REVIEW ARTICLE

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Government pharmaceutical pricing strategies in the Asia-Pacific region: an overview

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ABSTRACT

Background and objectives: Governments in Asia Pacific (APAC) are increasingly using pharmaceutical pricing strategies to contain rising healthcare costs. The objective of this narrative review is to discuss formal pricing strategies for reimbursed prescription medication in APAC, supported by relevant examples of implementation differences across countries. In the discussion section, we examine key advantages and disadvantages of each strategy.

Methods: A narrative review of the peer-reviewed and grey literature was undertaken to retrieve information, including strategy definitions, practising countries, country-specific implementation considerations, and merits and demerits of each strategy.

Results: Seven strategies (Internal Reference Pricing, External Reference Pricing, Special Pricing Agreements, Pharmacoeconomic Evaluation, Cost plus pricing, Price Maintenance Premium, and Tendering and negotiations) were identified as most commonly practised in APAC through the review process. Most countries use multiple strategies that differ in how they are implemented. **Conclusion**: APAC countries use multiple strategies simultaneously with varying implementation methods, including different formulae and sub-types of medication that a strategy applies to, whether the strategy is a mandate or guideline, and the extent of negotiations and transparency. Strategies are instituted partly with the aim of cost containment, and may also promote price stability, innovation, and increased access in the short and longer term.

Abbreviations: APAC - Asia Pacific; WHO - World Health Organisation; IRP - Internal Reference Pricing; ERP - External Reference Pricing; SPA - Special Pricing Agreement; MES - Managed Entry Scheme; PVA -Price-Volume Agreement; RSA - Risk Sharing Agreement; NHIS - National Health Insurance System; PE -Pharmacoeconomic Evaluation; CEA - Cost-Effectiveness Analysis; QALY - Quality-adjusted Life Year; BIA - Budget Impact Analysis; PMP - Price Maintenance Premium; R&D - Research & Development

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Introduction

Healthcare expenditures have risen dramatically in Asia-Pacific (APAC). In the past 15 years, several APAC countries, including Indonesia, Vietnam, Thailand, Singapore, Myanmar, and the Philippines, have seen growth in health spending exceed GDP growth [1]. Moreover, the public sector in many APAC countries, including Thailand, Vietnam, and Singapore, has taken on a greater share of health spending [1].

Pharmaceutical expenditures are a significant driver of rising healthcare costs, accounting for a quarter of all health expenditure in APAC [2]. With an annual growth rate of 6%, spending on medicines has outpaced general health spending by an average of 0.5 percentage points per year. Vietnam, Thailand, Laos, China, and the Philippines have experienced pharmaceutical expenditure growth of over 9% annually [3]. As with health spending in general, the public sector share of spending on medicines

in particular has also increased. Pharmaceutical spending now accounts for 31% of public sector health expenditures across the APAC region [1], and is even higher for lower-middle income countries [2].

In efforts to contain rising health care costs, many APAC countries have developed formal strategies aimed to influence prices of medicines financed by the public sector. Although there is a fair amount of information on these strategies available in the public domain, the information exists largely in the grey literature and is difficult to find. Therefore, the goal of this narrative review was to search the peer reviewed and grey literature to identify the most commonly practised public sector pricing strategies used by APAC countries, document key differences in implementation with examples across countries, and discuss the pros and cons of each strategy. This review will inform industry professionals, regulators, and academics interested to

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understand how APAC countries are addressing the rising costs of prescription medicines.

Methods

Since non-reimbursed medicines are often priced through market mechanisms, we employed a search strategy aimed to examine pricing policies for reimbursed prescription medicines only. We limited our search to the countries/provinces in APAC with GDP (in billions of USD) greater than \$100, which account for approximately 91% of the APAC population [4]. This includes 15 countries/provinces: China, Japan, India, South Korea, Australia, Indonesia, Taiwan, Thailand, Hong Kong SAR, Philippines, Malaysia, Singapore, Vietnam, Bangladesh, and New Zealand, and excludes Myanmar, Laos, Mongolia, Brunei, Fiji, Timor-Leste, etc [5].

