

# FACTORS AFFECTING CONSENT RATE FOR WHOLE GENOME SEQUENCING OF PATIENTS WITH CONGENITAL HEART DISEASE

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## Abstract

The Whole Genome Sequencing Project initiated by The Hospital for Sick Children of Toronto intends to enroll patients between 1 to 18 years of age with congenital heart disease to test genome sequencing methods for personalized diagnoses and treatments. Twenty-five patients were randomly selected to be observed for their consent rate to the project based on factors of age, gender, ethnicity, presence of heart diseases in the patient's family, and the type of congenital heart disease represented. Our studies found that females and ethnicities not of European descent, considered to be part of minority groups, were generally under-represented and had lower consent rates. There were no significant correlations between consent rates and familial history of heart disease, type of heart disease and age groups. These findings can aid in future studies conducted by the SickKids Hospital by indicating which patients may have higher consent rates and by raising inclusivity of minority groups to alleviate bias in medical studies.

Le Projet de Séquençage du Génome Entier initié par l'Hospital for Sick Children » de Toronto a l'intention de s'inscrire des patients âgés de 1 à 18 ans souffrant d'une cardiopathie congénitale pour tester les méthodes de séquençage du génome pour des diagnostics et des traitements personnalisés. Vingt-cinq patients ont été sélectionnés au hasard pour observer leur taux de consentement au projet en fonction des facteurs d'âge, de sexe, d'origine ethnique, de présence de maladies cardiaques dans la famille du patient et du type de cardiopathie congénitale représenté. Nos études ont montré que les femmes et les groupes ethniques d'origine non-européenne, considérés comme faisant partie de groupes minoritaires, étaient généralement sous-représentés et avaient des taux de consentement plus bas. Il n'y avait pas de corrélation significative entre les taux de consentement et les antécédents familiaux de maladie cardiaque, le type de maladie cardiaque et l'âge. Ces résultats peuvent aider dans les futures études conduit par L'Hospital SickKids en indiquant de comprendre quels patients pourraient avoir des taux de consentement plus élevés et d'aider à l'inclusion des groupes minoritaires pour atténuer le préjugé dans les études médicales.

## Keywords

*African-American; females; minority groups; underrepresentation*



# Introduction

## What is Congenital Heart Disease?

Congenital heart disease is defined as genetic inheritance of one or more genotypic heart disease alleles inherited through one or both parents (Andelfinger, 2014), detrimentally affecting children around the world. The rates of such disorders have increasingly caught the attention of clinicians, prompting interest in improving predictions of an offspring inheriting the disease. If successful, the understanding and reduction of pediatric congenital heart diseases could not only allow for the healthcare system to better address the needs of patients and their families, but also for the earlier commencement of treatments, thus reducing the chance of passing on the allele to the next newborn (Hannah-Shmouni, 2015). One testing method that is widely recognized for identifying genetic variants potentially implicated in congenital heart disease, is Whole Genome Sequencing (WGS).

## Whole Genome Sequencing

Over the last decade, there have been great advancements in genomic technologies, including WGS. This technology has enabled practitioners to identify potential genetic variants implicated in various genetic conditions, which has allowed for a better understanding of genetic makeup of the parent and offspring (Bowdin et. al, 2015). By identifying hidden genome markers and other underlying causes of the patient's genetic makeup, the tool has allowed for the typical user to better acknowledge the contributing causes for present disorders, as well as earlier preparation and the prevention of possible diseases suggested by the readings from the procedure (Blue et. al, 2014). Recently, the cost of WGS has drastically decreased and the use of this tool in clinics has increased (van El et. al, n.d.).

