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ORIGINAL ARTICLE

Cross-sectional survey on genetic testing utilization and perceptions in Wisconsin Amish and Mennonite communities

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Abstract

Amish and Mennonite (Plain) communities have increased prevalence of many recessively inherited disorders due to founder variants that can be identified using next-generation sequencing (NGS). We assessed newborn screening (NBS) utilization, prior genetic testing, and perceptions of genetic testing among Wisconsin Plain communities to guide implementation and utilization of a population-specific NGS gene panel testing. A mailed paper survey ($N=959$) of demographics, NBS utilization, prior genetic testing, and preferences for categorical genetic disorder and defined clinical context testing was developed. Overall response rate was 39% ($N=378$; 183 Amish, 193 Mennonite; 2 not Amish/Mennonite). Mennonites were more likely to respond in favor of carrier screening for metabolic disorders and other surgical conditions and less likely to respond in favor of asymptomatic testing for neurologic disorders and lethal disorders compared to Amish. Reported utilization of NBS was positively associated with stated interest in genetic testing for an asymptomatic child. Reported prior genetic testing was positively associated with stated interest in carrier screening and negatively associated with testing a symptomatic child. Although Plain community members share many common outward characteristics, our survey responses suggest diversity in their views of genetic testing and support laboratory methods that can be flexible to varied needs of individuals.

Keywords Amish · Mennonite · Plain · Genetic testing · Newborn screening

Introduction

The Amish and Mennonite (collectively called "Plain") communities are Anabaptist religious groups known for their simple dress, agrarian lifestyle, and selective use of technology. Present-day Plain communities arose from a few hundred European families who immigrated to North America beginning in the seventeenth century to escape religious persecution (Kraybill et al. 2013). Small founding populations settled in Pennsylvania, migrated west to neighboring states, and quickly increased in number. Currently, the Plain population in North America is over 350,000, and Wisconsin has fourth largest state population with an estimated population over 23,000 (Amish Population 2021).

The Plain population has continued to grow in numbers with sustained large family sizes. The Plain population has an estimated doubling every 20 years with rare instances of individuals from outside the Plain community joining the faith (Donnermeyer 2021). Together, this led to founder effects and genetic drift resulting in a higher incidence of recessively inherited genetic disorders among the Plain communities compared to the general population (Puffenberger 2003; Strauss and Puffenberger 2009). Plain community members do not typically participate in health insurance programs, so several non-profit, community-based clinics have been established in rural areas to care for children from the Plain communities with genetic disorders and special

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medical needs. Laboratory services within these clinics, including DNA sequencing technologies, have identified over 270 disease-causing founder variants among the Plain communities (Crowgey et al. 2019).

Originally, single founder gene variants were detected by quick and low-cost methods such as targeted Sanger sequencing or high-resolution melt analysis with an unlabeled probe (Crowgey et al. 2019). Single variant genetic testing provides rapid and affordable diagnosis for a symptomatic child, testing for an asymptomatic newborn with a family history of a genetic disorder, or carrier screening for members of the Plain community (Furnier et al. 2020). Advances in DNA sequencing techniques, particularly next-generation sequencing (NGS), now allow for testing of hundreds of Plain community pathogenic founder gene variants simultaneously. This technology has great potential to expand diagnostic capacity and cost-effectively identify pathogenic gene variants from a single sample collection.

Because of the potential increased value of NGS gene panel testing encompassing a multitude of medically actionable gene variants and the known challenges to accessing medical care for the Plain community, we sought to assess Wisconsin Plain community members perceptions and utilization of genetic testing through development and dissemination of a paper survey. Specifically, we inquired about interest in genetic testing in different contexts (asymptomatic children, symptomatic children, and carrier screening) and for a variety of genetic disorder categories. We aimed to determine if characteristics such as age, Plain community affiliation, experience with newborn screening (NBS), or prior genetic testing were associated with a particular response. Our goal is to use this information to develop education and communication materials, guide implementation, and optimize utilization of a population-specific NGS panel to meet the needs and interests of the Plain community in Wisconsin.