PubMed, Medline, and Cochrane databases were searched through April 2018 for English-language peerreviewed articles. Search strategies used the terms 'pharmaceutical pricing strategies', 'Asia Pacific', 'reimbursed medicines', 'prescription medicine pricing', and 'essential medicines list' for two or more words used together. A keyword search was also conducted by combining the terms 'pharmaceutical', 'strategy', 'medicines', 'Asia Pacific', and individual country names. An identical strategy was also used to search non-peer reviewed sources, including government websites, newspaper articles, reports from multilateral organisations such as the World Health Organisation (WHO), and white papers. For government websites, google translate was used to translate from local languages to English when possible. Though there may be strategies that are implemented informally, if no information was publicly available, those strategies were not included.

We scanned titles and abstracts to narrow our selection to relevant documents. The search was further supplemented by a review of relevant bibliographies for studies that met our criteria but that our search strategy may have missed. Information retrieved from our search included (i) definitions of pricing strategies (ii) countries that are using these strategies and (iii) differences in implementation across countries. After presenting these strategies, we discuss the advantages and disadvantages of each.

Results

All countries in APAC practise multiple strategies simultaneously. The review identifed the following pricing strategies as the most commonly practised in APAC: Internal Reference Pricing, External Reference Pricing, Special Pricing Agreements, Pharmacoeconomic Evaluation, Cost Plus pricing, Price Maintenance Premium, and Tendering and Negotiations (Table 1). Each strategy is discussed in detail below. Strategies

lable I.	Key pricing strategies used b	y gover.	nments in AF	AC TOL	reimbursed	prescri	ption me	edicatio	ns.							
		Australi	a Bangladesh	China F	long Kong I	India Inc	Jonesia J	apan M	lalaysia I	New Zealand	Singapore	South Korea	Taiwan	Thailand	The Philippines	Vietnam*
Strategy	Internal Reference Pricing	×		×				×		×		×		×		
	External Reference Pricing			×				×				×	×		×	×
	Special Pricing Agreements	×								×		×	×	×		
	Pharmacoeconomic Evaluation	×				×			×	×		×				
	Cost Plus pricing		×				×	×								×
	Price Maintenance Premium							×								
	Tendering and Negotiations	×	×	×	×	×	×		×	×	×	×			×	×

* Vietnam uses these strategies only to regulate prices

are ordered from most to least commonly implemented in APAC, with the exception of tendering and negotations since they require an understanding of the aforementioned pricing strategies.

Internal Reference Pricing

Definition

Internal Reference Pricing (IRP) is the practice of setting or negotiating reimbursed medicine prices by referencing prices of medicines within the country that are identical, similar, or therapeutically equivalent [6].

Practising countries

Australia [7], New Zealand [8], South Korea [9], China [10], Thailand [11], and Japan [12].

Implementation considerations

Governments often use IRP to determine the maximum reimbursed price for medicines in the class, either equivalent to the lowest priced medicine in the class, or derived as a percentage of a similar medicine in the class. Broadly, IRP can be classified based on whether medicines referenced are generics (i.e., have identical active ingredients as the patented medicine) or are therapeutically similar (i.e., somewhat equivalent products within the medicine class, but do not necessarily have the same chemical composition). In China [10] and South Korea [9], only generic medicines are referenced, whereas the remaining countries that practice IRP use a more extensive therapeutic criterion, such as similar dosage, indications, and clinical equivalence. Japan has two IRP strategies, one for medicines that are generic (these drugs are reimbursed at 80% of what is paid for branded medicines in the class; or 90% if there are 20 or more generics) and another for medicines that are therapeutically similar (i.e., 'me-too' medicines) but not identical [12]. For the latter, medicine reimbursement is usually set at a value that is lower than what is paid for the existing products.

In some cases, such as New Zealand and Australia, manufacturers can charge higher prices, but the government reimbursement is capped based on the reference price (which is the lowest-priced medicine for the group). New Zealand has at least one fully subsidised medicine in each medicine class and patients pay the additional cost if the price of another medicine in the class is higher than the price of the subsidized medicine [8]. However, as clinicians tend to prescribe the fully subsidized option, there is pressure for manufacturers to match that price. Similarly, Australia applies premiums on drugs represented in the drug formulary under a different brand or a different compound that is therapeutically equivalent in terms of health outcomes and safety. In both cases, the government subsidises the lowest priced drug in the category. The price difference is then paid by the consumer on top of the co-payment [13].

