fail to capture important political shifts created by crises such as pandemics that could influence health spending over and above the impact of the GDP. Several countries increased investments in health relative to the GDP following national crises. China increased investments in universal health coverage after the SARS-CoV outbreak,[8,9] as did Rwanda after the genocide.[10] Following the Asian financial crisis, Thailand increased spending but Indonesia did not.[11] Lastly, it is not clear that the model sufficiently captured the changing frequency of outbreaks, the differential impact on the economy, and the subsequent effect on development assistance for health.[12,13]

Taken together, these concerns illustrate the potential impact of COVID-19 on future government health expenditure and development assistance for health. The ultimate direction and magnitude of the impact is not certain and will depend on which of the counteracting forces prevail. It is therefore impossible to say exactly how health spending and development assistance for health will change over the next 30 years. Although these projections reflect the current state of knowledge, they might quickly become outdated as situations change and more evidence becomes available.

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Adjuvant PD-L1 blockade in non-small-cell lung cancer

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Lung cancer is the leading cause of cancer-related mortality worldwide.[1] Surgical resection is the mainstay of therapy for patients with stage I–II and select stage IIIA non-small-cell lung cancer (NSCLC). Despite complete surgical excision, patients with NSCLC have high rates of relapse.[2] Historically, strategies to mitigate risk of relapse have focused on adjuvant chemotherapy. In randomised studies, adjuvant chemotherapy improves overall survival, but the degree of benefit is modest, and treatment is associated with clinically significant toxicity.[3] Until recently, progress in developing adjuvant therapies for NSCLC had been largely stagnant, which is in stark contrast with advanced NSCLC, where new therapeutics have been driven by the emergence of two treatment strategies: immune checkpoint inhibitors and targeted therapy.[1] Immune checkpoint inhibitors, targeting PD-1 and its ligand (PD-L1), have since become the cornerstones of first-line therapy for patients with advanced NSCLC with no targetable alterations. With this success, efforts have focused on moving these agents into earlier stages of disease.

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In *The Lancet*, Enriqueta Felip and colleagues[4] report interim findings from IMpower010, a randomised, phase 3 study comparing the PD-L1 inhibitor atezolizumab with best supportive care in patients with stage IB–IIIA NSCLC after surgical resection and adjuvant chemotherapy. The study population was predominantly male (67% in both arms), and more than 95% of patients were white or Asian. With a median of 32·2 months' follow-up (IQR 27·4–38·3), the authors found that atezolizumab produced statistically significant improvements in disease-free survival in stage II-IIIA patients whose tumours expressed PD-L1 on 1% or more of tumour cells (hazard ratio [HR] 0·66; 95% CI 0·50–0·88; p=0·0039), and among all patients with stage II–IIIA disease regardless of PD-L1 expression (0·79; 0·64–0·96; p=0·020). In the intention-to-treat population, adjuvant atezolizumab did not cross the significance boundary (0·81; 0·67–0·99; p=0·040).

IMpower010 represents an important landmark in thoracic oncology, marking the first randomised study of adjuvant PD-L1 blockade in NSCLC. The findings have important implications for patients with resectable NSCLC and raise critical questions regarding clinical trial endpoints, predictive biomarkers, and future directions.

Historically, improvements in overall survival have been the gold standard in the adjuvant setting. Within the past year, however, regulatory bodies have granted approval of the EGFR inhibitor osimertinib as adjuvant therapy in patients with completely resected, *EGFR*-mutant NSCLC based on a disease-free survival improvement in the ADAURA study.[5] The magnitude of disease-free survival benefit (HR 0·17) coupled with the favourable safety profile are cited as key factors in support of adjuvant osimertinib. Like ADAURA, the primary endpoint in IMpower010 was disease-free survival. Although overall survival was a secondary endpoint, an important limitation of IMpower010 is that overall survival could not be formally tested on the basis of the hierarchical statistical design and follow-up time. Nonetheless, insights from the locally advanced, unresectable NSCLC setting suggest that prolongations in disease control might be clinically meaningful surrogates.[6,7] The PD-L1 inhibitor durvalumab was initially granted regulatory approval as consolidation therapy after definitive chemoradiation in unresectable stage III NSCLC based on improved progression-free survival. With additional follow-up, an improvement in overall survival was also observed.[7] This background, together with the favourable safety and efficacy data from IMpower010, supports use of adjuvant atezolizumab in a subset of surgically resected NSCLC.

