

# Genomic testing for children with interstitial and diffuse lung disease (chILD): parent satisfaction, understanding and health-related quality of life

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**To cite:** Kelada L, Wakefield C, Vidic N, *et al*. Genomic testing for children with interstitial and diffuse lung disease (chILD): parent satisfaction, understanding and health-related quality of life. *BMJ Open Resp Res* 2022;**9**:e001139. doi:10.1136/bmjresp-2021-001139

► Additional supplemental material is published online only. To view, please visit the journal online (<http://dx.doi.org/10.1136/bmjresp-2021-001139>).

Received 9 November 2021  
Accepted 2 February 2022



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## ABSTRACT

**Objective** Research is needed to determine best practice for genomic testing in the context of child interstitial or diffuse lung disease (chILD). We explored parent's and child's health-related quality of life (HRQoL), parents' perceived understanding of a genomic testing study, satisfaction with information and the study and decisional regret to undertake genomic testing.

**Methods** Parents of children with diagnosed or suspected chILD who were enrolled in a genomic sequencing study were invited to complete questionnaires pretesting (T1) and after receiving the result (T2).

**Results** Parents' (T1, n=19; T2, n=17) HRQoL was lower than population norms. Study satisfaction (T1) and perceived understanding (T2) were positively correlated ( $r_s=0.68$ ,  $p=0.014$ ). Satisfaction with information (T1 and T2) and decisional regret (T2) were negatively correlated (T1  $r_s=-0.71$ ,  $p=0.01$ ; T2  $r_s=-0.56$ ,  $p=0.03$ ). Parents reported wanting more frequent communication with staff throughout the genomic sequencing study, and greater information about the confidentiality of test results.

**Conclusions** Understanding of genomic testing, satisfaction with information and participation and decisional regret are inter-related. Pretest consultations are important and can allow researchers to explain confidentiality of data and the variable turnaround times for receiving a test result. Staff can also update parents when there will be delays to receiving a result.

Infant and child interstitial or diffuse lung disease (chILD) comprises a heterogeneous group of approximately 200 rare, chronic respiratory disorders characterised by abnormalities in the respiratory and immune systems.<sup>1</sup> The estimated incidence of chILD is 0.13–16.2 cases per 100 000 children/year, although exact incidence rates are difficult to determine.<sup>2</sup> chILD commonly presents as breathlessness, hypoxaemia and growth

## Key messages

### What is already known on this topic

- Parental regret for undergoing genomic testing for their child's illness is generally low and may be linked to poor understanding of testing.

### What this study adds

- This study shows that parents of children undergoing genomic testing for child interstitial or diffuse lung disease need more information about confidentiality and privacy of data, and updates throughout the process when there will be delays to receiving a result.

### How this study might affect research, practice or policy

- This research provides clinicians and genetic counsellors important information to support parents of children undergoing genomic testing for respiratory conditions.

abnormalities in children.<sup>3</sup> Morbidity can vary depending on the specific diagnosis and the severity of the respiratory compromise, but children with chILD may require care throughout their lifetime.<sup>2,3</sup> The mortality rate in high-income countries has been found to range from 6% to 30% for young people under 18 years.<sup>2</sup>

chILD presents many challenges for patients and their parents. For instance, children with chILD may be regularly hospitalised, frequently absent from school, restricted in their functional or recreational activities and experience disrupted psychosocial development.<sup>4,5</sup> Families may also experience uncertainty regarding treatments and prognosis.<sup>4</sup>

Previous research has shown that children with chILD have lower health-related quality of life (HRQoL) than their peers without chILD.<sup>5</sup> Clinical factors related to poorer HRQoL among children with chILD include a higher Fan severity score, extrapulmonary involvement, need for long-term oxygen therapy, use of enteral nutritional support and higher number of oral therapies.<sup>5</sup>

The burden of disease and treatment may also impact parents' HRQoL, however, research assessing the impact of chILD on families is lacking.<sup>2</sup> Research in other illness groups has shown that parents' poor mental health and well-being is associated with lower satisfaction with their child's care, and lower understanding of the illness and treatments.<sup>6,7</sup> As such, satisfaction with clinical care may therefore help buffer the impact of chILD on parents, although further research is needed to confirm this.

The aetiology of chILD is unknown in approximately 8%–27% of cases.<sup>8–11</sup> Genomic testing may help clinicians and families to better understand the aetiology of chILD and may be used to recommend personalised treatment plans and avoid unnecessary biopsies.<sup>1,12</sup> Nevertheless, managing parents' expectations regarding genomic testing is important<sup>13</sup> given that only 25%–50% of children will receive a diagnosis after testing for any condition.<sup>12,14</sup> While regret for undergoing genomic testing is generally low, regret may be linked to parental confusion regarding the test and test result.<sup>14</sup> This points to the importance of parental understanding of, and satisfaction with, the information provided to the family about genomic testing. Ensuring that parents are fully informed prior to consenting to genomic testing is therefore essential.<sup>15</sup>

Little is known about parents' satisfaction with, and understanding of, genomic testing for children with chILD. By examining parents' experiences with genomic testing for chILD, we can better determine areas for improvement to provision of emotional support and information during genetic consults.<sup>16,17</sup>

We aimed to explore:

1. HRQoL among parents and children enrolled in a genomic testing study for chILD, and whether parent's and child's HRQoL are related.
2. Parents' (i) understanding of information provided to them about the genomic testing study, (ii) satisfaction with information provided to them about the genomic testing study, (iii) satisfaction with their participation in the study and (iv) their regret in deciding to participate in the study.
3. Factors related to parent's and child's HRQoL, and parent understanding, satisfaction and regret over the course of the genomic testing study.

## METHODS

This study was part of a larger evaluation of whole exome sequencing for children with chILD, titled chILDRANZ. The larger study aimed to understand the value of genomic sequencing for children with chILD and the

impact on patient healthcare. The current study focuses on the psychosocial aspects of genomic sequencing from parents' perspectives. Parents/Guardians (parents used hereafter) could opt-in to genomic sequencing for their child without having to complete the psychosocial questionnaires.

## Participants

Children were eligible for the genomic test if they had either diagnosed or suspected interstitial or diffuse lung disease (chILD). Diagnostic labels are provided in online supplemental table 1. Suspected chILD included the following:

- ▶ Respiratory symptoms (eg, cough, tachypnoea or dyspnoea) at rest or with exercise, crackles, retractions, clubbing, failure to thrive, respiratory failure, systemic arterial hypoxaemia.
- ▶ Diffuse infiltrates on CT scanning.
- ▶ Abnormal pulmonary function tests with evidence of restrictive ventilatory defect, and persistence of these findings for >4 weeks or when the condition is clinically suspected in the case of acute neonatal respiratory distress.<sup>18</sup>

Children were not eligible for the genomic test if they had cystic fibrosis, primary ciliary dyskinesia or other 'common causes' of diffuse lung disease. Children were also not eligible if they exhibited 'masqueraders' (eg, congenital heart failure).<sup>19</sup>

In addition to these inclusion and exclusion criteria, parents were eligible for the psychosocial study if they were able to speak and read conversational English.

## Patient and public involvement

Patients were not involved in the development or design of this research.

## Procedure

Potentially eligible children were identified by the child's treating specialist during clinical care, through specialist clinical units or as inpatients at 19 Australian hospitals as part of the chILDRANZ network. The project manager provided the study genetic counsellor with the contact details of parents of eligible children. The study genetic counsellor then contacted the parents to discuss the study and consent procedure and to provide an information booklet and consent form. The information booklet provided to parents was 16 pages (including the consent form), and contained information about the purpose of the research, what would happen to their child's data including DNA samples, what genomic testing is and the risks, benefits and potential outcomes of genomic testing (online supplemental file 2) (The information booklets at each site contained the same content, with site-specific logos and contact details; an example booklet from one site is provided in online supplemental file 2). The study genetic counsellor's contact details were also provided on

the information booklet in the event that a parent was distressed or if they wanted to discuss any of the information in the booklet. The project manager emailed parents a link to a baseline questionnaire within 1 month of consenting to the genomic test (T1) and a follow-up questionnaire 3–6 months after receiving the test result (T2). Parents completed the questionnaires online, which took approximately 20 min.

## Measures

Parents completed a baseline questionnaire (T1) and a follow-up questionnaire (T2), which contained validated scales and purposively designed questions.

## Sociodemographics

Parents recorded their sex, highest level of education, employment status, whether they have private health insurance and the age and sex of their child undergoing genomic testing.

