



The personal utility and uptake of genomic sequencing in pediatric and adult conditions: eliciting societal preferences with three discrete choice experiments

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Purpose: To estimate the personal utility and uptake of genomic sequencing (GS) across pediatric and adult-onset genetic conditions.

Methods: Three discrete choice experiment (DCE) surveys were designed and administered to separate representative samples of the Australian public. Bayesian D-efficient explicit partial profile designs were used. Choice data were analyzed using a panel error component random parameter logit model.

Results: Overall, 1913 participants completed the pediatric ($n = 533$), symptomatic adult ($n = 700$) and at-risk adult ($n = 680$) surveys. The willingness-to-pay for GS information in pediatric conditions was estimated at \$5470–\$15,250 (US\$3830–\$10,675) depending on the benefits of genomic information. Uptake ranged between 60% and 81%. For symptomatic adults, the value of GS was estimated at \$1573–\$8102 (US\$1100–\$5671) and uptake at 34–82%. For at-risk adults, GS was valued at \$2036–\$5004 (US

\$1425–\$3503) and uptake was predicted at 35–61%.

Conclusion: There is substantial personal utility in GS, particularly for pediatric conditions. Personal utility increased as the perceived benefits of genomic information increased. The clinical and regulatory context, and individuals' sociodemographic and attitudinal characteristics influenced the value and uptake of GS. Society values highly the diagnostic, clinical, and nonclinical benefits of GS. The personal utility of GS should be considered in health-care decision-making.

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INTRODUCTION

Genomic sequencing (GS) is a transformative technology with demonstrated potential for the diagnosis, prognostication, and clinical management of genetic conditions. Internationally, governments are increasingly investing in genomics research and translation into clinical practice. It is estimated that over US\$4 billion of government funding has been used to support the development of translational genomics initiatives globally,¹ and the relevance of genomics is expanding across different clinical contexts and throughout the human life cycle.² Yet, implementation into mainstream clinical care has been slow and challenging. While a range of implementation barriers have been identified,^{3,4} there is a significant lack of empirical evidence on the determinants of GS uptake and the value components of GS that should inform reimbursement decisions in health care.

Ultimately, the extent to which individuals are willing to take up GS depends upon the value they place on GS information in a given clinical context. This value reflects the personal utility of GS, which includes diagnostic, clinical, and

nonclinical value components. A key methodological issue when assessing the value of genomics is the lack of evidence for the personal utility that they generate.⁵ As a result, nonhealth and process-related outcomes of genomics are rarely considered in health-care decision-making,⁶ which is likely to bias resource allocation decisions.⁷ There is real need to better understand individual preferences for GS to (1) value the personal utility benefits generated, (2) predict uptake, and (3) inform health-care priorities based on a composite evaluation of costs and benefits.

A method that enables an estimation of personal utility and uptake of GS is the discrete choice experiment (DCE). DCE is an established method to elicit preferences and values in health economics,^{8–10} and is increasingly applied in the context of rare disease and cancer.⁷ This study reports the findings from three DCEs conducted to elicit societal preferences for GS and to estimate its personal utility and uptake across pediatric and adult-onset genetic conditions. Our study provides empirical evidence on the value that society places on GS information in clinical situations

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involving different risk–benefit tradeoffs and evaluates how these tradeoffs and individual sociodemographic and attitudinal characteristics influence uptake.

MATERIALS AND METHODS

Study design and participants

Surveys were developed for pediatric (survey 1), symptomatic adult (survey 2), and at-risk adult (survey 3) conditions, following good research practice recommendations.^{11,12} As recommended,^{13,14} attribute development was undertaken using focus groups involving community representatives with lived experience of genetic condition, and clinical genomic and operational genomic staff. Detailed information about the process and outcomes of the focus groups is provided elsewhere.¹⁵

The final set of attributes were (1) chance of having a genetic condition, (2) severity of the condition, (3) availability of preventive or treatment options, (4) improving the process of medical care, (5) cost of testing to you, (6) disclosure of test results to others (i.e., life insurer), and (7) disclosure of secondary findings to you. The attributes and corresponding attribute levels are shown in Table 1. We used an iterative approach with all focus groups members to agree on attribute labeling.¹⁴ Attribute levels were selected in consultation with the genetic experts of our research team to ensure clinical face validity and applicability to a variety of genetic contexts.

