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Synthesis of the scientific contributions of the ECOgenomics conference 2021

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We are indebted to the European “Solve-RD” project for the opportunity to build an international network of economic researchers with an interest in genomic medicine. We are also grateful to the University of Burgundy, in particular to its President, Professor Vincent Thomas, who kindly accepted to open our conference. We thank both our centre for human sciences, the *Maison des Sciences de l’Homme* and our research centre, the *Laboratoire d’Economie de Dijon*, for their support throughout the project. Our thanks go also to our university’s digital media services, especially Eric Paul, who made it possible to hold the event by videoconference. Finally, we would like to thank our scientific and organising committees, and all the conference speakers and participants.

Foreword

The economic analysis of genomic medicine is one of two main lines of research of the Health Economics Team of the *Laboratoire d'Economie de Dijon*. Within the Université de Bourgogne-Franche-Comte (uBFC), genomic medicine is a topic that combines the human and social sciences with the Health line of research. The Health Economics Team is a member of FHU Translad and works with researchers from other research units at uBFC such as the Inserm U866 LNC Research Centre (GAD and Team 4). Despite the significance of its societal challenges, genomic medicine remains poorly developed as an aspect of Health Economics in France. The work of the Health Economics Team of the *Laboratoire d'Economie de Dijon* is innovative and has given rise to publications and oral communications. This topic is also consistent with the structuring of the research team's work around the dissemination of technological and organisational innovations in healthcare. For more about the Health Economics Team, click here.

The Health Economics Team's participation in the SOLVE-RD project is part of WP3 "Changing patient lives: translation to the clinic", Step 6 "Clinical utility". WP3 is shared with Lissenka Vissers (Radboud UMC, NL) who was in charge of Task 3.2 "NGS clinical utility and cost-effectiveness analysis".

As part of this task, this participation in the Solve RD project is described in objective A: "Perform a systematic review to gain insight into currently ongoing clinical utility studies for genomics strategies and their conclusions". Three consecutive approaches are planned:

- identify through a systematic review of literature, the consultation of public registries of ongoing studies and experts questioning the researchers on the clinical utility and efficiency of WES/WGS, published or in progress;
- organise a 2-day workshop in order to meet teams concerned by these questions and discuss their research and ours;
- provide a synthesis of the studies presented during the workshop.

Within the Health Economics Team at the LEDi, the conference was more specifically prepared and organised by Christine Peyron and Aurore Pélissier. Camille Level was recruited specifically to contribute to the project as a research assistant (*ingénieur d'étude*) (over an 18-month period).

This synthesis provides a presentation of each session of the conference. The program is presented in annex 1.

Scientific synthesis

1. Lectures

Although genomic medicine is experienced nowadays as a revolution by geneticists,[1] the spread of high-throughput sequencing technologies in healthcare systems raises important queries and runs up against many challenges. The three plenary sessions were designed to cast light on these through three disciplines in turn: genetics (Plenary 1), health economics (Plenary 2) and law (Plenary 3).

2.1 Plenary 1

"On the impact of diagnostic rare-disease research on the diffusion of genomic medicine" presented by Holm Graessner, 26 May 2021, 4.00 p.m. (GMT+2).

Access to diagnosis is a major issue for rare-disease patients today. Although, when considered individually, these diseases are certainly rare,[2] they nevertheless affect 30 million patients in Europe and 300 million patients worldwide.[3] Among them, 1 in 2 patients do not have an aetiological diagnosis for the disease they suffer from and for 25% of rare-disease patients, the diagnosis delay ranges from 5 to 30 years (Eurordis, 2009)[4]. The difficulty in diagnosing rare diseases leads to a prolonged diagnostic odyssey for many patients, sometimes with diagnostic errors, with difficulties in accessing specialised and adapted care, in obtaining treatment if any exists, and in securing medical and institutional recognition of the disease and its consequences.

In this context, high-throughput sequencing technologies have opened up an opportunity in recent years to improve access to diagnosis for patients suffering from rare diseases: diagnostic yields are significantly higher than with traditional analyses to date,[5] while time and costs of analysis fall drastically (McKinsey Global Institute, 2013[6]).

Even so, the spread of these technologies runs up against a number of challenges, especially in terms of healthcare provision. These challenges concern the organisation of health cover and especially the means of coordination among health professionals but also the possibilities for collecting, storing, sharing and re-analysing data (through the formation of biobanks) or the formation of treatment repertories that are under trial (like Treatabalome developed as part of the SOLVE-RD project). These elements, which may serve as levers for or obstacles to the spread of genomic medicine, are closely related to the regulation and financing arrangements put in place by the lawgiver nationally and across

[1] https://www.sfmpp.org/medecine-predictive/ (accessed 1 July 2021).
[2] A disease is rare if it affects fewer than one person in 2000. 72% of rare diseases are genetic and 70% start in childhood (https://www.eurordis.org/content/what-rare-disease, accessed 1 July 2021).
3 https://www.eurordis.org/content/what-rare-disease (accessed 1 July 2021).
[4] Eurordis. 2009. "The voice of 12,000 patients. Experiences and expectations of rare disease patients on diagnosis and care in Europe".
[5] In the diagnosis of heterogenous genetic diseases, exome sequencing reaches a diagnostic yield of more than 35%, making it at present the most powerful individual diagnostic test by far for such situations (Clark *et al.*, 2018). Proof-of-concept studies suggest that whole genome sequencing could lead to a diagnostic yield of 60% among individuals with development abnormalities involving intellectual deficiency (Gilissen *et al.*, 2014).
6 McKinsey Global Institute (2013). Disruptive technologies: Advances that will transform life, business, and the global economy. *McKinsey & Company*, 176p.