Although the clinical utility of this tool has advantages, it is also accompanied by complications. For example, it is vital to give the family an appropriate amount of time to make a decision on whether or not they will give consent,

along with counseling from a professional before final agreements are made. The resources required for the hospital to implement counseling methods and staff personnel to advise the patient and their family may be tremendous, not to mention the scientists that are hired to sequence the genomes in the lab once the project is underway. Counseling and decision periods may take as long as the patient desires, making the exact amount of time and resources needed for this study difficult to predict. Moreover, it must be stressed in counseling that one must understand that not all information obtained from this test is completely accurate; false positives and/or negatives are possible (Berg, J. S., Khoury, M. J., Evans, J. P., 2011). Patients and their families should also be informed of secondary information that does not relate to the topic of congenital heart diseases but provides insight into other possible genetic disorders (Bowdin et. al, 2015). This is in addition to the discussion on the types of alleles that patients wish to be disclosed and other genetic information that are used only by the clinician(s) for the purpose of WGS study. These decisions are approached through counseling with one or more healthcare professionals responsible for addressing advantages and risks possible to the technology.

## Our Aim

The goal of this study is to analyze and understand the reasons why a cohort of patients and/or their family will or will not decline the offer to participate in this project. Randomly chosen families and patients and their primary information are studied to determine if there is a pattern amongst those who have similar backgrounds. By performing this investigation, we may be able to understand how one's medical background may correspond to their willingness to accept WGS, improve the techniques and approaches for patients who are less willing, and ultimately decrease bias and increase diversity in the study.

## Methods and Procedures

### Population and Data Collection

Patients between the ages of 1-18 were recruited from the Division of Cardiology at The Hospital for Sick Children over a 4-month period (September 2016 to December 2016). Patients and their parents were eligible to participate in the study only if the patients had a primary cardiac diagnosis and were fluent in English. Data was initially obtained through verbal consultations then collected through electronic medical records. The 25 patients in this study were randomly selected out of all the patients approached in the Cardiology Clinic.

This study was approved by the Research Ethics Board at The Hospital for Sick Children and informed consent was obtained from all participants.

### Covariates

The data from 25 patients was taken, and all personal information including the participants name and contact information was removed. Data is shown for all patients and families approached including the gender (male, female, and unidentified), and ethnicity (European, Asian, African, Hispanic, and patients with two or more ethnicities). There was a total of seven types of congenital heart diseases represented in the approached patients: Pulmonary Stenosis, Atrial Septal Defect, Tetralogy of Fallot, Hypoplastic Left Heart Syndrome, Heterotaxy, Dilated Cardiomyopathy, and Transposition of Great Arteries. Finally, the data included whether consent was given by the individuals to participate in the procedure.

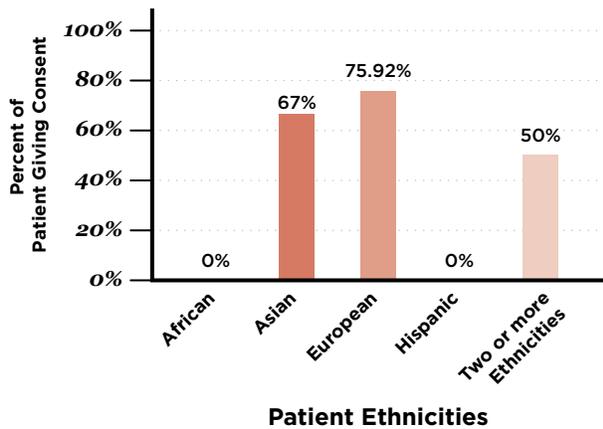
### Statistical Analysis

The data were graphed, and characteristics were observed by comparing consent rates to their respective factors. To further analyze this information, the characteristics were compared with the Chi-squared test to evaluate the statistical significance between the characteristics of the patients – age, gender, ethnicity, presence of familial congenital and the type of congenital heart disease – and the rate of consent to WGS. The percentage of patients who consented to WGS compared to the total number of patients listed under each of the characteristics was calculated. The age category was further divided into four sub-groups to improve the interpretation of the averages of consent rates, which were taken from each of the four sub-groups.