## Parents' HRQoL

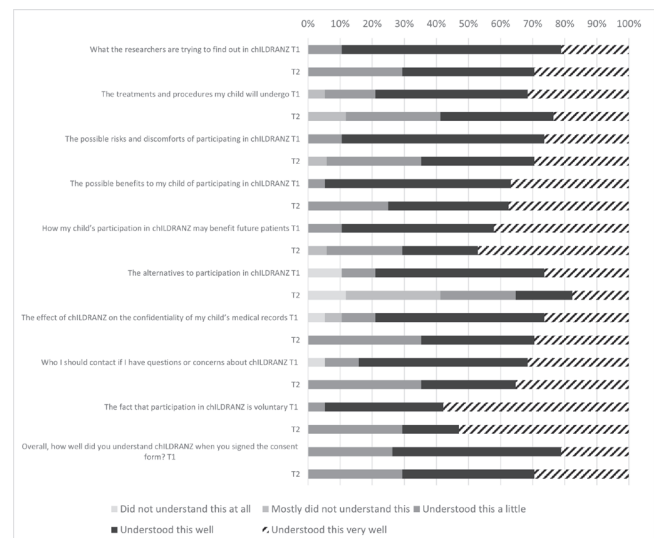
We used the 12-Item Short Form Survey version 2 (SF-12v2) to assess parents' HRQoL.<sup>20</sup> Respondents complete 12 items, with different rating scales. The SF-12v2 contains two subscales: the mental composite score (assessing mental functioning) and the physical composite score (assessing physical functioning). Scores are standardised,<sup>21</sup> so that scores range from 1 to 100, with a mean of 50 and SD of 10. Higher scores indicate better mental and physical functioning. The SF-12v2 displays strong validity and test–retest reliability.<sup>20</sup>

## Parent-reported HRQoL of the affected child

We used a measure of HRQoL designed specifically for children with chILD (chILD-QoL).<sup>4</sup> We used the parent-proxy reports for the current study. The measure has six versions adapted according to the child's age: 0–12 months (5 items), 13–24 months (8 items), 2–4 years (11 items), 5–7 years (11 items), 8–12 years (11 items), 13–18 years (11 items). Parents were asked how often over the previous month their child experienced a range of symptoms or issues (eg, 'getting out of breath'), which parents rated on a scale from 1 ('never') to 5 ('always'). Items were reverse-scored, linearly transformed to a scale of 0–100 and combined to form a total score including all age groups. Higher scores indicate higher HRQoL. The chILD-QoL has demonstrated strong internal reliability and convergent validity.<sup>4</sup> In the current sample, Cronbach's  $\alpha$  ranged from 0.66 to 0.92 for the different versions.

## Perceived understanding

We assessed parents' perceived understanding of the genomic sequencing study using purposively designed questions. Ten items (figure 1) asked parents to rate how well they understood different aspects of the chILDRANZ study on a scale from 1 ("I did not understand this at



**Figure 1** Parents' perceived understanding of key study elements.

all") to 5 ("I understood this very well"). Item responses were added together to create a total score (ranging from 10 to 50), with higher scores indicating higher parent-perceived understanding. The scale demonstrated strong internal reliability in the current study at both timepoints: T1 Cronbach's  $\alpha=0.85$ , T2 Cronbach's  $\alpha=0.94$ .

## Satisfaction with information

We assessed parents' satisfaction with the information provided to them about the study using purposively designed questions. The question stem stated: 'The information sheet and consent form was...'. Parents were then presented with six descriptors (clearly presented, informative, easy to read, useful to make a decision, visually appealing, easy to navigate) and asked to rate their agreement with each on a scale from 1 ('very') to 5 ('not at all'). Responses were then reverse-scored and summed to create a total score. Higher scores indicated greater satisfaction with the information. Internal reliability was adequate-to-strong with the current sample: T1 Cronbach's  $\alpha=0.69$ ; T2 Cronbach's  $\alpha=0.90$ .

Parents also completed open-ended questions and single items about their satisfaction with the information. Single items enquired whether parents were satisfied with the length of the information provided to them (1=too long; 2=just right; 3=too short), whether they needed help reading the information (1=yes, 2=no), if yes, who helped them read the information (open-ended) and how thoroughly they read the information (1=from cover to cover; 2=quite thoroughly; 3=just the parts I thought were relevant; 4=briefly; 5=I did not read the information). For this last question, we recoded the responses as 1=read thoroughly (answers 1–2) and 2=did not read thoroughly (answers 3–4) during analysis. Two scale items asked parents how worried and reassured the information made them feel, respectively, on a scale from 1 ('not at all') to 5 ('very much'). Parents then completed

two open-ended questions about what made them feel worried and/or reassured.

### Satisfaction with participation

Parents also reported their overall satisfaction with their involvement in the study on a scale from 0 (“I had a very poor experience”) to 10 (“I had a very good experience”). One open-ended question enquired about areas for improvement.

### Regret with decision to participate

We measured parents’ regret about participating in the genomic sequencing study with the Decision Regret Scale (DRS).<sup>22</sup> The DRS consists of five statements of distress or remorse after making a healthcare decision (eg, “I would go for the same choice if I had to do it over again”). Parents rated how much they agreed with each statement on a 5-point Likert scale from 1 (‘strongly agree’) to 5 (‘strongly disagree’). Scores were then converted to a scale of 0 (no regret) to 100 (high regret).<sup>23</sup> The DRS is validated, widely used and displays strong internal reliability and convergent validity.<sup>22 24</sup> The DRS had strong internal reliability at both timepoints: T1 Cronbach’s  $\alpha=0.92$ ; T2 Cronbach’s  $\alpha=0.72$ .

### Data analysis

We used SPSS V.24.0 to analyse the data. We used descriptive statistics to assess parent’s sociodemographic status. We used Pearson’s correlation to assess the relationship between parent’s and child’s HRQoL, and Spearman’s Rho correlations to examine the relationships between understanding of the study, satisfaction with information, satisfaction with the study, decisional regret, parent’s HRQoL and child’s HRQoL. Mann-Whitney U tests were used to determine whether these factors differed according to parent level of education and how thoroughly they read the information.

We analysed parents’ responses to the open-ended questions using directed qualitative content analysis, whereby we used the qualitative data to extend and validate the quantitative data.<sup>25</sup> We present illustrative quotes to supplement the quantitative findings.

## RESULTS

We sent the baseline survey (T1) to 34 parents whose children were enrolled in the larger genomic testing study, and 19 parents (58.8%) returned a completed questionnaire. After the genomic testing results were completed, we invited the 34 parents to complete a follow-up questionnaire (T2), and 17 parents (50.0%) returned a completed questionnaire. Fourteen parents completed the questionnaire at both T1 and T2.

At T1, 84% of parents were mothers (n=16). Affected children were mostly male (n=11, 58%) and aged 0–12 months (n=10, 53%). Sociodemographics are reported in table 1.

**Table 1** Sociodemographics of parent and their affected child

|  | Time 1<br>(n=19) | Time 2<br>(n=17) |
|--|------------------|------------------|
| <b>Parent sex</b>  |                  |                  |
| Female   | 16 (84.2%)       | 13 (76.5%)       |
| Male   | 3 (15.8%)        | 3 (17.6%)        |
| Prefer not to say  | –                | 1 (5.9%)         |
| <b>Parent highest level of education</b>   |                  |                  |
| High school  | 5 (26.3%)        | 1 (5.9%)         |
| Beyond high school   | 14 (73.7%)       | 16 (94.1%)       |
| <b>Employment</b>  |                  |                  |
| Employed: full-time/part-time/casual   | 10 (52.6%)       | 10 (58.8%)       |
| Not employed: actively seeking work/not seeking work/retired/student/home duties | 8 (42.1%)        | 7 (41.2%)        |
| <b>Private health insurance</b>  |                  |                  |
| Yes  | 9 (47.4%)        | 9 (52.9%)        |
| No (Medicare only)   | 9 (47.4%)        | 8 (47.1%)        |
| <b>Child age</b>   |                  |                  |
| 0–12 months  | 10 (52.6%)       | 7 (41.2%)        |
| 13–24 months   | 6 (31.6%)        | 5 (29.4%)        |
| 2–4 years  | 2 (10.5%)        | 4 (23.5%)        |
| 5–7 years  | 1 (5.3%)         | 1 (5.9%)         |
| <b>Child sex</b>   |                  |                  |
| Female   | 7 (36.8%)        | 6 (35.3%)        |
| Male   | 11 (57.9%)       | 11 (64.7%)       |

Fourteen parents completed questionnaires at both timepoints.

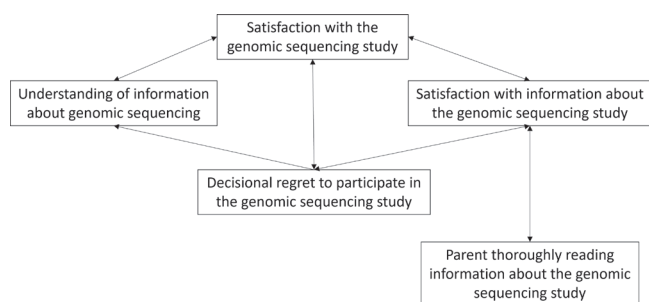
Parents report of satisfaction with the study, understanding of information provided to them, satisfaction with information and decisional regret were all inter-related as depicted in figure 2. Figure 2 outlines the correlations between these variables.

