

Genetics in Belgium : Today and Tomorrow

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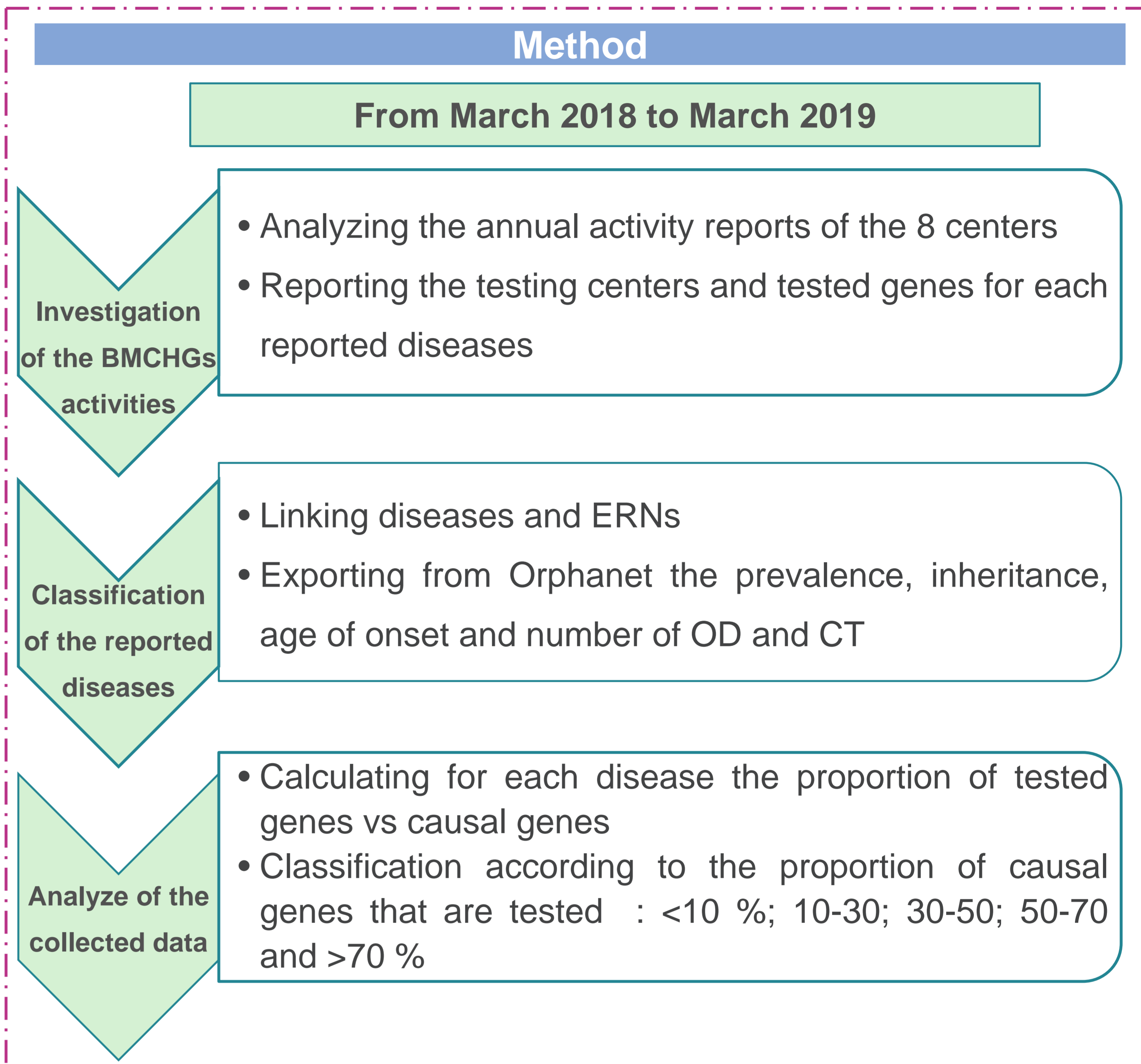
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Aims: Despite the annual discovery of more than 200 new implicated genes, rare diseases' complexity and low prevalence make them difficult to diagnose and treat. In this context, our goals were to (a) provide an overview of the RDs currently investigated by the eight Belgian Medical Centers of Human Genetics (BMCHGs), (b) put them into perspective with the scopes of the European Reference Networks (ERNs; [V. Héon-Klin, *Orphanet J Rare Dis*, 2017]) and (c) identify groups of RDs for which several diagnostic tests are accessible in at least one BMCHG and others for which a limited number of causal genes is tested.

