening test, and calls to screen ultimately drowned out some reservations by researchers and medical professionals over test reliability, false positive screens, and the lack of evidence concerning treatment effectiveness<sup>4</sup>. Based on a model law proposed by the NARC, by the mid 1970's, every state in the U.S. had enacted legislation for the screening of PKU<sup>4</sup>. Thus, despite differences in opinions regarding the state of the evidence required to go forward with screening programs, the development of an assay to detect pre-symptomatic individuals, along with the availability of a treatment to prevent progressive damage and severe morbidity resulted in the implementation of a national, state-led, and oftentimes mandatory public health screening program for congenital disease of newborns. The PKU case has continued to serve as one of the best examples of how population screening can reduce morbidity associated with rare diseases in infants.

As illustrated by this brief history, there are many parties who hold a stake in national and state NBS programs given its population-based nature (see Table 1). The variety of stakeholders and the range of issues at stake for each party results in a hugely dynamic and complex political environment in which there are likely to be "winners" and "losers" as the result of any particular NBS policy. For example, consider the recent controversy over the retention of dried blood spots within NBS programs: what may have seemed to be a simple logistical issue about obtaining consent for future research uses quickly escalated into a heated debate given what was at stake for the various parties<sup>5</sup>. While some families found the retention of dried blood spots to infringe upon privacy rights, other families found the same resource to be valuable in researching congenital disease or investigating an ambiguous cause of death in a child. Furthermore, varying interests by different stakeholders complicated the discussion because each focused on a different aspect of the issue: researchers hoped to utilize the vast resource of biological specimens, ethicists questioned whether consent was required by either the parent or child, and governmental officials sought to strike a balance between privacy and utilization of a valuable resource. Therefore, debates and policy within NBS are likely to never be straightforward, given the range

of issues at stake and the often emotional charge that accompanies issues of biological sampling and illness in newborns.

TABLE 1. STAKEHOLDERS IN NBS PROGRAMS

<u>Stakeholder</u>	<u>What's at Stake</u>
The Newborn	Stands to receive benefit or harm from screening. It is because the newborn is held as the most important stakeholder that screening is often mandatory and parents cannot easily opt out of screening <sup>6</sup> .
The Family of the newborn	Affected emotionally and financially by the health of other family members and parents may utilize screening information to make future reproductive decisions.
Patient or Genetic Advocacy Groups	Strive to "give a voice" to those affected by congenital disease and "believe that their disorder belongs on a higher plain of societal attention and to see the patients receive earlier and more effective therapy" <sup>7</sup> .
Healthcare Providers (including birthing facility staff and primary care physicians)	Responsible for properly submitting newborn blood samples in an efficient manner and for interpreting and relaying NBS results to the family. They often play a primary role in long term treatment and follow-up of newborns with positive screens.
Public Health and Public Health Laboratory Staff	Responsible for conducting screening tests that are sensitive and specific and to report positive screens so that newborns may undergo confirmatory testing promptly. They are charged with maintaining screening programs that improve the overall health of populations they serve.
Researchers and Pharmaceutical Companies	Seek to fund genetic/patient advocacy groups and utilize population-level data generated by NBS programs to elucidate disease etiology or develop new treatments,
Government Officials and Policy-makers	Charged with ensuring mandatory public programs are financially sound and in alignment with the goals and values of the population they serve <sup>6</sup> .

### Generating Standardized Criteria for Screening

Coinciding with the proliferation of NBS for PKU in the United States was a World Health Organization conference that commissioned James Maxwell Glover Wilson, the Principal Medical Officer at the Ministry of Health in London, and Gunnar Jungner, Chief of the Clinical Chemistry Department of Sahlgren's Hospital in Gothenburg, Sweden, to develop principles for the screening of disease<sup>8</sup>. Because of their positions, they were considered optimal authorities to consider how then-recent technical advances in medicine could be translated into population health gains while considering the practical controversies, such as whether earlier detection would in fact lead to improved outcomes or whether the information

learned from screening could produce null or even harmful results<sup>8</sup>. Although the principles they developed were originally commissioned regarding screening criteria for chronic diseases such as cancer and cardiovascular disease, the motives underlying screening for congenital disease in newborns were the same. The criteria that resulted from the Wilson and Jungner report were what came to be described as the “traditional” criteria; these criteria then formed the dominant discourse that would serve as the accepted way of viewing the subject and be most often perpetuated by those in power. Thusly, these criteria were used as guidelines in the United States for the addition of novel NBS tests, such as with the addition of congenital hypothyroidism in several states (see Table 2)<sup>2</sup>. However, opportunities to apply and test the criteria within NBS were limited since the panels of conditions offered by different states generally remained small and grew slowly<sup>4</sup>. In addition, now that the “traditional” criteria had been established as the dominant discourse, any criticism or alternative methods must garner substantial “voice” to be heard above the few stakeholders that typically hold most of the power in NBS.

TABLE 2. WILSON AND JUNGNER CRITERIA FOR APPRAISING THE VALIDITY OF A SCREENING PROGRAM<sup>8</sup>

“Traditional” Criteria for Screening

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1. The condition sought should be an important health problem.
2. There should be an accepted treatment for patients with recognized disease.
3. Facilities for diagnosis and treatment should be available.
4. There should be a recognizable latent or early symptomatic stage.
5. There should be a suitable test or examination.
6. The test should be acceptable to the population.
7. The natural history of the condition, including development from latent to declared disease, should be adequately understood.
8. There should be an agreed policy on whom to treat as patients.
9. The cost of case-finding (including diagnosis and treatment of patients diagnosed) should be economically balanced in relation to possible expenditure on medical care as a whole.
10. Case-finding should be a continuing process and not a “once and for all” project.

Evolution of NBS in the United States

The slow expansion of NBS in the United States came to an end in the early 1990's and can be in part attributed to the development of tandem mass spectrometry<sup>4</sup>. Mass spectrometry is an analytical method that measures the quantity and type of various molecules present in a biological sample; for NBS conditions, the molecules of interest most often include amino acids and acylcarnitines. The technology was a breakthrough since it can be used to detect an almost unlimited number of different molecules, and therefore conditions, from a single small blood sample. In contrast, prior to the development of mass spectrometry, a separate bacterial assay had to be conducted for each screening condition, which limited the total number of conditions that could be screened for by the volume of the biological sample that could be feasibly obtained<sup>2</sup>. Therefore, the use of mass spectrometry technology, which is also cheaper and more reliable than previous methods, made it possible to simultaneously screen for an almost unlimited number of biochemical congenital disorders<sup>9</sup>.

In addition to technological breakthroughs, rapid expansion of NBS programs has been attributed to a societal paradigm shift in the way NBS in the United States is viewed<sup>10</sup>. The original paradigm for NBS was based on that of a "public health emergency", whereby screening was employed to prevent "devastating harm to affected infants by providing immediate treatment after birth"<sup>10</sup>. In contrast, the suggested paradigm shift involves the move towards NBS as a "public health service"<sup>10</sup>. In this way, newborns are screened for conditions that no longer present as emergencies, but as those with less dramatic effects, such as conditions that are not immediately life-threatening but could benefit from treatment with prophylactic antibiotics, for example; another public health service may include knowledge that provides benefit to those other than the newborn, such as to the parents for reproductive purposes<sup>10</sup>.

Finally, the expansion of NBS was aided by a societal change in perspective surrounding the definition of benefit. In most historical reports concerning the criteria for NBS tests, "improved physical health for the infant via medical treatment" has been the primary criterion<sup>9</sup>. However, contemporary expert opinion and public commentary demonstrate growing support for criteria that broaden the definition of benefit beyond improved physical health to include "improved quality of life, availability of techniques to address learning and behavioral issues, and provision of supportive care"<sup>9</sup>.

#### Emerging Conflict Among NBS Stakeholders

Through the evolution of NBS programs in the United States, a conflict or debate has arisen. The nature of the conflict is based on differing perspectives concerning appropriate criteria to evaluate proposed NBS tests. Generally, one side in the debate supports “traditional” NBS criteria as defined by the Wilson and Jungner report, while the other side supports “expanded” screening criteria that encompass conditions that could receive the broader benefits described above. While position within a particular stakeholder group does not prescribe an individual’s support for one side of the debate or the other, in general, public health and medical professionals tend to support traditional criteria, whereas families and genetic advocacy groups tend to support expanded criteria.

