

2023

Assessing the Attitudes and Perceptions of the Old Order Amish toward Genetic Testing for Familial Defective Apolipoprotein B-100

Erin Sutcliffe
Genedx

Laura J. Conway
University of Pennsylvania

Alan Shuldiner
University of Maryland School of Medicine

Toni Pollin
University of Maryland School of Medicine

Follow this and additional works at: <https://ideaexchange.uakron.edu/amishstudies>



Part of the [Community Health and Preventive Medicine Commons](#)

Please take a moment to share how this work helps you [through this survey](#). Your feedback will be important as we plan further development of our repository.

Recommended Citation

Sutcliffe, Erin, Laura J. Conway, Alan R. Shuldiner, and Toni I. Pollin. 2023. "Assessing the Attitudes and Perceptions of the Old Order Amish toward Genetic Testing for Familial Defective Apolipoprotein B-100." *Journal of Amish and Plain Anabaptist Studies* 11(2):137-48.

This Original Research Article is brought to you for free and open access by IdeaExchange@Uakron, the institutional repository of The University of Akron in Akron, Ohio, USA. It has been accepted for inclusion in Journal of Amish and Plain Anabaptist Studies by an authorized administrator of IdeaExchange@Uakron. For more information, please contact mjon@uakron.edu, uapress@uakron.edu.

Assessing the Attitudes and Perceptions of the Old Order Amish toward Genetic Testing for Familial Defective Apolipoprotein B-100

ERIN SUTCLIFFE, MS, CGC
Supervisor/Genetic Counselor
Genedx

LAURA J. CONWAY, PhD
Assoc. Director, Master's in Genetic
Counseling
Perelman School of Medicine
University of Pennsylvania

ALAN R. SHULDINER, MD
Vice President, Regeneron Genetics Center,
and John Whitehurst Professor
University of Maryland School of Medicine

TONI I. POLLIN, MS, PhD, CGC
Associate Professor of Medicine and
Epidemiology & Public Health
University of Maryland School of Medicine

Abstract: Through a founder effect, one in eight Lancaster County, PA, Amish harbors the pathogenic *APOB* variant R3527Q, causing Familial Defective Apolipoprotein B-100 (FDB) that is rare in the general population. Affected individuals are at increased risk for high low density lipoprotein (LDL) cholesterol levels and cardiovascular disease and may benefit from early screening and treatment. A qualitative interview approach was used to investigate the genetic risk perceptions of the Amish and their attitudes towards genetic testing for FDB. The goal was to identify elements necessary for a successful program that would identify high risk individuals in the Lancaster County Amish community and provide them with potentially lifesaving education and interventions. Thirty interviews were conducted. Collected data were analyzed and coded for common themes. Participants felt genetic risk was important and were aware of the significant impact genetics have on health. Most individuals perceived genetic risk as more significant than family history. Twenty-four of 30 individuals would consider testing; of these, all 24 reported they would take proactive measures to reduce risks if given a positive result. Most would prefer diet modification and natural health remedies, with prescription medication only as a last resort. Several participants stated that most Amish people would be unlikely to test if they were feeling healthy. Cost was the most significant barrier to pursuing testing. Implementing a successful screening program would require community outreach and awareness, risk reduction education and support, and minimal out-of-pocket expenses. The program's success provides insights into the efficacy of predictive genetic screening for the general population. [Abstract by authors.]



Address correspondence to: Toni I. Pollin; tpollin@som.umaryland.edu.

Recommended citation: Sutcliffe, Erin, Laura J. Conway, Alan Shuldiner, and Toni Pollin. 2023. "Assessing the Attitudes and Perceptions of the Old Order Amish toward Genetic Testing for Familial Defective Apolipoprotein B-100." *Journal of Amish and Plain Anabaptist Studies* 11(2):137-48.

Publication type: Original research article (peer reviewed), open access (may be freely distributed). *JAPAS* is published by the Amish & Plain Anabaptist Studies Association (<http://amishstudies.org>) and the University of Akron

Keywords: Lancaster County, PA; LDL; familial hypercholesterolemia; hereditary diseases; autosomal dominant inheritance

Acknowledgements: The authors would like to thank all of the individuals who participated in this study. They would also like to extend their gratitude to the staff and liaisons at the Amish Research Clinic for their assistance in the coordination and completion of this research.” This project was completed in partial fulfillment of the requirements for the Master’s degree in genetic counseling at Arcadia University by Erin Sutcliffe.

INTRODUCTION

Through a founder effect, one in eight (12%) Lancaster County, Pennsylvania Amish (vs. <1/1000 in the general population) harbors the pathogenic *APOB* R3527Q variant (NM_000384.3:c.10580G>A, p.Arg3527Gln, ClinVar ID 17890) for Familial Defective Apolipoprotein B-100 (FDB). FDB manifests in affected individuals as higher than normal levels of low-density lipoprotein (LDL)-bound cholesterol, earlier onset cardiovascular disease, and xanthomas, cholesterol deposits that form under the skin (Marks, et al. 2003). FDB, caused by pathogenic variants in *APOB* resulting in defective Apolipoprotein B-100 (ApoB), follows an autosomal dominant pattern of inheritance, with homozygotes being more severely affected than heterozygotes (Austin, et al. 2003). The most common disease-causing *APOB* variant and the one responsible for the FDB observed in the Lancaster County Amish population is R3527Q (Shen, et al. 2010). This variant disrupts interaction between two amino acids which prevents proper folding of ApoB and binding to its receptor (Tybjærg-Hansen, et al. 1998; Shen, et al. 2010). ApoB is present on LDL particles and acts as a ligand facilitating binding between LDL and the LDL receptors involved in LDL-bound cholesterol uptake in cells (Tybjærg-Hansen, et al. 1998).

The Familial Hypercholesterolemia spectrum, of which FDB is a part, is associated with a 50% risk for cardiovascular disease (CVD) by age 50 in males and a 30% risk for CVD by age 60 in females (Marks, et al. 2003). Tybjærg-Hansen et al. (1998) estimated that the R3527Q variant, which is present in 0.08% of individuals of European ancestry in the general population and 12% of Lancaster County Amish (Shen, et al. 2010), increases the risk for CVD to seven times

that of the general population. One-time screening for LDL cholesterol (LDL-C) levels may not be a sufficiently sensitive marker for CVD risk in individuals with FDB as LDL-C levels can vary greatly between individuals with this pathogenic variant (Shen, et al. 2010). Because symptoms of FDB also present in individuals with other forms of hypercholesterolemia and do not always present in individuals with FDB, misdiagnosis may occur, and those affected may not be treated appropriately (Umans-Eckenhansen, et al. 2001; Marks, et al. 2003). Genetic testing may be necessary to identify patients with FDB in order to provide them with appropriate treatment.

