# *Tell Me Once, Tell Me Soon*:

# Parents' Preferences for Clinical Genetics Services for Congenital Heart Disease.

**Short running title:** Parents' preferences for pediatric cardio-genetics consultations

Nadine A. Kasparian BA Psych (Hons I), PhD[1,2*], Richard De Abreu Lourenco[3*] MEc, PhD, David S. Winlaw MD, FRACS[2,4], Gary F. Sholler MBBS (Hons I), FRACP[2,4], Rosalie Viney MEc, PhD[3], and Edwin P. E. Kirk FRACP, PhD.[1,5]

1. Discipline of Paediatrics, School of Women's and Children's Health, UNSW Medicine, The University of New South Wales, Sydney, NSW, Australia.
2. Heart Centre for Children, The Sydney Children's Hospitals Network (Westmead and Randwick), Sydney, NSW, Australia.
3. Centre for Health Economics Research and Evaluation, University of Technology Sydney, Ultimo, NSW, Australia.
4. Discipline of Child and Adolescent Health, Sydney Medical School, The University of Sydney, NSW, Australia.
5. Department of Medical Genetics, Sydney Children's Hospital, Randwick, NSW, Australia.

* Shared first authorship

**Please address correspondence to:** Associate Professor Nadine Kasparian, Heart Centre for Children, The Children's Hospital at Westmead, Locked Bag 4001, Westmead, NSW, 2145, Australia. Telephone: +61 2 9382 5510, Fax: +61 2 9845 3275, Email: n.kasparian@unsw.edu.au, Twitter: @NKasparian

**ABSTRACT**

**Purpose:** As the molecular basis of congenital heart disease (CHD) comes into sharper focus, cardiac genetics services are likely to play an increasingly important role. This study aimed to identify parents' preferences for, and willingness to participate in, clinical genetics services for CHD.

**Methods:** A discrete choice experiment (DCE) was developed to assess parents' preferences for pediatric cardio-genetics services described by four attributes: appointment format, health professionals involved, waiting time, and information format. Data were analyzed using a mixed logit model.

**Results:** One-hundred parents of a living child diagnosed with CHD requiring surgical intervention between 2000-2009 completed the DCE. Parents expressed a clear preference for cardiac genetics services featuring: (a) one appointment, (b) with both a clinical geneticist and genetic counselor, (c) providing verbal and web-based information about CHD and genetics, (d) within two weeks. If offered this service, 93% of respondents indicated they would attend. The choice of cardiac genetics service was most strongly influenced by the presence of both a clinical geneticist and genetic counselor.

**Conclusion:** Parents of children with CHD favor a single, timely genetics appointment with both a geneticist and genetic counselor present. If offered an appointment matching their preferences, uptake is likely to be high.

**Keywords:** Congenital heart disease; genomics; genetic counseling; discrete choice experiment; health economics.

## INTRODUCTION

Congenital heart disease (CHD), a spectrum of structural anomalies of the heart, affects one in 110 newborns or 1.35 million babies worldwide each year, and represents a major global health burden.[1] CHD is the most common cause of neonatal admission to pediatric intensive care,[2] and a leading cause of infant death[3] and disease-related disability in children under age five years.[4] Survival has markedly improved over the past two decades, and best estimates suggest there are now well over 65,000 people in Australia and 2 million people in the United States living with CHD.[5,6]

Understanding of the genetic contributions to CHD is rapidly evolving. Chromosomal microarray (CMA)[7] and massively parallel sequencing (MPS)[8] technologies have made significant inroads, in terms of both CHD diagnosis and our understanding of the mechanisms underlying this disease. In individuals with familial CHD, for example, the chance of achieving a molecular diagnosis with MPS is now 31-46%.[9,10] In individuals with sporadic CHD, *de novo* variation in known or novel CHD genes has recently been identified in a small proportion (~10%) of cases.[11] The genetic link between heart and brain development has also been established beyond the well-known genetic syndromes, expanding our knowledge of the mechanisms underlying the heightened vulnerability to neurodevelopmental impairment in children with CHD.[12]

As the molecular basis of CHD comes into sharper focus, cardiac genetics services are likely to play an increasingly important clinical role. The American Heart Association Scientific Statement on the genetic basis for CHD recommends the approach to all newly diagnosed patients includes routine examination of all relatives for a potential genetic contribution.[13] Within an interdisciplinary team approach,[13] cardio-genetics services require input from clinical geneticists specializing in the medical evaluation of people with CHD, and genetic counselors skilled in providing tailored education on inheritance, recurrence risk, risk management and family screening, as well as counseling to support informed decision-making and psychosocial adaptation.[14] For individuals and families affected by CHD, a genetic diagnosis has

implications for psychological and behavioral adjustment and family planning, and can also have important implications for clinical management and family screening. Individuals with variants in specific genes known to be associated with development of conduction abnormalities or cardiomyopathies, such as *NKX2-5*, *TBX5*, and *TBX20*, are key examples.[15-17] Individual genetic variation may also influence post-surgical outcomes including post-operative tachycardia,[18] tolerance to ischemic and re-perfusion injury,[19] neurocognitive impairment,[20] and risk of death or transplantation.[21] These findings suggest molecular diagnosis may lead to improvements in patient quality of life, and potentially even survival. Expanding application of genetic technologies also creates a growing need to assist individuals and families in navigating the complexities associated with incidental findings, or findings of uncertain clinical significance.[22,23]

While referral to cardiac genetics services is still relatively uncommon in day-to-day pediatric cardiology,[24] it is imperative we develop a deeper understanding of parents' perceptions of, and preferences for, such services.[25] In an earlier study,[24] we found most parents of a child with CHD (87%) perceived genetic factors as 'quite' or 'extremely important' in CHD development and many (73%) wanted information about CHD and genetics; however, only 36% of participants could recall receiving genetics information, most commonly from a pediatric cardiologist (73%) or website (56%).[24] Moreover, we found only 22% of families had previously accessed pediatric cardio-genetics services, with the presence of a syndrome associated with CHD (*OR*=17.93; $p<0.001$) and fetal cardiac diagnosis (*OR*=4.13; $p=0.02$) most strongly influencing attendance.[24] More recently, we found almost all parents (98%) perceived information on CHD recurrence risks as important, yet only 7% could recall receiving this information from a health professional.[26] Individualized genetic counseling sessions tailored to CHD have been shown to be highly beneficial for parents of children with CHD, with improvements in parents' knowledge of CHD causation and enhanced psychological wellbeing, including greater perceived personal control and reduced guilt, shame, depression, anxiety and emotional stress.[26] Developing

evidence-based models for the implementation of interventions such as these into clinical practice is a logical and much-needed next step.

Important when designing health services is to understand how individuals make healthcare choices, and what aspects of a health service they value most. Discrete choice experiments (DCE) are one means of investigating preferences for goods and services, and are increasingly used in health services research,[e.g.27] particularly when there is limited evidence on potential engagement with new services. In a DCE, respondents are asked to choose between a series of alternatives (or profiles) that present different health services or interventions. Services are described in terms of their characteristics (or attributes); for example, who provides the health service, and in what form. By systematically varying the combinations of attributes presented in each alternative, and asking respondents to choose their preferred option, the analysis of these repeated choices shows how individuals tradeoff between attributes when making their choice, hence describing their preferences for those attributes.[28]

To our knowledge, there are no published studies examining the preferences of parents of children with congenital heart disease for genetics services tailored to CHD. The primary aim of this study was to apply DCE methodology to estimate parents' preferences for clinical genetics services for CHD. A secondary aim was to examine the likelihood that parents would attend their preferred cardiac genetics service.