### Parent’s and child’s HRQoL

At T1 (M=36.50, SD=7.30) and T2 (M=37.44, SD=5.91), mean parent mental functioning scores as measured by the SF-12 were >1 SD lower than population norms (M=50 and SD=10; figure 3).

Parent-reported child’s HRQoL was also low, with parents reporting M=38.45, SD=21.82 at T1, and M=44.08, SD=24.86 at T2.

Parent mental functioning at T1 was positively correlated with their report of their child’s HRQoL at T1 (r=0.62, p=0.01) and T2 (r=0.61, p=0.03). Parent’s and child’s HRQoL did not appear to be related to parents’ ratings of their understanding, satisfaction or decisional regret.



**Figure 2** Relationships between parent satisfaction, perceived understanding and decisional regret.

### Understanding of the study

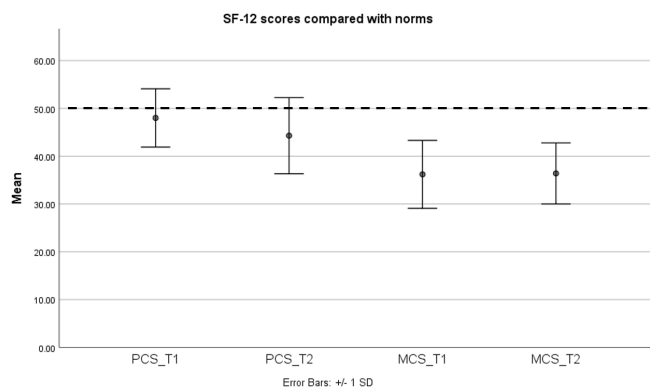
Parents reported overall high understanding of the study, with a median total score of 40/50 (IQR=39, 46) at T1 and 41/50 at T2 (IQR=30.5, 44.75).

Figure 1 shows how well parents reported understanding each aspect of the study. The percentage of parents reporting that they understood each aspect of the study ‘well’ or ‘very well’ appeared to decrease from T1 to T2. Parents particularly reported not understanding the alternatives to chILDRANZ at T2, with 79% at T1 and 41% at T2 reporting understanding this ‘well’/‘very well’.

At T1, parents with a high school level education reported higher perceived understanding of the information about the study than parents who were educated beyond high school: Mann-Whitney U test=11.50, SE=9.94, p=0.035.

### Satisfaction with information

Parents were generally satisfied with the information provided to them about the study, with a median total score of 26/30 for both T1 (IQR=25, 29) and T2 (IQR=23, 29). At T1, most parents felt the length of the information was ‘just right’ (n=12, 63%) while 6 (32%) felt it was too long. Just one parent reported they needed help to read the information from a genetic counsellor. Eleven



**Figure 3** Parents’ physical and mental functioning compared with norms. Dashed line, population mean; MCS\_T1, mental composite score time 1; MCS\_T2, mental composite score time 2; PCS\_T1, physical composite score time 1; PCS\_T2, physical composite score time 2; SF-12, 12-Item Short Form Survey.

parents (58%) reported thoroughly reading the information provided about the study, while eight parents (42%) briefly read the information.

Parents who read the information thoroughly at T1 reported greater satisfaction with the information they received than parents who briefly read the information: Mann-Whitney U test=18.00, SE=11.92, p=0.033.

Most parents reported the information helped them feel at least ‘a little’ reassured (T1=17, 90%; T2=13, 77%). Parent comments showed they felt reassured because they were able to ask professionals questions (“*The fact that we had a genetic counsellor to speak it over with*”), they could receive an explanation for their child’s illness (“*The possibility of finding a diagnosis*”) and could help other families (“*That we were making the right decision for our family and to hopefully help future families*”).

Several parents revealed that the information made them feel at least ‘a little’ worried (T1=8, 42%; T2=7, 41%). Parents’ comments revealed that they were worried about the test result (“*The thought that my child may have a lifelong condition*”). Parents were also worried that the test results may impact their child in the future (“*May affect insurance later in life*”) and about the privacy of their child’s genetic information.

Making sure that information about my son was only used in this research, I would hate to think at some later point having his genetic information on ‘file’ may have a negative impact on some aspect of his life.

### Satisfaction with participation

Parents were generally satisfied with their participation, with parents reporting a median score of 8/10 at both T1 (IQR=7, 10) and T2 (IQR=6, 10). Higher satisfaction was related to lower decisional regret at T1 ( $r_s=-0.48$ , p=0.038).

Eight parents (42%) at T1 and five parents (29%) at T2 reported no regret at all regarding their participation in the genomic sequencing study. Levels of regret in the remaining parents were low with a median score of 12.5/100 at T1 (IQR=0, 25) and 10/100 at T2 (IQR=0, 23.75).

Parents’ higher perceived understanding of the study at T2 was correlated with higher satisfaction with the study at T1 ( $r_s=0.68$ , p=0.014), and lower decisional regret at T1 ( $r_s=-0.60$ , p=0.038). Higher decisional regret at T2 was correlated with lower satisfaction with information at T1 ( $r_s=-0.71$ , p=0.01) and T2 ( $r_s=-0.56$ , p=0.03).

Parents’ comments regarding dissatisfaction with the study revealed that lack of communication was the most frequent complaint. Parents wanted to be kept updated about delays to receiving the test result.

There was a disconnect in communication from when we were discharged [from the hospital] to when we started the trial...The genetics team were extremely hard to get a hold of or communicate with. From all the teams we dealt with they were the most difficult



and stressful in regards to receiving information about the process of this trial...On numerous occasions the genetics team said they would come back to the ward to update us on [my daughter's] next steps, however they never did.

The time it takes to get results or be updated on where the results are at. This took a lot of follow up.

## DISCUSSION AND CONCLUSION

### Discussion

In this study, we aimed to explore (1) the HRQoL of parents and children enrolled in a genomic sequencing study for chILD, (2) parents' understanding, satisfaction and decisional regret regarding their participation in the genomic testing study and (3) factors related to HRQoL, parent understanding, satisfaction and decisional regret.

Parents reported a mean mental functioning score >1 SD below population norms. Research on the mental health of parents of children with chILD is limited,<sup>2</sup> so the current study adds to our understanding of the potential psychosocial toll of chILD on parents. Parent-reported child's HRQoL was also lower than what has been reported in previous literature.<sup>4 26</sup> Parents in the current study may have been more likely to complete the psychosocial questionnaire if their child was particularly unwell. Consistent with previous findings from other illness groups, parent mental functioning was lower when their perception of their child's HRQoL was also low.<sup>27</sup>

In general, parents' perceived understanding of, and satisfaction with, the study was high, and decisional regret was low. Parents' satisfaction with having participated in the genomic testing study was related to having a greater understanding of the study, higher satisfaction with the information provided about the study and lower decisional regret about taking part in the study. A unique finding from this study was how study satisfaction, understanding, satisfaction with information and decisional regret were all inter-related (figure 2). Previous genomic testing studies have found that simple, clear information about testing can facilitate understanding and information retention.<sup>28 29</sup>

Parents reported that the alternatives to participating in the study was the least understood aspect of the information provided to them. Confidentiality of medical records was also quantitatively one of the least understood aspects of the study, according to parents. Qualitatively, parents reported being worried about the privacy of their child's genetic information, and the future insurance implications of their child's test result, which has been found among other clinical populations.<sup>29 30</sup> These findings suggest that parents require further information about what would happen to their child's care if they chose not to have genomic testing, and confidentiality and privacy of test results. This information could be discussed with genetic counsellors, and also provided in writing so that parents can refer back to this information at later points.<sup>29</sup>

We found that, at baseline, parents with a high school level education reported greater perceived understanding of the study than parents who were educated beyond high school. Parents' median self-rated understanding of the study was generally quite high (40/50). As such, lower scores on 'understanding' may not reflect a lack of understanding of the study, but perhaps that they had more unanswered questions. Previous research has shown that patients with higher health literacy ask more questions in medical consultations, and are more likely to seek out further information than patients with low literacy.<sup>31 32</sup> Considering that higher health literacy is related to higher formal education,<sup>33</sup> this could explain our finding.

Parents' open-ended responses revealed that communication between families and clinicians may be an important contributor to parent satisfaction with genomic sequencing. Previous research has also found that parents are less satisfied with clinical services related to their child's genetic testing when the parent-clinician communication is inconsistent and sporadic.<sup>34</sup> Parents in our study especially wanted delays in receiving the result of their child's genomic test to be communicated to them, which has been found previously.<sup>35</sup>

### Practice implications

Our findings have key implications for clinical practice and research regarding communication between clinicians and parents of children with chILD undergoing genomic testing. First, genetic counsellors (or in the case of a research project, the study team) may ensure the parents understand how and where their child's results will be stored, who can access these data and whether the results will affect their child's insurance during the pretest consultation. Genetic counsellors may discuss with parents the variable turnaround times to receiving a result of a genomic test during the pretest consultation.<sup>35</sup> Genetic counsellors or the study team may also encourage parents to fully read the information provided to them prior to making a decision. The use of visual aids in these information booklets may be an important way to make the information more digestible.<sup>28 29</sup> Genetic counsellors or the study team may also briefly assess parents' satisfaction with information after initial genetic consultation. Parents with low satisfaction may require further information and consultation.

