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Using real-world evidence to inform value-based contract (VBC) design for cell and gene therapies (CGTs)

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ORIGINAL RESEARCH ARTICLE

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Using Real-World Data to Inform Value-Based Contracts for Cell and Gene Therapies in Medicaid

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Hemophilia gene therapies

- **Valoctocogene roxaparvovec (Roctavian)**
  - for severe hemophilia A in adults
  - list price $2.9 million

- **Etranacogene dezaparvovec (Hemgenix)**
  - for moderate and severe hemophilia B in adults
  - list price $3.5 million

Unique challenges in paying for cell and gene therapies (CGTs)

- Known uncertainties including cost offsets and health gains for patients on CGTs

Under-discussed sources of uncertainty for developing value-based contracts (VBCs)*

- **Identification of patients whose mean costs are representative of the SoC costs of the target group for gene therapies.**
  - How does eligibility definition affect cost projections for SoC, impacting potential cost offsets and break-even scenarios with CGTs?

- **Heterogeneity in real-world standard of care (SoC) costs:**
  - How do actual payer costs compare to the cost estimates based on recommended medication usage in clinical guidelines?

*Other terms used include outcomes-based agreements (OBAs), performance-based risk sharing agreements (PBRS), and managed entry schemes.

Case study objectives

- **Use Colorado Medicaid claims data to reveal**
  - Distribution of costs paid by Medicaid
  - Relationship between: eligibility – SoC costs – breakeven
  - Study period: 2018-2022

- **Combine data with “what-if” scenarios to inform**
  - Negotiations on contract time horizon in relation to payback amounts
  - Eligibility criteria

Prevalence of severe hemophilia without inhibitors in adults

Disease	Prevalence per 100 000 males*	Without inhibitors**	Est. patients in Colorado***
Hemophilia A	6.0	87.20%	118
Hemophilia B	1.1	90.90%	23

*Source: Iorio et al. (2019), https://doi.org/10.7326/M19-1208
** Source: Wight J, Paisley S. (2003) https://doi.org/10.1046/j.1365-2516.2003.00780.x, Male et al. (2021) https://doi.org/10.3324/haematol.2019.239160
** Based on a total adult population of 4,460,441, of which 50.7% were male in 2021. Source: State Demography Office, CO, https://demography.dola.colorado.gov/

Assumptions on eligibility

Target population for hemophilia gene therapies:

- Diagnosed adult patients on prophylactic treatments

Proxies of severity:

- Hemophilia A: ≥6 claims/year for factor VIII therapies or Emicizumab → *severe*
- Hemophilia B: ≥4 claims/year for factor IX therapies → *moderate and severe*

Additional eligibility scenarios tested:

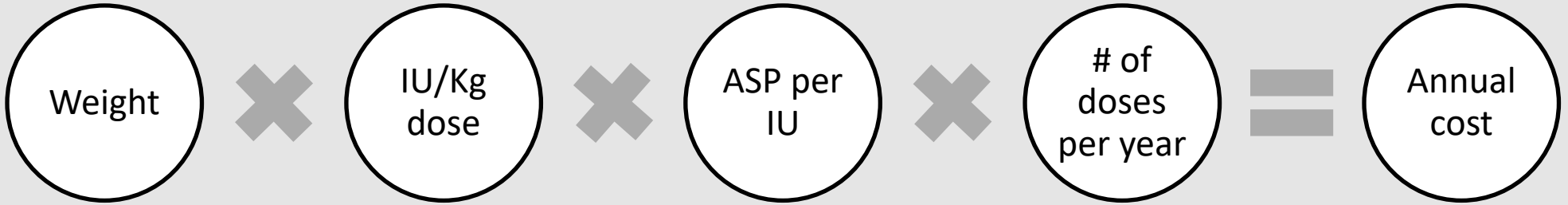
- Various scenarios explored using claim thresholds between ≥4 and ≥20 per year

Highlights of cost analysis methods applicable to RWE

- Factor claims treated as distinct if filed on different days
- Excluded zero-cost factor claims for dual-eligible Medicare-Medicaid patients
- Patients meeting criteria in a year are retained throughout observation
- Factor therapies are the focus, as they account for 95% of the total cost.
- Costs in 2022 US dollars