## MATERIALS AND METHODS

### Participants

Parents or guardians of a living child diagnosed with CHD between 2000-2009 and who had undergone cardiac surgery were identified via the Department of Cardiology databases at the Sydney Children's Hospital, Australia. Parents of children with heritable heart diseases (e.g., aortopathy, inherited arrhythmias, cardiomyopathies) were not included. Contactable, fully consented individuals were eligible

for participation if they were aged >18 years and could participate in English. To limit burden on families, one parent per family was invited, with the choice regarding who took part left up to each family.

**Procedure**

The study was approved by the South Eastern Sydney Illawarra Area Health Service Human Research Ethics Committee (HREC) (Approval Number: 08/202) and informed consent was obtained for all participants. A study package comprising an invitation letter from the child's pediatric cardiologist, participant information sheet, questionnaire and reply-paid envelope was mailed to all eligible families. Reminder letters and telephone calls were made, as appropriate, to parents who did not return the questionnaire within one month. Due to stipulation from the HREC, no further attempts were made to contact families after one telephone conversation and a second mailout.

**Discrete Choice Experiment Design**

A DCE was developed specifically to assess parents' preferences for various attributes of a hypothetical pediatric cardio-genetics service. A systematic review of the literature and consultation with experts from various fields (clinical genetics, genetic counseling, pediatric cardiology, medical psychology, health economics) informed the choice of four attributes included in the DCE (appointment format, health professionals involved, waiting time, information format), each with three possible levels (see Figure 1 for an example choice set and Supplementary Table A for the full list of attribute levels). From the initial 81 possible choice combinations in the full factorial, a fractional orthogonal design comprising nine choice sets was selected and tested using online design software.[29] Each respondent was presented with all nine choice sets. Prior to completing the choice sets, respondents were provided with a description of the context in which they were being asked to choose between options for CHD genetic risk assessment, and a description of each of the attributes and levels. Respondents could refer back to these definitions when needed. At each choice set, respondents were asked to indicate which appointment type they preferred, with a follow-up question on whether they would accept a referral to that appointment if

offered (**Error! Reference source not found.**). Prior to administration, the DCE was pilot-tested with a convenience sample of five parents of a child with CHD. Results showed the DCE was easy to understand and complete, and required no modification.

[Insert Figure 1 about here]

**Demographic and Clinical Characteristics**

Seven demographic items assessed: parent age, education, gross annual household income (categorized as above or below the National average based on the Australian Survey of Income and Housing[30]), birthplace, language most commonly spoken at home, relationship to the child with CHD (e.g. mother), and residence at time of childbirth. Participants were asked if their child had been diagnosed with, or if they suspected their child had, a chromosomal abnormality or syndrome, and if they had previously attended a genetics service to discuss their child's heart condition.

**Statistical Analysis**

DCE analysis exploits the relationship between respondents' choices and the choice profiles, revealing the impact on choice of differences between the attributes for the options being compared.[27,28] Our analysis adopted this approach, focusing on the mean choice coefficients across respondents using a multinomial logit analysis, then a mixed logit analysis to incorporate the extent to which there was heterogeneity across respondents in what influenced their choices.[28,31] Heterogeneity in preferences was explored by applying the method described by Hole,[31] which estimates the extent to which attributes influence choice (reported as means), as well as the extent to which respondents differ in the influence of those attributes (reported as the standard deviation around each attribute mean). For each multinomial logit and mixed logit analysis, we specified models with and without a constant, to test whether respondents were systematically choosing the left or right-hand profile in each choice set (the columns labelled 'Appointment A' and 'Appointment B' in Figure 1, respectively). Only respondents who

completed all nine choice sets were included in the analysis. The impact on the results of excluding respondents who completed fewer than nine choice sets was tested in a sensitivity analysis. An additional sensitivity analysis was carried out to examine the impact on preferences of respondents having previously attended a cardiac genetics service.

An important output from DCE analyses is the ability to predict the likelihood that individuals will use the service under investigation.[28] In the present study, the likelihood of service use was examined using the results of the mixed logit analysis, using pairwise comparisons to estimate the probability that respondents would use one of four new service models compared with the current approach to cardiac genetics service provision. The four new service models included one featuring the combination of the most influential levels for each attribute, and three other service models based on plausible combinations of the remaining attribute levels (see Table 2 for a description of each service). All analyses were carried out using StataCorp software, Stata 12 (Texas, USA).

## RESULTS

### Response rates and sample characteristics

Two-hundred fifty-seven eligible families were identified. Of these, 44 families were not contactable (incorrect address, disconnected telephone), 21 families declined participation, and 78 families did not return the questionnaire, resulting in 114 returned questionnaires; a participation rate of 53.5% among eligible, contactable families (114/213). Participants and non-participants did not differ according to child age ($p$=0.90), child sex ($p$=0.50), or presence of single ventricle CHD ($p$=0.29).

A total of 100 individuals (87.8% of 114 participants) completed all nine DCE choice sets. The mean age of respondents was 36.4 years ($SD$=5.4), the majority were mothers (80.0%), most were born in Australia (79.0%) and predominantly spoke English at home (90.0%). One-quarter of respondents (24.0%) had previously attended a genetics service for CHD, 79.2% of whom were parents of a child with a genetic

syndrome. Of those who had no previous exposure to cardiac genetics services, less than one-third (29.3%) could recall receiving information about CHD and genetics, and for those who could, the most common information sources were a pediatric cardiologist (22.4%), the internet (22.4%) and/or a leaflet (14.5%). Participants who did not complete all choice sets (12.2%) differed from those who did in terms of several demographic characteristics (Table 1). The implications of these differences for understanding respondents' preferences were tested in a sensitivity analysis.

[Insert Table 1 about here]

**Understanding Choices**

Results of both the multinomial logit and mixed logit analyses showed respondents were more likely to choose a cardiac genetics service involving: (i) only one appointment, (ii) with both a clinical geneticist and genetic counselor, (iii) providing web-based as well as verbal information about CHD and genetics, and (iv) available within two weeks (**Error! Reference source not found.** and Supplementary Table B). These were the attribute levels with the greatest positive influence. Model fit statistics (log-likelihood and $R^2$) indicated the mixed logit was a better representation of the choice data (Supplementary Table B). Based on Model 3, for example, we observed that offering an appointment with both a clinical geneticist and genetic counselor increased the likelihood of choosing the service by 1.54 ($p<0.01$) relative to the presence of a clinical geneticist only.