Genetic testing may also identify presymptomatic family members who would benefit from early, more aggressive treatment and lifestyle interventions. Preclinical signs of coronary artery disease have been identified in individuals with FDB as young as ten years old (Berenson, et al. 1987). Genetic testing of presymptomatic minors for an adult-onset condition, although not usually indicated, may thus be appropriate for FDB in order to facilitate early intervention and promote long-term survival, including adoption of heart-healthy habits, because of the early onset of subclinical features, particularly in homozygotes (individuals with two copies of the variant). Statin therapy in children with Familial Hypercholesterolemia significantly reduces coronary artery calcification (CAC, a subclinical measure of CVD) with no adverse effects on growth, maturation, hormones, or organ tissues (Wiegman, et al. 2004).

Statin therapy, which works by inhibiting cholesterol synthesis in the body, is effective in reducing the risk of CVD in patients with increased LDL-C levels (Scandinavian Simvastatin 1994; Long-Term Intervention 1998). Because smoking, limited physical activity, excess fat tissue, limited vitamin intake, and increased saturated fat intake

all are major risk factors for high LDL-C levels and CVD, interventions with individuals with FDB to promote healthier eating, lifestyle choices, and exercise habits may also be warranted (Austin, et al. 2004). A combination genetic screening and treatment program to detect individuals with inherited hypercholesterolemia and provide potentially life-saving treatments and interventions could be beneficial (Umans-Eckenhausen, et al. 2001).

The Amish are a distinct religion that sets itself apart from the rest of the world not only in their appearance and lifestyle but also in their effort to maintain their defining customs and values. They dedicate their lives to serving under God's will, and in doing so, reject pride and arrogance and strive for humility and composure (Brensinger and Laxova 1995). Their values are reflected in their healthcare practices, which often differ from mainstream American culture. The Amish are more likely to tend to their own medical needs, delay seeking medical attention, or try other "natural" remedies first. A natural remedy would be a non-synthetic material such as garlic, vitamins, and other herbal substances. The Amish are also less likely to practice preventive medicine (Weyer, et al. 2003). While the Amish may vary in their opinions and ideas of issues commonly debated in mainstream society, they tend to make decisions for uses of technology as a whole considering what would be best for the entire community (Patton 2005).

Although genetic testing may be relatively uncommon among the Amish compared to the general population, individuals do participate in genetic research at sites such as the Amish Research Clinic in Lancaster, PA, and testing for and treating pediatric genetic disorders at the Clinic for Special Children in Strasburg, PA. When asked about interest in carrier screening for a recessive disorder, Amish attitudes towards genetic testing are almost equally split between those who are and those who are not interested (Miller and Schwartz 1992; Brensinger and Laxova 1995).

Assessment of the general population's perceptions of genetic risk for developing a disease has identified heterogeneity. Two common scenarios that occur as a result of an individual learning of his/her genetic predisposition are: (1) he/she becomes increasingly proactive about taking preventative measures and practicing risk-reducing behaviors to avoid a disease outcome (Audrain, et al. 1997;

Westmaas and Woicik 2005) or (2) he/she develops a fatalistic outlook and believes that nothing he/she can do will prevent this genetic risk from resulting in the predicted illness and actively does nothing to reduce his/her risk (Senior, Marteau, and Peters 1999; Senior, Marteau, and Weinman 2000; Van Maarle, Stouthard, and Bonsel 2003). People faced with a genetic risk may also report feeling motivated to take risk-reducing action, but without an effective follow up treatment program, may not follow through (Audrain, et al. 1997).

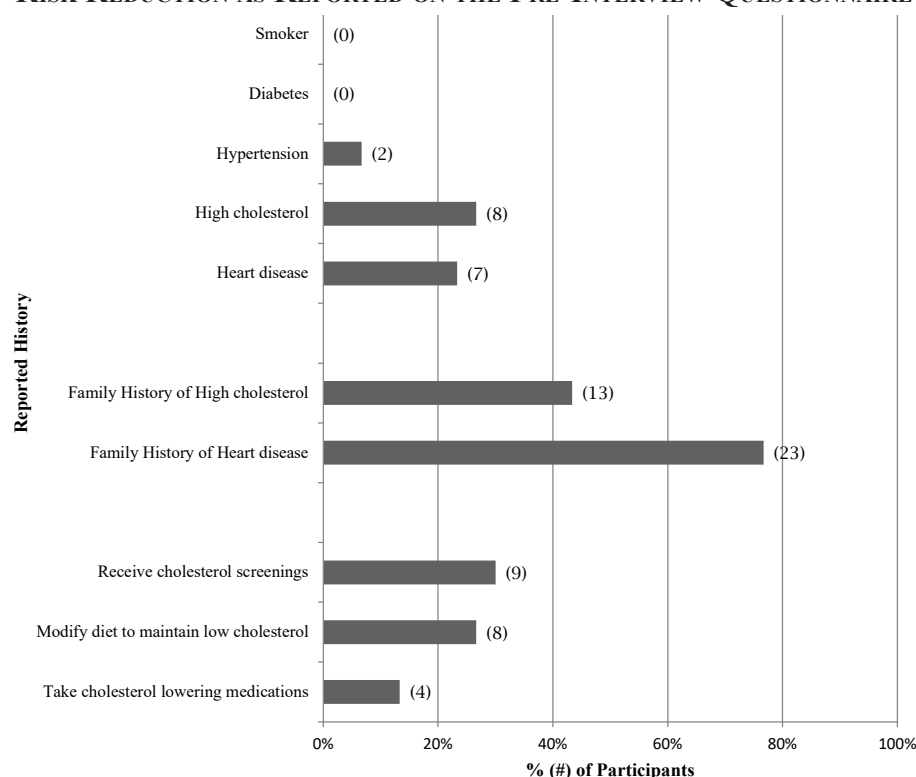
Having a family history of a disease also places one at increased risk to develop that condition. People may not differentiate between genetic risk and a family history risk (Hicken and Tucker 2002; Riggs and Giuliano 2007). Additionally, being presented with a genetic risk can have little effect on the perception of whether medical interventions are better risk-reducing tactics than behavioral or environmental preventative measures, such as diet and other lifestyle changes (Senior and Marteau 2007).