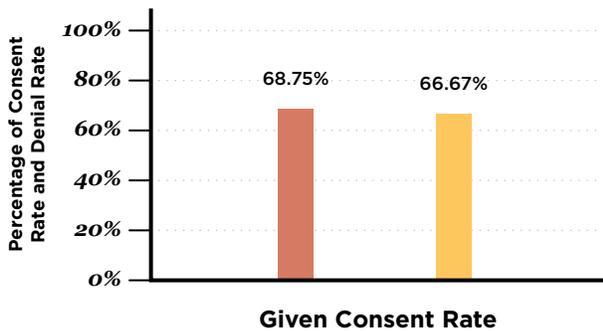
Since a large portion of the study's participants were of European ancestry, separate calculations were conducted on this subset of the sample. They are compared to the same categories created for all 25 patients (gender, age group, type of congenital heart disease and previous familial history) to compare the predominant ethnic group to other minorities of this study.



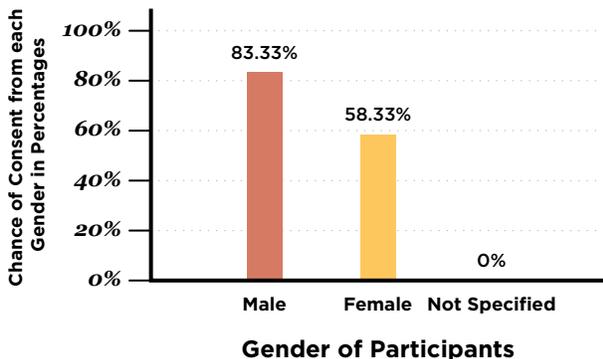
## Results



**Figure 1:** Percent Consent Rate by Patient Ethnicity: Analysis of data on the represented ethnicities of the approached patients and the chance of consent are shown in percentages. The African ancestry had a ratio of 0:1 given consent to total number of patients. The Asian ancestry had a ratio of 2:3 given consent. The European ancestry has a ratio of 13:18. The Hispanic ancestry had a ratio of 0:1. The subgroup of patients with two or more ethnicities had a ratio of 1:2.

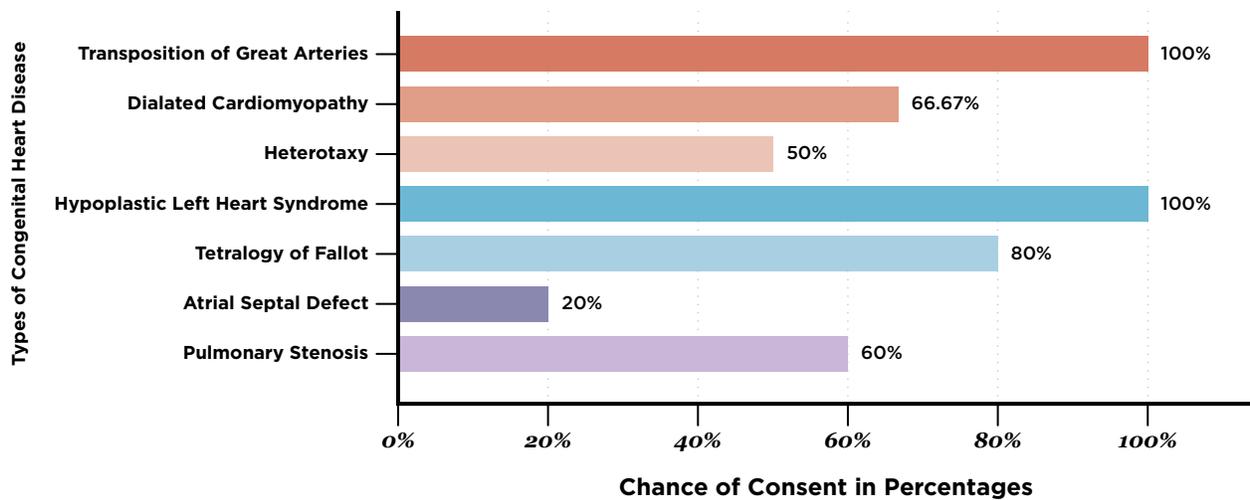


**Figure 2:** Previous Family History of Congenital Heart Disease Compared to Rate of Consent/Denial to SickKids Genome Project 68.75% of the subgroup with a pre-existing familial history provided consent. 66.67% of the subgroup without a pre-existing familial history of a congenital heart disease(s) provided consent to the SickKids Genome Project. The Chi-squared statistic is 0.0115. The  $p$ -value is 0.914641. This result is not significant at  $p < 0.05$ .

