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Correspondence

High cost of immunoglobulin replacement therapy

Causes and implications

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To the Editor,

We read with interest the recent Perspective on the *Annals of Allergy, Asthma & Immunology* titled "Immunoglobulin Replacement Therapy Stewardship in Modern Times."[1] The author of the article, Richard Wasserman, MD, PhD, attributed the high cost of immunoglobulin replacement therapy (IRT) in the United States to limited domestic plasma supply and proposed clinical immunologists contribute to controlling health care costs by IRT stewardship.

Although a important global concern, we find limited evidence that plasma scarcity meaningfully contributes to high IRT cost in the United States. The United States currently sources two-thirds of the world's plasma,[2] a quantity far exceeding its own therapeutic needs. Accordingly, the nation's surplus plasma is exported internationally for profit. Although unfractionated plasma is sold like a commodity, IRT product costs seem largely disconnected from the microeconomic forces of supply and demand. For instance, the most likely annual cost of IRT therapy for patients in the United States last year was $60,145, a sum 3 times higher than those of net plasma-import nations such as the United Kingdom, Australia, and Canada.[3-5] Clearly, domestic plasma surpluses have not generated much downward pressure on US IRT cost as Dr Wasserman suggests they would. Moreover, the United Kingdom, which suspended domestic plasma sourcing in the 1990s owing to Creutzfeldt-Jakob disease concerns, has not experienced ballooning IRT costs as Dr Wasserman's theory would predict.

Why are US IRT products more affordable when exported abroad? The likely answer is that other nations protect therapeutic affordability through value-based pricing.[6,7] Value-based pricing uses cost-utility measures to limit exorbitant pricing of marginally beneficial therapies and to incentivize development of highly effective, "game-changing" treatments.[8] Recently, we published a cost-utility analysis identifying lifelong IRT as a slightly more effective but much more costly strategy to treat US patients with congenital agammaglobulinemia than hematopoietic stem cell transplantation.[9] Although we did not promote a specific treatment strategy, we concluded that IRT was not a cost-effective therapy in the United States owing primarily to its excessive cost. Although we used mathematical models and virtual patient simulations to generate our results, in a real-world scenario the additional $900,000 spent for a lifetime of IRT is actually paid by real patients, their families, and the many stakeholders supporting public and private medical insurance.[9]

Regarding the second point of Dr Wasserman, although we agree that IRT should be prescribed to all patients who cannot generate protective antibody responses, we wish to highlight that cost remains a major obstacle to patients actually receiving prescribed therapies, especially recurring ones. Without value-based methods to set reasonable prices across markets, US insurers now routinely require extensive necessity documentation for each costly therapy. Although the utilization of prior authorization does limit insurance expenditures, it realistically creates little positive clinical impact while clearly harming patients.[10] For instance, weeks-long treatment delays waiting for insurance authorization are common in the US health care system as are payer refusals to cover therapies considered medically necessary by disease experts. Hence, although US clinical immunologists who practice good medicine can be good IRT stewards, our ability to treat patients with antibody deficiency is increasingly undermined by high IRT costs.

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