Europe. This is the background to Holm Graessner's lecture illustrating all of these aspects and presenting the European Solve-RD projects and Germany's Translate-NAMSE project.

Holm Graessner has been Managing Director of the Rare Disease Centre, since 2010, at the University and University Hospital Tübingen, Germany (www.zse-tuebingen.de). He is Coordinator of the European Reference Network for Rare Neurological Diseases (ERN-RND) www.ern-rnd.eu. In the Coordinator's Group of the European Reference Networks, he co-leads the joint – ERN coordinators and Board of Member States – working group on Integration. Together with Olaf Riess, he coordinates the H2020 Solve-RD project on "Solving the unsolved rare diseases" www.solve-rd.eu. He received his PhD "Summa cum laude" in 2004 and, then, he obtained his MBA degree in 2008. Since 2003, he has coordinated and managed more than 10 EU funded collaborative projects. The main focuses of these projects are rare and neurological diseases. The projects include EUROSCA, MEFOPA, SENSE-PARK, MULTISYN, NEUROMICS and PROOF.

2.2 Plenary 2

"What's important in the delivery of healthcare… and what does this mean for valuing Next Generation Sequencing?" presented by Mandy Ryan, 27 May 2021, 4.00 p.m. (GMT+2).

The notion of value is central in economics and has always been the subject of debate. In the context of genomic medicine, health economists are repositioning this debate by questioning in particular the value of this new technology, of the care it implies both upstream and downstream of genetic testing, of the information it produces and of the consequences it is likely to have for patients and their relatives.

In this sense, genomic medicine implies going beyond the mere consideration of clinical utility as a measure of value. For health economists, this means going beyond the traditional framework of medico-economic evaluation. Medico-economic evaluation compares the costs of a technology with its benefits. These benefits are measured either by an indicator expressed in physical units and reflecting a biological, clinical or pharmacological outcome, or by an indicator that makes it possible to capture an effect on life expectancy in terms of the number of years of life gained and quality of life (QALY; Le Pen and Lévy, 2018[7]). The utility of high-throughput sequencing technologies goes beyond the impact on mortality, morbidity or disability (Foster *et al.*, 2009[8]). Utility also includes non-medical dimensions and psychological or emotional aspects (Lee *et al.*, 2010[9]; McAllister *et al.*, 2007[10]; Pélissier *et al.*, 2016[11]).

Thus, economists are increasingly seeking to estimate the preferences of the various stakeholders (patients, health professionals, regulators, citizens) – in particular by means of discrete choice

[7] Le Pen C et Lévy P. (2018). L'évaluation médico-économique. Concepts et méthodes. LGM Sciences, 177p.
[8] Foster MW, Mulvihill JJ, Sharp RR. (2009). Evaluating the utility of personal genomic information. *Genet Med*, 11(8): 570-4.
[9] Lee DW, Neumann PJ, Rizzo JA. (2010). Understanding the Medical and Nonmedical Value of Diagnostic Testing. *Value in Health*. 13(2): 310-14.
[10] McAllister M, Payne K, Nicholls S *et al*. (2007). Improving Service Evaluation in Clinical Genetics: Identifying Effects of Genetic Diseases on Individuals and Families. *J Genet Counsel*, 16(1): 71-83.
[11] Pélissier A., Peyron C., Béjean S. (2016). Next-generation sequencing in clinical practice: from the patients' preferences to the informed consent process. *Public Health*, 38, 157-9.

experiments – with the aim of highlighting the dimensions that influence the usefulness of high-throughput sequencing technologies. This is the purpose of Mandy Ryan's lecture.

Mandy Ryan is Director of the Health Economics Research Unit at the University of Aberdeen. Her research interests focus on taking a person-centred approach to valuation in health economics. She is best known for her work challenging the clinical approach to valuation that is often adopted by health economists and for developing alternative person-centred approaches. She introduced discrete choice experiments (DCEs) into health economics in the early 1990s and her research has applied DCEs in a wide range of contexts to take account of user preferences in the delivery of healthcare. She has recently been awarded funding by the Scottish Government to conduct an economic assessment of whether Scotland should adopt Whole Genomic Sequencing for the diagnosis of rare disorders. She will talk about her research going beyond clinical outcomes in the valuation of healthcare and consider its relevance to her work evaluating whole genomic sequencing.

2.3 Plenary 3

"Introducing NGS in healthcare: challenges for patients' rights and for Public Health?" presented by Emmanuelle Rial-Sebbag, 28 May 2021, 4.00 p.m. (GMT+2).

The spread of high-throughput sequencing technologies also raises questions about whether patients are in a position to give their informed consent and whether it is possible to actively seek out and disclose to patient's certain genetic information unrelated to the initial grounds for consultation, i.e. what are called secondary data.

Genetics is a complex discipline and patients often have limited knowledge of it. New sequencing technologies further increases this complexity. They can produce information that exceed the primary objective of the test; one then speaks of secondary data or incidental data depending on whether or not they are actively sought out. These results as a whole may be (i) more or less certain, (ii) more or less usable for setting about preventive actions or treatment, (iii) more or less hereditary and therefore of relevance to patients but also to their relatives. In this context, the question arises both of patients' informed consent and of the legitimacy of restricting the scope of information that can be sought and disclosed to patients. The scientific community is divided on this point: some geneticists think that one should only pass on to patients the result for the initial purpose for which the test was prescribed while others argue secondary data are useful and justify an active search for them and their disclosure to those patients who so consent. The American College of Medical Genetics and Genomics publishes to this end a pre-established list of 59 medically actionable genes (Green *et al.*, 2013[12]; Kalia *et al.*, 2017[13]). In France, the *Société Française de Médecine Prédictive et Personnalisée* recommends disclosure to patients concerning 36 genes related to cancerology (Pujol *et al.*, 2018[14]). Recently a working group of the *Agence de la Biomédecine* has come out against such systematic analysis of

[12] Green RC, Berg JS, Grody WW *et al*. (2013). ACMG recommendations for reporting of incidental findings in clinical exome and genome sequencing. *Genet Med*, 15(7): 565-574.