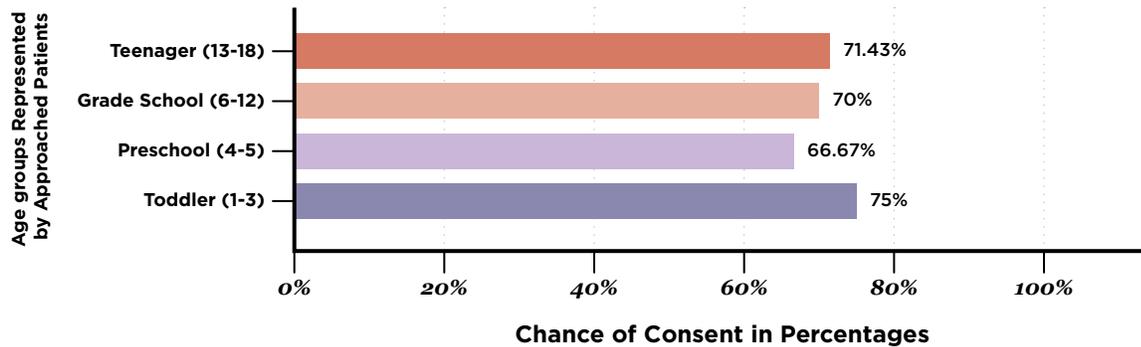


**Figure 3:** Consent Rate Compared to Gender of Patients: Male patients (12) have a consent rate of 83.33% (10). Female patients (12) have a consent rate of 58.33% (7). The patient that is not specified has a 0% chance of consent. The Chi-squared statistic is 1.8151. The  $p$ -value is 0.177895. The result is not significant at  $p < 0.05$ .





**Figure 4:** Type of Congenital Heart Disease of Approached Patients Compared to Consent Rate: Patients with Transposition of Great Arteries have a consent rate of 100%. Patients with Dilated Cardiomyopathy have a consent rate of 66.67%. Patients with heterotaxy have a consent rate of 50%. Patients with Hypoplastic Left Heart Syndrome have a consent rate of 100%. Patients with Tetralogy of Fallot have a consent rate of 80%. Patients with Atrial Septal Defect have a consent rate of 20%. Patients with Pulmonary Stenosis have a consent rate of 60%.



**Figure 5:** Age Groups of Approached Patients Compared to Consent Rate: Toddlers (ages 1-3) have a consent rate of 75%. Preschoolers (ages 4-5) have a consent rate of 66.67%. Grade-schoolers (ages 6-12) have a consent rate of 70%. Teenagers (ages 13-18) have a consent rate of 71.43%. The Chi-squared statistics, when calculated with age groups 1-5 and 6-18, is 0.0017. The  $p$ -value is 0.967162. This result is not significant at  $p < 0.05$ .

We have observed that 17 out of the 25 patients approached for participation in the SickKids Genome Clinic project gave consent. This places the initial consent rate, without the influence of other factors, at 68.00%.

**Figure 1** illustrates the consent rate in terms of ethnicity including all 25 of the approached patients. The majority of patients were of European descent (18), followed by patients of Asian (3), mixed race (2), African (1) and Hispanic (1) ancestry. 13 out of 18 patients of European ancestry agreed to participate (76%), which have made them the highest consenting group. Two out of three patients (67%) of Asian ancestry gave consent. Half of the patients (50%) of more than one ethnicity (mixed race) gave consent, while patients of African and Hispanic ancestry did not provide consent at all. The mean consent rate calculated for all ethnicities was 38.58%. The compared consent rates between European and non-European individuals were insignificant according to the Chi-squared test ( $p= 0.16962, p < 0.5$ ).