[Insert Figure 2 about here]

Results from the mixed logit analysis also indicated that respondents differed in the extent to which they were prepared to tradeoff between the attributes; the significant standard deviations on all attributes demonstrate preference heterogeneity among respondents. This was most evident for the number of appointments; 18% of participants preferred an initial and follow-up appointment relative to one

appointment only, while 23% of participants preferred an ongoing appointment compared with one appointment only. While most participants preferred having both clinician types present at their appointment, 1% of participants reported a preference for a clinical geneticist only. Respondents also differed in how they were influenced by the 6-week waiting time compared with 6 months; 56% of participants preferred the shorter waiting time, while 44% of participants preferred the longer waiting time. Finally, respondents differed in how information format influenced preferences; 36% of participants reported a preference for information presented verbally and in a booklet, compared with verbally alone. Respondents were consistent in how they viewed the tradeoffs between other attribute levels.

**Sensitivity Analyses**

Sensitivity of the results to variation in model structure, whether respondents completed all choice questions, and previous exposure to cardiac genetics services was tested. First, the inclusion of a constant term in Models 2 and 4 suggested that some respondents displayed a preference for the option that appeared on the right-hand side of the task ('Appointment B'). Given that: (i) the choice coefficients in these models did not differ from those in Models 1 and 3, (ii) a constant was not included in the underlying DCE design, and (iii) the experiment did not include an opt-out option, the main results reported are those from Models 1 and 3. The results examining potential differences in preferences based on whether or not all choice sets were completed, and prior cardiac genetics service attendance confirmed the choice preferences observed in the main analysis; thus, we did not identify any systematic differences in responses between participants who had versus had not previously attended a pediatric cardio-genetics service (results available upon request).

**Clinical Genetics Referral Acceptance**

In approximately 80% of cases, respondents indicated they would accept a referral to their preferred service if offered. The influence of attribute levels on choice is apparent in the impact on the probability of a service being chosen by a respondent. **Error! Reference source not found.** shows the average

probability of a service option being chosen when each attribute level is present, given all other possible service combinations, and based on the choice relationship in Model 3. This shows that having only one appointment, within two weeks, with both a clinical geneticist and genetic counselor, and both verbal and web-based information has the greatest impact on the probability of a service being chosen. Health professional type (i.e., presence of both genetics health professionals), was the most influential attribute.

[Insert Figure 3 about here]

Based on the relationships in Model 3, it is also possible to predict the probability of service use based on a combination of attribute levels that might apply. Four possible service models (Services 1-4), including the service associated with the most influential attribute levels, were chosen to test possible variations from the current service delivery model (Table 2). The probability of choosing each of these services was tested against that of the current model (Service 5). The resulting probabilities of uptake for each service (Services 1-4) in pairwise comparisons with Service 5 show that Service 1 was most popular; 93% of respondents indicated they would attend this service, if available. This is consistent with the attribute levels shown to be most favorable in Model 3.

[Insert Table 2 about here]

## DISCUSSION

An important determinant of people's experience of healthcare is how health services are delivered. This includes who provides the health service, in what format, how often, and when. Understanding how individuals might choose to participate in healthcare based on each of these factors is essential if we are to provide services that maximize participation in care. DCEs have been used to investigate these questions in several areas of healthcare, including participation in genetic screening and carrier testing.[e.g.32] To our knowledge, this is the first study to use DCE methods to identify parents' preferences for clinical genetics

services tailored to congenital heart disease. This approach allows estimation of preferences for novel technologies and health services prior to, rather than following, their implementation. This enables service design to better reflect the preferences of future users before implementation, maximizing potential uptake and impact. The challenge for service providers will be to design services that best match these preferences. Achieving rapid appointment times may be particularly challenging, given the demand for pediatric cardio-genetics services,[24-26] the high prevalence of CHD compared to other congenital anomalies,[1] and the limited number of specialists to provide such services. Awareness of the burden this could place on under-staffed genetics services, and strategies for addressing this, are much needed and reflect an issue affecting current practice models and the clinical genetics workforce globally.

This study provides further evidence of a high willingness to access pediatric cardio-genetics services.[24] Parents of children with CHD have an overwhelming preference for cardio-genetics services featuring: (a) one appointment, (b) with both a clinical geneticist and genetic counselor, (c) providing verbal and web-based information, (d) and occurring within two weeks. If offered this service, 93% of respondents indicated they would attend. This is an important finding, because it indicates that providing genetic counseling with reduced appointment waiting time would result in attendance by almost all parents offered a referral. Independent of patient preference, there are obvious advantages to this approach. While the diagnosis of CHD-associated syndromes is the province of the clinical geneticist, emphasis on both medical and emotional aspects of genetic assessment for CHD is consistent with the profound psychological consequences of complex CHD reported by parents.[33] Access to counseling and support of the type a genetic counselor can provide is likely to improve parents' understanding of, and psychological adaptation to, their child's heart condition[26] and is consistent with evidence on the clinical benefits of, and patients' preferences for, integrated interdisciplinary healthcare.[33]

DCEs examining preferences for genetic services in other clinical settings (e.g., cancer, mental health), have also found that individuals place high value on appointment waiting time,[34] mode of service

delivery,[34] and information provision.[32] Peacock et al. investigated women's preferences for genetic counseling for breast and ovarian cancer risk, focusing on amount of information provided, counseling in preparation for test outcomes, guidance regarding surveillance and risk management, and genetic testing recommendations.[32] Respondents valued information provision above all other factors, with women valuing information about cancer genetics nine times more than direct guidance regarding whether to undergo genetic testing. This is consistent with the goals of genetic counseling, which include providing information about disease and genetic factors that may influence risk, symptomatology or treatment, and facilitating autonomous health decision-making. Our finding that respondents preferred genetics information in both verbal and web-based formats is also consistent with previous research. In a study by Kasparian et al.,[35] parents of children with CHD reported a strong desire for web-based healthcare information, or eHealth, recommended by their pediatric cardiac team. Web-based information was reported to influence medical decision-making for over half the sample, despite relatively low levels of eHealth literacy.[35]

Several study limitations must also be considered. Unlike some DCEs in clinical genetics, we did not include cost in our study because pediatric cardio-genetics services are offered free of charge within our center, as in most Australian centers. This means it is not possible to estimate parents' willingness to pay for the presence of two clinicians, or shorter waiting times, for example. Previous DCEs have also considered the impact of genetic test results on respondents' preferences. In contrast, our research investigated parents' decision to attend a pediatric cardio-genetics service, irrespective of genetic testing availability. In so doing, we focused on how such services might be best structured, rather than on the nature of information provided within those services. This was considered important in a first study on parents' preferences for clinical genetics services for CHD, given limited available evidence on the clinical implications of such information and the rapidly evolving nature of the field.[9] We are not aware of evidence to suggest systematic differences in men and women's DCE responses, but acknowledge the low proportion of fathers who participated, potentially limiting the generalizability of results. Research

investigating the preferences of parents of more recently diagnosed children, of adolescents and young people with CHD, and of bereaved families, will broaden the evidence from which to inform best practice in pediatric cardio-genetics.

