

Health Technology Assessment: Reflections from the Antipodes

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Keywords: Australia, health technology assessment, HTA, PBAC.

Introduction

This paper is divided into three sections:

- Section I is largely descriptive and provides a brief inventory of the agencies that use health technology assessment (HTA) in Australia. First, the use of HTA by the Therapeutic Goods Administration (TGA) is discussed. The TGA is the principal agency regulating the availability and marketing of therapeutic products in Australia. An overview of the structure of the health-care system in Australia is then presented to provide a basis for understanding the subsequent discussion on the use of HTA by reimbursement agencies in Australia. The agencies in Australia that have the most highly developed and formalized systems incorporating HTA, including economic evaluation, are the Medical Services Advisory Committee (MSAC) and the Pharmaceutical Benefits Advisory Committee (PBAC). Thus, further details of the requirements of assessments that are undertaken to inform reimbursement decisions made by these committees are then presented.
- In Section II, the Australian situation with regard to a number of current issues in the conduct and use of HTA is discussed and represents our personal views.
- Section III is judgmental and represents our personal views on lessons learned from the HTA experience in Australia. It discusses the Australian situation with regard to a number of current issues in the conduct and use of HTA.

SECTION I: HTA AND ITS USE IN HEALTH-CARE DECISIONS IN AUSTRALIA

Overview of the Use of HTA by Regulatory Agencies in Australia

The Therapeutic Goods Act 1989, which came into effect on February 15, 1991, was introduced with the objective of providing a national framework for the regulation of therapeutic goods in Australia to ensure the quality, safety, and efficacy of medicines and ensure the quality, safety, and performance of medical devices. The Therapeutic Goods Act 1989, Regulations and Orders set out the requirements for inclusion of therapeutic goods in the Australian Register of Therapeutic Goods (ARTG), including advertising, labeling, product appearance, and appeal guidelines. The TGA, which is part of the Australian Government's Department of Health and Ageing, is responsible for administering the provisions of the legislation. Some provisions in relation to medicines, such as the scheduling of substances and the safe storage of therapeutic goods, are covered by the relevant state or territory legislation.

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 10.1111/j.1524-4733.2009.00556.x

The TGA carries out a range of assessment and monitoring activities to ensure that therapeutic goods available in Australia are of an acceptable standard. The approach adopted with respect to the assessment and monitoring activities conducted by the TGA differs slightly across the regulation of various medicinal products and medical devices. There are two levels of entry into the ARTG—"registered" products and "listed" products. All products that are classified as "registrable" by the TGA must undergo a detailed premarket risk assessment and evaluation by the TGA. Products that are "listed" on the ARTG are not subject to premarket evaluation because the TGA has determined, on the basis of a risk assessment, that the products are low risk.

The identification, analysis, and evaluation of risks associated with registrable medicines involve a number of steps. For details, see HTA: Reflections from the Antipodes *Value in Health* Supplementary Information, Part I at: http://www.ispor.org/publications/value/ViHsupplementary/ViH12s2_6.asp.

Overview of the Structure of the Health-Care System in Australia

The Australian health system comprises a mixture of public and private sector health service providers and is funded by a range of mechanisms. Figure 1 depicts the source of funding by health service type [1].

Individuals make financial contributions to the health-care system through taxes and an additional levy (Medicare levy), which is based on their income, and through private financing (either directly and/or through purchase of private health insurance).

Approximately 70% of total health expenditure in Australia is funded by government, with the federal government contributing two-thirds of this and state, territory and local governments the other third [2]. The federal government's major contributions include the two national subsidy schemes: Medicare Benefits Schedule (MBS) and the Pharmaceutical Benefits Scheme (PBS). These two schemes subsidize medical services (including optometry, psychology, pathology, and radiography services) and prescription medicines, respectively, for all Australians. State governments together with the federal government fund public hospital services (including emergency and outpatient services) and residential care for aged and disabled persons. The aim of the national health-care funding system is to give all Australians, regardless of their personal circumstances, access to health care at an affordable cost or at no cost, while allowing choice for individuals through substantial private sector involvement in delivery and financing [3].

Government also provides the following public health services:

1. immunization services and other communicable disease control (including biosecurity);
2. public health education campaigns (including health promotion in the areas of nutrition and physical activity);
3. injury prevention activities;

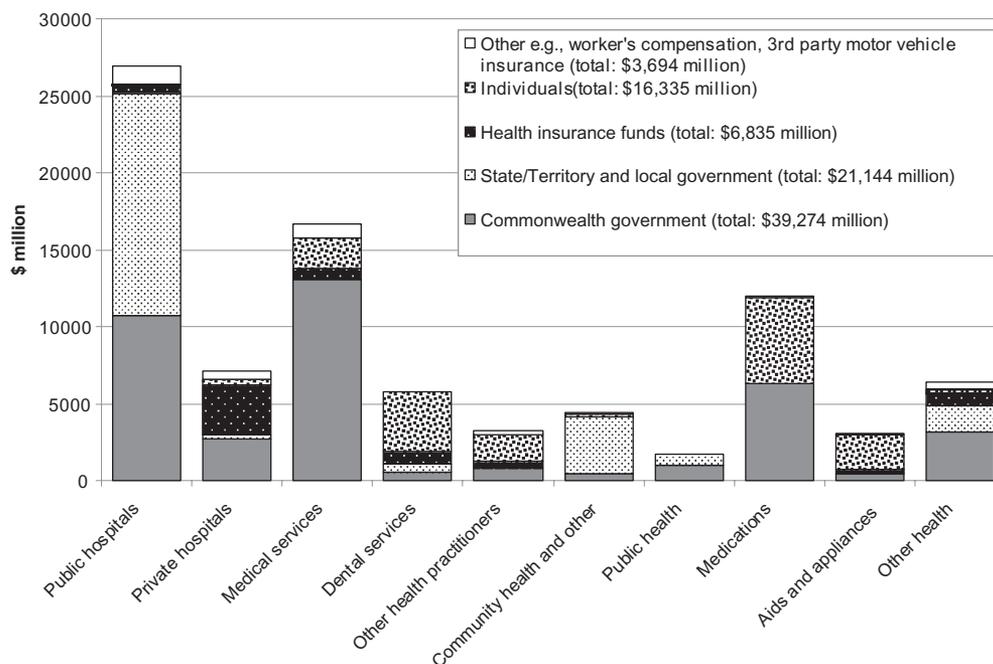


Figure 1 Source of funding by health service type (2006–2007) \$millions.

4. programs to reduce the use and harmful effects of tobacco, alcohol, and illicit drugs;
5. environmental monitoring and control; and
6. screening programs for diseases such as breast cancer and cervical cancer.

Services provided by dentists and other private sector health professionals such as physiotherapists, chiropractors, and natural therapists are generally funded directly by patients (with the support of private health insurance in circumstances where the patient is insured for the provision of such services).

Overview of the Use of HTA by Reimbursement Agencies in Australia

In Australia, as with most countries, the available health budget does not permit all patients in all circumstances to have subsidized access to the best possible health care. Therefore, reimbursement agencies have the responsibility of rationing of health-care resources. There is increasing pressure for health-care policymakers to provide explicit justification for their resource allocation decisions. This has resulted in a movement toward the use of HTA (including economic evaluation) to inform such decision-making, particularly in regard to whether a technology should be publicly subsidized. Interventions that are demonstrated to be effective and cost-effective compared with current practice are more likely to be subsidized than those for whom such evidence is not available. It also needs to be acknowledged, Nevertheless, that despite this increasing pressure for explicit justification of resource allocation decisions, HTA (including economic evaluation) is used by reimbursement agencies in Australia to varying extents to aid decision-making as to whether a technology should be publicly subsidized or not. The extent of assessment varies by health service type and the funder.

The strongest examples of the use of HTA (including economic evaluation) are at the federal level where it is currently pivotal to the processes by which screening programs, medical

interventions, pharmaceuticals, and vaccines are made available under national subsidy programs in Australia.

