York Health Economics Consortium

NHS Innovation Accelerator

Economic Impact Evaluation Case Study: Sapientia

1. BACKGROUND

SAPIENTIA™ is a genome analytics software which enables the human genome to be interrogated to identify pathogenic mutations. Although individually rare, collectively it is estimated that around 1 in 17 people will be affected by a rare disease in their lifetime and that over 75% of these will have a genetic aetiology.[1] Patients often undergo many tests and treatments, on a stepped diagnostic journey, to identify the cause of an inherited disease. Currently the average time to diagnosis for rare genetic diseases is 4.7 years, with an average of 7.4 different specialists involved.

Genome sequencing facilitates speedier diagnosis and better clinical decision support. The potential for healthcare savings comes from the patient receiving an unequivocal diagnosis rapidly, resulting in the avoidance of additional months or years without diagnosis and the associated unnecessary medical appointments, investigative tests and interventions.[2] However, as whole genome sequencing is currently very expensive, the decision as to when this is justified within the clinical pathway is not straightforward.

Sapientia has been developed by Congenica, following on from SBRI[3] funded research by the Wellcome Trust (the DDD study).[4] As whole genome sequencing becomes more widely available via the 100,000 Genomes Project, the Sapientia software will be an enabler and will support the 13 Genomics Medicine Centres across the UK to undertake genetic analysis. The NIA Fellow has provided clinical expertise and engagement with the UK genetics laboratories network to inform adoption and validation into clinical care, identification of clinical priorities and advising the software developers. Early work to gather evidence on how to implement Sapientia into the clinical pathway is underway in an initial partner site (Manchester) and in a number of laboratories over the next 12 months.

The early stage of development for Sapientia means that there are no robust data available relating to the implementation of the innovation. Furthermore, as costs become available they are likely to be commercially sensitive. This case study therefore comprises a cost consequence analysis, based on a sample clinical case provided by the NIA Fellow.

1 Haworth A. *NIA analysis framework: Sapientia.* March 2017.
2 Ibid.
3 SBRI: Small Business Research Initiative.
4 DDD: Deciphering Development Disorders Project. https://www.ddduk.org/

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2. INPUT COSTS

The development costs for Sapientia are incorporated into a multi-million pound company (Congenica) and are not available for this analysis.

Sapientia is a cloud based service and therefore involves minimal implementation costs. The revenue costs associated with Sapientia are for the exome sequencing and analysis, computer power and data storage. The software is aimed at increasing the volume of tests to be undertaken and there is an expectation that there no additional costs will be incurred relating to staff time.

As Sapientia is adopted into the clinical pathway, Congenica will need to develop a business case and a costing model that is viable within the healthcare system. For a provider location to access the software, the cost is likely to be based upon a number of criteria, such as: term; volume of tests; sample types to be analysed (gene panels, exomes or genomes); level of service required (access or clinical reporting); levels of data storage and additional added-value services such as training and customisation. The cost to providers may be met by an annual subscription, licence fee and/or unit costs and a stepped charging model may be introduced.

Although the costs of Sapientia are not currently available, indicative costs have been provided, of approximately £10 for a gene panel and £1000 for a whole genome.[5]

2.1 Sample Case Study

In order to demonstrate the potential costs and consequences of using Sapientia, a sample case has been provided by the NIA Fellow. In this case, a young child with a neurodegenerative disorder was diagnosed with a hereditary condition following exome sequencing. The poor prognosis associated with the condition, once diagnosed, led to a change in the care provided and also avoided a number of further tests that had been provisionally planned. The example costs used in this case study are shown in Table 2.1.

Table 2.1: Input costs (sample case)

Input	Description	Cost
Genome testing	Exome trio sequencing and analysis costs (2016) [6]	£1,900
	Data processing and storage	£100
Clinical analysis	Two clinical scientists for 1 hour (£50 x 2)	£100
Total		**£2,100**

[5] NIA Fellow, April 2017.
[6] Case study provided by the fellow (anonymised).

3. OUTCOMES

As the conditions being investigated are rare, each patient tends to undergo a different diagnostic journey, making it extremely difficult to generalise and identify consistent impacts of receiving an early diagnosis.

In the sample case study, examples of costs that have potentially been avoided by conducting the exome diagnosis are proposed as follows:[7]

- Repeat EEG (electroencephalogram);
- MRI brain after 6 month interval under general anaesthetic;
- Muscle biopsy;
- Repeat EMG (electromyography)/NCV (nerve conduction velocity);
- Moving patient from in-patient acute care setting to palliative care.

These are valued as in Table 3.1.