Given that life insurers in Australia can request and use GS results in certain circumstances,¹⁶ the attribute “disclosure of test results to others” was used to specifically capture the disutility associated with potential disclosure of results to life insurers and its effect on GS uptake. Based on evidence highlighting the importance of secondary (actionable and nonactionable) findings on individual preferences for GS,^{17,18} the attribute “disclosure of secondary findings to you” was used to account for the utility or disutility of disclosing information unrelated to the primary condition being suspected, and which may indicate a risk of developing a condition later in life.

Conventionally, a cost attribute is included in DCEs with fixed attribute levels and without interactions to account for income and substitution effects as cost changes (if such effects are present). Fixed cost levels, however, require disproportional income sacrifices from people of lower socioeconomic status. To ensure fairness in terms of the marginal disutility associated with each cost level across participants, choice tasks included individual-specific cost figures (in Australian dollars) relative to participants’ self-reported annual household income. This decision was made in response to equity concerns related to the cost attribute among the focus groups members, and in light of the large costs involved in the context of genomics. This method also reflects the way the Australian health-care system is funded with income proportional tax contributions. Individual-specific cost figures were implemented using fixed percentages of annual household income in the DCE design, and then pivoting these in choice tasks based on self-reported annual household income.

Table 1 Attributes and attribute levels included in the discrete choice experiment (DCE).

Characteristics	Levels
1. Chance of having a genetic condition	5 out of 100 10 out of 100 30 out of 100 50 out of 100 75 out of 100
2. Severity of the condition	Mild Moderate Severe
3. Availability of preventive or treatment options	No options are available Treatments to improve the condition are available Treatments to cure or prevent the condition are available
4. Improving the process of medical care	Not likely Somewhat likely Very likely
5. Cost of testing to you (% of annual household income) ^{a,b}	0.20% 1% 3% 5%
6. Disclosure of test results to others	Not required May be required to a life insurer
7. Disclosure of secondary findings to you	No Yes

^aIn choice tasks, percentages were pivoted based on individual’s reported annual household income. Thus, participants were given an actual cost figure (in Australian dollars) that was relative to their income.

^bMean cost after incorporating income adjustments, across the three surveys, was \$1840 (SD = \$2080). The median cost was \$900 (interquartile range = \$300 to \$2500).

Given that preferences for GS were expected to differ across the three contexts, each survey adopted a separate Bayesian D-efficient and explicit partial profile design developed using Ngene.¹⁹ The surveys shared common core elements, but the background information and choice tasks were tailored to the objectives of each survey. The survey used for the symptomatic adult DCE is provided as an example in the online Supplementary Materials. For each survey, there were 40 choice tasks split into four blocks, meaning that each participant had to complete 10 choice tasks. Blocking was performed to reduce task effort for the respondent and was implemented using the minimum correlation principle. Choice tasks were selected from a candidature set of all relevant attribute combinations using the modified Federov algorithm.¹⁹ Explicit partial profiles with two overlapping attributes were selected to reduce task complexity and avoid dominance issues.^{19,20} Overlapping attributes or attribute levels differed across choice tasks.

Choice tasks asked participants to indicate the situation under which they would choose to have a genomic test. Participants could choose between three options (situation 1, situation 2, or neither). The “neither” (opt-out) option was

labeled as “I would not like my child to have a genomic test” in the pediatric survey and as “I would prefer not to have a genomic test” in the adult surveys. The opt-out option was considered a third choice alternative. An example of a choice task, as shown in the survey, is provided in the Supplementary Materials (Figure S1). The final version of the surveys was approved by all members of the research team, the focus groups members, and a plain language advisor. The surveys were piloted in 196 members of the Australian public, recruited through an Internet-based survey panel (Dynata [formerly Research Now SSI]).

