Variation in healthcare services for specialist genetic testing and implications for planning genetic services: the example of inherited retinal dystrophy in the English NHS

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Abstract This study aims to identify and quantify the extent of current variation in service provision of a genetic testing service for dominant and X-linked retinal dystrophies in the English National Health Service (NHS). National audit data (all test requests and results ($n=1839$) issued between 2003 and 2011) and survey of English regional genetic testing services were used. Age- and gender-adjusted standardised testing rates were calculated using indirect standardisation, and survey responses were transcribed verbatim and data collated and summarised. The cumulative incidence rate of testing in England was 4.5 per 100,000 population for males and 2.6 per 100,000 population for females. The standardised testing rate (STR) varied widely between regions of England, being particularly low in the North-east (STR 0.485), with half as many tests as expected based on the size and demographic distribution of the population and high in the South-east (STR 1.355), with 36 % more tests than expected. Substantial and significantly different rates of testing were found between

regional populations. Specific policy mechanisms to promote, monitor and evaluate the regional distribution of access to genetic and genomic testing are required. However, commissioners will require information on the scope and role of genetic services and the population at risk of the conditions for which patients are tested.

Keywords Health services accessibility · Health services needs and demand · Genetic testing · Genetic services · Health planning

Introduction

Geographic variations in healthcare provision are ubiquitous and are observed for interventions for both common and rare disorders (Appleby et al. 2011). Although genetic testing is set

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to revolutionise health care for patients with rare inherited diseases through the advent of new technologies such as next-generation sequencing (NGS) (Singleton 2011; Yang et al. 2013; Jacob 2013; Biesecker et al. 2012), there is limited empirical evidence to identify the extent of variation in the current provision of testing. An important first step in planning an expansion of services is to identify, and then to quantify, if and where variation exists in current services. Evidence of variation will also facilitate understanding of the potential impact of variation in healthcare provision on the efficiency and equity of service delivery. In a publically funded healthcare system financed through taxation such as the National Health Service (NHS) in the UK, the whole population should receive the same access to services regardless of their ability to pay or where they live. The English NHS Atlas of Variation in Healthcare describes a requirement to increase value from resources allocated to the NHS by first searching for unwarranted variation and, once identified, to address the causes and drivers of this variation (NHS Right Care. The NHS atlas of variation in healthcare 2010). This study is one of the first to collate readily available empirical information on provision and uptake of specialist genetic diagnostic healthcare services in the UK, using the exemplar of genetic testing for inherited retinal dystrophy. Retinal dystrophies (RD) represent a highly genetically heterogeneous group of inherited conditions associated with visual loss and blindness. The group includes retinitis pigmentosa (RP), a group of clinically overlapping retinal disorders affecting between 1 in 3500–4000 people (Berger et al. 2010). A large number of genes have been associated with RP, which can be inherited in autosomal dominant, recessive or X-linked patterns, and with a range of other inherited retinal disorders such as cone-rod dystrophy, choroideraemia and X-linked retinosis (Daiger et al. 2007).

Currently, genetic testing for inherited retinal dystrophies such as RP has demonstrable clinical utility to direct management, define prognosis and inform genetic counselling and in future would direct novel genotype-specific treatments (Maguire et al. 2009; Farrar et al. 2010; Bainbridge et al. 2008; MacLaren et al. 2014). The recent advent of next-generation sequencing (NGS) has made molecular diagnosis applicable to significantly greater numbers of families (O'Sullivan et al. 2012; Shanks et al. 2013; Neveling et al. 2012), and there is a growing body of empirical evidence to demonstrate that individuals want and expect access to such genetic tests. For example, a recent survey of 200 RD patients in England revealed that 90 % of the sample would be likely to access a genetic test if it were offered (Willis et al. 2013). Findings from four recently published studies (Willis et al. 2013; Eden et al. 2013; Combs et al. 2013a, b) provide coherent and