→Mean costs and SD were inputs in a model-based simulation over a 12-year horizon

Recent (literature-based) estimates of SoC annual costs in economic evaluation



Hemophilia A factor VIII & emicizumab market basket **~$640,000**

Hemophilia B factor IX market basket **~$690,000**

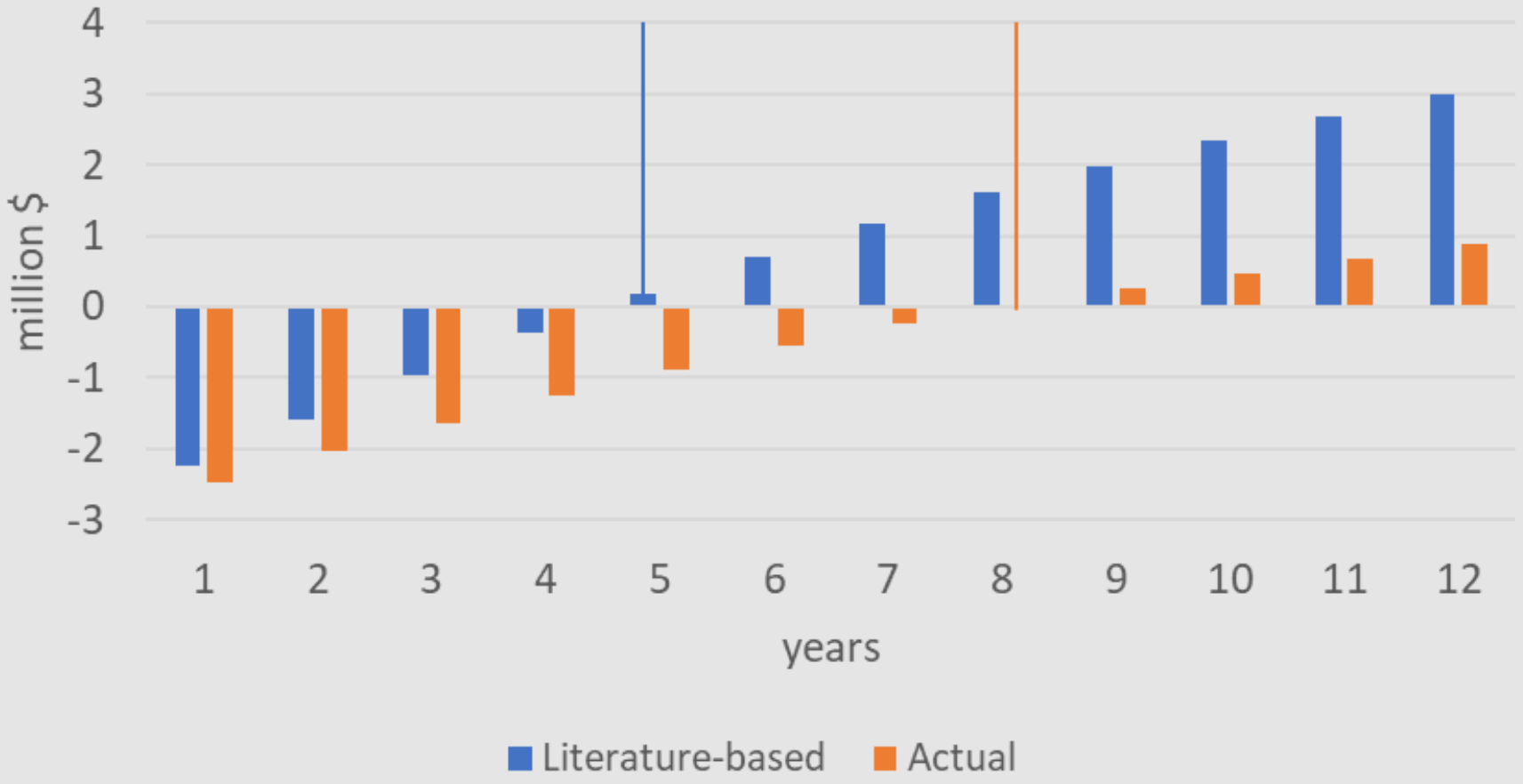
Tice JA, Walton S, Herce-Hagiwara B, Fahim SM, Moradi A, Sarker J, Chu J, Agboola F, Pearson SD, Rind DM. Gene Therapy for Hemophilia B and An Update on Gene Therapy for Hemophilia A: Effectiveness and Value; Evidence Report. Institute for Clinical and Economic Review, December 22, 2022.
https://icer.org/assessment/hemophilia-a-and-b-2022/

