CHAPTER 7
HEALTH ECONOMICS

7.1 Introduction

The development and application of new genetic technologies has the potential to provide significant benefits for health care. For patients, the potential benefits are improved knowledge about the risks of developing disease; the opportunity to mitigate risks through behaviour modification, screening or preventive treatment; and an opportunity to make more informed choices (Salari et al. 2012). For health care providers, there may be increased capacity to predict response to treatment and to target treatments more effectively, leading to greater certainty and potentially better health outcomes for their patients (Patel 2014). Instead of treating 100 people, with 10 per cent showing a response to treatment, 10 people identified through genomic testing could be treated with a 100 per cent response. However, all 100 individuals will require testing initially, and other treatments may be indicated for some of the other 90. This has the potential to decrease the cost of clinical trials and the time-to-market for new drugs. For industry, new technologies lead to new marketable products and potentially new sources of profit (Marketwatch 2014). The emergence of the capacity to identify genetic markers has, in some cases, rescued treatments previously thought to be ineffective or harmful, but which may be effective for a targeted population. For the health system, genetic technologies have the potential to lead to more targeted treatment, reducing health care expenditure on treatments that are unlikely to lead to benefits and improving overall efficiency. However, these new genetic technologies can also have significant costs,

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and many of the benefits remain uncertain (Deverka et al. 2010). The balance of costs and benefits will differ when considered from different perspectives in the health system and society.

In the short term, there are likely to be increased costs associated with new treatments and tests (Filipova-Neumann and Hoy 2014; Gazouli and Souliotis 2014). From the point of view of manufacturers of health care technologies, genetic technologies have the potential for increased revenue from new tests and treatments. But, in Australia, as in most developed health care systems, the prices paid for new technologies are generally related to the health outcomes gained, and the capacity to target may lead to higher prices for targeted treatments. This may have a direct impact on health expenditure through government-funded programs if there are excess profits or improved outcomes that are not offset by reductions in the number of people treated. Where new technologies are not funded or only partially funded by government, and especially during the period when new and old systems run in parallel, patients will face higher health care costs in terms of insurance premiums or out-of-pocket costs, often at levels that are beyond the reach of average income earners. This raises questions of equity of access to new technologies. It is also worth noting that the information from genetic screening is often indicative rather than definitive. As a result, there may be patients who undergo unnecessary treatment that entails costs and risks but does not provide benefit. Patients may also experience increased anxiety about potential future health outcomes and may choose, as a result, to seek more frequent follow-up and treatment even when this does not confer a health benefit (Hall et al. 1998).

There is also potential for increased anxiety if the ability to identify a risk of disease in an individual has outpaced the development of treatment options for that condition.

This chapter broadly examines the economic implications of these new technologies for the health care system. The gains in health may bring considerable benefits to Australian society, provided the associated costs are reasonable. Direct costs will include charges for genomic and other omic analysis. Even though the cost of DNA sequencing is falling rapidly, and is now in the order of US$1,000 for a complete genomic sequence, including interpretation, it is still considerable if applied to a population. Indirect costs, especially the costs of training existing and new staff in the delivery of genomic information for health benefit, will also be high.

As will be discussed in Chapter 8, both the skills and the equipment used in precision medicine and gene editing are the same as those used in agriculture and veterinary medicine and are relevant to sport and defence. The application of medical research is a highly competitive area of technology and, although Australia has some strengths in biotechnology, it is even stronger in agricultural innovation, where many commercial applications exist.

An estimate of the costs and benefits of precision medicine depends on how health care is funded, how value for the health dollar is determined and how the health technology market is regulated. Australia is a mixed public and private health care system (The Australian Institute of Health and Welfare 2016). This raises the question of what should be covered under universal health insurance (Medicare) and what should be left to private funding. Australia has a well-developed health technology assessment (HTA) approach, but evaluating genetic tests and genomically guided treatments presents new challenges. The rapid development of this technology is leading to lower upfront testing costs, although these may result in increased use of high-cost interventions, which presents challenges for market regulation. Further, the availability of low-cost testing may result in increased demand for treatments that may not yet have demonstrated benefits or for which the capacity for harm remains unknown (Miller et al. 2002). The medical market is becoming internationalised, and the fact that Australian medicine is regarded as safe and well-regulated should allow entrepreneurial medical units to become international centres for genomic diagnosis and treatment.