The MSAC advises the Minister for Health and Ageing on the strength of evidence relating to the safety, effectiveness, and cost-effectiveness of new and emerging medical services and technologies and under what circumstances public funding should be supported. The PBAC makes recommendations to the minister as to the pharmaceutical preparations (including vaccines) that should be subsidized. The PBAC is required by legislation to give consideration to the effectiveness and cost of therapy involving the use of the product, including by comparing the effectiveness and cost of that therapy with that of alternative therapies [4]. The processes for HTA for items that are to be considered by MSAC and PBAC are highly developed and formalized. For details of the requirements of assessments that are undertaken to inform these decision-makers are discussed below. For details, see HTA: Reflections from the Antipodes *Value in Health* Supplementary Information, Part II at: http://www.ispor.org/publications/value/ViHsupplementary/ViH12s2_6.asp.

Although decision-making regarding availability of technologies in public hospitals may be informed by HTA, less formal processes and less demanding requirements for these assessments are applied. Currently, there is no centralized assessment of health technologies (including drugs) that are proposed for use in hospitals. Most hospitals have therapeutics committees which consider requests to have drugs included on the hospital formulary, but the degree of assessment is generally less rigorous than the assessments required by MSAC and PBAC. Processes for availability of medical services and technologies in hospitals are generally less transparent than with drugs. This decentralized approach has the potential to result in differences in availability of health-care technologies across a state and even more so across the country. Over recent years, there have been some moves toward centralization of decision-making with respect to the adoption of technologies in hospitals. For example, the Victorian Department of Human Services has established the Victorian

Policy Advisory Committee on Clinical Practice and Technology to consider and make recommendations regarding the application of new and existing technologies and clinical practices in Victorian public health services. Centralization of processes could eliminate much of the duplication of effort by individual hospitals in determining whether a drug or technology should be made available and could result in more equitable access to health-care resources across the country. Some of the resources that are freed by elimination of duplication of effort could be directed toward the conduct of more rigorous assessments.

In the related area of prostheses, private health insurers are required, under the Private Health Insurance Act 2007, to pay benefits for a range of prostheses that are provided as part of an episode of hospital treatment or hospital substitute treatment for which a patient has cover and for which a Medicare benefit is payable for the associated professional service [5]. Prostheses include cardiac pacemakers and defibrillators, cardiac stents, hip and knee replacements, and intraocular lenses, as well as human tissues such as human heart valves, corneas, bones (part and whole), and muscle tissue. The Prostheses List contains prostheses and human tissue prostheses and the benefit to be paid by the private health insurers. For details on listing and prosthesis of devices, see HTA: Reflections from the Antipodes *Value in Health* Supplementary Information, Part III at: http://www.ispor.org/publications/value/ViHsupplementary/ViH12s2_6.asp. The Prostheses Devices Committee (PDC) is a ministerially appointed committee that makes recommendations to the federal minister on which prostheses should be included on the Prostheses List and the benefit payable. The PDC is not required to assess the cost-effectiveness of a device or prostheses before making a recommendation of listing or as the basis for determining the benefit. In setting up and changing the existing arrangements for listing prostheses and devices, the Federal Minister for Health and Ageing was focusing on establishing the need for relative clinical efficacy as a basis for listing with the aim that this would establish a base for which future cost-effectiveness assessment may be applied [6].

With respect to health technologies used in aged care, the federal government, in its 2007–2008 budget [7], announced an initiative to increase the availability and use of “assistive technology,” which refers to devices that could improve the independence of frail older people and help them remain safely in their own homes for as long as possible (e.g., devices that remotely monitor vital signs, systems to help people remember their medication). The measure establishes an industry body to promote the use of assistive technology by community care providers and to generate buying power for the large number of community care services. As there does not appear to be any requirement for the assessment of health technology in this process, it is likely that it will be used to a minimal degree to inform the selection of assistive technologies to be purchased.

Turning to health promotion, the federal government announced in its 2003 budget [8] that to ensure clear and informed decision-making, a formal priority setting mechanism for evaluating potential investment in disease prevention and health promotion would be established. In its annual report for 2003/2004, the Department of Health and Ageing reported that this mechanism had been successfully implemented; Nevertheless, no further details are available in the public domain about this mechanism.

Overview of the Use of HTA in PBAC Processes

The PBAC is an independent statutory body established on May 12, 1954 under Section 101 of the National Health Act 1953 to make recommendations and give advice to the minister about

which pharmaceutical preparations (including vaccines) should be publicly subsidized under the PBS or, in the case of vaccines, under the National Immunization Program Schedule (NIPS).

Submissions requesting the inclusion of a pharmaceutical product (or vaccine) on the PBS (or NIPS) are generally prepared by the manufacturer of the product, who holds the necessary data required to assess the effectiveness, safety, and cost-effectiveness of the product. Nevertheless, submissions from medical bodies, health professionals, and private individuals and their representatives are also considered. The PBAC has published comprehensive guidelines [9] to guide the preparation of submissions. The most recent version of the guidelines was released by the PBAC in December 2006. It is important to understand the purpose of the guidelines. The guidelines were developed to communicate to stakeholders the considerations that the PBAC makes in deciding whether a pharmaceutical should be publicly subsidized. The guidelines should not be interpreted as a set of prescriptive rules to follow, but instead, a reflection of the approaches that are likely to influence the PBAC to recommend a product for inclusion on the PBS. The guidelines are also intended to promote and reflect best practice in clinical and economic evaluation. Adherence to the guidelines across submissions promotes comparability across submissions and assists in identification of uncertainty for the PBAC.

The PBAC guidelines essentially request the presentation of detailed HTA and request the presentation of specific details in a submission. For PBAC guideline details, see HTA: Reflections from the Antipodes *Value in Health* Supplementary Information, Part II at: http://www.ispor.org/publications/value/ViHsupplementary/ViH12s2_6.asp. Drugs that are recommended by the PBAC for listing on the PBS fall into one of three categories—“unrestricted,” “restricted benefit,” and “authority required.” The latter two types of listing are used by the PBAC to target use to specific indications, patient groups, or clinical settings where optimum clinical benefit and cost-effectiveness are achieved [10]. To access the drugs, the patient’s doctor is required to confirm that the patient satisfies the criteria specified in the listing.

Patients are required to pay a copayment for drugs subsidized on the PBS and the government pays the rest. In 2009, there will be two copayment levels, “general” (\$32.90) and “concessional” (\$5.30), with the latter being for patients who are on social security or have other concessional status. This is the maximum price that a patient is required to pay for a PBS-listed drug dispensed at a pharmacy (Nevertheless, patients may pay more if they choose a brand of product that attracts a brand premium; where there are two or more brands of the same drug on the PBS, the Government subsidizes each brand to the cost of the lowest priced brand). Where drugs listed on the PBS are priced less than the patient copayment, then, patients just pay the cost of the drugs and the government makes no contribution.

Overview of the Use of HTA in Medicare Services Advisory Committee Processes

In its 1997–1998 federal budgets, the Government announced a measure aimed at improving health outcomes for patients by ensuring that new and existing medical procedures attracting Medicare benefits are supported by evidence of their safety, clinical effectiveness, and cost-effectiveness. A key element of this measure was the establishment of a new body, the MSAC, whose role is to advise the Federal Minister for Health and Ageing about the strength of evidence relating to new medical technologies and procedures and the circumstances under which, funding via the MBS should be supported.

The MBS lists and provides information on the professional services subsidized by Medicare. The assessment cycle for inclusion of a technology or service in the MBS involves five stages from application to possible funding. For details, see HTA: Reflections from the Antipodes *Value in Health* Supplementary Information, Part IV at: http://www.ispor.org/publications/value/ViHsupplementary/ViH12s2_6.asp. MSAC publishes two sets of guidelines (one for medical services and the other for diagnostic services). The guidelines are intended for use by applicants and by independent contractors. The MSAC guidelines, like the PBAC guidelines, essentially request the presentation of a detailed HTA.