in-depth explanations for why genetic testing is sought within genetic ophthalmology. Information from genetic tests is valued by individuals because a definitive diagnosis can lead to increased precision in the details of prognoses and patterns of inheritance. The opportunity to access this improved information was valued by patients because it facilitates informed decision making by individuals and their families (Eden et al. 2013). Short- and long-term plans could be formulated in response to a confirmed diagnosis. Whilst currently there are only limited options for test results to alter the clinical management of RD, an important perceived benefit of undergoing genetic testing was the possibility of enrolment into trials of novel treatments where inclusion criteria specifies a certain genotype (Willis et al. 2013; Eden et al. 2013). Acknowledging the limited possibility of exposure to an effective treatment, participants in these studies generally concur that test information is of value regardless of its ability to promote gains in health status. For example, in macular dystrophy, the identification of mutations in TIMP3 can predict the risk of neovascular macular damage, which is amenable to therapeutic intervention, and whilst adRP/xLRP testing does not alter clinical management, it enables children and young adults to plan careers and to implement holistic care plans that overcome visual disability. Additionally, the ability of test information to impact upon—and be of potential value to—the individuals' extended families was considered important. A negative genetic test result will provide relief for those who were potentially at risk of RD. Confirmation of an inherited disease in family members would still be valued for the reasons outlined above and also, for some, simply for the removal of uncertainty (Willis et al. 2013; Eden et al. 2013; Combs et al. 2013a, b).

New developments in genetic testing technologies consequently have important implications for expansion and commissioning of specialist services, and there is thus a need to understand how they will be accessed by ophthalmic and genetic specialists. This also has a broader relevance as the expansion of genetic testing to greater patient numbers will impact across all genetic medicine specialities and may exacerbate the serious inconsistencies in the provision of genetic services across the UK NHS that have previously been highlighted (House of Lords Technology Select Committee. Genomic medicine. 2nd Report of Session 2008). The aim of this study was to identify and quantify the extent of current variation in service provision for a specialist genetic testing service in the English NHS, specifically inherited RP. A secondary aim was to integrate quantitative findings with exemplars of current working practices and models of service delivery and funding.

Materials and methods

Sources of data

The Centre for Genomic Medicine in Manchester, UK, was the sole UK provider of a molecular genetic testing service for inherited retinal disease for the period covered by this dataset and analysis (Fig. 1). From 2003 to the end of December 2009, testing was funded by a charity and delivered free to all requesting clinicians. From January 2010, referring clinicians paid for all tests. The testing service is provided free to patients at the point of access, and the tests are primarily funded on a provider-to-provider basis within an NHS Commissioning Framework. There were no other UK-Genetic Testing Network-approved centres for testing for retinitis pigmentosa during the study period. Electronic records of all test requests and results for patients living in the UK maintained by the centre provide a reflection of the levels of testing across the country. This electronic database provided the sample frame to undertake a national audit of uptake of genetic testing for this condition. All data were collected and maintained in accordance with ISO 15189 (Technical Committee ISO/TC 212. 15189: Clinical laboratory testing and in vitro diagnostic test systems 2012).

The extent of variation in the provision of genetic testing for people with suspected inherited RP across the nine healthcare regions of the NHS in England was selected for

this analysis. This provides a contextual setting where access to the service should be based on patient need for the service (i.e. equitable access) in the population covered by this single publicly funded healthcare system. Given the range of genetically heterogeneous disorders that the tests are used for and the different inheritance patterns that give rise to the disorders, it was deemed reasonable to assume population need for the test is similar between regions after controlling for age and gender. In addition, a national survey of all English regional genetics centres (RGCs) ($n=17$) and three specialist ophthalmology centres collected information on models of provision and funding arrangements for testing.

To obtain provider perspectives on test provision, a semi-structured telephone survey of 20 lead contacts (14 consultants, five genetic counsellors and one specialist registrar) at care providers from all RGCs and specialist ophthalmology clinics delivering RD services in England was undertaken. These regional specialist genetic testing services are the same as those included in the quantitative analysis. This survey was designed as part of a larger study to understand current care models for inherited retinal dystrophies. The participants of survey comprised genetic counsellors, specialist registrars, genetic consultants and ophthalmologists. The survey contained closed and open-ended questions. Only the analysis of the open-ended questions is presented here. Open-ended questions were used to explore situations in which genetic testing is

Fig. 1 Regional specialist genetic testing services for RP and their relationship with the single accredited laboratory

used and the challenges to access including, for example, financial, organisational or other barriers to care provision in the context of RD.