As recommended in the health economics literature,²¹ values of the general public, who are the taxpayers and potential users of health care, were sought. Target sample sizes were determined based on the S-efficiency measure. Age, gender, and income quotas were applied to ensure representativeness of the sample, which was further validated against other national sources.^{22,23} People could participate in the survey if they were over the age of 18 and if they had not participated in any other of the surveys administered as part of this study. Participants were initially randomized to one of the two adult surveys. The pediatric survey was administered sequentially and recruited a separate sample of study participants. Participants were then randomized to one of the four blocks. Within each block, further randomization was applied in the order of choice tasks, in the order of the two GS situations, and to a version with or without pictogram for the attribute “chance of having a genetic condition.” Informed consent was obtained from all respondents prior to entering the survey. Ethics approval was granted from the Medicine and Dentistry Human Ethics Sub-Committee of the University of Melbourne (Ethics ID: 1852388).

Choice analysis

A panel error component random parameters logit model was estimated using NLOGIT 6 (Econometric Software, Inc., Waverton, NSW, Australia). Random parameters accommodate unobserved preference heterogeneity within the sample and the error component allows for a correlation between the two GS situations.¹¹ The primary analysis relied on a main-effects model specification of the DCE attributes. An additional analysis incorporated sociodemographic and attitudinal characteristics via main effects in the utility function of the two GS alternatives. The parameters were normalized to zero for the no-choice alternative. Continuous coding was applied for the attributes “chance of having a genetic condition” and “cost of testing to you.” Dummy coding was used for the remaining attributes. A constrained triangular distribution was used for the cost and the disclosure of test results to life insurer attributes given the known disutility associated with them.¹¹ A normal distribution was used for the other parameters. Random parameters were estimated using 1000 standard Halton sequences. Marginal willingness-to-pay (WTP) values for the DCE attributes were estimated using the unconditional population moments estimates.¹¹ Different clinical contexts, based on relevant permutations of

attribute levels, were constructed based on clinical expertise. For each context, we estimated (1) GS uptake based on the percentage of the population predicted to choose GS,⁹ and (2) WTP for GS based on the compensating variation formula,²⁴ using population simulated data that reflect identified preference heterogeneity.¹¹ Where available, real-world uptake evidence was compared against our study estimates. WTP values are reported in both Australian and US dollars (using 1 July 2019 Reserve Bank of Australia exchange rate of 0.70). The delta method was used to generate 95% confidence intervals (CIs).

RESULTS

Overall, 1913 individuals participated in the study and completed either the pediatric ($n_1 = 533$), symptomatic adult ($n_2 = 700$), or at-risk adult ($n_3 = 680$) surveys (cooperation rate of 73%). The composition of the three samples was not significantly different across all sociodemographic and attitudinal characteristics. As shown in Table S1, participants had a mean age of 46 years (SD = 16) and were mostly married or in a de facto relationship (59%; $n = 1120$) and female (52%; $n = 983$). About 41% ($n = 779$) of the sample had acquired higher-level education and 57% ($n = 1091$) were parents. Most participants had complementary private health insurance (58%; $n = 1102$) and 28% ($n = 531$) had life insurance. The majority of study participants (70%; $n = 1339$) had an annual household income below AU\$100,000. Compared with the national census summary and Household, Income and Labour Dynamics in Australia (HILDA) survey data,^{22,23} study participants appeared to be relatively more educated but on average similar in terms of age, gender, marital status, and household income. The distribution of participant responses in terms of familiarity with the effect of genetic conditions on patients and families, knowledge about genetics, attitudes toward GS, and health is shown in Figures S2–S4.