Materials and methods

Survey instrument and distribution

We developed a paper survey instrument that consisted of 28 questions (see Supplementary Materials). A glossary was provided for terms most likely to be unfamiliar to the survey respondent. The survey included 8 questions (multiple choice, yes/no, or open ended) related to demographics, family size, utilization of NBS, and experience with genetic testing. Nine additional questions inquired about testing for genetic disorders that were divided into disease categories (neurologic diseases, hearing loss, metabolic disorders, heart conditions, immune disorders, bleeding disorders, lethal conditions, other medical conditions, and other surgical conditions). The survey contained a brief explanation of each genetic disorder, including the availability of treatment and examples of genetic disorders included within that category (for some). For each genetic disorder category, respondents were asked to provide their preferred choice for genetic testing: (1) "*Before* my child had symptoms" (to indicate an asymptomatic child); (2) "*After* my child had symptoms" (to indicate a symptomatic child); (3) "To know if I am a carrier of the disorder" (to indicate carrier screening); (4) "Not at all"; (5) "I am unsure"; or (6) "I prefer not to answer." Respondents could select more than one preferred choice for each genetic disorder category. The survey also contained 11 questions (2 regarding cost of genetic testing, 3 related to the use of telemedicine, and 6 regarding carrier screening for spinal muscular atrophy) that are outside the scope of this report and will be described elsewhere.

The survey was mailed to Plain community households using mailing lists from our previous survey of NBS practices (Sieren et al. 2016) and a mailing list for the Center for Special Children, a rural health program in western Wisconsin that cares for children with genetic disorders from the Plain community. Each household received one survey and were asked to complete for their nuclear family. An incentive for survey completion was provided as $1 donation to the Center for Special Children for each returned survey. A total of 959 surveys were mailed on January 17, 2020. Surveys returned between January 18, 2020, and May 11, 2020, were included in the study. The University of Wisconsin Health Sciences IRB determined that this study is not human subjects research (45 CFR 46: Category 2) and is exempt from IRB review.

Data collection and statistical analysis

A Research Electronic Data CAPture (REDCap™) database was developed for deidentified survey data entry. Descriptive characteristics were summarized for the entire cohort and by community (Amish or Mennonite) with percentages rounded to the closest whole number or with the median and inter-quartile range (IQR). Characteristics were compared between communities using chi-squared or Fisher's exact tests (for categorical factors) or the Wilcoxon rank-sum test (for numerical characteristics of age and family size). The association between community and categorical factors of interest was summarized with odds ratios (OR); for age and number of children, the chance a respondent from a Mennonite family would be of greater age or have more children than an Amish. Univariate and multivariable logistic regression was used to identify associations between utilization of NBS or prior genetic testing and effects of age and community. Interest in genetic testing for each disorder type and time of testing was separately examined through similar models involving community, utilization of NBS, and prior genetic

testing. Data were analyzed using R version 4.0.3 (https://www.R-project.org) (R Core Team 2020). A p-value ≤ 0.05 was considered statistically significant with no adjustment for multiple testing in this exploratory research.

Results

Survey respondent characteristics

Three hundred seventy-eight of the 959 delivered surveys were returned (overall response rate 39%). Two surveys were returned by respondents who did not identify as Amish or Mennonite and were not included in the data analysis. Respondent characteristics are outlined in Table 1. Survey respondents were almost equally distributed between the Amish ($n=183$) and Mennonite ($n=193$) communities. The median age was slightly higher for Amish compared to Mennonite respondents but did not reach statistical significance. Most respondents (96% of Amish and 99% of Mennonite) had children with the family size significantly larger among Amish compared with Mennonite respondents (median = 8 children vs median = 7 children, respectively, $p=0.006$).

Relationships between reported prior NBS testing or genetic testing for any family member and Plain community affiliation were explored since both would suggest an openness to testing for genetic disorders. Mennonite respondents reported a significantly higher rate of NBS for all versus none of their children compared to Amish (OR 6.4, $p<0.001$, Table 1). In contrast, there was no significant association between reported prior genetic testing and Plain community affiliation.