HTAs (i.e., evaluations of the safety, clinical effectiveness, and cost-effectiveness of the technology) are produced by independent contractors (evaluators) in consultation with an “Advisory Panel.” The MSAC appoints a specialist advisory panel, chaired by a member of the MSAC, to assist in the assessment of each health technology. This panel provides expert input into the assessment process as well as ensures that the contractor’s assessment is clinically relevant. Given the number of applications MSAC receives for assessment, it can prioritize consideration of assessments based on clinical need, cost, likely benefit, and other factors determined by MSAC, such as access and equity.

Using the assessment report as a basis, MSAC formulates advice to the federal minister. If necessary, MSAC will request further assessments or analyses from the evaluators to assist it to come to a decision. MSAC can also rely on its previous decisions to inform its advice. Upon forwarding its recommendations to the Federal Department of Health and Ageing, MSAC’s formal role is finished. The Department is responsible for making a submission to the federal minister that combines MSAC’s final report, together with policy advice from the Department. To date, the minister has endorsed all MSAC recommendations [11].

For items listed on the MBS, the government will reimburse 85% of the scheduled price (or 75%, if the patient is an inpatient in a private hospital) and the patient is required to pay the gap. Because in Australia doctors are able to charge in excess of the recommended scheduled MBS listed fee, any excess would also be paid by the patient.

In addition to including restrictions with the descriptor for an MBS item to target use to specific indications, patient groups, or clinical settings where optimum clinical benefit and cost-effectiveness are achieved, the government also has another mechanism by which it can limit access to medical services—the issue of Medicare provider numbers to doctors (and other applied health professionals), which authorizes the practitioner to deliver services that are reimbursable under Medicare. The Medicare provider number uniquely identifies the medical practitioner (or health professional) and the location where they render services. There is no automatic link between medical registration and issue of a Medicare prescriber number. New graduates (and overseas trained doctors) are required to satisfy certain requirements before they are able to be issued a Medicare provider number and be eligible to provide Medicare-reimbursed services. In addition, MSAC can recommend that medical services only be provided at certain specialist centers to be eligible for reimbursement.

SECTION II: CURRENT ISSUES IN THE CONDUCT AND USE OF HTA

As the predominant use of HTA (including economic evaluation) is within the PBAC and MSAC processes in Australia, much of the discussion that follows is primarily in the context of these settings.

Australia has found that a process involving the formal use of HTA (including economic evaluation) to inform reimbursement decision-making for health technologies is both feasible and able to be effectively implemented. While acceptance of an evidence-based and cost-effectiveness process in health-care decision-making has been a little slower that advocates might have liked, it has gradually gained acceptance across the health sector. Nevertheless, there has been some resistance to the use of evidence-based medicine to guide availability of interventions especially if it conflicts with clinical freedom or reduces income to the health-care provider [12]. For cost-effectiveness evaluation to be an accepted part of the decision-making process, the use and acceptance of comparative clinical efficacy as a basis for decision-making needs to be well established. That is, there needs to be a culture of reliance on evidence-based medicine to guide medical practice. This can then be used as a foundation on which to build an HTA process.

Decision-makers in Australia aim to focus on the relative therapeutic value (i.e., the value of the health technology as compared with best current practice) rather than simply efficacy relative to control (often placebo) as may be demonstrated in a trial. As discussed in the guidelines published by PBAC and MSAC, the positioning of the proposed intervention in the management algorithm for the condition of interest is required to be explicit and the incremental effects of changing the algorithm from current practice to practice including the intervention is of paramount interest to the committees.

The use of HTA is now generally well accepted for the evaluation of pharmaceuticals but is less so for medical technologies (particularly for prosthesis and devices). This is partly because of the lack of availability of high-quality evidence as this sector does not have the same history of designing trials that correspond to the highest levels of evidence. Also, adoption of new technologies in the medical services areas can follow a different pathway to that for pharmaceuticals, i.e., new technologies can be adopted by clinicians in the absence of high-quality evidence demonstrating efficacy and safety.

Relationship between Decision-Making Agencies Using HTA and Government

As discussed in Section I, Australia has a universal health insurance scheme, Medicare, based on a philosophy that medical services should be delivered on the basis of ability to benefit rather than ability to pay. Like elsewhere, Australia has budget constraints on public health expenditure, and HTA has proven a useful measure to inform government, policymakers, and clinicians about the relative value of technologies. Nevertheless, the successful integration of HTA into a health-care system requires policymakers and HTA bodies, who are typically independent of each other in their decisions, to share a mutual set of principles underlying their decision-making. It needs to be recognized, for example, that pursuing “value-for-money” and pursuing “cost containment” are two quite different objectives, although often confused and conflated. HTA was not introduced into Australia with a main objective of cost containment but rather as a means of ensuring that funding of interventions was evidence-based and represented value-for-money.

This being said, it needs to be acknowledged that the Australian system is prone to affordability issues that generate ongoing tensions. This reflects the absence of any specified decision rule to define “acceptable cost-effectiveness,” the key role of fee-for-service in our health insurance payment arrangements, and the absence of any explicit expenditure caps on the MBS and PBS schemes. The increasing availability of effective but expensive

drugs and new technologies is likely to continue in the future. Accepting that a tension exists between the availability of cost-effective technologies and affordability, the key Australian HTA arrangements (as operated by PBAC and MSAC) does nonetheless provide a mechanism whereby the government can justify decisions in relation to health expenditure. To ensure that affordability is considered and to ensure that the system remains sustainable, the decision-making role of the PBAC is supplemented with a requirement that new drugs with a budgetary impact greater than \$5 million be considered by the Department of Treasury and Finance and that new drugs with a budgetary impact greater than \$10 million obtain approval from Cabinet (the decision-makers within the elected government) before any recommendation to make a drug available is implemented. If necessary, additional mechanisms to limit access can be introduced, policy advice may be issued, or an increase in public contributions through copayments or taxes can be arranged.

Transparency in Assessment and Decision-Making

Pharmaceutical companies and manufacturers of some other health technologies have been reluctant to have their submissions to the TGA, PBAC, and MSAC released in the public domain on the grounds that they contain commercially sensitive information. Sponsors requesting registration or subsidy of health technologies through these agencies are permitted to provide information on a commercial-in-confidence basis as part of their submissions. The TGA, unlike the Food and Drug Administration in the United States and the European Medicines Evaluation Agency, does not release any details of its evaluations.

In the past, the PBAC has accepted submissions on a commercial-in-confidence basis and the reasoning behind PBAC decisions was not publicly disclosed. Nevertheless, the recent Free Trade Agreement between Australia and the United States has influenced the PBAC to release their reasons for decisions publicly over the Internet, although much information (particularly details of economic analyses) is not disclosed. Generally, only summary clinical and economic information is released.

MSAC on the other hand, a more recent HTA initiative, releases its complete evaluation report, with censoring of information deemed commercial-in-confidence. Nevertheless, the MSAC guidelines [13] advise that “[d]ocuments in the possession of the Department of Health and Ageing are subject to the requirements of the Freedom of Information Act 1982. This means that the Department may be required to grant access to documents in its possession. Even if a document is stamped commercial-in-confidence, this does not mean that access under this Act can be denied. Nevertheless, the Department is required to consult with the author of the document when that document appears to contain commercial-in-confidence material, and take the author’s views into account when deciding to grant/not grant access to documents.” The release of the whole evaluation report by MSAC was in response to criticisms [14] that MSAC decisions were not clear and often at odds with the recommendations included in the evaluation reports. Therefore, recommendations arrived at by MSAC, and their reasoning, are publicly available documents along with copies of the evaluation report. Included with the reasoning is an indication as to whether commercial-in-confidence information was relied upon in coming to a decision.