The regression results from the pediatric survey are shown in Table 2. The results from the adult surveys are available in the Supplementary Material (Tables S2 and S3). Across surveys, participants demonstrated a negative preference for GS in the presence of higher costs and the disclosure of GS results to life insurers. Participants showed a positive preference for GS when the chance of having the genetic condition increased, when the severity of the condition increased, when there were options available to prevent or cure the condition or to improve the symptoms of the condition, when the information from GS could improve the process of medical care, and when they could receive secondary findings. Consistently across surveys, the standard deviation estimates of the attributes “chance of having a genetic condition,” “cost of testing to you,” “disclosure of test results to others (i.e., life insurer),” and the top levels of the “severity of the condition” and “availability of preventive or treatment options” attributes were statistically significant, which indicates preference heterogeneity among participants, and supports our modeling approach. The distribution of the

Table 2 Model estimation results (pediatric discrete choice experiment).

Attributes and personal characteristics	Main effects model		Model including characteristics	
	Mean	SD	Mean	SD
Chance of having a genetic condition (%)	0.01599 ^a	0.02508 ^a	0.01570 ^a	0.02549 ^a
Severity of the condition (moderate)	0.37130 ^a	0.04901	0.35943 ^a	0.03815
Severity of the condition (severe)	0.80142 ^a	0.59507 ^a	0.80357 ^a	0.65083 ^a
Availability of preventive or treatment options (improve condition)	1.00341 ^a	0.10757	1.00345 ^a	0.25353
Availability of preventive or treatment options (cure/prevent condition)	1.34510 ^a	0.99157 ^a	1.33651 ^a	0.98354 ^a
Improving the process of medical care (somewhat likely)	0.50200 ^a	0.02369	0.48779 ^a	0.07495
Improving the process of medical care (very likely)	0.65578 ^a	0.63296 ^a	0.66276 ^a	0.57324 ^a
Disclosure of test results to others	-0.14570 ^b	0.05948 ^b	-0.13879 ^b	0.05667 ^b
Disclosure of secondary findings to you	0.29280 ^a	0.77554 ^a	0.26783 ^a	0.73807 ^a
Cost of testing to you	-0.00028 ^a	0.00011 ^a	-0.00028 ^a	0.00011 ^a
Genomic sequencing constant	-0.97032 ^a	3.39515 ^a	-11.1476 ^a	0.18166
Age			-0.02792 ^c	
Higher education			0.79242 ^c	
Attitudes toward genomics			0.29037 ^a	
Log likelihood function	-3832.70		-3817.53	
McFadden pseudo R-squared	0.35		0.35	
Akaike information criterion	7707.00		7699.10	

^aStatistical significance at 1%.

^bStatistical significance at 5%.

^cStatistical significance at 10%.

Regression coefficients indicate the marginal effect of each attribute (or attribute level) on the utility for genomic sequencing. Positive (or negative) mean estimates indicate, on average, a positive (or negative) effect on utility. Standard deviation estimates describe the heterogeneity of preferences among study participants.

attributes “improving the process of medical care” and “disclosure of secondary findings to you” showed significant preference variability from the reported mean only in the pediatric and symptomatic adult surveys.

The second model specification in Tables 2, S2, and S3 additionally controlled for participants’ sociodemographic and attitudinal characteristics. The results across surveys suggested that older participants had on average less utility for GS compared with the younger ones, all else being equal, and that participants with higher-level education had more utility for GS relative to those with lower-level education, all else being equal. As expected, attitudes toward genomics, knowledge about genetics, and risk attitudes toward health influenced the utility for GS.

The marginal willingness-to-pay (WTP) for each attribute across the three DCEs is shown in Table 3. For every percentage point increase in the chance of having the

condition, the value of GS in pediatric conditions increases on average by \$57 (US\$40). For conditions of moderate severity and for severe conditions, participants in the pediatric survey were willing to pay on average \$1325 (US\$928) and \$2860 (US\$2002) more for GS compared with less severe conditions. If there were options available to prevent or cure the condition, a mean WTP of \$4800 (US\$3360) was estimated for pediatric conditions. If there were treatment options available to improve the symptoms of the condition, the estimated mean WTP was \$3580 (US\$2506). Participants were willing to pay on average an additional \$1790 (US\$1253) if it was “somewhat likely” to have an improvement in the process of medical care following GS and an additional \$2340 (US\$1638) if it was “very likely.” The mean WTP for not disclosing the test results to life insurers was \$520 (US\$364). Participants in the pediatric survey were also willing to pay an additional \$1045 (US\$732) on average to receive secondary findings.