Inclusion and exclusion criteria

Records were identified from the database for all patients tested for dominant and X-linked inherited retinal dystrophies between January 2003 and December 2011. During this time, a comprehensive repertoire of testing was offered including entire gene screening and targeted point mutation analysis for common/founder mutations (see Table 1). All six tests were available for the entire period of the study, and no NGS testing was available for retinal disease during the study period. Mutation analysis was carried out using Sanger sequencing (gene screens) or Pyrosequencing™ (founder mutations) using standard methodologies. Recessive retinal dystrophies were not tested for because the testing methodologies that were available were not applicable to these highly heterogeneous diseases. During the 9-year period, we obtained testing requests for both testing to aid diagnosis in the proband for the first affected family member who seeks medical attention for a genetic disorder (unknown mutation) and cascade tests in a family member (carrier or predictive—it can also be diagnostic) where the familial mutation is known. Each test was allocated a laboratory number and the patient's postcode of residence, date of birth and sex were recorded, along with the type of test conducted. This information was used to ensure that all test requests were for discrete individuals and no test requests in the dataset related to repeat tests performed on the same individual. Cascade tests in a family member for a known family mutation were excluded for the primary analysis as this type of testing could lead to clusters of tests in regions. No tests included in the analysis were performed for a future research trial-oriented reason or for other primary research reasons.

Table 1 Testing offered over the audit period

Clinical indication	Gene (OMIM #)	Extent of testing
xLRP	<i>RP2</i> (*300757)	Full gene screen
xLRP	<i>RPGR</i> (*312610)	Full gene screen (inc ORF15)
adRP	<i>RHO</i> (*180380)	Full gene screen
adRP and macular dystrophy	<i>PRPH2</i> (*179605)	Full gene screen
Sorsby fundus dystrophy	<i>TIMP3</i> (*188826)	p.(Ser181Cys)
Late-onset retinal degeneration (LORD)	<i>CIQTNF5</i> (*608752)	p.(Ser163Arg)

Statistical analysis

The analysis plan assumed that the need for testing would be equal within age and gender groups among all nine regions. Variation in service use was measured by 'standardised testing rates' with England set as the reference population. Data were extracted from the laboratory database and coded for analysis using STATA 12.1. Patients were allocated to one of nine regions of England using their postcode. Age- (18 5-year age bands) and gender-specific populations in each region were obtained for each year using annual mid-year population estimates for the 9-year period between 2003 to 2011 from the Office for National Statistics (ONS)(Office for National Statistics. All releases of Population Estimates for UK et al. 2013).

To place the number of tests into a population context, the cumulative incidence rate of testing was calculated. The cumulative incidence rate was calculated as the total number of tests during the 9-year study period divided by the total population (Hennekens and Buring 1987) (using the 2011 population estimates for England). To compare the rates of testing between regions, a 'standardised testing rate' (or STR) was then calculated using indirect standardisation following the method used to calculate standardised mortality ratios (SMR) (Hennekens and Buring 1987). This method divides number of tests that were observed in each region by the number of tests that would be expected for that region, if the rate of testing was the same as the overall rate for England. The expected number of tests was calculated using age group and gender-specific recorded testing rates for England for each year during the study period, which were then applied to the corresponding age group and gender-specific populations in each region for each of the years 2003 to 2011 and summed. Dividing the observed number of tests by this expected number of tests allows a comparison of the rate within a region to that of the underlying rate for England; a rate of one means the total number of tests in the region is the same as would be the case if the region's population were tested at the same age- and gender-specific rate as the England population. The exact confidence intervals around each of these STRs were calculated by assuming a Poisson process (Breslow and Day 1987).

Descriptive analysis of survey data

Survey responses were audio recorded, and responses to all open-ended questions were transcribed verbatim. Data were collated and summarised by two researchers (ME and KP) trained in qualitative research methods. A descriptive summary of findings is presented alongside illustrative quotes. A focus of the analysis of the survey data was to uncover examples of practice which could account for, or explain, variation in the uptake of genetic tests for RD.

Results

Between 2003 and 2011, 1839 tests were conducted for patients residing within England. A slightly higher proportion of tests were for males (62 %) as would be expected in an X-linked disease (Table 2). The cumulative incidence rate of testing in England was 4.3 per 100,000 population for males and 2.6 per 100,000 population for females (Table 2) over the 9-year study period. The highest cumulative incidence of testing over the 9-year period occurred within the age 30- to 64-year-old age groups.