Communication between parents and genetic counsellors or the study team while waiting for the test results could also be an important way to help parents feel satisfied with their decision to participate in genomic testing. Genetic counsellors or the study team could consider keeping parents updated about delays to help manage their expectations and associated distress.

## Limitations

The small sample size means further research is needed in order to confirm our findings. Research is particularly needed to assess the generalisability of our findings among families undergoing genetic evaluation in a clinical setting. The small sample precluded us from statistically assessing whether parents' understanding, satisfaction and HRQoL changed over the course of the study, or whether these factors are related to the child's test result.<sup>14</sup> Larger longitudinal research is needed given that a greater percentage of participants appeared to report understanding aspects of the study 'well' or 'very well' at T1 than T2 (figure 1). Nevertheless, chILD are rare conditions, and as such any data on this topic are valuable. Another limitation of the study was that we used a subjective measure of parent understanding. An objective measure would have helped elucidate further how well parents understood important aspects of the study. We also did not assess parent understanding of the test result, which may have shed further light on parent understanding of genomic testing for chILD. Our sample may have been biased, with 59% of parents of children undergoing genomic testing choosing to complete the questionnaire. Similarly, our sample was limited to English-speaking parents and fathers were under-represented. Finally, including a comparison group of caregivers of children with other chronic childhood conditions would have helped to contextualise our findings.

## CONCLUSION

The current study provides novel insights regarding families undergoing genomic testing for diagnosed or suspected chILD. We found that perceived understanding of the genomic testing study, satisfaction with the information they received, satisfaction with participation and decisional regret were inter-related. Clear, concise information about genomic testing—including what happens to genomic data, possible wait times and implications for insurance—may help parents to feel more satisfied with their decision to enrol their child in a genomic testing study. Information about privacy and confidentiality could also be discussed during pretest consultation with genetic counsellors. Genetic counsellors or the study team could also keep parents updated when there will be delays to receiving a result from the genomic test.

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**Acknowledgements** We would like to thank all the physicians, genetic counsellors, laboratory personnel and patients who took part in the children with interstitial lung disease research in Australia and New Zealand (chILD-RANZ). We would like to thank Gadiel Dumlaio for his contribution to the manuscript. We would like to thank chILD-EU for allowing us to use their chILD-QoL measure. We would like to acknowledge Luminesce Alliance—Innovation for Children's Health for its contribution and support. Luminesce Alliance—Innovation for Children's Health, is a not for profit cooperative joint venture between the Sydney Children's Hospitals Network, the Children's Medical Research Institute and the Children's Cancer Institute. It has been established with the support of the NSW Government to coordinate and integrate paediatric research. Luminesce Alliance is also affiliated with the University of Sydney and the University of New South Wales Sydney. The Chair in Genomic Medicine awarded to JC is generously supported by The Royal Children's Hospital Foundation. The research conducted at the Murdoch Children's Research Institute was supported by the Victorian Government's Operational Infrastructure Support Programme.

**Contributors** LK: writing—original draft, formal analysis. CW: writing—review and editing, supervision. NV: project administration, writing—review and editing, investigation. DSA: methodology, investigation, resources. BB: writing—review and editing, investigation, resources. KB: writing—review and editing, investigation, resources. JC: writing—review and editing, investigation, resources. JH: writing—review and editing, investigation, resources. GH: methodology, investigation, resources. NK: writing—review and editing, investigation, resources. SL-T: investigation, resources. TMcD: methodology, investigation, resources. DM: writing—review and editing, methodology, investigation, resources. AS: writing—review and editing, investigation, resources. HS: writing—review and editing, investigation, resources. AT: writing—review and editing, investigation, resources. AJ: guarantor, conceptualisation, methodology, writing—review and editing, supervision, funding acquisition.

**Funding** This study was funded by Australian Genomics HealthCare Alliance. Australian Genomics is funded by the NHMRC (GNT1113531, GNT2000001) and the Australian Government's Medical Research Future Fund. CW is supported by the National Health and Medical Research Council of Australia (APP1143767). LK is supported by the Golda Meir Post-Doctoral Fellowship Fund.

**Competing interests** None declared.

**Patient consent for publication** Consent obtained from parent(s)/guardian(s)

**Ethics approval** This study was approved by Melbourne Health Human Research Ethics Committee (HREC: 36378). Participants gave informed consent to participate in the study before taking part.

**Provenance and peer review** Not commissioned; externally peer reviewed.

**Data availability statement** Data are available on reasonable request. Deidentified participant data are available from the corresponding author (<https://orcid.org/0000-0001-9428-8807>) on reasonable request.

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### Supplementary file 1. Diagnostic labels of chILD

#### Classification of chILD (based on Deutsch et al, 2007)

| <b>DISORDERS MORE PREVALENT IN INFANCY</b>   | <b>DISORDERS LESS PREVALENT IN INFANCY</b>  |
|--|---|
| <b>Diffuse developmental disorders of the lung:</b><br>Acinar dysplasia<br>Congenital alveolar dysplasia<br>Alveolar capillary dysplasia with misalignment of pulmonary veins  | <b>Disorders related to systemic disease processes:</b><br>Immune mediated/collagen-vascular disorders<br>Storage disease<br>Sarcoidosis<br>Langerhans cell histiocytosis<br>Malignant infiltrates  |
| <b>Lung growth abnormalities reflecting deficient alveolarisation:</b><br>Pulmonary hypoplasia<br>Chronic neonatal lung disease<br>Related to chromosomal disorders<br>Related to congenital heart disease   | <b>Disorders of the normal host:</b><br>Related to infections<br>Related to environmental agents<br>- hypersensitivity pneumonitis<br>- toxic inhalation<br>Aspiration syndromes<br>Eosinophilic pneumonia                                  |
| <b>Specific conditions of undefined cause:</b><br>Neuroendocrine cell hyperplasia of infancy<br>Pulmonary interstitial glycogenosis  | <b>Disorders masquerading as ILD:</b><br>Arterial hypertensive vasculopathy<br>Congestive changes related to cardiac dysfunction<br>Venous-occlusive disease<br>Lymphatic disorders   |
| <b>Inherited surfactant disorders:</b><br>Surfactant protein B mutations<br>Surfactant protein C mutations<br>ABCA3 mutations<br>Histology consistent with surfactant dysfunction without a yet recognised genetic aetiology<br>- pulmonary alveolar proteinosis<br>- chronic pneumonitis of infancy<br>- desquamative interstitial pneumonitis<br>- non-specific interstitial pneumonia | <b>Disorders of the immunocompromised host:</b><br>Opportunistic infection<br>Disorders related to therapeutic intervention<br>Disorders related to transplantation and rejection syndromes<br>Diffuse alveolar damage of unknown aetiology |

Deutsch GH, Young LR, Deterding RR, Fan LL, Dell SD, Bean JA, Brody AS, Noguee LM, Trapnell BC, Langson CL. Diffuse lung disease in young children. Application of a novel classification system. *Am J Res Crit Care Med* 2007;176;1120-1128



## Supplementary File 2. Parent/Guardian Information Statement/Consent Form

### chILDRANZ Flagship Sydney Children's Hospital Network

|  |  |
|--|--|
| <b>Title</b>                               | <i>Australian Genomics Health Alliance: Preparing Australia for Genomic Medicine</i> |
| <b>HREC Number</b>                         | 2016.224   |
| <b>Coordinating Principal Investigator</b> | <i>A/Prof Meredith Wilson (CHW), Dr David Mowat (SCH)</i>                            |
| <b>Associate Investigator(s)</b>           | <i>Prof Adam Jaffe</i>   |
| <b>Location</b>                            | <i>SCHN</i>  |
| <b>Version no: 8</b>                       | <b>Version date: 24 April 2018</b>   |

This information statement and consent form is divided into three sections.

1. Information about the research project and genomic testing.
2. Consent to participate in the research.
3. Consent to participate in diagnostic genomic testing.

## **SECTION 1 - INFORMATION ABOUT THE RESEARCH PROJECT**

### **1 Introduction**

Thank you for taking the time to read this **Participant Information Statement and Consent Form**. We would like to invite you and your child to participate in a research project that is explained below.

This form tells you about the research project. It explains all the steps and procedures involved in the project. Knowing what is involved will help you decide if you want you and your child to take part in the research. Please read this Information Statement carefully.

Before you decide if you want you and your child to take part or not, you can ask us any questions you have about the project. You may want to talk about the project with your family, friends or health care worker.

Participation in this research is voluntary. If you don't wish you or your child to take part, you don't have to. Your child will receive the best possible care whether or not you take part.

If you decide you want you and your child to take part in the research project, you will be asked to sign the consent section. By signing it you are telling us that you:

- Understand what you have read.
- Consent for you and your child to take part in the research project.