We also analyzed the relationship between familial history of congenital heart conditions and consent (**Figure 2**). In this category, 16 of the 25 approached patients had a familial history of congenital heart disease(s), and 69.75% (11) of those patients gave consent to the SickKids Genome project. Two-thirds (6) of the patients that did not have a familial record of congenital heart disease(s) (9) also provided consent to the study. A Chi-squared test found no statistical significance between the presence of familial congenital heart disease and providing consent ( $p= 0.914641$ ).

Of the 25 patients, 12 were male, 12 were female, and one patient was unspecified. Male patients had a higher consent rate at 83.33%, while females had a lower consent rate, with only 58.33% agreeing to become a part of the Genome Clinic project. The patient who was not identified as either male or female did not provide consent. The Chi-squared was used to compare male and female patients consent

rates, resulting in a value of 1.8151, with a  $p$ -value of 0.177895. The result was not statistically significant at  $p < 0.05$ .

**Figure 5** explores the relationship between type of disease and the consent rate. Seven types of congenital heart disease are presented in this figure. More than half of the patients with conditions of Pulmonary Stenosis, Dilated Myocardopathy, Tetralogy of Fallot, Hypoplastic Left Heart Syndrome, and Transposition of Great Arteries provided consent to the test. All five patients exhibiting Transposition of Great Arteries and the three patients with Hypoplastic Left Heart Syndrome also provided consent to the Genome project. Two of three patients exhibiting Dilated Myocardopathy provided consent. A total of five patients exhibited Pulmonary Stenosis, three of which provided consent to the test. Less than half of the patients with either Heterotaxy or Atrial Septal Defect provided consent rate.

The ages of approached patients range from 1 to 18 years old. Due to the broad range of ages represented, four age groups were formed in order to better analyze patterns of consent between similar ages. Groups are loosely formed based on typical preschool kindergarten, elementary, and high school ages in North America. The toddler group, ages 1 to 3, were represented by a total of four patients, with 3 out of 4 patients who provided consent. Patients aged four and five are placed in the preschool group, with a total of three patients in that group, and two providing consent. Patients in the grade school group were 6 to 12 years of age, with ten patients in this category, with a consent rate of 70.00%. The last group, teenagers, consisted of patients aged 13 to 18, was represented by seven patients with 71.43% consenting to the test. The age groups ranked from highest to lowest according to their respective consent rates are: Toddler, Teenager, Grade School, and Preschool.

Referring back to **Figure 1**, patients of European descent have the highest consent rate of the five ethnic groups and is the dominant ethnicity represented by the sample – 13 of the total 25 approached families. Therefore, separate charts were created to test for possible patterns of consent rates with only patients of European descent, accounting for factors such as gender. There were a total of 9 male patients and 8 female patients, with 77.78% (7) and 50.00% (4) consent rates, respectively. The Chi-squared was used to compare these results and found no statistical significance ( $p= 0.231605$ ).

All patients of European descent with Hypoplastic Left Heart Syndrome and Transposition of Great Arteries provided consent. Patients in this category with Tetralogy of Fallot ranked second in providing consent. Patients with Pulmonary Stenosis and Dilated Myocardiopathy were ranked third, and patients with Heterotaxy were ranked fourth in provided consent. No patients with Atrial Septal Defect provided consent to the genome project.

## Discussion

The future application of WGS in providing personalized medicine is an important advancement in healthcare. The WGS project performed by the Hospital for Sick Children attempted to recruit patients with existing congenital heart diseases to participate in a genome study to test the advantages of using WGS for medicine and the factors that may cause patients to reject or accept the procedure. Though participation is free of charge and the resulting information may be valuable, some families did not give consent. It is important to understand the reasoning behind such decisions and this study attempted to do so by analyzing the factors provided in the patient's profile from SickKids Hospital. If a pattern in consent rate and these factors can be found, it will enable hospital staff to develop new methods to work with those patients who are less likely to provide consent.