External Reference Pricing (ERP)

Definition

External Reference Pricing (ERP), commonly known as International Reference Pricing, is a price control mechanism whereby a government considers the price of a medicine in other countries to inform or establish a price in its own country [6].

Practising countries

Japan [14], Taiwan [15], China [16,17], South Korea [18], Vietnam [19], and the Philippines [20].

Implementation considerations

The implementation of ERP varies significantly across countries. For example, in Taiwan, breakthrough innovative products are priced at the median price of ten reference countries [15], whereas Japan adjusts prices upwards or downwards if it differs significantly from the average of the drug's price in four reference countries [14]. For most countries, the price determined from ERP is taken as a starting point for benchmarking or price negotiations with industry, consistent with WHO recommendations for ERP [17]. The Philippines is unique in that it uses externally referenced prices to set price ceilings on select medicines; other criteria include addressing public health priorities and representing a significant share of the market [20].

Countries practicing ERP tend to reference other countries with similar economic characteristics, such as GDP per capita. As an example, South Korea, with a relatively high GDP per capita in the region, has a reference basket which includes two high income countries, Taiwan and Singapore [18], whereas Vietnam references lower income countries including Thailand, Malaysia, Indonesia, the Philippines, and Cambodia [19]. Another consideration for choice of reference countries and medicines to include is the number of price revisions and reductions that a medicine has already experienced in the reference country. Taiwan uses the median price of 10 countries (the UK, Germany, Japan, Switzerland, USA, Belgium, Australia, France, Sweden, and Canada) where medicines are introduced early and subsequently go through several price reductions over time as its reference price. For all except breakthrough medicines, Taiwan uses this highly revised and subsequently reduced ERP as a ceiling price in price negotiations, resulting in the prices of new medicines in Taiwan averaging 51 percent of the ERP [21].

Nearly all countries in APAC that practise ERP publicly disclose comprehensive information regarding reference countries, type of price (manufacturer's or retailer's price), formula, and method of implementation. In China however, implementation of ERP is comparatively ad-hoc and there is low visibility on methods used to select reference countries, formulae for ERP, and implementation strategies. In 2012, manufacturers were required to submit their own international reference prices for select countries, which resulted in price cuts for certain drugs nationwide [17]. Across the countries practising ERP, underlying processes of how the reference price has been established and frequency that it is updated were not easily available.

Special Pricing Agreements

Definition

Special Pricing Agreements (SPAs), a type of innovative agreement for payers and pharmaceutical companies to align on value, speed to market, and/or risk [22], are legal contracts between the government and the manufacturer.

Practising countries

Australia [23], New Zealand [24], South Korea [25], Taiwan [26], and Thailand [11].

Implementation considerations

SPAs typically include rebates, discounts and volume purchase agreements. For instance, SPAs in Australia allow manufacturers to set a higher public list price that is offset through rebates to the government based on predetermined criteria such as volume. New Zealand applies a similar approach via negotiating confidential discounts. This allows governments to obtain better prices without putting the manufacturer in a poorer negotiating position with the private sector and/or in other markets. New Zealand also practices bundling, another type of SPA, whereby the government agrees to offer subvention for a particular drug if the manufacturer agrees to discount prices on one or more of its other marketed medicines in the formulary list. This allows the government to attain price reductions for mature products and free up funding for new therapies [24].

Managed Entry Schemes (MES) are forms of SPA that enable access to and/or reimbursement for medicines subject to specified conditions. These agreements address uncertainty about medicines performance, uptake, or health outcomes [27]. Types of MES include Price-Volume Agreements (PVAs), refunds if medicines do not work as expected, and performance/outcome-based/value based Risk-Sharing Agreements (RSAs) [28]. South Korea, Taiwan, Thailand, and New Zealand practice MES in one or more forms. In South Korea, PVA related price cuts require several conditions to be met. For instance, if the consumption of a drug is 30 percent higher than predicted, the manufacturer provides the local drug subsidizing agency (National Health Insurance System (NHIS)) a price reduction of up to 10 percent [29]. South Korea is increasingly using risk-sharing agreements that are contractspecific and rely on metrics such as total sales, per patient cap etc. South Korea and Thailand also practise performance based risk-sharing for medicines to treat cancer and rare diseases, where the clinical benefits of a drug in each patient are monitored and costs are covered by the manufacturer if the drug fails to demonstrate effectiveness. In some cases, such as in Thailand, a maximum volume threshold (a form of PVA) is also calculated for high-cost onpatent medicines by estimating the number of eligible patients and the duration of the intervention. Costs exceeding the threshold are covered by the manufacturer [11].