Methods: Between March 2018 and March 2019, the BMCHG's activity scopes have been investigated by Sciensano (Belgian Institute for Health) based on an inventory of their annual reported tested genes for RDs. Secondly, these tests were classified according to (i) the scopes of diseases tackled by the 24 ERNs, and (ii) their prevalence, inheritance, age of onset, number of related orphan drugs (OD) and clinical trials (CT), and causal genes reported on Orphanet website.

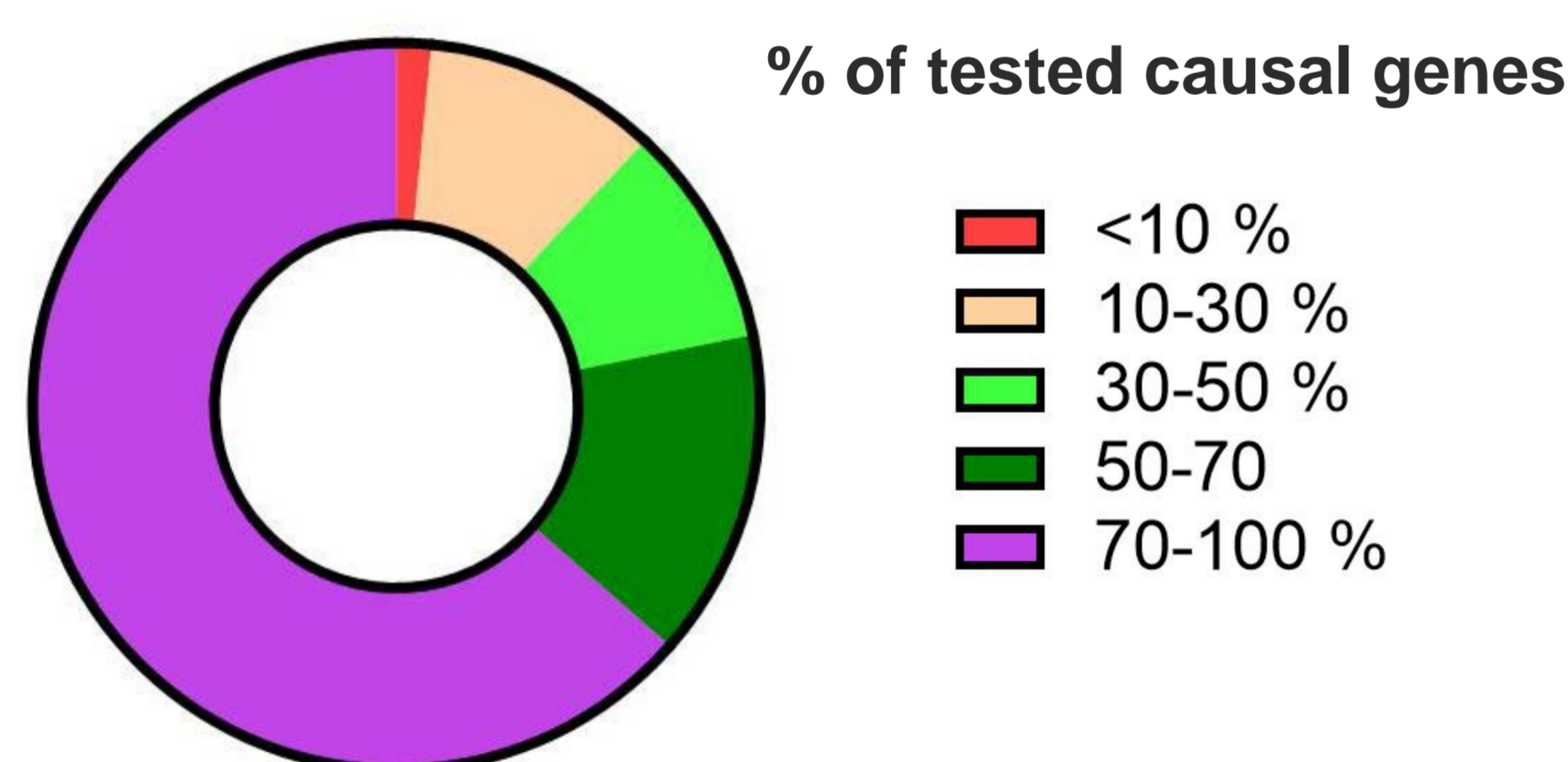
Results: For more than half of RDs covered by all ERNs excepted ERN LUNG, PaedCan, EPICARE and EURACAN, our results show that BMCHGs are testing at least 70% of causal genes. For some RDs covered by 10 ERNs, <10% of known causal genes are tested by the BMCHGs. Finally, collected data show that 28,5 % of those RDs have a prevalence of 1-9/100.000 and 57,1% occurs during childhood.