The standardised testing rate varied widely between regions of England (Table 3), indicating that some regions had higher rates of testing than expected whilst others had lower rates than expected. Standardised testing rates were particularly low in the North-east region (STR 0.435), approximately half of the expected rate, and notably high in the South-east region (STR 1.418), where there were approximately 42 % more tests than would be expected based on the size and demographic distribution of the population. Two regions (West midlands, East) had standardised testing rates that were not significantly different from the rates observed for the total population of England (Fig. 2).

Table 2 Total number of test reports issued and age- and gender-specific rates of testing per 100,000 population for England during the period 2003 to 2011

Age	Males			Females		
	England population ^a	Tests	Rate per 100,000	England population ^a	Tests	Rate per 100,000
0–4	1,698,200	13	0.766	1,620,300	8	0.494
5–9	1,521,400	43	2.826	1,451,400	9	0.620
10–14	1,577,100	64	4.058	1,504,000	7	0.465
15–19	1,706,500	69	4.043	1,633,700	15	0.918
20–24	1,810,300	59	3.259	1,785,000	22	1.232
25–29	1,820,500	82	4.504	1,830,200	49	2.677
30–34	1,754,900	99	5.641	1,754,400	63	3.591
35–39	1,765,600	122	6.910	1,783,500	75	4.205
40–44	1,923,500	100	5.199	1,962,500	76	3.873
45–49	1,919,700	106	5.522	1,960,100	94	4.796
50–54	1,687,800	94	5.569	1,712,500	69	4.029
55–59	1,481,700	80	5.399	1,515,300	67	4.422
60–64	1,557,100	76	4.881	1,615,200	57	3.529
65–69	1,218,000	56	4.598	1,290,200	35	2.713
70–74	967,800	38	3.926	1,076,300	22	2.044
75–79	755,600	14	1.853	913,600	18	1.970
80–84	519,800	10	1.924	738,900	12	1.624
85+	383,200	7	1.827	796,800	9	1.130
Total	26,068,700	1132	4.342	26,943,900	707	2.624

^a 2011 population for England

Table 3 Observed and expected testing rates and age and gender standardised testing rates by region of England

	Observed	Expected	STR	95 % CI	
				Lower	Upper
North-east	40	92	0.435	0.311	0.592
North-west	297	246	1.210	1.076	1.355
Yorkshire & the Humber	113	185	0.611	0.503	0.735
East midlands	90	158	0.568	0.457	0.699
West midlands	169	192	0.880	0.752	1.023
East	210	204	1.030	0.895	1.179
London	353	278	1.270	1.141	1.410
South-east	424	299	1.418	1.286	1.560
South-west	143	185	0.772	0.651	0.910

Views on variation in practice and access from the survey of English RGCS

Resources, constraints and practice variation

There was evidence of widespread variation in practice within and between regions, with RD patients seen in a variety of contexts (Fig. 1). Some participants expressed a desire to move towards standardised, multidisciplinary working involving geneticists, ophthalmologists and genetic counsellors. One centre was actively engaged in service redesign to achieve multidisciplinary working, but two others described past failures to achieve this due to organisational and practical constraints. No specific ring-fenced budgets were reported to exist for the provision of RD clinics. Instead, resources are drawn from overarching regional or hospital funds. Uncertainty about the sources of funding for RD clinics was evident, but there was a general perception that increased resources would improve service provision.

I think there are, sometimes, patients from other areas that are not getting the best deal, purely because of the way patients are managed within hospitals and trusts within our region. (Genetic Counsellor, RGC)

Provider-led variation in practice

A degree of subjectivity exists regarding providers' perceptions of clinical utility and patient benefit from testing. Some suggested a test would be offered if "it is going to give information that could benefit the rest of the family" (Genetic Counsellor, RGC), but, frequently, decisions on whether or not to offer a test were explicitly based on potential to inform clinical pathways.

Fig. 2 Standardised testing rates by region of England

We would offer genetic testing in any situation where the family want it and where it would alter management or treatment.... we don't do a huge lot of testing because for some eye diseases it doesn't alter anything. (Consultant Geneticist, RGC)

Four providers reported having ordered tests in a research context. In addition, centres attached to accredited laboratories recognised that they were “a special case” (Consultant Geneticist/Ophthalmologist, RGC) and were not subject to the same constraints as centres who incurred costs for ordering tests. Other providers indicated that they would take into consideration any future or ongoing trials when discussing genetic test possibilities with patients.

