Nordic Alliance for Clinical Genomics

WORKSHOP REPORT

NACG 7th Clinical Workshop
Helsinki, 6.-7. May 2019

About NACG

The Nordic Alliance for Clinical Genomics (NACG) is an independent, non-governmental, not-for-profit Nordic association. NACG gathers stakeholders in clinical genomics who collaborate to identify and address emerging challenges to the implementation of clinical genomics and precision medicine. NACG partners collaborate to identify and address emerging challenges to the implementation of clinical genomics and precision medicine. Learn more about the Nordic Alliance for Clinical Genomics at https://nordicclinicalgenomics.org/ or contact us at post@nordicclinicalgenomics.org.

Mission

NACG partners work together and learn from each other to lift performance standards. We aim at responsible sharing of trustworthy data for improved diagnosis and treatment, and as a resource for research.

Goals and activities

- Facilitate the responsible sharing of genomic data, bioinformatics tools, sequencing methods and best practices for interpretation of genomic data.
- Enhance quality of genomic data and processes, and explore methodologies to provide assurance.
- Understand legal barriers to the implementation of personalised medicine and to engage with key stakeholders that influence these barriers
- Develop demonstration projects that challenge perceived legal barriers that limit responsible and ethical sharing of genomic and health data.
- Build bridges between research and clinical communities, technologies and practices to foster innovation

Date of issue	Rev.	Prepared by
20190827	0	Guro Meldre Pedersen (Guro.Meldre.Pedersen@dnvgl.com) and Bobbie N. Ray-Sannerud (Bobbie.Nicole.Ray-Sannerud@dnvgl.com), DNV GL, with support from all workshop contributors.

Symbols

 Lecture / presentation

 Interactive workshop

Abbreviations

CNV	Copy number variation
GDPR	General Data Protection Regulation (EU) 2016/679
GMS	Genomic Medicine Sweden / Genomic Medicine Service (England)
HPO	Human Phenotype Ontology
NACG	Nordic Alliance for Clinical Genomics
NGS	Next-generation sequencing
OUS AMG	Oslo University Hospital, Department of Medical Genetics
PV	Pathogenic variant
SV	Structural variants
TVX	Trusted Variant eXchange
VP	Variant prioritization
VUS	Variant of uncertain significance
WES	Whole exome sequencing
WGS	Whole genome sequencing
WP	Work package

Contents

Executive summary

This report summarizes the 7th workshop of the Nordic Alliance for Clinical Genomics (NACG). The workshop took place at Biomedicum, Helsinki, 6.-7. May 2019, and gathered 64 participants from 21 organizations in five different countries (Table 1, Figure 1).

The objective of this workshop was to progress NACG work to share experiences, data and best practices relevant for the clinical implementation of genomics, and to collaboratively explore pain points in producing and using genomic data to the best of the patient (Figure 2).

Table 1 Summary of workshop participation

Country	Organization	Number of participants
Denmark	Aarhus University Hospital	4
	Rigshospitalet	6
Finland	CSC / NeIC	1
	Euformatics	3
	FIMM / University of Helsinki	6
	HUSLAB, Helsinki University Hospital	13
	Sitra, the Finnish Innovation Fund	1
Iceland	Landspitali - University of Iceland	1
Norway	DNV GL	5
	Haukeland University Hospital	1
	Oslo University Hospital	8
	St. Olavs Hospital	3
	The Norwegian Directorate of Health	1
	University of Bergen	1
	University of Oslo	2
Sweden	Karolinska Institutet	1
	Karolinska University Hospital	1
	SciLifeLab	5
	Twist Bioscience	1

Figure 1 Participants at the 7th NACG clinical workshop

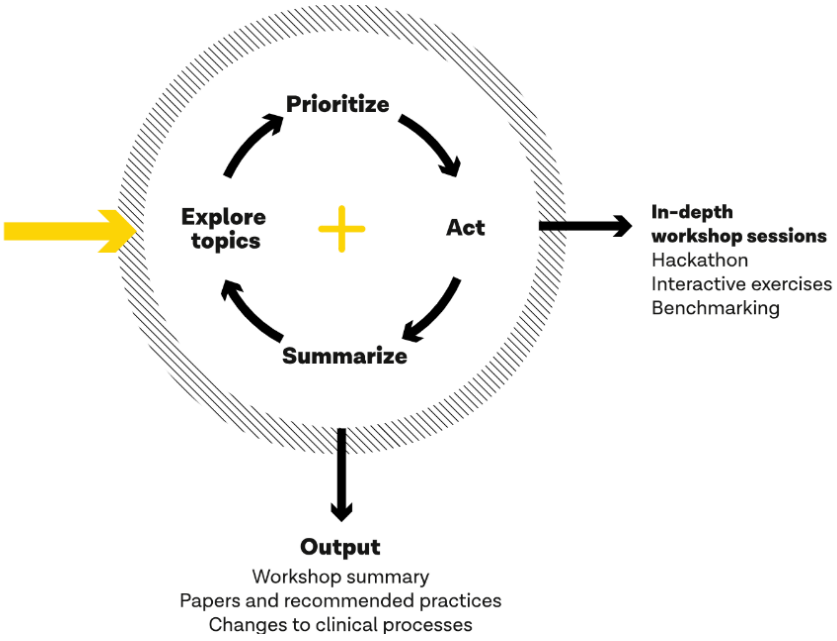


Figure 2 NACG members discuss and explore topics of interest to identify shared challenges and strategies for overcoming them. Prioritized topics are explored in in-depth interactive exercises. Findings and learnings are summarized in workshop summary reports and collaborative papers and contribute to lifting performance standards.

Workshop outline

The workshop was organized as illustrated in Figure 3 (detailed agenda available in Appendix 1). Setting the stage, the participants provided updates to the group on progress of NACG and relevant national activities in the Nordic countries. The workshop also provided an update on relevant European data sharing initiatives and suggested improvements of variant classification guidelines. Main topics discussed during the workshop group to three of the NACG working group themes;

- Benchmarking, harmonisation and standardisation / Enhancing quality of data and processes
- Bioinformatic tools development
- Vehicles for data sharing

Additionally, seeds of new topics were suggested to the NACG community.

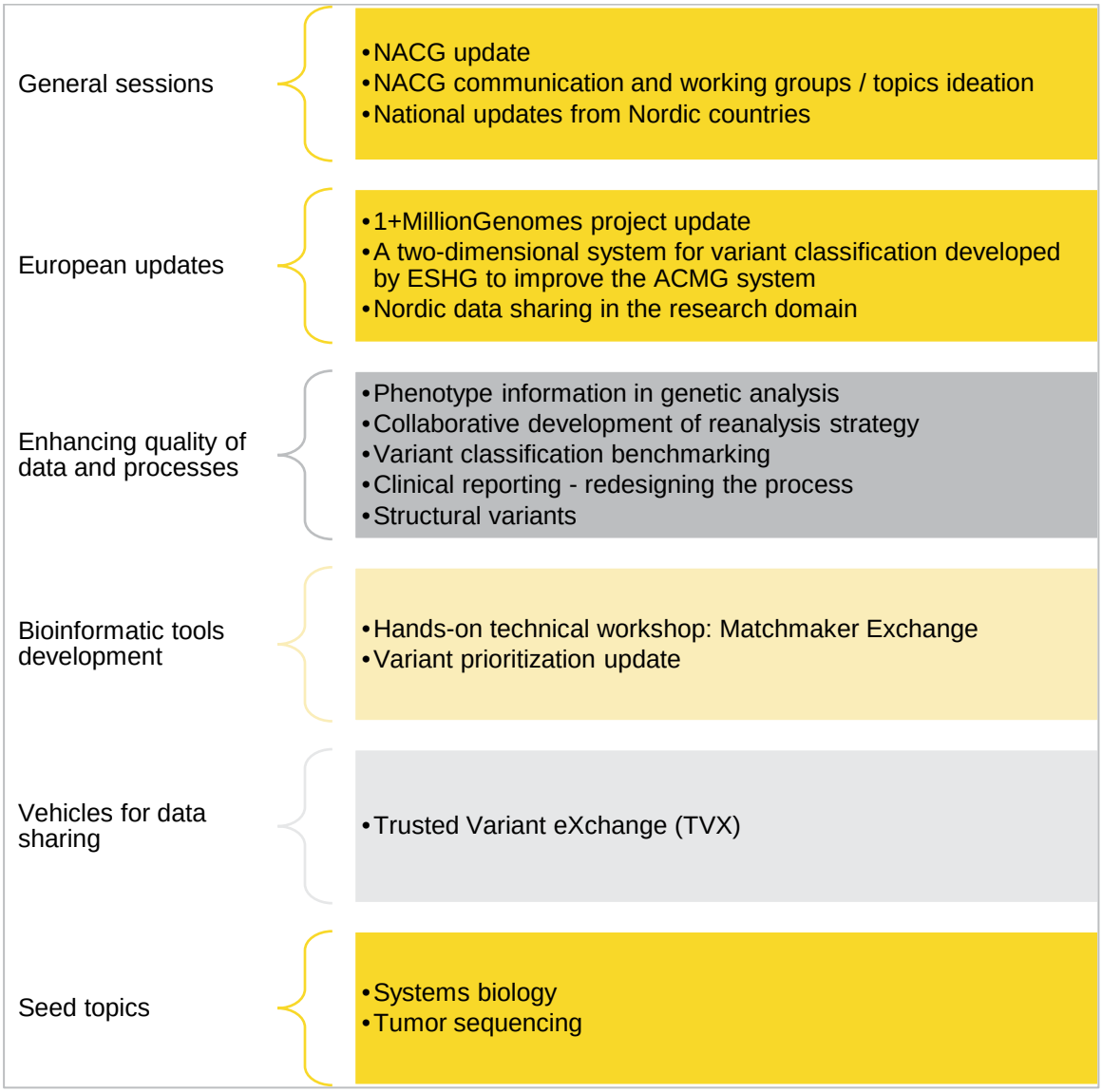
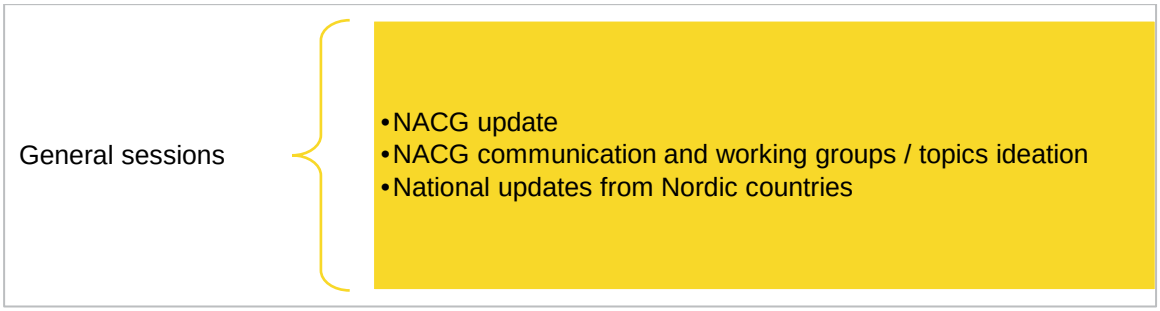