Little information is available on how the Amish view genetic risk for disease, predictive genetic testing, and the use of risk reduction. In this study, members of the Lancaster County Amish population were interviewed to investigate their feelings, thoughts, and reactions to the recent observation that R3527Q *APOB*, which causes FDB, is common in the Amish and the potential for a personalized testing/treatment program for the community. Their perceptions of genetic risk and their likelihood of engaging in risk-reducing behaviors and other treatments were assessed. Potential factors that may prevent this community from pursuing genetic screening were identified in order to anticipate and minimize barriers. The goal was to identify elements necessary for a successful program that will be able to identify people at increased risk for high cholesterol and CVD due to a genetic predisposition and provide them with life-saving treatments and interventions, some of which may be applicable to the general population.

METHODS

Research was conducted at the University of Maryland Baltimore (UMB) Amish Research Clinic in Lancaster, PA. Thirty participants were recruited from the ongoing studies at the clinic (convenience sample). Participants were recruited

FIGURE 1: PERSONAL HISTORY, FAMILY HISTORY, AND CARDIOVASCULAR RISK REDUCTION AS REPORTED ON THE PRE-INTERVIEW QUESTIONNAIRE



as they came to the clinic for testing procedures performed for the other clinic studies. Any Amish individual 18 years of age or older who was currently participating in a clinic study and visited the clinic for testing purposes between August and December of 2009 met inclusion criteria for this study and were interviewed at that time.

The participants were introduced to the researcher and the study during clinic check-in. Each participant was asked to complete a pre-interview questionnaire, read a brief educational presentation on FDB, and participate in an interview.

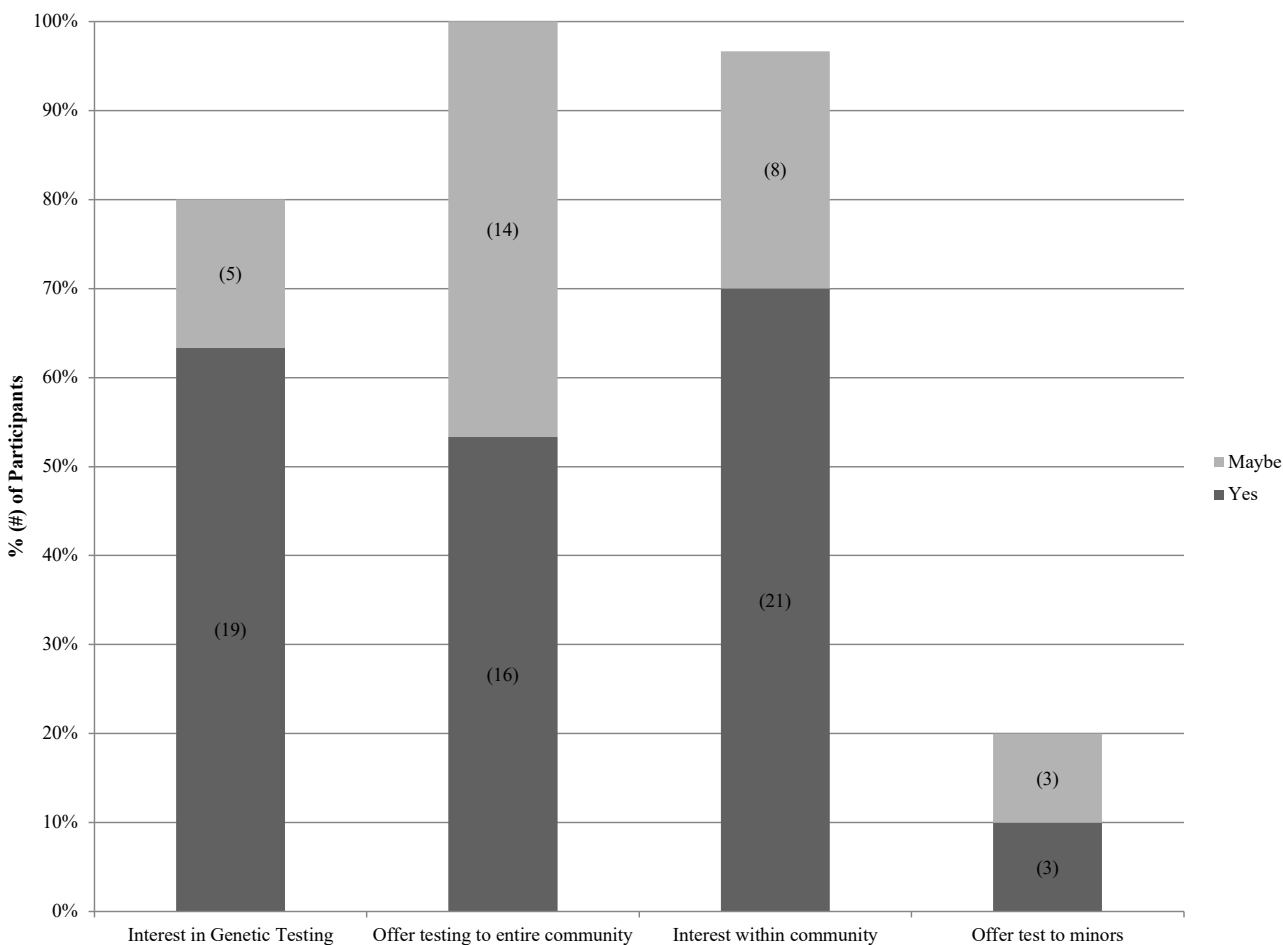
All procedures for the study were completed during breaks between clinic testing procedures. The pre-interview questionnaire collected demographic information including gender, height, weight, and age. Risk factors for high cholesterol and/or heart disease and any current risk reduction measures, including personal history, family history, and eating and exercise habits, were identified. The educational materials provided background information on FDB, the particular pathogenic variant found in the Amish community, and the health implications of having this variant. The interview included questions pertaining to the participant's attitudes and thoughts about genetic testing and opinions about how the community might

respond to the availability of testing for the genetic variant. Because Amish participants would not be comfortable with audio recording the interview session, responses were written by the interviewer on the interview guide.

