



Comparative effectiveness research around the globe: a valuable tool for achieving and sustaining universal healthcare

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Kalipso Chalkidou

Director, Global Health & Development Group, Institute for Global Health Innovation, Imperial College London, UK and

Visiting Professor, King's College, London, UK

k.chalkidou@imperial.ac.uk

Universal healthcare coverage (UHC) is now firmly on the global health agenda. In December 2012, the UN Assembly voted for UHC, with wide-ranging support including from the US and UK governments, and calling on countries to provide “access to key promotive, preventive, curative and rehabilitative health interventions for all at an affordable cost” [1]. The *Washington Post* ran the news with the headline ‘Obamacare Everywhere’ [2], drawing parallels with the US debate on expanding insurance to cover all Americans (although recent developments may curb the political commitment to UHC in the USA). Yet, given scarce resources, UHC cannot feasibly provide every beneficial health service to those in need. So, a critical first step to delivering on these aspirations is deciding which services and policies to prioritize and make available and at what cost, if any, to beneficiaries. As UHC is defined as ‘a comprehensive range of key services...well aligned with other social goals’ [3], the question naturally arises: ‘how comprehensive is comprehensive?’ The Institute of Medicine (IOM) Committee on designing essential health benefits [4], reporting around the same time as the UN resolution, exemplifies how balancing “the tensions between comprehensiveness and affordability” is faced not only by poorer countries but also by the world’s biggest spender on health, the USA. Far from making clear recommendations on what is in and what is out, the IOM Committee lim-

ited itself to general rules and principles for guiding others with the tough task of making coverage decisions.

One tool not mentioned by the IOM, and which can help policy-makers make and defend such hard choices for including or rejecting new or (less often) excluding existing interventions, is what in the USA is known as comparative effectiveness research (CER) and overseas as health technology assessment (HTA), a more pragmatic version of evidence-based medicine, where budgets and cost-effectiveness analyses (CEA) matter at least as much as comparative clinical effectiveness [5]. As UHC is necessarily country-specific, since the demography, epidemiology, spending requirements and prices or costs of products and interventions are different for every country, CER or HTA is also heavily context specific. So, it makes sense perhaps to discuss here how other countries around the world are setting out to attain or sustain UHC, whether they use CER as a means to such an ambitious end, and, if so, in what way. I use the terms CER and HTA interchangeably while being fully aware of the strange prejudice against considering resource constraints in the US context, which makes the term HTA less meaningful. In that sense, the USA is a policy (and expenditure) outlier.

The west (minus the USA) & Japan

CER is not new. Countries, such as Sweden, the UK, Australia and Canada, pioneered

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HTA as a decision-making tool, followed by the likes of Norway, The Netherlands, France and Germany, as well as eastern Europe and, though in a more fragmented geographically fashion, Italy and Spain and parts of southeast Europe [6]. Such efforts for a more streamlined, relatively explicit and informed by evidence process have been stifled to some extent in those countries most severely hit by the recession, especially in Europe, with Spain [7], for example, moving toward cost shifting and Greece, where HTA efforts had been in an infantile state for years, recently reverting to much less scientific and much more arbitrary price cuts and delisting of technologies. At the same time, Germany seems to have been backtracking away from economics in recent years, favoring instead a less transparent price and rebate negotiation approach through its Federal Joint Committee, the latter comprising professionals, providers and payers. Rather than an input in the negotiations, economic analysis is used instead as a last resort, a deterrent even, so that companies accept the deals offered by the Federal Joint Committee based on an early assessment of comparative clinical effectiveness and additional clinical benefit [8].

Far from being driven by economics alone, countries with universal healthcare systems and a commitment to solidarity often struggle with issues of distribution and equity alongside considerations of value for money. Norway is a good example, where successive priority setting committees have been set up by Parliament to work with the Ministry of Health and advise on how social justice can form part of the prioritization exercise. The third committee issued its proposals in 2016, recommending that cost-effectiveness is considered alongside disease severity, so that those worse off are given priority [9].

The most interesting and least publicized perhaps development on CER in Europe is the recently launched roadmap for strengthening the EU cooperation on HTA [10]. Intriguingly characterized as a 'likely legislative or non-legislative initiative', the roadmap defines HTA as "a key tool for Member States to ensure the accessibility, quality and sustainability of healthcare" and builds on the EU's HTA network, EUnetHTA and Joint Action, to which the EU has committed almost €40 million between 2010 and 2020, mostly devoted to methods development knowledge sharing. The roadmap, under consultation until early 2017, sets out five scenarios, ranging from the status quo (i.e., a loose methods development partnership in the form of EUnetHTA) to mandatory cooperation on and implementation of full EU-wide HTA reports including clinical and economic assessments, and related legislated fund-

ing directions by the EU as well as processing fees paid to the HTA bureaucracy by industry. With greater financial pressures on healthcare systems, and greater EU integration with free movement of people (including patients and professionals), goods and services across borders, HTA is gaining traction across the Union as a popular policy tool for managing escalating healthcare costs.