In our view, there is a strong argument that data submitted to support a request for public subsidy should be open to public scrutiny as public funds will be used to pay for the technologies. Furthermore, we contend that evaluations of these data conducted by government agencies should also be made available to

health professionals and consumers. The successful operation of the system is contingent on health professionals complying with restrictions applied to a technology and their cooperation is more likely if they can understand the reasons behind a decision to restrict the availability of a technology.

There have now been many calls for transparency in regulatory and reimbursement decisions in Australia and internationally. For example, there have been calls for an international register of clinical trials so that unfavorable results cannot be hidden [15,16]. The Australian HTA experience has been one of increasing transparency, in response to greater public demands for more information about the basis on which the PBAC and MSAC make their decisions, together with the impact of the Australia–United States Free Trade Agreement.

Factors Influencing Decisions

Some may consider it desirable for decision-makers to designate an explicit decision threshold (e.g., in terms of incremental cost per additional quality-adjusted life-year [QALY] gained) as constituting acceptable cost-effectiveness. Others argue that the nomination of a decision threshold is problematic as it may encourage “gaming” of the system (where interventions are priced at the maximum price that results in an incremental cost-effectiveness ratio (ICER) below the threshold) and because such formulae-driven approaches ignore other factors that influence whether a particular estimate of incremental cost-effectiveness is considered acceptable or not. These broader considerations include: 1) the degree of uncertainty around the point estimate of incremental cost-effectiveness; 2) the burden and severity of the disease or condition; 3) the prevalence of the disease or condition; 4) the availability of alternative treatments; and 5) the net financial implications of making the therapy available (including the potential for widespread use of the intervention outside any proposed restrictions).

In Australia, neither the PBAC nor the MSAC have nominated any decision threshold as representing acceptable cost-effectiveness and nomination of thresholds indicating that acceptable cost-effectiveness is unlikely to occur. The role of economic evaluation in decision-making in Australia remains as a part of the whole and not the “end game.” Results of an analysis conducted by Harris et al. [17] of the relative influence of factors in decisions for public insurance coverage of new drugs in Australia found that “there is no evidence of a fixed public threshold value of life years or QALYs, but willingness-to-pay is clearly related to the characteristics of the clinical condition, perceived confidence in the evidence of effectiveness and its relevance, as well as total cost to government.” No similar analysis has been reported in relation to MSAC decisions; Nevertheless, similar considerations underlie their decision-making.

As listed above, other factors, apart from economic considerations, can also be considered in deciding whether a particular estimate of incremental cost-effectiveness is “acceptable” or not. The potential for use of an intervention beyond any restriction that might apply (also known as “leakage”) is one of these considerations. For example, where a drug that is listed on the PBS for one reason may also be used for another purpose, needs to be considered, particularly where the market authorization (through TGA in Australia) is broader than the subsidy decision. Examples of use beyond a restriction (leakage) include use of therapy in patients with the same disease as those for whom the intervention is available but in whom cost-effectiveness has not been demonstrated (e.g., where the listing is restricted to a specific subgroup of patients with a disease, but evidence of cost-effectiveness is not available in other subgroups). To deal with

these potential issues, the PBAC and MSAC may require the establishment of a risk-sharing agreement (RSA). RSAs can be used to address at least three types of risk: 1) the overall financial cost to the government, which may be affected by uncertainties in the number of patients, daily dose, and duration of therapy; 2) cost-effectiveness of the therapy, which may be affected by the volume of use beyond any restriction; and 3) the extent of overall gain in health outcomes (although this is a risk that has been less commonly addressed in RSAs). There is currently very little information in the public domain with respect to what RSAs have been entered into and the outcomes of these agreements. Nevertheless, their use does appear to be increasingly adopted where estimates of financial implications for government budgets may be difficult to anticipate because of the issues identified above.

Another factor that the PBAC identifies as a special circumstance affecting its decisions is known as “rule of rescue,” which applies in exceptional circumstances and is particularly influential in favor of listing. The following three factors need to apply concurrently for the “rule of rescue” to be satisfied:

1. No alternative exists in Australia to treat patients with the medical condition meeting the criteria of the requested restriction. This is an absolute requirement.
2. The medical condition defined by the requested restriction is severe, progressive, and expected to lead to premature death. The more severe the condition, or the younger the age at which a person with the condition might die, or the closer a person with the condition is to death, the more influential the rule of rescue consideration is.
3. The medical condition defined by the requested restriction applies to only a very small number of patients. Again, the fewer the patients, the more influential the rule of rescue might be. Nevertheless, the PBAC is also mindful that the PBS is a community-based scheme and cannot cater for individual circumstances.

As with all considerations in the “other relevant information” category, the rule of rescue supplements, rather than substitutes for, the evidence-based consideration of comparative cost-effectiveness. A decision on whether the rule of rescue is relevant is only necessary if the PBAC would be inclined to reject a submission based on its assessment of comparative cost-effectiveness (and any other relevant factors).

Dealing with Uncertainty

Both the PBAC and MSAC generally require evidence that an intervention is statistically significantly superior to the comparator before they contemplate on recommending subsidization of the intervention at a higher price than the comparator (i.e., before they contemplate on the results of the supporting cost-effectiveness analysis). Some have argued that decisions should be based only on the mean net benefits, irrespective of whether differences are statistically significant and that decisions based on rules of inference will impose costs which can be measured in terms of resources or health benefits forgone [18]. It is our opinion that using this sequential process of first determining the clinical benefits of an intervention and then considering the economic merits of the intervention is preferable, as the alternative based on mean net benefits gives insufficient weight to genuine clinical/policy concerns that no harm is done to patients.

Both the PBAC and MSAC guidelines request the presentation of sensitivity analysis examining the impact of varying inputs to the economic evaluation. In addition, the guidelines requests the presentation of a stepped economic evaluation,

which helps the committees identify the aspects of modeling that have the greatest impact on the incremental cost-effectiveness ratio. The stepped evaluation explores the incremental effects of: 1) any adjustments to make the results of the trial applicable to the population of interest; 2) any extrapolation beyond the time horizon of the model; and 3) any transformation of outcomes assessed by the trial to patient-relevant outcomes. The committees are then able to focus on assumptions in the model that relate to the variable of interest (e.g., the degree of robustness around estimates, whether the estimates are the most appropriate, etc.). This approach makes explicit the underlying assumptions within the model, and allows a prioritization of the assumptions that may have the greatest relevance to the disease and interventions being evaluated and where the greatest uncertainty may lie.

Several guidelines for HTA mandate the presentation of probabilistic sensitivity analysis, in particular the United Kingdom. HTA guidelines in Australia differ from those in the United Kingdom, in that they caution against over-interpretation of results from probabilistic sensitivity analysis, particularly where data contributing to the analysis are not derived directly from individual patient data collected in the context of a direct randomized trial. Important sources of nonstatistical uncertainty are often introduced as various discrete pieces of information are combined with individual patient data. Statistical (probabilistic) uncertainty involves random error and can be reduced by increasing sample size. The many other sources of uncertainty may involve systematic error, which are harder to identify and cannot be reduced by increasing sample size. For example, they arise in the selection and measurement of information, the specification of the structure of the model, and the plausibility of the implicit and explicit assumptions relied on for the model, particularly in aggregating across the various sources of information. Without information about the correlation between certain variables within a model, the use of probabilistic sensitivity analysis may not be that helpful in identifying true uncertainty. Although probabilistic models generally allow for correlations to be specified, this information needs to be available with some degree of accuracy.

Both the PBAC and MSAC, in their guidelines, express a preference for evaluations that value outcomes in terms of overall quality and length of life, for example, in terms of QALYs gained, which facilitates comparability across submissions. The generally preferred method of eliciting utilities is by the repeated application of a valid, reliable, and responsive multi-attribute utility instrument to participants in a randomized, double-blind trial, together with the application of an appropriate scoring algorithm. Nevertheless, such instruments are not routinely included as an outcome measure in many trials, and sometimes, it is necessary to attach utility weights to health states not observed with a trial. Therefore, the preferences of the reimbursement committees of being able to compare across submissions needs to be weighed up against the Committees’ preference for minimizing uncertainty. For this reason, the presentation of cost-utility analysis may not be appropriate in all instances; particularly where the transformation of health outcomes to QALYs gained not only provides comparability but also adds an unacceptable degree of uncertainty.