7.2 Public and private payer systems

Health care in Australia is financed primarily by government, accounting for about two-thirds of health care expenditure (The Australian Institute of Health and Welfare 2016). The other main sources of finance are private health insurance and out-of-pocket expenditure. Funds are then expended through both public and private sectors. Medicare provides subsidies for treatment delivered by private medical practitioners, including diagnostic testing. Private health insurance covers private in-hospital treatment and general (largely dental) and other ancillary services and is prohibited from covering out-of-hospital services provided under Medicare. Over the past decade, there have been a series of initiatives using both subsidies and penalties to encourage the uptake of private insurance (e.g. the Australian Government private health insurance rebate). Slightly less than half the population have private insurance (Australian Prudential Regulation Authority 2017) at a cost of A$6.5 billion in public funding in the form

of rebates (Hawthorne 2016). Consequently, significant public funds have been directed to supporting the private health insurance industry and, by extension, the private health care sector.

The result of these complex arrangements is that any episode of care may be funded through different mechanisms and from different sources. We will consider the application of precision medicine to cancer treatment, as much of its cutting-edge application has occurred in oncology. The use of precision medicine will generally involve initial testing to determine the genetic make-up of the patient and the changes that have occurred in the genome of the tumour. The results of those tests may provide information that will allow the clinician to recommend the most appropriate therapy, particularly where there is a targeted treatment available or where there is information about potential harms of some therapies.

Consider a diagnostic test for a cancer that has an associated genomic marker with a potential targeted medicine. The test may or may not be covered by the MBS, but it may entail a consultation with a specialist, a biopsy and pathology tests, and will likely involve a private provider. The extent to which patients must pay out of their own pocket in the community setting will depend on the fees charged by their provider and the Medicare Schedule Fee. The Extended Medicare Safety Net (introduced in 2004) provides some additional financial protection for those patients who incur unusually high out-of-pocket costs (and higher costs for government) relating to Medicare services delivered in the out-of-hospital sector during a calendar year.

However, many different types of genomic tests are not listed on the MBS. Through their public hospital-linked facilities, state governments have established and funded genetic services that will offer genetic screening, as well as counselling and education. Such services are limited in their physical location, with different funding arrangements across states and territories, and they typically cater to people who have been identified as being at risk of a genetic condition. Any consequent treatment may be provided through a public hospital at no charge or, if the patient has private insurance, they may elect to be treated privately in a public hospital or in a private hospital. Each of these alternatives involves different costs for the patient, the private insurer and the state and federal governments. Subsidies may also distort the distribution of government benefits. These considerations also affect the ethical issues regarding distributive justice and the preferential allocation of resources to those with the greatest clinical needs.

7.2.1 Insurance

Medicare provides universal tax-financed comprehensive insurance, but it does not cover all health care services. This is particularly the case for emerging technologies that have not yet undergone HTA. The process by which new technologies are assessed for public subsidy is discussed in Section 7.4.1. In the context of precision medicine, it is important to note that Medicare has been intended to provide 'medically necessary services', which has not included population-based screening. Major population-screening programs, such as those for cervical cancer, breast cancer and colon cancer, have been funded as separate population health programs. There are some advantages to this approach, as national screening programs can be designed to encompass appropriate counselling, education and follow-up and to provide

a more efficient approach to recruitment, delivery and targeting of services. However, once a condition is detected, further investigation and treatment are deemed medically necessary and covered by Medicare.

The question arises of which genetic information testing and treatment technologies should be publicly funded. An individual pathology test for a specific genetic marker (e.g. for a hereditary disease) is managed through the evidence-based reimbursement decision-making process of the Medical Services Advisory Committee (MSAC). Genomic sequencing (as opposed to genetic testing related to specific risks of an individual) may be assessed through this process. If such an approach to screening becomes widespread, regardless of whether it is funded under Medicare, there will be inevitable consequent costs on Medicare for follow-up and treatment unless the fundamentals of Medicare are changed. There have also been suggestions that changing information can change behaviour in ways that can be difficult to predict, sometimes leading to avoidance and sometimes to seeking additional health care, therefore potentially increasing total costs; however, further studies are required (Macdonald et al. 1984).

Private insurers may choose to cover genomic sequencing, subsequent testing and follow-up through their general or ancillary products. Private insurers are allowed to operate 'health businesses' and some have recently established or acquired interests in dental and optical centres and primary care. Where genomic testing has clear benefits, and the tests are not yet covered by Medicare, this could be a significant challenge to the equity of the Australian health care system. Even when the benefits are not clearly demonstrated, this introduces differential access.