At the end of the interview, participants were informed that the purpose of this study was to gain knowledge on their opinions, attitudes, and perceptions regarding the genetic alteration for FDB and its potential impact on the community. The clinic was not providing any screening or treatment for this disorder. Participants were informed that the clinic will use the information from this study to structure a program that will offer genetic testing and treatment services for FDB to the

entire community. Notification of availability of testing/treatment would be mailed out once it becomes available.

The interview sheets documenting each participant's answers were used for results interpretation. Each question from the interview guide was organized into one of three categories: (1) personal interest in genetic testing, (2) use of information gained from testing, and (3) perception of the community's interest in genetic testing. Shortly after the conclusion of each interview, the researcher reviewed the completed questionnaires and created a spreadsheet tallying the responses for each question to group similar answers together. Using this spreadsheet, common and unique responses to each question were identified, and popular views and distinctive opinions on genetic testing were easily visualized. Emerging themes were apparent as subsequent interviews were completed and were coded within the results spreadsheet. These themes were further investigated in the details of each individual interview. This study was approved by the institutional review boards at the University of Maryland and Arcadia University.

FIGURE 2: PERSONAL AND BELIEVED INTEREST OF ENTIRE COMMUNITY AS REPORTED BY PARTICIPANTS

RESULTS

Participants

Thirty Amish individuals, who were volunteering for other research studies at the Amish Research Clinic, were approached about this study and all agreed to participate. These other studies included: a women's breast health/density study, an investigation on osteoporosis, and a pharmacogenomic study exploring resistance to cardiovascular medication. Twenty-four of the participants were female and six were male. Average age of the participants was 53 years, and the average BMI was 27.8 kg/m², which is considered overweight by the U.S. Department of Health and Human Services (2010).

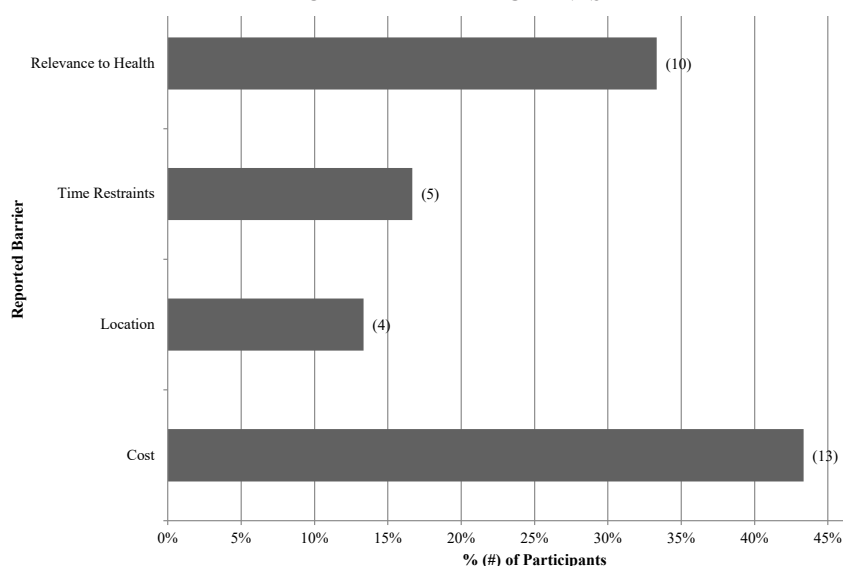
Family history of high cholesterol or heart disease was reported more frequently than a personal history (Figure 1). Participants were not specifically asked and did not reveal previous diagnosis

of a genetic disorder including FDB. Most reported eating meats including beef and chicken, dairy, fruit, potatoes, and other vegetables. About half reported that they tried to avoid fatty foods and only ate sweets occasionally. Women commonly reported cleaning, cooking, sewing, gardening, and childcare as their daily activities. Some of the women helped out at a family business or store. Men reported working in the fields, yard work, and office/store work for those who owned a business.

Summarized Interview Responses

Participants were asked to indicate their personal interest and their perceived interest of the community in genetic testing along with whether it should be offered to adults and minors within the community (Figure 2). The majority of participants (24/30, 80%) reported that they would either definitely pursue or consider pursuing genetic testing for FDB. Only one person reported that they believed the entire community would not be

FIGURE 3: BARRIERS TO PURSUING GENETIC TESTING AS REPORTED BY PARTICIPANTS



interested. All participants were at least willing to consider that this testing should be offered to the community, with 16/30 (53%) stating that it definitely should. However, most of the participants (24/30, 80%) indicated that genetic testing should not be offered to minors.

Participants were also asked to comment on the perceived barriers to testing (Figure 3). The most common barriers were cost of the test (43%) and relevance to health (33%); many participants reported that they would be less likely to pursue testing if they were feeling healthy. Follow-up questioning revealed that the majority of the participants (53%) believed the test should cost \$100 or less, and \$200 was the maximum amount of money willing to be paid by half of the group. Interestingly, two individuals reported that they would no longer pursue testing if it were not free.

Use of information gained was explored with the 24 people who would at least consider testing. If the results were negative (no pathogenic variant found in the *APOB* gene), the majority (83%) stated that they would do nothing different. The remaining four participants stated they would use the information to benefit themselves and their family. None of the participants reported they would feel a sense of false reassurance. False reassurance occurs when an individual believes him or herself to be at no risk for the disease in question because he or she was found not to carry the genetic risk factor. In this situation, these individuals tend to overlook other risk factors associated with the disease that are environmental.

If the results were positive (deleterious variant found in the *APOB* gene), all 24 participants stated that they would attempt to reduce their risks for high cholesterol and heart disease. None of the participants expressed a fatalistic outlook. A person is said to possess a fatalistic outlook when he or she believes there is nothing that he or she could do to prevent this genetic risk from resulting in the disease and may actively do nothing to reduce his or her risk. Diet modification was the most commonly favored risk reduction tactic followed by additional exercise, and the least favored was cholesterol lowering medications (Figure 4). Even though “use natural supplement” was not given as an