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- Consent to the use of your and your child's personal and health information as described.
- Have had a chance to ask questions and received satisfactory answers.

You will be given a copy of this Participant Information Statement and Consent Form to keep.

## 2 What is the research project about?

Genes are the instructions inside you that tell your body what to look like and how to work. Genes get passed down in families from parents to children.

Genes are made up of DNA and appear on thread-like structures called chromosomes. Genes are inside almost every cell of your body. There are over 20,000 genes in each of your cells, and together these genes make up your "genome". Each gene has a specific function, however the function of all genes is not yet known. Variations in genetic information in different people can occur, which is why we are all unique. Some variations are harmless, but other variations can make a gene not work, resulting in a health condition. Identifying variations may help to find the cause of your child's genetic condition.

Previously, testing to look for variations in genes involved looking at only one gene at a time. There are now new types of tests that can look at many or all of our genes at once. This testing is known as "genomic" sequencing.

This research is trying to determine the impact of "genomic sequencing" on patient care. The test being provided is a clinical test carried out in a diagnostic laboratory, and the performance of the test itself is not being evaluated.

This type of testing may or may not provide your child with a diagnosis for their condition. Your child's doctor or genetic counsellor will describe the test and research to you.

The aims of this research study are:

- a) to look at how providing this test to certain populations of patients with suspected genetic conditions can impact on their clinical management,
- b) to determine the cost effectiveness of offering this test, and
- c) to evaluate if providing further research as part of this study for undiagnosed patients will provide more diagnoses and further our understanding of your disease.

We will collect a blood and/or saliva sample from your child, which will be used for the clinical test being provided. We will also ask you as a parent for a sample of your blood and/or saliva, as this can assist in determining the cause of your child's condition. If no cause is found in a known gene and you agree, your and your child's samples will be used in research to further understand how the condition occurs by looking at new genes. In some rare cases, we may also collect a skin sample, hair follicles or bone marrow from your child to provide cells that can be used for research as part of this study. We will use the blood and/or saliva samples to extract DNA and look at the genes and how they function. We can use the blood cells, skin cells and hair follicles to provide a constant source of material so recollecting samples should not be necessary. We plan to collect excess tissue if your child is required to have surgery for their condition to look for possible genetic causes.

Advances in technology means we can use new tests to give us more information to better understand the structure of genes and how they work. We may use the skin samples provided to:

- perform functional cellular studies: where we can look at skin fibroblasts (a type of cell that is responsible for making connective tissue) so we can find out more about the structure of the cells and how they work.
- generate an Induced pluripotent stem cell (iPS) line: where we take skin cells and use them to make stem cells which can be re-programmed and turned into another type of cell. This means that we can study the specific type of cell that is not working properly in the affected

individual. For example, if the heart is not working properly we can generate heart cells to try and understand what is wrong. These cells will give us more information about how a genetic change affects the formation of different cell types in the body.

In addition to this, the potential outcomes of genomic testing on families will be assessed. As part of this we would like you to participate in questionnaires on the health, financial, social and emotional impacts of living with a child with a rare genetic disorder, along with questionnaires about the patient/parent/guardian experience of having genomic testing.

We would also like to store any remaining samples and data that we have collected for the purpose of the research outlined in this document. If you consent to this, there is no limit on the length of time that we can store your and your child's sample/s and information.

Together this research will allow us to gather the information needed to determine the most appropriate and cost effective way of providing genomic testing to patients in the future.

### **3 What is the purpose of this research?**

The purpose of this research study is to find out if information obtained from genomic sequencing is useful for the diagnosis and/or management of your child's condition compared to the routine care that is usually offered to people with your child's condition.

The research also seeks to understand your experiences and obtain your views of your child having the test and what you think is important for doctors to consider when offering the genomic sequencing test to people. The cost effectiveness of this type of test for people with your child's condition will also be examined.

This study will also examine if making your and your child's samples and data available for further laboratory research (beyond the first genomic test) within this project, helps us to provide more patients with a diagnosis and understand more about their disease.

Genomic sequencing is not usually funded for your condition and is therefore not widely available. However, the test will be provided to you as part of your participation in this research so the researchers can answer the questions above. It will be provided as part of your care and will be ordered by your doctor and performed in an accredited laboratory.

### **4 Why am I being asked to participate in this research project?**

We are collecting evidence on the usefulness of genomic sequencing for a select group of health conditions. Your child has been asked to take part in the study because they have one of the conditions for which we are trying to determine if genomic sequencing is useful.

### **5 What does participation in this research involve?**

Participation in this study requires your child to provide a blood and/or saliva sample (as advised by the clinician). In some rare cases, we may also collect a skin sample or hair follicles to provide cells that can be used in the study.

We would also like to collect a blood and/or saliva sample from you as a parent, as having your information from your DNA can help to determine the cause of your child's condition and may provide you with information about the possibility of future children having the same condition.

Participation in this study involves having a genomic sequencing test so the impact of this test on your child's healthcare can be investigated. In addition we will collect information about your understanding, views and preferences regarding the test, along with health, social and financial information. Specifically, we would like to:

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- collect and store you and your child's DNA (at a diagnostic laboratory) from you and your child's blood and/or saliva sample and carry out a clinical grade genomic test on your child's sample.
- access the stored DNA and you and your child's identified or re-identifiable data, including clinical photos, for research if a diagnosis is unable to be made by the initial genomic test, or where further understanding of how your child's disorder occurs is required. This research may include more in depth genomic sequencing and/or other laboratory studies on your and your child's samples, either in Australia or overseas, to see if a cause can be found for your child's condition. [This research may also require access to other tissues and samples that may be collected as part of your child's standard clinical investigations as listed below. If these samples are required for this research and they are available and are no longer needed for clinical purposes we will contact the laboratory storing them directly. We will provide the clinical laboratory with your consent for your child to participate to this study to access them and you will not be required to fill out another consent form. These tissues include:  
Lung tissue and lung washings (lavage) for lung diseases]
- collect information about your child's condition, the tests your child has had, treatments your child has received, any other health problems and history of related health problems in your family. We will collect this information from your child's medical records, but the researchers may also ask you for more detail if required. This information will help the study doctors interpret your child's results and understand how genomic sequencing may change how care is provided for your child's condition in the future. We may also continue collecting medical information on your child, for up to ten years, from your child's doctors after genomic sequencing is completed to help us determine the long-term implications of our research.
- ask you about your views on genomic sequencing and experiences related to this testing, to help us decide how this testing should be offered in the future. We will ask you to complete two surveys to gather this information; one around the time the genomic sequencing test is ordered and the other no sooner than one month after genomic sequencing is completed.
- offer you the opportunity to participate in focus groups or workshops so that we can ask you questions about your experience of genomic testing.
- ask you about social and financial factors, that will be used help us understand the costs of living with a child affected by a genetic disorder and to determine if the genomic sequencing test is cost effective for people with your child's condition. We will ask you to complete surveys to gather this information; before you receive your child's genomic testing results and the other no sooner than one month after you have received your child's genomic testing results. Examples of the types questions asked may be your ability to work, quality of life, family planning and impact on relationships. This includes personal questions about your relationships and family planning.
- link your child's identifying information (e.g name, date of birth, address) to gather your child's data from hospital and emergency datasets. Throughout our lives, information is collected about our health and health care. Hospitals, health departments and other groups or organisations that provide health services collect this information. The collection of this information is usually required by law and is securely stored by the service or agency that collects it. Health research is very important as it looks at how health care is managed and how services are delivered and used. This study will collect your child's hospital and emergency records that are related to your child's conditions through data linkage. Data linkage is a technique for creating links between data sources (in this case hospital and emergency datasets) so that information that is related to the same person can be brought together. In brief, we will supply the data linkage agency with key fields for linkage, including but not limited to name, date of birth, address. The data linkage agency will then

create a unique ID for your child and send it to hospital and emergency data custodian. Your child's hospital and emergency records will be merged with the unique ID, and be provided to us. We will access information from 2007 (or the date of your child's birth) through to the end of the study, which is up to 14 years. We will then know about the healthcare resources your child has used. This will help us to study the potential economic impact of genomic sequencing in comparison to current standard care. We will collect information about your child from the following databases through third party data linkage agencies:

- hospital datasets
  - Victorian Admitted Episodes Dataset
  - NSW Admitted Patient Data Collection
  - ACT Admitted Patient Care
  - QLD Hospital Admitted Patient Data Collection
  - WA Hospital Morbidity Data System
  - South Australia Inpatient Hospital Separations
  - Northern Territory Inpatient Activity
  - TAS Public Hospital Admitted Patient Collection
- emergency department datasets
  - Victorian Emergency Minimum Dataset
  - NSW Emergency Department Data Collection
  - ACT Emergency Department Data Collection
  - QLD Emergency Department Information System
  - WA Emergency Department Data Collection
  - SA Emergency Department Data Collection
  - NT Emergency Department Activity Collection
  - Tasmanian Public Hospital Emergency Department Presentations
- collect information about your child's Medicare Benefits Schedule (MBS) and Pharmaceutical Benefits Scheme (PBS) data. You will be asked to fill out a consent form authorising the study access to your complete MBS and PBS data as outlined here. Medicare collects information on your child's medical visits and procedures, and the associated costs, while the PBS collects information on the prescription medications you have filled at pharmacies. The consent form is sent securely to the Department of Human Services who holds this information confidentially.