The opportunity for this debate to enter the national dialogue came with the 2006 publication of the Recommended Uniform Screening Panel (RUSP)<sup>11</sup>. The aim of the RUSP was to serve as national guidance on the best candidate conditions for newborn screening, especially given rapid developments in genetics, screening technologies, and some treatments<sup>11</sup>. To develop the RUSP, the American College of Medical Genetics (ACMG) was commissioned by three federal agencies (the Maternal and Child Health Bureau [MCHB], Health Resources and Services Administration [HRSA], and the United States Department of Health and Human Services [DHHS]) to conduct an analysis of the scientific literature and gather expert opinion to “delineate the best evidence for screening for specified conditions and develop recommendations focused on newborn screening”<sup>11</sup>. To be considered as a primary NBS target, the condition had to meet several minimum criteria that included: the ability to be detected 24 to 48 hours after birth when it typically wouldn’t be identified clinically, the availability of a test with appropriate sensitivity and specificity parameters, and for which there are demonstrated benefits to early detection with an efficacious treatment<sup>11</sup>. To evaluate these minimum and accompanying more complex criteria that were developed by the committee, a two phase method was employed. The first phase involved a more subjective survey that was distributed to a variety of individuals and organizations with an interest in NBS, including the listservs of the Genetic Alliance, Association of Public Health Laboratories, Association of State and Territorial Health Officials, as well as to experts in the conditions under investigation. The second phase of evaluation was a more objective algorithm to weigh the scientific evidence available for the criteria on Pubmed, through professional guidelines, and from cost/economic models, among other sources<sup>11</sup>. Data from both phases were translated into scores, and those conditions with combined scores

above a certain threshold were considered suitable targets for NBS. The results of these efforts resulted in an initial RUSP that included 29 core conditions considered to warrant newborn screening, as well as 25 secondary conditions that are identified in the course of screening for the core conditions<sup>11</sup>.

Subsequently, HRSA requested public commentary on the report, which resulted in 155 letters and e-mails over the 60 day period with 32 arriving later<sup>12</sup>.

At the time of the development of the RUSP, NBS panels varied substantially across states, with some mandating screening for only 3 conditions, while others screened for up to 43 conditions<sup>11</sup>. Today, most states have adopted the 29 core conditions from the RUSP onto their screening panels, which has had an overall effect of dramatically increasing the number of conditions being screened for across the country.

While all stakeholders generally supported the development of a uniform screening panel as a way to promote equity in NBS, reactions to the final list of conditions that made up the RUSP were mixed. In all cases, the underlying satisfaction or disapproval of the RUSP can be viewed as being rooted in the debate over what criteria were used to justify the addition of a NBS test. It may be hypothesized that although a variety of stakeholders were able to respond to the survey and provide feedback as to how well conditions met the given criteria, the fact that the expert group, made up exclusively of medical and public health professionals, were the only ones involved in the development of the criteria in the first place was problematic and may have contributed to the lack of broad support for the final product.

#### Role of Genetic Advocacy Groups in Shaping NBS

Whether explicit or not, those affected by congenital conditions that can be detected through NBS have historically played, and increasing play, a crucial role in shaping NBS programs in the United States. As referenced previously, patient organizations such as the National Association for Retarded Children were a driving force in securing mandatory nation-wide screening for PKU, and disease-specific genetic advocacy groups continued to champion for additional screening, as well as for the development of a recommended uniform screening panel<sup>4</sup>. This is demonstrated by the fact that over 60% of the comments made during the open comment period of the RUSP were by individuals connected to someone affected by a congenital disease; nearly all of the comments endorsed expanded NBS panels and many rejected

historical screening criteria<sup>4</sup>. In public debates over NBS, genetic advocacy groups have been described as holding an inherent advantage through their personal and moving testimony that portrays how NBS programs directly impact their lives. This is in contrast to researchers or public health professionals who discuss hypothetical future patients that may receive harm or benefit from NBS and are thus easily perceived as being “self-serving, petty or abstract”<sup>4</sup>.

Another advantage available to genetic advocacy groups is the unique structure of NBS politics in the United States<sup>7</sup>. This structure has been argued to be unique through the “extent to which a group of individuals who are press-savvy and politically connected can influence the introduction of new programs into the national and state health mandates in the absence of careful prospective consideration of the impact”<sup>7</sup>. This political structure deviates substantially from what is typical in European countries, where newborn screening is only implemented with the recommendation from an expert panel following evidence of test effectiveness and cost-benefit analyses<sup>7</sup>. This authority lies in stark contrast to similar expert panels in the United States that make recommendations following evidence-based reviews, but whose recommendations are just that: recommendations which are not at all binding. Such differences can result in vastly different decisions in NBS policy and programs in light of the same data.

One example of the power of genetic advocacy groups is the case of NBS for Krabbe disease in New York State. In this case, reviews made by two expert groups (the New York State Newborn Screening Task Force and the federal Discretionary Advisory Committee on Heritable Disorders in Newborns and Children) recommended against screening for Krabbe disease because they found insufficient evidence that screening offered potential net benefit due to gaps in knowledge about the disease and potential harms from screening and/or treatment<sup>13</sup>. However, despite these recommendations, Krabbe disease was subsequently added to the state screening panel; this action was generally attributed to influence generated by genetic advocacy groups in the state who argued that early identification offers the best chance at effective treatment<sup>13</sup>.

In addition, genetic advocacy groups have become increasingly linked to the pharmaceutical industry, which has increased the reach and professionalism of these groups, but also the ethical quandaries<sup>4</sup>. While pharmaceutical industries often sustain or even create genetic advocacy groups, the ties become

problematic when a group's funding is not transparent and issues of how industry may influence the group's motivation to expand screening are called into question<sup>4</sup>. Lastly, NBS is not the only example of national policy being effectively influenced by advocacy groups. For example, advocacy undertaken by those affected by HIV and AIDS in the United States starting in the 1980's has been described as one of the most successful public policy change models ever observed. Thus, the power of genetic advocacy groups to generate substantial and long-lasting change within major political and industry systems must not be overlooked.

While the above passages aim to evidence a few of the inherent strengths of genetic advocacy groups and their potential to generate policy change in the U.S. (especially as compared to other countries), the reality remains that these groups are mostly working as outsiders who can only challenge existing policies (rather than be active stakeholders developing policies) because medical and public health professionals persist as gatekeepers to NBS policy and programs. Thus, genetic advocacy groups are forced to mount extraordinary efforts to have their perspectives included in a formal way.

## B. Research Purpose

While it is possible to infer the specific motives, values, and perspectives that underlie genetic advocacy groups' efforts to expand NBS criteria through statements produced by the groups or from similar, well-studied efforts such as by HIV/AIDS advocates, these features have not been elucidated. Similarly, members of genetic advocacy groups and the general public of NBS consumers are commonly cited to be motivated to expand newborn screening criteria based on an American tendency to consider any and all facts useful as a means to make things better<sup>14</sup>. In other words, "if a child has a problem, American parents simply want to know everything they can about it", and the information itself is valued, above and beyond what clinical utility the information may offer<sup>14</sup>. This is congruent with the consistent support by American consumers for genetic screening and for diagnoses in the newborn period; they attest that knowledge of a child's genetic abnormalities is a right, regardless of whether that abnormality may be medically treated<sup>14</sup>. However, this too seems to be singular dimensional analysis.

Therefore, the purpose of this discourse analysis is to elucidate the underlying motives, values, and perspectives of public health and genetic advocates that each represents a side of the U.S. debate over NBS criteria. This analysis will reveal areas of agreement and disagreement between the stakeholders, illuminate the nature of the debate and suggest recommendations to enhance collaboration to meet shared goals.

## II. Methods/Approach

### A. Methodology

#### Discourse Analysis

Discourse analysis is a qualitative method of research that recognizes that rather than simply conveying information, language serves many functions for members of a society. Discourse analysis as a methodology evolved from linguistic studies, literary criticism, and semantics<sup>15</sup>. Specifically, discourse analysis involves study of language-in-use to illuminate how individuals or groups accomplish personal, social, and political projects through language<sup>15</sup>. It can be argued that through language reality is constructed, social roles are defined, and identities are able to be enacted in a society<sup>15</sup>. By investigating the way language is used, connections may be drawn that allow researchers to speak in a novel way to social and political issues and perhaps offer recommendations to intervene on these issues. In short, language is an abundant, yet taken-for-granted medium that is brimming with deep rooted meaning that can be used to generate informed conclusions about societal groups or processes to generate solutions to conflicts.

### B. Discourse Analysis and Discourse Tracing as a Method

Discourse analysis as a method primarily utilizes “language-in-use” data from recorded conversations or extant texts. Careful examination of language-in-use allows the study of the ways in which language combines with particular actions, beliefs, symbols, and places to create particular identities<sup>16</sup>. Each individual participates in and enacts multiple Discourses or identities in their lives. Discourse analysis also studies “Conversations”, or public debates such as the “abortion Conversation” that are prevalent in the media and in which you know the positions that comprise each “side’s” main views and what type of

people are likely to belong to each side<sup>16</sup>. Conversations are specific examples of language-in-use that reveal the core values, beliefs, identities, places, and objects of members of the different sides or positions<sup>16</sup>

Discourse tracing is a specific form of discourse analysis that evolved from ethnographers, discourse critics, case study scholars, and process tracers<sup>17</sup>. Discourse tracing is especially useful in critical-interpretive and applied analysis of discourse that allow for the study of social processes, facilitation of change and institution of new processes<sup>17</sup>. This is accomplished through the study of micro, meso, and macro levels of discourse and interaction across a social issue to provide insight regarding transformation and change<sup>17</sup>. Micro discourses are defined as local uses of text and language within a specific context. Meso discourses then, consider how micro discourses are connected across contexts. Finally, macro discourses are defined as broader social narratives and systems of enduring thought<sup>17</sup>. Discourse tracing involves four distinct phases including, research design, data management, analysis, and evaluation<sup>17</sup>.

