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The Global Access Crisis for GLP-1 Receptor Agonists: From Scientific Breakthrough to Health Equity Challenge

Jindong Xie[1, #], Gujie Wu[2, #], Lin Cheng[3, *], Hailin Tang[1, *]

1. Department of Oncology, State Key Laboratory of Oncology in South China, Guangdong Provincial Clinical Research Center for Cancer, Sun Yat-sen University Cancer Center, Guangzhou, Guangdong, 510060, China.
2. Clinical Research Unit, Zhongshan Hospital, Fudan University, Shanghai, 200032, China.
3. Regenerative Medicine Institute, School of Medicine, National University of Ireland, H91 TK33 Galway, Ireland.

[*]Correspondence to: Dr. Hailin Tang (tanghl@sysucc.org.cn); Department of Oncology, State Key Laboratory of Oncology in South China, Guangdong Provincial Clinical Research Center for Cancer, Sun Yat-sen University Cancer Center, Guangzhou, Guangdong, 510060, China. Dr. Lin Cheng (L.Cheng1@universityofgalway.ie); Regenerative Medicine Institute, School of Medicine, National University of Ireland, H91 TK33 Galway, Ireland.

[#] These authors contributed equally to this work.

Dear Editor:

Glucagon-like peptide-1 receptor agonists (GLP-1 RAs) are currently undergoing an unprecedentedly explosive growth in clinical application and public market popularity. Spanning from well-known Hollywood celebrity groups who adopt these agents for body weight management to widespread online weight-loss sharing trends prevalent across multiple social media platforms featuring regular body mass tracking and intervention outcome check-ins, two representative novel long-acting GLP-1 RAs, namely semaglutide and tirzepatide, have acquired extensive popular acclaim and are widely dubbed as revolutionary "miracle drugs" for metabolic and adiposity control among the general public and part of clinical practitioners. A recent genetic study elucidated individual efficacy heterogeneity, while SELECT, FLOW, and SOUL trials confirmed transformative cardiovascular and renal benefits [1]. The SELECT trial showed semaglutide could reduce major adverse cardiovascular events (MACE) by 20% in overweight/obesity with cardiovascular disease (CVD) but without diabetes (HR 0.80; 95% CI 0.72–0.90, $P < 0.001$) [2]. In parallel, the FLOW trial demonstrated a 24% reduction in composite kidney outcomes (decline in eGFR, onset of kidney failure, or renal death) in type 2 diabetes with chronic kidney disease (CKD) (HR 0.76; 95% CI 0.66–0.88, $P = 0.0003$) [3]. Most recently, the SOUL trial, with 9,650 participants, confirmed once-daily oral semaglutide reduces MACE by 14% in type 2 diabetes with CVD or kidney disease (HR 0.86; 95% CI 0.77–0.96, $P = 0.006$) [4]. Despite this transformative evidence, the global distribution and utilization of GLP-1 RAs have devolved into a stark illustration of health inequity.

In high-income settings, an alarming proportion of prescriptions is being diverted toward what can only be described as off-label cosmetic use in individuals without documented obesity or related comorbidities. A French nationwide observational study of insurance databases from 2017 to 2023

identified 4,683 individuals—approximately 2.2% of all new GLP-1 users—who received these medications without any documented diagnosis of diabetes or obesity [5]. These recipients were predominantly younger women, and semaglutide was the most frequently dispensed agent. While 4,683 may seem modest, the scale of such wastage is economically non-negligible. Meanwhile, a global modeling study estimated that 799 million adults worldwide—27% of the adult population—meet contemporary eligibility criteria for GLP-1 RAs therapy for weight management alone. However, the overwhelming majority reside in precisely those nations where these agents remain unavailable or catastrophically unaffordable. In the lowest-income quintile of countries, only an estimated 11.7% of adults who could benefit actually qualify by clinical indication, yet the real-world treatment coverage is a negligible fraction of that figure [6].