**Potential practice models in pediatric cardio-genetics**

Our findings suggest at least three potential models for the integration of clinical genetics services into CHD care, each with strengths and weaknesses. The model most strongly supported by our results is one in which all children with CHD are referred to an interdisciplinary pediatric cardio-genetics service, ideally co-located with the referring cardiac center. Genetics assessment would include consideration of family history, potential teratogenic exposures and examination for features suggestive of an underlying syndromal cause. Although most CHD is multifactorial in causation, parents (particularly those considering further children) would benefit from reassurance around exposures during pregnancy and empiric recurrence risks, informed by expert opinion about the likelihood of a Mendelian cause. Genetic counseling would be offered hand-in-hand with medical evaluation, and would be tailored to meet the psychosocial needs of families, including referral to medical psychology services, when indicated. It is, however, unlikely that such a model could deliver the speed of appointment preferred by parents, and the resource and funding implications are prohibitive.

Given these constraints, other models require consideration. There is a strong case for further development of genetic counselors' role in CHD care.[26] There are existing models in cardiac genetics (e.g. cardiomyopathies, disorders of cardiac rhythm) for participation of genetic counselors in cardiologist-led services,[36] with consultation with clinical geneticists as required. Some upskilling of pediatric cardiologists and cardiac surgeons would be needed, to ensure equitable access and to triage patients for genetics review. While this would not directly match the preferred model suggested by our data, it would meet some of the requirements - particularly for speed and genetic counselor involvement. Building on, rather than replacing, existing models has obvious advantages.

Lastly, consideration could be given to focusing almost entirely on empowering pediatric cardiologists and cardiac surgeons to take on a substantial part of the genetics assessment and even counseling. While this group of health professionals has considerable relevant knowledge and immediate access to the patient, it seems unlikely that most cardiologists would have time for these tasks. At a minimum, a proportion of the required information could be streamlined through the use of eHealth (online) resources.[35] These would not replace clinical assessment or care provided by genetics professionals, but could provide an educational grounding to facilitate clinical interactions and support informed decision-making. eHealth resources, developed by an interdisciplinary team, also have the advantages of being easy for patients and families to re-access at various points throughout the care trajectory, and of being inexpensive for health professionals to maintain and update as genetic knowledge and technologies evolve. Irrespective of the service model, our data suggest best practice is for every pediatric cardiac center to have access to clinical genetics services and resources for CHD.

## CONCLUSION

As the molecular basis of CHD comes into sharper focus, cardiac genetics services are likely to play an increasingly important clinical role. Research shows that genetic factors play a role in almost all parents' causal attributions for CHD.[24] Understanding families' preferences for novel genetic technologies and services prior to, rather than following, their implementation is vital for informing health policy and shaping future health services. Modeling the factors that influence engagement with cardiac genetics services can ensure that such services are designed to meet participation targets. In this study, we found parents espoused a *'tell me once, tell me soon'* model of clinical genetics services for CHD. Gaining a deeper and more precise understanding of the aspects parents value most in relation to these services - and developing, testing and implementing innovative practice models to improve service access, use, outcomes and cost - is a necessary next step.

**ACKNOWLEDGEMENTS**

We very gratefully acknowledge Dr Stephanie Knox for her contribution to DCE design, and Drs Stephen Cooper, David Murphy, Christoph Camphausen, Owen Jones, Blake Fidock and Ritik Kaul for assistance with data collection. A/Professor Kasparian is the recipient of a National Heart Foundation of Australia Future Leader Fellowship (101229).

**REFERENCES**


1. van der Linde D, Konings EE, Slager MA, et al. Birth prevalence of congenital heart disease worldwide: A systematic review and meta-analysis. *J Am Coll Cardiol.* 2011;58(21):2241-7.
2. Australian and New Zealand Intensive Care Society. *Report of the Australian and New Zealand Paediatric Intensive Care Registry (ANZPIC).* Brisbane: Centre for Outcome and Resource Evaluation; 2014.
3. Australian Institute of Health and Welfare. *A Picture of Australia's Children 2012. Cat. No. PHE 167.* Canberra: AIHW; 2012.
4. Australian Institute of Health and Welfare. *Australian Burden of Disease Study: Impact and causes of illness and death in Australia 2011. Australian Burden of Disease Study Series No. 3. Cat. No. BOD 4.* Canberra: AIHW; 2016.
5. Celermajer D, Strange G, Cordina R, et al. Congenital heart disease requires a lifetime continuum of care: A call for a Regional Registry. *Heart Lung Circ.* 2016;25(8):750–4.
6. Gilboa SM, Devine OJ, Kucik JE, et al. Congenital heart defects in the United States: Estimating the magnitude of the affected population in 2010. *Circ.* 2016;134(2):101-9.
7. Helm BM, Freeze SL. Genetic evaluation and use of chromosome microarray in patients with isolated heart defects: Benefits and challenges of a new model in cardiovascular care. *Frontiers Cardiovasc Med.* 2016;3:19.
8. Blue GM, Kirk EP, Giannoulatou E, et al. Advances in the genetics of congenital heart disease. *J Am Coll Cardiol.* 2017;69(7):859-70.
9. Blue GM, Kirk EP, Giannoulatou E, et al. Targeted next-generation sequencing identifies pathogenic variants in familial congenital heart disease. *J Am Coll Cardiol.* 2014;64:2498–506.
10. Jia Y, Louw JJ, Breckpot J, et al. The diagnostic value of next generation sequencing in familial nonsyndromic congenital heart defects. *Am J Med Genet A.* 2015;167(8):1822-9.

11. Zaidi S, Choi M, Wakimoto H, et al. De novo mutations in histone-modifying genes in congenital heart disease. *Nature.* 2013;498:220–3.
12. Homsy J, Zaidi S, Shen Y, et al. De novo mutations in congenital heart disease with neurodevelopmental and other congenital anomalies. *Science.* 2015;350(6265):1262-6.
13. Pierpont ME, Basson CT, Benson DW, Jr., et al. Genetic basis for congenital heart defects: Current knowledge. A scientific statement from the American Heart Association Congenital Cardiac Defects Committee, Council on Cardiovascular Disease in the Young, Endorsed by the American Academy of Pediatrics. *Circ.* 2007;115(23):3015-38.
14. Parrott A, Ware SM. The role of the geneticist and genetic counselor in an ACHD clinic. *Prog Ped Cardiol.* 2012;34(1):15-20.
15. Kirk EP, Sunde M, Costa MW, et al. Mutations in cardiac T-box factor gene TBX20 are associated with diverse cardiac pathologies, including defects of septation and valvulogenesis and cardiomyopathy. *Am J Human Genet.* 2007;81(2):280-91.
16. Costa MW, Guo G, Wolstein O, et al. Functional characterization of a novel mutation in NKX2-5 associated with congenital heart disease and adult-onset cardiomyopathy. *Circ Cardiovasc Genet.* 2013;6(3):238-47.
17. Zhang XL, Qiu XB, Yuan F, et al. TBX5 loss-of-function mutation contributes to familial dilated cardiomyopathy. *Biochem Biophys Res Commun.* 2015;459(1):166-71.
18. Smith AH, Flack EC, Borgman KY, et al. A common angiotensin-converting enzyme polymorphism and preoperative angiotensin-converting enzyme inhibition modify risk of tachyarrhythmias after congenital heart surgery. *Heart Rhythm.* 2014;11(4):637-43.
19. Zhang H, Gong DX, Zhang YJ, Li SJ, Hu S. Effect of mitochondrial aldehyde dehydrogenase-2 genotype on cardioprotection in patients with congenital heart disease. *Eur Heart J.* 2012;33(13):1606-14.
20. Carey AS, Liang L, Edwards J, et al. Effect of copy number variants on outcomes for infants with single ventricle heart defects. *Circ Cardiovasc Genet.* 2013;6(5):444-51.

