Deliverable

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Explanation according to GA Annex I:

Publication on the synthesis of existing studies assessing cost effectiveness and clinical utility of WES/WGS.

Abstract:

This report is the deliverable of Objective A "Perform a systematic review to gain insight into currently ongoing clinical utility studies for genomics strategies and their conclusions" described in Task 3.2 of WP 3 "Changing patient lives: translation to the clinic?" and led by Christine Peyron and Aurore Pélissier from the Health Economics Team of the *Laboratoire d'Economie de Dijon* (University of Burgundy).

The report sets out: (i) the work done to organise the conference proposed in Objective A; (ii) the summary of the research presented at the conference.

In addition to reporting on the work by the Dijon Health Economics Team, it provides a fairly complete overview of the issues and research currently being developed in the social sciences with respect to genomic medicine.

Introduction:

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**[1]. 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[2] 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.

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 have been 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 (part 1);
- organise a 2-day workshop in order to meet teams concerned by these questions and discuss their research and ours (part 2);
- provide a synthesis of the studies presented during the workshop (part 3).

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 (ingénieure d'étude) (over an 18-month period).

[1] https://ledi.u-bourgogne.fr/les-equipes-du-ledi/economie-de-la-sante.html

[2] http://www.translad.org/presentation.html

This report sets out the work accomplished in preparing the conference, as initially planned and then held by videoconferencing. The organisation of the conference was greatly disrupted by the COVID pandemic. The conference had to be postponed for one year and then be organised in the form of a videoconference.

Report:

- **Part 1 – Scientific preparation through a systematic review of the literature**

A literature review was conducted before deciding for the conference. Considerable work was done on defining the keywords so as to be as exhaustive as possible and to be in a position to programme automatic searches:

1. Keywords initially identified by the team
2. Processing with the HeTOP and MeSH thesauruses
3. Bibliographic research using these keywords in Google Scholar, PubMed and Science Direct (title, abstract and keywords) + Similar articles in PubMed
4. Each time a paper of interest was included, the keywords were taken from it and added to the search as necessary until all possible keywords were exhausted
5. Analysis of keywords automatically encoded by Zotero in Excel
6. Processing in HeTOP and MeSH thesauruses
7. Addition of relevant keywords as necessary
8. Bibliographic research using these keywords in Google Scholar, PubMed and Science Direct (title, abstract and keywords) + Similar articles in PubMed.

On completing this step, we had 121 keywords and 7523 papers identified for the period from 3 September 2018 to 12 September 2019. In all, 1245 papers were selected after reading their abstracts. They were analysed through Nvivo.

- **Part 2 – Organization of the two-day conference**

The operational organisation of the conference was based on the literature review described above and on two workshops held ahead of it. The conference was initially devised as a two-day event to be held in Dijon (29-30th May 2020). Subsequent circumstances meant it had to be changed into a three-day videoconference (26-28th May 2021).

- ***Identification and consolidation of a national network: the ECOgen workshops***

For the purpose of forging a research network on economic approaches to genomics, we organised ahead of the conference two ECOgen workshops: one in 2018 (5th October: here ECOGen2018) and one in 2019 (9th November: here ECOgen2019). Both workshops received financial support from the University of Burgundy and its AnDDI-Rares department.

These annual workshops bring together health economists, researchers in the social and human sciences and health professionals, all with a concern for genomic medicine, its challenges and the evaluation of it. The objective is to foster exchange on the issues, methods and results of current research and to explore the multiple possible points of view (patients, practitioners, establishments, insurers, financers) in order to cast light on expectations, levels, obstacles and possible means of dissemination.

- ***Organisation of a European Conference on the Diffusion of Genomic Medicine***

The conference was designed to contribute to the development of research in genomic medicine concerning its evaluation, its dissemination and the public policies accompanying this new type of medicine. This being so, we entitled the ECOgenomics conference: “European Conference on the Diffusion of Genomic Medicine: Health Economics & Policy”. Please see the website of the conference here.

We defined 10 target topics: Preferences, expectations, representations of patients and professionals; Medico-economic evaluation; Diffusion in health systems; Big data: uses and risks;

Financial access; Legislation, public regulations and policies for diffusion; Patient management and care pathway; Organisational and relational changes for professionals; Open access, access inequalities and equity; Dissemination to the general public.

We formed two *ad hoc* committees for the conference: a **local organising committee** and an **international scientific committee**. The composition of the scientific committee was international and wide in terms of disciplines and countries represented. The scientific committee totalled 37 members representing 9 disciplines and 10 countries. More details: here and here and also here.

We received 52 proposals for oral presentation. Each proposal was read by at least two members of the scientific committee on the basis of a predefined scoring grid. The final list was approved by all members of the scientific committee[3]. In all, 44 presentations were selected including 9 organised sessions.