This information will only be used by the current study and will not be shared.  
\*Please note that if your child is on both parents' Medicare cards, i.e. not family Medicare card, it is important to obtain signed consent from both parents for us to obtain the complete Medicare record of your child.
- share your child's anonymised data with other researchers. To do more powerful research, it is helpful for researchers to share information they get from studying your and your child's samples. They do this by putting it into one or more restricted access databases, where it is stored along with information from other studies. Your and your child's data and sample/s may also be shared in an anonymised way with other laboratories involved in research for your child's condition, under appropriate agreements with the Australian Genomics Health Alliance.
- ask you to use a website to manage your choices about being in the study and to allow you to engage with the study on an ongoing basis. This website, that can also be used like an App on your phone, is called CTRL. The person who you provide consent to for being in the study will tell you how to register. We are introducing this website as a small pilot study which will tell us whether having more consent choices and ongoing contact with the study is better for you.

#### Optional Consent:

- a) You will also be asked if you agree to share your and your child's data (health related, genomic and self-reported information) and sample/s for use in ethically approved research

outside this study. If you do agree to this you will not be contacted for further consent, and your and your child's data and sample/s will be shared in a de-identified way.

- b) We may like to contact you in the future about the possibility of you or your child participating in other ethically approved research projects. This is optional and you can indicate your willingness to be involved in such research on the consent form.

#### Optional Parental Sample Consent:

As mentioned we would like to collect parental (biological) blood and/or saliva samples at the time of collecting your child's samples if possible. Having these samples can allow us to confirm a finding in your child, determine the possibility of having further children that may be affected by the same condition, or even find a new previously unknown cause for your child's condition. This is optional and you can indicate your willingness to provide your samples individually on the consent form.

There are no additional costs associated with participating in this research project, nor will you be paid.

A summary table of your and your child's direct involvement in this study is provided below:

|   |  |
|---|--|
| <b>Visit 1 – Regular appointment</b><br>Consent   | You will have the study purpose and procedures explained to you by your child's treating clinician and will be asked if you are interested in you and your child taking part in the study. You may either sign a consent form on the day of your child's visit or be given the option to provide your consent with a genetic counsellor over the phone or at another appointment. If possible, arrangements can be made for your and your child's samples to be taken at this visit too, or at a later date if it is more convenient.                                    |
| <b>Patient Experience Questionnaire(s)</b><br>(pre-test)                                    | You may be sent a letter or email requesting your participation in a survey to allow the researchers to understand your experience of genomic testing and how it may best be provided to patients with your child's condition in the future, to determine the lifetime cost of your child's condition and if offering genomic testing for patients with your child's condition is going to be cost-effective. The survey may ask questions about the social and financial situation of you and your family. You may complete it online or on a paper copy mailed to you. |
| <b>Visit 2 – Regular appointment</b><br>Return of results                                   | At a regular appointment with your child's treating clinician the results of the genomic testing performed in a diagnostic laboratory will be provided to you. This may or may not result in a diagnosis. If there is no initial diagnosis found your and your child's samples may be accessed for further research related to your condition to try to find a diagnosis. You will not be required to sign another consent form.   |
| <b>Patient Experience Questionnaire(s)</b><br>(post-test > 1 month after return of results) | You will be sent a letter or email requesting your participation in a follow-up survey regarding your experience of genomic testing. It may ask whether genomic testing has resulted in any changes in the social and financial situation of you and your family. Again, you may complete it online or on a paper copy mailed to you.  |

## 6 Who is funding this research project?

This research is being led by the Australian Genomics Health Alliance (AGHA), a collaboration of major research institutions, universities and clinical services across Australia, and is funded by the National Health and Medical Research Council. The study doctors and researchers are employees of the major collaborating institutions, universities and clinical services.

## 7 Do I have to take part in this research project?

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Participation in a research project is voluntary. Please talk to your clinician about alternative testing options available to you and your child if you decide not to participate.

It is your choice to take part in this research. You do not have to agree if you do not want to. If you give your consent and change your mind, you can withdraw from the project. You do not need to tell us the reason why you want to stop being in the project. If you leave the project we will use any information already collected unless you tell us not to. To opt out, please contact the clinical contact person listed in section 14. If however you have consented for your data to be shared, it may not be possible to retrieve and remove all your data should sharing have occurred prior to withdrawal of consent. If you withdraw from the research before the genomic sequencing test is started, the test may not be performed and will not be funded by the research project. You can speak with your doctor about other options for obtaining this test if you decide not to participate in the research.

If you withdraw your child from the research before data linkage to hospital and emergency datasets, the data linkage will not be performed. If you withdraw your child from the research before MBS/PBS information is collected, we will not collect your child's MBS/PBS information. Hospital and emergency datasets, as well as MBS/PBS datasets collected prior to your child's withdrawal will be retained unless you tell us not to.

## **8 What are the possible benefits of taking part?**

The genomic sequencing test is not currently routinely funded for people with your condition. By taking part in this study you will be able to access this new test. The results may confirm or provide a diagnosis and may influence your healthcare. Expert advice and counselling will be available at your hospital to provide you with more information about the possible outcomes of genomic sequencing.

However, there may be no direct benefit to you or your child from taking part in this research, although the outcomes may provide valuable information about whether this test should be part of routine care for patients with your child's condition in the future.

## **9 What are the possible risks and disadvantages of taking part?**

### Blood Test

There are no major risks associated with a blood test. It is possible you or your child may feel some discomfort during the blood test. It is possible there may be some bruising, swelling or bleeding where the needle enters the skin. Some people can feel a little light-headed when blood is taken.

### Skin Biopsy

A skin biopsy is generally a simple and safe procedure but your child may experience bleeding and/or bruising where the skin is taken. The procedure will leave a small scar measuring 3mm. In some cases, infection may occur. If your child is having another procedure under anaesthetic, we may ask if we could collect a skin biopsy at the same time to minimise the discomfort for your child.

### Hair Follicle

A minimum of 20 hair follicles is required for collection. The follicle should be attached to the hair shaft on removal, to enable DNA extraction. Hairs may be taken from your child's head, face or body. Your child may suffer slight discomfort from the collection of these specimens, including a small amount of pain when the hair is removed and some redness in the surrounding skin after removal of the hair.

### Tissue collection

If your child is having tissue removed as part of a planned surgery, we would like to access this tissue for this project. As no extra tissue would be removed for this study, there is no extra risk involved in the collection of tissue.



### Genomic Test

Genomic testing can raise important issues. Although we do not expect many issues to arise, you should be aware of the potential risks and think carefully before agreeing for you and your child to participate in this research project.

We are only searching for genes that are related to your child's condition but it is possible that we may find genes responsible for other genetic conditions that you do not know about. If we find that you or your child have any genetic condition that you do not know about, your child's doctor will contact you to discuss the findings and refer you to a genetic counsellor.

On rare occasions, we may find a genetic change unrelated to the research that could have implications for your health. If changes are found in you or your child's genes, your child's doctor will discuss this with you. If we do find an unusual gene change and tell you about it, you and/or your child's health can be managed in the most appropriate way.

It is possible that we will find a change in your or your child's genes but not know for certain whether it is important or how it relates to your child's condition. If we find a change in you or your child's genes that we are certain about, your child's doctor will contact you to talk about it.

The genetic tests we perform may tell us something about you or your wider family. Learning about the results from genetic research may affect you and your family emotionally and could interfere with family relationships. You may need to decide about making your family aware of the existence of genetic information. Family members may or may not wish to know this information.

Some people in your family might want to know about your child's results and whether the result has implications for them. Your child's results will only be provided with your permission.

You may be required to inform insurance companies or employers in the future of any genetic information that you learn about yourself or your child through this project.

Because this research involves whole families, by chance, we may discover that parents and children or siblings may not be biologically related. Information regarding paternity or maternity will not be made available through this project.

Some people may find it distressing to receive information about their or their child's genetic make-up and future health. There is also the possibility that genetic information may be important in understanding the risks of having another child with your family's condition in the future.

### Health Economic and Patient Experience Surveys

Being asked your experience of genomic testing, or the impact of your child having a genetic disorder on your social and financial situation may be upsetting for some people, but your child's genetic health care provider or specialist is available to discuss any concerns with you.

### Data Sharing into national and international scientific databases

Your and your child's name and other information that could directly identify you (such as address or hospital number) will never be placed into these scientific databases. However, because your genetic information is unique to you, there is a small chance that someone could trace it back to you or your child. The risk of this happening is very small, but may grow in the future. As these databases are all access restricted and have traceable access the risk is minimised, and researchers will always have a duty to protect your and your child's privacy and to keep your and your child's information confidential.

