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Cost-Effectiveness of Cardiovascular, Obesity, and Diabetes Mellitus Drugs: Comparative Analysis of the United States and England

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Multiple drugs for cardiovascular disease, obesity, and diabetes mellitus have been recently approved; however, it can be challenging to determine whether these drugs represent worthwhile improvements in cost-effectiveness over standard treatment regimens. England is one of several high-income countries that integrates evidence-based value assessments within pricing decisions and consistently has one of the lowest pharmaceutical expenditure per capita.[1] In England, the cost-effectiveness of new drugs is evaluated by the National Institute for Health and Care Excellence (NICE), a national public agency, while the Institute for Clinical and Economic Review (ICER) is an independent nongovernmental organization providing recommendations to private insurers for coverage decisions in the United States. We compared ICER's assessments of cardiovascular, obesity, and diabetes mellitus drugs with those similarly assessed by NICE in order to determine whether there are differences in how these organizations, from 2 of the largest pharmaceutical markets, evaluate cost-effectiveness and make coverage recommendations.

We analyzed assessment reports for drugs indicated for cardiovascular disease, obesity, and diabetes mellitus until April 2020 since ICER began publishing assessments in 2006. Drugs with assessments for cost-effectiveness measured using the incremental cost-effectiveness ratio (cost per quality-adjusted life-year [QALY]) from ICER were compared with public appraisal documents from NICE. Additional characteristics including comparator treatment, coverage recommendation, price, and the methodology of the economic evaluation (perspective, model, time horizon, outcome, and discount rate) were also compared. The authors declare that all supporting data are available within the article.

Ten drugs were similarly assessed for cost-effectiveness measured in cost/QALY indicated for cardiovascular disease, obesity, or diabetes mellitus (Table). In the United States, 5 drugs were within ICER's acceptable range for cost-effectiveness ($100–$150K/QALY) and below the threshold (sacubitril/valsartan, ranibizumab, pegaptanib, dronedarone, and naltrexone/bupropion), while 5 drugs were not recommended for coverage from private insurers at their current list or net price unless prices were discounted.

In England, 8 drugs were recommended for public coverage in England's National Health Service (NHS), while 2 were not approved (pegaptanib and naltrexone/bupropion). Confidential discounts were negotiated between manufacturers and the NHS to improve the clinical and cost-effectiveness of drugs for public coverage subject to price reductions. Five of the 8 drugs approved by NICE for coverage in England's NHS were subject to price discounts to improve cost-effectiveness as they were evaluated as cost-ineffective at their list price.

ICER and NICE were in concordance for 3 drugs (sacubitril/valsartan, ranibizumab, and dronedarone),

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Table 1. Cost-Effectiveness Evaluations and Coverage Recommendations

Indication	Drug	Cost Per QALY		Recommendation		Concordance of Recommendations	Reason for Discordance
		ICER	NICE	ICER	NICE		
Congestive heart failure	Sacubitril/valsartan (Entresto)*	$50 915	$37 736–$43 541	Clinical benefit over standard of care and cost-effective (but with significant budget impact)	Cost-effective and approved	Yes	NA; cost-effective in both the United States and England
Diabetic macular edema	Ranibizumab† (Lucentis)	$22 611–$28 747	$21 295–$43 022	Cost-effective but no clear recommendation	Cost-effective if manufacturer covers cost of >14 injections. Approved subject to financial agreement	Yes	NA; cost-effective in both the United States and England
	Pegaptanib (Macugen)‡	$22 720	$49 430–$246 296	Cost-effective but no clear recommendation	Significant clinical benefit (visual acuity) but cost-ineffective. Not recommended	No	Discordance regarding cost-effectiveness
Atrial fibrillation	Dronedarone (Multaq)§	$103 892–$120 398	<$21 583	Comparable clinical and cost-effectiveness	Cost-effective and approved	Yes	NA; cost-effective in both the United States and England
	Dabigatran (Pradaxa)	$178 483–$244 121	<$28 490	Unproven comparative clinical effectiveness, cost-ineffective	Cost-effective and approved	No	Higher price in the United States
High cholesterol	Alirocumab (Praluent)‖	$251 000	$29 028–$72 569	Cost-ineffective at net price or WAC, considerable uncertainty for clinical benefit	Approved subject to financial agreement	No	Higher price in the United States
	Evolocumab (Repatha)¶	$799 596	$42 380–<$54 717	Cost-ineffective at net price or WAC, moderate certainty of small net clinical benefit	Approved subject to financial agreement	No	Higher price in the United States
Obesity management	Naltrexone and bupropion	$122 737–$173 469#	$34 824	Cost-effective but no clear recommendation	Cost-ineffective given substantial uncertainty of long-term clinical effectiveness. Not recommended	No	Higher cost-effectiveness threshold in the United States, discordance regarding clinical effectiveness
Amyloidosis	Patisiran (Onpattro)	$835 000	$117 170–$181 794	Substantial net health benefit but current pricing exceeds cost-effectiveness	Approved subject to financial agreement	No	Higher price in the United States
	Inotersen (Tegsedi)	$1.7 million	$140 344	Substantial net health benefit but current pricing exceeds cost-effectiveness	Approved subject to financial agreement	No	Higher price in the United States