Actual cost of SoC

Cohort	N	Mean age (SD)	Mean annual cost (SD)
Hemophilia A			
Patients with claims	238	40.4 (16.6)	$105,000 ($246,000)
Patients with Factor VIII or Emicizumab utilization	59	34.3 (14.8)	$298,000 ($338,000)
Patients on prophylaxis (>=6 relevant claims per year)	36	30.8 (12.3)	**$426,000 ($353,000)**
Hemophilia B			
Patients with claims	54	36.8 (12.9)	$151,000 ($353,000)
Patients with Factor IX utilization	<30	33.5 (12.9)	$301,000 ($451,000)
Patients on prophylaxis (>=4 relevant claims per year)	<30	30.6 (12.8)	**$546,000 ($542,000)**

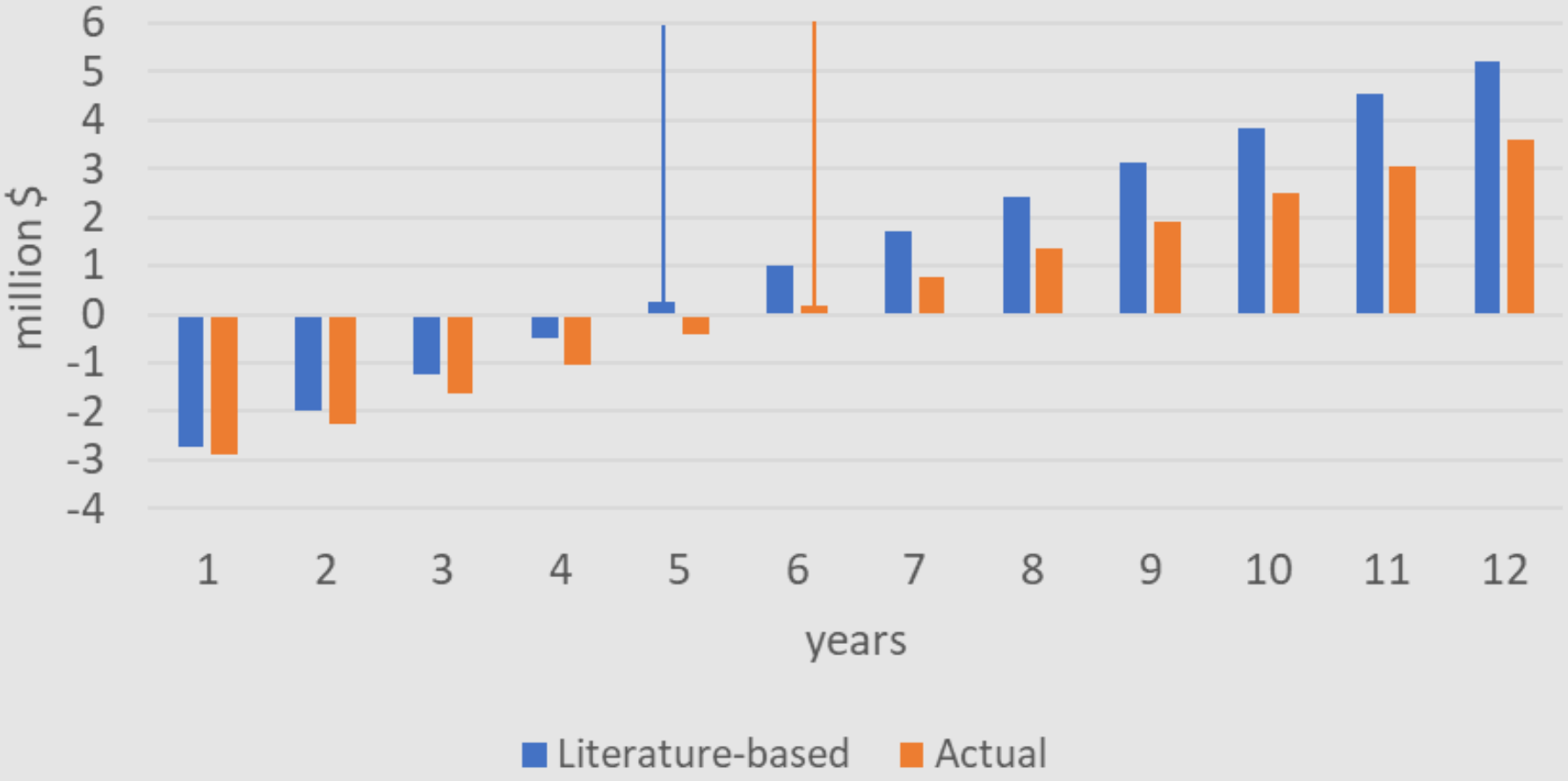
Hemophilia A: literature-based cost ($640,000) was only representative of the top 5% of all patients
Hemophilia B: literature-based cost ($690,000) was representative of the top 13% of all patients