The programme (available here) proposed was rich, varied and particularly stimulating:

- 3 plenary lectures led by H. Graessner (Plenary 1), M. Ryan (Plenary 2) and E. Rial-Sebbag (Plenary 3)[4];
- 9 organised sessions;
- 11 parallel sessions.

Part 3 – Synthesis of the three-day videoconference

Lectures

Although genomic medicine is experienced nowadays as a revolution by geneticists[5], 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).

- **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).
- **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).
- **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).

For a presentation of the keynote speakers, please see this page.

Plenary sessions

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[6]) 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

[3] https://ecogenomics.sciencesconf.org/resource/page/id/28
[4] https://ecogenomics.sciencesconf.org/resource/page/id/8
[5] https://www.sfmpp.org/medecine-predictive/ (accessed 1 July 2021).
[6] McCarthy JJ, McLeod HL, Ginsburg GS. (2013). Genomic medicine: a decade of successes, challenges, and opportunities. *Sci Transl Med*, 5(189).

by 15 countries[7] have been identified by Stark *et al.* (2019)[8] for the period 2013–19. That number is growing: in July 2021, the Global Genomic Medicine Initiative[9] listed 68 initiatives in 36 locations. The experiences are nevertheless very varied. According to Stark *et al.* (2019)[8] 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.

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[10]). No fewer than 14 stakeholders are identified by Mitropoulo *et al.* (2020)[11]. The dissemination of genomic medicine in our healthcare systems will depend in particular on the preferences and expectations of all 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 focused on the views of patients and Canadian society through a qualitative study on cancer. Chloé Mayeur presented the results of a large-scale survey of Belgian citizens. And, finally Wendy Ungar explained 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 showed 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.

[7] Australia, Brazil, Canada, China, Denmark, Estonia, France, Japan, Netherlands, Qatar, Saudi Arabia, Switzerland, Turkey, UK, USA.
[8] Stark *et al.* (2019). Integrating Genomics into Healthcare: A Global Responsibility. *The American Journal of Human Genetics*, 104(3), 13-20.
[9] https://www.genomicspolicy.org/catalogue-introduction (accessed 1 July 2021).
[10] Burton, H., Adams, M., Bunton, R., Schröder-Bäck, P. (2009). Developing Stakeholder Involvement for Introducing Public Health Genomics into Public Policy. *PHG*. 12, 11-19.
[11] 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.

- ***Parallel sessions***

B1 “How to assess the cost effectiveness of WES/WGS?”, 27 May 2021, 5.10 p.m. (GMT+2).	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)
B2 “Preferences, expectations, representations of patients, professionals and general population”, 27 May 2021, 5.10 p.m. (GMT+2).	“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
B3 “Addressing evidentiary uncertainty in precision medicine health technology assessment” Proposed by Dean REGIER (CA), 27 May 2021, 5.10 p.m. (GMT+2).	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)
C1 “Methodological considerations for measuring preferences for genome sequencing”. Proposed by Wendy Ungar, 27 May 2021, 6.30 p.m. (GMT+2).	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)
C2 What place and articulation for professionals? 27 May 2021, 6.30 p.m. (GMT+2).	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)
C3 Use and value of genetic information 27 May 2021, 6.30 p.m. (GMT+2)	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)
D1 Cost effectiveness of genomic medicine: Beyond the cost of diagnosis – Proposed by Deborah SCHOFIELD, 28 May 2021, 10.00 a.m. (GMT+2).	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)
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).	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)
E1 Comparative evaluation of two strategies	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)
E3 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).	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)
E3 Theoretical microeconomics in genomic medicine	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)

Conclusion:

ECOgenomics conference, 26-28th May, 2021
Number of speakers: 47
Number of sessions: 3 plenary sessions and 11 parallel sessions
Number of presentations: 47
Number of people registered: 87

The organisation of the event as a videoconference went without difficulty or technical hitches. Over the three days, the conference attracted a loyal audience, who participated assiduously in the various sessions. The presentations were the subject of questions and debates of genuine scientific quality. The organisation by videoconference allowed meaningful exchanges among researchers despite everything.

Given the matter of time zones, some participants could not log in to all the sessions. For that reason, but also to enable staggered access for everyone who registered, image captures were made available for several weeks.

Many participants spoke to us after the conference of their enthusiasm and the quality of the programme. This is therefore a very positive result.

The organization of the symposium allowed us to gain visibility in the health economist community. We were contacted by James Buchanan to join the **SIG Economics of Genomics and Precision Medicine** associated with the **International Health Economics Association** (iHEA). Camille, Christine and Aurore are now members of this international working group. For additional information: https://www.healtheconomics.org/page/EGPM.