



## Global article collection: essential reads from around the world

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At the beginning of 2022, the *Journal of Medical Economics* (JME) published a Commentary highlighting the top five cited articles in 2021 [1]. This Commentary also included six articles from 2021—chosen by the Editor in Chief and Deputy Editor in Chief—that had a significant impact on the study of health economics.

However, the JME editorial team noticed that the articles in the Commentary focused on research in the U.S. rather than reflecting the global diversity of the Journal's content. This realization led to the publication of this Commentary that represents authors and articles from regions beyond North America.

To create this Commentary, the Journal's Editorial Board members and some of its highly-cited authors selected impactful and thought-provoking articles from the following global regions: Western and Eastern Europe, Africa, Asia, Australia, and South America. Continue reading for the full list of articles and accompanying commentaries.

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### Western Europe

**Burden of caring for Alzheimer's disease or dementia patients in Japan, the US, and EU: results from the National Health and Wellness Survey: a cross-sectional survey**

Numerous people are caring for partners, children, and family members or relatives with chronic diseases. Being a caregiver can have a large impact on the health, activities of daily life, and professional work of the caregiver. In 2021, a paper [2] published in JME reported the burden of caring for Alzheimer or dementia patients in Japan, the USA, and five EU countries. This paper reported a substantial caregiver burden in all three regions across the world, with some similarities and differences. Compared to non-caregivers, caregivers were associated with lower health outcomes (measured by the EQ-5D, the mental component summary, and the physical component summary from SF-12) in all countries. Significant higher absenteeism and presentism were also observed for caregivers compared to non-caregivers in Japan and the USA, but not in Europe.

Quantifying the burden of caregivers on health-related quality of life (HRQOL) is important to adequately report the full burden of diseases and to assess the complete effects of a healthcare intervention. The inclusion of caregiver burden in economic evaluation has, therefore, gained importance in recent years. Excluding the caregiver burden from a cost-effectiveness study may provide incomplete information on the effectiveness and cost-effectiveness of a healthcare intervention.

In 2013, the National Institute for Health and Care Excellence (NICE) in the UK stated that economic evaluations should include direct health effects for all individuals, including carers where relevant. In a recent review [3] of all published NICE technology appraisals (TAs) and highly specialized technologies (HSTs), only 16 out of 422 (3%) documents included carers disutility in their cost-effectiveness analysis. Inclusion of carers disutility is limited by the absence of guidance and consensus on specific methods to incorporate caregivers' utilities, and further research is therefore needed on the technical aspects of the inclusion of carers HRQOL in cost-effectiveness models [4]. The final NICE manual published in early 2022 stated that evidence should be provided to show that the condition is associated with a substantial impact on carer HRQOL without setting minimum standards at this time [5]. Studies, such as the study of Ohno et al. [2], quantifying the caregiver burden are expected to increase in the future, while further research and guidance are needed for the measurement and inclusion of caregiver burden in health technology assessment.

Mickael Hilgsmann

**Eastern Europe**

**Economic implications of adding a novel algorithm to optimize cardiac resynchronization therapy: rationale and design of economic analysis for the AdaptResponse trial**

Cardiac resynchronization therapy has gained much attention in both the seminal literature and clinical practice over the past two decades. This procedure relies on the insertion of electrodes in the left and right ventricles of the heart to treat heart failure via an implanted pacemaker. Typical patients that are recruited suffer from an ejection fraction lower than 35% coupled with prolonged QRS interval duration of well over 120 ms. This type of therapy has been hailed as one of the most promising approaches to resolve life threatening terminal stage heart failure by increasing bioelectrical and biomechanical efficiency of the myocardium [6]. The clinical aspects of this therapy have been well documented; however, there is a certain scarcity of evidence in terms of health economics, which is why I selected this recently published original research article to highlight in this commentary.

AdaptResponse itself is the largest trial conducted amongst randomized cardiac resynchronization therapy (CRT) interventional global trials in this area (ClinicalTrials.gov Identifier: NCT02205359) with an estimated patient enrollment of 3,700 participants. In their findings, the authors note that CRT improves cardiac performance and consequently reduces morbidity and mortality. Distinctive added value of the AdaptivCRT algorithm lies in its ability to improve response rates and hemodynamic optimization of CRT pacing. The use of post-hoc analysis proved significant in reducing the risk of all-cause readmission. Furthermore, the economic evaluation indicates incremental gains in the average patient survival and quality of life associated with cost savings. The authors have also carefully designated all core methodological limitations, with the main one simply being a lack of maturity of the data. However, this will come in time as the AdaptResponse trial's estimated study completion date is September 2024. These pilot findings were published in October 2020, four years prior to final outcomes being determined.

