**Supplementary Materials**

# Next-generation sequencing-based newborn screening initiatives in Europe: an overview

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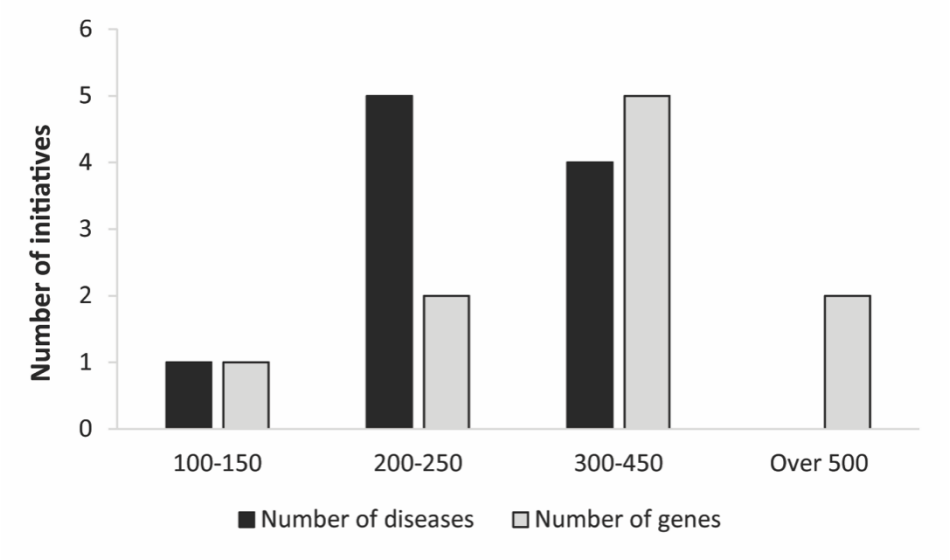
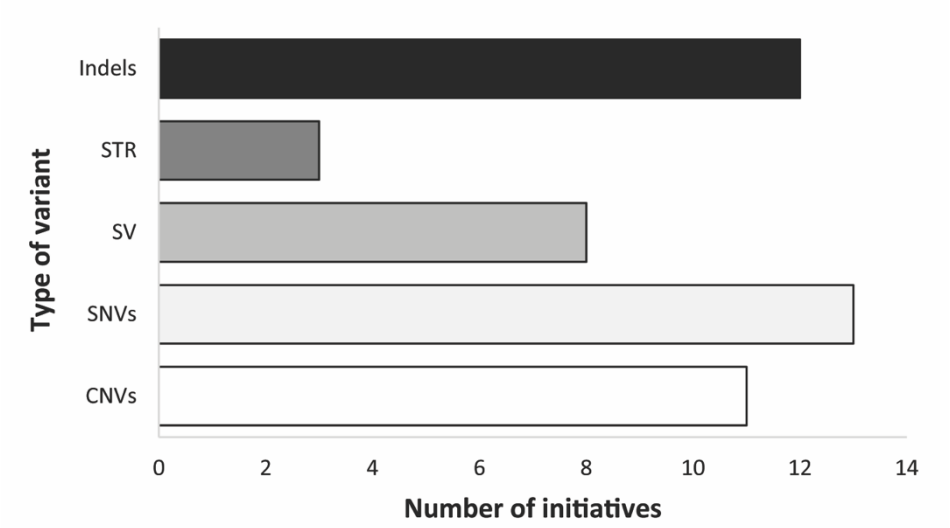



**Supplementary Figure 1.** Number of diseases and genes to be screened within the surveyed initiatives. Note that only ten initiatives have responded to this question, as four initiatives have yet to confirm the number of diseases and genes that will be included with their respective tests.




**Supplementary Figure 2.** Types of variants to be included in the NGS tests. Responses included in the figure are from 13 initiatives, as one initiative had yet to confirm the selection of the types of variants to include in the test.

**Supplementary Table 1. Wilson and Jungner's principles of screening[26]**

| | |
|---|---|
| 1 | The condition sought should be an important health problem. |
| 2 | The natural history of the condition, including development from latent to declared disease, should be adequately understood. |
| 3 | There should be a recognizable latent or early symptomatic stage. |
| 4 | There should be a suitable test or examination. |
| 5 | The test should be acceptable to the population. |
| 6 | There should be an agreed policy on whom to treat as patients. |
| 7 | There should be an accepted treatment for patients with recognized disease. |
| 8 | Facilities for diagnosis and treatment should be available. |
| 9 | The cost of case-finding (including diagnosis and treatment of patients diagnosed) should be economically balanced in relation to possible expenditure on medical care as a whole. |
| 10 | Case-finding should be a continuing process and not a "once and for all" project. |

General information
IRDiRC-driven initiative: the goal of this survey is to collect information about ongoing or planned Next-generation sequencing-based Newborn Screening (NGS-based NBS) initiatives within the framework of the International Rare Diseases Research Consortium (IRDiRC- https://irdirc.org/) Working Group on "Real World Applications and Technology" for NBS.
Survey responses will be aggregated and analysed by the IRDiRC working group in order to write a manuscript to be published within a special series of articles on NBS by IRDiRC in the Rare Diseases and Orphan Drugs Journal.