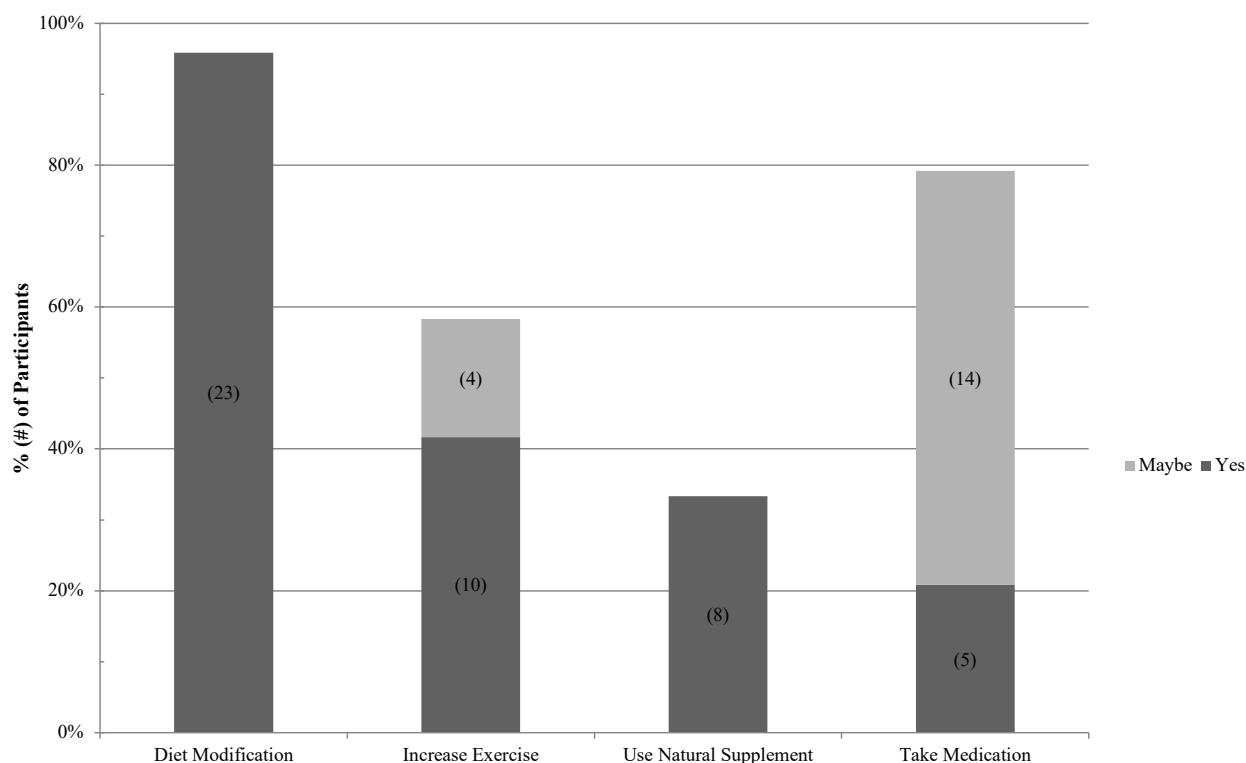
option on the interview guide, eight participants indicated that they would be interested in using a natural remedy to reduce risks. Furthermore, 16 participants (67%) believed that a genetic risk for high cholesterol would definitely or probably be more of a motivator to implement risk reducing behaviors than a personal/family history risk.

The participants were also asked to brainstorm some ways in which they thought a genetic testing program, which would be implemented to identify and help Amish individuals with the genetic predisposition, would benefit their community. Perceived benefits of the proposed genetic testing program included: increasing awareness of population specific cholesterol and CVD risks, providing information about their personal health risks, and assisting with implementing health improvement behaviors. While most could not think of any concerns about such a program, some expressed a concern for the potential for people to feel pushed into pursuing testing and/or receiving information that they may not want to know about themselves.

Emerging Themes

IMPORTANCE

Participants understood the significance of genetic impact on health in conjunction with the environment. If the test results were negative, the majority of the participants would “continue

FIGURE 4: ACTION PARTICIPANTS WOULD TAKE IF FOUND TO TEST POSITIVE FOR A MUTATION IN APOB.

Note: Only the 24 participants who would consider genetic testing are represented here.

living life the same,” implying that without the genetic risk, there is no need for increased risk reduction. They also appreciate the impact that lifestyle and environment, in addition to genetics, have on health because they would not interpret a negative test result as falsely reassuring. No participants indicated that they would engage in risky lifestyle habits, ignoring the environmental risk factors, as if they believed a negative genetic test result would eliminate any and all risk for high cholesterol and heart disease.

The perception that a genetic risk can have more consequences for their health than a family/personal history risk was evident. When asked, “Would having the gene make you more likely to make changes than if you just had a family history of heart disease?” participants responded:

It would make me more likely to change my behaviors. I think you have to fight harder.

Yes, definitely. If it's just in the family it's not necessarily a personal risk, but a genetic risk would mean it is definite in me.

Probably, but having a family history would still motivate me to do something. It's just that genetic risk would motivate me more.

RELEVANCE

Participants perceived the (predictive) test as only being relevant to ‘unhealthy’ individuals and families. It was evident that many of the participants would not pursue testing if they were feeling healthy. When discussing reasons to pursue or not pursue testing, one participant stated, “I don’t wanna bother...if I’m healthy; if there is nothing wrong.” Another woman stated, “If I’m healthy, I don’t need to go to the doctor. What you don’t know can’t hurt you. Don’t worry about your health if you feel healthy.” When asked about the perceived interest of the entire community in genetic testing, one individual stated, “A lot of the attitude is that ‘I’m healthy.’ There may be more concern for those with heart disease.”

Even though FDB is a common disease in the population, several people indicated that the decision to test would be influenced by a relevant personal or strong family history, as illustrated by this quote: “I am not really concerned about my personal history of cholesterol. I have a concerning family history. The test might explain why high cholesterol is running in my family.”

Furthermore, if no concern for health existed, most participants believed they and others would

be less likely to make efforts to overcome barriers to testing, as illustrated in this quote, “If I had a heart problem, I might be more likely to have the testing done or pay to have the testing done.”

This concept was also addressed when discussing testing of minors. The majority agreed that testing should be restricted to adults, as illustrated in this participant’s response, “My reason would be that cholesterol is not really a problem for children. It would make more sense to test them as adults because it is not a problem until they are older.” Overall, the value of predictive testing in an asymptomatic individual was not appreciated by several of the participants nor something believed to be appreciated by the entire Amish population.

PROACTIVITY

All who would consider testing would be proactive about risk reduction if found to have a positive result. No participants indicated they had a fatalistic outlook, that they would actively do nothing to reduce their risk. While diet modification was the preferred method of risk reduction, many participants were also willing to increase physical activity and try natural health supplements. Even though medication was the least preferred method of risk reduction, many proactive participants stated that they would use it as a last resort. One participant replied, “I wouldn’t be happy (about taking medication), but I would not refuse if my doctor saw the need.”