For adult-onset conditions, the marginal WTP across attributes was, on average, 40% less compared with pediatric conditions. The relative importance of the different attributes differed between symptomatic and at-risk adult conditions but WTP estimates were generally larger in the symptomatic survey apart from the value of secondary findings. To avoid disclosure of test results to life insurers, participants in the symptomatic and at-risk surveys were willing to pay on average \$690 (US\$483) and \$378 (US\$265) respectively (Table 3).

Tables 4 and 5 present the uptake and WTP for GS across different scenarios selected to reflect groups of pediatric and adult-onset genetic conditions that differ in the chance of having the condition or the potential benefit derived from GS information. The scenarios estimate the value and uptake of GS as part of a publicly funded health-care system, where there are no out-of-pocket costs for accessing the test, compared with current standard of care, where GS is not publicly reimbursed. The results suggest that for pediatric conditions, such as complex neurological conditions, where the major benefit of GS is shortening the diagnostic odyssey (scenario 1), the WTP for GS was estimated at \$5470 (US \$3830) and the predicted uptake at 60%. For conditions such as mitochondrial conditions, where GS is more likely to benefit the process of medical care (scenario 2), WTP was estimated at \$6915 (US\$4840) and uptake at 65%. For conditions where treatments to improve symptoms exist (scenario 3), for example severe epilepsy, or where there is also an opportunity to prevent or cure the condition (scenario 4), for example retinoblastoma, the value of GS increased to \$10,090 (US\$7063) and \$15,250 (US\$10,675) respectively, while the corresponding predicted uptake rate increased to 73% and 81%.

For symptomatic adult conditions that involve similar risk-benefit tradeoffs to the four pediatric conditions (scenarios 5–8 in Table 5), the WTP for GS was estimated at \$1573–\$8102 (US\$1100–\$5671) and uptake at 34–82%. For at-risk adult conditions, scenario 9 represents predictive GS

Table 3 Marginal willingness-to-pay (WTP) estimates across surveys (in Australian \$).

	Pediatric Mean (95% CIs)	Symptomatic adult Mean (95% CIs)	At-risk adult Mean (95% CIs)
Chance of having a genetic condition (%) ^a	57 (42 to 72)	29 (23 to 35)	32 (24 to 40)
Severity of the condition (moderate) ^b	1325 (806 to 1843)	692 (368 to 1015)	490 (218 to 762)
Severity of the condition (severe) ^b	2860 (2230 to 3490)	1670 (1230 to 2042)	882 (562 to 1203)
Availability of preventive or treatment options (improve condition) ^c	3580 (2915 to 4245)	2422 (2049 to 2794)	2209 (1846 to 2573)
Availability of preventive or treatment options (cure/prevent condition) ^c	4800 (4014 to 5583)	3043 (2634 to 3452)	2972 (2592 to 3352)
Improving the process of medical care (somewhat likely) ^d	1790 (1231 to 2350)	1152 (824 to 1480)	1011 (730 to 1292)
Improving the process of medical care (very likely) ^d	2340 (1675 to 3005)	1625 (1262 to 1986)	1177 (869 to 1485)
Disclosure of test results to others ^e	−520 (−965 to −75)	−690 (−948 to −428)	−378 (−571 to −184)
Disclosure of secondary findings to you ^f	1045 (503 to 1586)	302 (38 to 566)	567 (310 to 826)

CI confidence interval.

^aThe additional value that participants would be willing to pay on average for genomic sequencing (GS) for every percentage point increase in the chance of having a genetic condition.

^bThe additional value that participants would be willing to pay on average for GS if the condition was moderate or severe relative to mild.

^cThe additional value that participants would be willing to pay on average for GS if there were available preventive or treatment options.