Figure 3 Workshop outline

General sessions



NACG update

	Session lead:	Dag E. Undlien/ OUS AMG & NACG steering committee chair
	Objective:	Share information on development and status of NACG.
Key information:	- Dag introduced the rationale for collaboration across Nordic clinical genomic stakeholders as technology and knowledge are developing rapidly and the leading production of genomic data is shifting from research to clinic. - Linking the Nordic value proposition to the mission and aim of NACG, old and new participants were encouraged to seek NACG membership and engage in the working group activities to contribute to the NACG collaborative efforts to advance clinical genomics in the Nordic countries together. - Dag emphasizes that the alliance should be agile and continue to organize working groups and activities according to the membership's interests. - The next NACG meeting (Nov 2019) will include a broader symposium in addition to the workshop activities. Adjacent to these, a Nordic legal symposium focusing on relevant topics will take place, further information to come. - Henrik Stranneheim and Kjell Petersen have decided to discontinue their responsibilities as working group leads after this workshop and were thanked for their contributions to their respective working stream activities.	
Conclusions:	As NACG is growing, members are encouraged to come with ideas to improve workshop format, ways of collaboration, ideas for improving existing working group topics or add new.	

NACG communication and working groups / topics ideation

	Session lead:	Guro Meldre Pedersen and Bobbie Ray-Sannerud, DNV GL
	Objective:	- Discuss needs and alternatives for NACG communication - Secure ideas for further NACG working group focus
NACG communication	A communications professional has delivered a suggestion for a NACG communication strategy. Among the recommendations were:	

	1) Establish communication tool to foster communication between workshop; to capitalize on knowledge and experience of other NACG members and create more dynamic topic ideation between workshops. 2) Establish NACG presence in social media to share information and strengthen NACG recognition among relevant stakeholders inside and outside of membership. Workshop participants were invited to a discussion on the need for internal communication channels to continue discussions and work between the workshops. The value of connecting more is recognized, but communication tools vary across groups. Further follow up on specific channels will probably be driven by working group-specific needs. Different social media platforms were discussed, and LinkedIn was confirmed to be the most relevant and valuable channel. Members were encouraged to contribute with relevant content and actively use the #NACG tag. NACG presence also established at Twitter and Facebook, mainly referring to the NACG website for further information.
NACG working groups / topics ideation	At the end of the workshop the participants were inquired about topics they would like to see in the future NACG agenda. As summarized in Figure 4,topics most frequently nominated were: - Structural variants - Classification benchmarking - Somatic variant calling - Transcriptomics - Long read sequencing - Auto-classification - CNV filtering - RNAseq Other topics mentioned included: - Tools mapping - ML in clinical genomics - Variant calling benchmarking - ACMG interpretation - DPIA and risk assessment examples - Somatic pipeline - CNV analysis - SV tools - ESHG modified ACMG - Clinical reporting; effective reports
Conclusions:	To complement external communication through the NACG website (https://nordicclinicalgenomics.org/), LinkedIn will be used as the primary social media channel. The community is encouraged to use the #NACG tag for relevant content. Internal communication channels / platforms will be developed per working group needs. Input from the participants on preferred topics will be used for planning of the Nov 2019 NACG event. Ideation output will be included in the planning of the next workshop.

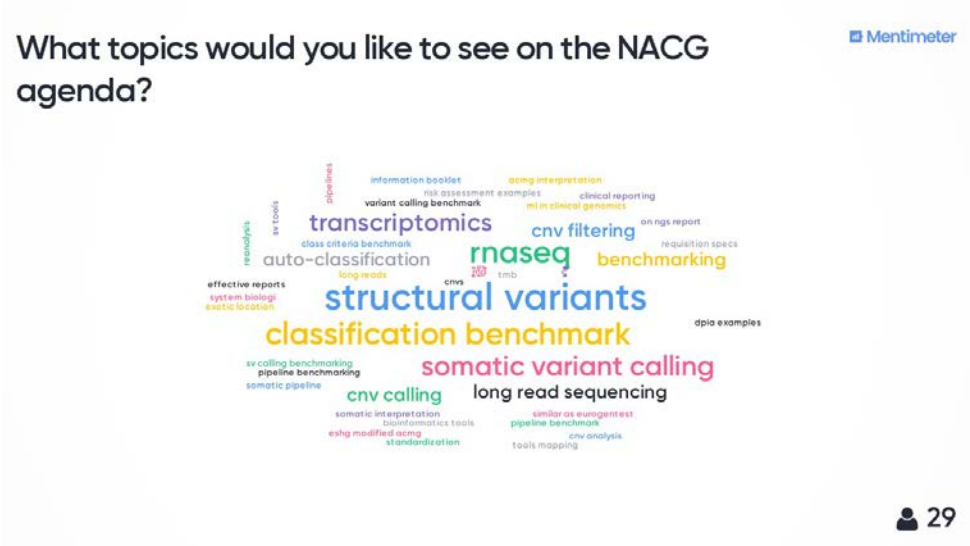


Figure 4 NACG Ideation output

National updates from the Nordics

The objective of this session was to share key updates from the Nordic countries.

	Country:	Finland
	Session lead:	Janna Saarela, FIMM
Key information:	Janna informed the group on changes in the Finnish regulatory environment including: - National Genome Centre: Genome act in parliament - Renewal of the Biobank act - Act in progress for secondary usage of health data Other relevant activities and projects include: - Reorganization of healthcare - Plan for a drug development centre - FinnGen - iCAN project	

	Country:	Iceland
	Session lead:	Jón J. Jónsson, Medical Director, Dept. of Genetics and Molecular Medicine, Landspitali
Key information:	Jon informed the workshop about the development of key infrastructure in Iceland, including: - Building of a national university hospital in Reykjavik initiated. - Update to the use of the Heilsuvera Health Portal for communication with patients and sharing of lab results. DeCODe has started sharing of BRCA2 founder PV, where more than 50,000 signed up to check their genotype. There are about 350 confirmed carriers of the BRCA2:999del5 gene mutation, 40 of these were previously known carriers.	

	Country:	Norway
	Session lead:	Dag E. Undlien, OUS AMG
Key information:	Dag update the group on the National Strategy for Implementation of Personalized Medicine including: - Ongoing work to establish a variant database - Network of regional centres for personalised medicine - Revision of biotechnology act in progress - Legal process to clarify anonymity of variants - Legal process to figure out possibilities for sharing of non-anonymous genetic data and variant classifications - Ministry of Health desire for regional health authorities to develop combined clinical / research patient pathways - Directorate of Health is considering if Norway should sign an agreement on European data sharing initiative - Research strategy ongoing on personalized medicine	

	Country:	Sweden
	Session lead:	Valtteri Wirta, SciLifeLab
Key information:	Valtteri updated the workshop participants on the Genomic Medicine Sweden (GMS) project, a national program with a key concept to include seven genomic centres working within five different clinical areas supported by technical work streams. - For the rare diseases, the 5000-sample milestone has been achieved in Stockholm. The GMS will focus on initiating a mini-pilot to enable all six healthcare regions with clinical genetics departments to get started in WGS. - For solid tumours, somatic analysis is more panel focussed (from May 2018) and used as a basis for National strategy on solid tumours in terms of cost efficiency and value.	

- A WGS pilot is designed for paediatric cancer
    - One-year project funded with expectations to go to 3-years
    - Three phases (build capability, demonstrate capability, production)
    - Provide evidence for assessing clinical utility of WGS in terms of cost, clinical value, ability to replace current tests, and turnaround time.
- Informatics work package includes preparing a pilot infrastructure for compute and storage, exploring a genome database to include raw data as well as coordinating the bioinformatic workflows and interface solutions. Work is also in progress to pilot infrastructure, a data lake to capture all the data for compute and storage.

Country: Denmark

Session lead: Ane Yde Schmidt, Center for Genomic Medicine, Rigshospitalet

Key information:

Ane updated the group on the developments of the Danish National Genome Centre. The Novo Nordisk Foundation has approved a framework grant of DKK 990 million (€133 million) over 4.5 years for establishing and operating the infrastructure of the National Genome Centre, which will kick off July 1st, 2019. Focus will be on patients and not healthy people, but focus patient groups are yet to be selected.

The update also included information about Østdansk Infrastruktur for personlig medicin, a joint effort between Region Hovedstaden, Region Sjælland og Københavns Universitet (KU) SUND, Institut for Klinisk Medicin og Danmarks Tekniske Universitet (DTU). In phase 1, focus is on datacenter (patient data lake), genomcenter and biobank.