7.2.2 Assessment of risk factors

Genomic testing will provide more precise familial information about individual risk factors. These results may have implications for a person's relatives even if they choose not to be tested. This risk assessment may alter eligibility for private health insurance, other insurance and occupation selection.

Although private health insurance in Australia is community rated (so individual risk should not affect the premium charged), firms do attempt to encourage healthy people ('better risks') to take out insurance by, for example, targeting policies to young people. Genomic testing could provide new approaches to favourable risk selection and while this will improve private firms' profitability, it runs counter to the social goals of community rating for private health insurance. Should firms be obliged to provide cover to individuals with known conditions where the probability of an insurance payout becomes higher, or to provide packages that cover all conditions? There are also questions relevant to the individual's responsibility to disclose risk and, equally, at what point they should seek treatment.

The same issues arise in the context of other insurance, where the markets are not as highly regulated – particularly life insurance and income protection, although we may also include travel insurance.

Finally, more precise information may provide insights into risks associated with certain occupations. In the future, this may benefit the individual in selecting an occupation and could also be valuable to employers in recruiting staff. It is feasible that, just as psychological testing for job attributes has become widespread, employers could seek genomic testing as one basis of candidate selection. This has implications for regulation in terms of mandating the pooling of risks

and the level at which this risk pooling should occur for the population. Further, this raises concerns about an increased risk of discrimination against individuals by employers or insurance providers.

7.3 Cost-effectiveness and resource allocation

The previous section identified how, in Australia's mixed public-private system, the developments of precision medicine can lead to changes in the costs of health care and the distribution of those costs across governments and individuals. The way that these new technologies are financed and funded has a significant bearing on the efficiency, equity and sustainability of the system. It is also important to recognise that the funding mechanism will have consequences; for example, fee-for-service models will generally result in increased volumes of services offered or provided. New technologies generally have high overhead costs associated with the process of discovery and bringing them to market. Funding mechanisms that recompense these fairly and provide incentives for additional advancement, while not allowing providers to capture abnormally high profits, should be considered.

7.4 Costs of implementation

The costs of implementation can be considered in two categories:

- The cost of providing the service based on the technology itself; and
- The need for associated infrastructure.

The cost of any service delivery is a combination of fixed and variable costs. The relationship between the two determines whether there are economies of scale. In many health care services, there are volume-outcome relationships, whereby a minimum level of activity is required to ensure good quality outcomes. Investigation of economies of scale, economies of scope and volume-outcome relationships is required to ensure technical efficiency in the delivery of these services.

It is important to understand that testing in itself does not deliver improved health outcomes, but it can provide information that serves as a basis for further intervention (Cairns and Shackley 1993; Rubin et al. 2014). The information changes the consequences in terms of health care use and costs. Overall, the net costs may be negative or positive (but should be weighed against health gains, as discussed in Section 7.4.1). It is well established that fee for service is associated with increased volumes of services provided and that some of those services will be of little, no or negative benefit. Health reform is seeking new funding approaches that provide more appropriate incentives for practice. Where a service is part of an episode of care, bundling those services may well be a more effective funding mechanism (Dawda 2015). Another consideration is funding mechanisms that will enhance care quality. In the context of precision medicine, such funding mechanisms might ensure that services are better targeted to those who stand to benefit, and that the use of the resulting information leads to the appropriate downstream use of health care. The development and implementation of such innovative funding approaches have not proven easy so far, but will have significant effects on the cost of delivery.

There will also be an associated infrastructure required for the storage of genetic material and the confidentiality of data (see Chapter 6) (McGowan et al. 2014). Storage of information and the capacity to retest will be important because, as more information from research becomes available, there may be changes in the interpretation of results (e.g. there may be retesting of new markers or changes in management based on new information about the existing and known markers). Health information is known to be valuable, and there are increasing risks associated with cybersecurity. There are also medicolegal and ethical implications regarding the responsibility to act on information. For example, if a test identifies a familial risk of a potentially severe condition, should family members be informed even though they have chosen not to be tested?