21. Kim DS, Kim JH, Burt AA, et al. Burden of potentially pathologic copy number variants is higher in children with isolated congenital heart disease and significantly impairs covariate-adjusted transplant-free survival. *J horacic Cardiovascul Surg.* 2016;151(4):1147-1151.e1144.
22. Green RC, Berg JS, Grody WW, et al. ACMG recommendations for reporting of incidental findings in clinical exome and genome sequencing. *Genet Med.* 2013;15(7):565-74.
23. American College of Medical Genetics and Genomics (ACMG) Board of Directors. ACMG policy statement: Updated recommendations regarding analysis and reporting of secondary findings in clinical genome-scale sequencing. *Genet Med.* 2014;17(1):68–9.
24. Kasparian NA, Fidock B, Sholler GF, et al. Parents' perceptions of genetics services for congenital heart disease: The role of demographic, clinical, and psychological factors in determining service attendance. *Genet Med.* 2014;16(6):460-8.
25. Fitzgerald-Butt SM, Klima J, Kelleher K, Chisolm D, McBride KL. Genetic knowledge and attitudes of parents of children with congenital heart defects. *Am J Med Genet A.* 2014;164(12):3069-75.
26. Blue GM, Kasparian NA, Sholler GF, Kirk EP, Winlaw DS. Genetic counselling in parents of children with congenital heart disease significantly improves knowledge about causation and enhances psychosocial functioning. *Int J Cardiol.* 2015;178:124-30.
27. Clark MD, Determann D, Petrou S, Moro D, de Bekker-Grob EW. Discrete choice experiments in health economics: a review of the literature. *PharmacoEconomics.* 2014;32(9):883-902.
28. Muhlbacher A, Johnson FR. Choice experiments to quantify preferences for health and healthcare: State of the practice. *Applied Health Econ Health Policy.* 2016;14(3):253-66.
29. *Discrete Choice Experiments* available from http://maths.science.uts.edu.au/maths/wiki/SPExpts [computer program]. Sydney, Australia: Department of Mathematical Sciences, University of Technology, Sydney; 2007.
30. Australian Bureau of Statistics. Survey of Income and Housing. 2007-08; http://www.abs.gov.au/ausstats/abs@.nsf/1020492cfcd63696ca2568a1002477b5/5f4bb49c975c64c9ca256d6b00827adb!OpenDocument. Accessed 12th February, 2010.

31. Hole A. Fitting mixed logit models by using maximum simulated likelihood. *Stata J.* 2007;7(3):388-401.
32. Peacock S, Apicella C, Andrews L, et al. A discrete choice experiment of preferences for genetic counselling among Jewish women seeking cancer genetics services. *Brit J Cancer.* 2006;95:1448-53.
33. Kasparian NA, Winlaw DS, Sholler GF. 'Congenital heart health': How psychological care can make a difference. *Med J Australia.* 2016;205(3):104-6.
34. Buchanan J, Wordsworth S, Schuh A. Patients' preferences for genomic diagnostic testing in chronic lymphocytic leukaemia: A discrete choice experiment. *Patient* 2016;9(6):525-36.
35. Kasparian NA, Lieu N, Winlaw DS, Cole A, Kirk E, Sholler GF. eHealth literacy and preferences for eHealth resources in parents of children with complex CHD. *Cardiol Young.* 2017;27(4):722-30.
36. Caleshu C, Kasparian NA, Edwards KS, et al. Interdisciplinary psychosocial care for families with inherited cardiovascular diseases. *Trends Cardiovasc Med.* 2016;26(7):647-53.

## FIGURE LEGENDS

**Figure 1. Example of a choice task offered to participants.** Each participant completed nine such tasks. Hypothetical services differed on four attributes: appointment format, health professionals who provide the service, appointment waiting time, and the format in which information is provided. In each task, participants were asked to choose between two cardiac genetics service models. Participants were also asked to indicate whether they would accept a referral to attend their preferred service.

**Figure 2. Results of the mixed logit analysis (Model 3), illustrating parents' (*N*=100) preferences for genetics services for congenital heart disease.** The top portion of the figure (above the dotted line) shows the mean coefficient values, while the bottom portion (below the dotted line) shows the extent of deviation (standard deviation) among individual for those values.

**Figure 3. Influence of the four attributes on mean probability of choice.** Base levels for each attribute are presented in green. Note: The mean probability of choice at each attribute level was generated by non-parametric bootstrapping of predicted probabilities, given the overall model results and over 1,000 replications. This method utilizes the likelihood of choice from the mixed logit without a constant.

## Conflict of Interests Statement

The authors declare no conflict of interest.

Figure 1

**Figure 1. Example of a choice task offered to participants.** Each participant completed nine such tasks. Hypothetical services differed on four attributes: appointment format, health professionals who provide the service, appointment waiting time, and the format in which information is provided. In each task, participants were asked to choose between two cardiac genetics service models. Participants were also asked to indicate whether they would accept a referral to attend their preferred service.

***Which type of appointment would you prefer?***

| | **APPOINTMENT A** | **APPOINTMENT B** |
|---|---|---|
| **Appointment Format** | One appointment and ongoing support provided over the telephone | One appointment only |
| **Health Professional** | Clinical Geneticist and Genetic Counsellor | Clinical Geneticist only |
| **Waiting Time** | Six weeks | Six months |
| **Information Format** | Verbal information and an information booklet to take home | Verbal information and the link to a relevant website |

***Which would you prefer?*** Appointment A ☐ Appointment B ☐

***If your preferred appointment was offered, would you accept a referral to the clinic?*** Yes ☐ No ☐

Figure 2. Results of the mixed logit analysis (Model 3), illustrating parents? (N=100) preferences for genetics services for congenital heart disease.

The top portion of the figure (above the dotted line) shows the mean coefficient values, while the bottom portion (below the dotted line) shows the extent of deviation (standard deviation) among respondents for those values.