Conclusion: These results highlight the importance to develop new tests within the centers of human genetics to improve the accuracy and availability of RDs' genetic diagnosis. Patients with a RD characterized by a low prevalence are particularly affected by the incomplete testing of causal genes. This lack in RD genetic testing may also impact clinical trials and orphan drugs development.



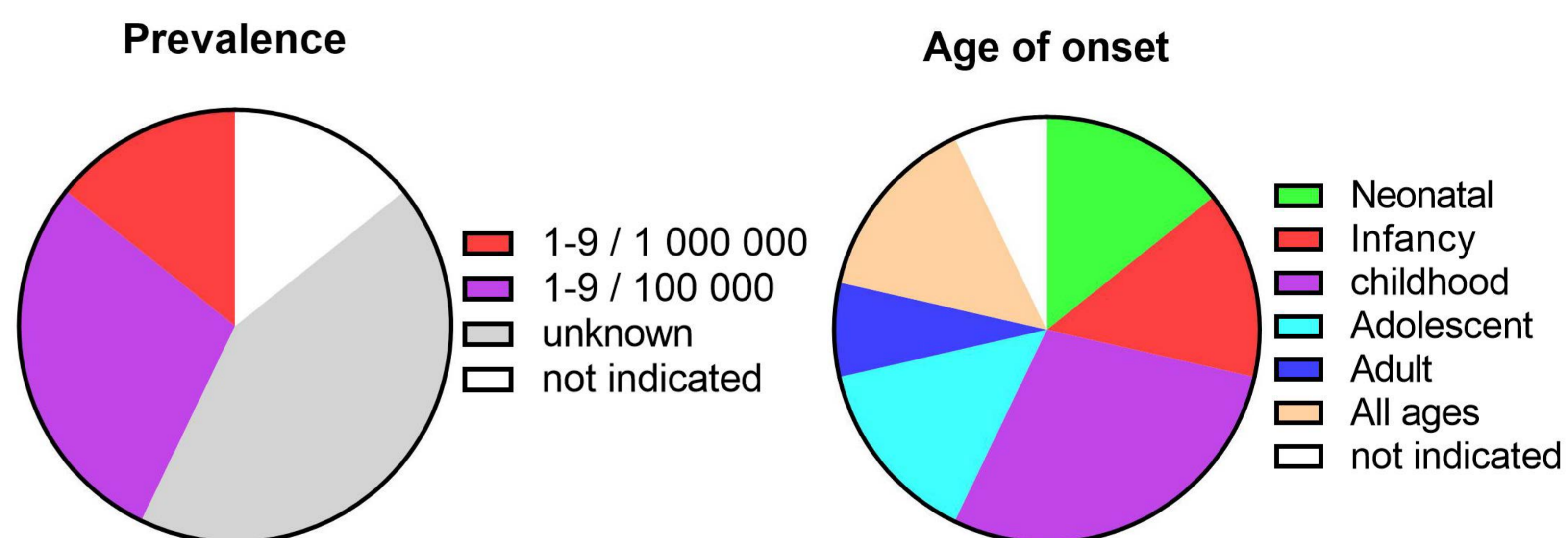
Rare disease testing in Belgium: current overview