Thus, we conclude this health economic evaluation opens the floor for debate on appealing Health Technology Assessment (HTA) issues, which depart from common medical technology innovations competing for public reimbursement. The case of complexity of such interventions is particularly prominent in Asian Pacific countries, despite their sound legacy in HTA [7]. We believe that intriguing cases like this one may serve as a knowledge platform for rapidly developing low- and middle-income countries (LMICs) market access systems across the Global South [8].

Mihajlo Jakovljevic

## Africa

### Cervical cancer prevention in Morocco: a model-based cost-effectiveness analysis

Cervical cancer is a preventable disease. Despite this, the annual incidence globally is projected to increase from 570,000 cases currently to 700,000 by 2030, and most of these will be among young, under-educated women in low- and middle-income countries (LMICs) [9,10]. The human papillomavirus (HPV) vaccine offers the potential to eliminate cervical cancer if made routinely available and used based on recent studies [11]. This is especially important in LMICs where the cost of cancer care can be prohibitive including for biological medicines [12]. It is for this reason that the recent study of Messoudi et al (2019), which assessed the cost-effectiveness of the HPV vaccine in Morocco, is both necessary and impactful to guide future healthcare funding strategies across Africa and wider. As a result, it will help achieve the WHO goal of eliminating cervical cancer as a public health problem [9, 10].

The authors successfully developed a Markov model to determine the cost/ life year saved (LYS) from the HPV vaccination program versus traditional screening approaches or combined approaches, which were based on a previous model from Spain and subsequently calibrated with data from Morocco including current incidence figures. Annual transition probabilities with respect to the natural history of HPV infections and cervical cancer were taken from published studies on the assumption that the natural history would not differ between countries [10]. This appears a reasonable assumption, along with the cost of the vaccine based on the negotiated price of the Revolving Fund of the WHO Pan American Health Organisation [10]. The price could even be lower based on current estimates of the manufacturing costs.

The authors calculated that the cost/LYS from the HPV vaccines would be \$1,150 (USD) assuming a 70% coverage among pre-adolescent girls and a reduced lifetime risk of cervical cancer of 62% [10]. The cost/LYS increases if the programs are combined (e.g., HPV vaccines combined with visual inspections with acetic acid every 3 years); however, the lifetime risk is reduced by 69%. This compares with a cost/LYS of \$551 (USD) and an expected 14% reduction in the lifetime risk of cervical cancer with current screening approaches in Morocco. The recent study of Falcaro et al. (2021) suggests that the HPV vaccine is more effective in reality, almost eliminating cervical cancer in women born in the UK since autumn 1995 [11]. These results, coupled with the findings of Messoudi et al., argue for the routine availability of the HPV vaccine across all countries. This can be funded through donors, non-government organizations, governments, and other sources. The next stage is

to reduce current rates of vaccine hesitancy by including educational programs among parents (mothers and fathers) and teenage girls to ensure improved uptake and lower cervical cancer rates in the future. Similar cost effectiveness analysis can be conducted in GAVI-supported LMICs for comparison.

Brian Godman and Sylvia Opanga

## Asia

### **Cost-effectiveness and budget impact analyses of colorectal cancer screenings in a low- and middle-income country: example from Thailand**

This article highlights the importance of including preference research in Health Technology Assessment (HTA) to inform clinical and policy decisions. HTA is recognized for evidence-informed decision making, but the evidence lacks preference data, especially in the case for low- and middle-income countries (LMICs). Understanding these preferences may lead to more nuanced decision making and can help policymakers optimize successful campaigns (e.g., increased uptake via better intervention design or implementation of interventions). Discrete-choice experiments (DCE), a stated-preference method, are gaining more popularity in healthcare nowadays and have been widely used to elicit and analyze preferences [13]. Yet, LMICs lack this kind of evidence; this article shows the importance of preference research in relation to colorectal cancer (CRC) screening in Thailand.

In 2019, a paper investigating the cost-effectiveness and budget impact analyses of CRC screenings in Thailand was published. This paper concluded that the screening test colonoscopy was the best value for money, while the fecal immunochemical test (FIT) was found to be more affordable [14]. Despite value for money, the screening participation rate of colonoscopy and FIT were (only) 47% and 63%, respectively, indicating suboptimal uptake. Using a DCE, the study showed that FIT had the highest Willingness-To-Pay, indicating it as the preferred screening method. Insights are also provided into which screening characteristics people prefer, allowing campaigns to highlight favorable or concerning attributes of screening tests. The article demonstrates that adding preference research to previous cost-effectiveness evidence may lead to more nuanced HTA conclusions. For instance, if investing in colonoscopy as a CRC screening method in Thailand (due to its better value for money), then behavior change interventions (incorporating messages to address

perceptions related to the screening attributes) are needed to maximize uptake, which is critical for successful screening campaigns. This is important for LMICs to optimize their public health resources.