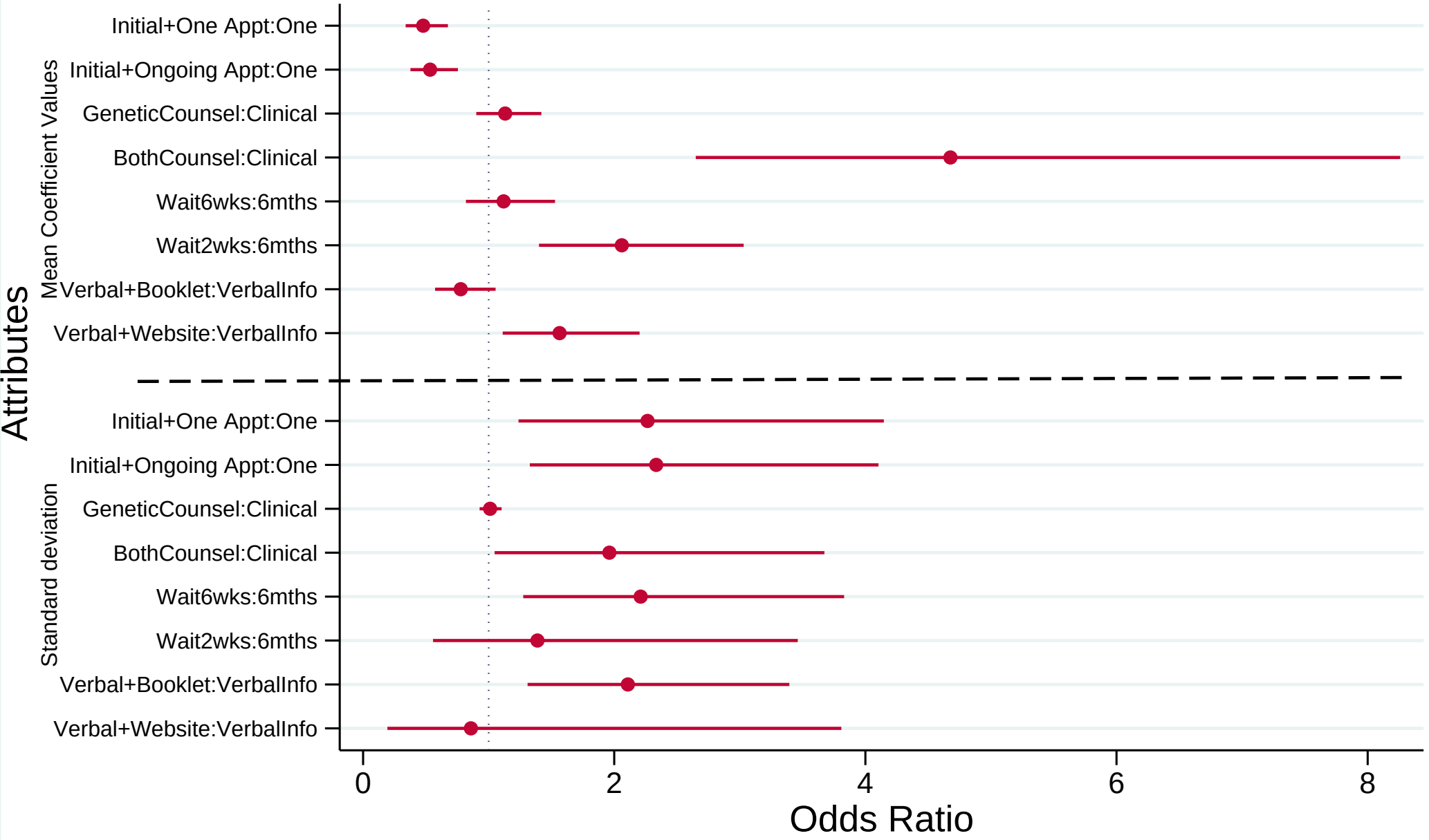

Figure 3

**Figure 3. Influence of the four attributes on mean probability of choice.**

Base levels for each attribute are presented in grey. Note: The mean probability of choice at each attribute level was generated by non-parametric bootstrapping of predicted probabilities, given the overall model results and over 1,000 replications. This method utilizes the likelihood of choice from the mixed logit without a constant.

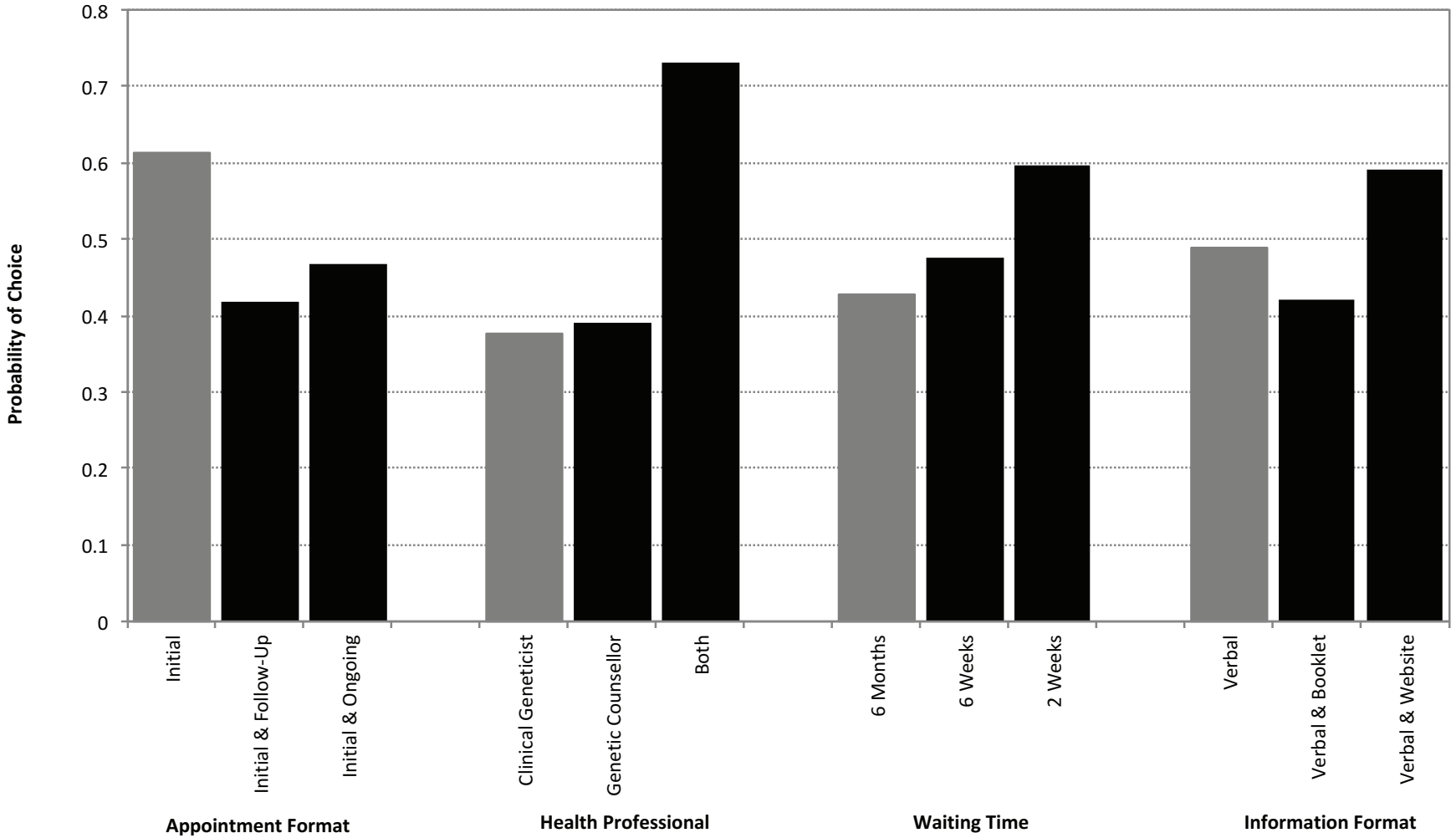

**Table 1. Demographic characteristics presented separately for the total sample (*N*=114) and DCE respondents (*N*=100).**