We are doing more and more [testing] on retinal dystrophy because treatment is coming along....a molecular diagnosis allows us to, potentially, get them enrolled in new therapy trials. (Consultant Geneticist, RGC)

Current and future impact of next-generation sequencing

Respondents reported they expected referrals to increase as new genetic tests such as NGS become available.

We're certainly going to start increasing the number of DNA tests we do because next gen costs have come down and we see a much greater need to have molecularly confirmed diagnoses in the foreseeable future... we really just want to test as a routine rather than as the exception. (Consultant Geneticist, RGC)

The potential impact of NGS was also highlighted, driving expectations of increased opportunities for testing because

multiple mutations can be screened simultaneously, even for patients with ambiguities in family history and/or phenotypic features which may previously have precluded the ordering of single gene tests.

Discussion

Substantial and statistically significantly different rates of testing were found among regional populations. Testing for autosomal recessive retinal disorders was not included in the analysis thereby removing differential rates of consanguinity, which varies across the UK, as a risk factor. Although no information was available on any differences in risk factors among these populations, it seems unlikely that the observed rates of provision could be explained simultaneously by differences in needs or risks across a range of conditions which have different molecular causes, different inheritance patterns and different phenotypic effects. The variations are observed similarly across all conditions analysed; this would appear to provide reasonable evidence of regional inequalities in access to services which compromise both the efficiency (allocating resources in accordance with levels of need) and equity (equal service provision for equal need) of resource utilisation. Furthermore, the differences between regions do not appear to be readily explained by differences in material deprivation between regions as measured by the index of multiple deprivation (IMD). Although provision was highest in the area with the lowest levels of deprivation (South-east) and lowest in the region with the highest levels of deprivation (North-east), the overall rank correlation of provision and deprivation was low (Spearman's rank $r_s=0.33$). The findings from the survey of provider perspectives on test provision confirmed the lack of a

clear strategy to address access to services. These findings should not be seen as surprising because there was no policy mechanism in place to promote equitable access to testing. Although NHS resources are allocated among regions based on the relative needs of regions' populations, this resource allocation policy produces, in principle, equitable capacities to care between regions. There is no attempt to earmark these resources for particular services within regions. Instead, regions are left to determine use of the resources allocated to them in accordance with local priorities. Yet, at the same time, the notion of "postcode lotteries" in healthcare provision, whereby access to a particular service is dependent upon where one lives, is considered to be inappropriate under the NHS.

The differences in levels of provision within England (NE 0.435 to SE 1.418) are consistent with differences in levels of provision between countries of the UK (Northern Ireland 0.265 to England 1.098 (Online Appendix A)). The differences in levels of provision between constituent parts of the UK are to be expected as each country has its own dedicated NHS resource budget and is responsible for determining NHS policies including allocating those resources in accordance with its own priorities, population needs and service configurations. However, there is a long-standing policy context for a regional analysis within England with explicit policies aimed at providing equitable access across England and the avoidance of postcode lotteries in healthcare provision. Consistent with this aim, the operating model for commissioning specialised services published by NHS England in 2012 outlined the need for equal access to services for patients regardless of their location as a key ambition (NHS Commissioning Board. Securing equity and excellence in commissioning specialised services 2012). In this context, the finding of greater differences in provision between regions across England is concerning. Findings of variations in age-standardised rates of genetic testing have also been reported for a broader range of tests (Huntington's disease, breast cancer and Fragile X) between and within countries of the UK (UK Genetic Testing Network. Molecular genetic test activity rates in the United Kingdom 2011). Scotland had consistently higher rates of testing for these conditions than England, Wales or Northern Ireland, but no consistent patterns in testing rates for these conditions were apparent between high-level commissioning health areas within England.

The perception of clinical utility of testing for XL-AD retinitis pigmentosa and retinal dystrophies may vary between providers and commissioners. XL-AD retinitis pigmentosa and retinal dystrophies are untreatable conditions, and for this reason, clinical utility is reflected by achieving a positive diagnosis, assessing accurate prognosis, supporting family decision making and excluding the diagnosis in non-gene carriers. At the time of this study, there was limited evidence of the clinical utility of testing and the variation in provision

we observe highlights the importance of evidence of clinical utility. Since clinical geneticists have a limited budget and come from diverse backgrounds, the perception of relative clinical utility would be expected to differ between different individuals. In contrast, ophthalmologists had no budget to test for genetic conditions during the study period, although those with a special interest run clinics for patients with inherited retinal disease and would be impacted by the variability in genetic testing rates. This variability in testing rates is the outcome of decisions made by clinical geneticists operating under locally determined budget constraints.