Respondent associations with prior genetic testing

Because NBS is a universal public health program aimed at early detection of many genetic disorders, we conducted further analyses to explore crude (univariate) and adjusted (multivariable) associations between reported utilization of NBS and independent characteristics (Plain community affiliation, survey respondent age, and reported prior genetic testing for any family member). For these analyses, reported NBS for all or some children in a family were aggregated. In univariate analysis, Mennonite community affiliation was significantly associated with reported NBS utilization compared to Amish (OR 4.35, $p<0.001$, Table 2). There was a linear relationship between age and reported utilization of genetic testing, so OR represents the effect per 10 years of age of the respondent. Older parental age was linearly associated with decreased likelihood of indicating newborn screening for all or some children (OR 0.29 per decade of age, $p<0.001$, Table 2). Reported prior genetic testing (OR 2.82, $p=0.002$, Table 2) and reported uncertainty about prior genetic testing (OR 6.38, $p=0.020$, Table 2) were each separately associated with increased likelihood of utilizing NBS for all or some children. Multivariable analysis controlling for respective independent characteristics (community affiliation, age, and prior genetic testing use) showed relationships between reported NBS utilization and Mennonite community affiliation (aOR 6.85, $p<0.001$), age (aOR 0.25, $p<0.001$), and reported prior genetic testing use ("Yes" [aOR 3.65, $p=0.003$] or "Unsure" [aOR 7.44, $p=0.033$, Table 2]).

Next, we examined relationships between reported prior experience with genetic testing by two independent characteristics (Plain community affiliation and age). Because we

Table 1 Study participant characteristics

	Amish $N=183$	Mennonite $N=193$	Estimated effect[a]	p-value
Age (years), median (IQR)	45 (35–56)	42 (34–51)	44.3% (38.4–50.2%)	0.059
Respondents with children, N (%)	176 (96)	191 (99)	3.79 (0.83–26.6)	0.097
Number of children, median (IQR)	8 (5–11)	7 (5–9)	41.8% (36.6–47.0%)	**0.006**
Newborn screening for children, N (%)				
None	40 (23)	13 (7)	Reference	
Some	37 (21)	4 (2)	0.33 (0.10–1.11)	0.074
All	76 (43)	158 (83)	6.40 (3.23–12.70)	**<0.001**
Unsure	23 (13)	15 (8)	2.01 (0.81–4.95)	0.130
Prior genetic testing, N (%)				
No	103 (57)	106 (55)	Reference	
Yes	60 (33)	73 (38)	1.18 (0.76–1.83)	0.452
Unsure	17 (9)	14 (7)	0.80 (0.38–1.71)	0.564

[a]For numerical characteristics (age and number of children), the estimated effect is the probability (expressed as a percentage) that the response is greater for Mennonites than for Amish. For categorical factors (respondents with children, newborn screening for children, and prior genetic testing), the estimated effect is the odds ratio of Mennonite to Amish

Table 2 Association between reported newborn screening utilization in all or some children and Plain community affiliation, age, and prior genetic testing

	Crude odds ratio (95% CI)	*p*-value	Adjusted odds ratio (95% CI)[a]	*p*-value
Plain community affiliation				
Amish	Reference		Reference	
Mennonite	4.35 (2.27–8.82)	**< 0.001**	6.85 (2.99–17.1)	**< 0.001**
Age				
Per 10 years	0.29 (0.20–0.39)	**< 0.001**	0.25 (0.16–0.36)	**< 0.001**
Prior genetic testing				
No	Reference		Reference	
Yes	2.82 (1.42–6.01)	**0.002**	3.65 (1.54–9.38)	**0.003**
Unsure	6.38 (1.28–116)	**0.020**	7.44 (1.15–149)	**0.033**

[a]Multivariable logistic regression adjusted for Plain community affiliation, age, and prior genetic testing. Analysis includes $N = 319$ respondents ($N = 148$ Amish and $N = 171$ Mennonite) with complete responses for all independent variables (Plain community affiliation, age, and prior genetic testing)

observed that the association with age for this response was not strictly linear, the OR is computed over one IQR of age (25th to 75th percentile, i.e., 34 to 54 years). Using both univariate and multivariable analyses, there was no significant association between reported prior genetic testing and Plain community affiliation or age (Table 3).