| Level | All Participants *N*=114 (%) | Completed DCE *N*=100 (%) |
|---|---|---|
| **Age** | | |
| ≥25 years | 4 (3.5) | 3 (3.0) |
| 26 to 35 years | 46 (40.4) | 42 (42.0) |
| 36 to 45 years | 55 (48.3) | 50 (50.0) |
| ≤46 years | 9 (7.9) | 5 (5.0) |
| **Education** | | |
| Tertiary | 57 (50.0) | 51 (51.0) |
| No tertiary | 56 (49.1) | 48 (48.0) |
| Not reported | 1 (0.9) | 1 (1.0) |
| **Gross annual household income** | | |
| Below national average | 48 (42.1) | 40 (40.0) |
| Above national average | 50 (43.9) | 48 (48.0) |
| Not reported | 16 (14) | 12 (12.0) |
| **Birthplace** | | |
| Australia | 83 (72.8) | 79 (79.0) |
| Elsewhere | 31 (27.2) | 21 (21.0) |
| **Language spoken at home** | | |
| English | 101 (88.6) | 90 (90.0) |
| Other | 13 (11.4) | 10 (10.0) |
| **Relationship to child with CHD** | | |
| Mother | 91 (79.8) | 80 (80.0) |
| Father | 20 (17.5) | 19 (19.0) |
| Other | 1 (0.9) | 0 |
| Not reported | 2 (1.8) | 1 (1.0) |
| **Residence at time of childbirth** | | |
| Metropolitan NSW | 80 (70.2) | 70 (70.0) |
| Regional/Rural NSW | 31 (27.2) | 27 (27.0) |
| Overseas | 3 (2.6) | 3 (3.0) |
| **Child chromosomal abnormality** | | |
| No | 74 (64.9) | 65 (65.0) |
| Yes/Unsure | 39 (34.2) | 34 (34.0) |
| Not reported | 1 (0.9) | 1 (1.0) |
| **Previously attended a genetics service for CHD** | | |
| No | 89 (78.1) | 76 (76.0) |
| Yes | 25 (21.9) | 24 (24.0) |

**Table 2. Predicted service use, indicating the probability of each service being used, based on the relationships observed from the mixed logit regression model without a constant.**

| | SERVICE 1 | SERVICE 2 | SERVICE 3 | SERVICE 4 | SERVICE 5 Currently Available |
|---|---|---|---|---|---|
| **Appointment Format** | One appointment only | Initial appointment and follow-up | One appointment only | Ongoing appointments | One appointment only |
| **Health Professional** | Clinical geneticist and genetic counselor | Clinical geneticist only | Clinical geneticist and genetic counselor | Clinical geneticist and genetic counselor | Clinical geneticist only |
| **Waiting Time** | 2 weeks | 6 months | 6 months | 2 weeks | 6 months |
| **Information Format** | Verbal and web-based information | Verbal information and booklet | Verbal information only | Verbal and web-based information | Verbal information and booklet |
| **Probability of Service Uptake** | **93%** (7%) | **34%** (66%) | **82%** (18%) | **86%** (14%) | |

Probabilities of service uptake relative to Service 5 (probability of uptake for Service 5 shown in brackets).

**Supplementary Table A. The four attributes, each with three levels, included in the discrete choice experiment examining parents' preferences for pediatric cardio-genetics services.**

**Attribute 1: APPOINTMENT FORMAT**
The number of appointments offered may vary.
Level 1: One appointment only.
Level 2: One appointment and one follow-up appointment.
Level 3: One appointment and ongoing support provided by telephone.

**Attribute 2: HEALTH PROFESSIONALS**
A Clinical Geneticist is a doctor who specializes in the assessment and medical care of people with a genetic condition. A Genetic Counselor has specialist training in providing information, education and counseling to individuals and families affected by a genetic condition.
Level 1: Clinical Geneticist only.
Level 2: Clinical Geneticist and Genetic Counselor.
Level 3: Genetic Counselor only.

**Attribute 3: APPOINTMENT WAITING TIME**
The length of time that families may need to wait to see a Clinical Geneticist and/or Genetic Counselor may also vary.
Level 1: Two weeks.
Level 2: Six weeks.
Level 3: Six months.

**Attribute 4: INFORMATION FORMAT**
Information provided in a genetics appointment can be communicated in a variety of ways. Verbal information simply involves listening to what is said during the appointment. Families may also want to take home some written information, or be given a link to a relevant website.
Level 1: Verbal information only.
Level 2: Verbal information and an information booklet to take home.
Level 3: Verbal information and the link to a relevant website.

**Supplementary Table B. Results of the conditional logit and mixed logit regression analyses, each examined without (Models 1 and 3), and with (Models 2 and 4), a constant to test the potential for position bias.**

| | Conditional Logit | | Mixed Logit | |
|---|---|---|---|---|
| | **MODEL 1** | **MODEL 2** | **MODEL 3** | **MODEL 4** |
| *Coefficient Means* | | | | |
| **Appointment Format: <u>One appointment only</u>** | | | | |
| Initial and follow-up appointments | -0.592 (0.123)** | -0.578 (0.128)** | -0.737 (0.176)** | -0.751 (0.195)** |
| Ongoing appointments | -0.535 (0.121)** | -0.550 (0.117)** | -0.628 (0.177)** | -0.694 (0.194)** |
| **Health Professional: <u>Clinical geneticist</u>** | | | | |
| Genetic counselor | 0.068 (0.082) | 0.104 (0.084) | 0.123 (0.116) | 0.184 (0.131) |
| Clinical geneticist and genetic counselor | 1.139 (0.114)** | 1.183 (0.125)** | 1.543 (0.290)** | 1.687 (0.342)** |
| **Appointment Waiting Time: <u>6 months</u>** | | | | |
| 6 weeks | 0.138 (0.117) | 0.090 (0.120) | 0.112 (0.159) | 0.066 (0.169) |
| 2 weeks | 0.584 (0.119)** | 0.545 (0.114)** | 0.723 (0.197)** | 0.725 (0.210)** |
| **Information Format: <u>Verbal only</u>** | | | | |
| Verbal and booklet | -0.231 (0.108)* | -0.204 (0.112) | -0.251 (0.156) | -0.234 (0.167) |
| Verbal and web-based (eHealth) | 0.276 (0.109)* | 0.351 (0.117)** | 0.448 (0.174)* | 0.570 (0.202)** |
| **Constant** | | 0.237 (0.074)** | | 0.341 (0.108)** |

