Fluctuation in Treatment Initiation: Increasing the Accuracy when Modeling Patient Entry in Budget Impact Analyses

Authors: Neves C[1], Bappoo Y[2], Bjerke A[3], Bruette R[3], Meng Y[4]

Affiliations: [1]Lumanity, Utrecht, The Netherlands; [2]Lumanity, London, UK; [3]Lumanity, Bethesda, MD, USA; [4]Lumanity Inc., Las Vegas, NV, USA

INTRODUCTION

Standard budget impact analyses assume annual patient entry intervals

- Budget impact (BI) projections are widely used for assessing affordability of health care interventions to support reimbursement and formulary decisions (from determining the tier [copayment and coinsurance] on a health plan's formulary to negotiating drug prices and discount rates)[1]
- While accurate estimation of the target population is key, guidance on modeling the pattern of patient entry in BI analyses is limited and it is typically assumed that the entire cohort expected to initiate treatment each year does so on January 1st
- This annual entry assumption does not capture any fluctuation throughout the year in disease incidence, screening, diagnosis and, ultimately, treatment initiation seen in real-world practice. For example, analyses of US patient registries suggest there are seasonal trends in diagnosis of acute myeloid leukemia (AML)[2], influenza[3], legionellosis[4], rotavirus[5], and several enteric diseases[6]

OBJECTIVES

Our budget impact analysis tests multiple patient entry patterns

- To explore whether accounting for fluctuations in patient entry affects BI projections
- To shed light on the use of real-word data (RWD) to inform patient entry patterns

METHODS

- We developed a model in Microsoft Excel® using dummy data to test the BI projections from January 1st in Year 1 to December 31st in Year 3 under six patient entry patterns: 1) annual entry; 2) weekly entry, even distribution; 3) weekly entry, 70% of entries in winter; 4) weekly entry, 70% of entries in spring; 5) weekly entry, 70% of entries in summer; 6) weekly entry, 70% of entries in fall
  - Winter: December–February; spring: March–May; summer: June–August; fall: September–November
- The model traces costs incurred continuously (with the Intervention, the Comparator and subsequent treatments) in weekly cycles (Figure 1 and Figure 2)
  - Constant treatment discontinuation rates, derived from the median duration of treatment (assuming an exponential distribution), are used (model inputs in Table 1 and Table 2)
- Sensitivity analyses include testing:
  - Fixed number of patients initiating treatment (150 each year)
  - Multiple starting points of the model time horizon (winter, spring, summer or fall start)