[13] Kalia SS, Adelman K, Bale SJ *et al.* (2017). Recommendations for reporting of secondary findings in clinical exome and genome sequencing, 2016 update (ACMG SF v2.0): a policy statement of the American College of Medical Genetics and Genomics. *Genet Med*, 19(2): 249-55.

[14] Pujol P, Vande Perre P, Faivre L *et al.* (2018). Guidelines for reporting secondary findings of genome sequencing in cancer genes: the SFMPP recommendations. *Eur J Hum Genet*, 26(12): 1732-42.

secondary data on a pre-established list of genes unrelated to the initial indication (Isidor *et al.*, 2019[15]).

In her lecture, Emmanuelle Rial-Sebbag enquires into these two debates by tracing more specifically the history of ethical thinking since the rise of genetics after the Second World War. She emphasises the strains that may be found between individual and collective interests; questions that also reflect research by health economists particularly when they look both to reveal the preferences of the various stakeholders (patients, health professionals, citizens) and to highlight the points of agreement and disagreement.

Emmanuelle Rial-Sebbag, Lawyer, Graduate in health law (Bordeaux, France), Ph.D in Health Law (European mention, University Paul Sabatier Toulouse). She is Director of research in health law and bioethics at the Inserm. She is the leader of a multidisciplinary team, Health innovations' trajectories: bioethical challenges and impact on public health, at the Inserm/Paul Sabatier University 1027 Unit. She is an associate lecturer in bio-law and bioethics at the University of Medicine in Toulouse (Purpan). She is involved in several research projects at national, European and international level, on the topics of biobanking and personal data, innovative therapies, biomedical research involving human beings, genetic testing and Big Data. She was the coordinator of the EUCelLEX project (FP7 2013-2016, Cell-based regenerative medicine, new challenges for EU legislation and governance, GA 601806, https://www.eucellex.eu/). She holds the UNESCO Chair "Ethics, Science and Society" (https://chairee2s.hypotheses.org/).

2. Plenary sessions

2.1 Session A

"Implementation of Exome and Genome Sequencing: Who Has Access, Who Pays, and What are Solutions? for Implementation Challenges?" - Session organised by Deborah Marshall, with the participation of Kathryn Phillips, Sarah Wordsworth and James Buchanan, 28 May 2021, 5.00 p.m. (GMT+2).

Genomic medicine is spreading and gradually transforming our health systems. Genomic medicine enlarges the potential uses of genetic testing in medicine (McCarthy *et al.*, 2013[16]) at a drastically decreasing cost (McKinsey Global Institute, 2013). Thus, the implementation of genomic medicine in clinical practice is accelerating. US$ 4 billion worth of initiatives supported by 15 countries[17] have been identified by Stark *et al.* (2019)[18] for the period 2013–19. That number is growing: in July 2021, the Global Genomic Medicine Initiative[19] listed 68 initiatives in 36 locations. The experiences are

[15] Isidor, B., Nizon, M. & Vincent, M. (2018). Données secondaires : un enjeu scientifique et éthique. In: E. Hirsch (éd.), Traité de bioéthique : IV - Les nouveaux territoires de la bioéthique, pp. 261-70. Toulouse: ERES.

[16] McCarthy JJ, McLeod HL, Ginsburg GS. (2013). Genomic medicine: a decade of successes, challenges, and opportunities. *Sci Transl Med*, 5(189).

[17] Australia, Brazil, Canada, China, Denmark, Estonia, France, Japan, Netherlands, Qatar, Saudi Arabia, Switzerland, Turkey, UK, USA.

[18] Stark et al. (2019). Integrating Genomics into Healthcare: A Global Responsibility. *The American Journal of Human Genetics*, 104(3), 13-20.

[19] https://www.genomicspolicy.org/catalogue-introduction (accessed 1 July 2021).

nevertheless very varied. According to Stark *et al.* (2019) three types of national approach to support the development and dissemination of genomic medicine can be distinguished. The approaches differ in their coverage objective, funding modalities and infrastructure development. Session A thus offers an illustration of this for three countries: Canada, the UK and the USA.

2.2 Session F

"Perspectives on Genomic Medicine: Between Public Policy and Citizens." 28 May 2021, 6.30 p.m. (GMT+2).

The deployment of genomic medicine in healthcare systems involves many stakeholders (Burton *et al.*, 2009[20]). No fewer than 14 stakeholders are identified by Mitropoulo *et al.* (2020)[21]: 1. Academic and research organisations, 2. Private and public genetic laboratories, 3. Physicians, 4. Payers, 5. Genetics and genomics professional associations, 6. Pharmaceutical and biotechnology corporate entities, 7. National Medicines Organisation, 8. Ministry of Health, 9. National Bioethics Council, 10. Various religious organisations and the church, 11. Public and private providers in the field of genomics and personalised medicine, 12. Pharmacy practices, 13. Consumers and citizens, 14. Press and the media.