7.4.1 Ensuring value for money

Australia has a well-developed process for assessing new medical technologies for public subsidy, by way of the health technology assessment process. The need for a rational process, and one that is consistent across funding programs in deciding whether to fund a new technology, is driven by the limited resources available to pay for health care. Australia has introduced formal structures to assess the cost-effectiveness of new technologies, and these are part of both the PBS and the Medicare Benefits Scheme and are in addition to the regulatory structures that are in place to consider the safety and efficacy of new technologies.

There have been a number of reviews of economic evaluation studies in precision medicine (see, for example, Jarrett and Mugford 2006; Vegter et al. 2008; Wong et al. 2010; Beaulieu et al. 2010; Djalalov et al. 2011; Antoñanzas et al. 2012; Assasi et al. 2012; Yang et al. 2013; Buchanan et al. 2013; Simonds et al. 2013; Marzuillo et al. 2014; Miller et al. 2014; Phillips et al. 2014). As precision medicine can vary in its focus, from screening to targeted therapy, and across diseases, it is difficult to reach general conclusions about the cost-effectiveness of the technology. There are inconsistencies in the approach taken in individual studies and in the ratings of quality by reviewers. For example, in an extensive review of cost-effectiveness analyses for colorectal cancer, Frank and Mittendorf (2013) observed significant variability across studies, concluding that the key drivers of the results were: how the costs for the detection of predictive biomarkers were included (not at all, only for patients who received the targeted agent, for all patients); the clinical characteristics of predictive biomarkers (sensitivity, specificity, validity, reliability, timing, prognostic value, testing sequence and incidence); and the data for the targeted agent (based on retrospective subgroup analyses, incorporating heterogeneity of effects, or individualised dosing). However, some general findings about the challenges for economic evaluation emerge.

Although genetic technologies are just another category of new health care technology, and so should be assessed within the same broad HTA framework, there are particular issues that arise in consideration of their cost-effectiveness (Grosse et al. 2008; Deverka et al. 2010). It is important to identify how genomic technologies, and particularly different sorts of technologies (e.g. whole genome sequencing, tests for specific genes or tests for tumour markers), change the treatment algorithm at different points and what the implications are for treatment. The choice of comparative technology against which costs and outcomes are assessed is another issue (Buchanan *et al.* 2013). The choice of comparator for genomically guided cancer care should ideally involve a mix of genomic and non-genomic care. Multiple

comparators may also be of value, particularly when applied to diagnostic tests where there is potential for the use of in-house custom tests of differing cost and analytical validity.

The choice of perspective is key to identifying the scope of outcomes and costs included in the analysis. Choosing a narrow perspective, such as one that emphasises benefits to the health care sector rather than to the economy as a whole, may overlook many of the potential benefits and costs of genomic-based technologies. An example of this is the value that consumers may place on information provided by genetic tests that potentially goes unmeasured or unvalued when the study's perspective is restricted to a health system perspective. Similarly, information may have a negative value if it increases consumer anxiety or concern.

Economic studies of genomically-guided cancer care also require appropriate timeframes to ensure that all downstream costs and benefits are captured. Importantly, economic evaluations of many genomically-guided cancer care technologies are an amalgam of two different technologies: the test and the treatment. This inevitably makes the evaluation more complex and generates more uncertainty about some of the key parameters of the study, such as the sensitivity and specificity of the test results. This makes it important to undertake well-specified sensitivity analyses that can provide information on the importance of such uncertainty to the overall results.

Current HTA approaches rely on clinical evidence produced by clinical trials. Robust trials require large groups of homogeneous patients to achieve statistical significance. In contrast, precision medicine is exploiting the differences between individuals to better target therapy. This produces a challenge in generating scientifically valid evidence. Adding to this complexity, scientific knowledge is expanding at a rapid rate and is likely to change the relationship between genetics, disease progression and therapy. This complex relationship suggests that it is difficult to assess (or predict) the overall impact of genomics on the health care system in terms of health outcomes, costs and delivery.

The decision-making processes for listing pharmaceuticals on the PBS were designed in an era when blockbuster drugs, prescribed to large groups of patients, were commonplace. The additional costs that HTA processes imposed on pharmaceutical companies and governments (such as the costs of producing a health technology report, conducting economic evaluations and undertaking rigorous assessments) were relatively small compared with the overall revenue that could be gained by listing a drug on the PBS. However, the blockbuster era has gone, and the current pharmaceutical market is characterised by more therapeutics for multiple indications and smaller patient groups. This trend is likely to continue with expansion of genomically-guided treatments, where the patient population is getting smaller and the volume of sales for each new therapy is decreasing.