#### Phase 1: Research Design

The research design phase involves defining the “case” using a rupture or turning point, as well as reviewing the literature to investigate potential research directions<sup>17</sup>. For the purposes of my study, the rupture point, or the event that signals a moment of discursive organization or reorganization surrounding NBS criteria, is the 2006 publication of “Newborn Screening: Towards a Uniform Screening Panel and System” that included the original Recommended Uniform Screening Panel (RUSP). As described earlier, the publication of this document by several expert groups determined a set of NBS criteria and generated national guidance on the best candidate conditions for NBS. Following the publication of this document, a renewed Conversation regarding NBS criteria ensued and will serve as the societal issue upon which discourse tracing will be applied in order to better understand the debate and develop recommendations to enhance collaboration between the two sides.

#### Phase 2: Data Management

The second phase of discourse tracing involves data management that begins with the gathering of data<sup>17</sup>. Data sources included extant texts representing micro, meso, and macro levels of discursive

practices of those parties discussing NBS criteria and were chosen to include as many primary sources as possible to support claims and to generate a rich description of the conversation surrounding criteria for inclusion in NBS panels<sup>17</sup>.

For my purposes, macro discourses primarily consisted of formal documents by national organizations aimed at informing programs and policy nation-wide, while micro discourses were defined as first person narratives. Meso-level discourses included examples of how macro and micro discourses intersected at the organizational and state levels. While discourse tracing involves specifically identifying discourses at each level, emphasis is also placed on recognizing connections between and across the levels that connect the local to the broad societal level issues<sup>17</sup>.

### Macro

To collect my data, I first sought to include examples of the macro level discourses. To do so, I started with the document serving as my rupture point, the RUSP. The Discretionary Advisory Committee on Heritable Disorders in Newborns and Children (DACHDNC) "Reports" webpage where the RUSP was published also included several other reports that I collected and had been published subsequently to either clarify the criteria used in the RUSP, to update the Committee's evidence review process, or to respond to other national commentaries regarding the RUSP.

[<http://www.hrsa.gov/advisorycommittees/mchbadvisory/heritabledisorders/reportsrecommendations/index.html>] From this initial collection of eight reports, I utilized reference lists to identify other documents that addressed the topic of NBS criteria. In addition, by navigating to other links from the DACHCNC web resources, I was able to download other applicable documents from national resources such as by the U.S. Department of Health and Human Services, Health Resources and Services Administration, U.S. Preventative Services Task Force, and the President's Council on Bioethics. This tactic also led me to collect legislative documents such as pertaining to the "Newborn Screening Saves Lives Act of 2007" and Reauthorization Act. These texts were likely to be characteristic of the broad social narratives and systems of enduring thought regarding NBS in the U.S. because of the role that national government agencies have in terms of being granted authority to recommend NBS policy and collect rigorous and robust data to determine best practices,

### Meso

Meso- level sources included position statements or other written statements regarding NBS criteria by organizations or groups. My first tactic to collect these texts was to use the Google™ Search engine ([www.google.com](http://www.google.com)) and the following search terms: newborn screening AND position statement, newborn screening AND policy statement, newborn screening AND recommended panel, newborn screening AND criteria.

I followed this with another Google™ Search for webpages of those organizations that had been mentioned by name in any of the documents collected thus far. If the organizations did have a webpage, I then searched to the best of my ability for any organizational statements regarding NBS criteria. In this way, I was able to identify statements by organizations such as Genetic Alliance, Baby's First Test, Save Babies Through Screening Foundation, March of Dimes, Association of State and Territorial Health Officials and the Association of Public Health Laboratories.

To capture other meso-level discourses that may exist in forms besides a formal statement or position on the organization's web page, I conducted a search of the LexisNexis Academic database. This database was used to identify newspaper articles pertaining to NBS criteria across the United States in national, regional, and local publications. The search term applied was "newborn screening" and the results were limited to those published between May, 2006 and December, 2013. This resulted in approximately 575 newspaper items. However, the majority were irrelevant to my study and excluded; to be included, the articles had to allude to some aspect of why a NBS test should/should not be added, or why NBS should/should not be expanded. Essentially, the author or interviewee had to be speaking to some aspect of the criteria that should be utilized to make NBS decisions, although the exact term, "criteria" was almost never used. The newspaper articles included a different set of meso level discourses that primarily represented state public health organizations, health departments, regional research facilities, local chapters of medical organizations and local chapters of genetic or patient advocacy groups.

As a final means to seek organizational statements concerning NBS criteria, I browsed support group resources linked from the Baby's First Test webpage. The Baby's First Test webpage serves as a national clearinghouse for all conditions for which states conduct NBS, including those who screen for additional

conditions beyond the RUSP. These organizational and group statements served as good examples of the interplay between the macro and micro levels, since they often included implications from federal policy, coupled with individual experiences or goals.

### Micro

Micro-level discourse took the form of individual family members or health care providers sharing their stories related to NBS criteria. These texts came in the form of newspaper articles derived from the LexisNexis search, as well as in legislative testimonies and as personal stories published on web pages that provide NBS information or advocacy resources such as on the Save Babies Through Screening site.

Overall, the search resulted in 61 extant texts and included 813 pages of data with which to conduct a discourse tracing analysis (see Appendix A for the complete list of data texts).

TABLE 3. DISCOURSE TRACING DATA

Discourse Tracing Data			
Level of Analysis	Data Type	Example Data Sources	Pages
Macro	<ul style="list-style-type: none"> <li>• Formal National Reports</li> <li>• High Profile Commentaries on National Reports</li> <li>• National Legislation</li> </ul>	<ul style="list-style-type: none"> <li>• President's Council on Bioethics</li> <li>• Secretary's Advisory Committee on Heritable Disorders in Newborns and Children</li> </ul>	629
Meso	<ul style="list-style-type: none"> <li>• Organization Position Statements</li> <li>• State Policy</li> <li>• News items pertaining to state NBS programs</li> </ul>	<ul style="list-style-type: none"> <li>• Association for Public Health Laboratories</li> <li>• Association of State and Territorial Health Officials</li> <li>• Genetic Alliance</li> <li>• Save Babies Through Screening Foundation</li> <li>• State Departments of Health</li> </ul>	121
Micro	<ul style="list-style-type: none"> <li>• Family Stories</li> <li>• Commentaries by medical professionals</li> <li>• Personal Testimony to Legislature</li> </ul>	<ul style="list-style-type: none"> <li>• Local Newspapers: Star Tribune (Minneapolis, MN), Tampa Tribune</li> <li>• Regional Newspapers: The Oklahoman,</li> <li>• National Newspapers: USA Today, New York Times</li> </ul>	63

### Phase 3: Data Analysis

Once I collected a sampling of various texts at each level of analysis, I ordered the data chronologically and conducted a careful reading of the data in chronological order to illuminate how the different parties have been involved in the Conversation surrounding newborn screening criteria over time (see Appendix

A). This initial, careful reading allowed me to gain an initial grasp on the social processes taking place across time and context, the presence or absence of the various stakeholders, as well as how macro-level discourse both enabled or restricted the micro-level discourses and vice versa<sup>17</sup>.

From my chronological reading of the 61 texts, I identified several key features of how the various stakeholders have been involved in the Conversation surrounding NBS criteria. First, some stakeholders were more visible in the Conversation than others. For example, the most visible parties were national NBS committees and workgroups at the macro level, genetic advocacy groups and state public health organizations at the meso level, and parents and family members of those affected by congenital conditions, as well as medical professionals who treat those conditions at the micro level. Notably, although NBS has been taking place in the U.S. for 50 years, the voice of the most important stakeholder, the “newborn”, was absent from the Conversation at all levels of discourse. I had anticipated that given this length of time, there would be more discourse by those who had been directly affected by NBS, such as a grown person with a congenital condition detected by NBS.

Second, the macro-level discourse directly affected the meso- and micro-level discourses over time. In this way, the 2006 publication of the RUSP not only reengaged and restructured the Conversation surrounding NBS criteria, but also directly enabled and informed the meso and micro level discourses. For example, the March of Dimes developed state “report cards” based on how well each state’s panel of NBS conditions met those on the RUSP. This resulted in a flurry of articles in the news by both state organizations and individuals that most often resulted in either a charge to “bring the state in line with federal recommendations” or praise when a state was found to screen for most, all, or even a surplus of conditions as compared to the RUSP.