European updates

European updates

- 1+MillionGenomes project update
- A two-dimensional system for variant classification developed by ESHG to improve the ACMG system
- Nordic data sharing in the research domain

The 1+MillionGenomes project

Session lead: Valtteri Witra, SciLifeLab

Objective: Share updates on the 1+Million Genomes project

Key information:

The project goal is to provide secure and authorized cross-border access to 1 million genomes and linked health data in the EU by 2022 through a federated network of genomic datasets at national / regional level. The partners will also join forces on analytical capabilities to advance the understanding of genetic associations that cause or predispose diseases measures and to facilitate further development of personalized medicine.

The project is a Member States driven initiative supported by the European Commission, and the list of EU countries that have agreed to cooperate in linking genomic data across borders is continuing to grow. Additionally, eight countries currently have observer status in the project. Ten working groups have been identified to further define the way forward and the position / role of this initiative, as well as to identify current status and gaps.

Suggested timeline is to have a first draft by end of September with a roadmap initiative by the end of the year.

Further information is available at https://ec.europa.eu/digital-single-market/en/european-1-million-genomes-initiative .

A two-dimensional system for variant classification developed by ESHG to improve the ACMG system

Session lead: Gunnar Houge, ESHG President

Objective: Share information about the ESHG prototype system for variant classification, and get feedback on the proposed system

Key information:	Gunnar provided a swift review of the ACMG / AMP variant interpretation guidelines[1], and the work done by the ESHG to refine and improve these guidelines by adding a clinical grading of a variant to the molecular dimension. VUSes are a general cause of confusion as some clinicians fail to understand this class and debates are ongoing on whether they should be reported. The ESHG prototype suggest re-grading the molecular score of VUSes to 0 and shifting the score 3 to describe "variants of potential interest, possibly pathogenic", so that the score scale is a continuum, tentatively also introducing the -1 score to describe a protective variant ("den Dunnen variant"). The clinical score refers to a variant's pathogenicity and penetrance. By combining the molecular and clinical score, a combined and more robust grading is achieved. Using the ESHG system will require training of clinical geneticists in basic biology, and clinical information is essential. Challenging variants should be evaluated by evaluation teams. Gunnar was clear that the ESHG prototype is not a diagnostic system, but a tool aimed to help the clinicians. Key to success in precision medicine will be collaboration and efficient transfer of clinical / lab information between departments, including the necessary dialogue when insufficient information is available. Gunnar also emphasized the importance of sharing information about variants between laboratories.

Nordic data sharing in the research domain

	Session lead:	Antti Pursula, NeIC / CSC / ELIXIR Finland
	Objective:	Share information about infrastructures for research with sensitive data, such as the NeIC Tryggve project.

Key information:

- For research based on personal data, scientific goals and societal benefits must be balanced with the protection of privacy and integrity of individuals.
- Tryggve (https://neic.no/tryggve/) is a collaboration of NeIC (Nordic e-Infrastructure Collaboration) and Nordic ELIXIR (European research infrastructure for life science information) nodes (DK, FI, NO, SE) to develop and provide data and compute services for human data across borders
- The Nordic countries are joining forces in NeIC to tackle e-infrastructure challenges beyond singular national capabilities. NeIC is a part of NordForsk and is operating a portfolio of Nordic projects.
- Tryggve's objective is to develop and facilitate access to secure e-infrastructure for sensitive data, suitable for hosting large-scale cross-border biomedical research studies.
- Tryggve activities include
    - Development of sensitive data archiving technology
    - Development of secure tools for analyzing sensitive data across borders, based on a secure distributed platform for sensitive data.
    - Operating a use case program (https://neic.no/tryggve/usecase)
    - Targeted development of the secure Tryggve platforms
    - Implementing ELIXIR AAI based authentication and authorization solutions

[1] Richards, Sue et al. "Standards and guidelines for the interpretation of sequence variants: a joint consensus recommendation of the American College of Medical Genetics and Genomics and the Association for Molecular Pathology." *Genetics in medicine: official journal of the American College of Medical Genetics* vol. 17,5 (2015): 405-24. doi:10.1038/gim.2015.30

- Providing assistance with GDPR related issues
- Other initiatives and frameworks for data sharing in research domain discussed included:
  - Danish National Genome Center
  - Genome center in Finland
  - ELIXIR Research Infrastructure
  - Federated EGA
  - GA4GH - Developing standards for international data sharing

Enhancing quality of data and processes

Working group lead: Sharmini Alagaratnam, DNV GL & Kaisa Kettunen, HUSLAB & FIMM

Enhancing quality of data and processes

- Phenotype information in genetic analysis
- Collaborative development of reanalysis strategy
- Variant classification benchmarking
- Clinical reporting - redesigning the process
- Structural variants

Phenotype information in genetic analysis

Session lead:	Sharmini Alagaratnam, DNV GL & Kaisa Kettunen, HUSLAB /FIMM
Objective:	Share experiences in collecting phenotypes for rare disease diagnosis by NGS
Workshop outline:	1) Gauging of current status of phenotype information accompanying genetic analysis 2) Discussion on selection of diagnostic test or panel 3) Review of requisition forms. 4) What would the perfect requisitioning system look like? 5) How could NACG contribute to developing the perfect system?

1) Gauging current status of phenotype information accompanying genetic analysis

Plenary discussion on how to get an accurate description of a patient's phenotype and symptoms.

Do you generally get sufficient phenotypic information from requisitions?	- No: 17 - Yes: 7
What format is best for collecting phenotypic information?	- Structured (e.g., HPO): 6 - Non-structured: 0 - Combination: 22
How are you currently getting phenotypes?	Examples included order form, excel sheet, free text, journal, HPO, oral, free text through email, psychedelic, form, phone call, check marks, scribbles, database, hand written, non-structured.

2)	**Discussion on selection of diagnostic test or panel**	Who should choose the diagnostic test or panel: the requisitioning clinician or the genetics lab?
		- Lab:
		  o Based on the purpose of the test, the lab should be in a position to argue why we have the panel we have.
		  o It is difficult for a clinician to understand and follow the changes in genomics that would justify changes to the panels but concerns of clinical geneticists should be heard.
		- Both:
		  o There is value in consolidating opinions based on the unique perspectives
		  o There is a risk if the lab chooses a panel that the patient has not consented to. The lab cannot change a panel without patient having consented.
		  o Caveat: Requires a good process and effective collaboration to be able to choose the test together

3)	**Review of requisition forms**	As basis for discussion, in-house NACG examples of how background information is transmitted to the genetic lab were shared from: - Rigshospitalet by Maria Rossing - Oslo University Hospital by Eidi Nafstad - HUSLAB by Pia Alhopuro - Karolinska by Nicole Lesko Requisitioning forms from the commercial NGS provider Baylor Genetics were also made available for discussion. Through group work the participants compared the requisition forms to identify preferred and not preferred traits. The outcome is available in Table 2 below.
4)	**What would constitute the perfect requisition form?**	A group work was organized to explore features of a perfect requisition form. The group discussions are summarized in Table 3.
5)	**How could NACG contribute to developing the perfect system?**	The workshop participants discussed how the NACG can contribute to the development of the perfect system. Suggestions included: - Describe/establish of the “perfect system” with specifications and publish on the NACG website. - Provide guidelines for what form should include and how - Develop a generic demo version - Sharing good solutions and working on standardization Developing a prototype was discussed; all agree it is difficult to develop a prototype as it has to be integrated into multiple hospital systems

Table 2 Review of Nordic requisitioning forms – group work findings

Like	- Information to identify family members - Combination of free text and click boxes as an option - Danish / Iceland: space for family tree and questions about siblings. - Observed that the forms are adapted to clinician environment – Karolinska has tick boxes which is good for those who do not understand all the terms. - Assistance in selecting HPO terms. - HPO terms to tick off - Check boxers for phenotype - OUS: ease of completing family information - If there is an option to be read digitally
Dislike	1) Too small space to write free text clinical information 2) Baylor form – too many pages and too much information 3) Observed that many have no space for phenotype 4) Observed that many don't have a request for HPO terms 5) No space for any extra text. 6) Value of going digital – i.e., clinician starts typing the word and drop down menu populates. Will save time and eliminate need to have forms with so many pages. 7) List of single genes 8) HUSLAB – too much free text 9) Prefer not to have gene panels on the form at all. Maybe have this on a webpage?