Preferences for categorical genetic disorder testing and varied clinical context

To better understand Plain community family preferences for genetic testing, our survey segregated genetic disorders into nine distinct disease categories and three defined clinical contexts (asymptomatic, symptomatic, or carrier screening). Collectively, the average stated affirmative interest was 39% for asymptomatic testing, 28% for symptomatic testing, and 32% for carrier screening. Among those who stated an interest in genetic testing, 40% indicated interest in genetic testing for one clinical context, 40% stated interest in two contexts, and 20% stated interest in all three contexts. For those who responded in favor of genetic testing in at least one of these clinical contexts, most respondents (72% of those interested in asymptomatic testing, 81% of those interested in symptomatic testing, and 64% of those interested in carrier screening) selected some, but not all, disease categories. The remaining respondents stated an interest in testing for all disease categories in that clinical context. Among specific disease categories, the highest level of stated interest was for asymptomatic testing for metabolic disorders (48%, Table 4), while the lowest level of interest was for symptomatic testing of metabolic disorders (20%, Table 4).

Twenty-eight respondents (57% Amish, 43% Mennonite) with a median age of 42 years (range 26–70 years, missing data $N = 1$) indicated they were "Not at all" interested in genetic testing for at least one genetic disorder category, with a range of 1% and 4% for any given category (Table 4). It is important to note that respondents could choose "Not at all" for more than one disorder, so the aggregate reported lack of interest in genetic testing represents 73 responses obtained from these individuals. The greatest lack of interest in genetic testing was indicated for disorders treated with surgery (4%) and immune disorders (3%). Seven of these respondents (25%) reported prior experience with genetic testing, and 20 of these respondents (71%) indicated they utilized NBS for all children. Although one respondent selected "Not at all" interested for all 9 disease categories,

Table 3 Association between reported prior genetic testing and Plain community affiliation and age

	Crude odds ratio (95% CI)	*p*-value	Adjusted odds ratio (95% CI) [a]	*p*-value
Plain community affiliation				
Amish	Reference		Reference	
Mennonite	1.13 (0.73–1.76)	0.588	1.12 (0.72–1.76)	0.610
Age				
54 years vs 34 years (1 IQR)	1.08 (0.72–1.61)	0.709	1.09 (0.73–1.62)	0.678

[a]Multivariable logistic regression adjusted for Plain community affiliation and age. Analysis includes $N = 334$ respondents ($N = 159$ Amish and $N = 175$ Mennonite) who responded to questions regarding age and affiliation and who were also certain about prior experience with genetic testing (either yes or no; excludes unsure)

Table 4 Reported interest in genetic testing

	Total	Reported interest in genetic testing					
		Asymptomatic	Symptomatic	Carrier	"Not at all"	"Unsure"	"I prefer not to answer"
Type of disorder	N	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)
Neurologic diseases	355	121 (34)	113 (32)	128 (36)	6 (2)	78 (22)	3 (1)
Hearing loss	345	124 (36)	126 (37)	96 (28)	7 (2)	58 (17)	3 (1)
Metabolic disorders	347	167 (48)	68 (20)	132 (38)	6 (2)	53 (15)	4 (1)
Heart conditions	343	153 (45)	78 (23)	112 (33)	4 (1)	70 (20)	2 (1)
Immune disorders	345	127 (37)	110 (32)	98 (28)	11 (3)	70 (20)	2 (1)
Bleeding disorders	343	142 (41)	87 (25)	104 (30)	9 (3)	65 (19)	4 (1)
Lethal conditions	340	134 (39)	92 (27)	110 (32)	10 (3)	62 (18)	3 (1)
Other medical conditions	343	142 (41)	95 (28)	110 (32)	7 (2)	66 (19)	1 (< 1)
Other surgical conditions	343	116 (34)	110 (32)	101 (29)	13 (4)	85 (25)	2 (1)

the majority (68%) indicated "Not at all" interested for 1 or 2 disease categories.

