Accéder au séquençage des gènes: ambivalence et incertitude. Comprendre les préférences et l'expérience de parents d'enfants atteints de retard du développement (Étude Sequapre)

Aline Chassagne, Aurore Pélissier, Françoise Houdayer, Elodie Cretin, Elodie Gautier, Dominique Salvi, Sarah Kidri; Aurélie Godard, Christel Thauvin-Robinet, Alice Masurel, Daphné Lehalle, Nolwenn Jean, Julien Thevenon, Gaetan Lesca, Audrey Putoux, Marie-Pierre Cordier, Sophie Dupuis-Girod, Marianne Till, Yannis Duffourd, Jean-Baptiste Riviere, Lorraine Joly, Christine Juif, Pierre Ancet, Anne-Sophie Lapointe, Paulette Morin, Patrick Edery, Massimiliano Rossi, Damien Sanlaville, Sophie Béjean, Christine Peyron, Laurence Faivre
Challenges and role of research

New ethical issues:
- Anticipation: preference, benefit/risk?
- Choice: access to what results? (VUS and SF)
- Return the result: What and how to say it?
Describe and understand the experience of families concerned by access to the TEST in terms of preferences and representations

**Pre-TEST Quantitative Study**
- Analysis of individual preferences
  - Questionnaires
- Parents of patients candidates for diagnostic WES

**Post-TEST Qualitative Study**
- Analysis of representations (expectations and reactions)
  - Interviews
- Parents of patients following WES results
  - 10 positive diagnosis
    - 19 interviews
  - 6 uncertain result
    - 11 interviews
  - 14 negative result
    - 27 interviews

528 questionnaires
- 65% mothers
- Mean age of children = 7 years

57 interviews (29 mothers, 28 fathers)
- Mean age of children = 8
Methodology of quantitative study
C. Peyron, A. Pélissier, S. Béjean (Health Economics team, University of Burgundy)

- **Discrete choice methods:** Choose among hypothetical configurations of alternatives (scenarios), which are distinguishable by the modalities (levels) of predefined dimensions (attributes)
- 36 scenarios, in 6 blocks of 6 per respondents

<table>
<thead>
<tr>
<th>Attributes</th>
<th>Levels</th>
</tr>
</thead>
<tbody>
<tr>
<td>VUS</td>
<td>None</td>
</tr>
<tr>
<td></td>
<td>Most likely</td>
</tr>
<tr>
<td></td>
<td>All</td>
</tr>
<tr>
<td>Secondary findings</td>
<td>None</td>
</tr>
<tr>
<td></td>
<td>Actionnable</td>
</tr>
<tr>
<td></td>
<td>All</td>
</tr>
<tr>
<td>Reanalysis</td>
<td>Never</td>
</tr>
<tr>
<td></td>
<td>Yearly and automatic</td>
</tr>
<tr>
<td></td>
<td>At my request</td>
</tr>
<tr>
<td>Who decide?</td>
<td>Myself</td>
</tr>
<tr>
<td></td>
<td>My geneticist</td>
</tr>
<tr>
<td></td>
<td>An ethical committee</td>
</tr>
<tr>
<td>Accompaniment</td>
<td>The geneticist</td>
</tr>
<tr>
<td></td>
<td>A psychologist</td>
</tr>
<tr>
<td></td>
<td>A nurse</td>
</tr>
<tr>
<td></td>
<td>With other families</td>
</tr>
<tr>
<td>Cost</td>
<td>1€, 300€, 600€, 900€</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>CHOICE N°2</th>
<th>TEST A</th>
<th>TEST B</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Variants of unknown significance</td>
<td>None</td>
</tr>
<tr>
<td></td>
<td>Secondary findings</td>
<td>Possible action</td>
</tr>
<tr>
<td></td>
<td>Reanalysis in the future</td>
<td>Automatically</td>
</tr>
<tr>
<td></td>
<td>Persons choosing the type of results that should be given back</td>
<td>My geneticist</td>
</tr>
<tr>
<td></td>
<td>Type of accompaniment while waiting for the results</td>
<td>Meetings with other families</td>
</tr>
<tr>
<td></td>
<td>Willingness to pay</td>
<td>1 euro</td>
</tr>
<tr>
<td></td>
<td>I choose test (tick)</td>
<td>X</td>
</tr>
</tbody>
</table>

