# NGS expanded carrier screening in the Netherlands: initial implementation results

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## Introduction:

Expanded carrier screening (ECS) has broadened in recent years from high risk population-targeted testing to general public screening, and the main challenge now is choosing the most applicable test design for the intended population. Here we describe the ECS test developed at our department of Genetics and our initial results.

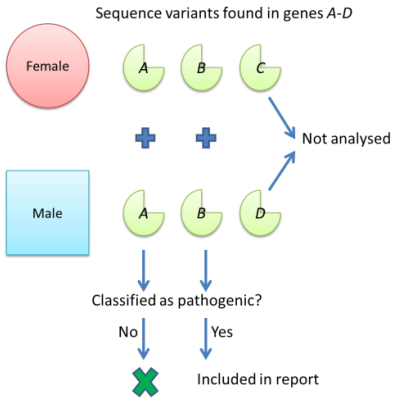
Note: Juliette Schuurmans will present results on the psychological impact of this test in Session: EPL6.5 - Perinatal decision-making | Date: Tuesday, June 19, 2018 | Time: 11:00 - 12:30 hrs

## Materials & Methods

Based on an international multidisciplinary expert meeting, we designed and implemented a couple-based ECS multi-gene test for 70 rare, early onset and serious recessive Mendelian conditions using NGS technologies. Concentrating on **couple-based screening**, emphasis was on the **combined risk** for having affected children.
The *a priori* risk of being a carrier couple is approximately 1 in 150 and increases for those referred for medical reasons (e.g. ethnicity or consanguinity). Only results with high predictive value regarding severely affected offspring were reported in the combined result.

## Results & Discussion

A total of 169 couples were tested, 52 potential high-risk couples and 117 general public couples as part of an population-based implementation study. 5 couples, referred for medical reasons, shared carriership of one of the diseases tested. All remaining couples tested normal. Reporting times averaged at 38 days, and in some cases results were available in 2 weeks.




| High-risk couple | Consanguinous | Previous children with severe AR condition |
|---|---|---|
| 1 | - | X |
| 2 | X | X* |
| 3 | - | X |
| 4 | - | X |
| 5 | X | X |

*Severe AR condition or mutations were not known prior to testing

| High-risk couples: increased risk of following conditions |
|---|
| Cystic Fibrosis (*CFTR*) |
| Mitochondrial DNA depletion syndrome (*POLG*) |
| Mucopolysaccharidose I (Hurler) (*IDUA*) |
| Osteogenesis imperfecta, type VII (*CRTAP*) |
| Propionicacidemia (*PCCA*) |
| Spinal muscular atrophy (*SMN1*) |

## Conclusions

Our combined approach to ECS testing allows for a fast, simplified procedure to report combined risk to couples, forestalling the burden of individual findings. Broader implementation (e.g. general public via their GP) seems warranted, and is supported by these first results. Future international discussions will guide further development and implementation of such important screening tests, taking into account the internationally different health-care systems.