The dissemination of genomic medicine in our healthcare systems will depend in particular on the preferences and expectations of these stakeholders. They may act as levers for or barriers to the spread of genomic medicine. The literature on views, expectations and preferences as to genomic medicine is growing and sessions B2 and C1 are examples of this. The aim is, of course, to reveal the preferences of each of these stakeholders but also to highlight commonalities and differences in order to identify issues that could influence the diffusion of genomic medicine in different contexts. In this session, Samantha Pollard focuses on the views of patients and Canadian society through a qualitative study on cancer. Chloé Mayeur presents the results of a large-scale survey of Belgian citizens. And, finally Wendy Ungar explains how Ontario is trying to develop an approach to produce HTA evidence in order to rapidly implement these technologies in the health system while trying to consider the objectives of the different stakeholders. Each presentation shows that despite the popularity of these technologies, it can be difficult to reconcile different perspectives, objectives and timeframes to ensure ethical and equitable access for patients and the general population.

3. Parallel sessions

2.1 Session B1

"How to assess the cost effectiveness of WES/WGS?" 27 May 2021, 5.10 p.m. (GMT+2).

The medico-economic evaluation of next-generation sequencing technologies faces methodological challenges whether one is interested in measuring the effectiveness, or more broadly the benefits of these technologies, or their cost. However, this evaluation is essential to justify and guide the dissemination of these technologies and to help public decision-making. Evaluations are multiplying

[20] Burton, H., Adams, M., Bunton, R., Schröder-Bäck, P. (2009). Developing Stakeholder Involvement for Introducing Public Health Genomics into Public Policy. *PH*G. 12, 11-19.
[21] Mitropoulo, C., Politopoulou, K., Vizikis, A., Patrinos, G.P. (2020). Assessing the stakeholder landscape and stance point on genomic and personalized medicine. In: Applied Genomics and Public Health. Ed. Patrinos G.P. Elsevier, Academic Press. 404p.

with various methodologies and results that allow us to begin to make progress on how to evaluate these technologies and to establish reference values. Camille Level analyses the heterogeneity of recently published studies and the difficulty of comparing their results to produce a quality meta-analysis. Based on two prospective studies currently being conducted in France on the care of patients with intellectual disabilities, Catherine Lejeune highlights the contribution of multidisciplinary evaluations and qualitative studies. Michael Abbot shows that it is not easy to compare costs between WGS or WES and standard care. He presents the results obtained in Scotland on the costs of WGS and WES for patients with rare diseases, but highlights the great variability in the costs of the standard care diagnostic pathway, which are highly dependent on the patient diagnostic odyssey.

Systematic review or meta-analysis: how to consider the high heterogeneity of studies to access the clinical utility of WGS/WES? – Camille LEVEL (speaker)
Genomic testing in the field of developmental disorders: the added value of human and social sciences studies – Catherine LEJEUNE (speaker)
Next Generation Sequencing for the next generation of patients: building the economic evidence base – Michael ABBOTT (speaker)

2.2 Session B2

"Preferences, expectations, representations of patients, professionals and general population" 27 May 2021, 5.10 p.m. (GMT+2).

The literature on preferences towards genomic medicine has developed particularly in health economics in recent years. It is part of the recurrent debate on the value of genetic information and the scope of this information beyond the results that concern the primary indication of the test. Should secondary data be actively sought or not? Who should make this choice? What secondary data? For what purpose? Based on a qualitative study conducted in Vancouver, Samantha Pollard shows that parents of children with rare diseases value genetic information beyond the diagnosis alone, from the perspective of access to treatment, changes in their child's care or their lifestyle. The results have a medical value, but not only that. In the literature, we find this idea that the usefulness of genomic medicine is not only linked to the primary indication of the test or to the medical value of the results: this is the so-called "personal utility". It can also extend beyond this to non-health outputs. Martin Eden and Aurore Pélissier each present the results of two population-based SHDs, in the UK for Martin Eden and in France for Aurore Pélissier, which support this view. Deborah Marshall presents an approach that allows patient preferences to be taken into account in the economic evaluation of genomic medicine. Session C1 below discusses the methodology for measuring these different dimensions that make up the utility of genomic medicine.

"Anything to make things a bit better for my child": parental preferences for genomic testing in rare childhood diseases – Samantha POLLARD (speaker)
Quantifying how individuals trade health for non-health value deriving from genomic-based diagnostic information – Martin EDEN (speaker)
Simulation modelling methods for economic evaluation in precision medicine that consider patient preferences – Deborah MARSHALL (speaker)
"It is written in our genes! What we would like to know?" Understanding the demand for genetic testing using a discrete choice experiment to assess the French population's preferences – Aurore PELISSIER (speaker), Nicolas KRUCIEN, Christine PEYRON

2.3 Session B3

"Addressing evidentiary uncertainty in precision medicine health technology assessment." - Proposed by Dean REGIER (CA), 27 May 2021, 5.10 p.m. (GMT+2).

The individualisation that characterises precision medicine implies extreme heterogeneity in the clinical, genetic and environmental characteristics of patients, their treatments and their pathways. Health technology assessment must be able to control this heterogeneity in order to produce results that are general enough to contribute to collective health policy decisions. Methods and strategies must be developed to exploit the available data in this way. James Buchanan shows how big data can be used to integrate rare situations into more homogeneous groups of patients, while reducing heterogeneity. Big data also make it possible to jointly exploit data from different domains (pathways, health outcomes, socio-demographic data) and to broaden the dimensions taken into account in the evaluation. Deirdre Weymann proposes to use quasi-experimental methods and machine learning to identify comparators for precision medicine in the event of missing data. In a single-arm study, control patients are matched to treated cases and the impacts of genomic sequencing on overall survival compared to usual care can then be estimated. Dean Regier presents the contribution of life-cycle based evaluation. He builds on the construction of a database for cancer management in Canada and a framework for life-cycle assessment of precision medicine applications.

