Methods of Incorporating Changes in Drug Price over Time into Health Economic Evaluations: A Targeted Literature Review

EE447

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INTRODUCTION

- Drug prices are innately dynamic across their life cycle: competition and loss of exclusivity, among other factors, influence drug prices
- However, conventional economic evaluation, including cost-effectiveness analysis (CEA), assumes a constant price over time, which may lead to biased estimates of a product's cost-effectiveness
- While some healthcare decision makers, including the Institute for Clinical and Economic Review, accept the use of dynamic pricing in CEA under certain circumstances, limited guidance is provided on how this should be done

OBJECTIVES

This targeted literature review aimed to identify and characterize different approaches that have been used to implement life-cycle drug pricing (LCDP) into CEAs.

METHODS

A targeted search strategy using PubMed® and a snowballing-based approach (looking at articles being cited or cited by other key papers) was conducted to identify English-language articles that explored dynamic pricing in CEAs. Relevant articles were reviewed, and their methods summarized.

Figure 1. PRISMA diagram

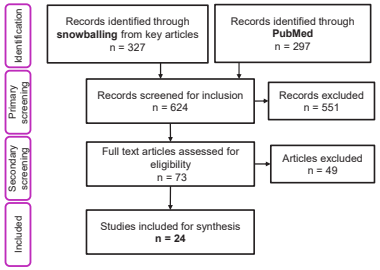


Table 1. Overview of articles reviewed

Source	Geography	Retrospective or prospective	Drug-specific or drug-agnostic	Models price trends	Adjusts price trends	Cohorts and weighting	Other novel methods
Neumann et al. 2022	WW	NA	NA	NA	NA	NA	NA
Schöttler et al. 2022	NL/ UK	Pro Retro	Spec	Reg	NA	CU	NA
Rubin et al. 2022	US	Pro	Spec	Step	NA	No	NA
van der Schans et al. 2020	NL	NA	NA	NA	NA	NA	NA
Stevens et al. 2019	US	Retro	Spec	Obs	Infl	CW	Effect
Hua et al. 2019	US	Retro	Spec	Step	Share	No	NA
Heath 2018	UK	Pro	Spec	Step	NA	No	Delay
Moreno et al. 2016	UK	Pro	Spec	Step	NA	CW	Innov
Park et al. 2016	SK	Retro	Spec	Step	NA	No	NA
Grimm et al. 2016	UK	Pro	Agn	Reg	NA	CU	Diffus Vol
Guertin et al. 2015	CAN	Pro	Spec	Step	NA	No	NA
Pistollato 2015	WW	Pro	Agn	Step	Share	No	NA
Camejo et al. 2013	UK	Retro	Spec	Obs	Infl	CW	Dyn
Camejo et al. 2012	UK	Retro	Spec	Obs	NA	CU	Dyn
Lu et al. 2012	US	Retro	Spec	Obs	Share	CW	Mult
Camejo et al. 2011	WW	NA	NA	NA	NA	NA	NA
Hoyle 2011	UK	Pro	Spec	Step	Infl	CW	NA
Grabner et al. 2011	US	Pro Retro	Spec	Obs, Step	Share	No	NA
Hoyle 2010	UK	Retro	Agn	Reg	Share	CW	NA
Ohsfeldt et al. 2010	US	Pro	Spec	Step	NA	No	NA
Garrison et al. 2009	US	Pro	Spec	NA	Share	CW	Mult
Hoyle 2008	UK	Retro	Agn	Obs, Reg	Infl, Share	No	NA
Shih et al. 2007	US	Retro	Spec	Step	NA	No	BRM
Shih et al. 2005	US	Pro	Spec	Step	NA	No	NA

Key: **Agn**, drug-agnostic; **BRM**, Bayesian regression model to incorporate price drop; CAN, Canada; **CU**, includes unweighted cohorting; **CW**, includes weighted cohorting; **Delay**, compared early vs delayed treatment; **Diffus**, model's effect of diffusion (uptake) on costs; **Dyn**, dynamic analysis (not comparing the same intervention/comparator for each cohort); **Effect**, time-varying cohort clinical effects; **Infl**, corrects for inflation; **Innov**, innovation; **Mult**, c/e across multiple indications; NA, not available; NL, Netherlands; **Obs**, observed data used; **Pro**, prospective; **Reg**, regression model; **Retro**, retrospective; **Share**, incorporating market share/volume; SK, South Korea; **Spec**, drug-specific; Step, step-wise price drop; **Vol**, value of information; WW, worldwide.

