Editorial

Pharmaceutical Policy, Impact and Health Outcomes

Hye-Young Kwon[1], Brian Godman[2,3,4]

[1]Division of Biology & Public Health, Mokwon University, Daejeon, South Korea. Email: haeyoungkwon0111@gmail.com
[2]Department of Public Health Pharmacy and Management, School of Pharmacy, Sefako Makgatho Health Sciences University, Pretoria, South Africa; Email: brian.godman@smu.ac.za. ORCID number: 0000-0001-6539-6972 (BBG)
[3]Strathclyde Institute of Pharmacy and Biomedical Sciences, University of Strathclyde, Glasgow G4 0RE, United Kingdom; Email: Brian.Godman@strath.ac.uk
[4]Centre of Medical and Bio-allied Health Sciences Research, Ajman University, Ajman 346, United Arab Emirates

Pharmaceutical policy is essential given increasing expenditure on medicines and only finite resources, with global expenditure on medicines estimated to reach US$1.5 trillion by the end of 2023 (1). This represents an annual compounded growth rate of 3–6% a year in recent years, driven by increasing prevalence of non-communicable chronic diseases (NCDs) with ageing populations and resultant increase in medicine use alongside the increasing costs of new medicines especially for orphan diseases and cancer (2-5). The cost of cancer care is a particular issue with world-wide sales of oncology medicines expected to reach $237 billion by 2024, and continue growing (4). This increase is driven by the increasing prevalence rates of patients with cancer alongside the increasing costs of new oncology medicines, with requested prices per life year gained for new oncology medicines rising four-fold or more during the past years after adjusting for inflation (4). This increase is exacerbated by the emotive nature of the disease area (6). These growth rates though are unsustainable leading to greater scrutiny over the cost and value of new oncology medicines, which will continue (4).

Alongside this, there needs to be greater scrutiny over the costs and use of existing medicines to ensure maximum value, with more than half of all medicines prescribed or dispensed inappropriately (2). In addition, health authorities may not always realise the full potential for available savings. This happens when there are limited demand- and supply-side measures to encourage the preferential prescribing of low cost multiple-sourced medicines or biosimilars as seen in South Korea compared with Western European countries including Sweden and the UK (2, 7, 8). The ideal is that patients receive medicines appropriate to their clinical needs, in doses and duration cognisant of their requirements, and at the lowest cost to them and the health service. However, this is not always the case. Alongside this, we are aware there are concerns with rising rates of antimicrobial resistance (AMR), increasing morbidity, mortality, and costs (9). This results from excessive use of antibiotics especially for self-limiting conditions alongside patients with tuberculosis not fully complying with their course of treatment (9, 10). Both areas need addressing going forward to reduce rising AMR. Similarly, polypharmacy can increase healthcare expenditure alongside increase adverse outcomes in patients; consequently, potential patients need careful management once the size of the problem has been calculated (11, 12). In their study, Cho et al demonstrated in South Korea that the rate of polypharmacy remained high in the elderly during the past 10 years with the rate of hyper-polypharmacy (currently prescribed 10 or more medicines) had increased, which needs actively addressing (12).

In view of these multiple issues, this research topic sought to examine the strengths and weaknesses of pharmaceutical policy across countries, and its impact on medicine use and health outcomes to provide future guidance. Overall, 22 papers were published as part of this research topic across a wide-variety of areas and countries.