Table 3 The perfect requisition form – summary of group discussions

- Electronic, integrated with lab systems (LIMS), ease of typing and readability, self-guided with suggested typing, interactive, provides digital copy (pdf) of the printout
- Info nudging of clinician: guide not demand, suggested genes/terms digitally to clinicians, help functionality to describe test types, etc.
- Short time fill time (5 min?)
- HPO terms: Converter for phenotypes, controlled vocabulary output, drop down box
- Ability to pick symptoms, disease, and single genes
- System/decision tree that recommends gene panel/relevant assays based on information
- Test purpose (diagnostic vs predictive)
- Extra information on the sample type, ethnicity, pedigree, family history
- Optional: digital free text field
- Covers legal aspects
- Information about limitations
- Tick box for informed consent
- Allow capturing of negative phenotypes

Collaborative development of reanalysis strategy

	**Session lead:**	Sharmini Alagaratnam, DNV GL & Kaisa Kettunen, HUSLAB /FIMM
	Objective:	Workshop to design a reanalysis strategy for NGS
	Workshop outline	1. Review of reanalysis survey from NACG April 2019 2. Review of guidelines for reanalysis 3. Group-wise design of reanalysis strategy, presentation in plenary
Workshop to design a reanalysis strategy	The workshop participants were challenged to design a reanalysis strategy that would serve their needs today. Components discussed included - What to reanalyse and when - Prerequisites - Barriers The workshop outcome is summarized in Table 4.	
Conclusions:	- What do patients want in terms of reanalysis? Are there cases where patients have declined reanalysis? - Implications from IVDR when designing own internals tools. - Not a duty to reanalyze but represents a huge opportunity for undiagnosed patients	

Table 4 Summary of group discussions on reanalysis strategy

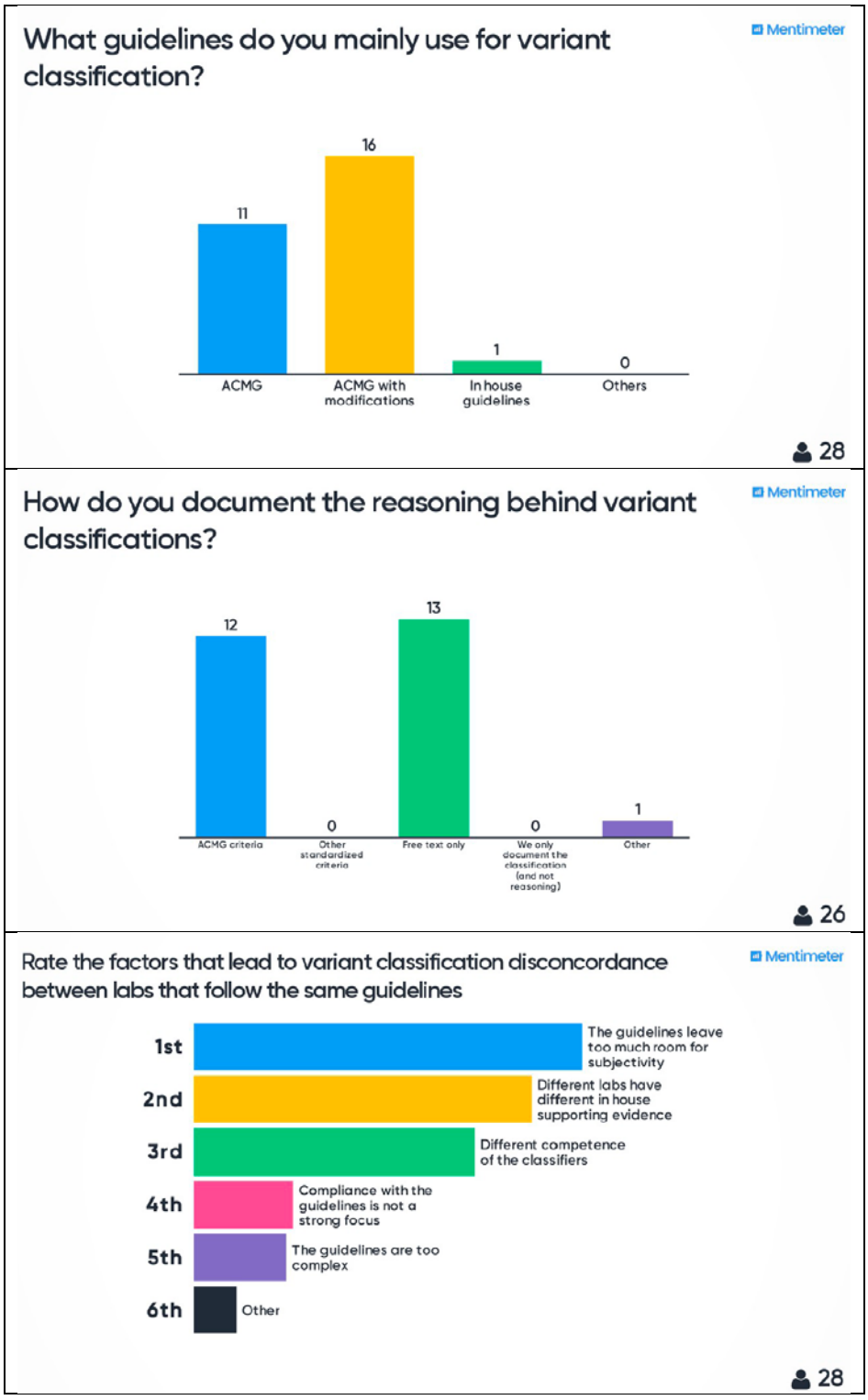
	What to reanalyse and when?	**Prerequisites**	**Barriers**
Group 1	- Reanalysis defined as a new sequencing from DNA. - VCF, FastQ, Classification - Triggers: Requisition from clinician and new gene, you have a new software, expanding a panel, wet-lab problems, validation of a pipeline, re-classification of a variant.	- Prerequisites associated with barriers. - Need metadata: what did the patient consent to and ensure data follows the sample. - Variant prioritization – large numbers of variants, need a way to prioritize/ automatically classify - Need good communication between lab and clinic to discuss reanalysis. For example, what is in the requisition form? - Validation dataset – set of samples to return to so you can benchmark - Desire to have a database for an overview (i.e., in which samples has this variant been seen before).	- Lack of automation - Lack of personnel (resource demanding) - Lack of consent of the patient (does the patient want us to look into this?) - Lack of a legal framework in terms of consent but also for what can be shared.
Group 2	Scenario: Broad analysis (WES / WGS) without result, strong suspicion of genetic disease. Reanalysis triggered by new clinical information, new gene-to-disease evidence, improved bioinformatic pipeline, new resources, or a certain amount of time passing.	- Solid consent process - Data lake – know what you have and how it is analysed - Structuring of data and logs - Cost of compute and storage - Need an automated bioinformatic workflow - Should be a very conservative decision to what bring up to integrate - Variants in class (4), 5 - Clinician initiated re-evaluation	- Ethical and legal aspects with consent so patient is aware of the process - Time for re-interpretation - Suitable reimbursement model
Group 3	Triggers: 1) new knowledge 2) patient info (signs and symptoms) 3) advances in technologies	- A challenge is patient info – argues for free flow of data EHR to lab - Semi-automatic IT solutions - Do not limit to relevant genes	- Legal requirements around data sharing - IT systems – lack of interoperability
Group 4	- Changed phenotype - New pathogenic genes, updated classification - New treatment options - Updated panels - Updated software for variant calling - Frequency: scope dependant and clinical evaluations	- Undiagnosed syndrome patients, treatable conditions - Funding dedicated to cost codes - Grouping and selection of patients eligible for reanalysis triggered by a clinician	- Resources to do interpretations
Group 5	- Sample -> library->variant calling->annotation (focused on VC and annotation) -> Clinical report - Within lab system, can do reanalysis frequently- and only release this when clinician is requesting?	- With annotation, there is version control - Consider periodic reanalysis – but what is the frequency? - Controls in place to ensure it is cost-effective: what do we know works? - Time it takes to reanalysis: a week? Competence dependent.	- Legal barriers – decipher legal or best practice, then national, regional, international levels - Conflicts in departments - Finland- new law to take place that can do a reanalysis without patient consent. - Cost – does it make sense to pay for this? What is the economical benefit? - Use of cloud services?

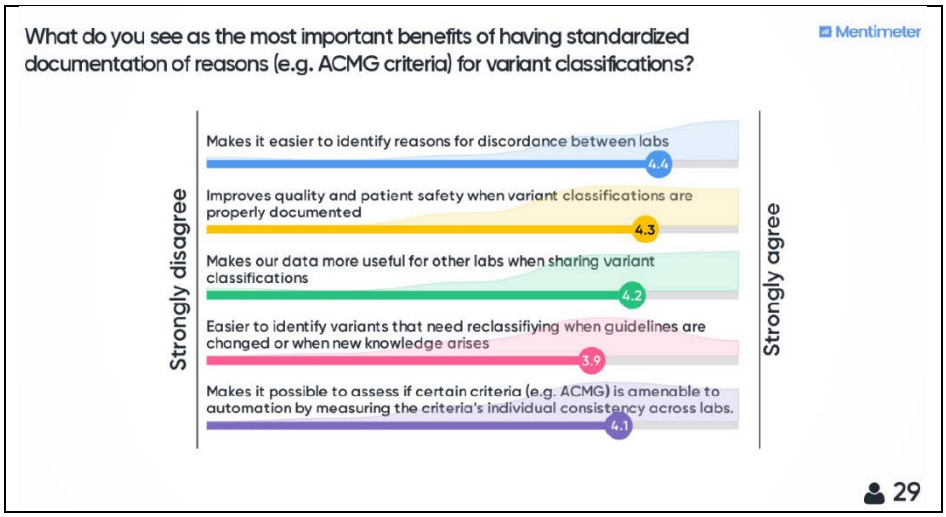
			- New annotations good for patient but there is feedback from the clinical report that implies the next step – how to articulate this?
Group 6	- Panels are only done upon request unless, there is a re-classification, re-analysis - Come up with clear consensus if it should be done automatically	- Clear policy and protocol so patient knows what is done with their sample - In house database or shared	- Cost - Personnel (resources) - Bioinformatic tools - Changing evolving phenotype - Contact person (physician and patient)
Group 7	- Changing panel - On request - Changing pipeline - Re-classification of variants	- Automated re-analysis pipeline that reacts only when the relevant consent is valid - consent platform to facilitate it	- Legal grounds for going back to reanalyze - Consent? - Right to get the best health care - Right to not know - Required to reanalyze - Ethics

Variant classification benchmarking

	**Session lead:**	Dag Undlien, OUS and Stephen McAdam, DNV GL
	Objective:	Variant Classification – should we do more to improve it?
Introduction	Stephen and Dag reviewed studies that demonstrate high discordance in clinical classification underlining the quality and patient safety issues linked to this process. Results from Canada demonstrated that the simple act of sharing classification data led to high concordance between laboratories. This is also a challenge amongst NACG laboratories where a previous informal benchmarking exercise suggested that 12 out of 39 differences found could affect clinical management.	
Discussion	A live survey was conducted to: - Map guidelines used for variant classification - Map documentation of reasoning behind variant classifications - Rate factors that the participants see leading to variant classification discordances between labs following the same guidelines - Capture opinions on the most important benefits of having standardized documentation of reasons (e.g. ACMG criteria) for variant classifications. The results from the live survey are provided in Table 5.	
NACG benchmarking of variant classification	A live survey was conducted to gauge if NACG should continue to do more benchmarking of variant classification, revealing a broad interest in the group (20 Yes, 2 no, 9 I have no opinion). The majority agreed that benchmarking should include the reasoning behind the variant classification (25 yes using ACMG criteria, 5 yes using other criteria, 1 no). The opportunity of testing ESHG criteria for VUSes was also brought up, although several participants indicated that while individual laboratories might want to test the draft guidelines they are still under development and it may be best to wait until the guidelines have matured before NACG invest in doing a Nordic benchmarking exercise.	
Conclusions	Stephen and Dag will consider the input collected and report back to NACG with a proposal.	