| | | | | |
|---|---|---|---|---|
| *Coefficient Standard Deviations* | | | | |
| **Appointment Format: <u>One appointment only</u>** | | | | |
| Initial and follow-up appointments | | | 0.818 (0.309)** | 0.974 (0.334)** |
| Ongoing appointments | | | 0.848 (0.288)** | 0.873 (0.316)** |
| | | | | |
| **Health Professional: <u>Clinical geneticist</u>** | | | | |
| Genetic counselor | | | 0.012 (0.044) | 0.020 (0.037) |
| Clinical geneticist and genetic counselor | | | 0.674 (0.320)* | 0.766 (0.319)* |
| | | | | |
| **Appointment Waiting Time: <u>6 months</u>** | | | | |
| 6 weeks | | | 0.793 (0.281)** | 0.925 (0.306)** |
| 2 weeks | | | 0.328 (0.466) | 0.387 (0.436) |
| | | | | |
| **Information Format: <u>Verbal only</u>** | | | | |
| Verbal and booklet | | | 0.746 (0.243)** | 0.799 (0.267)** |
| Verbal and web-based (eHealth) | | | -0.152 (0.760) | -0.294 (0.478) |
| | | | | |
| *Observations* | 1,800 | 1,800 | 1,800 | 1,800 |
| *Individuals* | 100 | 100 | 100 | 100 |
| Pseudo R-Squared | 0.18 | 0.19 | 0.19 | 0.21 |
| Wald Chi | 144.90 | 124.70 | 36.33 | 34.12 |
| *df* | 8 | 9 | 8 | 9 |
| *p*-value | 0.00 | 0.00 | 0.00 | 0.00 |
| Log-likelihood | -508.81 | -504.42 | -499.80 | -493.74 |

*$p$<0.05, **$p$<0.01, ***$p$<0.001

The omitted level for each independent variable is shown in bold and underlined typeface, alongside the category name.

Pseudo R-squared for Models 3 and 4 estimated as 1-(log-likelihood$_m$/log-likelihood$_c$), where *m* denotes the relevant model and *c* denotes a model with a constant only random term. *df*: degrees of freedom.

Corresponding Author Name: Nadine Kasparian
Manuscript Number: GIM-D-17-00491

# Reporting Checklist

This checklist is used to ensure good reporting standards and to improve the reproducibility of published results. **Please respond completely to all questions relevant to your manuscript. For sections that are not applicable please fill in NA.** For more information, please read the journal's Guide to Authors.

⬓ Check here to confirm that the following information is available in the Material & Methods section:

- the **exact sample size (*n*)** for each experimental group/condition, given as a number, not a range;
- a **description of the sample collection** allowing the reader to understand whether the samples represent **technical or biological replicates** (including how many animals, litters, culture, etc.);
- a **statement of how many times the experiment shown was replicated in the laboratory**;
- **definitions of statistical methods and measures**: (For small sample sizes (n<5) descriptive statistics are not appropriate, instead plot individual data points)
  - very common tests, such as *t*-test, simple $\chi^2$ tests, Wilcoxon and Mann-Whitney tests, can be unambiguously identified by name only, but more complex techniques should be described in the methods section;
  - are tests one-sided or two-sided?
  - are there adjustments for multiple comparisons?
  - **statistical test results**, e.g., ***P* values**;
  - definition of **'center values'** as **median or mean**;
  - definition of **error bars as s.d. or s.e.m. or c.i.**

Please ensure that the answers to the following questions are reported both **in the manuscript itself and in the space below.** We encourage you to include a specific subsection in the methods section each for statistics, reagents and animal models. Below, provide the text as it appears in the manuscript as well as the page number.

| **Statistics and general methods** | **Text AND page number from manuscript** |
|---|---|
| 1. How was the sample size chosen to ensure adequate power to detect a pre-specified effect size? (Give text and page #) | NA |
| For animal studies, include a statement about sample size estimate even if no statistical methods were used. | NA |
| 2. Describe inclusion/exclusion criteria if samples or animals were excluded from the analysis. Were the criteria pre-established? (Give text and page #) | Page 6: Parents or guardians of a living child diagnosed with a congenital cardiac malformation between 2000-2009 and who had undergone cardiac surgery, were identified for study participation via the databases of the Department of Cardiology at the Sydney |
| 3. If a method of randomization was used to determine how samples/animals were allocated to experimental groups and processed, describe it. (Give text and page #) | NA |
| For animal studies, include a statement about randomization even if no randomization was used. | NA |

| | |
|---|---|
| 4. If the investigator was blinded to the group allocation during the experiment and/or when assessing the outcome, state the extent of blinding. (Give text and page #) | NA |
| For animal studies, include a statement about blinding even if no blinding was done. | Page 8: Heterogeneity in preferences was explored by applying the method described by Hole,34 which estimates the extent to which |
| 5. For every figure, are statistical tests justified as appropriate? | Page 8: DCE analysis exploits the relationship between respondents' choices and the choice profiles, revealing the impact on choice of |
| Do the data meet the assumptions of the tests (e.g., normal distribution)? | NA |
| Is there an estimate of variation within each group of data? | Page 8: Heterogeneity in preferences was explored by applying the method described by Hole,34 which estimates the extent to which |
| Is the variance similar between the groups that are being statistically compared? (Give text and page #) | NA |

| **Reagents** | **Text AND page number from manuscript** |
|---|---|
| 6. Report the source of antibodies (vendor and catalog number) | NA |
| 7. Identify the source of cell lines and report if they were recently authenticated (e.g., by STR profiling) and tested for mycoplasma contamination | NA |

| **Animal Models** | **Text AND page number from manuscript** |
|---|---|
| 8. Report species, strain, sex and age of animals | NA |
| 9. For experiments involving live vertebrates, include a statement of compliance with ethical regulations and identify the committee(s) approving the experiments. | NA |

10. We recommend consulting the ARRIVE guidelines (*PLoS Biol.* **8**(6), e1000412,2010) to ensure that other relevant aspects of animal studies are adequately reported.

| **Human subjects** | **Text AND page number from manuscript** |
|---|---|
| 11. Identify the committee(s) approving the study protocol. | Page 6: The study was approved by the South Eastern Sydney Illawarra Area Health Service Human Research Ethics |
| 12. Include a statement confirming that informed consent was obtained from all subjects. | Page 6: informed consent was obtained for all participants. |
| 13. For publication of patient photos, include a statement confirming that consent to publish was obtained. For more information, please see http://www.icmje.org/recommendations/browse/roles-and-responsibilities/protection-of-research-participants.html. | NA |
| 14. Report the clinical trial registration number (at ClinicalTrials.gov or equivalent). | NA |

15. For phase II and III randomized controlled trials, please refer to the CONSORT statement and submit the CONSORT checklist with your submission.

16. For tumor marker prognostic studies, we recommend that you follow the REMARK reporting guidelines.

| **Data deposition** | **Text AND page number from manuscript** |
|---|---|
| 17. Provide accession codes for deposited data. Data deposition in a public repository is mandatory for:<br>a. Protein, DNA and RNA sequences<br>b. Macromolecular structures<br>c. Crystallographic data for small molecules<br>d. Microarray data | NA |

Deposition is strongly recommended for many other datasets for which structured public repositories exist; more details on our data policy are available in the Guide to Authors. We encourage the provision of other source data in supplementary information or in unstructured repositories such as Figshare and Dryad. We encourage publication of Data Descriptors (see Scientific Data) to maximize data reuse.

| | |
|---|---|
| 18. If computer code was used to generate results that are central to the paper's conclusions, include a statement in the Methods section under "**Code availability"** to indicate whether and how the code can be accessed. Include version information as necessary and any restrictions on availability. | NA |