^dThe additional value that participants would be willing to pay on average for GS if it was somewhat likely or very likely to improve the process of care instead of unlikely.

^eThe value that participants would be willing to pay on average to avoid a potential disclosure of their test results to a life insurer.

^fThe value that participants would be willing to pay on average to find out about secondary findings from GS.

for conditions, such as Huntington disease, where diagnostic information cannot currently change the course of disease. For this group, the WTP for GS was estimated at \$2036 (US \$1425) and predicted uptake at 35%. For conditions such as familial cardiomyopathy, where surveillance can be initiated to prevent the condition (scenario 10), the value of GS was \$3584 (US\$2509). For conditions where GS can lead to cure or prevention (scenario 11), like familial cancers including Lynch syndrome, the value of GS was estimated at \$5004 (US \$3503) and uptake at 61%. The risk of disclosing test results to life insurers across the selected scenarios reduces GS uptake by approximately 5–10%.

DISCUSSION

This study elicited societal preferences and estimated the personal utility and uptake of GS in pediatric and adult-onset genetic conditions. The results indicated that personal utility and uptake increase when the chance of having a genetic condition increases, the condition severity increases, there are treatment or preventive options available, the chance to improve the process of medical care increases, or when secondary findings are disclosed to patients and families. Personal utility and uptake decline as the test becomes more expensive and when test results can be disclosed to life insurers.

For pediatric conditions, the WTP for GS increased from \$5470 to \$15,250 (US\$3830 to \$10,675) as the likely benefit from genomic information increased. Uptake increased from 60% to 81%. The value of GS was on average 56% less in symptomatic adult conditions, ranging between \$1573 and \$8102 (US\$1100–\$5671), and 62% less in at-risk adult conditions, ranging between \$2036 and \$5004 (US\$1425–\$3503). Similarly, uptake was found to be 20% less in symptomatic adult conditions and 30% less in at-risk adult conditions. Personal and attitudinal characteristics appeared to have a statistically significant effect on the value and uptake of

GS. For example, age and higher-level education were important across the three surveys. Similarly, risk attitudes toward health, knowledge about genetics, and attitudes toward genomics consistently had a significant effect on the utility for GS.

The value of GS in pediatric rare genetic conditions was recently explored in a DCE study by Marshall *et al.*²⁵ The study elicited preferences for diagnostic testing from parents of children in Canada with either confirmed or suspected rare genetic condition ($n = 319$). The study estimated that the value of GS was US\$4943 compared with operative procedures that might be experienced in the diagnostic odyssey. This figure is approximately equivalent to the average value of the first three pediatric scenarios in our study, which probably represent the majority of pediatric rare diseases in Australia. The study by Marshall *et al.* also estimated that parents of affected children were willing to pay US\$6038 for obtaining knowledge about cause, progression of the disease and risk to family, and US\$5768 for having improvements in disease management. Although these estimates are higher compared with our results, potentially due to differences between societal and patient preferences, they support our conclusion that the value of GS is not fixed but dependent upon the risk–benefit tradeoffs involved.

Evidence for the value of GS in symptomatic or at-risk adults is limited, and no evidence relevant to rare genetic conditions exists. A DCE study by Regier and colleagues²⁶ explored the demand for precision medicine among symptomatic adults based on preferences of people with recent health-care experience in the United States ($n = 1124$). The authors estimated that for every percentage point increase in the chance of having the genetic marker participants were willing to pay an additional US\$16 for GS, which is very close to the US\$20 estimate that we found for the attribute “chance of having a genetic condition.” In their case study, Regier *et al.* estimated the value of the 21-gene recurrence

Table 4 Uptake and willingness-to-pay estimates for genomic sequencing in selected pediatric conditions.