Distribution of the diseases in each category



Mean percentage of diseases in each category regardless ERNs

Common characteristics between diseases with <10 % of known causal genes that are tested

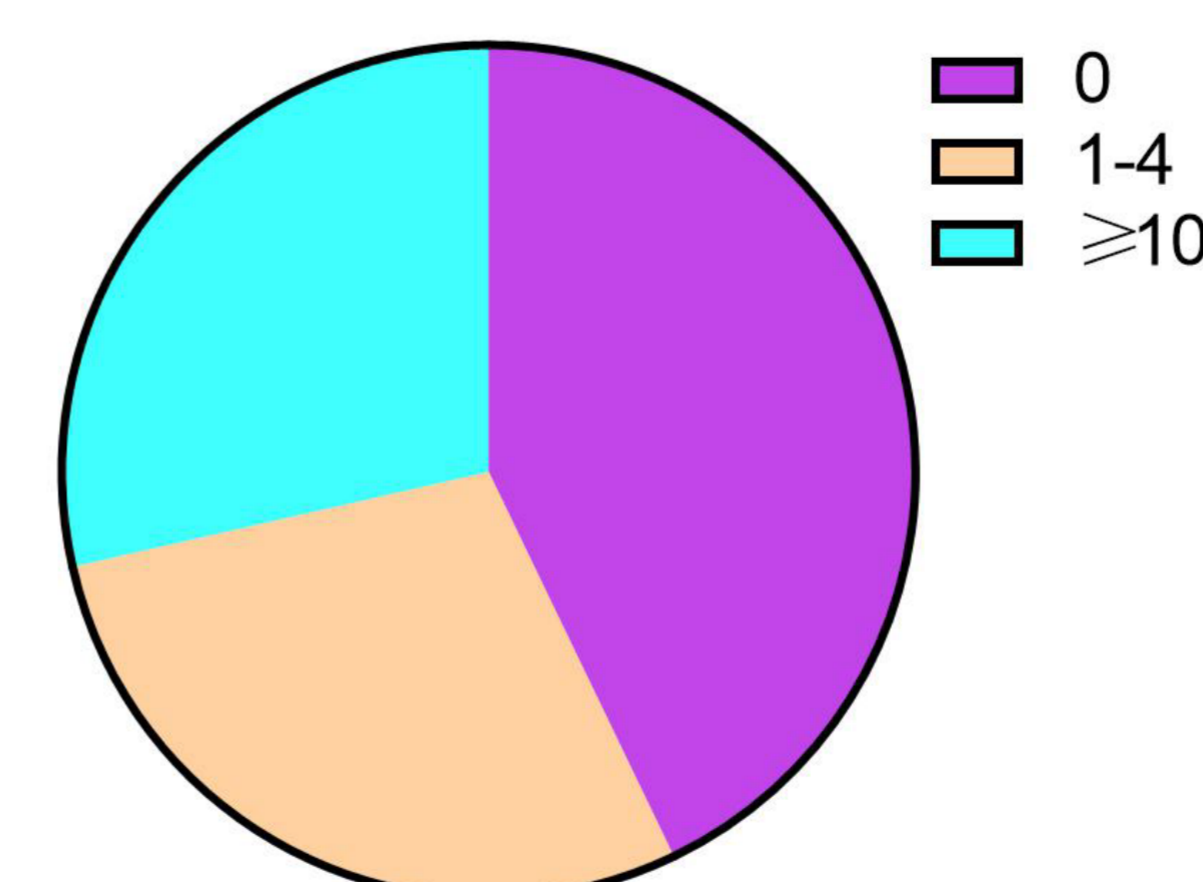


Distribution of the ERNs when > 70 % of diseases' causal genes are tested

Number of diseases in the category with >70 % of tested causal genes	<50 %	50-70 %	>70 %
Number of ERNs concerned	4	11	9