Therapeutics with smaller potential markets may increase the relative costs of undertaking HTA compared with the potential volume of sales. Given that the costs of conducting an HTA is are relatively fixed (i.e. the costs are unlikely to vary much regardless of the sales volume), its expense may begin to put additional pressure on drug prices. These issues may come to the fore with the development of precision medicine. Under circumstances where the target population is small, Australia's current HTA and decision-making processes may become too cumbersome, and alternative priority-setting mechanisms for deciding which technologies to adopt and diffuse may need to be designed.

Box 24: Rare disease economics

Rare diseases are typically complex, debilitating or life-threatening disorders and are a major cause of intellectual and physical disability in childhood. About 8,000 rare diseases have been identified worldwide, and 6 to 8 per cent of the Australian population are affected (Rare Voices Australia 2017). There are an estimated 15,000 new rare disease diagnoses in Australia every year (based on 300,000 births annually), and they account for one-quarter of inpatients in children's hospitals at any one time. As advocates have argued, although rare when considered individually, collectively these diseases have a significant economic and health impact. The rarity of each of these diseases means that diagnosis is often complex, lengthy and can require repeat assessments. Once a diagnosis has been made, many rare diseases have no effective treatment. Improved diagnosis, early intervention and prevention could significantly improve the quality of life of affected patients and reduce the economic burden of rare diseases.

The use of precision medicine to diagnose rare diseases, particularly whole exome sequencing conducted early in the diagnostic pathway, has been shown to increase the diagnostic rate, provide greater accuracy and reduce the cost per diagnosis compared with traditional diagnostic pathways (Stark et al. 2017). Rare diseases are also considered to be good candidates for precision therapeutics that are capable of treating at the level of the gene. Indeed, they have been proposed as good targets of gene editing interventions.

However, the prevalence of individual rare diseases means they pose an economic challenge to traditional models of drug funding. Whereas blockbuster pharmaceuticals are designed to be suitable for broad swathes of the population, the market for a rare disease drug could be as small as a handful of patients. In some cases, this has led to exorbitantly high prices for novel medications. For example, Europe's first approved gene therapy, alipogene tiparvovec (marketed as Glybera and designed to compensate for lipoprotein lipase deficiency, which can cause severe pancreatitis), was made available at a cost of US$1 million per patient; the drug's manufacturer recently announced it would not be seeking renewal for its market licence due to low demand (UniQure 2017). Regulatory measures in some countries, such as orphan drug designations, seek to minimise risk and expedite the work of drug development for rare diseases.

7.5 Regulation of private markets

There are large potential benefits offered by precision medicine, alongside the potential for increased cost pressures on health care budgets. With the rapid development of technology leading to lower costs for genetic sequencing, and the potential for new market-driven opportunities, it is important to ensure appropriate regulations (and incentives) exist to ensure cost-effective use of these new technologies. The policy response will have to address better targeting of genetic tests to population groups, as well as influencing and informing patients and clinicians about appropriate surveillance activities and ensuring that post-market surveillance is part of the infrastructure.

Health care is seen as a growth industry by investors in the Australian economy because Australians are prepared to commit considerable discretionary spending to health, the population is ageing and most health care services are underwritten by government. This provides a context in which private profit can conflict with social objectives. Achieving an economically sustainable precision medicine field will necessitate balancing the cost-effectiveness of new technologies and treatments with effective mechanisms for upholding intellectual property rights, including incentives for the parties developing those innovations.

7.5.1 Pop-up clinics and diagnostic services

New health technologies often provide a niche market for new providers to specialise and develop new customers. This is particularly so when consumers can be recruited directly, without referrals from GPs. A screening test can be useful as a marketing tool and may be offered as a loss leader, particularly if covered by Medicare and thus eligible for bulk billing. People with positive test results can then be recalled for further investigation or treatment. Of course, this provides an incentive to err on the side of classifying more test results as positive and to recoup costs on further tests or treatments.

The development of skin cancer clinics is a case in point. These have proliferated and have been accompanied by a tendency to excise lesions at a rate that is perhaps greater than necessary (The Royal Australian College of General Practitioners 2014). Although such services appear specialised, they are usually staffed by generalist trained doctors rather than dermatologists (House of Representatives Standing Committee on Health 2015).