## Ethnicity

Ethnicity is perhaps one of the most interesting factors to analyze since one ethnicity is represented by the majority of patients, whereas the remaining ethnicities only represent a small portion of the sample. It was observed that the patients of European descent had the highest consent rate, when compared to patients of Asian, African, Hispanic, or two or more ethnicities. However, the differences in consent rates by ethnicity were not statistically significant. Though the sample is ethnically diverse, only patients who are fluent in English were approached and those with the potential to require a translator were excluded. This places Europeans – most with English as their first language – in the majority of all the approached patients. This finding suggests that further efforts should be made to provide equal chances of participation in scientific studies to patients who do not have English as their first language. Not only will this promote equity in the sample of patients that are often provided less opportunities, but also decrease potential biases in this study towards certain races or cultures.

A comparison can be made to another study that highlighted the reasons why consent rates are lower for ethnicities other than the European ancestry. In Wendler's study, a comprehensive literature search was conducted on 20 health research papers that reported enrollment rates due to race or ethnicity (Wendler et. al, 2005). It was found that patients representing ethnicities in the minority were willing to participate only if they were eligible and invited to participate, not because they had a lower consent rate compared to the dominant ancestry (Wendler et. al, 2005). Hispanics and African-Americans agreed to participate more than Europeans, but the differences in consent rates between the European ancestry and the other ethnicities were minimal (Wendler et. al, 2005). Wendler lends further evidence that past speculated theories of historic abuse leading to mistrust of scientific studies from minority ethnicities in North America are false; however, another study found that Europeans were more likely



to provide consent (Street et. al, n.d.). Though the procedures of these studies and the targeted population differ drastically from the WGS study, commonalities were found in the explanations with regards to low participation rates. They all address the fact that low consent rates were not by chance; instead, it may be due to other underlying causes such as exposure of a race to scientific opportunities or faults in history that have caused certain groups to remain doubtful of experimental studies.

Comparatively, other studies observed significant differences in the consent rates of Europeans and other minority groups. In correspondence to the findings in the present study and in Street et al. (Street et. al, n.d.), there were more Europeans than minority ethnicities giving consent to participation in medical studies (Mucsi et. al, 2017). This may also be due to the European ancestry dominating 54% of approached sample size.

The research on the rates of participations amongst African American populations in North American health studies indicates that African Americans always had a lower participation rate since more Europeans are approached. African Americans are often excluded as well due to language barriers in complex medical surveys and studies (Street et. al, n.d.). When asked what their feelings were towards medical studies, many have referred to the Tuskegee Syphilis Study – a medical study that has been ridiculed for its unethical practices (Reverby, S. M., 2017). The participants were in fear of being “guinea pigs” and did not want the potential to become infected or to be injected with a virus via needles. Another famous example may be from the case of Henrietta Lacks who had her biopsy of tumour cells taken and grown in a lab without her or her family’s permission. Though her cells were the first to successfully grow and contributed to the polio vaccine, the discovery of human telomerase, and countless other advances, it was an unethical approach. An adequate response on what was done to the biopsy was answered 30 years after the incident (Callaway, E., 2013). Furthermore, research with

African-American participants is limited due to racial discrimination and poverty, and since the study will not directly benefit the African American population, participation is seen as a waste of time (Corbie-Smith et. al, 1999).

In addition to ethnicity, a history of familial congenital heart disease can affect decisions of participation due to fear of unknown outcomes from genome sequencing or poor experiences with past medical studies. In this study, the differences between the two groups of patients were not significant (3.08% difference,  $p= 0.914641$ ). There are currently not many studies targeting the participation rates of patients in research studies that can provide reasoning for this finding. It can be hypothesized that patients with a previous family history of heart disease are more motivated to participate in the study since they are eager to learn about the potential underlying cause of their disease. Without previous exposure to risks of heart diseases, the group with no familial records may not see the benefits of the study and therefore may not have provided consent to participating due to that reason. However, further research is needed to ascertain the reason(s) why there were no significant differences between the two groups.