Between 15 and 25% of respondents selected "I am unsure" when asked about genetic testing for a genetic disorder category (Table 4). The greatest amount on uncertainty was indicated for disorders treated with surgery (25%) and neurologic disorders (22%), and less so for metabolic disorders (15%). Again, individuals could respond with uncertainty for more than one disorder. A total of 608 responses of uncertainty were collected from 149 individuals (53% Amish, 47% Mennonite) with a median age of 44 years (range 22–84 years, two not specified). Forty-five (30%) individuals who indicated uncertainty about genetic testing also reported prior experience with genetic testing, and 85 (57%) indicated they utilized NBS for all their children.

For a given genetic disorder category, between 1 and 4 individuals indicated they "prefer not to answer" regarding their interest in genetic testing. The collective 24 responses came from 10 individuals (70% Amish, 30% Mennonite) with an age range of 29–51 years. Two of the respondents had prior experience with genetic testing. None selected "I prefer not to answer" for every disease category; however, two individuals selected "I prefer not to answer" for 6 or 7 genetic disorder categories and identified as Amish. Remaining respondents chose "I prefer not to answer" for 1 or 2 genetic disorder categories. Nine (90%) of the 10 respondents had children, and of those, 7 reported newborn screening for all or some of their children.

The relationship between reported affirmative interest in genetic testing for asymptomatic children, symptomatic children, and carrier testing adjusting for independent characteristics (community affiliation, utilization of NBS for any of their children, and prior genetic testing) was determined using multivariable logistic regression analysis. Mennonites were more likely to respond in favor of carrier screening for metabolic disorders (aOR 3.06, $p < 0.001$, Fig. 1, left panel) and other surgical conditions (aOR 2.01, $p = 0.018$, Fig. 1, left panel) compared to Amish. Mennonites were less likely to respond in favor of asymptomatic testing for neurologic disorders (aOR 0.51, $p = 0.012$, Fig. 1, left panel) and lethal disorders (aOR 0.55, $p = 0.024$, Fig. 1, left panel) compared to Amish.

Utilization of NBS was associated with reported interest in asymptomatic testing for eight of the nine disease categories. These disease categories included neurologic disorders, hearing loss, metabolic disorders, heart conditions, immune disorders, bleeding disorders, other medical conditions, and other surgical conditions (each disease category with an aOR ≥ 2.5, $p < 0.04$ for all, Fig. 1, middle panel).

Reported prior genetic testing was positively associated with stated interest in carrier screening for all the defined disorder types (aOR 1.79–2.56, $p < 0.03$, Fig. 1, right panel). Reported prior genetic testing was negatively associated (aOR < 0.60 for each, $p < 0.05$ for each, Fig. 1, right panel) with stated interest in symptomatic testing for hearing loss, metabolic disorders, heart conditions, immune disorders, bleeding disorders, and other surgical conditions.

Discussion

In this survey study, we found higher reported utilization of NBS among Mennonites, younger respondents, and those who indicated prior experience with genetic testing. Although there was some level of interest in genetic testing for each of the disease categories and testing contexts presented in our survey, stated interest varied significantly by community affiliation, utilization of NBS, and prior genetic testing. There was also a small, but notable, reported lack of interest in genetic testing from respondents from both the