Pharmacoeconomic Evaluation

Definition

Pharmacoeconomic Evaluations (PEs) often involve a costeffectiveness analysis (CEA) to examine the value of medicines, usually defined in terms of its consequences (e.g., Quality-adjusted Life Years (QALYs) gained) relative to its cost [6]. Other types of PE include cost-minimisation, and cost-benefit analysis. PE is particularly useful for identifying value for money of a medicine, which most countries use to inform their subvention decisions and some countries use to determine drug prices.

Practising countries

New Zealand [30], Australia [23], South Korea [31–33], India [34], and Malaysia [35] (all countries that use PE to inform prices).

Implementation considerations

Most often PEs involve CEAs to determine prices of medicines. Some countries, such as South Korea, use CEA to compute the price at which the medicine is cost-effective to direct its pricing negotiations with manufacturers [31–33]. Other countries, like New Zealand, use CEA only for medicines that are first in class. They then set the maximum price for the class based on this drug and their internal CEA threshold. In India, new products, for which a wholesale price does not exist, have price ceilings based on PE assessments with a 16 percent retail mark-up [34]. Else, the ceiling prices of medicines on its national list are calculated by the simple average price of all brands with market shares greater than or equal to 1 percent of total market turnover for that medicine.

Cost-minimisation is often conducted when interventions display the same level of effectiveness. For example, in South Korea [31–33], if a medicine has similar therapeutic benefits compared with the current standard, a costminimization analysis is conducted to determine the maximum reimbursed price. South Korea also uses Budget Impact Analyses (BIAs) as part of PE based price-setting to assess the net impact of reimbursement on the healthcare or medicines budget, considering market prices, uptake, and the influence of subvention on demand for substitute and complementary products [31–33].

Cost Plus Pricing

Definition

Cost Plus Pricing is a cost-based method for setting prices of medicines, where the production costs, research and development (R&D), administrative costs, overheads and profit, and promotional expenses are summed to determine the reimbursed price [6].

Countries

Japan [36], Bangladesh [37,38], Vietnam [39], and Indonesia [40].

Implementation considerations

Japan uses it to calculate prices for medicines with no comparator on the market [36], and Bangladesh uses it to calculate prices for all medicines on its essential medicines list [37,38]. In Japan, the formula takes manufacturing costs, sales and general administrative cost, operating profit, distribution, and marketing cost into account [36], whereas Bangladesh's formula includes only cost of raw materials and packaging materials, and a mark-up [37,38]. Vietnam uses the cost plus method to ensure fairness of declared prices, however, no specific formula is published [39]. In Indonesia, the Ministry of Health uses this method to set a price ceiling on the retail price at 40 percent of the wholesale price [40].

Price maintenance premium (PMP)

Definition

Price Maintenance Premium is a policy which awards one or multiple premiums to prices of drugs should they meet certain criteria. This strategy aims to incentivise manufacturers to launch in a certain country because it allows them to recuperate larger returns on investment.

Practising countries Japan [41]

Implementation considerations

Japan's PMP considers premium(s) for newly approved drugs that have higher efficacy than comparable drugs based on innovativeness/usefulness (new action mechanism, high efficacy/safety, improvement in treatment method), support for small market size (e.g., orphan drug), support for paediatric indications, and/ or drug approval in Japan before other countries [42]. After Japan's 2018 pricing reform, the range of drugs considered for premiums was narrowed from drugs that had been marketed for less than 15 years or without a generic comparator to first-in-class therapies, two next-in-class therapies launched within three years of listing the first-in-class drug, orphan drugs, and drugs developed at the health ministry's request [43]. Manufacturers have the opportunity to present to pricing authorities the criteria that their product addresses and the number of points (i.e., premium) that they believe they should be eligible for. Ultimately, pricing authorities decide the appropriate premium to be applied.