When the European ancestry was included with the same factors (age, gender, familial history, type of disease) compared to participation rate, the results were similar to comparisons made amongst the entire sample of patients. Though statistically insignificant, the percentage of females providing consent to the genome project was lower than males of Europeans descent (consent rates 77.78% males, 50.00% females.  $P= 0.231605$ ). This finding was supported by a study performed by Street et al. (2005), where they found more women expressed negative concerns about scientific studies than men but contradicts a consent rate study performed on a sample of 25,000 by Dunn et al. (Dunn, K. M., 2004) stating that men before 59 had a lower consent rate than women in the same age range. Further analysis was performed on the types of heart disease and age group, and the findings were similar to

the data found for the complete sample. These findings may suggest that even though patients of European descent may be more represented and have a higher consent rate, ethnicity may not be strongly influential in the likelihood for certain genders or age groups to give consent.

### Gender

Furthermore, gender plays a role when determining the likelihood of participation in medical studies (Murthy, V. H., Krumholz, H. M., Gross, C. P., n.d.). Though statistically insignificant when placed into the Chi-squared test, 25% more males gave consent to participate in a study rather than females (consent rates 83.33% male, 58.33% female,  $p= 0.177895$ ). Of note, sex preference is found to be a function of age, for example, 30 to 60-year-old men and women had an equally likely chance of providing consent, whereas older men (60+ years) tend to have a noticeably higher consent rate than women (Murthy, V. H., Krumholz, H. M., Gross, C. P., n.d.). Even though the sample sizes and targeted purpose in Street and Stone's studies differ to the current study, they may still explain the reason why less than 60% of female patients have given consent to the WGS study compared to over 80% of male patients.

Similarly, a correlation may arise when looking at the effects of gender and race on consent rates. When a cancer clinical study was analyzed, more than one third of women of colour agreed that scientists cannot be trusted, while only 4.1% of white women had the same belief (Mouton et. al, n.d.). Similar results were found in an AIDS Clinical Studies, stating that females are less likely to participate because most of the women in that cohort study were from communities of colour (Stone et. al, 1997). Of the four females in the WGS study that are of non-European background, three gave consent to the study and only one did not, while only half of European females gave consent. This may suggest that Mouton and Stone's findings are not accurate for this sample. The statement cannot fairly represent the results

of this genome study since the participants included only one more female patient than male that is not of European descent. Of the 25 patients in the sample, one had an unidentified gender. Because the subject's sexuality is unknown, he or she must be excluded from the analysis of gender versus participation.

### Disease

On the other hand, this study's results indicate that there were no differences in consent rates amongst the seven different heart diseases. The diseases cannot be ranked in order of severity since each type affects a different part of the circulatory system, nor could we determine to what degree the patients were being affected by their diseases without being provided more detailed information. While there has been some evidence that the type of disease will yield a different participation rate, specifically in cancer clinical trials (Mouton et. al, n.d.), there were few research studies on consent rates focusing specifically on patients with congenital heart diseases.

The three diseases with the lowest consent rates (Atrial Septal Defect, Heterotaxy, Pulmonary Stenosis) were represented by twelve patients, and characteristics of these patients were observed for this study. Nine of the patients were European, and only one of the latter three was African American. Research on consent rates of Europeans has previously found patients of the three diseases have higher consent rates. However, eight of the twelve patients were female; the gender considered to be a part of the minority in medical studies and is expected to have a lower consent rate than a group with more males. Further analysis showed that the remaining four diseases, with higher consent rates did match consent patterns found in previous research. Since most of these patients are male and/or European, consent rates were between 66.67% and 100%. Regardless, patients with any of the diseases had a low representation of people from minority ethnicities.