Table 5 Results of live survey on variant classification





Clinical reporting - redesigning the process

	Session lead:	Sharmini Alagaratnam
	Objective:	Reporting on results of the project 'User-driven redesign of clinical genomics reports'

Key information:

Sharm reviewed the NACG paper on clinical reporting of NGS data published October 2018 (available at https://nordicclinicalgenomics.org/), where results indicated:

1. Evaluators state reports are generally clearly written;

2. But evaluators can't always find specific information in the reports;

3.Improving reporting of NGS results would have a beneficial effect on information flow between interested parties

DNV GL, in collaboration with Dept for Medical Genetics at OUS, have received funding for a design driven innovation project from DOGA and the Norwegian Research Council to redesign clinical reporting based on user insight. At the NACG meeting in April 2019 in Copenhagen, NACG members were invited to give their input into their perceived needs and challenges of report users, and to invite their users to participate in this project.

The users of the reports are diverse, making the information flow complex;

1) Patient/guardian;
2) specialist close to / far from NGS lab;
3) NGS lab producers
4) Primary doctors/GPs.

For the project, 12 users were interviewed in 30-90 min interviews, within 5 target groups. The results indicated variation among the users:

- **Expert clinicians** want to understand the whole picture, the less expert just need a clear yes or no.
- **Expert users** read reports with uncertain findings thoroughly and spend time digging into references and literature
- **Non-expert users** want guidance and more training
- **Patients** don't always receive the report – but it is valuable to them

	Highlights of findings related to specific topics:
	- Requisitioning
	  o It is time-consuming to select the right test when referring
	  o Labs believe it is their mandate to decide which tests to run
	- Communication and collaboration
	  o Clinicians have both small and big questions for the lab
	  o Communication and collaboration between the clinician and the lab is crucial
	  o The less experience, the higher the threshold is for contacting the laboratory.
	  o Multi-disciplinary meetings and cross-team discussions are essential
	  o Some clinicians believe that the patient cannot manage or need the information in the report
	- Report content
	  o Large variation in how the report is written, from lab to lab and from case to case
	  o Today's IT systems are a limitation
	  o The 'dead' pdf leads to additional work, loss of reports and human errors.
	  o Clinicians feel that suggested treatment is their responsibility, not the laboratory.
	  o Experts users say they are generally happy with the content and structure of the report
	  o Expert users want to know about VUSes

Conclusions	Based on the insights gathered, the next step is to conceptualize and test redesigned clinical reporting, also in a 10-15 year perspective. Through iterative testing, a concept will be selected to be tested with labs.

Structural variants knowledge sharing

Session lead:	Oleg Agafonov, DNV GL
Objective:	To share knowledge around challenges and solutions for managing structural variants
Workshop outline:	1) Setting the stage 2) Review of NACG SV activities 3) Sharing of knowledge on challenges and solutions for SVs through structured group discussions 4) Status updates on implementation of SV pipelines from NACG partners.

1) Setting the stage	Henrik Stranneheim, SciLifeLab, introduced the rationale for why SV is important in NACG. Introducing WGS in 2015, the labs did not know how to handle SVs. The last two years they have started exploring the topic, and in 2019 standardized SV analysis is implemented in the lab. Knowledge is developing, and it is of value to learnings and experiences.
2) Review of NACG SV activities	Oleg reviewed previous NACG SV seed activities, starting with the Nov 2018 activities to identify challenges related to SVs. These are today used as suggested topics for the group discussions, with the goal to share knowledge about SV implementation in the labs – at different stages – and with different perspectives and approaches

3)	**Sharing of knowledge on challenges and solutions for SVs - structured discussions**	The participants were split in groups, addressing challenges, experiences and solutions related to a set of SV-relevant topics. Main take-aways from the group discussions are summarized in Table 6 below.
4)	**Status updates on implementation of SV pipelines from NACG partners**	The different labs were invited to provide status updates on implementation of SV pipelines. **1. Filipe Vieira, Rigshospitalet, Center for genomic medicine** Performed a benchmarking study, with following research questions: • Which tools have a better performance • Compared performance for WGS and WES • Compared performance for CNV calling with respect to size, variant type and chromosome type 50 tools were considered, and 11 tools were selected for testing. At the time of the study no benchmarking references were available, therefore 50 internal samples, for which WGS or WES was performed together with CytoScan HD array or MLPA. In addition, GIAB NA12878 WGS and WES were used. The study was ongoing at the time of presentation, results will be announced later. **2. Mads Bak, Rigshospitalet, Department of Clinical Genetics (DCG)** For exome sequencing Library preparation: - TWIST, TruSightOne, AmpliSeq Variant callers: - VarSeq CNV(GoldenHelix) - CNVkit For genome sequencing: - Manta (high level of noise and FP) - CNVKit Focus of current work: - sensitivity & specificity; - include more SV callers; - set of control samples with known SVs. DCG performed an analysis of 100 WGS samples and established and internal database of SVs. **3. Tony Håndstad, OUS AMG** - In production: WES CNV calling with inhouse depth cased caller - Under development: WGS SV calling, targeted sequencing CNV calling - WGS SV calling based on Parliament 2 – adding other callers to see how they perform. Run, genotype, merge calls within 1000 bp (survivor) - Frameworks developed by DNA nexus - Runs and merges results of 6 callers - 3 h of wall-clock time and around 60 core-hours - Docker image available, but several bugs and challenges using it outside cloud/DNANexus

	- Parliament2 delivers quality values making it easier to balance sensitivity and precision - Only just started validation against GIAB SV v0.6 - Manta + delly / TIDDIT / survivor = cover most of what you can cover - Plans for annotation: Ensembl Variant Effect Predictor and frequency database (inhouse + gnomAD SV) - Targeted CNV calling with CoNVaDING (detection of small (single exon) CNVs in high coverage sequencing of targeted panels **4. Henrik Stranneheim Karolinska** - Work from Clinical Genetics at Karolinska presented - 68 cases diagnosed through arrays - Clinical implementation of calling SVs from WGS a. Detects all variants detected by array CGH b. Diagnostic rate increased from 10 to 27% c. Detects a wide range of structural variants with high accuracy and resolution d. Comprehensive genetic test in a clinical diagnostic setting e. SVs are confirmed through sanger sequencing - *Reference publication: Anna Lindstrand et al: from cytogenetics to cytogenomics: WGS as a first line test comprehensively captures the diverse spectrum of disease-causing genetic variation underlying intellectual disability (manuscript)*
Conclusion	Recent developments in characterization of structural variants, and development of benchmarking sets, enhance implementation of SV detection in clinical practice. Nevertheless, transfer of the technology from research environment to clinics is not trivial. During the workshop participants shared knowledge on implementation of SVs in clinic, and agreed to continue work in this direction. Mads Bak (Rigshospitalet) and Oleg Agafonov (DNV GL) volunteered to take a lead in the structural variants' activities. It was acknowledged that it would be of value to have an online platform for continuous knowledge sharing on SVs.

Table 6 Summary of discussions on SVs

Group / topic	Take-aways	Comments
Use of multiple callers	1. Need to use multiple callers; specialized on different things. Challenge is combining output. Merging is challanging. Tools: survivor, custom scripts 2. Combine short and long reads to give more power to the calls. Difficult to annotaet and pinpoint when using only short reads 3. Fuzzy boarders; same call identifed slightly differently, difficult to identify break points. 4. Difficult to merge result from multiple callers. Needs testing and verification. Create own tool? 5. Challenges with vcf file format; some tools not following specifications and working together.	• OUS work based on reports from DNA nexus, performing slightly different. Not compared with anything you can buy off the shelf. • Manta – really good fort the smaller ones • Delly – better for larger ones. Has also improved for the smaller ones. • CNVnator – specific about size able to call. Works really well. • Henrik: manta and CNVnator will get you far. • Different callers optimized for different sizes. Difficult to compare without gold standards.
Handling of false positive (FP) calls	- WGS is a prefferebe technology for calling SVs. - Use multiple callers and IGV to filter false positives. However can be challanging to use IGV to find all FP calls. Look at break points. Is there additional evidence for the variants? - Use databases of known / common variants. - Can you use other methods than short reads? - Long reads may better identify SV. Higher confidence.	
Verification and benchmarking	- Lacking truth datasets was a problem - Recently GIAB released a benchmark set for SV (HG002/NA24385) - Software: use multiple variant callers as they are developed for different purposes; combine output. - Verify with orthoganal technologies MLPA, aCGH. - No benchmark set for inversions - There is a need for new and better standards to enable sharing. - Share what you can!	- When missing truth – which consensus is the right one? - St Olavs: in house developed algrithm to detect CNVs.