Variants of unknown significance
Secondary findings
Reanalysis in the future
Persons choosing the type of results that should be given back
Type of accompaniment while waiting for the results
Willingness to pay
I choose test (tick)
528 respondents in Dijon and Lyon University Hospitals between February and December 2015 – 65% of the respondents were mothers

Results of quantitative study

-0.4  -0.2  0   0.2  0.4  0.6  0.8  1

Only the most probable VUS  0.859
All VUS  0.776
Only actionable secondary findings  0.665
All secondary findings  0.69
Automatic yearly reanalysis  0.72
Reanalysis at my request  0.647

-0.276
-0.281
-0.224
-0.272
0.00514
-0.0000621

I decide the information I want back
An ethical committee decide which results should...
Accompaniment with a nurse waiting for results
Accompaniment with other families waiting for results
Cost 1
Cost 2
Post NGS - Design of the qualitative study
(A. Chassagne, E. Cretin, A. Godard and F. Houdayer)

30 situations
14 boys, 16 girls
57 interviews (29 mothers, 28 fathers)
Mean age of children = 8

- What were your expectations before the test was done?
- How did you react?
- At what moment was WES proposed to you during care trajectory? By whom?
- Will this result lead to modifications in your child’s care?
- And in the daily life?

- Understanding the procedure
- Experience
- Impact

- Expectations

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Interviews</th>
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<tbody>
<tr>
<td>Positive</td>
<td>10</td>
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<tr>
<td>Uncertain</td>
<td>6</td>
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<tr>
<td>Negative</td>
<td>14</td>
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<table>
<thead>
<tr>
<th>Interviews</th>
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<tbody>
<tr>
<td>19</td>
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<tr>
<td>11</td>
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<tr>
<td>27</td>
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<td>19</td>
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<td>11</td>
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<td>27</td>
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</table>
Results (1) Expectations from WES

- “We were really expecting a name for what she has, that's it. That is what motivated the research, to push a little further the research, to be able to have an answer” (mother, n°1-04).

- “So the goal is to know... finally to know... the name for it, to project ourselves in the future more easily” (father, n°1-06).

- High expectations towards the test
Results (2) experience of return of the result

- Difficulty in understanding genetic language
- The diagnosis served a purpose of identification, of repair, of relief
- Mixed feelings of both relief and worry
- Parents who received diagnosis differed in their reactions in terms of result and also according to their gender
Results (3) the expected repercussions of the result and the anticipation of the future follow-up

• An important step

• Two thirds of parents in group 1 (positive result) said that the result would not modify the care

• For half of the group 1 (positive result), even when a diagnosis was made, a feeling of helplessness and of uncertainty could persist.

• In uncertain and no result cases, the parents wished to continue the diagnostic investigations.

Social expectation, to give a label, to provide explanations and to have easier access to social rights New odyssey/uncertainty
Production de données quantitatives et qualitatives
Démarche comparative

528 Parents

Résultats Pré-ES (E)

<table>
<thead>
<tr>
<th>Attente ciblée (25%)</th>
<th>Attente prospective (75%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>+ Résultats incertains probables</td>
<td></td>
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<tr>
<td>• DS</td>
<td></td>
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<tr>
<td>• Résultats incertains probables</td>
<td></td>
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<tr>
<td>• Réanalyse</td>
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<tr>
<td>-</td>
<td></td>
</tr>
<tr>
<td>• DS</td>
<td></td>
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<tr>
<td>• Coût inversé (U-inversé)</td>
<td></td>
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<tr>
<td>• Décision (Moi ou comité)</td>
<td></td>
</tr>
</tbody>
</table>

57 Parents

Résultats post-ES (Entretiens)

- Avoir un nom
- Trouver l’origine
- Gérer l’avenir

Synthèse croisée

Vivre l’incertitude
Poursuivre l’investigation
Sentiments ambivalents

57 Parents
Discussion

- **Interdisciplinary team** to study the complexity of the phenomenon with **mixed methods**
- Investigate patient experiences throughout **all the process of WES**
- Parents favored the **central role of the geneticist** in the WES prescription and return of results
- Parents, in general, wish to have **full information**, including VUS and secondary results
- **Contradictions** between expectations and tangible impacts of the result
- **Modalities of information disclosure** before and after the WES are particularly important
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Publications
- Chassagne et al. (2018), Eur J of Hum Genet (IF-4.580)
- Peyron et al. (2018), Social Science and Med (CNRS-1, HCERES-A)
- Pélissier et al. (2016), Public Health (CNRS-3, HCERES-B)