Increasing access to medicines, and enhancing their rational use, are extremely important to countries, especially low- and middle-income countries (LMICs) where there are concerns with the current management of patients (13, 14). In their study, Lu et al discuss the impact of the recent Chinese centralised drug procurement policy, called the '4 + 7' policy, on drug utilisation patterns among public medical institutions (15). Lu et al found that the policy had an appreciable impact with the utilisation of bid-winning medicines increasing from 17.03% to 73.61% of procured medicines. Alongside this, the utilisation of multiple-sourced medicines increased by 67.53% and originators decreased by 26.88% as a result of the policy (15). The use-proportion of quality-guaranteed medicines also increased from 56.69% to 93.61% of procured medicines (15). Long et al showed similar findings; however, there were no significant price changes in medicines that were not part of this policy (16). This mirrors the findings from studies conducted across Europe where the introduction of multiple demand- and supply-side measures can enhance the prescribing of target medicines whilst appreciably reducing expenditure without compromising care (2). The same is not true in countries with limited supply- and demand-side measures (2). In the case of selective serotonin re-uptake inhibitors (SSRIs), Wen et al showed that the '4 + 7' policy resulted in an appreciable increase in their utilisation (76.7%) alongside decreasing expenditure (3.39%) benefitting patients (17). The same has been seen for instance in Scotland where multiple measures resulted in a 73.7% reduction in overall SSRI expenditure between 2001 and 2017 despite their utilization increasing 2.34-fold during this period (18).

There have also been similar benefits among hospitals in China as part of a national stewardship policy. Under this policy, key medicines of concern, i.e. those which currently have high prices and utilisation but unconfirmed or limited therapeutic effects, have been subject to close scrutiny with the help of clinical pharmacists (19). Prior to implementation, there was typically increasing usage and spend on these medicines. However, after implementation in one tertiary hospital with 1300 beds, Li et al demonstrated 430 fewer DDDs (defined daily doses) per month in 20 medicines under scrutiny alongside a reduction in overall expenditure of US$4,682 per month in the 19 months post implementation (p=0.003). However in their study, Galimberti et al failed to show that multiple demand-side measures including feedback reports and online courses failed to appreciably improve GP prescribing in Italy (20). This contrasts with Sweden where the prescribing of an agreed list of medicines appreciably improved through education and monitoring of prescribing, with a similar situation seen in Sweden and the UK when multiple sourced proton pump inhibitors (PPIs) and statins first became available (2). The differences in findings may be a result of differences in intensity, dissemination and follow-up of the various demand-side measures (2).

There are also concerns with access to medicines and their affordability within the Brazilian healthcare system as it strives to provide universal access (21, 22). In their study, Luz et al assessed the impact of the ERAF (Estratégia de Regionalização da Assistência Farmacêutica) policy to promote technical cooperation between the State and municipal governments with the aim of improving medicine procurement and distribution. The rationale is to promote the purchasing of high-quality products with reliable suppliers at the lowest-possible prices and transaction costs (23). We have seen such procurement activities obtain very low prices for medicines among European countries (24). However, Luz et al had concerns that the ERAF policy did not fulfil its goals, with the need to introduce a more sustainable long-term policy to achieve lower prices for medicines as demand grows (23). There are similar concerns with the availability of essential medicines within the State of Minas Gerais in Brazil with a need to strengthen funding and public purchasing processes to continue to provide universal healthcare alongside growing demands on available resources (25).

On the other hand, the instigation of the Korean Pharmaceutical Information Service (KPIS) to increase transparency in the pharmaceutical supply chain, including the prevention of recalled medicines as well as a decrease in inventory and disposal of out-of-date medicines, resulted in appreciable savings (26). Kim et al calculated the net benefit of the introduction of KPIS at US$571.6 million over 12 years, justifying its introduction (26). Such systems can also help monitor possible medicine shortages, which are an increasing concern globally (27). Shortages are more likely to occur with multiple-sourced medicines and older parental medicines where issues of profitability can be a concern, especially where the supply of raw materials is concentrated in only a limited number of manufacturers. In addition, where information systems are lacking to track utilisation and where there are delays in payment (27-29). These concerns are leading to pro-active measures across countries to address the situation including planning for shortages with antibiotics (30, 31).