Figure 1. Patient trace

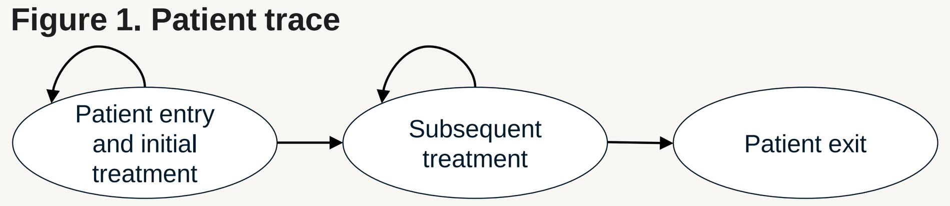


Figure 2. Analysis overview

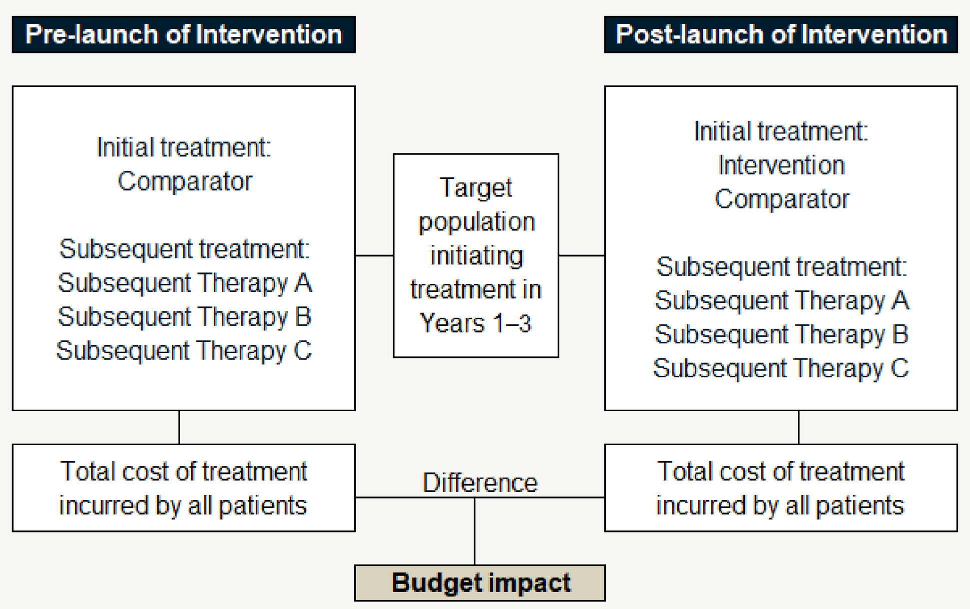


Table 1. Patient population and market shares

	Year 1	Year 2	Year 3
Patients initiating treatment	150	200	250
Market shares for patients initiating treatment each year – pre-launch of Intervention			
Comparator	100%	100%	100%
Market shares for patients initiating treatment each year – post-launch of Intervention			
Intervention	10%	30%	50%
Comparator	90%	70%	50%
Market shares for subsequent treatment on discontinuation of:		Intervention	Comparator
Subsequent Therapy A		30%	50%
Subsequent Therapy B		30%	50%
Subsequent Therapy C		40%	0%

Table 2. Treatment duration, dosing schedule and costs

Treatment	Median tx duration (weeks)	Weekly discont. prob.	Tx admin schedule	Cost of tx per admin
Intervention	60	1.15%	Q2W	$150
Comparator	40	1.72%	Q3W	$250
Subsequent Therapy A	20	3.41%	Q1W	$30
Subsequent Therapy B	30	2.28%	Q2W	$40
Subsequent Therapy C	40	1.72%	Q4W	$100

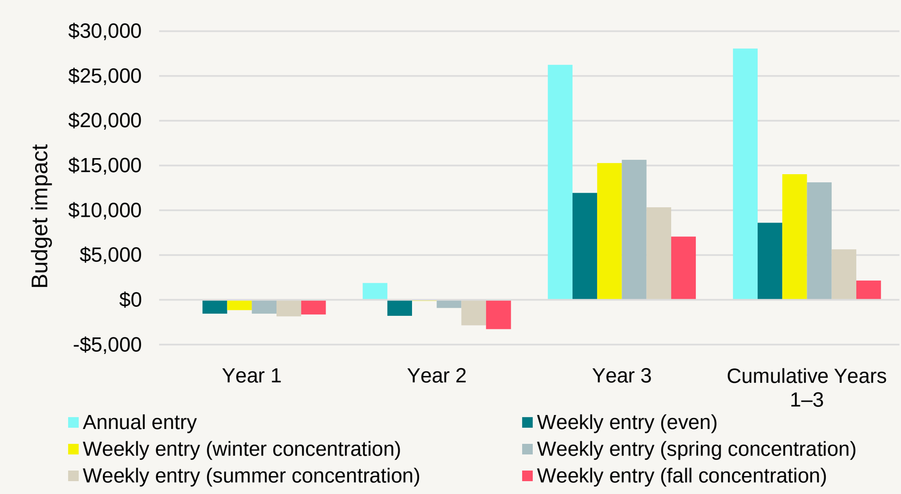
Key: admin., administration; discont., discontinuation; prob., probability; QW, once weekly, Q2W, once every two weeks; Q3W, once every three weeks; Q4W, once every four weeks; tx, treatment.

RESULTS

The budget impact varies substantially across patient entry patterns

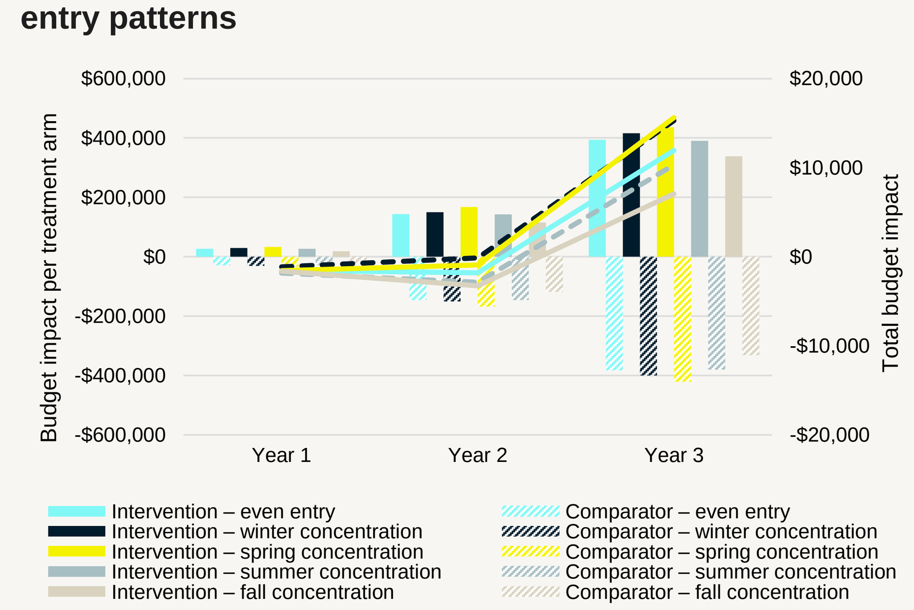
- The cumulative BI for Years 1–3 for the six patient entry patterns is: $28,045 (annual entry); $8,615 (weekly entry, even distribution); $14,018 (weekly entry, winter concentration); $13,129 (weekly entry, spring concentration); $5,627 (weekly entry, summer concentration); $2,148 (weekly entry, fall concentration)
  - The differences between annual patient entry and any of the weekly patient entry scenarios are particularly stark, with the cumulative BI being 50% to 92% lower in weekly patient entry scenarios (Figure 3). This is in line with previous research[7]