On the other side of the world, Japan has launched this year an official pilot to incorporate HTA in its pricing negotiations. Japan has included the option of submitting pharmacoeconomics analyses as part of the process of listing and pricing new products since the early 1990s. However, without this being mandatory nor clear guidelines for such submissions or a process for how such information will be used by the payer, companies very rarely produced such information. In 2012 and under escalating insurance premiums and a growing healthcare technologies bill, the Ministry of Health, Labour and Welfare set up, under the Social Insurance Medical Council (Chuikyo), a committee on cost-effectiveness, which was empowered by relevant legislation as part of the country's economic and fiscal reform plan of 2015 to launch a pilot for using CER including economic evidence as an input in price negotiations for pharmaceutical and healthcare products. During the 2015/16 pilot, only existing pharmaceuticals and devices with high profit margins and sales volumes were considered, including sofosbuvir and trastuzumab; and autologous cartilage implants and thoracic stent graft systems, respectively. Ratified by Chuikyo, the Ministry of Health, Labour and Welfare has set out guidelines for economic evaluation and the pilots are on track for informing price renegotiations for the selected products in the planned 2018 medical revision fee round [11] [PERS. COMM. AND PRESENTATIONS BY TAKASHI FUKUDA AT HTAi (Tokyo, May 2016) AND ISPOR ASIA-PACIFIC (Singapore, September 2016)]. It is expected that full-blown implementation of HTA as a requirement for all new drug and device submissions will follow the pilot evaluation in 2018.

Affordability matters

One interesting trend in the HTA world is the increasing emphasis on affordability, exemplified perhaps by the case of NICE in England and Wales. After a decade of record levels of investment in health, the English National Health Service is faced with unprecedented pressures to cut costs and generate efficiency savings, with projections of billions of pounds shortfall if the current spending trend with near zero growth, continues [12].

In response, a debate between NICE and academics as well as NHS national and regional budget hold-

ers is being played out, with the latter two arguing that the NICE threshold, that is the cutoff below which a technology is deemed to be cost effective and therefore ought to be funded by the NHS, is far too generous [13]. NICE is refusing to amend its threshold but the consistent pressures have resulted in a radical change in the workings of the famous HTA watchdog: instead of issuing its advice directly to the NHS with a statutory requirement that the latter finds the funds to pay for them within 3 months, the decision-making center is slowly shifting toward the budget holders. This started with the NHS executive with budgetary responsibilities (known as NHS England) being part of and having decision-making powers over decisions to take drugs down the recently reviewed and highly controversial Cancer Drugs Fund [14]. The trend was further reinforced by recent proposals by an independent review commissioned by government to look at ways of accelerating access to innovation for the NHS, to place a price-negotiating center downstream of NICE and within NHS England [15]. Finally, a proposal regarding highly specialized technologies (also known as ‘orphan’), jointly put forward by NICE and NHS England, openly to include affordability as a final step in the decision-making process with products deemed to be cost effective by NICE likely to remain unfunded or have their funding delayed if their budget impact is deemed too high by NHS England, suggests that things will never be the same for the world’s best known HTA proponent [16].

As budgets are starting to trump CEA at least in richer countries, and delays in uptake of cost-effective products seem legitimate where the total bill is just too high, as the hepatitis C experience in the UK and other European countries demonstrates [17], the whole rationale for going down the route of a time- and resource-consuming (albeit accountable and legitimate) priority setting process based on HTA/CER information is becoming less obvious to governments and payers acutely aware of the need to balance their books year after year.

Emerging economies

In emerging markets on the other hand, HTA has been gaining ground [18]. A growing number of countries seem to be following the example of so-called developed economies with Thailand at the forefront with a most sophisticated and high policy impact agency, the Health Intervention and Technology Assessment Program (HITAP) [19]. In operation for over 10 years now, HITAP informs the country’s essential medicines list as well as its package of services offered by the Thai Universal Coverage Scheme reaching 70% of its population. Often citing the 2014 World Health Assembly

resolution calling on national governments to push ahead with introducing HTA as a tool for achieving UHC, countries like the Philippines, Indonesia, Ghana and Vietnam with relatively young but expanding health insurance schemes are following the Thai example, supported by both WHO regional and country offices and regional and global networks such as HTAsiaLink [20] and the international Decision Support Initiative (iDSI) [21]. iDSI is a multicountry initiative funded by the Bill and Melinda Gates Foundation, the UK’s Department of International Development (DFID) and the Rockefeller Foundation to support, through the local application of CER, countries faced by the growing challenges of growing and aging populations, chronic diseases and expensive new technologies spend their limited resources more efficiently. The Thai HITAP, the South African Priority Cost Effective Lessons for System Strengthening [22], the US Centre for Global Development [23] and the UK’s Imperial Global Health and Development Group, the latter continuing the legacy of NICE International, are all major partners in the initiative.