This study highlights the need to embed preference eliciting research (e.g., DCEs) in behavior change theory. Perceptions of screening attributes (that influence screening preferences) may be linked to different determinants of behavior change (e.g., attitude, self-efficacy) [15]. The study also showed that many participants were not aware of CRC and CRC screening, indicating the need to incorporate behavior change in the public health program, targeting people in different stages of change. Thus, it is important to combine cost-effectiveness evidence with preference research and behavior change theory to optimize the success of public health efforts.

Kei Long Cheung and Mickael Hiligsmann

## Asia

**Treatment patterns and medical cost of systemic lupus erythematosus patients in Japan: a retrospective claims database study**

**Treatment patterns and direct medical costs of metastatic colorectal cancer patients: a retrospective study of electronic medical records from urban China**

Real-world data (RWD) refers to data relating to patient health or healthcare delivery in real-world clinical settings, usually derived from sources such as patient health records, administrative or claims database, and disease registries. There is an increase in use of RWD due to its closer representation of clinical practice and patient outcomes compared to data from clinical trials. Over the last few years, the use of real-world evidence (RWE) has consistently emerged as a leading trend in health economics and outcomes research [16]. The prominence of RWD is further underscored by its use in regulatory decision-making by the Food and Drug Administration in recent years [17]. These trends have expanded globally, and the demand for RWE will continue to grow, including in the Asia Pacific region.

Two papers published in this journal last year are essential reads to understand the use of RWD in the Asia Pacific region in answering questions on disease burden and treatment patterns. Miyazaki et al. employed data from the Japan Medical Data Center on inpatient, outpatient, and pharmacy claims under the Health Insurance Association in Japan [18]. Interesting trends were revealed based



on data from 4733 patients with systemic lupus erythematosus (SLE) across multiple medical institutions. A high use of glucocorticoids was noted, and a heavy economic burden was found to be associated with SLE where a mean annual direct medical cost of up to \$20,276.90 (USD) per patient was estimated among those with severe disease [18]. In another study using an oncology database with information extracted from electronic medical health records across 12 tertiary hospitals in China, Shen et al. showed that the use of biologicals among patients with metastatic colorectal cancer was low, despite guideline recommendations of this drug class. A sharp increase in treatment cost at the third line of treatment regardless of treatment type was also demonstrated [19].

Real-world studies have important policy implications. Both Miyazaki et al. and Shen et al. demonstrated the significant economic burden associated with both diseases evaluated, especially with increasing severity or in later lines of therapy [18,19]. Using glucocorticoid use as an indicator, Miyazaki et al. postulated that treatment for SLE patients remained suboptimal, leading to a higher rate of disease flare-ups, while Shen et al. suggested that there remains limited access to biologicals due to their low use among patients with metastatic colorectal cancer [18,19]. Such findings, derived from RWD, are critical to evaluate and guide the allocation of healthcare resources to improve patient outcomes, highlighting the value of real-world studies.

Given its importance, the use of RWD should be expanded in the region. An important takeaway from these studies is the crucial role of RWD sources that can provide data that is complete, comprehensive, and of good quality. For example, when designing electronic medical health records or disease registries for clinical use or performance monitoring, consideration should be given to whether the data collected could be used for research, including regulatory requirements for data access and logistic issues involved in data extraction. Taking such measures will be critical to drive real-world studies in the Asia Pacific region, not only in line with global trends but also to identify unmet needs and potential treatment gaps, hence improving patient outcomes in this region.

Chia Jie Tan and Nathorn Chaiyakunapruk

## **Australia**

### **The Global South political economy of health financing and spending landscape – history and presence**

This political economy article is something I would not normally read; however, I was drawn to this piece through intrigue in the “Global South” part of the title, not knowing where the Global South started and ended, and because it was published in JME. In addition, I was interested to learn more about the two Australian authors who contributed to this article: Professor Wijeratne and Dr Khatri.