7.5.2 DIY kits

The market for direct-to-consumer genetic tests, where consumers submit samples and receive information on their genetic profile without the mediation of a GP or other health care professional, has expanded rapidly, facilitated by internet sales and international commerce. Some of the most popular tests are offered through companies such as 23andMe and Ancestry.com, which have been described as offering recreational genomics. 23andMe had to withdraw the links of its ancestry tests to health information after a US FDA warning stated that the company did not have data to justify provision of all the risk analyses it was offering. It has since relaunched with a limited range of health-related advice, concentrating on SNPs associated with high risk of developing several well-characterised diseases, including breast cancer and Alzheimer's disease. The motivation for those taking part in tests offered by 23andMe or Ancestry.com is often an interest in ethnicity or ancestry, but the tests also offer access to a great deal of genetic information, at a low cost.

When direct-to-consumer test companies are based overseas (as is the case for 23andMe), it is difficult to regulate their local use, and they are not subject to NATA accreditation and inspection. However, more than two million people have provided DNA samples to 23andMe, which has also entered into agreements with pharmaceutical companies for the associated data linking gene patterns to health. Even though much of the information offered by the direct-to-consumer companies is accurate and well presented, it cannot give the depth of information tailored to an individual that would be offered by a fully knowledgeable health care provider. As such, the potentially adverse consequences of this form of testing include possible poor

standards of non-accredited providers, variable relevant information, lack of follow-up and counselling services, lack of connection to other health care providers, consequent anxiety for consumers and increased demand on in-country health services (to deal with the results of such testing, regardless of its accuracy or relevance to care). State governments and professional societies in Australia have recognised the need for proper regulation of this market, issuing position statements on the role of direct-to-consumer tests in relation to the health system (see, for example, Australian Medical Association 2012; Office of Population Health Genetics 2013).

7.5.3 Pharmaceutical industry

The pharmaceutical industry has the potential to benefit from the development of targeted treatments, which may command substantially higher prices than established treatments. Currently, the highest returns are made from products for which consumers comprise large segments of the population. Products that will only benefit a small number of patients are less commercially attractive. The industry also bears most of the costs of drug development (although the underpinning basic science is still supported by government in universities and medical research institutes), and these have to be recouped whether the product is for a common or a rare disease. To date, the Australian Government has recognised the need to provide different arrangements for the funding of treatments for rare conditions, including rare genetic conditions, through the Life Saving Drugs Program. The challenge is to encourage inclusion of more therapies that can be directed towards smaller patient groups within the general PBS. It is of note that the prices paid by government are often related to therapeutic benefit for a particular patient group; consequently, the same drug could attract different funding in different patient groups.

The use of economic evidence in determining public funding is a powerful tool for policy makers to increase value for health care expenditure, but decisions are more uncertain where economic evidence is lacking. Clinical and economic evidence takes time to develop, and patients may be denied beneficial treatments in the meantime. One response to this challenge is to provide coverage alongside evidence development, such as through risk sharing arrangements, with the condition that more evidence is collected and with the supplier at risk for a product that proves to be less effective. Thus far, risk sharing arrangements have taken on many forms:

- Agreements that are designed to limit uncertainty regarding costs without considering the health outcome experienced by the patient. For example, a manufacturer pays for a genetic test in order for patients to gain access to a drug that is subsidised on the PBS for individuals with tumours that exhibit specific mutations.
- Price volume arrangements that restrict the financial liability of the payer by placing a cap on their total expenditure. These agreements allow the payer to be reimbursed if the total expenditure exceeds the cap.
- Performance-linked reimbursement arrangements that are designed to limit uncertainty regarding the cost-effectiveness of a new drug in the real-world. For example, under the funding of ipilimumab for melanoma, the funder only pays for the treatment for those patients who respond.

Box 25: Precision medicine health economics questions for further consideration

Insurance

- Where should the responsibility for funding of genomic technologies fall, particularly in a mixed public–private health system such as Australia's?
- Which genomic technologies should be funded or subsidised publicly, and what are the implications of access through the private system in terms of equity and efficiency?

Assessment of risk factors

- What are the implications of genomic technologies, including genetic testing and precision medicine, for private health insurance in Australia?
- Should individuals be required to disclose their testing history to insurers, employers or others?
- Should insurers, employers or others be prohibited from seeking information about testing history from individuals?
- What are the implications for other insurance markets, including life, income and travel insurance?
- Should employers be able to require genetic testing?