Transferability of Economic Information

As noted by Drummond and Pang [19], transferability of results of economic evaluations across contexts may be limited by factors including: differences in the demographic and clinical characteristics of patients with the condition; differences in

disease epidemiology; differences in availability of health-care resources; variations in clinical practice; differences in costs of health-care resources; and differences in the way a population may value an outcome. Submissions requesting subsidy of health-care technologies are required to present economic evaluations that reflect clinical practice and costs in Australia. As a small country (in population terms), Australia has frequently relied on economic evaluations conducted for other jurisdictions but adapted to make them applicable to the Australian setting. For example, if there are differences in terms of unit costs for health-care resources, but in other respects, the trial setting and the Australian context are similar (e.g., results from trials are applicable to the Australian population, the utilization of resources is likely to be similar in the Australian context, the comparator included in the evaluation reflects standard practice in Australia), it should be possible to modify the economic evaluation to reflect unit costs in Australia if the cost data have been reported in a transparent way (e.g., explicit statement of the number of units of health-care resources utilized).

More generally, there is a need for the decision-makers in HTA to not have to be constantly reinventing the wheel. Information on reimbursement decisions should be available in sufficient detail to enable decision-makers in other jurisdictions to be able to replicate an HTA, with allowances for local conditions. Reimbursement bodies in larger jurisdictions are encouraged to recognize the needs of smaller stakeholders and jurisdictions.

Generating and Using Real-World Data

Real-world data are routinely used by the TGA to monitor the safety of therapeutic goods (e.g., reports of device failure and adverse outcomes associated with a product). To date, the PBAC and MSAC have generally not been involved in commissioning the generation of further evidence of the safety, effectiveness, or cost-effectiveness of an intervention (e.g., by recommending funding only for patients prepared to enroll in a clinical trial). As explained in the description of MSAC processes, MSAC, unlike the PBAC, may recommend interim funding of an intervention where the evidence is inconclusive but suggests that the intervention could be safer, more effective, and more cost-effective than comparable procedures that attract public funding. Interim funding enables time for data collection and further evaluation of the intervention. A mechanism permitting conditional funding of an intervention while further evidence is being generated might be valuable for drugs as well as medical interventions. The topic of funding conditional on evidence development (also known in the literature as Coverage with Evidence Development) is a topic likely to be discussed greatly in the literature over the next few years.

Timing of Assessment

Different approaches to assessment will influence the timeliness of decisions for public subsidy. If submissions to the PBAC are received by a specified cutoff date, usually 17 weeks before the next PBAC meeting, then the drug is considered at the next PBAC meeting. Following the meeting, the secretariat is provided with a summary of products that have been recommended for listing on the PBS. This information can then be provided to the applicant. On average, MSAC HTAs have taken 13 months to complete [13].

A critical comparison is sometimes made between the time frames applying to assessments by the PBAC and by MSAC. Nevertheless, a comparison of the two is not entirely valid because there are some major differences between the two assessment processes. Applicants to the PBAC are required to submit a

complete assessment, which is then scrutinized by independent evaluators and the different subcommittees which assist the PBAC. The onus of proof in this process resides with the applicant. This is in contrast to the MSAC process where applications may be received but where a full independent HTA is commissioned (more analogous to the UK National Institute for Clinical Excellence [NICE] process). This independent assessment is the primary basis upon which MSAC makes its decision. Thus, the onus of proof rests with the evaluation group producing the HTA. The MSAC process can also be delayed due to a number of causes, not all within its control. For details, see HTA: Reflections from the Antipodes *Value in Health* Supplementary Information, Part V at: http://www.ispor.org/publications/value/ViHsupplementary/ViH12s2_6.asp.

Continuous Innovation

The PBAC guidelines are considered a living document that is open to regular review and improvement. The revision process is managed by the Economic Sub-Committee (ESC) in consultation with other stakeholders, including those who prepare submissions to PBAC. One of the functions of ESC is to advise the PBAC on technical aspects of requiring and interpreting economic evaluations. Although no explicit selection criteria appear to have been articulated to guide the selection of members for the ESC, members are typically people who are active in academia and who could be considered technical experts in a field. Reviews of various aspects of the PBAC process have been conducted since its inception. For example, a review of post-PBAC meeting processes [20] was published in 2004. It is anticipated that implementation of the recommendations of the report would result in the period between PBAC recommendations and actual listing being reduced to no more than 4 months [21].

The current MSAC process for assessment of medical technologies in Australia is a relatively recent development, but already, there have been two reviews of its workings. MSAC undertook a review of its procedures and methods in 2004, with the final report released in May 2005. This final report included both responses to the review by interested parties, responses by MSAC, and actions agreed to by MSAC. One of the responses to the review was the release of new guidelines for diagnostic services (August 2005) and updated medical technologies (September 2005). The Productivity Commission, the federal government's principal body for reviewing regulation and micro-economic policy in Australia, has also produced a major report [22] into the impacts of advances in medical technology. Nevertheless, many of the recommendations contained in this report require action by the whole of government rather than the bodies reviewed.

Independence, Health Policy, and Politics

Members of the PBAC and its subcommittees are independent experts in their fields. Members are required to complete general conflict of interest statements before joining the committee and at each meeting [23]. Given that PBAC is a statutory authority, it is relatively immune to political interference. Nevertheless, there are instances where such interference appears to have occurred. Two stand out. The first involved the dissolution of the PBAC membership in 2000. It was reported by journalists that a confidential background paper had been prepared for a meeting of then Prime Minister John Howard and a group of CEOs of pharmaceutical companies located in his electorate in 2000. The press coverage cited aspects of the background paper, viz: "[i]ndustry is greatly concerned about membership of the PBAC, particularly the public hostile attitude of some members and staff

to industry” [24]. The background paper was reported as including comments along the lines that industry supported proposed legislation that would enable the membership of the PBAC to be spilled but were concerned that changes to legislation would be held over until 2001. On December 31, 2000, PBAC and its subcommittees were dissolved under legislation passed precipitately through the Federal Senate [25].

The second example involved Herceptin, used to treat metastatic breast cancer. It is reported that the manufacturer of Herceptin had applied unsuccessfully three times to the PBAC for PBS listing. The federal government cannot include a pharmaceutical product on the PBS without a PBAC recommendation to do so. For details, see HTA: Reflections from the Antipodes *Value in Health* Supplementary Information, Part II at: http://www.ispor.org/publications/value/ViHsupplementary/ViH12s2_6.asp. On December 1, 2001, following ministerial intervention, the government implemented a new “unique” program administered completely separately to the PBS program to finance the drug costs of Herceptin to eligible patients [26]. It has been postulated that it was intense lobbying that led the government to subsidize Herceptin by creating a special program outside the normal PBS mechanisms [27].

Members of MSAC are appointed by the Federal Minister for Health and Ageing. As with the PBAC, MSAC members are required to declare any conflict of interest at each meeting. Where a conflict of interest exists, members abstain from voting on the committee’s decisions that relate to the area where there is such a conflict. It has been agreed that any conflicts of interest relating to advisory panel members should be recorded, including in assessment reports. Nevertheless, conflicts of interest are not a straightforward issue in the case of the advisory panels and it is not clear how conflicts of interest are managed at this level. Clinicians are appointed to the advisory panels because of their expertise in the area under consideration and may well be regularly performing the medical procedure being assessed. They are often not free of conflicts of interest, including pecuniary interests in the technology. Clinicians involved in the advisory panels, therefore, may not necessarily take the role of impartial judge of the clinical evidence, but rather may take the role of advocate for the procedure/technology. There have been allegations of political interference in MSAC decision-making and the government’s commitment to evidence-based medicine. Ware et al. [28] allege that, in regard to the assessment of extended Medicare funding for positron emission tomography, which had the potential to be a major expense for the federal government (and was occurring shortly after a scandal and cost blowout for the government over funding magnetic resonance imaging scans), “normal” MSAC processes were not followed.