While the World Health Organization (WHO)'s 2025 inclusion of four specific GLP-1 RAs (semaglutide, dulaglutide, liraglutide, and tirzepatide) in its Model List of Essential Medicines—approved exclusively for adults with type 2 diabetes accompanied by established cardiovascular disease, chronic kidney disease, or obesity—represents a meaningful symbolic advance, insights derived from decades of insulin deployment indicate that essential medicine designation alone fails to secure affordable access; without enforceable provisions for tiered pricing, patent exemptions and coordinated global bulk procurement, the affordability crisis persists unresolved [7]. The 2026 safety alert issued by the Pan American Health Organization, which flags safety hazards stemming from inappropriate GLP-1 RAs misuse—spanning severe pancreatitis, bowel obstruction, and perioperative aspiration under general anesthesia—as well as the tightened safety warnings released by the UK Medicines and Healthcare products Regulatory Agency, underscore a secondary equity challenge [8]. Between 2007 and 2025, the UK Yellow Card Scheme logged 1,296 adverse event submissions linked to severe pancreatitis, among which 19 fatal outcomes

were documented (although these spontaneous reports cannot establish causality or incidence rates) [9]. Collectively, these regulatory actions signal a critical structural barrier: even with the abrupt rollout of affordable generic formulations, under-resourced nations equipped with rudimentary pharmacovigilance infrastructures will lack sufficient capacity to monitor, identify, and clinically mitigate these uncommon yet life-threatening adverse drug reactions. In the absence of internationally coordinated allocation protocols and structured global supply distribution architectures, the rollout of generic GLP-1 RAs alone cannot mitigate pronounced cross-national disparities in treatment access. Though certain key patents for core active ingredients are set to begin expiring in some regions starting in 2026, an event projected to ease overall supply constraints and reduce baseline manufacturing costs, pharmaceutical developers continue to tilt their commercial development and distribution strategies toward the high-margin obesity market dominated by high-income economies, while allocating minimal investment to affordable, scalable diabetes and cardiorenal therapies designed for low- and middle-income countries. From an equity-focused epidemiological lens, marginalized subgroups—including socioeconomically disadvantaged women, geographically remote rural inhabitants and impoverished demographic cohorts—disproportionately bear the brunt of unmet therapeutic needs and avoidable health harms arising from inequitable drug availability.

As clinical researchers, we argue that the prevailing market and regulatory trajectory surrounding GLP-1 RAs is both ethically indefensible and clinically unsound. The scientific community ought to rally behind a globally harmonized drug allocation framework centered on populations with the most pressing unmet medical needs: individuals living with type 2 diabetes complicated by established CVD, CKD, or clustered cardiometabolic risk factors, subgroups poised to accrue the largest absolute reductions in all-cause mortality. We urge the WHO, the World Trade

Organization, and originator pharmaceutical firms to co-design an inclusive international access scheme for GLP-1 RAs, drawing on actionable successes and empirical shortcomings accumulated from global vaccine equity programmes. We organize the required policy interventions into three interconnected thematic clusters to deliver coherent, actionable global solutions: (1) Affordability frameworks: Implement legally binding tiered pricing caps linked to national per capita income levels, broaden the Medicines Patent Pool to cover all core GLP-1 RAs, and establish standardized, transparent technology transfer agreements to lower local manufacturing barriers. (2) Equitable supply and distribution systems: Roll out coordinated cross-national bulk procurement mechanisms, mobilize targeted multilateral development bank financing, and scale up cold-chain logistics and basic healthcare infrastructure in low- and middle-income nations to guarantee steady drug delivery. (3) National safety monitoring capacity: Allocate sustained public investment to build comprehensive national pharmacovigilance infrastructures, avoiding gaps between rapid treatment expansion and post-marketing adverse event surveillance and clinical management capacity. Concurrently, sustained public funding for comprehensive pharmacovigilance infrastructures is essential to prevent rapid treatment scale-up from outstripping post-marketing safety monitoring and adverse event management capacity. In parallel, regulatory authorities in high-income economies need to tighten prescription control measures to deter off-label diversion for cosmetic weight loss among people lacking documented obesity or cardiometabolic comorbidities, while preserving constrained drug supplies for patients with evidence-based metabolic indications (***Figure 1***).

The scientific value of GLP-1 therapies should not be fractured by wealth disparities. Only by ensuring breakthroughs reach those in greatest clinical need—rather than serving as privileges for the affluent—can their public health mission be fulfilled.

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Figure Legends

Figure 1. Schematic overview of the global access crisis for GLP-1 RAs. Disproportionate commercial prioritisation of cosmetic weight-loss demand in high-income countries drives off-label misuse and supply shortages, exacerbating cross-national health inequities between high-income and low- and middle-income nations; this imbalance creates an ethical imperative for coordinated global policy interventions covering affordability, equitable drug distribution and pharmacovigilance capacity building.

Figure 1