Cost of implementation

- Are there delivery system implications (such as economies of scale, volume–outcome relationships) for genomic testing and treatment?
- What are the appropriate funding mechanisms to ensure efficient provision of appropriate and high-quality services?
- Who is responsible for the provision of infrastructure associated with genomic technologies (including storage of genetic information and genetic samples)?
- What are the ethical and legal responsibilities for provision of information to other parties?

Ensuring value for money

- Are the current structures for assessing new technologies, such as MSAC and the Pharmaceutical Benefits Advisory Committee (PBAC), appropriate for assessing new genomic testing and treatment?
- Are structures available for assessing the economics of chronic disease prevention or onset delay?

Pop-up clinics and diagnostic services

- How should the provision of clinics and diagnostic services be regulated to ensure appropriate use of these technologies and to safeguard patient interests?

DIY kits

- Can direct-to-consumer advertising be regulated?
- Can the use of these services be managed to ensure appropriate use of these technologies and to safeguard patient interests?
- Can the quality of laboratories providing genomic profiling be regulated, especially if they are based outside Australia?

Pharmaceutical industry

- How do we ensure that benefits of genetically guided treatment are appropriately shared between the developer of the technology and the taxpayer?
- How do we design payment arrangements for genetically guided treatment to ensure a fair sharing of risks between the developer of the technology and the taxpayer?
- How can we build on existing data collection systems to facilitate monitoring for new risk sharing arrangements?

- Coverage with evidence development arrangements that link population-level payment or reimbursement to prospective data collection.

Despite the obvious attraction, risk sharing agreements have frequently been difficult to implement (Neumann et al. 2011). Some risk sharing arrangements require substantial new capacity to monitor costs and outcomes of new therapies in real-world settings, particularly those that are based on performance-linked reimbursement arrangements that require patient-level outcome measurement. This capacity is often lacking or requires substantial investment.

Thus far, risk sharing agreements have typically been established between the payer and the pharmaceutical manufacturer. However, Ramsey and Sullivan (2014) propose that in the case of genomically guided care, risk sharing agreements between payers and cancer care institutions are worth considering. One of the main reasons for this proposition is that treatment outcomes are not just predicated on the effectiveness of a drug but also on the accuracy of the genomic tests, as well as clinical decisions of who and how to treat. Hence, under traditional risk sharing agreements between payers and manufacturers, the drug company stands to make losses on the basis of decisions that are possibly not in its control. Realigning the agreement between payers and cancer care facilities could address this issue. Under such an agreement, the facility receives greater flexibility to offer patients new therapeutic treatment but bears the financial costs of these decisions if certain predetermined clinical benchmarks are not met. This creates strong incentives within facilities to ensure that the most accurate genetic tests are offered and that treatments are matched to patients most likely to benefit. Despite these potential advantages, such risk sharing agreements would still require a sophisticated data infrastructure to enable outcome measurement, as well as measures to protect facilities from excessive risks.

7.6 Cost-effectiveness of precision medicine

The economic benefits of precision medicine are difficult to assess because they will not only depend on the rate at which the cost of tests comes down, but also on the extent to which the new precision testing can be implemented in practice to reduce the amount of preventable illness. To ensure diagnosis and treatment are considered jointly as part of the cost-effectiveness process, the PBAC and the MSAC will need to review evaluation processes for precision medicine.

Some reviews have found reasonable rates of cost-effectiveness and, to a lesser extent, cost savings (Berm et al. 2016; Verbelen et al. 2016). For example, Verbelen and colleagues (2016) found that a pharmacogenetics-informed treatment strategy was more cost-effective than the alternative in more than half of the studies they reviewed.

Yet other reviews have been less conclusive (Hatz et al. 2014; Phillips et al. 2014; Douglas et al. 2016). For example, Hatz and colleagues (2014b) found that 'personalized medicine in terms of stratifying care by genetic characteristics seems to be neither more nor less economically efficient than conventional medicine'.

A common feature of these reviews and other commentary has been discussion of the challenges in evaluating economic benefits of precision medicine technologies (Antoñanzas et al. 2015; Lu and Cohen 2015; Shabaruddin et al. 2015; Bertier et al. 2016). The challenges span both methodological and data-availability issues. A particular challenge alluded to by Lu and Cohen (2015) is identification of the 'broader impacts on the use and costs of related and/or downstream health services'.