Next, I developed a set of structured questions to “ask” of the data as a way to systematically trace out discursive practices in the Conversation regarding NBS criteria and identify the underlying motives, values and perspectives of the public health side of the debate as they compare and contrast with those of genetic advocates.<sup>17</sup> The structured questions were informed by the literature review, my research questions, and the close reading of the chronological data. The resulting questions were designed to help “lift out” patterns and arguments from the data in order to generate themes and included the following:

1. What language is being used to construe particular types of benefit as justifying NBS, and thereby either upholding or rejecting traditional NBS criteria?
2. What language is being used to make different claims regarding the role of technology in shaping NBS programs?
3. What language is being used to construe particular distributions of social goods in NBS as “good” or “acceptable” or not?

The final task of the data analysis phase of discourse tracing is to generate a case study. After I applied the structured questions to the chronological data, I translated the resulting raw data regarding the identified discursive practices and themes into a more accessible and cohesive narrative. Developing the narrative is akin to storytelling and often includes a plot, characters, and outcomes<sup>17</sup>. This step also required a heightened sense of critical reflection to assess how legitimate my emerging claims were based on the data and how much I may have been reading into the texts based on my own interests<sup>17</sup>.

The completion of this step resulted in the a written case study aimed at public health professionals and policy-makers involved in NBS that described narratives relating to issues of language and identity, relationships, and perspectives of the distribution of social goods. These narratives elucidate the underlying motives and values of each side of the debate over NBS criteria. The case study also concludes with recommendations to increase collaborative policy that better accomplishes the shared goals of the two groups.

#### Phase 4: Evaluation

Evaluation of the theoretical and practical implications of the case study is the final phase of the discourse tracing method. The results from this phase are presented in the Discussion section of this paper.

#### Steps to Assure Data Quality in Discourse Analysis

The nature of qualitative research is inherently subjective given the role of the researcher in making decisions regarding the data sources included in the sample, as well as coding, categorizing, decontextualizing, and recontextualizing the data<sup>15</sup>. Therefore, I employed a variety of tactics to monitor, document, and evaluate my analytic process so as to inject rigor and trustworthiness into my analysis<sup>15</sup>.

This included consultations with colleagues and mentors, as well as memoing of my progress throughout the analytic process that documented how my thoughts and ideas changed as I engaged more deeply with the data. Specifically pertaining to discourse analysis, it was critical to remain thoughtful of my position within the public health Discourse and to be aware of how this positionality differs from those within the genetic advocacy Discourse from which many of the texts of analysis come from. Readers of this analysis will benefit from keeping in mind that I am a member of the public health side of the Conversation at the center of this study. So, although I do not belong to the Discourse from which I obtained data for analysis, I provide substantial detail regarding my data selection and analytic strategy to enhance the rigor and trustworthiness of my conclusions.

### III. Results

#### Evaluating the “Sensitivity and Specificity” of the NBS Debate

The concepts of “sensitivity” and “specificity” serve as unique and fundamental elements of all screening programs, including NBS. Employing a discursive move of their own, the two familiar words are used in a technical way to shape NBS programs, with substantial consequences. “Sensitivity” within screening programs describes how well a test produces a “true positive” result when the individual being tested does in fact have the condition of interest. Conversely, “specificity” describes how well a test produces a “true negative” result when the individual does not have the condition<sup>18</sup>. The values for the sensitivity and specificity of a screening test exist across a continuum in which the “best” answer is not inherently known because of the relationship between the two concepts: increasing the accuracy of one comes at the cost of decreasing the accuracy of the other. Therefore, this subtle and seemingly technical aspect of NBS programs actually involves significant value judgments, since for whatever cutoffs are chosen, there are consequences: in order to detect all cases of a given condition, the number of false positives may increase, just as to reduce the number of false positives, a program may risk missing a newborn with a serious or life-threatening condition. However, in most NBS programs, thresholds are set to assure 100% detection of true positive cases, while reducing the number of false positives as much as possible<sup>18</sup>. The implications of sensitivity and specificity parameters within screening programs involve the tradeoff between population and individual benefit. For example, maximizing sensitivity to detect 100% of true

positive cases will likely provide a great deal of benefit to a small number of individuals, but at the expense of population benefit, which is likely to receive comparably less benefit and bear extra burden in the form of false positives. Similarly, if specificity is maximized in a screening program, the population is likely to receive cost-effective improvements in population health, while reducing false positives. However, the individual may bear the burden in this scenario through delays in diagnosing their rare disease, potentially leading to delays in treatment initiation and poorer outcomes. Therefore, just as screening programs inherently include tradeoffs when determining sensitivity and specificity parameters, the debate between public health and genetic advocates too, is largely a debate over which tradeoffs to make in providing population and individual benefits.

Thus, the model for evaluating a screening test by its sensitivity and specificity also serves as an elucidating and useful model for describing the nature of the debate over NBS criteria. Revisiting this sensitivity/specificity model, it becomes clear that after determining the cutoff values for screening tests, four outcomes become possible once a newborn is screened for a given condition: a true positive, a true negative, a false positive, or a false negative (see Table 5). Each test outcome is accompanied by specific actions and potential implications for the newborn, their family, medical providers, and other stakeholders. Following this rationale, I have superimposed my findings of the discourse analysis onto the binary model for evaluating a screening test (see Table 6). This is possible since the underlying values, motives, and perspectives of stakeholders involved in the debate over NBS are tied to the various outcomes of the screening test model, which now serves as a useful framework to elucidate the underlying nature of the debate.

TABLE 5. POSSIBLE OUTCOMES FOLLOWING A SCREENING TEST

		Test Classified As:	
		Positive	Negative
Newborn Really Is:	Positive	True Positive	False Negative
	Negative	False Positive	True Negative

TABLE 6. TAKE HOME ISSUES ASSOCIATED WITH EACH POTENTIAL NBS CASE

The Case:	True Positive: Proper identification of a newborn with a serious congenital condition	False Positive: Identifying a newborn as potentially having a serious congenital condition when in fact, they do not	False Negative: Failure to identify a newborn with a serious congenital condition	True Negative: Identifying a newborn as not having a serious congenital condition when in fact, they don't
Take-home Issue:	Genetic Advocates want to expand the benefit criteria that justify NBS, resulting in many more "True Positive" cases	Public Health wants to reduce the number of False Positive cases as much as possible	Genetic Advocates want to reduce the number of hypothetical False Negatives that exist as a result of failing to maximize technology	Public Health wants to more broadly distribute the social goods represented by True Negative cases, while Genetic Advocates want to increase the proportion of social goods allocated to NBS

### The True Positive

The "True Positive" represents the founding goal of NBS programs: identification of an asymptomatic newborn with a serious health condition. Following the positive screen, the family will be alerted, the newborn will receive confirmatory diagnostic testing, and a plan to efficiently deliver evidenced efficacious treatment will be made. This goal to save or improve the lives of newborns through NBS is shared by both public health and genetic advocates and is the fundamental area of agreement that unites the stakeholders in their shared passion. As an example of how the lifesaving nature of NBS is valued, the Association of Public Health Laboratories shared the story of a little girl who will go on to live a relatively normal life with a modified diet following a diagnosis of propionic acidemia, saying "Maren is just one of the more than 12,000 babies each year in the United States whose lives are saved or improved through newborn screening. She is part of what the Centers for Disease Control and Prevention have called one of the greatest public health achievements of the 20th century"<sup>19</sup> Similarly, one teenager who received a diagnosis of galactosemia following NBS as an infant said, "I think that it saved my life...I've benefited so much from it. Without newborn screening, my life would have been so different."<sup>20</sup>

Thus, focusing on the lifesaving nature of NBS, the ability to provide improved health outcomes to newborns, most often through a medical treatment, became the fundamental criteria used to evaluate a proposed NBS condition. In this way, while both sides of the debate value improved medical outcomes as an important feature of NBS, disagreement arose over the other types of benefit that may also justify NBS. Specifically, genetic advocates describe four other benefits of NBS, including: “elimination of the ‘diagnostic odyssey,’ the provision of reproductive risk information to parents, fostering research with affected children, and the developmental, psychological, and social benefits that occur from early disease detection.”<sup>21</sup>