Can big data from precision medicine observational cohorts reduce evidentiary uncertainty? A Perspective from the UK 100,000 Genomes Project – James BUCHANAN (speaker)
Quasi-experimental Methods for Evaluating Precision Medicine: Case Studies in Personalised OncoGenomics – Deirdre WEYMANN (speaker)
Life-cycle health technology assessment to enable sustainable precision medicine diffusion – Dean REGIER (speaker)

2.4 Session C1

"Methodological considerations for measuring preferences for genome sequencing." - Proposed by Wendy Ungar, 27 May 2021, 6.30 p.m. (GMT+2).

If we stick to medico-economic evaluation as we know it today, the value of genomic medicine is certainly underestimated. It is known that preferences for genetic information extend beyond the primary indication for which the test is performed, but also beyond the medical elements that might concern other pathologies highlighted in the secondary data. Dean Regier's presentation shows how these different elements are valued by the Canadian public.[22] Genetic information from genomic medicine can have an impact on the lives of patients but also on those of their relatives. That said, it is not easy to incorporate these different elements to evaluate the benefits of genomic medicine. Wendy Ungar presents an attempt based on measuring QALYs for different members of the patient's family. Robin Hayeems presents another way to highlight the different values associated by patients with genetic information through the P-Guide: the Patient-reported Genetic testing Utility InDEx (P-GUIDE),

[22] Readers might also refer to sessions B2 and F for other studies about the preferences and expectations of patients or the general public.

a patient-reported measurement tool for genomic medicine to highlight the preferences related to psychosocial, behavioural, ethical and familial impacts of genomic sequencing.

Family matters: measuring the preferences of family members for genome sequencing – Wendy UNGAR (speaker)
Demand for precision medicine: a discrete choice experiment and external validation study – Dean REGIER (speaker)
Defining and measuring the value of genetic testing from patients' perspectives: developing the patient-reported genetic testing utility InDEx (P-GUIDE) – Robin HAYEEMS (speaker)

2.5 Session C2

"What place and articulation for professionals?" 27 May 2021, 6.30 p.m. (GMT+2).

The diffusion of WGS in clinical practice will depend on the usefulness that professionals perceive and the reorganisation of their activity that this new technology will require. The notion of clinical utility is a multidimensional concept that can be apprehended differently depending on the evaluator considered. Robin Hayeems first presents the work of a group of experts who proposed a framework that can be adapted to different WGS applications and that is operational for evaluating this clinical utility through four dimensions and specific indicators. She then presents the construction of the Clinician-reported Genetic testing Utility InDEx which should lead to a standardised and robust tool to evaluate the clinical utility of genetic tests. Based on a survey of clinical geneticists and genetic counsellors, Léa Gaudillat shows that these professionals anticipate changes in their practice in connection with the dissemination of the WGS, in particular in order to respond to the increased need for support in prescribing and reporting results.

Clinical utility of genomic sequencing: a measurement toolkit – Robin HAYEEMS (speaker)
The development of the clinician-reported genetic testing utility index (C-GUIDE): a novel strategy for measuring the clinical utility of genetic testing – Robin HAYEEMS (speaker)
The evolution of the profession of clinical geneticist and genetic counsellors with the arrival of new technologies in genetics – Lea GAUDILLAT (speaker)

2.6 Session C3

"Use and value of genetic information" 27 May 2021, 6.30 p.m. (GMT+2)

In genomics, the data made available to clinicians and researchers is a key element. It implies a donation upstream and then takes on a collective informational and economic value. Patients' consent must be a constraint when they give their data, agree to share them but also for the use that will be made of them in terms of medical results as well as for research. Wannes Van Hoof reports on the conclusions of expert workshops and citizens' forums that indicate both a willingness to share genetic data and the importance of a protective legal framework to govern this sharing. Laurence Faivre looks at the results available to patients after analysis of their data, and particularly at the secondary data made possible with next generation sequencing, and how patients may or may not wish to access them. Sarah Carvallo analyses how genetic data take on a bio-economic value and how the donation of genetic data integrates (or not) all dimensions of this value. Marie Darrason develops the idea that

the more data that are available, the more possible outcomes can mean more uncertain and more complex information.

My DNA, everybody's business? A citizen forum on the use of genomic information in society – Wannes VAN HOOF (speaker), Chloé MAYEUR
Additional data obtained from exome/genome sequencing: two national studies to discuss the risk-benefit balance for implementation in France – Laurence FAIVRE (speaker)
Donation, free and informed consent, genetic data – Sarah CARVALLO
Next Generation Sequencing techniques and the "information illusion" – Marie DARRASON (speaker)

2.7 Session D1

"Cost effectiveness of genomic medicine: Beyond the cost of diagnosis." - Proposed by Deborah SCHOFIELD, 28 May 2021, 10.00 a.m. (GMT+2).

The medico-economic evaluation of genomic medicine still faces obstacles due to the lack of reference values, the difficulty of finding a relevant comparator and, finally, because for many genetic diseases the costs are societal and not only health-related. In response to these difficulties, three studies present innovative methodologies. Deborah Schofield presents an estimate of the costs of intellectual disability for the community but also for the families who bear a heavy economic and psychological burden. Evelyn Lee and Rupendra Shrestha propose a model to evaluate the costs and effectiveness of preconception screening for genetic diseases. They use their modelling to compare the cost-effectiveness of such screening for spinal muscular atrophy with standard care. Owen Tan develops a microsimulation model to evaluate the costs and benefits of using next-generation sequencing (NGS) in the management of childhood cancer.