As mentioned, the “Global South” was an unfamiliar term to me. After some digging, I learned about the Brandt line [20], the Maddison Historical Statistics Project [21], and that the South and North are divided by more than the equator. The Global South and Global North are predominantly geographical classifications of lower- and middle-income countries and high-income countries, respectively. The Global South is not a fixed entity but bound by time and place; that is, the borders of nation-states and jurisdictions, populations, wealth, prosperity, and technology all change over time.

Putting the boundaries of the Global South aside, the article provides a succinct history of the economic history and health for the last two millennia and is peppered with interesting facts throughout. For instance, the article discusses the richest countries based on their ability to extract gold (e.g., Mali); the sexual revolution and the female labor force needed to achieve “five-year plans”; the industrial revolution with the population drift from agrarian to urbanization; and the one-child policy of China and its growth in wealth to be the richest country in the world (total GDP in USD) [22]. The epidemiologic impact of economic development with the changing patterns in longevity, causes of mortality, and burden of disease are put in context of access to medicines and insurance plans.

The takeaway is that most nation states in the Global South, from Chile to Serbia and Korea to Vietnam (with the exceptions of Sub-Saharan Africa and Afghanistan), have increasingly aging populations and declining fertility. The ageing population has increasing burdens on health systems due to chronic diseases, including dementia, and the income generated by younger populations is used to support those no longer in the labor force. Health technology assessment goes some way to rational decision-making for efficient allocation and use of health resources, but the universal health coverage project [23] is pushing governments to increase their healthcare budgets to build and staff hospitals, enhance primary care, and fund public health interventions. A key consideration that is often not factored into healthcare planning and financing decisions is that healthier older people can remain in a productive workforce for longer and therefore contribute to the future costs of healthcare and social welfare. We are seeing this phenomenon in high income countries where the age of retirement (and eligibility for a pension) is increasing. However, the future “payback” is

typically not factored into budget decisions on healthcare financing, and healthcare budgets are driven by political parties who may be in power for relatively short election periods.

Regarding the two Australian authors, Professor Tissa Wijeratne is the Director of Academic Medicine and Director of International Affairs at Western Health, Melbourne, along with many other key leadership positions. He is a senior neurologist with a research focus on neuroscience, stroke, movement disorders, and headache. Dr Resham Khatri is a Post-doctoral Research Fellow in the School of Public Health at the University of Queensland. His research focus is on health systems and services, health policy, and child and maternal health, especially in low- and middle-income countries. Both have made important contributions to this article with regard to summarizing the economic and health financing history in the Global South.

I encourage others to read this article; it is well presented and an easy and interesting read. Understanding the economic history, geopolitics, technological change, population dynamics, and the history of healthcare is fundamental to development of sustainable long-term healthcare systems with appropriate financing mechanisms. The bottom line is knowing the historical context of “time and place” for big decisions.

Paul A Scuffham

## **South America**

### **A discrete choice experiment to assess patients’ preferences for HIV treatment in the rural population in Colombia**

In the last few decades, HIV therapy has evolved significantly, achieving outcomes that were thought to be unreachable. Nowadays South American countries, such as Brazil and Colombia, have guidelines aligned with the most recent therapeutic strategies launched. In parallel, patient-centered healthcare has gained a lot of relevance as the main pillar of value-based healthcare approaches. Thus, understanding patients’ preferences has become a must in the current and future settings of healthcare. In this context of value-based healthcare and patient centricity, while slower than other parts of the world, the South American region has evolved rapidly.

In this complex scenario, Goossens et al. developed a discrete choice experiment study to understand HIV patient preferences in the rural population of Colombia. Interestingly, younger and highly educated patients valued the effects of the therapy on their physical activity, which was in

contrast with older patients and less educated patients who, in general, valued life expectancy and accessibility to the clinic. This study brings to light several important factors:

- 1) Differences in what patients with distinct sociodemographic characteristics value the most (e.g., older, highly educated).
- 2) The importance of patient preference studies, still scarce in South America, to support healthcare decision making and patient pathway care design.
- 3) Describing the preferences of the rural population, a part of the population that is usually the focus for most research projects, but which is 25% of the total population in the continent.

In summary, real-world studies such as the one developed by Goossens et al. are essential to support a better decision-making process in South America and should be encouraged, especially when they bring to light patient preferences in a trend of patient-centered approaches.

Guilherme Silva Julian

### **Closing remarks**

We hope you have enjoyed reading the articles and commentaries that we have collected in this Commentary, and that you found them as interesting as we did. The JME editorial team is always on the lookout for more high-quality, globally representative content for the Journal. Please visit the Journal's website for more information on article submission and to reach out to our team with pre-submission queries and questions.

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