Parallel Trade

The term “parallel trade” or “importation” is taken to refer to the practice where products sold by a single firm in more than one country are imported (by third parties) from the country where prices are lower. The Australian government does not permit the parallel importation of pharmaceutical or medical products. Criticisms of the statutory restrictions on parallel imports under copyright law include that they enable unjustified price discrimination between countries, that they hinder and distort competition, and that they impose draconian restrictions on international trade.

Within Australia, drug prices are reported to be low by world standards, with prices around 60% less than US prices [29]. Given Australia’s relatively small size (representing approximately 1% of the global market), the impact of its pricing poli-

cies might be expected to be small. Nevertheless, it has become an increasing concern for pharma as other larger markets, such as the United States and Europe, have become ever more aware of the disparity in prices globally (even across first-world developed countries) and, in some cases, have begun to reference their prices to Australia and New Zealand [30]. The decision by several countries to legalize parallel importing has added to this concern. To the extent that Australia is viewed to materially contribute to the risk of untenable price reductions for the pharmaceutical industry (due to global pricing considerations, parallel import concerns, and the export of its reimbursement schemes overseas), Australia has been threatened [31] that it will be characterized by the industry as a country where investment should be limited (e.g., new drugs should not be marketed here). Nevertheless, the credibility of such threats is uncertain.

Patient and Provider Choice

The regulation of pharmaceuticals and medical technologies in Australia is in recognition that patients, and doctors as their agents, have limited access to information upon which to assess the safety and quality of these products. The regulatory mechanisms provide patients and providers with a degree of confidence to enable them to participate in the health market. As noted in the section describing the overall structure of the health system in Australia, the aim of the national health-care funding system is to give all Australians, regardless of their personal circumstances, access to health care at an affordable cost or at no cost, while allowing choice for individuals through substantial private sector involvement in delivery and financing [32].

Every individual in the community is able to choose their general practitioner and through them gain referral to specialist care. Patients in the community and their doctors have a reasonable degree of flexibility in deciding what health-care interventions should be employed to treat a patient’s condition. Nevertheless, the government does impose some restrictions on availability of subsidy for many health-care interventions. Where a patient does not satisfy the restrictions, he/she may choose an alternative that is subsidized or may elect to pay for the intervention himself/herself.

Patients treated as public patients in a hospital, Nevertheless, are not able to choose their doctor or specialist. Patient choice with respect to interventions delivered in public hospitals is limited by whether the hospital provides the procedure and whether the patient is eligible to receive the treatment under any restrictions the hospital imposes on availability of that intervention. Patients with private health insurance are able to choose their doctors. Doctors in the private sphere are able to provide medical services or procedures that are not reimbursed through the MBS, but patients bear the full cost. Listing on the MBS increases the number of patients for which medical services are affordable. Private patients in both public or private hospitals can gain earlier access to new technology compared with public patients [33].

Effects on Budgets, Reimbursements, and Access

Total health expenditure in Australia was 9.7% of gross domestic product (GDP) in 2003 to 2004, up from 8.3% in 1993 to 1994. Most of this increase has been funded from growth in federal government health expenditure, which has increased from 3.7% to 4.4% of GDP. This rate of increase was around double that of both the private sector (from 2.8% to 3.1% of GDP) and state and local governments (from 1.8% to 2.2% of GDP) [34].

Figure 2 depicts the change in expenditure on health (by source of funding) over time [35].

**Total health expenditure, constant prices by source of funds,
1993-94 to 2003-04**

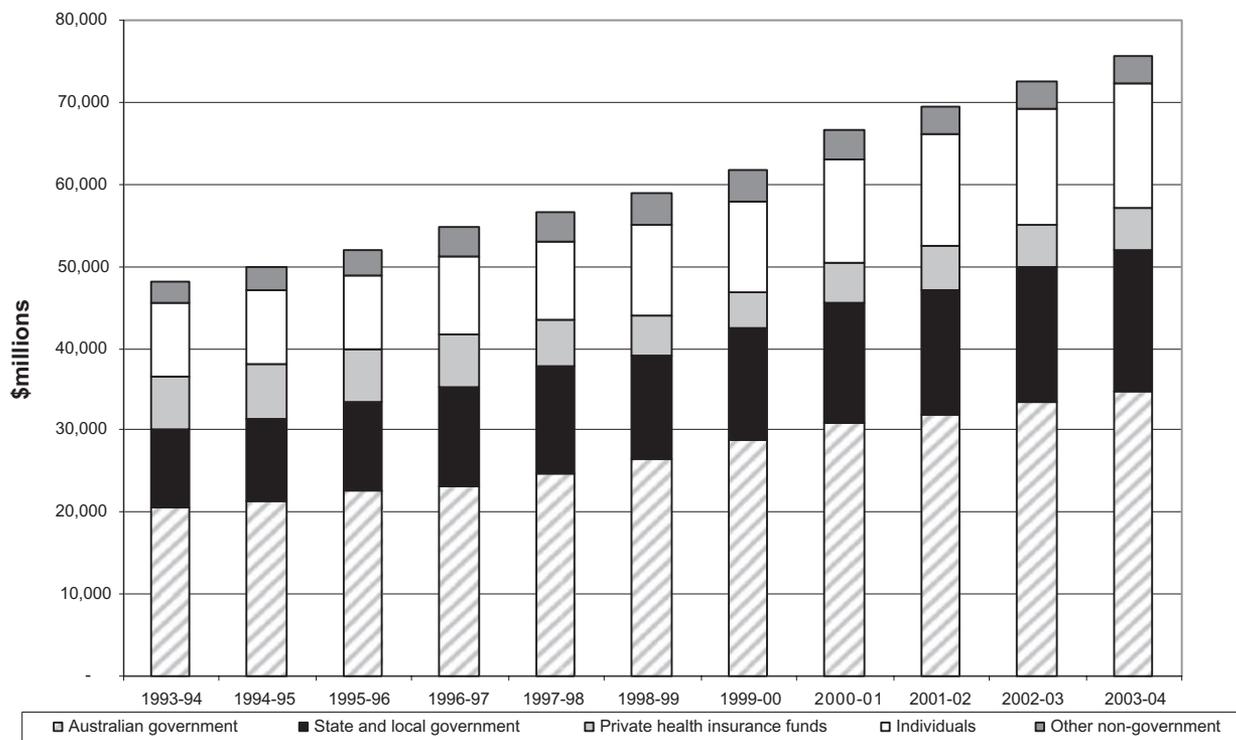


Figure 2 Change in expenditure on health (by source of funding) in Australia over time.

Government budgets for health interventions are administered as part of the overall general health budget. HTA has direct policy relevance in Australia as it is part of health service funding within the Australian setting and forms the basis on which most new interventions are taken up, unlike countries such as Canada in which the role of HTA does not appear to directly inform decision-making [36]. The Medicare health-care system is controlled by a number of regulatory constraints. Direct budget caps constrain public hospital spending and most of the smaller health-care and aged-care programs. Medical services (MBS) and drugs (PBS) are uncapped. Nevertheless, and are characterized by fee-for-service arrangements. Affordability and sustainability of the MBS/PBS systems has been an ongoing policy issue for governments of both political persuasions in Australia. Restrictions on the supply of doctors through limits on medical school intakes and doctor immigration have been used to control Medicare outlays, but this is a blunt instrument that can deliver embarrassing shortfalls. Increasing patient copayments to dampen demand for services and reduce government outlays is another policy approach, but this can have unwelcome equity implications. While there are no explicit caps on expenditures on the PBS, the growth in expenditure is carefully monitored and positive recommendations with projected costs over \$10 million must go to Cabinet for approval.