Tendering and Negotiations

Definition

Tendering is a process whereby the government engages manufacturers to submit quotations for a particular contract [6], usually in a competitive bidding process. It usually takes place towards the end of the pricing process, once the government has determined an initial price to reference the bids, and is often used to reduce prices of medicines that have existing competition in the market. It simultaneously works as a procurement strategy to aid supplier and volume decisions for certain medicines and typically relies on some form of negotiation.

Practising countries

Australia [44], New Zealand [24], South Korea [25], Hong Kong [45], China [46], India [47], Malaysia [20], The Philippines [48], Singapore [49], Vietnam [50], Bangladesh [37], and Indonesia [51,52].

Implementation considerations

Almost all APAC countries use tendering and negotiations to reduce the prices of medicines. In China, tendering is carried out for drugs that have existing market competition at the provincial level [16]. Most provinces in the country implement some variation of the 'twoenvelope' system to decide the winning bid, where one envelope considers quality and the second envelope focuses on price. This bidding scheme may only apply to specific drugs. In New Zealand, for example, tenders are fixed term-contracts and apply to generic drugs only [24]. However, since tendering is not linked to procurement, hospitals must engage in secondary negotiations with manufacturers about specific prices and volumes. China is one of several countries that engages in negotiations, independent of tendering, for drugs with little market competition.

Despite the wide use of tendering and negotiations, transparency in the process differs substantially across APAC countries. In Indonesia, all reimbursed medicines are listed on-line [51,52], and in Hong Kong, medicines, supplier, and total value of tender are published, but tender prices remain confidential [45]. The Philippines [48] and China [46] offer more transparency, with a Drug Price Reference Index that provides the lowest net price for each medicine in the former, and published tender prices after bidding in the latter.

Discussion

This narrative review presents publicly available information on the most common formal pricing strategies for reimbursed medicines practiced by APAC governments. The review identified the following strategies in the order that they are most frequently practised: Internal Reference Pricing, External Reference Pricing, Special Pricing Agreements, Pharmacoeconomic Evaluation, Cost Plus pricing, Price Maintenance Premium, and Tendering and Negotiations. For each strategy, countries tend to use a highly personalized approach and rely on multiple strategies to obtain best prices.

Governments have adopted pricing strategies, partly to contain rising costs and achieve fiscal sustainability [10,20,53,54]. Some strategies, by design, may contribute to this aim by directly invoking price competition. IRP achieves this by reducing price variability within the class and pushing prices down to the least expensive medicine [55], which is typically the generic. It may also put downward pressure on prices of therapeutic substitutes even when not subject to referencing [55]. When manufacturers place their bids to win a tender, they too engage in a form of price competition. Other strategies, such as ERP, provide price stability across countries [56,57]. Aside from directly influencing prices, strategies may have other effects favourable to manufacturers, governments, and patients. PMP aims to promote innovation and increase access, partly by encouraging manufacturers to launch guickly. Evidence suggests that Japan, the sole implementer of PMP, may have benefitted in this respect pre-2018 reform, with the increase in percentage of new drug applications filing lag less than 1 year from 18% 2007-2011 (preimplementation of the PMP) to 71% in 2015-2017 (postimplementation of PMP) [54]. Tendering and SPAs further help ensure the supply of the medicine for the stated period at the agreed price. SPAs are also useful because such contracts protect the interests of both government and manufacturers by providing some degree of risk sharing. Such agreements provide governments with avenues for cost saving and incentivise manufacturers keen on introducing new medicines. Moreover, since the effective price paid by the government is typically undisclosed, manufacturers are protected from the knock-on effect of low prices through IRP or ERP. Lastly, strategies that explicitly place a limit on prices, like Cost Plus pricing, help protect patient populations with rare diseases from manufacturers who may dominate the market and wish to charge monopoly prices.

Although pricing strategies can be advantageous to payers in several respects, the most attractive being ability to control costs, several concerns remain. Firstly, strategies often lack transparency [58,59]. For instance, it is unknown whether external reference prices include confidential rebates and discounts, which if not included could lead to artificially high prices being referenced [60]. With SPAs, patient advocacy groups argue that more transparency would help to lower prices whereas industry groups believe that it provides unfair advantages to larger companies who can offer a greater suite of products. Moreover, several informal strategies may be used by governments but are not disclosed publicly. Secondly, the theoretical and empirical grounds of some strategies, such as PE, may be called into question. On the theoretical front, many argue that QALYs are not truly preference-based [61], the thresholds are set arbitrarily [62] and are assumed to apply to all conditions and people equally. These assumptions are unlikely to hold in reality. Moreover, even if one ignores these issues, PE studies often rely on many assumptions, which may not hold in reality.