Other countries, such as India and South Africa, with federal systems and a devolution of healthcare policy and as well as fund raising to the state or province level, further confounded by strong private sectors and significant private expenditure through formal private insurance (South Africa) or individual out-of-pocket (India), are faced with a different set of challenges, but their governments still view HTA as a means for addressing issues of efficiency, quality and access *en route* to UHC. In South Africa, the National Department of Health, for instance, includes a series of explicit references to HTA in the White Paper setting out the government’s 10-year vision for high-quality UHC and a dedicated taskforce has been set up to consider HTA among other tools as a means to designing a high-quality affordable package of health services to be made available. In India, states like Kerala are experimenting with HTA while the Union government has launched a program of work to establish the Medical Technologies Advisory Board, which will use CER to inform national-level decisions on value for money, influencing the country’s budding National Health Plan and State-level schemes. iDSI and its partners are heavily involved in both sets of reforms with funding support by the BMGF.

Finally, China is also committed to HTA as a means of informing its urban and rural health insurance schemes, experimenting with value-based purchasing approaches informed by HTA-type analyses not only regarding products but also services at the province level. Indeed, so-called value-based healthcare, very much an application of HTA to a broad set of interven-

tions including technologies but also services and whole models of care, is gaining traction, with countries and regions from the USA to China, experimenting with different regulatory and provider payment reforms, technology innovations and alternative models of human resource development and deployment [24].

The most exciting development in HTA in China and perhaps, globally, was the recent announcement, in December 2016, by Vice Minister Xiaowei Ma and in the presence of several officials from the Health and National Planning Commission, the country's Finance Ministry as well as the Ministry of Labour and Social Security, of a China Health Policy and Technology Assessment Network. Numbering 29 universities across the country, including Peking, Fudan and Renmin, and with small teams of administrators and analysts across several provincial and city health authorities, including Xiamen, QingDao and Chengdu, the network is led by the China National Health and Development Research Centre and is meant to make HTA a major input into national health policy. Launching the network, Vice Minister Ma called HTA a 'prerequisite for achieving Health China 2030' the country's forward looking national health plan and a means to 'innovation driven development' [25].

Latin America is very much at the forefront of HTA reforms. Countries such as Brazil (CONITEC) and Uruguay (FNR) have for years operated committees that consider HTA for making listing and pricing decisions. In 2012, Colombia launched IETS, having worked closely with NICE International and technical experts from Argentina and supported by the Inter-American Development Bank, with an increasing influence on or pricing decisions [26,27]. Chile has from early on used CEA as one of several inputs in designing Acceso Universal con Garantías Explícitas, the explicit guarantees package developed in the early 2000s, and has more recently established a dedicated HTA team within the MoH, while Cost Rica is in the process of launching an HTA body to inform its technology adoption decisions. Interestingly, and perhaps worryingly, a growing number of countries including Colombia and Chile [28] are setting up High Cost Drugs Funds, emulating the English Cancer Drugs Fund, which, having overspent for 7 years or so on cancer drugs NICE rejected, has now been placed under NICE's jurisdiction with severe CEA and budget controls. Such Funds aimed at bypassing the science of HTA and play to politicians' populist instincts are a significant drain on resources, especially in resource-constrained countries with significant distributional discrepancies, and have a real opportunity cost on health as the English example demonstrates.

They fragment decision-making processes introducing different types of criteria, methods and bureaucracies, and divert attention away from low-cost, high-value technologies such as vaccines, often not yet available to all, especially the poorest of the population.

HTA networks are also abundant: Red de Evaluación de Tecnologías en Salud de las Américas (RedETSA) in partnership with Pan-American Health Organisation (PAHO) in Latin America, HTAsiaLink in Asia, EUnetHTA in Europe, as well as professional societies such as HTAi and International Society for Pharmacoeconomics and Outcomes Research (ISPOR), the latter with major country and regional chapters, all contribute to knowledge sharing and capacity building for HTA, especially ones like HTAsiaLink [20], operating free of commercial sponsorship and with a focus on mentoring young Asian researchers working closely with their countries national governments [29].

As demonstrated earlier, the relevance of CER is far from restricted to richer or emerging economies. In fact, it has been argued that the scarcer the financial and other (e.g., human and infrastructure) resources for UHC, the more important it is that the investment choices made account for the opportunity cost of such investment [24,30,31]. Indeed, in addition to the accountability brought by its scientific nature, HTA can be a powerful governance-enhancing tool with potentially an important role in realizing the vision of a country-led and aid-independent world [32].

In different shapes and forms, contextualized to local settings and used for different purposes, HTA is here to stay. Whether strategic purchasing or commissioning as we call it in the English NHS, HTA is a powerful tool for improving the efficiency and equity of resources allocated to healthcare and hence arming policy makers and those who hold them to account with a handle on spending and (expected) outputs whether the aim is an all-inclusive and equitable UHC [18] or a functioning healthcare market.

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