In addition to initiating some type of strategy to reduce personal risks for high cholesterol if found to test positive, 29/30 (97%) of individuals would share the information with their family members and extended relatives in order to allow them to be proactive about their health. A common response amongst the individuals already making attempts to live healthier was that they would try harder to reduce their risks if found to have a genetic predisposition. If a participant expressed that they would not be likely to increase exercise, it was usually because they felt that they already got enough physical activity in a day.

Many individuals described a genetic testing program tailored to the Amish community as very useful. They stated that the program would increase the health of the population by providing an opportunity to learn more about their personal health risks. Such a program would also help indi-

viduals with a positive test result implement effective preventative health practices. By taking action to reduce their risks they would also increase their quality of life. A few people believed that it would save money in the future, as explained in this individual’s response, “It would be less costly in the long run if you could take care of the problem before they have a heart attack. There would be fewer medical bills.” Although most of the participants believed that testing was not useful for children, five of the six individuals who agreed with the idea of offering testing to children indicated that it would only be acceptable if knowing this information would benefit the child through risk reduction. One individual replied, “It would be good to test early on. The more you can do earlier, the better.”

DISCUSSION

The proposed genetic testing and treatment program for Familial Defective Apolipoprotein B-100 (FDB) would likely be used by this population. The participants placed a great deal of importance on genetic risk and would seek out proactive measures to reduce risks if found to have an *APOB* pathogenic variant. Diet modification was acceptable to the majority of participants. Therefore, education about the benefits of incorporating a healthy diet and advice on how to implement diet modification would be the most valuable to individuals with a positive *APOB* test result.

Due to the interest of this population in taking natural supplements to improve their health as opposed to medications, informing Amish individuals of the effectiveness of natural products, such as red yeast rice, in lowering LDL-C levels and offering them as an alternative to statin medications would be well-received. Red yeast rice, *Monascus purpureus*, contains compounds known to inhibit cholesterol synthesis and has been used for some time as a common dietary supplement in China (Zhao, et al. 2004). It contains a lower dose of statins, as compared to prescribed statin medications, but the mechanism is the same. A metaanalysis of 93 randomized trials comparing red yeast rice to placebo, no treatment, statins, or other lipid-lowering agents showed that red yeast rice resulted in significant lipid reduction in patients with high cholesterol and was as effective at reducing cholesterol levels as prescription statin

medications (Liu, et al. 2006). Red yeast rice also appears to be an effective alternative in individuals with prescription statin intolerance (Venero, et al. 2010). Additionally, its lipid-lowering effects have been shown to significantly improve endothelial function in individuals with coronary heart disease (Zhao, et al. 2004).

As discussed previously, statin therapy may be considered as a last resort if other interventions such as diet, exercise, or natural supplements are not sufficiently effective. Providing education on the benefits, risks, and limitations of statin therapy and directing patients to their primary care doctor if interested in seeking such treatment, may be most beneficial in this type of program. Additionally, ApoB antisense inhibitors may work well since they target the actual molecule that is defective. Administration of an antisense inhibitor resulted in a 50% reduction in ApoB and a 35% reduction in LDL cholesterol in 36 individuals with mild hyperlipidemia (Kastelein, et al. 2006). This therapy is currently in clinical trials and may be an option for the near future.

An increase in physical activity often reduces the risk of CVD. Due to the active and busy lifestyles already adopted by most Amish individuals, this method for risk reduction may not be feasible. Making suggestions for simple yet effective ways to increase exercise may motivate the individuals who need it most to add it to their daily routine.

Because most of the participants expressed that they would want to inform their family members of a positive result, it may also be appropriate to offer support and guidance for individuals in informing other relatives about the significance of their test results. Providing strategies for sharing the information with family members or even assisting in a type of information session may be a valuable tool for this community.

Those who test positive would likely be concerned about the risks to their family, especially their children. A pathogenic *APOB* variant would predispose an individual to typical adult-onset disorders, high cholesterol and CVD. Children who inherit this genetic predisposition would likely not experience disease related issues until they were older; however, one could argue that early interventions to maintain low cholesterol levels and reduce risk for CVD would improve long term health. Additionally, given the prevalence of *APOB* in the community, the likelihood

for homozygous, early-onset FDB is more common. Although early intervention can have some additional benefit, most participants in this study viewed testing minors for FDB as unfavorable. Even though this may reflect limited understanding of possible medical benefits for minors, perhaps restricting the access of the test to adults may be in the best interest of this community. Further discussion and education in the community about the risk of the earlier onset homozygous form of FDB may generate interest in a limited application of testing minor children of couples in which both partners have FDB and have at least a 25% chance of having a homozygous child.

Many participants reported that they and others in the community would only seek testing if feeling unhealthy. Therefore, it may be in the best interest of the community to reach out and provide awareness education on the implications of the *APOB* variant found to be common in their population and explain the benefit of taking action now to prevent any health problems in the future (including the financial benefits of reducing risk of hospitalization for major cardiac events). This type of education could be done in a newsletter or by word-of-mouth. Practical information, such as the question of cost and testing location, as well as where to obtain follow-up care, could be included. It appears from responses that the Amish would be more likely to take advantage of the services provided by this program if the cost of the test could be reduced to under \$100. Therefore, attempts at reducing the out-of-pocket expenses would be essential for the success of this program.

As technological advances continue to be made in genetic screening, general population testing for low frequency, high penetrance genetic variants is becoming more feasible and would facilitate the identification of presymptomatic high risk patients. In the Netherlands, where there is a 1/400 carrier frequency for FH, a genetic screening program has been developed to identify presymptomatic FH mutation carriers (Huijgen, et al. 2010). Over a period of 16 years, 9,000 FH carriers have been identified, which led to an increase in the utilization of cholesterol-lowering therapy and a significant reduction in LDL cholesterol levels (Huijgen, et al. 2010). Almost 86% of Netherlands patients diagnosed with FH via DNA testing were in compliance with the recommendation for cholesterol-lowering medication two years post

test (Umans-Eckenhuis, et al. 2003). Eighty-one Amsterdam residents diagnosed with familial hypercholesterolemia (FH) via genetic testing all reported pursuing risk reduction; 99% utilized medication and almost half reported adoption of a healthier lifestyle, including improved diet and increase in physical activity (Claassen, et al. 2010).