Government pricing strategies have also been criticized on the grounds of dis-incentivising manufacturers. With ERP in place in several countries, manufacturers may refrain from launching a new product in a country that only accepts low prices so as not to jeopardise their product's prices in other markets [4]. IRP may also lead to the delayed launch of new products by manufacturers wary of having to accept a low price, reflected in a case in New Zealand [55,63]. With smaller markets, if the price ceiling is too low, suppliers may decide not to provide the medicine for that market, which would limit availability. Furthermore, government intervention in pricing may not allow manufacturers to cover their costs of extensive R&D. Because of the nature of the pharmaceutical industry, whereby costly R&D may result in only a small proportion of medicines successfully reaching the market, if drug prices are based on manufacturing and distribution costs alone, such as in cost plus pricing, costs of failed

R&D efforts would not be recovered, which could adversely influence these investments. This issue would be a concern if larger markets, such as China and India, adopted such a strategy. For all pricing strategies mentioned above, a broader concern may be that a focus on low prices may compromise on quality in the absence of strict regulations and checks.

Moreover, if not implemented meticulously, certain strategies could result in more expenses for governments which are already concerned with high costs. Japan's initial introduction of PMP illustrates this possibility. Drugs eligible for premiums and criteria for awarding premiums were overly generous, which led to higher prices and promoted expensive new drugs entering the market, thus Japan responded by limiting eligible drugs [43]. Furthermore, some strategies, such as PE, require high-quality research infrastructure and reliable health care data, making it costly and difficult to implement.

Trends in the region indicate that more countries, most recently Japan [64], are moving towards using health technology assessment involving pharmacoeconomic evaluation to inform drug pricing and subvention decisions. Strategies in China, the second largest pharmaceutical market in APAC, may also set the precedent for changes in other countries. The ongoing expansion of China's subsidized formulary is predicted to spark increased interest in price volume agreements since manufacturers are willing to accept pricing cuts of 40-60% due to large volumes of sales [64]. Within China, there are shifts in tendering and negotiations from local to regional levels. An aggressive tendering process was announced in late 2018 whereby 11 major cities were asked to combine their tender proposal to receive the lowest procurement price from the manufacturers [65]. Given the high demand and high cost of medicines, change is inevitable. Governments in APAC will continue to look for strategies that serve the dual role of increasing access while promoting fiscal responsibility.

Although this study contributes to the knowledge base by providing a broad overview of pricing strategies practised by the largest APAC countries, it has several limitations. Due to the narrative nature of the review design, we did not identify all strategies or implementation differences across countries. We did however use country-specific examples where possible. Our inclusion of only literature published in English and reliance on Google translate for certain governmental websites may have limited information retrieved in the search. Furthermore, given the low levels of transparency about these strategies, and the speed in which policies change, it is possible that there could be differences between what countries report to do and what is practised currently. Future studies should include interviews with key stakeholders, such as pricing strategy experts or health ministry officials, to incorporate these 'on-the-ground' insights. In addition, due to the fast-changing nature of pricing policy, this topic should be continually updated.

Lastly, we did not identify which strategies are most effective in promoting cost containment and/or greater access. A systematic review that examined the effects of select pricing policies in LMICs [66], including China, Bangladesh, Thailand, Taiwan and Indonesia, found that many strategies are not proving effective in containing rising costs of medications due to poor enforcement, lack of governance, and noncompliance. This reveals that one cannot examine the effectiveness of the policies without understanding the context and broader policy setting within which they operate. More research that explores implementation fidelity, effectiveness across various domains, and unintended consequences within each country in APAC is needed. Lack of such evidence hinders our ability to understand how best to ensure affordable access to medicines without compromising patient well-being while still promoting a vibrant market for high value medicines.

Disclosure statement

EAF is a consultant for Roche and other pharmaceutical corporations. NRV, SA, and JB report no conflict of interest. YB is an employee of Roche Singapore. EAF and YB have disclosed those interests fully to Taylor & Francis, and have in place plans for managing any potential conflicts arising from that involvement.

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