The incremental cost-effectiveness ratio was measured in US$ per quality-adjusted life-year (QALY) from the Institute for Clinical and Economic Review (ICER) and in GB£ per QALY from National Institute for Health and Care Excellence (NICE; converted to US$ gross domestic product purchasing power parity). Economic evaluations conducted with different comparators are included in the subtext of the Table. Drug evaluations from ICER and NICE differ because of their function within the 2 healthcare systems. In the United Kingdom, NICE makes recommendations for funding decisions in the National Health Service, whereas in the United States, ICER does not have a funding mandate and does not make formal decisions for reimbursement. Therefore, the recommendations from the 2 agencies are distinct and presented differently.

*ICER's economic evaluation was compared with lisinopril. NICE's was vs angiotensin-converting enzyme inhibitors and angiotensin receptor blockers.

†ICER's economic evaluation compared ranibizumab with grid laser therapy. NICE's evaluation provided multiple ICER's that were nondefinitive. Using the guidance from NICE, the most likely estimate is between $28 471 to $42 857/QALY vs best supportive care.

‡ICER's economic evaluation was compared with grid laser therapy. NICE'S was compared with best supportive care. The range of cost-effectiveness from NICE appraisals was dependent on the visual acuity of the subgroup.

§ICER's economic evaluation included dronedarone followed by amiodarone vs amiodarone alone, whereas NICE's evaluation was dronedarone vs sotalol, class 1a antiarrhythmics, and amiodarone.

‖ICER's economic evaluation for alirocumab with a statin was compared with a statin alone. NICE's evaluation was alirocumab, a statin, and ezetimibe vs a statin and ezetimibe (range depending on the subtype of hypercholesteremia and low-density lipoprotein cholesterol level).

¶ICER'S economic evaluation for evolocumab was with a statin compared with a statin alone. The incremental cost-effectiveness ratio was based on the net price, using the wholesale acquisition cost, the cost/QALY was $1 336 221. NICE'S evaluation was compared with ezetimibe (depending on the subtype of hypercholesteremia).

#The cost/QALY for ICER's evaluation of naltrexone and bupropion varies depending on body mass index.

which were approved in both the United States and England and evaluated as cost-effective. In contrast, both agencies had discordant recommendations for 7 drugs. For 5 drugs (dabigatran, alirocumab, evolocumab, patisiran, and inotersen), the discordance was attributed to the higher price of drugs in the United States, which resulted in higher cost/QALY evaluations. For example, both amyloidosis drugs were well above NICE's commonly accepted cost-effectiveness threshold but were accepted for coverage with price discounts because of their efficacy. Similarly, ICER concluded that both were clinically effective, but they exceeded the cost-effectiveness threshold from ICER because of their prices. For the remaining 2 drugs, both agencies were in discordance regarding the cost-effectiveness evaluations for pegaptanib (with NICE having a significantly higher estimate for cost-effectiveness) and the long-term clinical effectiveness of naltrexone/bupropion (with NICE hesitant when evaluating cost-effectiveness because of the long-term uncertainty of benefit).

Our analysis shows that only 5 cardiovascular, obesity, and diabetes mellitus drugs assessed by ICER and 8 drugs from NICE were considered cost-effective (based on the negotiated price discounts achieved by NICE), indicating that some newer drugs do not represent strong value for the money. Despite similar methodologies and results for evaluating cost-effectiveness, the high discordance for recommendations to payers on whether to include a new cardiovascular, obesity, or diabetes mellitus drug in their formularies is mostly a result of the United States' higher drug prices and thresholds for value. In England, NICE negotiated price discounts on multiple drugs to a point where they could be considered cost-effective, whereas these same drugs assessed by ICER, which has no bargaining role, were valued using a higher list or net price that firmly positioned these drugs as cost-ineffective. Comparatively, when ICER determined that a drug was cost-effective using its higher value threshold of $100K to $150K/QALY, NICE was often unable to negotiate a cost-effective price below their comparatively low threshold of £20K to £30K/QALY.

Our investigation was limited to publicly available data. Stratifying cost-effectiveness into clinical modeling for efficacy and drug prices was not possible as the former was largely redacted from NICE appraisals, while drug prices were not uniformly reported among ICER and NICE assessments. The cost/QALY estimate from NICE's appraisal documents was inclusive of confidential price discounts, whereas ICER's cost/QALY was based on an assumed net or list price. Therefore, our study will likely overestimate the difference in cost-effectiveness.

ICER's decisions are increasingly referenced by private insurers for formulary decisions[2]; however, there is an absence of a public government agency in the United States, which evaluates the cost-effectiveness of medicines for coverage within public insurance programs including Medicare and Medicaid. Integrating value-based evidence in formulary listings, such as in England, has significant potential to reduce pharmaceutical expenditure in the United States by sending price signals to the market that cardiovascular, obesity, and diabetes mellitus drugs with high prices and marginal improvements in effectiveness over current standards of care will not be covered by public insurers.

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