The findings here suggest that the Amish would react similarly to other populations when presented with a genetic risk for high cholesterol by proactively reducing their risks. Implementation of a testing and treatment program in the Amish community would allow us to investigate further the efficacy of population screening and increase knowledge as to whether general population screening for hereditary predispositions for common diseases would be clinically useful. The high FDB carrier frequency in the Amish (12%) (Shen, et al. 2010) would provide information more quickly than in the general population.

At least two major differences between the Amish and general public limits the ability to extrapolate findings. First, whereas individuals in the general population tend to practice preventive medicine and, therefore, might be more likely to seek genetic testing prior to becoming symptomatic, this study suggests that most Amish would not consider genetic testing for FDB unless they were experiencing symptoms of high cholesterol or heart disease. This potential difference in timing of testing could be the difference between developing a reactive treatment regimen as compared to a potentially more effective proactive treatment regimen. However, the identification of a symptomatic FDB carrier could potentially result in identification of presymptomatic family members who would benefit from proactive treatment. Second, while individuals in other populations may favor risk reduction in the form of medication (Claassen, et al. 2010), this study indicated a preference among the Amish for dietary modification and use of natural health supplements. The difference in treatment strategies between the two populations could impact the outcome of genetic screening for FDB in the Amish as compared to screening in the general population.

Limitations

This study had several limitations. Most importantly, a significant selection bias existed, such

that the entire Amish population was not well represented. All of the participants were recruited from other studies being performed at the Amish Research Clinic. Therefore, these individuals already have a heightened awareness of the value of preventive medicine and/or genetic testing. One could argue that people who are willing to participate in research in order to benefit society would also be more likely to pursue non-routine medical care and seek information through genetic testing to benefit themselves. Perhaps these Amish individuals' attitudes towards genetic testing would be more favorable than the average Amish person.

Additionally, this study sample was biased towards females. This was a result of the decreased availability of male volunteers. During the recruitment period, the number of women coming to the clinic for research procedures far exceeded the number of men most likely because the major project being carried out by the clinic staff was a breast health study.

Another concern with limiting the study sample to ARC research participants was that the clinical research atmosphere might influence several individuals' perception of the purpose of this study and the interview. During the enrollment process for the other ARC studies, the participants received an in-depth education and interview where they are informed of the tests and procedures involved and asked several personal health, family history, and other related questions. The enrollment for this study was not as lengthy, and the interview itself may have been similar to the consent process the participants experienced for other studies. During this interview, some of the participants were under the impression that they would receive genetic testing for FDB as part of this research. Upon re-explaining the purpose of this study and clarifying the intent of the interview, the participants seemed to understand that they needed to indicate their actions given the hypothetical scenario of being offered testing. The extent to which the clarification process may have been effective at addressing any misconceptions and potentially influenced answers is not known. However, one could argue that if the individual was assuming they were responding to the real prospect of considering genetic testing, then their answers are credible.

These limitations suggest further investigation is needed to obtain a more representative sample

and comprehensive outlook of the Amish population on testing for a genetic predisposition. The information gathered from this research can be used as a starting point.

CONCLUSION

This study reveals that there is some interest in pursuing genetic testing for a predisposition to high cholesterol and heart disease in the Amish. The perception that a genetic risk can have more consequences for their health than a family/personal history risk is evident. Proactive measures to reduce health risks identified by a positive test result would be pursued by all participants. However, several participants indicated that most Amish individuals would be less likely to take advantage of genetic testing if they were feeling healthy. Furthermore, cost of the test appeared to be the most significant barrier to pursuing testing. Therefore, the most successful testing/treatment program for the Amish would involve community outreach and awareness, risk reduction education and support, and minimized out-of-pocket expenses. Further investigation into the generalization of these findings to the rest of the community and future research regarding the perceptions of the Amish surrounding genetic testing is warranted. After more exploration, perhaps the healthcare needs of this population can be best addressed. The outcome of such a screening program may provide insight into how best to develop genetic screening programs for the general population.

REFERENCES

- Audrain, Janet, Neal Boyd, Joan Roth, David Main, Neil Caporaso, and Caryn Lerman. 1997. "Genetic Susceptibility Testing in Smoking-Cessation Treatment: One-Year Outcomes of a Randomized Trial." *Addictive Behaviors* 22(6):741-51.
- Austin, Melissa, Carolyn Hutter, Ron Zimmern, and Steve Humphries. 2004. "Familial Hypercholesterolemia and Coronary Heart Disease: A HuGE Association Review." *American Journal of Epidemiology* 160(5):421-29.
- Austin, Melissa, Carolyn Hutter, Ron Zimmern, and Steve Humphries. 2004. "Genetic Causes of Monogenic Heterozygous Familial Hypercholesterolemia: A HuGE Prevalence Review." *American Journal of Epidemiology* 160(5):407-20.
- Berenson, G. S., S. R. Srinivasan, D. S. Freedman, B. Radhakrishnamurthy, and E. R. Dalferes Jr. 1987. "Atherosclerosis and Its Evolution in Childhood." *The American Journal of the Medical Sciences* 294(6):429-40.
- Brensinger, Jill, and Renata Laxova. 1995. "The Amish: Perceptions of Genetic Disorders and Services." *Journal of Genetic Counseling* 4(1):27-47.
- Claassen, Liesbeth, Lidewij Henneman, Iris Kindt, Theresa M. Marteau, and Danielle Timmermans. 2010. "Perceived Risk and Representations of Cardiovascular Disease and Preventive Behaviour in People Diagnosed with Familial Hypercholesterolemia: A Cross-Sectional Questionnaire Study." *Journal of Health Psychology* 15(1):33-43.
- Hicken, B., and Diane Tucker. 2002. "Impact of Genetic Risk Feedback: Perceived Risk and Motivation for Health Protective Behaviours." *Psychology, Health & Medicine* 7(1):25-36.
- Huijgen, Roeland, Iris Kindt, Sjoerd BJ Verhoeven, Eric JG Sijbrands, Maud N. Vissers, John JP Kastelein, and Barbara A. Hutten. 2010. "Two Years after Molecular Diagnosis of Familial Hypercholesterolemia: Majority on Cholesterol-Lowering Treatment but a Minority Reaches Treatment Goal." *PLoS One* 5(2):e9220.
- Kastelein, John, Mark Wedel, Brenda Baker, John Su, JoAnn Bradley, Rosie Yu, Emil Chuang, Mark Graham, and Rosanne Crooke. 2006. "Potent Reduction of Apolipoprotein B and Low-Density Lipoprotein Cholesterol by Short-Term Administration of an Antisense Inhibitor of Apolipoprotein B." *Circulation* 114(16):1729-35.
- Liu, Jianping, Jing Zhang, Yi Shi, Sameline Grimsgaard, Terje Alraek, and Vinjar Fønnebo. 2006. "Chinese Red Yeast Rice (*Monascus purpureus*) for Primary Hyperlipidemia: A Meta-Analysis of Randomized Controlled Trials." *Chinese Medicine* 1:1-13.
- Long-Term Intervention with Pravastatin in Ischaemic Disease (LIPID) Study Group. 1998. "Prevention of Cardiovascular Events and Death with Pravastatin in Patients with Coronary Heart Disease and a Broad Range of Initial Cholesterol Levels." *New England Journal of*