Description of the session: Determining the cost effectiveness of genomic medicine has been limited by available data. Many studies have focused on the cost of genomic sequencing with cost effectiveness often assessed on the basis of the cost per additional diagnosis. However, due to the relatively recent capacity to provide a molecular diagnosis for many conditions, and lack of direct access to clinical cohorts, many studies have been unable to take account of the impact of health outcomes using standard measures such as QALYs. This is a particular limitation when studies are required to support access to public funding as there is no recognised threshold for funding of a diagnosis alone. Further, genetic information is often of benefit to other family members including to inform reproductive planning where there is a risk of recurrence of the condition. Due to the highly disabling and life-long nature of many genetic conditions, the costs beyond the health system are also often large, suggesting the importance of taking a societal perspective. In this session we demonstrate how we are addressing these issues in several ground-breaking studies of the benefits and cost effectiveness of genomic medicine.

Capturing the widespread ripple effects of familial intellectual disability and potential benefits of genomics – Deborah SCHOFIELD (speaker)
An economic-modelling framework to assess the impact of population-wide preconception carrier screening for genetic disease with specific reference to spinal muscular atrophy – Evelyn LEE and Rupendra SHRESTHA (speakers)
Modelling the economic impact of next generation sequencing on childhood cancer management: a microsimulation approach – Owen TAN (speaker)

2.8 Session D2

"Implementing new generation sequencing in care for paediatric cancers: impacts for patients, healthcare providers and public policies." - Proposed by Sandrine DE MONGOLFIER and Sylvain BESLE, 28 May 2021, 10.00 a.m. (GMT+2).

The spread of genomics in paediatric oncology practice has consequences for the relationships and expectations of stakeholders such as public authorities, professionals, children and their parents. With three different perspectives, this session shows the transformations underway or desirable. Catherine Bourgain looks at two types of regulation of the use of and access to genetic testing, regulation by the state and regulation by professionals. She analyses how professionals react and resist to what could limit their professional autonomy. Solenne Carof and Lucile Hervouet develop the challenges of genetic screening for paediatric cancers from three points of view: professionals, parents and children. Emmanuelle Rial Sebbag is also interested in oncopaediatrics and the three parties involved, i.e. children, their families and their doctors, but she approaches their relationship within the current French legal framework and analyses its relevance.

Negotiating the regulation of routine genome sequencing in a care setting – Catherine BOURGAIN (speaker)
Routinisation of sequencing techniques: What impact on patient care pathways in oncopaedatrics? – Solenne CAROF and Lucile HERVOUET (speakers)
Legally assuring minors patients' rights in oncopaediatrics: between rights and practices – Emmanuelle RIAL SEBBAG (speaker)

2.9 Session E1

"Comparative evaluation of two strategies" 28 May 2021, 5.05 p.m. (GMT+2).

There is still a lot of variability in measuring the cost and effectiveness of sequencing. Strategies and methods need to be sought to control this variability and produce relevant measures to inform access and reimbursement decisions. This session presents four original contributions for measuring costs or effectiveness. Wendy Ungar uses a bottom-up micro-costing approach to estimate the costs of care for two cohorts of paediatric patients who have undergone sequencing. She shows that there are significant differences in sequencing costs and analyses the determinants of these differences. Deirdre Weymann looks to measure the effectiveness of genetic information by comparing time on treatment and time to next treatment initiation for cancer patients according to whether or not management has integrated this information. Using a difference-in-difference method that eliminates patient heterogeneity, she shows the effectiveness of genetic information. Jason Wassy shows that the use of polygenic risk scores has clinical utility, shortening the time to diagnosis of one of the six common diseases targeted in his study. Liliana Sousa demonstrates that preventive management of CDH1 mutation carriers is less costly and saves more lives than treating patients with a clinical expression of diffuse gastric cancer.

Accurate and comprehensive micro-costing of genome sequencing in paediatric populations – Wendy UNGAR (speaker)
Time-varying effects of genomics-informed treatment in patients with advanced cancers: a difference-in-difference analysis – Deirdre WEYMANN (speaker)
The GenoVA Study: design of a pragmatic randomised trial of polygenic risk scoring for common diseases in primary care – Jason VASSY (speaker)
A cost-effective model for the pathway of care of CDH1-related hereditary diffuse gastric cancer syndrome – Liliana SOUSA (speaker)

2.10 Session E2

"Genome sequencing: new evidence on costs, and challenges for health technology assessment." - Proposed by James Buchanan, 28 May 2021, 5.05 p.m. (GMT+2).

While it is not easy to estimate the benefits of genomic medicine, evaluating its costs is also problematic for health economists. And yet the increasing inclusion of genomic medicine in clinical practice will be increasingly reliant on medico-economic analysis to guide resource allocation. The challenges of cost-estimation are crucial for integrating genomic medicine into clinical practice and financing it. Wendy Ungar sets out the challenges confronting health economists looking to evaluate genomic medicine: the possibility of estimating costs and comparing different healthcare strategies are two major issues. In the domain of rare diseases, for instance, John Buckel looks to highlight the costs that could be avoided through healthcare provision that includes genomic medicine and that could shorten the diagnostic odyssey and the medical costs it entails. Patrick Farh nonetheless shows that it is very difficult for economists to evaluate these avoided costs and the medical costs entailed by the different episodes of healthcare provision despite the wealth of databases completed by clinical practitioners. It is not enough just to have these data; the real challenge for health economists now lies in being able to use them.