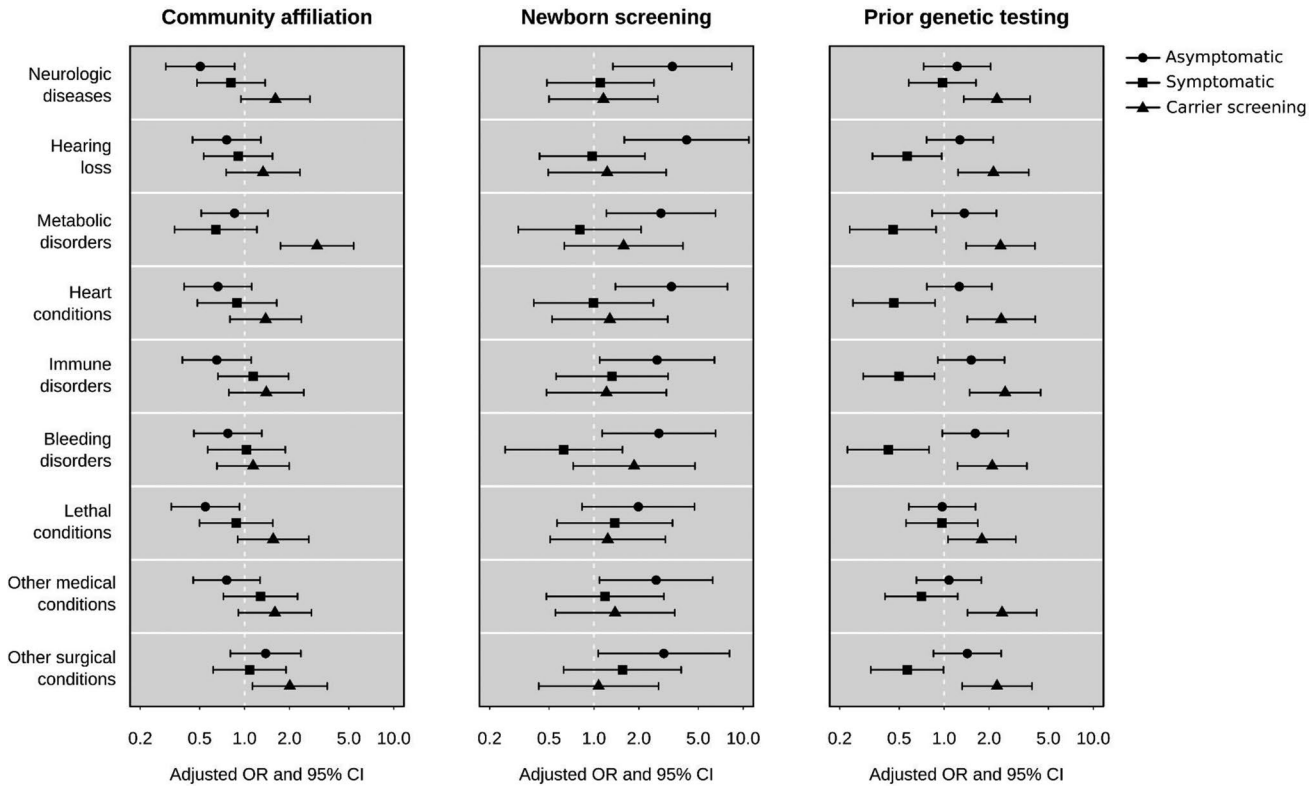

Fig. 1 Association between stated interest in genetic testing and Plain community affiliation, utilization of newborn screening, and prior genetic testing. Adjusted odds ratios for stated interest in genetic testing stratified by clinical context (asymptomatic, symptomatic, carrier). Left panel: Community affiliation (Mennonite/Amish) adjusted odds ratios for age, utilization of newborn screening, and reported prior genetic testing. Values left of 1 indicate that Mennonites are less likely than Amish to favor genetic testing. Values right of 1 indicates that Mennonites are more likely than Amish to favor genetic testing. Middle panel: Newborn screening for all or some children, adjusted odds ratios for age, reported prior genetic testing, and community affiliation. Right panel: Reported prior genetic testing, adjusted odds ratios for age, utilization of newborn screening, and community affiliation. For middle and right panels, values left of 1 indicate that responses favor no genetic testing, and values right of 1 indicate that responses favor genetic testing

Amish and Mennonite communities representing a wide age range and including those who reported prior genetic testing and utilization of NBS.

We found an overall reported NBS rate of 73% among survey respondents, which is equal to or above NBS rates reported among Pennsylvania Plain communities (28–73%), with the exception of Lancaster County Mennonites who report NBS in 81.3% (Miller et al. 2017, 2019). The overall reported rate of NBS in the current study is nearly identical to a previous report of NBS practices among Wisconsin Plain communities from 2016 (Sieren et al. 2016). We found notable differences in reported NBS practices based on community affiliation, age, and prior genetic testing. Specifically, we found that Mennonites were more likely to report utilizing NBS for all their children compared to Amish, which is consistent with prior studies of Pennsylvania and Wisconsin Plain communities (Sieren et al. 2016; Miller et al. 2017, 2019). Reported utilization of NBS was more common in younger survey respondents, similar to prior studies of Wisconsin Plain communities (Sieren et al. 2016), as well as those reporting prior experience with genetic testing. Higher utilization of NBS in younger respondents may reflect a shift in NBS practices over time; however, poor recall cannot be excluded because of differences in time intervals.