In response to this debate, public health maintains that screening for a congenital condition is only warranted when doing so will provide a direct medical benefit to the newborn; these are the only “True Positives” that ought to be detected. For example, the founders of the “traditional” screening criteria, Wilson and Jungner commented “Of all the criteria that a screening test should fulfill, the ability to treat the condition adequately, when discovered, is perhaps the most important...Unless this is so, there can be no advantage to the patient and, in fact, in alerting him or her to a condition that has not been shown to benefit by treatment at an earlier stage actual harm may be done.”<sup>8</sup> Agreeing with Wilson and Jungner, one epidemiologist stated that “the ‘old dogma’ in fact remains a sound principle...There would need to be special and compelling reasons to screen for a disorder for which no effective remedy was available.”<sup>22</sup> In addition, another scientist addressed the debate by saying “Advocates of an expanded notion of ‘benefit’ often extol the utility of newborn screening for helping parents make future reproductive decisions...But this notion of “benefit to the family” is not unproblematic. At what point have we crossed the line from legitimate family planning to capricious and morally dubious eugenics?”<sup>14</sup>

Conversely, genetic advocates would like to expand the definition of benefit within NBS criteria, which would increase the number of True Positive cases to identify. One public health professional described the conflict saying, “With the potential of greatly expanded testing, many have begun to question one standard tenet of newborn screening . . . that it’s appropriate to screen only for conditions for which an effective treatment already exists. The tenet served a useful purpose in early years, but it’s now being challenged as outmoded, because it fails to consider other benefits.”<sup>21</sup> As a testament to this notion, a

spokesperson for a national alliance of genetic advocacy groups addressed those who developed the criteria for the RUSP, saying

“...as the ACMG’s expert groups evaluated conditions for inclusion in the uniform panel, significant consideration was given to whether or not there was a “efficacious treatment” available... we believe that the traditional medical model that this type of criterion reflects may not be the most appropriate one for newborn screening. That is, while the medical community may not consider a particular treatment “efficacious,” an affected family might find that same treatment essential. Our community of consumers—14 million people living with genetic conditions—knows that the medical definition of treatment is more narrow and limited than the one they experience.<sup>23</sup>”

In agreement with the above sentiments, one mother described how information alone was a benefit, saying “... to know one way or the other was really important to us, and when I found out what it [Krabbe disease] was and how quickly it hit, that knowing part would be so vital because the amount of time that you would have is so short...<sup>24</sup>”

While both public health and genetic advocates find value in identifying True Positives that stand to receive medical benefit, public health seeks to limit the proportion of tested individuals characterized as True Positives through application of traditional NBS criteria. This is in contrast to genetic advocates who support greatly expanding the pool of True Positives to include newborns and their families that may receive more broad types of benefit, such as increased information, for example.

### The False Positive

The “False Positive” represents some of compromise inherent in screening programs: while screening facilitates the investigation of an entire population for health conditions that can be acted upon, they are not diagnostic tests. This means that a certain number of healthy individuals will falsely “test positive” for a given condition. Therefore, through efforts to detect 100% of True Positives in a population, False Positives are an undesired side effect of the screening process. Depending on how NBS assays and programs are set up, a false positive test result may require a subsequent test of the sample, an additional blood sample from the newborn (which is often collected routinely), or diagnostic testing of the

newborn to confirm the screening test was in fact, a false positive and that the infant is not affected by the condition of interest<sup>18</sup>. While the first two of the three options are unlikely to affect the newborn or their families in any way, the third option has at times been associated with harm for the family. Specifically, a literature review of studies investigating the impact of false positive newborn screens found mixed results; some studies did not find any negative impact on families, while others found negative psychosocial consequences such as parental stress, anxiety, or dysfunction within the parent-child relationship<sup>18</sup>. In aggregate, these studies, which investigated families who received false positives of cystic fibrosis, metabolic conditions, and hearing, found that while each family will experience receiving a false positive differently, most families were willing to endure the false positive in order to ensure all True Positives are detected. In addition, most did not experience lasting negative outcomes<sup>18</sup>.

Given the above findings, there would seem to be insufficient evidence for either side of the debate to slow the expansion of NBS on the basis of avoiding false positives, since parents endorse that the benefit of detecting every True Positive case is worth the minor harms they experienced following a False Positive screen. However, it is important to note that the above studies were for conditions that doctors were able to quickly and confidently rule out upon follow-up testing and inform parents that their child did not have the condition, with little additional discomfort afforded to the patient. This is not the case for all NBS conditions. For example, as discussed in the Background section, Krabbe disease was added to the state panel due to the efforts of local advocacy groups despite expert recommendations not to screen. After several years of the program, the state has detected far more positive screens than were expected and diagnostic tests have not been able to consistently determine which newborns will ever develop symptoms. Therefore, parents are given a “low”, “moderate”, or “high” risk prediction for their child to ever develop Krabbe disease; asymptomatic infants deemed at some risk are tested every three months during the first year of life with a neurologic examination, magnetic resonance imaging (MRI), lumbar punctures, audio and visual evoked response tests, and nerve conduction studies<sup>25</sup>. Overall, approximately 25 children have been identified as positive screens, and 2 have developed symptoms of Krabbe disease; both of whom received the stem cell transplant treatment. Following treatment, which carries a 10% mortality rate, one child died as a result and the other's Krabbe disease is not progressing, but has left the child “developmentally delayed”<sup>25</sup>.

The Krabbe disease example differs in several ways from the false positive studies of Cystic Fibrosis and other conditions covered in the review discussed previously; parents were not provided a definitive diagnosis and the infant underwent extended and sometimes uncomfortable testing. Because of this, it is reasonable to assume the harms associated with false positives for Krabbe disease may also be different. This view seems supported by interviews with parents, who describe more substantial harms than were reported in the previous literature review. For example, one mother described receiving the news that her infant had a positive screen, saying “I had a really hard time that time, I even went to the doctor and they gave me a lot of pills for depression and stuff like that...Well, I had trouble. I started hurting myself after that. It was a way to get the pain off of me, I guess, even though the pills weren't helping.”<sup>13</sup> Other parents described life following a positive screen carrying a “low risk” prediction, saying “...for the first six months of his life, any time he cried or if he didn't want to eat or if something was wrong, you know, not that I expect the worst and hope for the best, but I always did wonder in the back of my mind. What if they were wrong?”<sup>13</sup>

The issues raised with Krabbe disease highlight the rationale for two of the traditional criteria (#4 and #7) which focus on known trajectories and recognizable stages of disease. For public health, False Positives are a paramount concern. In the open commentary period following publication of the RUSP, analysis of comments made by health professionals found that “The most common theme was risk to the child from the impact of false positive results or results of uncertain clinical value. Identification of disorders for which therapies might be ineffective or dangerous was also viewed as a risk for the child. Three statements noted risks to the family, including parental anxiety related to false positives, insufficient information on disorders, early identification of carriers, and privacy concerns.”<sup>12</sup> Another public health professional described the issue of false positives, saying “screening tests almost always generate numerous “false positive” results that are frightening and often expensive and risky to address. If the harms from evaluating false positive results (e.g., tissue biopsies) outweigh the benefits of the program, then screening programs can be more harmful on balance than no program at all.”<sup>21</sup>

Of note, comments from genetic advocates are generally absent on this point. Indeed, analysis of lay and advocacy group comments to the RUSP found “no mention of any risks or burdens of screening”<sup>12</sup>. While

it is unlikely that genetic advocates support screening that increases harmful false positives experienced by families, the number of False Positive cases is not an expressed major concern. For public health, however, False Positives are an explicit concern that should be limited as much as possible.

### The False Negative

The “False Negative” case represents those newborns that have a congenital condition, but are not picked up by the screening test. Instead, those infants will likely be detected clinically following the development of symptoms and may experience poorer outcomes as a result of delayed treatment initiation. While NBS programs cannot be sure how many False Negative cases exist, given the tendency to develop test cutoff values to provide a high sensitivity that attempt to detect 100% of True Positives, they are likely to be relatively rare.

While the prevalence of False Negative cases that exist from the current panel of conditions routinely included in NBS was not present in the discourse as a major concern of either public health or genetic advocates, the False Negative case can instead be seen to highlight an underlying feature to the debate over NBS criteria concerning the role of technology. Without a doubt, both sides of the debate acknowledge technology as a driving force in NBS programs that allows congenital conditions to be detected. However, debate exists concerning the best role for technology in NBS programs, especially as science enters the age of genomic medicine.