Examples of genetic conditions	Scenario 1 Complex neurological conditions	Scenario 2 Mitochondrial conditions	Scenario 3 Severe epileptic disorders	Scenario 4 Pediatric-onset cancer (e.g., retinoblastoma)
Chance of having a genetic condition	30%	50%	50%	50%
Severity of the condition (moderate)	X	X	X	X
Severity of the condition (severe)	✓	✓	✓	✓
Availability of preventive or treatment options (improve condition)	X	X	✓	✓
Availability of preventive or treatment options (cure/prevent condition)	X	X	X	✓
Improving the process of medical care (somewhat likely)	✓	X	X	X
Improving the process of medical care (very likely)	X	✓	✓	✓
Disclosure of test results to others	X	X	X	X
Disclosure of secondary findings to you	X	X	X	✓
Cost of testing to you	No cost	No cost	No cost	No cost
Mean uptake (%) (95% confidence intervals)	60 (59 to 61)	65 (64 to 66)	73 (72 to 74)	81 (79 to 82)
Median uptake (%) (95% confidence intervals)	70 (67 to 72)	78 (76 to 80)	91 (90 to 92)	98 (97 to 98)
Real-world uptake (%)	No evidence	No evidence	No evidence	No evidence
Mean willingness-to-pay (AU\$) (95% confidence intervals)	5470 (5272 to 5668)	6915 (6677 to 7152)	10,090 (9788 to 10,390)	15,250 (14,860 to 15,638)
Median willingness-to-pay (AU\$) (95% confidence intervals)	4438 (4052 to 4805)	5726 (5334 to 6107)	8830 (8335 to 9272)	14,388 (13,802 to 14,826)

X non-applicable; ✓: applicable.

score assay for breast cancer at US\$2940 and uptake at 66%. These figures match with scenario 7 in our analysis. Weymann *et al.*²⁷ conducted a DCE to elicit patient preferences for GS in the context of colorectal cancer (*n* = 122). The study estimated the WTP for GS relative to standard genetic testing at US\$400–\$1541 depending on the risk–benefit tradeoffs involved, with the uptake of any genetic or GS ranging between 39% and 82%. Our study estimates appear to also align with the broader literature on genomic (or genetic) testing uptake, particularly for individuals at risk of genetic conditions, where more real-world evidence exists (Table 5). Nevertheless, differences between rare genetic conditions and cancers; differences in socioeconomic and cultural characteristics across countries; as well as differences in study designs, samples, and objectives may well explain variations in preferences and values for GS. For example, in our GS scenarios there were no out-of-pocket costs assumed, which differs from the cited studies that either predicted uptake for an assumed cost level or estimated personal utility without assuming a cost level.

Our study benefited from a generic design that enabled an estimation of personal utility and uptake across a range of genetic pediatric and adult-onset conditions in the rare disease and cancer space. Given the so-far questionable performance of conventional health economics outcome measures for capturing important value components of GS information to patients and families,^{7,28,29} cost–benefit

analyses may become a valuable tool for informing evidence-based policy decision-making in this context. Our results demonstrate that society values highly health, nonhealth, and process utility outcomes, which is a finding that consistently comes across in the context of genomics and personalized medicine.^{25,26,30–32} The design of the study enables the inclusion of personal utility and uptake probabilities in the economic evaluation of GS. Our findings are also timely to the current debate in Australia and beyond around the disclosure of diagnoses or test results to life (and potentially health or travel) insurers. We concluded that the risk of disclosing GS results to life insurers was associated with significant disutility, leading to a 5–10% reduction in the uptake of GS. Thus, this is a risk that some people are unwilling to take, which may have important health and economic implications.

The study, however, has limitations. As recommended for informing health-care priorities,²¹ the study relied on preferences of nationally representative samples of the general public. However, only about 35% of participants had heard about GS prior to completing the surveys. Thus, societal preferences are likely to be less informed and different from the preferences of people who currently experience a diagnostic odyssey or seek clinical GS. Further research directly comparing population and patient preferences in this context would be beneficial. There is also a growing body of evidence identifying notable differences between description-

Table 5 Uptake and willingness-to-pay estimates for genomic sequencing in selected adult conditions.