The survey data have provided a snap shot of working practice from respondents with experience of current models of service delivery which is undergoing a process of adaptation in response to the ongoing technological revolution seen in medical genetics. To varying degrees, dependent upon centre, RD service provision is already subject to resource constraints. Providers are confident that NGS has the potential to improve patient outcomes but recognise the potential demands on finances, time and providers' input to care. However, the advent of NGS has meant that some laboratories are now not testing their own samples. The impact of NGS on equity of access to testing needs to be tested empirically, but it would be intuitive that this has introduced additional possibilities of inequity of access to testing by NGS as not all laboratories in the UK are offering this service.

Our analysis has a number of limitations. Firstly, to place the number of tests into a population context, we estimate a rate of testing for the total population within a given region. This introduces an implicit assumption that the entire population is at risk; however, this is not the case and the results should not be interpreted this way. Furthermore, in line with this implicit assumption, we do not remove people who were tested from population for all future years even though they would not be tested again and are therefore no longer part of the "at-risk" population. However, removal of people from the populations introduces further, arguably weaker, assumptions that the populations are stable over time. This assumption would assume that there is no inflow or outflow of populations through, for example, migration and death. In practice, the numbers of people tested are so small (<0.01 % of the population) that it is highly unlikely that they would make any real difference to the results. Additionally, we excluded gene-specific tests due to the possibility that cascade testing within families could lead to clusters of tests in regions. However, a secondary analysis indicated that our results were robust to the inclusion of targeted tests (range 0.989; NE 0.485 to SE 1.474) (Online Appendix B).

A second potential limitation is the possibility that some of the diagnostic tests may have been available to referring clinicians free of charge during the periods in which they were under development. Although all tests are free to the patients at the point of access, the majority of tests were funded on a provider-

to-provider basis within an NHS commissioning framework. If access to tests that were provided free of charge was unequal between different centres, then this could explain some of the variation we observe in test provision. However, as the number of free tests relates to a small number of samples and is made available to all referrers, we do not believe that this has influenced the patterns of test provision. Furthermore, no cohorts of “research” samples were included in our analysis.

Finally, it is unclear whether the variation in rates of testing observed is due to differences in the way that tests are explained and presented to patients by clinical geneticists and genetic counsellors, or due to geographical differences in patient decisions to undergo testing. It would be difficult to create a single, national policy for uptake, but a consistent approach about how to provide information about the availability and perceived value of testing could improve equity of demand through a shared decision-making process between counsellor and patients. One difficulty of developing a single strategy is the lack of a strong evidence base supporting testing. Currently, the UK GTN approves Gene Dossiers to evaluate new genetic tests to inform decisions about whether these tests should be funded by the NHS. These Gene Dossiers consider clinical validity and clinical utility and cost implications, although clinical utility as supported in the gene dossier remains a subjective decision. We suggest that a sufficiently robust evidence base that supports the value of genetic testing for RD based on clinical and economic evidence of clinical utility is required to promote the development of a single national strategy for provision of testing.

Equitable access to particular services across regions is unlikely to happen by chance (i.e. without specific policy mechanisms to promote, monitor and evaluate the regional distribution of access to care). Instead, service delivery is likely to reflect the distribution of clinical expertise and leaders in the field and hence depend upon the case being made for improving access to services by these clinical leaders. In this way, the distribution of services will be “supply” driven as opposed to needs based.

Future expansion of technologically driven testing capacity will not overcome all barriers to genetic and genomic testing. If more equitable access to genetic testing is to be achieved, commissioning authorities will need to be provided with information on the scope and role of genetic services and the size and nature of the population at risk of the conditions for which patients are being tested. Such data are urgently required to facilitate the rapid advances in health care that are presaged by the NGS revolution.

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Conflict of interest Mark Harrison, Stephen Birch, Martin Eden, Simon Ramsden, Tracey Farragher, Katherine Payne, Georgina Hall, and Graeme Black declare that they have no conflict of interest.

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