Table 3.1: Impacts, outcome metrics and proxy values (sample case)

Impact	Outcome metric	Value
Avoided diagnostic tests	Diagnostic tests: • Electroencephalogram • MRI under GA • Muscle biopsy • Nerve conduction velocity • Electromyography	Not available – some will be incorporated into the specialty appointment (below)
Avoided healthcare appointments	Example specialties seeing child: • Paediatric neurology* • Clinical genetics* • Radiology (*Treatment Function does not have a national tariff price for OP in 2017/18) Five avoided out-patient (OP) appointments at indicative cost e.g. follow-up appointment for paediatric out-patients 5 x £131[8]	£655
Avoided hospital costs	Net difference between acute bed day and palliative care bed day for 3 weeks Acute bed day £400[9] Palliative care bed day £289[10] Net saving of £111 per day x 21 days	£2,331
Improved wellbeing of patient and family	Reduced anxiety for family and ability to plan for future	Not appropriate
Total		**£2,986**

[7] Case study provided by the fellow (anonymised).
[8] NHS Improvement. *National Tariff Payment System 2017/18 Annex A: The national prices and national tariff workbook.* 2016.
[9] https://data.gov.uk/data-request/nhs-hospital-stay.
[10] Ibid.

In addition to the intangible benefits such as improved wellbeing, there may be other benefits, such as provision of reproductive choice for future pregnancies, counselling and diagnosis of other family members and increased likelihood of accessing other forms of care following diagnosis (e.g. social care). It has also been suggested that parents may be able to maintain employment due to earlier diagnosis and treatment for their child, although there are no data available to quantify this benefit from a societal perspective.

4. ECONOMIC ANALYSIS

The information available from the sample clinical case has been used to conduct a cost-consequence analysis. This involves using the available information to describe and compare the potential costs and consequences of introducing Sapientia into a sample clinical pathway.

The following assumptions underpin the sample case:

- The proposed additional diagnostic tests would have been performed if exome sequencing had not taken place;
- As the costs are not available for the individual diagnostic tests, an estimate has been used based on the value of an avoided out-patient appointment in the relevant speciality.

The costs and consequences in the clinical case are summarised in Table 4.1.

Table 4.1: Costs and consequences of genome sequencing in a sample case

Costs	Consequences	
Genome testing (including clinical analysis) £2,100	Cost savings	Avoided healthcare appointments, diagnostic tests and hospital stay to the value of £2,986
	Patient & family outcomes	Appropriate care provided for the child Reduced anxiety for family members following confirmation of diagnosis Ability to make reproductive choices for the future
	Productivity	Potential for the parents to maintain employment and plan for the future

The figures available from the sample case show that the exome sequencing has most probably avoided additional healthcare, yielding a positive return on investment from a healthcare perspective. Furthermore, the clinician involved in the case suggested that additional savings would have been achieved if the exome testing had been carried out earlier in the diagnostic journey.

In cases where the patient is not at ‘end of life’ as in this case, there is the potential for earlier treatment leading to better patient outcomes, i.e. extended life in a better health state. There are also additional intangible benefits to which it is not possible to ascribe a monetary value but may bring unquantified quality of life improvements and would have considerable value to the family e.g. obtaining a diagnosis, appropriate care and ability to plan for the future. These benefits bring. Societal benefits may also be accrued by the ability to maintain productive work.

5. IMPACT ON EMPLOYMENT

As an organisation, Congenica has grown from three employees in 2015 to 40 people in the UK at the end of 2016. This is expected to increase to 70 by the end of 2017, around 60 of which will be UK based, with other teams based in the USA and China. At an average UK salary of £28,200 per annum,[11] this equates to an estimated £1,692,000 in productivity gains.

6. CONCLUSION

As the Sapientia innovation is in the early stages of implementation into clinical practice there is currently little evidence of cost-effectiveness. The sample case shows however, that it has promising potential to provide a positive return on investment from a healthcare perspective, by considerably shortening a patient's diagnostic journey in some cases.

Evidence from studies in the USA supports this, with one study finding that if sequencing had been performed at symptom onset, diagnoses may have been made 77 months earlier, with the cost of prior negative tests in non-acute patients averaging $19,100 per family.[12] Similarly, another study found sequencing resulted in diagnostically useful outcomes in 29.4% of patients, resulting in average cost savings of $3,547 for genetic and metabolic investigations in diagnosed patients and $1,727 for genetic investigations in undiagnosed patients.[13]

In addition to the improvement in wellbeing for the family there is also the potential for wider societal benefits for the family and via the employment generated by Congenica within the UK. For the wider benefits which cannot be easily valued, decision makers will place their own weights on these either implicitly or explicitly.

The future scaling of Sapientia into practice will potentially occur with the progression of the 100,000 Genomes project and the NIA Fellow has assisted with the clinical engagement informing the adoption into clinical care. Linked to this, Sapientia provides an example of UK funded research which has the potential to lead to an economically viable development with global reach.

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August 2017

[11] ONS Annual Survey of Hours and Earnings 2016
[12] Sabatini LM et al. *The Journal of Molecular Diagnostics*, Vol. 18, No. 3. 2016.
[13] Monroe GR et al. Effectiveness of whole-exome sequencing and costs of the traditional diagnostic trajectory in children with intellectual disability. *Genet Med.* 2016 Sep;18(9):949-56.