We found similar reported aggregate interest in genetic testing for asymptomatic children, symptomatic children, and carrier screening for each disorder category presented in the survey. Of note, Mennonites reported significantly more interest in carrier screening for metabolic disorders compared to Amish. Although both communities have an increased incidence of several metabolic disorders, the Mennonite community has an increased incidence of maple syrup urine disease (MSUD, OMIM 248,600). This is a disorder of branched-chain amino acid metabolism that causes early (often prior to NBS results) neonatal encephalopathy, metabolic instability, and risk of cerebral edema, leading to intensive medical care and substantial healthcare costs for affected newborns. Mennonites carry a founder variant in the MSUD causative gene *BCKDHA* (c.1312 T > A, p. Tyr438Asn) with a carrier frequency as high as 1 in 10 in

some communities (Puffenberger 2003) and resulting in an incidence of MSUD of 1 in 400 births (Strauss et al. 2020) compared to the general population rate of 1 in 150,000 births (Hinton et al. 2014; Therrell et al. 2014). In Wisconsin and other states, many Mennonites utilize targeted *BCKDHA* gene variant carrier screening to identify individuals or couples who are at-risk for having an affected child (Furnier et al. 2020). This practice has facilitated early genetic testing (prior to NBS) for the *BCKDHA* founder variant in at-risk newborns and has dramatically reduced newborn hospitalization rates for MSUD and spared substantial medical costs for the Mennonite community each year (Strauss et al. 2012). The success of MSUD genetic carrier screening may have been reflected in the positive responses toward carrier screening for metabolic disorders.

Amish respondents expressed significantly more interest in asymptomatic testing for neurologic disease and lethal disorders. Although both the Amish and Mennonite communities collectively have a higher frequency of many genetic disorders compared to the general population, the disorders that occur are often distinct for each of the communities. Compared to the general population, the Amish community has an increased frequency of several disorders that cause severe neurologic disease in infancy without a known treatment (Fox et al. 2018; Johnston et al. 2000; Kelley et al. 2002; Puffenberger et al. 2004, 2012). The increased interest in asymptomatic testing for neurologic and lethal disorders among the Amish respondents may reflect the high prevalence of these disorders and desire for early recognition to avoid prolonged uncertainty or a lengthy diagnostic workup.

Interestingly, we found that reported prior utilization of NBS was associated with interest in asymptomatic testing for nearly all disorders presented in the survey, except for lethal disorders without treatment. The philosophy of identifying treatable disorders in asymptomatic newborns aligns with most state NBS guidelines. This reported preference in our survey suggests Plain community openness to expanded genomic NBS for infants in addition to the recommended state screen for all newborns. However, this preference in testing asymptomatic children was not universal among respondents, so proposing genomic screening for all infants from the Plain community would likely be viewed negatively by those who indicated little or no interest in genetic testing. Additionally, broad genetic testing in a well newborn would raise ethical and policy issues related to disclosure of carrier status. Typically, carrier status is reserved for individuals of adult age who can choose to have this information for themselves, arguing for withholding this information from NBS reports. However, a child who is a carrier of any disorder with autosomal recessive inheritance almost certainly has a parent who is also a carrier. That information may be valuable to parents as they may elect to pursue carrier testing as a couple, which could affect the testing and care of future children. In line with population-wide genomic NBS, clear guidelines would need to be established for disclosing results and appropriate counseling when offering testing of parents.

We also found that survey respondents who reported prior experience with genetic testing were more likely to indicate support for carrier screening for all disorder types presented in the survey, suggesting that some Plain community members may be interested in utilizing a NGS panel for carrier screening. If utilized for carrier screening, an NGS panel would likely identify carrier status for several disorders, stressing the importance of sound genetic counseling at the time of informed consent and during the discussion of results.