Individual responses will not be shared outside of the working group. Survey responses will not be used for commercial purposes nor shared with third parties.
Please do not share any confidential or personal information in your responses.
If your initiative has not yet started, please answer to the best of your knowledge based on the plans defined thus far.

If you have any question, please contact Virginie at vbros@illumina.com

Virginie Bros-Facer, PhD - On behalf of IRDiRC
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## Page 1: General information

**Q1**

Please select your laboratory type

**Q2**

What is the name of your initiative

(optional)?

**Q3**

Country - please list if more than one countries involved

Italy

**Q4**

Is there a public website with information on your initiative?

**Yes,**
If yes - please share the website address
If not yet -please explain:

## Page 2: Study design

**Q5**

What is the scope of the initiative/catchment area?

**Q6**

Please describe the framework of your initiative. For example, is it a research pilot or service driven? Please describe in the comment box

**Q7**

How is your initiative funded?

**Q8**

Are there patient advocacy groups or members of the public involved in the initiative?

**Q9**

Is the National NBS committee (or equivalent authority in your country) involved in your initiative?

**Q10**

For which groups do you anticipate the initiative having the most impact/interest? Please select all that apply

**Q11**

Please select your study design

**Q12**

How many samples do you plan to include in your prospective study?

**Q13**

How many samples do you plan to include in your retrospective study?

**Q14**

When will the sample be collected (e.g. 3 days after birth)?

**Q15**

When will participants be enrolled (select all that apply)?

**Q16**

Which healthcare practitioner will be responsible for the enrolment? Please select all that apply

**Q17**

When will you start providing information regarding the genetic testing to the participants (prior to obtaining the consent)?

**Q18**

When will informed consent be obtained?

**Q19**

Study duration (enrolment period in months)

**Q20**

Please describe the testing method(s) being utilised in the initiative - Describe all if more than one apply (e.g. Panels, WES, WGS etc.)

**Q21**

Is confirmatory testing planned?

**Q22**

If you answered yes to Q20, where will this confirmatory testing be done?

**Q23**

Is this initiative linked to the current NBS program in your country?

**Q24**

Will genetic screening results be returned to the participants/families?

**Q25**

What is the estimated/desired time between sample receipt and return of results (if applicable)?

**Q26**

What is the selected sample type for the initiative (select all that apply)?

**Q27**

How many conditions will be screened?

**Q28**

Are you focussing on a specific group of diseases to be screened (e.g. only metabolic disorders)?

**Q29**

Are clinical care pathways identified and available for each of the conditions screened?

**Q30**

How many genes will be included?

**Q31**

What type of variants will be included in the test? Please tick all that apply

**Q32**

Will any conditions be excluded because of the type of variants?

**Q33**

According to ACMG guidelines, what type of variants are you planning to report?

**Q34**

What inclusion criteria were applied for the disease selection?

**Q35**

Will it be possible to add or subtract conditions on the disease list while the initiative is active?

**Q36**

Should this disease selection remain flexible in the future?

**Q37**

Are you planning to validate your test?

**Q38**

If you answered yes to Q36, can you please indicate which of the following best apply?

## Page 3: Data & follow-up

**Q39**

What type of analytical software are you planning to use (e.g; commercially available, in-house, hybrid)? Please explain

**Q40**

Where will data be analysed and/or stored?

**Q41**

What type of files will you store (e.g. vcf, FASTQ, etc.)?

**Q42**

For how long are you planning to store data following the end of the study?

**Q43**

Will genetic screening results be linked to clinical dataset in the long-term?

**Q44**

Are you planning any recollection/post-service calls with the parents who agreed to participate in your initiative?

**Q45**

Is your initiative going to follow up on clinical outcomes?

**Q46**

If you answered yes to Q44, when will you conduct the follow up?

**Q47**

If you answered yes to Q44, please select all that would apply in the follow up

**Q48**

If you answered yes to Q44, will these clinical outcomes be tied up to Electronic Health Records or other data source?

**Q49**

Are you planning to federate any data from this initiative?

Page 4: Health economics and Outcomes

**Q50**

Will you be performing a micro-costing analysis of your NGS-based NBS test to understand the operational cost of the workflow?

**Q51**

If you are planning long-term follow up of individuals with identified etiological variants, will you be collecting data on economic utility?

**Q52**

If you answered yes to Q50, please indicate which of the following would demonstrate the potential economic value of screening (with NGS-based NBS). Please tick all that apply

**Q53**

What data will you be able to collect to address the long term economic impact?

**Q54**

Please describe how the comparator (control) group (.e.g; individuals who did not receive an early diagnosis through NBS) will be established.

**Q55**

Will you be attempting to capture cost data in conjunction with healthcare resource utilisation data

## Page 5: Future Vision

**Q56**

When do you see your initiative having an impact within the healthcare system of your country (i.e. adopted as first-tier genomic screening test offered to every newborn)

**Q57**

Do you see genomic screening replacing one day conventional (biochemical) screening or used in parallel to conventional screening