Despite these affordability concerns, Australia has been relatively successful at controlling health-care costs, has an extensive, well-developed and easily accessible health-care system, and a skilled health workforce. It achieves better health outcomes than many comparable countries. In terms of the health outcomes obtained from investment in health care, apart from some specific population groups, such as the Aboriginal population, Aus-

tralia has high levels of population health, long life expectancy, and low infant mortality (estimated at 4.57 deaths per 1000 live births) [37]. Central to this effort are the Medicare and PBS programs and continued high levels of government involvement in health-care funding and delivery. Australians recognize this by their continued high level of support for these programs.

SECTION III: LESSONS FOR OTHER JURISDICTIONS

HTA in Australia has developed in response to the needs of the Australian health-care system, involving a mix of public and private health-care providers. The Australian system is fragmented (drugs vs. medical services, federal vs. states, public vs. private systems) and duplication can occur in HTA assessment [38]. It is argued that this may be justified as the evaluation needs of drugs and medical services differ, with drugs having a longer history of reliance on clinical evidence and more straightforward evaluation methods compared to medical services. Furthermore, it is important to recognize that the different funders, state versus federal and private versus public, have differing responsibilities that may be best served by dedicated evaluation efforts [39]. Nevertheless, it remains a task for the Australian system to improve its level of efficiency and remove any unnecessary duplication, especially as people with the skill set required to carry out HTA is quite limited and duplication can result in exercises more concerned with moving the cost of providing services to other payers than with the most efficient way to provide services.

The key weaknesses in the Australian system can best be summarized as:

1. the use of silo budgeting;
2. focus on clinical decision and not public health;
3. lack of attention to disinvestments; and
4. capacity to fund/instantiate research

The health of the Australian community can be affected by a broad range of government policies, such as health care, taxation, employment, education, housing, transport, regional development, and social security. Therefore, a cohesive approach across various government portfolios would result in the most efficient use of resources. Nevertheless, in Australia as elsewhere, funding of services potentially affecting health status (e.g., housing, education, environment, health care, etc.) is compartmentalized, not only across broad areas, but even within an area. For example, funding of health technologies in Australia is compartmentalized with separate funding for various programs (PBS, MBS, hospitals, etc) and is likely to result in “silo” decision-making. In the conduct of financial analyses for MSAC and PBAC, there is only limited consideration of the opportunity cost of funds that may be spent on a proposed health technology. For example, if a new drug becomes available to treat Alzheimer’s, the financial analysis would identify the additional expenditure for the PBS budget; Nevertheless, potential other uses of the funds (e.g., provision of assistance to carers of patients with Alzheimer’s) are rarely considered.

One of the biggest challenges for government is coordination of decision-making not only across various portfolios but across health-care services. The Australian approach has led to challenges when trying to evaluate interventions that cross over agencies, as it is difficult to determine which agency should have overarching responsibility. For example, photodynamic therapy (PDT) with verteporfin, in which the PDT part of the health intervention is listed on the MBS and verteporfin is listed on the PBS.

Also, this “silo budgeting” mentality has kept the focus of HTA in Australia on clinical care decisions as opposed to the wider issue of population health and the use of HTA in evaluating preventative interventions with a public health objective. The exceptions here are screening interventions and a number of researcher initiated studies funded through competitive research grants. With that said, Nevertheless, other reasons aside from “silo budget” mentality may contribute to this lack of HTA emphasis on public health interventions, as in this area, development of a rigorous evidence base provides greater challenges. Even though some quite sophisticated models have been proposed to address the complexity of modeling public health interventions, the lack of well-designed and credible efficacy results inhibit this area the most.

Another weakness of the Australian HTA process, a weakness shared with HTA in other countries, is the issue of “disinvestments.” The Australian HTA process is mainly user led, that is, responding to applications from industry or users of the procedures (although it is reported that around 30% of MSAC work involves requests from the Federal Department of Health and Ageing). There is not a clear process by which old technologies, which are receiving subsidies, are evaluated and if found to be not cost-effective, are removed from listings. The use of evidence as a basis for decision-making should include the need for more routine evaluation of old technologies to be included as part of the HTA system. The exception to this is where a “drug” or “medical service” has been found to be unsafe, in which case, speedy removal from reimbursement listings occurs.

Although Australia has introduced horizon scanning which allows the federal and state departments of health to identify any emerging medical technologies that may influence future health-

care systems, current HTA bodies are not able to instigate any direct research in areas where they may think the evidence is insufficient for robust decision-making. This is in contrast to the NICE in the United Kingdom, which increasingly is able to nominate areas in which more research is needed, to enable a more robust scientific assessment of research questions, or to generate data for emerging areas such as preventative interventions. Hopefully, future funding will be made available to allow HTA agencies in Australia to instigate their own research agendas in collaboration with the public.

Conclusion

There are inevitably tensions between the objectives of achieving: 1) a rigorous evidence-based assessment; 2) administrative feasibility; and 3) due process. In Australia, for example, these tensions have been found to exist between:

- *The level of assessment required to be presented to the committees and the tractability of the reimbursement process.* The information requirements for a PBAC and MSAC submission have increased over time with the development of the guidelines. As information requirements and the complexity of analyses presented increase, the process becomes more difficult to manage and also becomes more expensive (particularly with respect to time). The average duration of a PBAC meeting, for example, has increased from 2 days to 3 days in recent years.
- *The furnishing of due process to stakeholders and timeliness of the reimbursement process.* As more opportunities are provided for stakeholders to respond to various inputs to the decision-making process, the more time will be required to reach the point of decision. The frequency of PBAC meetings was reduced from quarterly to tri-annually in 2004 to permit greater feedback to sponsors through the process.

It is not clear yet from the Australian experience whether the appropriate balance between analytic rigor, administrative feasibility, and due process has been achieved. Finding this balance is an ongoing enterprise that requires goodwill and collaboration from all stakeholders.

Source of financial support: ISPOR provided a modest honorarium.

Liliana Bulfone, Sandra Younie, and Rob Carter have no conflicts to declare.

References

- 1 Australian Institute of Health and Welfare 2008. Health expenditure Australia 2006–2007. Health and Welfare Expenditure Series no. 35. Cat. no. HWE 42. Canberra: AIHW, 2008. Data source: Table a.3 (p. 120). Available from: <http://www.aihw.gov.au/publications/hwe/hea06-07/hea06-07.pdf> [Accessed January 2, 2008].
- 2 Australian Institute of Health and Welfare. Australia’s health 2006. AIHW cat. no. AUS 73. Canberra: AIHW, 2006. Available from: <http://www.aihw.gov.au/publications/index.cfm/title/10321> [Accessed August 6, 2007].
- 3 Medicare Australia Information Sheet. Department of Health & Ageing (DOHA). Available from: <http://www.medicareaustralia.gov.au/about/whatwedo/medicare.jsp> [Accessed August 6, 2007].
- 4 The National Health Act 1953 as amended. Commonwealth of Australia. Available from: http://www.austlii.edu.au/au/legis/cth/consol_act/nha1953147/s101.html [Accessed August 7, 2007].