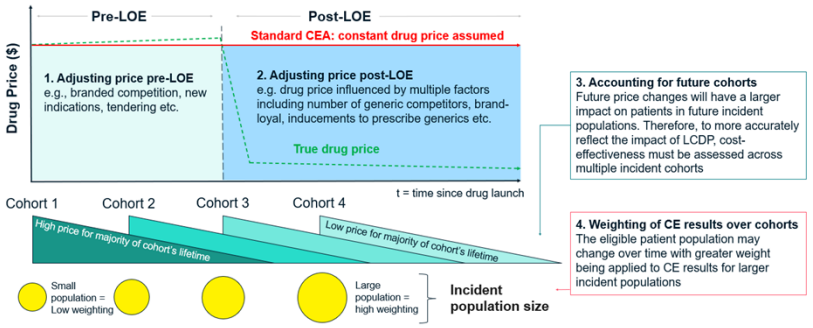
RESULTS

- 624 records were screened based on title and abstract. 73 were reviewed for eligibility, and 24 studies were included (**Figure 1**), most of which were US- or UK-focused (each 9/24)
- Of these 24 studies, 21 described the incorporation of LCDP into CEAs. These were categorized based on timing of analysis (retrospective versus prospective) and breadth of focus (technology-specific versus technology-agnostic; **Figure 2**). The remaining three articles did not contain economic evaluations but instead provided considerations for the inclusion of LCDP in CEAs
- Modeling approaches were divided into four categories: (1) methods for modeling price trends, (2) methods for adjusting price trends, (3) methods for accounting for future multiple cohorts ("cohorting"), and (4) weighting of cost-effectiveness results over time (**Table 1**; **Figure 3**)
- Price trends modeled prospectively typically included a step-wise price drop following loss of exclusivity (LOE) and regression models fitted to historical data. The most common method of adjusting price trends was via market share (present in 9/24 articles); this is where separate prices for originator and generics after LOE are accounted for, with a variable rate of generic uptake over time to account for factors such as brand loyalty
- Cohorting was implemented in less than half of the studies. For these studies, there was a lack of consensus as to whether results should be weighted based on the size of future cohorts.

Figure 2. Types of dynamic pricing CEAs described in literature

	Retrospective CEA (n = 11)	Prospective CEA (n = 12)
Technology-specific (n = 17)	Cost-effectiveness analysis based on **observed** changes in price  n = 9	Cost-effectiveness analysis based on **expected** changes in price  n = 10
Technology-agnostic (n = 4)	Theoretical framework for exploring impact of LCDP on CE in general  n = 2	Framework of LCDP in CEA to be applied to specific cases prospectively  n = 2

Figure 3. Modeling approaches captured to account for dynamic pricing in CEAs



Key: CEA, cost-effectiveness analysis; CE, cost-effectiveness; LCDP, life-cycle drug pricing; LOE, loss of exclusivity.

DISCUSSION

- Models in the literature vary in their methodology, the therapeutic areas they have been applied to, and the impact of applying LCDP. Some studies perform retrospective analysis by looking at observed changes in prices, while others use step-wise price drops after LOE or perform regression analysis to project future trends in prospective analysis
- Inclusion of LCDP is likely to reduce the incremental cost-effectiveness ratio (ICER) when the intervention is branded but comparator is generic, and increase the ICER when both the intervention and the comparator are branded drugs, but the comparator's patent expires first
- When drug costs are incurred over a longer time horizon, it is important to consider modeling multiple incident cohorts and weighting cost-effectiveness results across these cohorts based on changes in population size
- Models incorporating LCDP should use methods that are transparent, intuitive, and interpretable to aid acceptability. Modeling assumptions for factors affecting price trends (e.g. number of competitors, generic uptake over time) should be made clear
- LCDP could have a profound impact on the value assessment and consequent reimbursement decision. As such, further work is needed to reach a consensus on when LCDP should be incorporated, which methodological approaches are appropriate, and how to account for uncertainties in the data sources used for predicting future pricing trends

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An electronic version of the poster can be viewed by scanning the QR code.

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