Examples of genetic conditions	Symptomatic survey			At-risk survey			
	Scenario 5 Complex neurological conditions	Scenario 6 Mitochondrial conditions	Scenario 7 Cardiac arrhythmias	Scenario 8 Lynch syndrome	Scenario 9 Huntington disease	Scenario 10 Familial cardiomyopathy	Scenario 11 Familial cancer (Lynch syndrome)
Chance of having a genetic condition	30%	50%	50%	50%	50%	50%	50%
Severity of the condition (moderate)	X	X	X	X	X	X	X
Severity of the condition (severe)	✓	✓	✓	✓	✓	✓	✓
Availability of preventive or treatment options (improve condition)	X	X	✓	✓	X	X	X
Availability of preventive or treatment options (cure/prevent condition)	X	X	X	✓	X	✓	✓
Improving the process of medical care (somewhat likely)	✓	X	X	X	X	X	X
Improving the process of medical care (very likely)	X	✓	✓	✓	X	X	✓
Disclosure of test results to others	X	X	X	X	X	X	X
Disclosure of secondary findings to you	X	X	X	✓	X	X	X
Cost of testing to you	No cost	No cost	No cost	No cost	No cost	No cost	No cost
Mean uptake (%) (95% confidence intervals)	34 (33 to 35)	44 (43 to 44)	62 (62 to 64)	82 (81 to 83)	35 (34 to 36)	51 (50 to 52)	61 (60 to 62)
Median uptake (%) (95% confidence intervals)	31 (30 to 32)	42 (40 to 43)	67 (66 to 68)	90 (89 to 90)	23 (22 to 25)	53 (51 to 55)	71 (68 to 73)
Real-world uptake (%)	No evidence	No evidence	48 ³⁵	81–85 ³⁶	46 ³⁷	39–51 ^{38,39}	34–52 ³⁶
Mean willingness-to-pay (AU\$)	1573 (1473 to 1673)	2518 (2356 to 2680)	4394 (4127 to 4660)	8102 (7645 to 8560)	2036 (1883 to 2190)	3584 (3272 to 3896)	5004 (4572 to 5435)
95% confidence intervals							
Median willingness-to-pay (AU\$)	915 (886 to 948)	1326 (1278 to 1396)	2683 (2591 to 2781)	5310 (5145 to 5471)	590 (546 to 630)	1615 (1525 to 1716)	2596 (2462 to 2743)
95% confidence intervals							

X: non-applicable; ✓: applicable.

based and experienced-based choices.³³ These differences are driven by the psychological decision processes that individuals adopt when they make choices under conditions that involve risk. More research is needed to explore psychological processes under risk in discrete choice analyses, which could further enhance the external validity of stated preference methods. To ensure the external validity of our findings, we developed our surveys with support from community representatives who had lived experience of genetic conditions, professionals specializing in clinical genomics, and a plain language advisor. DCEs have been shown to have reasonable external validity,³⁴ and similar to the study by Regier *et al.*,²⁶ our study offered reasonably close predictions compared with the very limited available evidence. As the evidence base becomes more established, we will be able to better understand the value of GS, the factors that determine its uptake across clinical contexts, and the transferability of our study findings beyond the Australian context.

Our study provided empirical evidence for the personal utility and uptake of GS in pediatric and adult-onset genetic conditions and the way these are influenced by different risk–benefit tradeoffs and individuals’ socioeconomic and attitudinal characteristics. This evidence provides useful insights for the implementation of genomics into clinical care and enables the inclusion of personal utility in cost–benefit analyses for informing health-care priorities. Our findings demonstrate that societal preferences for GS are not restricted to treatment availability but expand to benefits in the process of medical care and to the intrinsic value of genomic information. It is pertinent that reimbursement decisions in the context of genomics and beyond reflect societal values and the maximization of personal utility.

SUPPLEMENTARY INFORMATION

The online version of this article (<https://doi.org/10.1038/s41436-020-0809-2>) contains supplementary material, which is available to authorized users.

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DISCLOSURE

The authors declare no conflicts of interest.

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