- 5 Health Insurance: Prostheses List. Available from: <http://www.health.gov.au/internet/main/publishing.nsf/Content/health-privatehealth-prostheseslist.htm> [Accessed September 3, 2007].
- 6 Productivity Commission 2005, Impacts of Advances in Medical Technology in Australia, p. 257. Submission of DoHA to Productivity Report. Research Report, Melbourne. Available from: <http://www.pc.gov.au/projects/study/medicaltechnology/docs/finalreport> [Accessed September 3, 2007].
- 7 Department of Health & Ageing—Media Release. Available from: [http://www.health.gov.au/internet/budget/publishing.nsf/Content/BC823217D493393CCA2572D400376387/\\$File/afact11.pdf](http://www.health.gov.au/internet/budget/publishing.nsf/Content/BC823217D493393CCA2572D400376387/$File/afact11.pdf) [Accessed August 27, 2007].
- 8 Budget 2003-2004-Health Budget: Health Fact Sheet 3—A focus on Prevention. Department of Health & Ageing. Available from: [http://www.health.gov.au/internet/main/publishing.nsf/Content/health-budget2003-fact-hfact3.htm/\\$FILE/hfact3.pdf](http://www.health.gov.au/internet/main/publishing.nsf/Content/health-budget2003-fact-hfact3.htm/$FILE/hfact3.pdf) [Accessed August 27, 2007].
- 9 PBAC Publications: Guidelines for preparing submission to the PBAC. Department of Health and Ageing. Available from: http://www.health.gov.au/internet/main/publishing.nsf/content/pbac_guidelines-index [Accessed August 27, 2007].
- 10 Birkett DJ, Mitchell AS, McManus P. A cost-effectiveness approach to drug subsidy and pricing in Australia. *Health Aff* 2001;20:104–14.
- 11 Available from: <http://www.msac.gov.au/internet/msac/publishing.nsf/Content/evaluation-cycle-1> [Accessed August 6, 2007].
- 12 Harris A, Bulfone L. Getting value for money: the Australian experience. In: Jost TS, ed., *Health Care Coverage Determinations: An International Comparative Study*. Maidenhead: Open University Press, 2005.
- 13 MSAC Application Process: Guidelines. Available from: <http://www.msac.gov.au/internet/msac/publishing.nsf/Content/guidelines-1> [Accessed August 28, 2007].
- 14 Report of the review of the Medical Services Advisory Committee: May 2005. Available from: <http://www.msac.gov.au/internet/msac/publishing.nsf/Content/review-1> [Accessed September 2, 2007].
- 15 DeAngelis C, Drazen JM, Frizelle FA, Haug C, et al. Clinical trial registration [editorial]. A statement from the International Committee of Medical Journal Editors. *Med J Aust* 2004;181:293–4.
- 16 DeAngelis C, Drazen JM, Frizelle FA, Haug C, et al. Is this clinical trial fully registered? [editorial]. A statement from the International Committee of Medical Journal Editors. *Med J Aust* 2005;182:609–10.
- 17 Harris AH, Hill SR, Chin G, et al. The role of value for money in public insurance coverage decisions for drugs in Australia: a retrospective analysis 1994–2004. *Med Decis Making* 2008;28:713–22.
- 18 Claxton K. The irrelevance of inference: a decision-making approach to the stochastic evaluation of health care technologies. *J Health Econ* 18:341–64.
- 19 Drummond M, Pang F. Transferability of economic evaluation results. In: Drummond M, McGuire A, eds. *Economic Evaluation in Health Care*. Oxford: Oxford University Press, 2001.
- 20 Working Together to Improve the Pharmaceutical Benefits Scheme: Review of Post PBAC Processes Report. 2004 Department of Health and Ageing. Available from: [http://www.health.gov.au/internet/main/publishing.nsf/Content/B3CE8CB96E0E3A6CA2573FC001C4319/\\$File/pbacprocess.pdf](http://www.health.gov.au/internet/main/publishing.nsf/Content/B3CE8CB96E0E3A6CA2573FC001C4319/$File/pbacprocess.pdf) [Accessed September 2, 2007].
- 21 Media Release: Minister of Health and Ageing. Available from: <http://www.health.gov.au/internet/ministers/publishing.nsf/Content/health-mediarel-yr2004-ta-abb270704.htm?OpenDocument&yr=2004&nth=7> [Accessed September 2, 2007].
- 22 Productivity Commission 2005, Impacts of Advances in Medical Technology in Australia, Research Report, Melbourne.
- 23 Official Committee Hansard. Senate: Community Affairs Legislation Committee. Consideration of Additional Estimates. Monday, 19 February 2001. Canberra. Available from: <http://www.aph.gov.au/HANSARD/senate/commtee/s4564.pdf> [Accessed September 2, 2007].
- 24 Paying the Price: How the pharmaceutical industry broke the scheme which delivers Australians cheap medicines? Australian Broadcasting Corporation. Four Corners. Reporter Liz Jackson. Available from: <http://www.abc.net.au/4corners/stories/s248583.htm> [Accessed September 2, 2007].
- 25 Henry DA, Birkett DJ. Changes to the Pharmaceutical Benefits Advisory Committee: Any proposed change in the Committee's role should be communicated widely. *MJA* 2001;174:209–10. Available from: http://www.mja.com.au/public/issues/174_05_050301/henry/henry.html [Accessed September 2, 2007].
- 26 Brown L, Walker A, Waters AM, Harding A, Thurecht L. Funding of High Cost Biotechnology and Other Innovative Targeted Therapies under the Pharmaceutical Benefits Scheme. National Centre for Social and Economic Modelling. NATSEM. University of Canberra. Position Paper. 27 February 2002. Available from: <http://www.pc.gov.au/projects/study/medicaltechnology/docs/submissions> [Accessed September 2, 2007].
- 27 Kaye KI, Lu CY, O'Day R. Can we deny patients expensive drugs? *Aust Prescr* 2006;29:146–8. Available from: <http://www.australianprescriber.com/magazine/29/6/146/8> [Accessed September 3, 2007].
- 28 Ware R, Francis H, Read K. The Australian government's review of positron emission tomography: evidence-based policy making in action. *Med J Aust* 2004;180:627–32; and responses: Davies P. The Australian government's review of positron emission tomography: an open door. *Med J Aust* 2004;180:633; Ware R, Francis J, Read K. *Med J Aust* 181:516–7.
- 29 Productivity Commission 2003. Evaluation of the pharmaceutical industry investment program, Research Report, AusInfo, Canberra. Page 3.10. Available from: <http://www.pc.gov.au/projects/study/piip/docs/finalreport>.
- 30 Reference Pricing Subcommittee Report (Fifth Draft). West Virginia Pharmaceutical Cost Management Council (Rx Council). Available from: http://www.state.wv.us/got/pharmacycouncil/ReferencePricingReport_Draft5.pdf [Accessed August 6, 2007].
- 31 The Allen Consulting Group. Drivers of pharmaceutical industry investment. 2006. Available from: <http://www.medicinesaustralia.com.au/pages/images/Drivers%20of%20Pharmaceutical%20Industry%20Investment%20FINAL%20060915.pdf> [Accessed January 28, 2009].
- 32 The Australian Health System. Department of Health and Ageing. Available from: <http://www.medicareaustralia.gov.au/about/whatwedo/health-system/index.jsp> [Accessed August 6, 2007].
- 33 Productivity Commission 2005. Impacts of Advances in Medical Technology in Australia, Research Report, Melbourne. Available from: <http://www.pc.gov.au/projects/study/medicaltechnology/docs/finalreport> [Accessed September 3, 2007].
- 34 Health and Ageing Factbook 2006. Department of Health and Ageing. Canberra. Chapter 2. Available at: <http://www.health.gov.au/internet/main/publishing.nsf/Content/Factbook2006-1> [Accessed September 4, 2007].
- 35 Australian Institute of Health and Welfare (AIHW). Health expenditure Australia 2003–2004. AIHW Cat. No. HWE 32 (Health and Welfare Expenditure Series No. 25). Canberra: AIHW, 2005. Available from: <http://www.aihw.gov.au/publications/index.cfm/title/10204> [Accessed September 4, 2007].
- 36 Hailey DM. Health technology assessment in Canada: diversity and evolution. *Med J Aust* 2007;187:286–8.
- 37 Central Intelligence Agency. The World Factbook. Australia. Available from: <https://www.cia.gov/library/publications/the-world-factbook/geos/as.html> [Accessed September 3, 2007].
- 38 Productivity Commission. Impacts of advances in medical technology in Australia, research report. Melbourne. p. 257 submission of DoHA to Productivity Report. 2005. Available from: <http://www.pc.gov.au/study/medicaltechnology/finalreport/index.html> [Accessed September 3, 2007].
- 39 Jackson TJ. Health technology assessment in Australia: challenges ahead. *Med J Aust* 2007;187:262–4.