Long read sequencing technologies	Potential of long read technologies: - Improved resoulution - Calling methylations (with some long read sequencing technologies) - Much better understanding of SV (do not rely on aligning reads) Challenges: - Integration short / long reads to get complete picture (however there is software out there) - DNA extracted limit the possible length of reads. Second extraction to get long molecules? - Cost of doing long reads –is it worthwhile? RNA seq - future potential for detections of fusions and isoforms	- When will long reads be feasible fo clinical implementation? - When we have the money to buy something. Not here now, perhaps 2 years into the future.
Challenges describing SVs by existing sequence variation nomenclature	- HGVS nomenclature is not designed for large and complex SV - Use ISCN nomenclature for complex SV?	
SVs interpretation	- Exclude repeat region - No database available - Validation: visual inspection with IGV - In-house database is extremely important (local db – looking at observation counts). - Second judgement is frequently needed due to poor quality.	
Annotation of SV	- VEP (will anotate anything across break-points) - Genotyping information from SV annotation varies,and should be improved - There is a need in a frequency database - In SciLifeLab an internal database is used - Need classification database - IGV is needed for inspection of SVs, IGV can be scripted to display snapshots of ROIs.	

Bioinformatic tools development

Working group lead: Kjell Petersen, University of Bergen and Tony Håndstad, Oslo University Hospital AMG

Bioinformatic tools development	•Hands-on technical workshop: Matchmaker Exchange •Variant prioritization update

Hands-on technical workshop: Matchmaker Exchange

Session lead:	Tony Håndstad, OUS AMG
Objective:	Familiarize participants with MME through sharing of practical experiences and hands-on experience with MME.
Workshop outline:	1) Setting the stage 2) Sharing of experiences from SciLifeLab 3) Practical introduction to MME

1)	**Setting the stage. Tony Håndstad, OUS AMG**	Tony introduced how the magic number in rare diseases diagnosis often is 2; finding the second case similar to the patient in question. Matchmaker Exchange is a tool made available by GA4GH, and the goal for this workshop was to become more familiar with MME, reducing perceived complexity, and to share experiences from OUS and SciLifeLab to enable MME implementation in the other labs.
2)	**Sharing of experiences from SciLifeLab. Chiara Rasi, SciLifeLab**	Chiara introduced MME (https://www.matchmakerexchange.org/) including current setup and rules for becoming an MME node (MME requirements: https://www.matchmakerexchange.org/assets/files/Matchmaker%20Exchange%20Service%20Requirements_March2019.pdf). To join the MME network you can submit data to an existing node or create your own node. Phenotype information are given as HPO terms, and it is possible to include and exclude phenotypes in the search. SciLifeLab: PatientMatcher – https://github.com/Clinical-genomics/patientMatcher - Open source, not approved by MME yet - Python, MongoDB database - Implements the MME API - Accepts and returns patient data validated against MME JSON scheme 50 patients spanning 22 disorders included in the testing. Patient score = genotype score + phenotype score - Floating point number between 0 (no matching) and 1 (perfect match) - You can customize Genotype and Phenotype scores (→ their sum is 1)

	Genotype matching algorithm - Only based on genotype features - Default max GT score is 0.75 - Max 3 variants / genes per submitted patient (not enforced in patient-Matcher, but recommended) – do not want to have too many matches as this would trigger a lot of notifications in the MME network Phenotype matching algorithm - Calculated matching into account feature (HPO) and disorders (OMIM) of patients - Disorder: 50% of phenotype score. - If no diagnosis is provided, phenotype score is only calculated based on similarity of HPO terms - Semantic similarity computation using HPO terms (simGIC score) The legal basis is consent from patient or data owner, and it is possible to withdraw patient data from the MME service. The PatientMatcher is designed to be able to include patient data from several different organizations (one can easily upload new patient cases via the API).
3) Practical introduction to MME. Tor Solli-Nowlan, OUS AMG[2]	The purpose of this workshop session was for people to get a better understanding of what the Matchmaker Exchange does, how to use it, and what is required to create a new Matchmaker node of your own. Since Matchmaker consists of specifications, but leaves the actual implementation up to the individual nodes, the workshop used two different implementations: 1. patientMatcher - https://github.com/Clinical-Genomics/patientMatcher o Uses on Python 3.6 and MongoDB o Written by Chiara Rasi at SciLifeLab o Designed to integrate with Scout 2. mme-async - https://gitlab.com/ousamg/mme-async o Uses python 3.7, PostgreSQL, Celery and Redis o Written by Tor Solli-Nowlan at OUS o Designed to be integrated with Ella in the secure computing environment TSD (a more secure environment which also complicates setup). o Not fully Matchmaker compliant, as responses cannot be sent synchronously due to security restrictions The goal was to be able to send queries, see responses to those queries, and add/delete patients using both systems. It's important to note that while there is specification that all implementations need to adhere to, there is also variability in how they do so. Scoring methods will vary from node to node, and some may provide additional fields that others do not. For example, patientMatcher includes the specific _genotype and _phenotype scores in addition to the required overall patient score. The workshop participants were provided an IP address, username and password to access a VM that had been pre-configured with docker, both implementations and some conveniences for working with them.

[2] An outline of the MME workshop is available at https://gitlab.com/ousamg/matchmaker-exchange-workshop

	After setup and configuration, the group used a quiz created by Chiara Rasi on www.classmarker.com with a number of exercises to get used to working with the API.

Variant prioritization update

	**Session lead:**	Kjell Pettersen, University of Bergen
	Objective:	Inform/update all participants on activities and status on previous activities, including preparing a synthetic variant data set.
Key information	Since the previous NACG workshop in Copenhagen, the major NACG progress on VP has been on collecting and summarizing our work stream's activities. The information is available in this location: https://tinyurl.com/NACG-VP-2018	
Conclusions	A code base exists, and a good collection of use case examples have been gathered to start off activities on VP. The form and shape of activities can be varied; there are opportunities for virtual hackathons, student projects etc., in addition to the regular NACG WSs.	

Vehicles for data sharing

Working group lead: Henrik Stranneheim, SciLifeLab

Vehicles for data sharing	• Trusted Variant eXchange (TVX)

The Trusted Variant eXchange (TVX)

Session lead:	Stephen McAdam, DNV GL
Objective:	Updates from preparations for beta testing of the TVX that enables secure sharing of variant classifications and evidence between trusted partners.

Key information:

To gauge interest in sharing of variant classification data, Stephen used a digital tool to query the audience, on a scale from 0 (strongly disagree) to 5 (strongly agree), about impact of widescale sharing of clinical variant classification data to improve

- patient safety and quality of services (4.5)
- Efficiency of services (4.4)

Current data sharing practices and channels were investigated (Figure 5), as well as current factors limiting data sharing (Figure 6) and levels of data sharing that would provide value to the participant labs (Figure 7).

Stephen then introduced DNV GL as an independent foundation providing independent 3rd party services related to standards, assessments and risk management, where the TVX represents piloting of a new role to enable data sharing as a party disinterested to the data themselves.

- TVX started with BigMed funding and workshops in NACG in a first attempt to share anonymous data.
- TVX enables sharing of classification data in a simple way that provides opportunities for quality control and variant classification management as well as benchmarking and harmonization.
- A main challenge has been clarifications on the legal basis for sharing of classification data. A DPIA has been developed with input from BigMed, OUS and UiO. Currently, there is a process in the Norwegian Directorate for Health and Care to review the issue of classification data and privacy.
- The risk assessment identified free text fields as triggering medium risk for reidentification of patients, and these are therefore put on hold in the first release but can potentially be included later if risk can be reduced through other mechanisms such as standardized text options.

Next steps:	-	TVX converted to MVP and Beta Testing to kick off after summer. Laboratories intending to be involved in the beta testing includethe Danish Breast Cancer Consortium, Oslo University Hospital and Scilifelab/Karolinska Hospital.
	-	Audience agreed that at the Nordic level (over national or NACG level) the secure sharing of anonymous clinical variant classification data would create value for their labs.