Not surprisingly given that new cancer medicines dominate the medicines' pipeline with over 500 companies actively pursuing the development of new oncology medicines (4), there were an appreciable number of papers examining the cost-effectiveness of different oncology medicines. Such analyses are particularly important in LMICs where there are already issues of cost-effectiveness with existing oncology medicines to treat patients with breast cancer (14). In their paper, Zhu et al documented that toripalimab combined with gemcitabine and cisplatin had a greater chance of being cost-effective compared to camrelizamub combined with gemcitabine and cisplatin or gemcitabine and cisplatin combined from a Chinese payer's perspective for first-line treatment of patients with recurrent or metastatic nasopharyngeal carcinoma (32). Similarly in their study, Chen et al demonstrated that capecitabine and oxaliplatin appeared more cost-effective than gemcitabine and oxaliplatin again from the perspective of the Chinese healthcare system (33). In their network meta-analysis, Li et al also found that sintilimab plus biosimilar bevacizumab was cost-effective compared to sorafenib in patients with unresectable hepatocellular carcinoma again from the perspective of the Chinese healthcare system (34). However, whilst adding atezolizumab to platinum-based chemotherapy as first-line treatment of patients with metastatic urothelial cancer improved survival times, Liu et al did not find this combination was cost-effective in the Chinese setting (35). There were also mixed findings in the systematic review of Chan et al regarding Poly ADP-Ribose Polymerase (PARP) inhibitors across a variety of cancers (36). The authors concluded that in advanced ovarian cancer, PARP inhibitors should be prioritised for upfront maintenance for patients with BRCA mutation or BRCAness at recurrence in view their cost-effectiveness in this situation (36). The same was not seen in recurrent maintenance in patients with advanced ovarian cancer even with genetic stratification (36).

Sensitivity analyses are particularly important when reviewing potential reimbursement and funding for new cancer medicines given that an increasing number are being launched early with only limited effectiveness and safety data (4). This aspect is discussed further by Bae et al, who urge caution when using immature data especially if this diverts funding away from proven cost-effective technologies and subsequently wastes valuable resources (37, 38).

In the case of other NCDs, Oh et al in their study assessed the appropriateness of using EQ-5D-3L and EQ-5D-5L when assessing the role and value (39). Unsurprisingly, the pooled utility of patients with asthma declined with worsening control and severity of asthma. The authors concluded that both these health-related quality-of-life instruments are useful when assessing the value of asthma treatments (39). Kim et al showed that easing the criteria for reimbursing statins among patients with type 2 diabetes reduces CV events and their related costs (40). This mirrors other studies, demonstrating the need for multiple demand- and supply-side measures to ensure low prices for statins alongside increased use to benefit both patients and the healthcare system (2, 41). There were though concerns with the improper use of PPIs for patients undergoing stress ulcer prophylaxis in non-critical patients in the study of Li et al (42). The authors concluded that effective intervention strategies including education executed by clinical pharmacists could help address the situation (42). Effective interventions are also needed to reduce prescription opioid misuse in South Korea highlighted by Kim et al in their study (43).

AMR is an increasing concern across countries exacerbated by appreciable purchasing of antibiotics without a prescription in LMICs (9). Dispensing of antibiotics without a prescription is exacerbated by patient pressure even for self-limiting conditions such as acute respiratory illnesses (9). Consequently, it was encouraging to see in the study of Arshad et al that the public in Pakistan appeared to be aware of the problems associated with multidrug-resistant pathogens and their responsibilities in helping to reduce AMR (44). In their study, Pradipta et al found that strengthening ambulatory care facilities, including adequate resources and personnel, is important to ensure patients with TB are adequately managed and adherent to prescribed therapies (45). Otherwise, resistance will develop, which needs to be avoided to help eradicate TB.

In conclusion, there were a considerable number of papers covering this Research Topic. This demonstrates considerable interest across countries to develop and implement pharmaceutical policies to enhance the rational use of medicines. This includes improve access as well as procurement of medicines. In addition, ensuring value for money within finite resources. A number of initiatives can act as exemplars for the future, building on existing initiatives.

Conflict of interest

The authors declare that the editorial was written in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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