If you require extra support as a result of participating in this study, your child's genetic health care provider can refer you to an independent counsellor if you wish.

## **10 How will the results be provided to me?**

Your child's individual genomic test result will be given to you by your child's treating specialist/genetic healthcare professional.

Research results beyond the diagnostic report may be provided if available. This could include a summary of the impact of the genomic sequencing test for the conditions that are being studied as part of this research.

## 11 What will happen to information about me and my child?

By signing the consent form you consent to the study doctor and relevant research staff collecting and using personal health information about you and your child for the research project. The personal information collected in this study may include, but not be limited to:

- Your child's medical history including information about your child's condition and other medical conditions
- Your child's test results (e.g. blood tests, x-rays, scans or other test reports)
- Your child's information from Medicare and Pharmaceutical Benefits Scheme relating to medical investigations ordered and medications prescribed – a separate consent form will be provided for this data as required by the Department of Human Services.
- Reports about your child's treatment and side effects
- Family history of any related medical conditions
- Genetic and genomic testing results and information

Any information obtained in connection with this research project that can identify you or your child will remain confidential, except as required by law. Details of how you and your child's confidentiality will be protected and who will have access to you and your child's information are provided below.

All information that is collected/recorded about you and your child during the research study ("study data") will not be labelled with any personal details (such as name, date of birth or hospital number) but instead will be identified by a unique study identifier number (UIN) assigned to your child by the central coordination site of the AGHA when they join the study. Only the study doctors and their relevant research staff will be able to re-identify the UIN and study data back to you and your child.

Data will be stored for at least 5 years after the publication of the results to comply with the recommendations of the Australian Code for Responsible Conduct of Research. The laboratory performing the test according to standard clinical laboratory guidelines stores data generated from the genomic sequencing. These data may also be stored in a national data repository, as your child's individual data in combination with others' may assist in further discoveries for the genetic health of others. For this reason your and your child's data may also be shared in an anonymised way with approved genomic databases nationally and internationally. Further information about this is provided below under large-scale data sharing.

All study data will be stored in a secure, password-protected electronic database/registry. Only the study doctors, study researchers and personnel working directly with this study will have access to the database/registry.

Data related to MBS, PBS, and hospital and emergency datasets will be stored on the Murdoch Children's Research Institute's and University of Sydney's secured server and access to the data will be limited to authorised researchers in this study via assigned login password. Hard copy consent forms will be stored in a locked cabinet where it is only accessible by authorised researchers in this study. All data related to MBS, PBS, and hospital and emergency datasets will be destroyed after 7 years from the publication of the final project report. Hard copies will be shredded and destroyed by secured destruction service provider. Non-identifiable data will be

stored indefinitely as the economic model will be critically appraised by the scientific community, and update and running of the model will require access to the non-identifiable data files.

Your child's health information will be used for the purpose of this research project, and subject to your agreement, may also be used in future research projects which are approved by a Human Research Ethics Committee.

Information about your child's participation in this research project may be recorded in your child's health records.

Your child's health records and any information collected and stored by the study doctors during the research project may be reviewed for the purpose of verifying the procedures and the study data. This review may be done by the ethics committee that approved this research project, regulatory authorities, or as required by law. In these circumstances, these parties will review only, not collect or record, your child's personal information. By signing the consent form, you authorise release of, or access to, this confidential information.

In accordance with relevant Australian and/or State privacy and other relevant laws, you have the right to request access to your and your child's information collected and stored by the study team. You also have the right to request that any information with which you disagree be corrected. Please contact the study team member named at the end of this document if you would like to access your information.

It is anticipated that the results of this research project will be published and/or presented in scientific and medical meetings. In any publication and/or presentation, information will be provided in such a way that you or your child cannot be identified.

#### Large-scale data sharing

To do more powerful research, it is helpful for researchers to share information they get from studying human samples. They do this by putting it into one or more scientific databases, where it is stored along with information from other studies. Researchers can then study the combined information to learn even more about health and disease.

If you agree to participate in this study your and your child's de-identified or anonymised genetic and health information may be placed into one or more scientific databases. It may allow study investigators to identify the cause of your child's condition, as features of your child's rare condition can be matched to other individuals with the same genetic variants or similar features. There are many different kinds of scientific databases; medical research institutions maintain some while governments maintain others. For example, the National Institutes of Health (an agency of the US Government) maintains a database called "dbGaP." Other databases in which your or your child's data may be shared in a de-identified way include but are not limited to PhenomeCentral, PhenoTips, MatchMaker Exchange and Genematcher. These secure databases are shared by the international rare diseases community including Canada, the United States, Europe and Australia. They store descriptions of the features of the condition and genetic variation(s) that may identify the cause of that individual's rare condition.

Access to these databases is restricted to approved medical researchers. A researcher who wants to study the information must apply to the database. Different databases may have different ways of reviewing such requests. Researchers with an approved study may be able to see and use your and your child's information, along with that from many other people.

Your and your child's information will be handled so that you will not be readily identifiable. These safeguards to protect your privacy include:

- Personal identifiers are removed (i.e. name/date of birth);
- Personal details are kept separate;
- Data is coded;
- Only information relevant to the question being asked will be shared;
- Stringent security measures prevent unauthorized access or misuse.

This use of your or your child's information has the potential to improve understanding of normal and abnormal variants, as it will allow the variants in the genomes of thousands of people to be compared. Your child may not benefit directly from this work, but your and your child's information may be used for advancement of knowledge generally.

You will only be contacted about this data sharing if researchers from the AGHA find a result that is relevant to your clinical care. Results from research carried out by other approved researchers on information available in these databases will not be returned to you as they will not have access to your child's identifying information.

When your child reaches the age of 18 and if your child is able to provide informed consent, we will attempt to contact your child for their acknowledgement and continued consent to be involved in this research, if it is ongoing at that time.

## **12 What will happen to the samples collected for these studies?**

Samples (blood and/or saliva) will be collected at an appropriately located pathology collection facility and will be sent directly onto an accredited diagnostic laboratory for DNA extraction for both your and your child's samples and testing on your child's sample only. In the diagnostic setting these samples will be identifiable as a requirement of sample tracking.

Other samples (where required) will be collected by your clinical team and passed on to relevant diagnostic or research laboratories as mentioned above.

As part of this study you are also consenting to your and your child's samples being accessed by researchers on this study where further testing may be carried out as described above in sections 2 and 5. These samples will be provided to researchers with your child's study UIN, so any information relevant to your child's condition may be passed back to your child's clinician. These samples will also be stored in a research laboratory in an area with restricted access.

Your and your child's samples will be kept indefinitely unless you request the destruction of these samples. We will track your and your child's samples through our study database and hence will know where your samples are if you request this.

As part of this study for your child's specific condition, your child's samples will be tested at:

Department of Molecular Genetics, The Children's Hospital at Westmead (NSW) or Women's and Children's Hospital (SA)

with both your and your child's samples being sent to, research (as described above) carried out and stored at:

1. Kids Research Institute (NSW) and/or Murdoch Childrens Research Institute (VIC)
2. Murdoch Childrens Research Institute (VIC)
3. Harry Perkins Institute for Medical Research (WA) and/or the Kids Research Institute (NSW) and/or the Broad Institute (USA).
4. NSW Health Pathology Randwick Genetics (NSW)
5. South Australian Health and Medical Research Institute (SA)
6. The Garvan Institute for Medical Research (NSW)
7. The Centre for Personalised Immunology (ACT)

9. The Garvan Institute for Medical Research (NSW) and/or Kinghorn Cancer Centre (NSW) and/or Victor Chang Cardiac Research Institute (VCCRI) (NSW) and/or Royal Prince Alfred Hospital (NSW) and/or Centenary Institute (NSW) and/or PathWest (WA) and/or Victoria Clinical Genetics Services (VCGS) (VIC)

If you consent to your and your child's samples being used in future ethically approved research, your and your child's samples may be provided to other researchers who are not part of this project in an unidentified way.

### 13 Who has reviewed the research project?

All research in Australia involving humans is reviewed by an independent group of people called a Human Research Ethics Committee (HREC). The ethical aspects of this research project have been reviewed by the HREC of Melbourne Health

This project will be carried out according to the *National Statement on Ethical Conduct in Human Research (2007)*. This statement has been developed to protect the interests of people who agree to participate in human research studies.