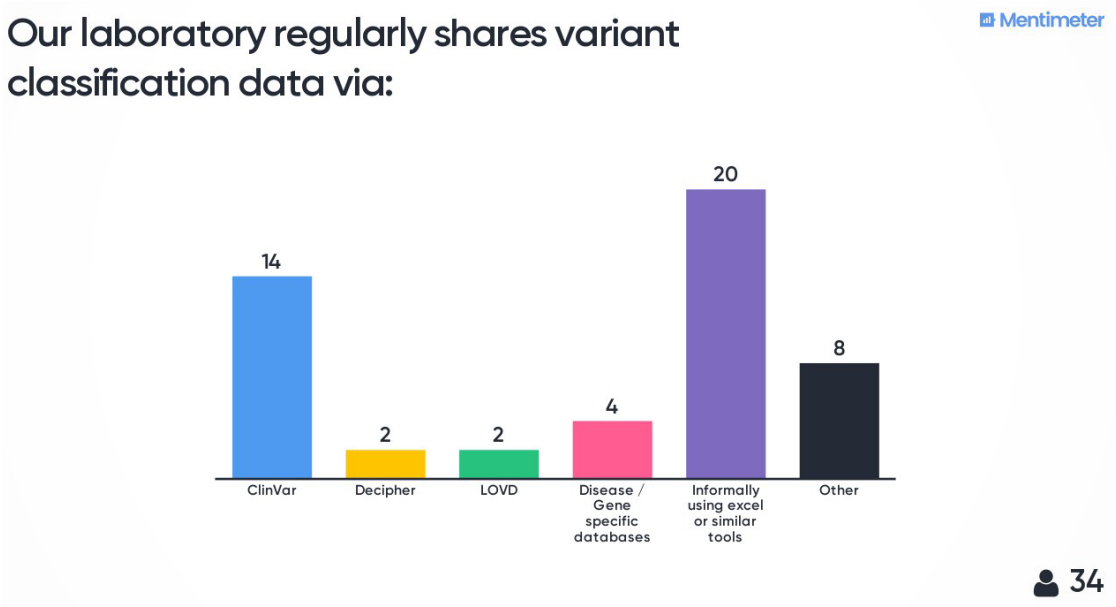


Figure 5: Current data sharing practices

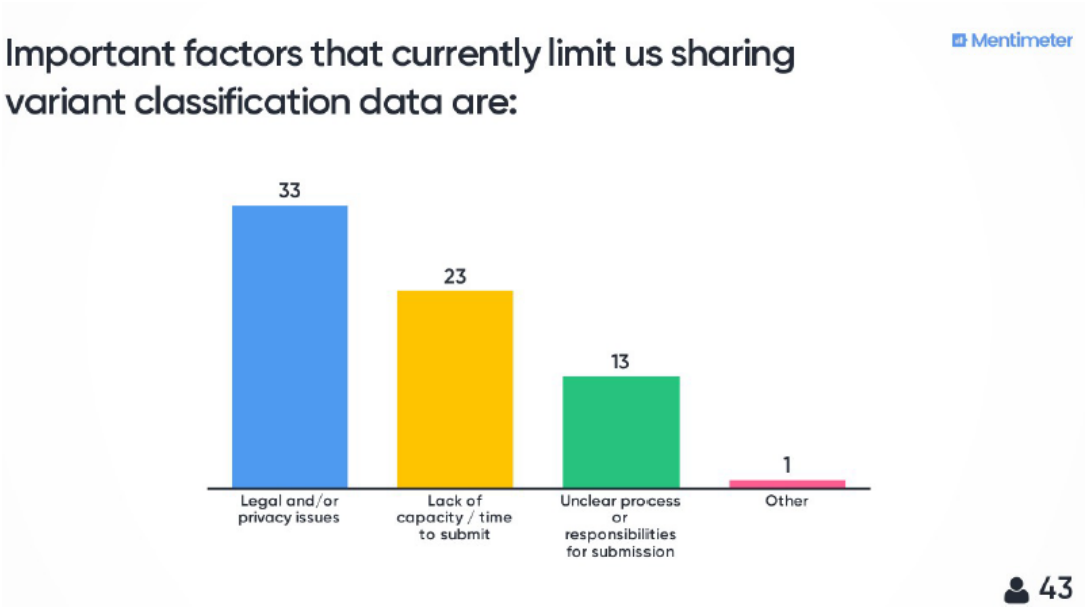


Figure 6 Factors limiting data sharing

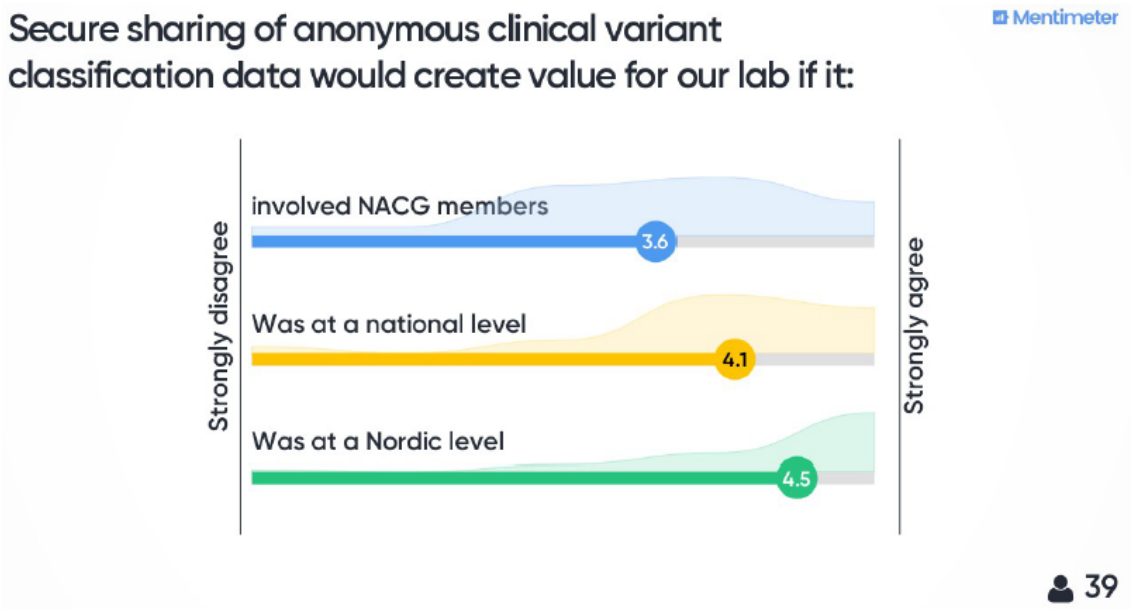
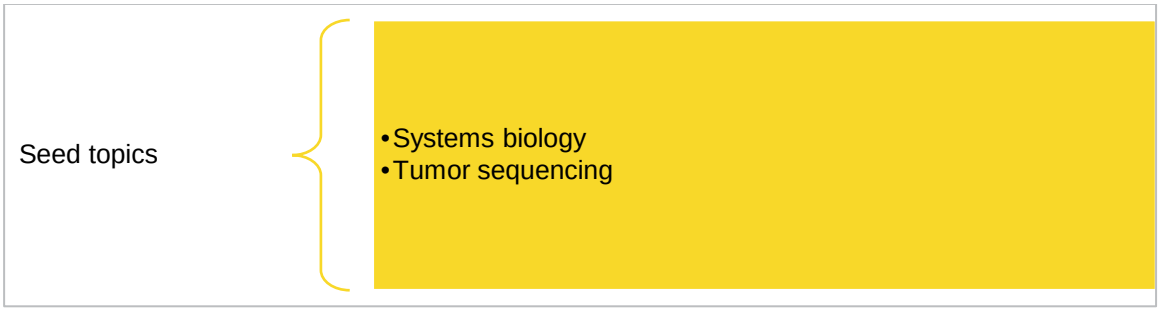


Figure 7 Levels of data sharing that would provide value to the participant labs.

NACG seed topics



Systems biology beyond the genome

Session lead: Henrik Stranneheim

Objective: Discuss systems biology as a topic and level interest for further NACG activities

Key information

Henrik introduced systems biology as a technology driven opportunity.

Next-generation sequencing is already implemented in clinical utilisation, as reduction in sequencing time and costs has enabled the transition from reference genome via population scale studies to individual genomes. Massive parallel WGS covers a variety of genetic variations including SNVs, INDELs, SVs and MT genome analysis. Missing pieces in WGS include

- Hard to call regions (centromeres, telomeres, low-complexity regions)
- Hard to call variants in window between SNVs/INDELs and SVs
- Interpreting regulatory regions:
    - Introns
    - 5'-UTRs, 3'-UTRs
    - Intergenic regions
    - Synonymous variants

Henrik advocated for the systems biology approach, adding layers of information about biological variations to the patient analysis, and introduced examples of information that could be added and patient cases where additional layers of information were critical for solving the cases.

At SciLifeLab, although not yet put into clinical routine, there is an opportunity to use the Scout tool to connect information such as:

- DNA (Snv/Indels, SV, Mosaicism)
- RNA (Mono allelic expression, Reference assembly, Transcript abundance, Fusion transcripts)
- Clinical (Pedigree, HPO)
- Biochemistry (Pathway, Protein function)

Tumour sequencing

	**Session lead:**	Maria Rossing, Rigshospitalet and Valtteri Wirta, SciLifeLab
	Objective	Discuss tumour sequencing as a topic and level interest for further NACG activities on somatic sequencing.

Key information:

Maria and Valtteri introduced somatic sequencing to the workshop participants to understand overlapping activities and interest in developing this track further in future NACG activities.

Half of audience reported working in somatic analysis (approx. 15 persons)

- Helsinki: Geneticist interpretation and reporting of somatic analysis (Three panels)
- FIMM: Exome sequencing on leukemia patients
- Rigshospitalet: initial experimental phase with BRCA, Ovarian, pediatrics, etc.
- OUS AMG: BRCA genes, biomarker parameters, molecular pathology currently in this and AMG serves as a supportive role (just starting)
- Aarhus: three patients (uknown primary cancer, looking for phase I trials, and pediatrics) WES, RNAseq (in house classifier), looking to cut down repetitive sequencing.
- SciLifeLab: all clinically relevant fusions put into design (also BRCA), design to capture copy number and genes to be relevant for this for solid tumors.

Somatic analysis pipeline development was described as a moving target.

A pre-workshop between DNV GL and SciLifeLab had concluded opportunities for work with NACG on:

1. Harmonization /standardization / quality assurance of bioinformatic workflows
2. Efforts needed to collect, organize, share and analyze data on
    a. genomic profile of tumour,
    b. therapy, and
    c. outcomes short and long term
3. Legal track – Nordic view on what is shareable

Other ideas possible to explore:

1. MSI Panel
2. Tumor Mutation Burden
3. Copy Number Analysis
4. Tier Classification Somatic: how to?
5. Tumor clinical report format
6. Methylation assay
7. Fusion genes
8. RNA seq /array
9. NGS panels
10. WGS for signatures on tumor samples

Discussion & conclusion

For NACG to extend focus to include somatic analysis, it was agreed that it would be key to identify and engage the right labs and people, such as molecular pathologists.

It was suggested to do some initial work to define the scope and initial activities for NACG in somatic analysis space through establishing a somatic sequencing working group and pilot activities to demonstrate / probe interest.

The participants expressed interest in including this topic in NACG, specifically in terms of how to share data and the legal issues implied; would it be possible for NACG to come up with basic statements for the need to share data?

Conclusions:	Maria and Valtteri will take lead in completing a mapping exercise ahead of next NACG workshop to find contact persons and identify topics. Contact should be initiated with legal departments to find the right people to be involved in further potential NACG legal work streams. The Steering Committee will work on integrating legal activities across working streams.