Notably, survey respondents reporting prior experience with genetic testing were less likely to indicate interest in testing for symptomatic children. One interpretation of this relationship is those individuals had a negative experience with genetic testing and would not pursue it again. Alternatively, it may be those individuals are not opposed to testing symptomatic children but preferred testing prior to symptom onset. The latter explanation is supported by the positive association between prior genetic testing and interest in carrier screening.

A small, but notable, lack of interest in genetic testing was reported among both Amish and Mennonite communities from respondents of various ages, utilization of NBS, and prior experience with genetic testing. Survey respondents also indicated a fair amount of uncertainty regarding genetic testing, underscoring the importance of educational materials and trained healthcare providers to obtain informed consent and discuss results from genetic testing in any context.

Although our study was conducted exclusively among the Plain communities, our varied findings are consistent with studies of the general population. Qualitative studies using semi-structured interviews report mixed views of personalized genetic information, citing potential for improved personal healthcare as well as concerns over the psychological effects, reproductive implications, and varied views on personal autonomy (Smit et al. 2020a). In a second study, participants indicated it was acceptable to offer personalized genetic testing to the general population, but their own preference for utilizing the testing was based on family history, disease incidence, and possibility of disease prevention (Smit et al. 2020b). Participants also indicated utilization of testing should be based on individual preferences and that decision should be supported by a genomics healthcare professional (Smit et al. 2020b).

Studies of expanded carrier screening (ECS) for autosomal recessive disorders in the USA and European populations noted interest in ECS (32–76%) but lower rates of actual utilization of ECS (8–50%). Utilization of ECS was

highest in pregnant women or woman considering IVF and lower in the preconception population (Steijvoort et al. 2020). In a study of the Dutch reproductive age population, the majority indicated that ECS should be offered to all prospective parents, and 31% indicated they would take the test themselves. The most common reason for participating in ECS was to spare a child from a life with a severe hereditary disorder (Nijmeijer et al. 2019). Those considering a future pregnancy were more likely to participate in ECS, and those with religious views were less likely (Nijmeijer et al. 2019).

A potential limitation of our study is that surveys were distributed to households who had participated in a prior survey of NBS practices or had some affiliation with the Center for Special Children, a program dedicated to caring for children with genetic disorders from the Plain community. This approach has the potential for selection bias for families that are more likely to seek medical care and genetic testing. However, about one-third of respondents from both the Amish and Mennonite communities had prior experience with genetic testing, suggesting that most survey respondents were generally unbiased by prior experiences with genetic testing. Additionally, survey responses indicated a hypothetical interest or lack of interest in genetic testing, which may not directly reflect actual utilization of genetic testing among the Plain communities in varied clinical contexts. Even for those respondents with a stated interest in genetic testing, several barriers (lack of access, cost, etc.) may still limit its use.

Collectively, these findings suggest a flexible NGS platform with the ability to expand or limit results may be beneficial to allow for customizable testing for individuals from the Plain community. Although survey results indicate a NGS panel could be applied in diagnostic settings, NBS, or for carrier screening, there was not universal interest in these applications, suggesting elective testing would be preferable. Given the many outward similarities among Plain community members, it is easy to generalize and assume that views on healthcare and genetic testing are comparable among members. However, this survey demonstrates there is significant diversity of views among the Plain community, stressing the importance of personalized care based on an individual's informed decision.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s12687-022-00621-z.

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Author contribution Conceptualization: K.B.W., M.B., C.M.S. Data curation: K.B.W. Formal analysis: M.R.L. Funding acquisition: C.M.S. Writing (original draft): K.B.W. Writing (review and editing): K.B.W., M.R.L, M.B., C.M.S.

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Availability of data and material Survey instrument and supporting documents are submitted as supplemental materials. Deidentified response data are available upon request.

Declarations

Ethics approval The University of Wisconsin Health Sciences IRB determined that this study is not human subjects research (45 CFR 46: Category 2) and is exempt from IRB review.

Conflict of interest The authors declare no competing interests.

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