Moving forward, the most pressing question is which patients are most likely to benefit from adjuvant atezolizumab? Consistent with previous studies in metastatic NSCLC,[8,9] IMpower010 suggests that PD-L1 expression might enrich for clinical benefit among stage II–III patients receiving adjuvant atezolizumab. However, these same data raise crucial questions on the optimal PD-L1 expression cutoff. Although IMpower010 met its primary endpoint in the stage II–IIIA population with PD-L1 expression on 1% or more of tumour cells, the improvement in disease-free survival appears to be largely driven by patients with PD-L1 expression on 50% or more of tumour cells (HR 0·43; 95% CI 0·27–0·68). In a post-hoc exploratory analysis of the stage II–IIIA population with PD-L1 expression on 1–49% of tumour cells, the disease-free survival HR was only 0·87 (0·60–1·26). Although such post-hoc analyses must be interpreted with caution, these results align with standard PD-L1 cutoffs in the metastatic setting (≥50%, 1–49%, and <1%) and are consistent with findings from KEYNOTE 042.[8]

In KEYNOTE 042, the PD-1 inhibitor pembrolizumab produced a significant improvement in survival in patients with advanced NSCLC with PD-L1 expression on 1% or more of tumour cells, but this survival benefit was predominantly driven by patients with PD-L1 expression on 50% or more of tumour cells. Ultimately, findings from IMpower010 support a new role for PD-L1 testing in surgically resected NSCLC, although they underscore the need for additional studies to further define which subpopulations benefit most from adjuvant atezolizumab.

IMpower010 represents an important step forward. In my view, adjuvant atezolizumab should be a new standard of care for patients with surgically resected, PD-L1-positive stage II–IIIA NSCLC after completion of adjuvant chemotherapy, with particular emphasis on those patients with PD-L1 expression on 50% or more tumour cells. In the near future, the therapeutic landscape for resectable NSCLC is likely to become more complicated as additional data emerge from other, ongoing studies of immune checkpoint inhibitors in the adjuvant setting and parallel studies evaluating neoadjuvant approaches. More broadly, the success of adjuvant PD-L1 blockade in patients with NSCLC, along with recent data in melanoma,[10] sets the stage for continued expansion of immune checkpoint inhibitors into the adjuvant setting across disease areas over the ensuing decade.

JFG has served as a compensated consultant for Genentech/Roche, unrelated to the topic of this Comment; has also served as a compensated consultant or received honoraria from Bristol–Myers Squibb, Takeda, Loxo/Lilly, Blueprint, Oncorus, Regeneron, Gilead, Moderna, AstraZeneca, EMD Serono, Pfizer, Novartis, Merck, GlydeBio, and Karyopharm, unrelated to the topic of this Comment; has received research support from Novartis, unrelated to the topic of this Comment; has received institutional research support from Bristol–Myers Squibb, Tesaro, Moderna, Blueprint, Jounce, Array Biopharma, Merck, Adaptimmune, Novartis, and Alexo, unrelated to the topic of this Comment; and has an immediate family member who is an employee with equity at Ironwood Pharmaceuticals, unrelated to the topic of this Comment.

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Functioning of the International Health Regulations during the COVID-19 pandemic

When the International Health Regulations (IHR) came into force in 2007, WHO announced that "the global community has a new legal framework to better manage its collective defences to detect disease events and to respond to public health risks and emergencies".[1] The IHR aim to enable the prevention, detection, and containment of health risks and threats, the strengthening of national capacities for that purpose, and the coordination of a global alert and response system.

In the prolonged and unprecedented COVID-19 pandemic, some have stated that the IHR "are a conservative instrument that constrain rather than facilitate rapid action".[2] What we, the Review Committee on the Functioning of the IHR (2005) during the COVID-19 Response, found instead was that much of what is in the IHR is well considered, appropriate, and meaningful in any public health emergency. However, many countries only applied the IHR in part, were not sufficiently aware of these

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For the **Review Committee on the Functioning of the IHR (2005) during the COVID-19 Response** see https://www.who.int/teams/ihr/ihr-review-committees/covid-19