Conclusions and next steps

In line with the organization's Constitution, the NACG will continue to work to include more stakeholders to clinical genomics in the Nordic countries in the meetings and encourage them to seek membership in line with governing documents available at the organization's website.

The NACG working groups and their focuses should be continuously re-evaluated to ensure that relevant topics from the group are prioritized and resulting in learnings and outcomes that are useful to clinical work processes for the membership. The membership is encouraged to continuously nominate seed topics to the Working Group leads, the Steering Committee or to the Secretariat. Current active working groups and responsible working group leads include:

Enhancing quality of data and processes	• Sharmini Alagaratnam, DNV GL • Kaisa Kettunen, HUSLAB & FIMM
Bioinformatic tools development	• Tony Håndstad, OUS AMG • To be appointed
Structural variants	• Oleg Agafonov, DNV GL • Mads Bak, Rigshospitalet
Tumor sequencing (exploring)	• Maria Rossing, Rigshospitalet • Valtteri Wirta, SciLifeLab

It was agreed that the working group "Vehicles for data sharing" is put on hold and can be revitalized later. The NACG will continue to seek opportunities for joint projects.

Next NACG meeting

The next NACG meeting will take place in Høvik, Oslo. A NACG symposium on the 19. - 20. November will be followed by a NACG workshop 20. - 21. November 2019. The events will be announced to the NACG membership per email and on https://nordicclinicalgenomics.org/.

As part of the process of exploring the inclusion of a legal work stream in the NACG organisation, a legal symposium on topics relevant to clinical genomics will be held at the same venue 18. – 19. November 2019.

Table 7 Outline of November 2019 NACG relevant events

	Monday 18th	**Tuesday 19th**	**Wednesday 20th**	**Thursday 21st**
Morning		Legal symposium	NACG symposium	NACG workshop
Afternoon	Legal symposium	NACG symposium	NACG workshop	

Appendix 1: Agenda

Agenda – 6. May 2019

Parallel 1: Lecture room 3 - Biomedicum I (Haartmaninkatu 8)

Time	Session	Session lead
General sessions		
12:00	Welcome and NACG updates	Dag Undlien, OUS AMG & Guro Meldre Pedersen, DNV GL
13:00	Lunch	
13:45	Key updates from the Nordic countries	NACG Steering Committee
Working group: Vehicles for sharing Lead: Henrik Stranneheim		
14:15	Update on the Million European Genomes Alliance (MEGA)	Valtteri Wirta, SciLifeLab
14:35	Trusted Variant eXchange (TVX) - beta testing of secure sharing of variant classifications between trusted partners.	Stephen McAdam, DNV GL
General sessions & seeds for new NACG topics		
14:45	What is systems biology and how can the NACG forum collaborate on this?	Henrik Stranneheim, SciLifeLab
15:00	Guided tour of HUSLAB / FIMM (note: parallel session on tumor sequencing)	Janna Saarela & Kaisa Kettunen, HUSLAB & FIMM

Shift to Seminar room 1-2 – Biomedicum I (Haartmaninkatu 8)

16:00	A two-dimensional system for variant classification developed by ESHG to improve the ACMG system	Gunnar Houge, ESHG President
16:30	Benchmarking of bioinformatics tools - session tbc	To be confirmed
17:00	Structural variants	Oleg Agafonov, DNV GL
18:30	End of day 1	
18:30	*NACG Steering Committee meeting (Meeting room D307a - Biomedicum II)*	

Parallel 2: Seminar room 3 - Biomedicum I (Haartmaninkatu 8)

General sessions & seeds for new NACG topics		
15:00	Tumor sequencing – a future NACG topic?	Maria Rossing, Rigshospitalet & Valtteri Wirta, SciLifeLab

Agenda – 7. May 2019

Parallel 1: Seminar room 3 – Biomedicum I (Haartmaninkatu 8)

Working group: Enhancing data quality and processes Lead: Sharmini Alagaratnam, DNV GL & Kaisa Kettunen, FIMM		
9:00	Workshop: Phenotype information in genetic analysis	Sharmini Alagaratnam, DNV GL & Kaisa Kettunen, HUSLAB & FIMM
11:00	Mini-hackathon: Collaborative development of reanalysis strategy	Sharmini Alagaratnam, DNV GL & Kaisa Kettunen, HUSLAB & FIMM
12:00	Lunch	
13:00	Plenary discussion: Collaborative development of reanalysis strategy	Sharmini Alagaratnam, DNV GL & Kaisa Kettunen, HUSLAB & FIMM
14:00	Variant classification benchmarking	Dag E. Undlien, OUS & Stephen McAdam, DNV GL
14:30	Clinical reporting – redesigning the process	Sharmini Alagaratnam, DNV GL
General sessions		
15:00	NACG working groups ideation	Guro Meldre Pedersen, DNV GL
	Update from Steering Committee	Dag Undlien, OUS AMG
16:00	End of day 2	

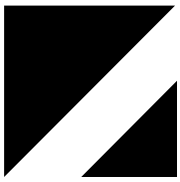
Parallel 2: Meeting room D307a - Biomedicum II (Tukholmankatu 8 U)

Working group: Bioinformatics tools development Lead: Kjell Petersen, University of Bergen & Tony Håndstad, Oslo University Hospital AMG		
9:00	Hands-on technical workshop: Matchmaker Exchange	Kjell Petersen, UiB & Chiara Rasi, SciLifeLab & Tony Håndstad, Svein Tore Seljebotn & Tor Solli-Nowlan, OUS
12:00	Lunch	
13:00	Hands-on technical workshop: Matchmaker Exchange – continued	
14:00	Variant prioritization update	Kjell Petersen, UiB & Tony Håndstad, OUS AMG
14:15	Nordic data sharing in the research domain - NeIC Tryggve, federated EGA, Elixir and other initiatives	Antti Pursula, Program director at CSC and project manager for NeIC Tryggve
15:00	End of parallel 2 → join general sessions	

Appendix 2: List of participants

Country	Organisation	First name	Last name
Denmark	Aarhus University Hospital	Michael	Knudsen
Denmark	Aarhus University Hospital	Ole Halfdan	Larsen
Denmark	Aarhus University Hospital	Piotr	Starnawski
Denmark	Aarhus University Hospital	Søren	Vang
Denmark	Rigshospitalet	Ane Yde	Schmidt
Denmark	Rigshospitalet	Filipe	Vieira
Denmark	Rigshospitalet	Mads	Bak
Denmark	Rigshospitalet	Maria	Rossing
Denmark	Rigshospitalet	Peter	Johansen
Denmark	Rigshospitalet	Ulf	Birkedal
Finland	CSC / NeIC	Antti	Pursula
Finland	Euformatics	Allyana	Thomas
Finland	Euformatics	Christophe	Roos
Finland	Euformatics	Jukka	Matilainen
Finland	FIMM	Henrikki	Almusa
Finland	FIMM	Johanna	Lehtonen
Finland	FIMM	Maija	Lepistö
Finland	FIMM	Sari	Hannula
Finland	FIMM / HILIFE / UH	Pekka	Ellonen
Finland	FIMM / University of Helsinki	Janna	Saarela
Finland	Helsinki University Hospital	Anna-Kais	Anttonen
Finland	Helsinki University Hospital	Emma	Andersson
Finland	Helsinki University Hospital	Heli	Nevanlinna
Finland	Helsinki University Hospital	Kaisa	Kettunen
Finland	Helsinki University Hospital	Matti	Kankainen
Finland	HUSLAB	Anu	Närhi
Finland	HUSLAB	Eevi	Kaasinen
Finland	HUSLAB	Maarit	Lappalainen
Finland	HUSLAB	Minna	Pöyhönen
Finland	HUSLAB	Nina	Horelli-Kuitunen
Finland	HUSLAB	Pia	Alhopuro
Finland	HUSLAB	Reetta	Vainionpää
Finland	HUSLAB	Tarja	Niini
Finland	Sitra, the Finnish Innovation Fund	Pia	Heikkurinen
Iceland	Landspitali - University of Iceland	Jon J.	Jonsson
Norway	DNV GL	Bobbie	Ray-Sannerud
Norway	DNV GL	Guro Meldre	Pedersen
Norway	DNV GL	Oleg	Agafonov
Norway	DNV GL	Sharmini	Alagaratnam
Norway	DNV GL	Stephen	McAdam
Norway	Haukeland University Hospital	Gunnar	Houge

Norway	Oslo University Hospital	Beate	Skinningsrud
Norway	Oslo University Hospital	Cathrine	Nordhus
Norway	Oslo University Hospital	Dag	Undlien
Norway	Oslo University Hospital	Eidi	Nafstad
Norway	Oslo University Hospital	Morten C.	Eike
Norway	Oslo University Hospital	Oda	Bakken
Norway	Oslo University Hospital	Svein Tore	Seljebotn
Norway	Oslo University Hospital	Tony	Håndstad
Norway	St. Olavs Hospital	Christa	Schmidt
Norway	St. Olavs Hospital	Maren F.	Olsen
Norway	St. Olavs Hospital	Silje	Vean
Norway	The Norwegian Directorate of Health	Grethe	Foss
Norway	University of Bergen	Kjell	Petersen
Norway	University of Oslo	Gjertrud Bøhn	Mageli
Norway	University of Oslo	Tom	Sørlie
Sweden	Karolinska Institutet	Hassan	Foroughi
Sweden	Karolinska University Hospital	Nicole	Lesko
Sweden	SciLifeLab	Adam	Rosenbaum
Sweden	SciLifeLab	Anders	Jemt
Sweden	SciLifeLab	Chiara	Rasi
Sweden	SciLifeLab	Henrik	Stranneheim
Sweden	SciLifeLab	Valtteri	Wirta
Sweden	Twist Bioscience	Christofer	Flood



Nordic Alliance for Clinical Genomics