Figure 3. Overall budget impact across annual and weekly patient entry patterns



- Results also vary substantially across the weekly patient entry scenarios. The higher the concentration of entries at the start of the year, the higher the cumulative BI (the highest cumulative BI is with entries concentrated in the winter and the lowest cumulative BI is with entries concentrated in the fall). Additionally, the cumulative BI with even distribution is close to the average BI of the seasonally varied patient entry scenarios (Figure 4)

Figure 4. Detailed budget impact across weekly patient entry patterns



The budget impact is further affected by the starting point of the model time horizon

- The direction of the results is not impacted by changes in the overall target population size: the difference in cumulative BI for fixed versus increasing number of patients initiating treatment is between -$1,987 (annual entry) and $3,714 (weekly entry, fall concentration)
- The closer the starting point of the model time horizon is to the concentration of patient entry, the higher the cumulative BI. For example, for a spring start of the model time horizon, the highest cumulative BI is with entries concentrated in the spring and the lowest cumulative BI is with entries concentrated in the winter (Table 3)

Table 3. Cumulative budget impact across multiple starting points of the model time horizon

Patient entry pattern	Starting point of model time horizon				
	Winter start	Spring start	Summer start	Fall start	Jan. 1st start (base case)
Weekly entry, even	$8,615	$8,615	$8,615	$8,615	$8,615
Weekly entry, winter conc.	$19,210	$1,500	$3,388	$10,356	$14,018
Weekly entry, spring conc.	$10,311	$19,144	$1,500	$3,446	$13,129
Weekly entry, summer conc.	$3,388	$10,280	$19,144	$1,500	$5,627
Weekly entry, fall conc.	$1,500	$3,388	$10,280	$19,210	$2,148

Key: conc., concentration; Jan., January.

CONCLUSIONS

Budget impact analyses should model patient entry patterns that are reflective of the indication of interest. Additionally, the model time horizon should align with stakeholders' financial years

- The pattern of patient entry (including both length of entry intervals and seasonality) affects BI projections. Given the potential impact on reimbursement decisions and price negotiations, modeling the patient entry pattern accurately is crucial
  - Seasonal fluctuations in incidence, screening, diagnosis, and/or treatment initiation are well reported in the literature, which reveal the importance of capturing the disease-specific patient entry patterns in BI analyses
- The starting point of the model time horizon also affects BI projections when coupled with patient entries concentrated in given periods
  - We recommend that the starting point of the model time horizon is in line with the starting point of the stakeholder's financial year

REAL-WORLD DATA OPPORTUNITIES

- The expansion of access to RWD, in the form of electronic health records or medical claims data, presents opportunities to capture details along the patient journey, including the timing associated with entering the healthcare system up to the moment the patient's concerns are addressed
- We recommend using RWD to understand the cyclical patterns of treatment initiation, and, in turn, inform patient entry in BI analyses, improving the accuracy of BI projections
- Importantly, there may be more than fluctuation in diagnosis to consider when modeling patient entry – for example, delays in care from initial health care visit to treatment initiation[8]
  - The annual patient entry assumption (on January 1st each year) can be acceptable when there is a trend in RWD of high concentration of treatment initiation early in the year, as seen in AML[2] and influenza[3]
  - If no seasonal trend is known and RWD cannot be used, we recommend that BI analyses use weekly intervals, testing both even entry distribution and varied entry concentration scenarios

REFERENCES

1. Ghabri and Mauskopf. *Eur J Health Econ.* 2018; 19(2): 173-5. **2.** Calip et al. *Br J Haematol.* 2013; 160(3): 343-50. **3.** Shaman et al. *PLoS Biol*. 2010; 8(2): e1000316. **4.** Fisman et al. *J Infect Dis*. 2005; 192(12): 2066-73. **5.** Turcios et al. *Pediatr Infect Dis J.* 2006; 25(5): 451-4. **6.** Naumova et al. *Epidemiol Infect.* 2007; 135(2): 281-92. **7.** Neves et al. *Value Health*. 2022; 25(12): S134. **8.** Vidaver et al. *J Oncol Pract.* 2016; 12(6): e643-53.

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