### 14 Further information and who to contact

If you want any further information concerning this project, you can contact the Prof Adam Jaffe on 02 93825500 or any of the following people:

#### Clinical contact person

|           |  |
|-----------|--|
| Name      | Kirsten Boggs  |
| Position  | Genetic Counsellor   |
| Telephone | 0476 807 324   |
| Email     | <a href="mailto:kirsten.boggs@health.nsw.gov.au">kirsten.boggs@health.nsw.gov.au</a> |

If you have any complaints about any aspect of the project, the way it is being conducted or any questions about being a research participant in general, then you may contact:

#### Reviewing HREC approving this research and HREC Executive Officer details

|                        |                           |
|------------------------|---------------------------|
| Reviewing HREC name    | <i>Melbourne Health</i>   |
| HREC Executive Officer | <i>HREC manager</i>       |
| Telephone              | <i>03 9342 8530</i>       |
| Email                  | <i>research@mh.org.au</i> |

#### Local HREC Office contact (Single Site - Research Governance Officer)

This project has also been authorised to be conducted at The Children's Hospital at Westmead / Sydney Children's Hospital Randwick. If you have any concerns about the conduct of this study, at this site please do not hesitate to contact the Research Governance Officer on (02) 9845 3011.

**SECTION 2 - CONSENT TO PARTICIPATE IN RESEARCH**

**This consent form is divided into 2 parts. The first part is for participation in the research and the second part is the consent for the clinical genomic sequencing test. You must sign both section 2 and 3 to consent to the clinical testing and the research.**

**Consent Form for participation in research**

|  |  |
|--|--|
| <b>Title</b>                               | <i>Australian Genomics Health Alliance: Preparing Australia for Genomic Medicine</i> |
| <b>HREC Number</b>                         | 2016.224   |
| <b>Coordinating Principal Investigator</b> | <i>A/Prof Meredith Wilson (CHW), Dr David Mowat (SCH)</i>                            |
| <b>Associate Investigator(s)</b>           | <i>Prof Adam Jaffe</i>   |
| <b>Location</b>                            | <i>SCHN</i>  |

I have read, or had read to me in my first language, the information statement and I understand its contents.

I believe I understand the purposes, procedures and risks of the research described in the project.

I voluntarily consent for myself and my child to participate in this research project as described and understand that I am free to withdraw my consent for myself and my child any time during the project without affecting my child's future health care.

I have had an opportunity to ask questions and I am satisfied with the answers I have received.

I understand I will receive a copy of this Information Statement and Consent Form to keep.

I give permission for my child's doctors, other health professionals, hospitals, federal and state agencies or laboratories outside this hospital to release my child's re-identifiable information to the Australian Genomics Health Alliance (AGHA) concerning my child's condition and treatment for the purposes of this project. I understand that this information may be collected for up to 10 years following genomic testing. I understand that such information will remain confidential.

I give permission for the diagnostic laboratory undertaking the testing to release my child's identifiable genetic and genomic data associated with this study to the AGHA, and I acknowledge that the responsibility for the appropriate use and storage of the released data lies henceforth with the AGHA.

I understand that this project has been approved by the Melbourne Health Human Research Ethics Committee and will be carried out in line with the National Statement on Ethical Conduct in Human Research (2007).

**Optional consent for future research:**

I do  I do not consent to my and my child's data (health related, genomic and self-reported information) and samples being used for future ethically approved research projects.

I do  I do not consent to being re-contacted by the study team about related future research projects that me or my child may be eligible for.

**Optional consent for parental samples:**

I do  I do not consent for my blood and/or saliva to be collected and used in this research project.

\_\_\_\_\_  
Mother's Name

\_\_\_\_\_  
Mother's Signature

\_\_\_\_\_  
Date

*(a parent providing a sample must sign)*

I do  I do not consent for my blood and/or saliva to be collected and used in this research project.

\_\_\_\_\_  
Father's Name

\_\_\_\_\_  
Father's Signature

\_\_\_\_\_  
Date

*(a parent providing a sample must sign)*

***PARENT/GUARDIAN CONSENT for participation in RESEARCH as part of this study***

\_\_\_\_\_  
Child's Name

\_\_\_\_\_  
Parent/Guardian Name

\_\_\_\_\_  
Parent/Guardian Signature

\_\_\_\_\_  
Date

\_\_\_\_\_  
Name of Witness to  
Parent/Guardian's Signature

\_\_\_\_\_  
Witness Signature

\_\_\_\_\_  
Date

Declaration by researcher: I have explained the project to the participant who has signed above, and believe that they understand the purpose, extent and possible risks of their involvement in this project.

\_\_\_\_\_  
Research Team Member Name

\_\_\_\_\_  
Research Team Member  
Signature

\_\_\_\_\_  
Date

Note: All parties signing the Consent Form must date their own signature.

**SECTION 3 - CONSENT TO PARTICIPATE IN CLINICAL GENOMIC TESTING****Consent Form for Genomic Sequencing**

Genomic sequencing has been explained to me by a health professional and I have been given the information sheet describing the test.

I understand that my child's DNA will be tested for genes associated with

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by genomic sequencing. Only variants in genes known to be associated with the condition above will be analysed and interpreted in the first instance. **This test is NOT a general health test and will not identify all gene changes that could contribute to health problems in the future.**

I understand:

1. the potential outcomes of the test, including the potential risks and benefits, as outlined in Information Sheet 1: Exome sequencing.
2. knowledge about genetic conditions is likely to improve in the future. If new information comes to the attention of the laboratory that alters the meaning of the result for my child's health, the laboratory may inform my healthcare provider of this. Alternatively, I can ask my child's healthcare provider to contact the diagnostic laboratory to check if such information has become available.
3. there is a small chance that mutations may be identified that are associated with an unrelated condition that may develop in the future, or that may reveal carrier status of an unrelated condition. In this circumstance, my child's healthcare provider will arrange appropriate follow up care, as necessary.
4. the result can be used to facilitate the counselling and testing of other family members.
5. my DNA sample and genomic data will be stored by the testing laboratory in accordance with national laboratory guidelines.
6. the genomic data and associated healthcare information can be used and disclosed in accordance with the applicable health privacy laws.
7. the result and associated health information will be stored by my healthcare provider and may be made available for my child's ongoing treatment and healthcare.
8. my child's genomic data and associated health information may be shared, in a way that does not identify my child (anonymised), for the purpose of advancing knowledge generally, including understanding of genetic variation in humans. I understand that my child is unlikely to gain any personal benefit from this and I will not be notified if the information is shared.
9. I may be contacted to obtain my consent for the use and disclosure of my child's DNA, genomic data and associated health information for other purposes not specified above.
10. Genomic testing will not affect the ability to obtain health insurance but may affect applications for some types of life or other insurance.

**Additional use of DNA and genomic data.**

Please specify if you agree or not to the following:

Tick one box:

10.  I agree  I do not agree for my child's DNA, genomic data and associated health information (information) to be shared with third parties other than the AGHA after the initial analysis for activities that may benefit healthcare. Examples of how the information may be shared are listed overleaf. If you agree, the information will be shared in such a way that it may be possible to identify your child so results can be returned (if necessary/applicable). If I do not agree, the information will not be shared for activities that may benefit my child's healthcare.

**Examples of how information that identifies you may be used#**

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Some examples of how your / your child's or relative's information could be used in a way that may identify you are listed below. These uses may reveal information that may be important to your health, or the health of your blood relatives. For all the examples below, your information can be linked to you so any information with important health implications can be returned to you.

**Example of use:**

**Activities to clarify the cause or management of your condition.\***

For example, your doctor may share your information with international groups trying to identify variants common to people who all have the same condition. The greater the number of patients with the same condition and the same variants, the more likely the variants are to contribute to the condition.

**Research to identify new genes associated with your condition.\***

Research opportunities aimed at finding the cause of your condition may be offered. This may involve a re-analysis of your genomic data. With your permission, your doctor and the laboratory could share your information, meaning researchers may not need to re-sequence your genome and you would not need to provide another sample.

**Trying to clarify what a specific variant does in the cells of the body.\***

To help clarify whether the variant affects cell functioning, the laboratory may ask for your information so they can do further work that may provide clues to the role of the variant.

\*You may be asked to sign a separate consent form for this use.

**PARENT/GUARDIAN CONSENT for Clinical Genomic Testing**

\_\_\_\_\_  
Child's Name

\_\_\_\_\_  
Parent/Guardian Name

\_\_\_\_\_  
Parent/Guardian Signature

\_\_\_\_\_  
Date

Parent/Guardian email \_\_\_\_\_

\_\_\_\_\_  
Name of Witness to  
Parent/Guardian's Signature

\_\_\_\_\_  
Witness Signature

\_\_\_\_\_  
Date

**Declaration by researcher:** I have explained the potential clinical utility (including the risks and benefits) of the requested test, as well as the clinical implications of not undergoing the test, and answered questions asked of me by the patient and/or the patient's guardian or authorised representative.

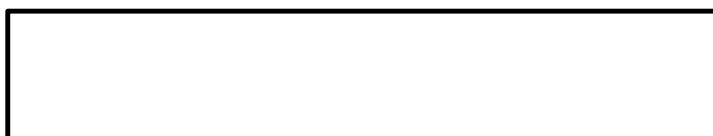
\_\_\_\_\_  
Health Professional Name

\_\_\_\_\_  
Health Professional Signature

\_\_\_\_\_  
Date

Note: All parties signing the Consent Form must date their own signature.

NOTE: Copy of this clinical consent is to be sent to testing laboratory with sample.



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*Affix identifier information here*

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