Estimating the diagnostic pathway costs of patients with suspected rare genetic diseases – John BUCKEL (speaker)
Costing genome sequencing in large-scale, national initiatives: challenges and opportunities – Patrick FAHR (speaker)
Considerations for cost-effectiveness analysis of genome sequencing – Wendy UNGAR (speaker)

2.11 Session E3

"Theoretical microeconomics in genomic medicine." 28 May 2021, 5.05 p.m. (GMT+2).

Personalised medicine is an attractive and relevant field of research for microeconomic theory. Personalised medicine modifies the information potentially available to patients, professionals and insurers, whether public or private. Without eliminating uncertainty in decisions (medical or insurance), it stratifies more finely the probabilities of pathologies as well as those of the effectiveness of treatments. A certain number of models used in health economics can then be re-examined, firstly those of health insurance supply and demand behaviour, but also those of prevention behaviour or doctors' activity. In all these theoretical models, the evolution of the level of information associated with personalised medicine will modify equilibria and optimal behaviour. Philippe De Donder models the impact of genetic information on the prevention behaviour of policyholders and the nature of

insurance contracts at equilibrium. Samuel Kembou Nzale uses an experimental economics approach to determine which remuneration methods would encourage physicians to integrate the benefits of personalised medicine into their practice.

Welfare impacts of genetic testing in health insurance markets: Will cross-subsidies survive? – David BARDAY, Philippe DE DONDER (speaker)
Physicians' incentives to adopt personalised medicine: experimental evidence – Samuel KEMBOU NZALE (speaker)

Annex 1 - Program of the conference

Please click on Join here to go directly to the session of your choice. Don't forget to log in with the guest IDs that were sent to you for the conference.
If you have any technical problems during the conference, please send an email to dominique.salvi@chu-dijon.fr
Enjoy the conference !

PROGRAM

Wednesday 26th May 2021

-9 (Vancouver)	-6 Quebec, NY, ...)	-1 (London, Lisbon)	Paris (ref.)	+8 (Melbourne, Sydney)	
06:30 a.m.	09:30 a.m.	02:30 p.m.	*03:30 p.m.*	11:30 p.m.	*Welcome and Introductions* Join here
Plenary 1 (1h)					
07:00 a.m.	10:00 a.m.	03:00 p.m.	*04:00 p.m.*	00:00 p.m.	"Solve-RD - on the impact of diagnostic rare disease research on the diffusion of genomic medicine" **Holm GRAESSNER** *(Centre for Rare Diseases, University Hospital Tübingen, Germany)* Join here
Session A (1h)					
08:00 a.m.	11:00 a.m.	04:00 p.m.	*05:00 p.m.*	(Day +1) 01:00 a.m.	*A - Implementation of exome and genome sequencing: who has access, who pays, and what are solutions for implementation challenges?* Proposed by Deborah Marshall **Deborah MARSHALL, Kathryn A. PHILLIPS, Sarah WORDSWORTH, James BUCHANAN, Dean REGIER** Join here

Thursday 27th May 2021

-9 (Vancouver)	-6 Quebec, NY, ...)	-1 (London, Lisbon)	Paris (ref.)	+8 (Melbourne, Sydney)			
Plenary 2 (1h)							
07:00 a.m.	10:00 a.m.	03:00 p.m.	*04:00 p.m.*	00:00 p.m.	***"What's important to you in the delivery of health care... and what does this mean for valuing Next Generation Sequencing?"*** **Mandy RYAN** *(Health Economics Research Unit, University of Aberdeen, United Kingdom)* Join here		
Short break (10min)							
Sessions B (1h15)							
08:10 a.m.	11:10 a.m.	04:10 p.m.	*05:10 p.m.*	01:10 a.m.	*B1 - How to assess the cost effectiveness of WES/WGS?* *Systematic review or meta-analysis : how to consider the high heterogeneity of studies to access the clinical utility of WGS/WES ?* - **Camille LEVEL** *Genomic testing in the field of developmental disorders: the added value of human and social sciences studies* - **Catherine LEJEUNE** *Next Generation Sequencing for the next generation of patients: building the economic evidence base* - **Michael ABBOTT** Join here	*B2 - Preferences, expectations, representations of patients, professionals and general population* *"Anything to make things a bit better for my child": parental preferences for genomic testing in rare childhood diseases* - **Samantha POLLARD** *Quantifying how individuals trade health for non-health value deriving from genomic-based diagnostic information* - **Martin EDEN** *Simulation modeling methods for economic evaluation in precision medicine that consider patient preferences* - **Deborah MARSHALL** *"It is written in our genes! What we would like to know?" Understanding the demand for genetic testing using a discrete choice experiment to assess the French populations' preferences* - **Aurore PELISSIER** Join here	*B3 - Addressing evidentiary uncertainty in precision medicine health technology assessment* Proposed by Dean REGIER (CA) *Can Big Data from Precision Medicine Observational Cohorts Reduce Evidentiary Uncertainty? A Perspective from the UK 100.000 Genomes Project* - **James BUCHANAN** *Quasi-experimental Methods for Evaluating Precision Medicine: Case Studies in Personalized OncoGenomics* - **Deirdre WEYMANN** *Life-cycle Health Technology Assessment to Enable Sustainable Precision Medicine Diffusion* - **Dean REGIER** Join here
Short break (5min)							
Sessions C (1h15)							
09:30 a.m.	12:30 p.m.	05:30 p.m.	*06:30 p.m.*	02:30 a.m.	*C1 - Methodological considerations for measuring preferences for genome sequencing* Proposed by Wendy UNGAR (CA) *Family matters: measuring the preferences of family members for genome sequencing* - **Wendy UNGAR** *Demand for precision medicine: a discrete choice experiment and external validation study* - **Dean REGIER** *Defining and mesuring the value of genetic testing from patients' perspectives: developing the patient-reported genetic testing utility InDEx (P-GUIDE)* - **Robin HAYEEMS** Join here	*C2 - What place and articulation for professionals ?* *Clinical utility of genomic sequencing: a measurement toolkit* - **Robin HAYEEMS** *The development of the clinician-reported genetic testing utility index (C-GUIDE): a novel strategy for measuring the clinical utility of genetic testing* - **Robin HAYEEMS** *The evolution of the profession of clinical geneticist and genetic counsellors with the arrival of new technologies in genetics* - **Lea GAUDILLAT** Join here	*C3 - Use and value of genetic information* *My DNA, everybody's business? A citizen forum on the use of genomic information in society* - **Wannes VAN HOOF** *Additional data obtained from exome/genome sequencing : two national studies to discuss the risk-benefit balance for implementation in France* - **Laurence FAIVRE** *Donation, free and informed consent, genetic data* - **Sarah CARVALLO** *Next Generation Sequencing techniques and the "information illusion"* - **Marie DARRASON** Join here