- Medicine* 339(19):1349-57.
- Marks, Dalya, Margaret Thorogood, H. Andrew W. Neil, and Steve E. Humphries. 2003. "A Review on the Diagnosis, Natural History, and Treatment of Familial Hypercholesterolaemia." *Atherosclerosis* 168(1):1-14.
- Miller, Shelley R., and Robert H. Schwartz. 1992. "Attitudes toward Genetic Testing of Amish, Mennonite, and Hutterite Families with Cystic Fibrosis." *American Journal of Public Health* 82(2): 236-42.
- Patton, Michael A. 2005. "Genetic Studies in the Amish Community." *Annals of Human Biology* 32(2):163-67.
- Riggs, Abigail L., and Traci A. Giuliano. 2007. "Running in the Family or Swimming in the Gene Pool: Discriminating between Family History and Genetic Risk in Illness Perceptions." *Journal of Health Psychology* 12(6):883-94.
- Scandinavian Simvastatin Survival Study Group. 1994. "Randomised Trial of Cholesterol Lowering in 4444 Patients with Coronary Heart Disease: The Scandinavian Simvastatin Survival Study (4S)." *The Lancet* 344(8934):1383-89.
- Senior, Victoria, and Theresa Marteau. 2007. "Causal Attributions for Raised Cholesterol and Perceptions of Effective Risk-Reduction: Self-Regulation Strategies for an Increased Risk of Coronary Heart Disease." *Psychology and Health* 22(6):699-717.
- Senior, Victoria, Theresa Marteau, and Timothy Peters. 1999. "Will Genetic Testing for Predisposition for Disease Result in Fatalism? A Qualitative Study of Parents Responses to Neonatal Screening for Familial Hypercholesterolaemia." *Social Science & Medicine* 48(12):1857-60.
- Senior, Victoria, Theresa Marteau, and John Weinman. 2000. "Impact of Genetic Testing on Causal Models of Heart Disease and Arthritis: An Analogue Study." *Psychology & Health* 14(6):1077-88.
- Shen, Haiqing, Coleen Damcott, Evadnie Rampersaud, Toni Pollin, Richard Horenstein, Patrick F. McArdle, Patricia A. Peyser, et al. 2010. "Familial Defective Apolipoprotein B-100 and Increased Low-Density Lipoprotein Cholesterol and Coronary Artery Calcification in the Old Order Amish." *Archives of Internal Medicine* 170(2):1850-55.
- Tybjærg-Hansen, Anne, Rolf Steffensen, Hans Meinertz, Peter Schnohr, and Børge Nordestgaard. 1998. "Association of Mutations in the Apolipoprotein B Gene with Hypercholesterolemia and the Risk of Ischemic Heart Disease." *New England Journal of Medicine* 338(22):1577-84.
- Umans-Eckenhausen, Marina, Joep Defesche, Eric Sijbrands, Robert Scheerder, and John Kastelein. 2001. "Review of First 5 Years of Screening for Familial Hypercholesterolaemia in the Netherlands." *The Lancet* 357(9251):165-68.
- Umans-Eckenhausen, Marina, Joep Defesche, Marjel J. van Dam, and John JP Kastelein. 2003. "Long-Term Compliance with Lipid-Lowering Medication after Genetic Screening for Familial Hypercholesterolemia." *Archives of Internal Medicine* 163(1):65-68.
- U.S. Dept. of Health and Human Services. 2010. Retrieved Dec. 6, 2010 (www.nhlbi.nih.gov/health/dci/Diseases/obe/obe_diagnosis.html).
- Van Maarle, M., M. Stouthard, and G. Bonsel. 2003. "Risk Perception of Participants in a Family-Based Genetic Screening Program on Familial Hypercholesterolemia." *American Journal of Medical Genetics Part A* 116(2):136-43.
- Venero, Carmelo V., Jose V. Venero, Dale C. Wortham, and Paul D. Thompson. 2010. "Lipid-Lowering Efficacy of Red Yeast Rice in a Population Intolerant to Statins." *The American Journal of Cardiology* 105(5):664-66.
- Westmaas, J. Lee, and Patricia Butler Woicik. 2005. "Dispositional Motivations and Genetic Risk Feedback." *Addictive Behaviors* 30(8):1524-34.
- Weyer, Sharon M., Victoria R. Hustey, Lesley Rathbun, Vickie L. Armstrong, Samantha Reed Anna, Jeanne Ronyak, and Carol Savrin. 2003. "A Look into the Amish Culture: What Should We Learn?" *Journal of Transcultural Nursing* 14(2):139-45.
- Wiegman, Albert, Barbara A. Hutten, Eric De Groot, Jessica Rodenburg, Henk D. Bakker, Harry R. Büller, Eric JG Sijbrands, and John JP Kastelein. 2004. "Efficacy and Safety of Statin Therapy in Children with Familial Hypercholesterolemia: A Randomized Controlled Trial." *JAMA* 292(3):331-37.
- Zhao, Shui Ping, Ling Liu, Yan Chun Cheng, Mehdi H. Shishehbor, Ming Hui Liu, Dao Quan Peng, and Yu Ling Li. 2004. "Xuezhikang, an Extract of Cholestin, Protects Endothelial Function through Antiinflammatory and Lipid-Lowering Mechanisms in Patients with Coronary Heart Disease." *Circulation* 110(8):915-20.