Cumulative cost difference of Roctavian vs standard care in Hemophilia A



Break-even reached in 8 years vs. literature suggesting 4 years

Cumulative cost difference of Hemgenix vs standard care in Hemophilia B



Break-even reached in 6 years versus literature suggesting 5 years.

Variation in eligibility and financial outcomes: Hemophilia A, Roctavian

Eligibility claims per year	Reaching break-even (years)	Balance		Probability of breakeven	
		5 years	10 years	5 years	10 years
≥4	10	-$1,048,548	$187,315	18%	40%
≥5	9	-$941,415	$373,983	22%	45%
≥6 (base case)	8	-$880,280	$480,506	23%	48%
≥7	8	-$828,862	$570,098	25%	50%
≥8	7	-$663,862	$857,594	29%	55%
≥9	7	-$479,092	$1,179,540	30%	58%
≥10	6	-$371,746	$1,366,580	33%	60%
≥15	5	$204,654	$2,370,904	45%	77%
≥20	4	$1,682,565	$4,946,028	81%	97%

Variation in eligibility and financial outcomes: Hemophilia B, Hemgenix

Eligibility claims per year	Reaching break-even (years)	Balance		Probability of breakeven	
		5 years	10 years	5 years	10 years
≥4 (base case)	6	-$428,742	$2,490,018	32%	59%
≥5	6	-$428,742	$2,490,018	32%	60%
≥6	6	-$12,407	$3,299,490	38%	70%
≥7	5	$123,867	$3,564,444	42%	71%
≥8	4	$918,720	$5,109,862	57%	87%
≥9	4	$1,199,590	$5,655,952	61%	90%
≥10	4	$1,199,590	$5,655,952	60%	91%
≥15	3	$3,450,253	$10,031,870	99%	100%
≥20	3	$3,981,483	$11,064,729	100%	100%

Limitations

- Data is specific to Colorado.
- Analysis did not consider loss to follow-up.
- The number of factor claims may not accurately represent prophylactic therapy utilization

Key findings

- Actual data may yield substantially **different break-even time estimates** compared to those derived from published clinical trials and evaluations

- Estimated costs, cost-offsets, and break-even times are **contingent upon treatment eligibility criteria**, including factor utilization, which is a proxy for prophylaxis and disease severity

Key takeaways

- Incorporating real-world data into the design of VBCs for CGTs can provide Medicaid agencies with a **more accurate understanding of budget projections** for CGTs

- Inform negotiations by **trading off** higher (lower) **payback amounts** with shorter (longer) **contract durations** evaluated at varying levels of eligibility

- Leverage improves if Medicaid **negotiates as a group of states**