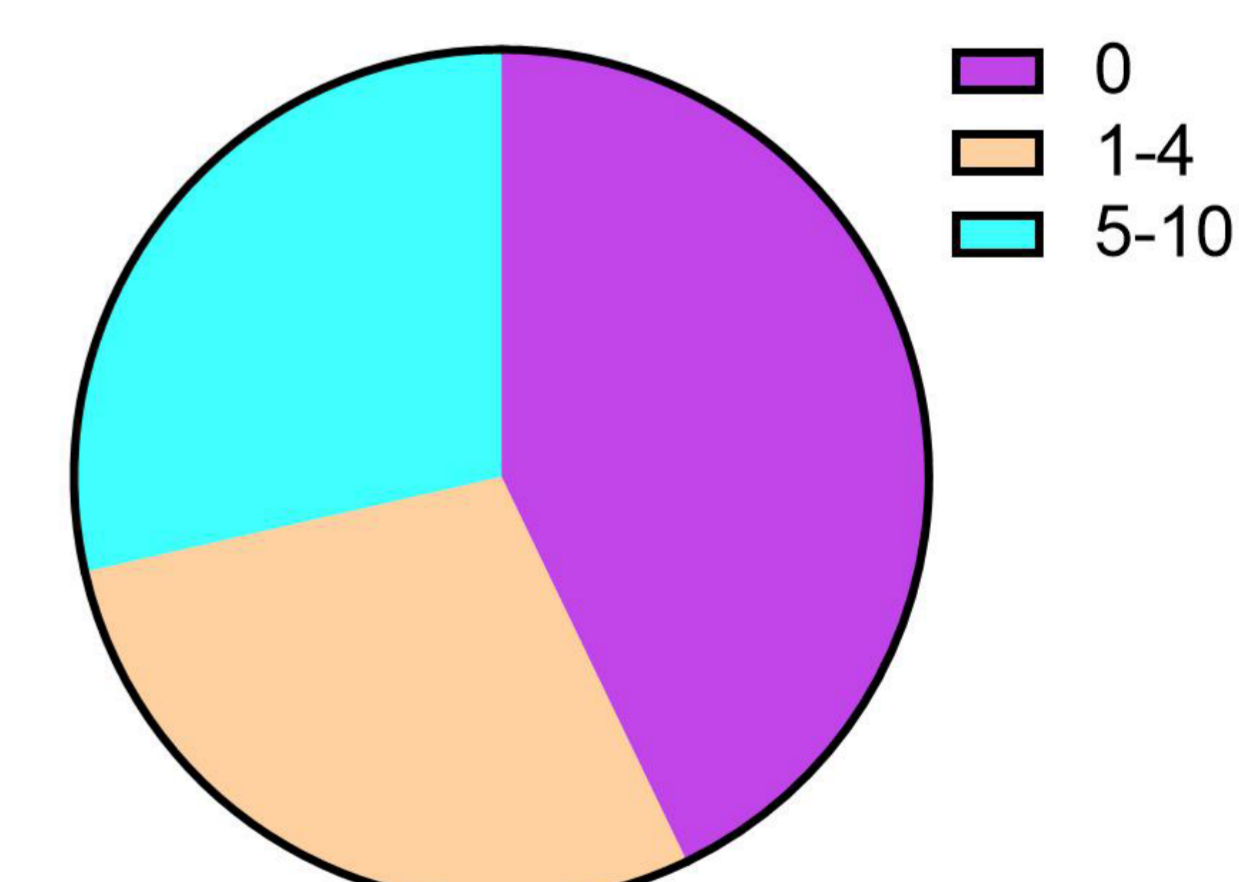
- For 20 ERNs, more than half of the diseases have at least 70 % of their causal genes that are tested in one of the 8 BMCHGs.
- 261 different diseases have at least 70 % of their causal genes that is tested

Number of clinical trials



→ 28,5% of diseases have a low prevalence (1-9/100,000) and 57,1% occurs during childhood

Number of Orphan Drugs



→ 43 % of them have neither clinical trials nor orphan drugs reported

General conclusions and perspectives

- ✓ The scope of the diseases tested in the Belgian Medical Centers of Human Genetics is broad as all the 24 ERNs are covered.
- ✓ For approximately half of the diseases tested in our centers, more than 70 % of the causal genes are tested.
- Development of new tests is required to :
 - improve accuracy and availability of the diagnosis of a RD notably for patient with a RD characterized by a low prevalence
 - increase the development of orphan drugs and clinical trials