For public health, technology is a tool to be used within the scope of traditionally-defined criteria and goals, and the presence of additional “False Negative” cases that hypothetically exist following restraint in utilizing technology to develop additional NBS tests is not a concern. As one public health professional stated “The availability of a suitable screening test does not justify screening for a disease unless the disease is important, relatively prevalent, and amenable to early treatment...<sup>22</sup>” However, despite these guidelines, it can be argued that a technological imperative remains at play in NBS; as one stakeholder put it, “the test itself is what gets the most attention, and the technology available for the test has been a critical factor driving the growth of newborn screening.<sup>26</sup>” For the public health side of the debate, NBS dictated by technological developments is risky, since it threatens to bypass traditional criteria thought to

be upheld to prevent harm and ensure the newborn is the primary beneficiary of screening. To that end, one stakeholder commented, “Above all, as thoughtful human beings, we cannot and must not permit what we do in medicine to be driven by the possession of technologies. We must keep technology in its proper place, which is a subordinate one to the overarching goal—if medicine is the focus—of the well-being of the individual patient. Here, surely, *do no harm* remains the surest guide.<sup>22</sup>” Negative implications stemming from a technological imperative in NBS are thought to include the transformation of the newborn into a “research subject”, whereby it is possible to detect the condition in the newborn and learn about the disease’s progression, but for which no efficacious treatments yet exist for the child. One epidemiologist described it in the following way: “early detection might provide the opportunity for research into preventive therapies...Even so, this is not what most people expect from screening. They expect a personal benefit, not to be a potential candidate for a research study.<sup>27</sup>” Or as another stakeholder said, “Expanded newborn screening is essentially *research* carried out for the public good, not the good of the infants being screened.<sup>22</sup>”

Conversely, for genetic advocates, failure to utilize the full potential of technology to develop and utilize NBS tests for as many congenital conditions as possible means that many “False Negative” cases will exist. The result of this is viewed as leaving many individuals and families without the benefits attributed to expanded screening, such as elimination of the diagnostic odyssey or increased information. One researcher described the promise held by technology to detect more conditions, saying “The technology could be expanded to screen for additional disorders as mutational analysis or other multiplex technology becomes available, with decisions being based more on what not to screen for (perhaps Huntington disease) than on what to include.<sup>21</sup>” Another physician added that additional NBS tests facilitated by new technology “adds to the capacity of the system to recognize things that pediatricians or family-practice doctors or nurse practitioners may not be thinking about or seeing every day,<sup>28</sup>” One mother described the importance of testing, saying “My son never got the chance at life because there was no testing, The more that we know, the more we can help them have a healthy, long, successful life.<sup>29</sup>”

While public health does not appear to be concerned with additional False Negatives in the population as a result of limiting the application of technology in NBS, this is a primary concern for genetic advocates.

According to genetic advocates, technology should be maximized to expand NBS tests and therefore reduce the number of hypothetical False Negatives that are not receiving the benefits of screening.

### The True Negative

The “True Negative” case represents the majority of individuals who undergo NBS. For that majority, NBS tests will give a negative result, which is congruent with the individual’s status as being unaffected by the rare congenital disorders being investigated. Following this result, the newborn’s parents are appropriately not contacted and most likely do not even recall undergoing NBS. This, of course, is the expectation of properly designed screening programs and both sides of the NBS criteria debate are satisfied with this result.

However, this seemingly ideal outcome reveals an underlying conflict between public health and genetic advocates over NBS. Following a True Negative screen, taxpayers, governmental agencies, and individual families have all made an investment in money or other resources that will not result in any particular net benefit for that newborn, other than to know the newborn did not screen positive for a rare congenital condition. Therefore, the True Negative case highlights the debate over the distribution of social goods within NBS programs; as the number of screening test increases, so does the cost, and the debate then revolves around questions of “who foots the bill?” and “what doesn’t get funded as a result?”

Public health, while dedicated to improving the health of newborns, also views careful distribution of social goods as part of their professional responsibility in accordance with their identity as public stewards. In this way, resources must be allocated in a way that maximizes benefits to a community in the face of competing needs. This leads to a broad consideration of NBS that considers its place among other resources that could provide other benefits to individuals and populations, such as healthcare and research funding, NBS infrastructure, other public health aims, and alternative options to improve newborn health. One public health professional considered this broad view and describing the need to reduce infant mortality said, “The final harms or costs to newborn screening programs are the opportunity costs ...Public health programs in the US are poorly funded in many states. Given this situation, more lives may be saved by devoting full attention and resources to programs that we know can be effective

rather than adding more and more tests for poorly understood conditions.<sup>21</sup> Another professional suggested that even for rare diseases, expanded NBS may not be the answer, saying instead that “perhaps it would be better to improve pediatricians’ abilities to recognize early symptoms<sup>14</sup>”. Finally, even when public health agrees that social goods should be allocated to additional NBS, in today’s economic climate, coming up with funding can be challenging. DHHS Secretary John Law spoke to this issue when he said “The biggest obstacle to offering all the tests continues to be finding the funding for the infrastructure...This includes purchasing the equipment needed to perform the tests and finding competent personnel to interpret the tests, as well as finding the necessary personnel to follow up with the children tested.<sup>30</sup>”

In contrast, genetic advocates support a greater distribution of social goods towards NBS, citing the cost savings for both families and society following efficient treatment for an affected newborn. One mother described her frustration with the lack of NBS for Severe Combined Immunodeficiency, saying: “It frustrates me that the state hasn’t passed this bill. My son is already costing them more in 10 months than they would pay in a whole year for testing.<sup>31</sup>” Another supporter described the cost-benefits of NBS in this way: “At a time of budget constraints, some might say that’s too much to pay, but consider the alternative...according to the Department of Health, the average lifetime medical costs for a child afflicted with these disorders can exceed \$1 million dollars. Treatment, on the other hand, can be as simple as a change in diet.<sup>32</sup>” Finally, one grandmother who lost her granddaughter to a condition not on the RUSP described the consequences of not supporting NBS, saying “the test only costs a few dollars, much less than the loss of income that families may face, the lack of productivity that organizations those families work for may face, the unpaid medical bills that poor families will leave to taxpayers. In short, this is the humane and economical right thing to do.<sup>33</sup>”

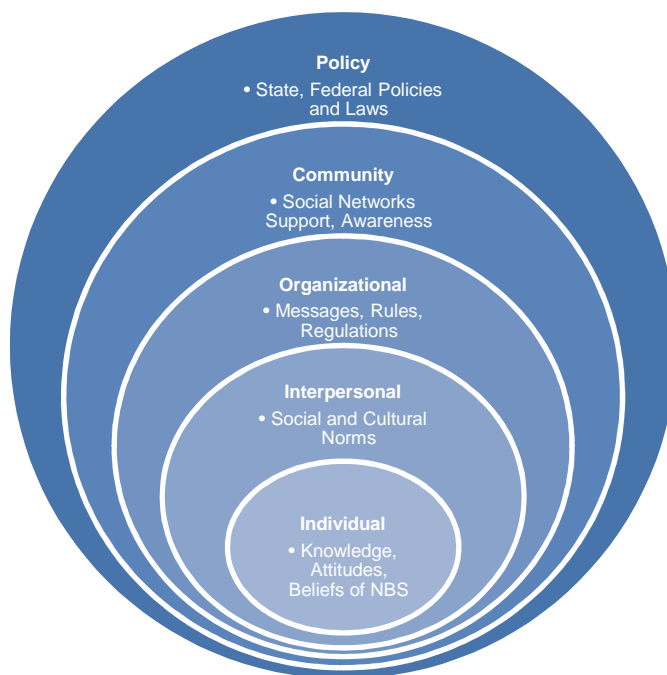
The True Negative case highlights differences in perception regarding the best distribution of social goods with public health supporting a broader distribution of social goods that considers alternative public needs and methods to address newborn illness and mortality. Genetic advocates on the other hand, highlight the cost-benefit that often results from NBS and suggests additional social goods be contributed to the effort.

#### IV. Discussion

##### A. Theoretical Implications

The underlying motives, values, and perceptions of each side of the NBS criteria debate may be best understood if kept within the context of how each side supports different tradeoffs regarding population versus individual benefit. Since decisions regarding NBS are not formulated in a vacuum, the different foci of the two sides are well-represented by different layers of the Social Ecological Model (SEM), which is a person-in-environment model that helps visualize how the context shifts as the focus moves along a continuum from the individual to society as a whole<sup>18,34</sup> (see figure 1). The first level of influence includes the individual themselves, where behaviors regarding NBS may be affected by real or perceived value of NBS, the risks and benefits of NBS, and issues of access to screening as well as access and affordability of diagnosis and treatment that may result from screening. The second level includes influence from interpersonal relationships with family members, friends, healthcare providers and professional peers that affect the social and cultural norms regarding NBS. The third level represents organizational activities that influence NBS behavior. Such organizations may include healthcare systems, professional organizations, and patient or genetic support groups that deliver NBS messages. The fourth level of the SEM includes influence by the community that delivers regional communications and support. Community activities may include messages by health departments, advocacy coalitions, and the media to promote public awareness and leverage resources. The fifth and final level of the SEM includes NBS messages at the policy level and may include interpreting and implementing existing policy as well as support of new policies<sup>34</sup>.