## Age

Since the genome project was performed at the SickKids Hospital, only children from birth to 18 years of age were approached, therefore the age range in this study does not accurately reflect findings from other studies that are focused on the adult population (Dunn, K. M., 2004). Upon analysis, all four age groups had similar consent rates (**Figure 5**). This is likely because all patients approached are 18 years old or younger, thus it can be assumed that the decision for participation is made by the patient's parent or guardian. As mentioned before, women and men ages 30 to 60 years of age have an equal chance of providing consent. So, if parents and guardians are near that age range, then the consent pattern would correlate with this finding.

Moreover, age cannot be precise in determining consent rates regarding such a young age group. Parents may believe that participating may provide few to no benefits to the child and family members, which would limit their willingness to participate. Additionally, the SickKids WGS project is an early phase clinical trial. It did not provide families with information regarding the treatment(s) that can be determined through WGS, nor were the families offered any financial compensation. Due to these reasons, many may have seen the project as a waste of personal time, refusing to participate. Ultimately parental biases and preconceptions may have had an effect on patient consent, due to the young age of patients.

## Limitations

Though the data collected are recent, the sample size may be too small to determine whether the differences were statistically significant. With a random sample of 25 patients, it is difficult to ascertain the strength of a relationship between two or more variables. Findings may continue to change as the sample grows larger. It is also difficult to apply findings in this study to other potential medical studies. The WGS Project performed at SickKids Hospital in Toronto is specifically targeted towards children under the age of 18 and is only open to those in the

cardiology department. Other studies that require patients of all ages or those above 18 years of age will not be able to apply the findings in this study since clarity was not provided who made decisions of consent; the patient, or the parent/guardian. Furthermore, this sample only represents seven congenital heart diseases in children. A larger sample with more diseases may be able to determine whether the type of defect has a correlation to consent rate, but otherwise the findings for this factor were inconclusive and were not considered reliable for application to other studies.

Based on the results of the study, some changes that can be made in the future are the representation of minorities in medical studies. A general pattern was observed when research was conducted showing that patients of African ancestry or of the female gender are less likely to be present in medical studies than patients of European descent and males. The under-representation of minority groups (ex. gender and race) poses a bias in studies that hope to yield findings to benefit the general population. In the genome sequencing project, only families fluent in English were approached, placing those with language barriers in the minority. The same patients may also feel less welcome in scientific studies since they believe that racial discrimination will continue to exist and that their contributions will be minimal in medical advancements. Efforts can be made to allow patients of African descent to feel more inclusive, achieving a more accurate representation of the African population in Canada. Moreover, accommodations can be made by providing translators to those who are not fluent in English to account for the increasing number of immigrants from other countries. Further information can also be provided to female patients to boost participation of this gender to make the number of both genders as equal as possible. All of these suggestions are made in hopes that the WGS study can promote social equity to lessen biases linked to gender and age and to bridge the gaps that exist between different cultures and races.

## Conclusions

In conclusion, our results suggest the comparably low consent rates of female and/or patients representing ethnicities in the minority may be due to the underrepresentation of these groups in the initial sample, not because men or Europeans are more likely to participate in the WGS Project. The importance of factors such as age, familial history, as well as types of disease in understanding the likelihood of participation remains inconclusive as results yielded did not reach statistical significance. These outcomes highlight that while there are limitations to which patients meet the requirements to participate in this project, patients in minority groups should never be overlooked. A fair enrollment of all genders and ethnicities will result in more diverse opinions on advancing technology, helping to improve the health care system to benefit all members of the society. Moreover, there were no benefits in favoring one factor when deciding which patients will more likely provide consent; variance amongst patients highlights the diversity of our present-day culture and the need for a representative sample in medical studies. Ultimately, further research with a larger sample size will be needed to validate findings and conclusions.

## Abbreviations

Abbreviation	Full Form
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WGS	Whole Genome Sequencing
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## Acknowledgements

Thank you to the participants and their families for consenting to this study, as well as the staff from The Hospital for Sick Children in Toronto, Ontario, Canada for data collection. I would like to give special thanks to Dr. Brad Bass, a mentor at the University of Toronto, and Priya Dhir, a teacher and researcher at The Hospital for Sick Children, for their relentless patience, inspiration, and guidance on this article.



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