Friday 28th May 2021

-9 (Vancouver)	-6 Quebec, NY, ...)	-1 (London, Lisbon)	Paris (ref.)	+8 (Melbourne, Sydney)			
Sessions D (1h15)							
01:00 a.m.	04:00 a.m.	09:00 a.m.	*10:00 a.m.*	18:00 p.m.	*D1 - Cost effectiveness of genomic medicine: Beyond the cost of diagnosis* Proposed by Deborah SCHOFIELD (AUST) *Capturing the widespread ripple effects of familial intellectual disability and potential benefits of genomics* – **Deborah SCHOFIELD** *An economic-modelling framework to assess the impact of population-wide preconception carrier screening for genetic disease with specific reference to spinal muscular atrophy* – **Evelyn LEE and Rupendra SHRESTHA** *Modelling the economic impact of next generation sequencing on childhood cancer management – a microsimulation approach* – **Owen TAN** Join here	*D2 - Implementing new generation sequencing in care for pediatric cancers: impacts for patients, healthcare providers and public policies* Proposed by Sandrine DE MONGOLFIER and Sylvain BESLE *Negotiating the regulation of routine genome sequencing in care setting* - **Catherine BOURGAIN** *Routinization of sequencing techniques: what impact on patient care pathways in oncopediatrics?* – **Solenne CAROF and Lucile HERVOUET** *Legally assure minors patients'right in oncopediatric: between rights and practices* – **Emmanuelle RIAL SEBBAG** Join here	
Long break							
Plenary 3 (1h)							
07:00 a.m.	10:00 a.m.	03:00 p.m.	*04:00 p.m.*	24:00 p.m.	*"Introducing Next Generation Sequencing in healthcare: challenges for patients' rights and for public health"* **Emmanuelle RIAL-SEBBAG** *(Laboratoire d'épidémiologie et de santé publique, Université de Toulouse, France)* Join here		
Short break (5min)							
Sessions E (1h15)							
08:05 a.m.	11:05 a.m.	04:05 p.m.	*05:05 p.m.*	(Day +1) 01:05 a.m.	*E1 - Comparative evaluation of two strategies* *Accurate and comprehensive microcosting of genome sequencing in pediatric populations* - **Wendy UNGAR** *Time-varying effects of genomics-informed treatment in patients with advanced cancers: a difference-in-difference analysis* - **Deirdre WEYMANN** *The GenoVA Study: design of a pragmatic randomized trial of polygenic risk scoring for common diseases in primary care* - **Jason VASSY** *A cost-effective model for the pathway of care of CDH1-related hereditary diffuse gastric cancer syndrome* - **Liliana SOUSA** Join here	*E2 - Genome sequencing: new evidence on costs, and challenges for health technology assessment* Proposed by James BUCHANAN (UK) *Estimating the diagnostic pathway costs of patients with suspected rare genetic diseases* - **John BUCKELL** *Costing genome sequencing in large-scale, national initiatives: challenges and opportunities* - **Patrick FAHR** *Considerations for cost-effectiveness analysis of genome sequencing* - **Wendy UNGAR** Join here	*E3 - Theoretical microeconomics in genomic medicine* *Welfare impacts of genetic testing in health insurance markets will cross-subsidies survive ?* - **Philippe DE DONDER** *Implementation of personalized medicine in a context of moral hazard and uncertainty about treatment efficacy* - **Stéphane ALCENAT** *Physicians' incentives to adopt personalized medicine: experimental evidence* - **Samuel KEMBOU NZALE** Join here
Short break (10min)							
Sessions F (1h15)							
09:30 a.m.	12:30 p.m.	05:30 p.m.	*06:30 p.m.*	02:30 a.m.	*F - Perspectives on Genomic Medicine: Between Public Policy and Citizens* *Stakeholders perspectives for precision oncology: balancing patient and public support with evidentiary uncertainty* - **Samantha POLLARD** *DNA debate: engaging citizens on genomics* - **Chloé MAYEUR** *Health technology assesment and funding of genomic medicine technologies in Ontario, Canada* - **Wendy UNGAR** Join here		
10:45 a.m.	01:45 p.m.	06:45 p.m.	***07:45 p.m.***	03:45 a.m.	***Close of the conference***		

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