Figure 1: The Social Ecological Model of NBS



Not surprisingly, I found evidence to suggest that the public health side of the debate is primarily influenced by the outer layers of the SEM, which is congruent with their charge to focus on population health that balances benefits and harms for both affected and unaffected individuals. That is, influence from state and national NBS policy, and the community of state and national NBS recipients shaped the underlying motives, values, and perspectives of public health stakeholders who seek outcomes on the population-level and who experience a sense of duty to the population to distribute benefits and minimize harms in an equitable fashion. Conversely, I found discursive evidence to suggest that genetic advocates are more heavily influenced by the inner rings of the SEM, and messages from organizations of which they are a part, as well as interpersonal connections and personal experiences have shaped their underlying motives regarding NBS criteria. Genetic advocates seek outcomes on the individual level and experience a duty to provide benefit and prevent harm for the individual who is rare within the population. Therefore, it is important to recognize these generally differing spheres of influence while considering the perspectives of individual speakers within the debate over NBS criteria, especially since they seem to confer different normative standards regarding to whom each side perceives to owe a moral duty to. Of course, however, all stakeholders are affected by all levels of the SEM. That is, it would be impossible for

a public health stakeholder to be unaffected by a personal experience with NBS, just as it would be impossible for a genetic advocate to be unaffected by national NBS policy. In general, these findings help to contextualize how the opposing sides of the NBS criteria debate fall into different categories of the sensitivity/specificity model and will guide practical implications.

In addition, differences in each side's focus and moral duties can be mapped onto the disagreement regarding which thresholds are used to evaluate the sensitivity and specificity of a particular screening test (see Table 7). In one example, the True Positive case highlights differences in perception regarding the types of benefit that justify NBS; with public health seeking to limit identification of True Positive cases to those who are likely to experience improved health outcomes following treatment, while genetic advocates support expanding the population of True Positives that are detected so that families can receive other types of benefit such as information or earlier access to behavioral resources. Given that the sensitivity/specificity assessment is a unique feature of screening programs, conceptualizing the debate as though each side were applying different cutoff values to a screening test, resulting in differing sensitivities and specificities, and therefore different outcomes, is a unique and useful way to elucidate the underlying motives, values, and perspectives. Doing so makes a complex debate more theoretically manageable, as it becomes clear which of the four potential outcomes on the chart each side of the debate focuses on and the values and perspectives that influence those positions.

TABLE 7. QUOTES REPRESENTATIVE OF PUBLIC HEALTH AND GENETIC ADVOCATE'S PERSPECTIVES ON ISSUES IN THE NBS CRITERIA DEBATE

Issue:	Public Health Perspective	Genetic Advocate Perspective
The True Positive Case: Benefit Justifying NBS	"If we have the assay that can work, and we can intervene...and we can do so with all the state economics working, we should be testing everywhere." <i>Jelili Ojodu, APHL</i> <sup>19</sup>	"ALL babies should be screened as fully as possible AT BIRTH ~ and NOT through an autopsy!" <i>FOD support group</i> <sup>35</sup>
The False Positive Case: Balancing Benefit and Harm in NBS	"Screening tests almost always generate numerous "false positive" results that are frightening and often expensive and risky to address. If the harms from evaluating false positive results (e.g., tissue biopsies) outweigh the benefits of the program, then screening programs can be more harmful on balance than no program at all." <i>Donald B. Bailey, Jr.</i> <sup>21</sup>	"There was no mention of any risks or burdens of screening other than to discount arguments that conditions for which there is no proven medical treatment for the child should not be included in newborn screening." <i>Donald B. Bailey, Jr.</i> <sup>21</sup>
The False	"The availability of a suitable screening test	"My son never got the chance at life

Negative Case: Role of Technology in NBS	does not justify screening for a disease unless the disease is important, relatively prevalent, and amenable to early treatment..." <i>President's Council on Bioethics</i> <sup>22</sup>	because there was no testing, The more that we know, the more we can help them have a healthy, long, successful life." <i>Carol Cross</i> <sup>29</sup>
The True Negative Case: Distribution of Social Goods in NBS	"The states are using public dollars and weighing the benefits...A screen may be picking up one baby every 10 years, and they have to weigh this against the cost of providing clean water for the state." <i>Jelili Ojodu, APHL</i> <sup>19</sup>	"The test only costs a few dollars, much less than the loss of income that families may face, the lack of productivity that organizations those families work for may face, the unpaid medical bills that poor families will leave to taxpayers. In short, this is the humane and economical right thing to do." <i>Sherri Daniels</i> <sup>33</sup>

## B. Practical Implications

These results suggest several practical implications for both public health and genetic advocates within the debate over NBS criteria. First, there is value in determining what exactly both sides of the debate agree and disagree on. Identifying specific issues of agreement or controversy, as well as the underlying motivations behind them, allows both sides to grant each other "recognition" in the form of genuine understanding of each other's values and perspectives. In this way, a safe space of appreciation may be generated, facilitating productive conversations where the two sides are no longer simply "talking past one another".

Additionally, public health and genetic advocates have more areas of agreement concerning NBS criteria than disagreement. This reinforces the sentiment that the two stakeholders are rightful partners in their passion and mission to improve newborn and population health. However, differences do exist regarding the motives, values, and perspectives that each side holds toward NBS criteria that are congruent with their differing sense of moral duty. Since we cannot expect or desire that either side will change the group to whom they feel a moral obligation to provide benefit and limit harm, practical steps forward must address other routes.

One solution would be to acknowledge that value differences require that there be "winners" and "losers" regarding NBS criteria. In this way, one argument may be found to be much more compelling than the other, and would thus dictate the nature of NBS programs. If this were the case, it would be important to

ensure that adequate supports, whether resources, alternative programs, or otherwise are available to the “loser”.

Another solution may be adopt a mutual framework or end goal and collaborate honestly to assess what compromises must be made to reach that goal. For example, both sides could adopt a consequentialist framework and identify mutual outcome goals. In this way, if both sides determined that a specific goal, such as identifying 100% of true positive cases or that a certain cost-benefit threshold should not be breached, that would dictate other policy decisions.

Overall, the fact that public health and genetic advocates differ in their duties to provide benefit and minimize harm with NBS is a positive feature that promotes an inclusive NBS process. However, the resulting differences in motives, values, and perspectives regarding NBS criteria requires that difficult decisions be made in order to move forward in the debate and work collaboratively in their shared mission to improve newborn health.

### C. Evaluation

Discourse analysis as I applied it here is especially useful when investigating the power of language within a specific Conversation, including specific groups. However, the interpretative aspect of this method requires a great deal of reflexivity and the method is not designed to inform issues of causality or personal experience<sup>17</sup>. One specific limitation of this study is the lack of participant involvement. That is, funding/time did not allow me to include individuals taking part in various sides of the Conversation in the study, who would have been able to provide valuable insight as to whether the interpretations I made and conclusions I drew were in line with their own interpretations of their motives, values and perspectives.

### V. Conclusion

Despite being declared as one of the greatest public health achievements of the 20<sup>th</sup> century, NBS has not proceeded into the 21<sup>st</sup> century without challenges. Entering an era characterized by breakthrough medical technologies, savvy consumers, and inadequate funding, NBS programs in the United States can be viewed as resting upon a tipping point: poised to either fall back into the “public health emergency” model or proceed with the “public health service” philosophy<sup>36</sup>. While society’s fascination with technology

as a driver has seemed to seal the fate of the latter philosophy in NBS, debate over several other facets remains. Namely, public health and genetic advocacy stakeholders disagree over the nature of criteria that should be used to evaluate potential NBS tests. A study of the discursive practices of both sides of this debate helped to elucidate the underlying values, motives, and perspectives. Specifically, I found that the issues of the debate were well characterized by a model routinely used within screening programs to evaluate the outcomes of a screening test. In this way, it became possible to describe how the two sides in the debate were differentially influenced by layers of the SEM to provide benefit to either entire populations or individuals, and how their values and perspectives translated into different goals and attitudes regarding the various possible outcomes of a NBS test. Theoretically viewing the debate in this way also pointed to practical implications to enhance collaboration and included “recognition” of the other side’s values and motivations as an important step forward. Following this moral recognition of the opposing views, honest collaboration must take place that may weigh the strength of arguments or work backwards from agreed upon goals. In this way, there is little doubt that public health and genetic advocacy stakeholders will continue to act as partners to develop mutual NBS criteria and by doing so will ensure that NBS’s legacy as a substantial public health achievement continues.

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#### Appendix A: Chronological Ordering of NBS Criteria Data

Chronological Ordering of NBS Criteria Data	
Year	List of Events
2006	<ul style="list-style-type: none"> <li>• "ALENA AND MIA ROSE" Save Babies Through Screening Foundation (Jan 2006)<sup>37</sup></li> <li>• "From Public Health Emergency to Public Health Service: The Implications of Evolving Criteria for Newborn Screening Panels" Commentary (Mar 2006)<sup>10</sup></li> <li>• ACMG Report: Newborn Screening: Towards a Uniform Screening Panel (May 2006)<sup>11</sup></li> <li>• Genetic Alliance Policy Statement: Comments to Secretary's Advisory Committee on Heritable Disorders and Genetic Diseases in Newborns and Children (May 2006)<sup>23</sup></li> <li>• "A healthier start for children" Opinion piece in <i>The Oklahoman</i> by John J. Mulvihill, MD (Jun 2006)<sup>38</sup></li> <li>• "The PKU Test Has Come A Long Way, Baby!" by Laura Weathers, MD for the <i>Tampa Tribune</i> (Jun 2006)<sup>39</sup></li> <li>• "Gene disorder tests start at birth" <i>The Oklahoman</i> (Jun 2006)<sup>40</sup></li> <li>• "Saved by a drop of blood; States expand routine testing of newborns" <i>USA Today</i> (Jul 2006)<sup>41</sup></li> <li>• "Newborn testing Screening lessens risks posed by genetic illnesses In the Midlands" <i>Omaha World-Herald</i> (Jul 2006)<sup>42</sup></li> <li>• "Virginia screens babies for 28 rare diseases; when treated early, serious effects can be limited or prevented" <i>Richmond Times Dispatch</i> (Jul 2006)<sup>28</sup></li> <li>• "State to expand newborn screening; At present, W.Va. tests for only 7 of 29 serious disorders, March of Dimes reports" <i>Charleston Daily Mail</i> (Jul 2006)<sup>30</sup></li> <li>• "Ohio to begin testing babies for cystic fibrosis; Screening also required for second illness"</li> </ul>

	<ul style="list-style-type: none"> <li>The Blade (Ohio) (Aug 2006)<sup>43</sup></li> <li>“Changing Perspectives on the Benefits of Newborn Screening” (Sept 2006)<sup>12</sup></li> <li>Committee Report: Evidence-based Evaluation and Decision Process for the SACHDNC (Oct 2006)<sup>44</sup></li> </ul>
2007	<ul style="list-style-type: none"> <li>“‘Bubble boy’ illness targeted; State may lead way in screening newborns” The Milwaukee Journal Sentinel (Jan 2007)<sup>45</sup></li> <li>“Doctors screening for early ‘bubble boy disease’” The Maryland Gazette (Jan 2007)<sup>46</sup></li> <li>“Up for vote; simple, required screening could save infants” The Charleston Gazette (Mar 2007)<sup>47</sup></li> <li>“Screening in State Reveals a Surprise About Hmong Babies” Wisconsin State Journal (Apr 2007)<sup>48</sup></li> <li>“Newborn testing expands to more states, disorders” USA Today (Jul 2007)<sup>49</sup></li> <li>SACHDNC Report: Advancing the Current Recommended Panel of Conditions for NBS (Aug 2007)<sup>50</sup></li> <li>“Newborn Screening: The Spigot is Open and Threatens to Become a Flood” Editorial, Journal of Pediatrics (Aug 2007)<sup>7</sup></li> </ul>
2008	<ul style="list-style-type: none"> <li>Newborn Screening Saves Lives Act of 2007 (Jan 2008)<sup>51</sup></li> <li>“States Rapidly Adopt CF Newborn Screening” Pediatric News (Jan 2008)<sup>52</sup></li> <li>“The Future of Newborn Screening: Clouds on the Horizon?” Staff Discussion Paper, The President’s Council on Bioethics (Mar 2008)<sup>14</sup></li> <li>“Test Newborns for Treatable Disorders; Pennsylvania Could Save Lives and Money by Requiring More Pre-Screening” Editorial by Catherine Houska, March of Dimes for the Pittsburgh Post-Gazette (Apr 2008)<sup>32</sup></li> <li>“Expanding Newborn Screening: Process, Policy, and Priorities” U.S. Preventative Services Task Force Report (May 2008)<sup>26</sup></li> <li>“Cause drives Kelly: Newborn screening” Buffalo News (Jun 2008)<sup>53</sup></li> <li>“Genomic Medicine Newborn Screening” Family Practice News (Oct 2008)<sup>54</sup></li> <li>“The Changing Moral Focus of Newborn Screening: An Ethical Analysis by the President’s Council for Bioethics” (Dec 2008)<sup>22</sup></li> </ul>
2009	<ul style="list-style-type: none"> <li>“Saved by a screening; Newly mandatory test for newborns was a lifesaver for Raynham girl” The Patriot Ledger (Massachusetts) (Jan 2009)<sup>55</sup></li> <li>“Assessing the new newborn screening criteria” by Jeffrey Botkin, MD, MPH, Chief of Medical Ethics at University of Utah, in Health Matrix (Feb 2009)<sup>21</sup></li> <li>“ALEC” Save Babies Through Screening Foundation (Apr 2009)<sup>56</sup></li> <li>“Kelly wants Obama’s help in testing issue” Buffalo News (Jun 2009)<sup>57</sup></li> </ul>
2010	<ul style="list-style-type: none"> <li>SACHDNC Commentary: Method for Evaluating Conditions Nominated for Population-based Screening of Newborns and Children (Jan 2010)<sup>58</sup></li> <li>“Emma’s Story” Letter to Congressman (Feb 2010)<sup>33</sup></li> <li>ACMG Review: An Evidence Development Process for Newborn Screening (Mar 2010)<sup>59</sup></li> <li>IDF Advocate: The National Newsletter of the Immune Deficiency Foundation “Newborn Screening for SCID – The Time is Now” (Mar 2010)<sup>60</sup></li> </ul>
2011	<ul style="list-style-type: none"> <li>SACHDNC Commentary: Response to President’s Council on Bioethics Report on the Changing Moral Focus of NBS<sup>61</sup></li> <li>“Scott bursts bubble” The Tampa Tribune (Jun 2011)<sup>62</sup></li> <li>“Baby’s big screen test. Blood samples are an infant’s first line of defense against metabolic disorders” Daily News (New York) (Jul 2011)<sup>63</sup></li> <li>Association of State and Territorial Health Officials: Newborn Screening - Position Statement (Oct 2011)<sup>64</sup></li> <li>“Dangerous and Expensive Screening and Treatment for Rare Childhood Diseases: The Case of Krabbe Disease” (Nov 2011)<sup>24</sup></li> </ul>
2012	<ul style="list-style-type: none"> <li>“A test that saves lives and money” The Tampa Tribune (Jan 2012)<sup>65</sup></li> <li>“Screening could save infants’ lives” Tampa Bay Times (Apr 2012)<sup>31</sup></li> </ul>

	<ul style="list-style-type: none"> <li>• “Commentary Quality Newborn Screening” Pediatric News (May 2012)<sup>66</sup></li> <li>• “Debate over baby testing; Some Experts Question Extensive Medical Screening of Infants” St. Louis Post-Dispatch (Oct 2012)<sup>29</sup></li> </ul>
2013	<ul style="list-style-type: none"> <li>• “Department of Health: Newborn screenings turn 50 this year” Las Cruces Sun-News (New Mexico) (Jan 2013)<sup>67</sup></li> <li>• “Lawmaker hopes to save babies by mandating simple newborn screening test” Deseret Morning News (Utah) (Feb 2013)<sup>68</sup></li> <li>• “Blood tests ‘saved my life’” Star Tribune (Minnesota) (Mar 2013)<sup>20</sup></li> <li>• Association of Public Health Laboratories “The Newborn Screening Story: How One Simple Test Changed Lives, Science, and Health in America” (May 2013)<sup>19</sup></li> <li>• SACHDNC Statement: Decision-making Process for Conditions Nominated to the RUSP (Jun 2013)<sup>69</sup></li> <li>• “Screening of infants finds hidden defects” Herald News (New Jersey) (Jul 2013)<sup>70</sup></li> <li>• March of Dimes Testimony “Newborn Screening Saves Lives: The Past, Present and Future of the Newborn Screening System” (Sept 2013)<sup>71</sup></li> <li>• “Brigham and Women’s Hospital Awarded \$6 Million to Study Genome Sequencing in Newborns” India Pharma News (Sept 2013)<sup>72</sup></li> <li>• “Utah: NIH program explores the use of genomic sequencing in newborn healthcare” US Official News (Sept 2013)</li> <li>• “Simple newborn screening saving babies’ lives” Deseret Morning News (Utah) (Oct 2013)</li> <li>• “The Test That Babies Need” The New York Times (Oct 2013)</li> <li>• “Va. celebrates newborn screening; State looks to further expand its program, which began in 1966” Richmond Times Dispatch (Virginia) (Nov 2013)</li> <li>• “ALD-AMN Global Alliance Position Statement on addition of newborn screening of X-Linked Adrenoleukodystrophy (X-ALD) to the SACHDNC recommended uniform panel and to individual state newborn screening programs” (current)</li> <li>• “Support Expanded Newborn Screening in Your State” Hunter’s Hope Foundation (current)</li> <li>• “Newborn Screening” Fatty Oxidation Disorders Family Support Group (current)</li> </ul>