BUDGET IMPACT ANALYSIS OF PROACTIVE THERAPEUTIC DRUG MONITORING FOR INFLAMMATORY BOWEL DISEASE PATIENTS IN THE UNITED STATES ON INFLIXIMAB THERAPY

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Background and Objective

Infliximab (IFX) efficacy for the treatment of inflammatory bowel disease (IBD), including Crohn's disease and ulcerative colitis varies amongst patients. Some do not respond to treatment, experience adverse effects or develop drug resistance, likely resulting from inadequate IFX levels. Proactive therapeutic drug monitoring (TDM) of IFX involves assessment of serum IFX concentrations, prior to loss of response, followed by regimen adjustments to achieve evidence-based IFX levels. Optimal IFX exposure can mitigate treatment failure, relapse and has been associated with improved treatment outcomes and reduced total healthcare costs.[1-3] Conversely, reactive TDM and empiric dosing involves assessment of treatment regimen *after IBD symptoms appear* followed by ad-hoc adjustments to recapture lost response.

This study aims to estimate the 2021 incremental budgetary change per member per year (PMPY), in the US, comparing proactive TDM, reactive TDM and empiric dosing approaches for IFX treated IBD patients.

Methods

A 2-year Markov model (2-week cycles), compared 3 common IFX dosing scenarios in a simulated cohort of 161,781 IFX-treated US IBD patients for 2021 (DRG, 2021).

Clinical event probabilities[1] (Fig. 1) were considered with health care resource utilization (HCRU), drug and TDM costs[2,3]. Costs were adjusted to 2021 consumer price index (Fig. 2) and clinical assumptions validated by an IBD expert.

- **Proactive TDM**: Routine monitoring strategy (2x per year)
- **Reactive TDM**: TDM prompted by disease recurrence (1x per year)
- **Empiric dosing scenario**: No TDM testing

The Markov model uses a series of equations to calculate the costs and clinical outcomes associated with each patient state per cycle.

$$[P(n+1) = P(n) \times T]$$

- $P(n)$ = Probability vector of being in each state at time n
- T = Probability of moving from one state to another
- $P(n+1)$ = Updated probability vector after one time step

For example: Cycle 1 hospitalizations are calculated by obtaining the number of patients who discontinued therapy subtracted from the total number in cycle 0, and then multiplying by the probability of hospitalization (1.5%) for cycle 1.

Iterating this equation over the 2-year follow up yielded expected cost and number of IBD related hospitalizations. (Discount rate: 3%). Simulated cohorts were distributed according to typical IFX induction and maintenance regimens (Fig. 3).

Notably, as ≈90% of IBD patients receive outpatient treatment, this assumption provides a more accurate and robust estimation of the simulation's results.

Results

Results suggest proactive TDM strategies may be associated with a 1-year average savings of $5,520 and $9,229 PMPY compared to reactive and empiric strategies, respectively (Fig. 4). Proactive TDM had higher IFX and testing costs than reactive but lower HCRU (procedures, visits, IBD-related hospitalizations). Compared to empiric, proactive TDM had higher testing costs, lower IFX costs, and significantly lower HCRU.

Conclusions

A proactive TDM strategy is associated with total cost-of-care savings of 10% and 15.6% compared to reactive TDM and empiric dosing, respectively, resulting primarily from lower IBD-related HCRU, which are expected from suboptimal dosing and subsequent disease complications. This budget impact analysis highlights the cost value of efficiently maintaining optimal IFX dosing via proactive TDM and avoiding drug waste, thereby reinforcing the importance of using the right dose for the right patient.

Fig. 1 – Probabilities[1]

	Proactive TDM		Reactive TDM		Empiric Dosing	
	Probability per year	Converted by cycle	Probability per year	Converted by cycle	Probability per year	Converted by cycle
IBD related hospitalizations	5.3%	0.2%	33%	1.5%	43%	2.1%
IBD related surgeries	3.3%	0.1%	19%	0.8%	40%	2%
Procedures	56%	3.2%	83%	6.8%	80%	6.2%
ER visits	17%	0.7%	38%	1.8%	25%	1.1%
Therapy persistence (year 1)	94%	10.8%	72%	4.9%	76%	5.5%
Therapy persistence (year 2)	89%	8.5%	65%	4.0%	61%	3.6%
	Per year per patient	Per cycle per patient	Per year per patient	Per cycle per patient	Per year per patient	Per cycle per patient
Office visits	4.2	0.16	6.6	0.25	5.28	0.20

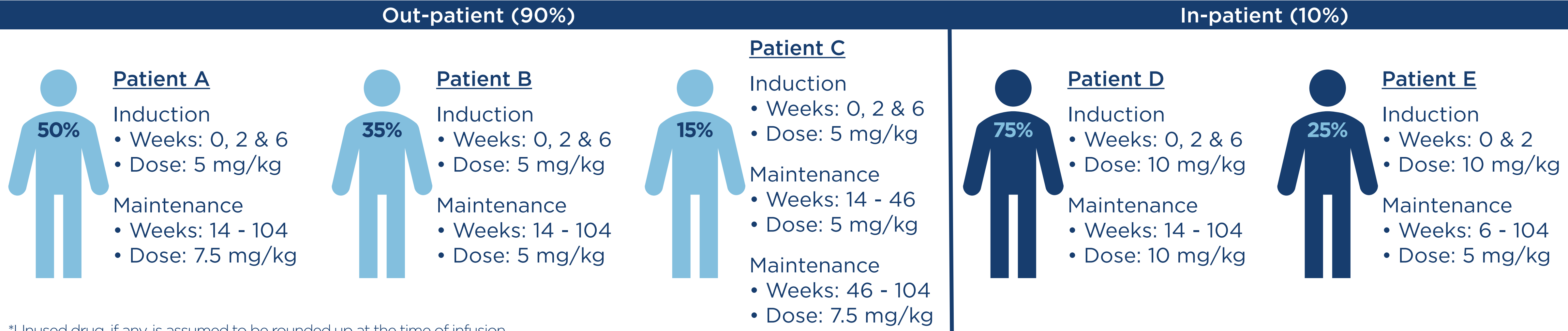Incidence rates were assumed on 100 people in one year[1]

Fig. 2 – Costs[2-4]

	Value	Year	Frequency	Adjusted Value**
IBD related hospitalizations	$12,379	2014	USD/discharge	$14,581
IBD related surgeries	$11,613	2016	One time	$13,304
ER visits*	$118	2016	One time	$135
Procedures	$1,252	2016	One time	$1,434
Blood and stool work	$70	2016	One time	$80
CT scan	$265	2016	One time	$304
Colonoscopy	$878	2016	One time	$1,006
Surgical pathology	$40	2016	One time	$45
Office visits	$55	2016	8-week period	$63
Infliximab doses	$1,021	2015	USD/vial	$1,194

*ER visit defined as the office visit (ER) plus procedures performed[5] **Costs adjusted, according corresponding year's consumer price index[5]

Fig. 4 – Per Member Per Year (PMPY) Costs

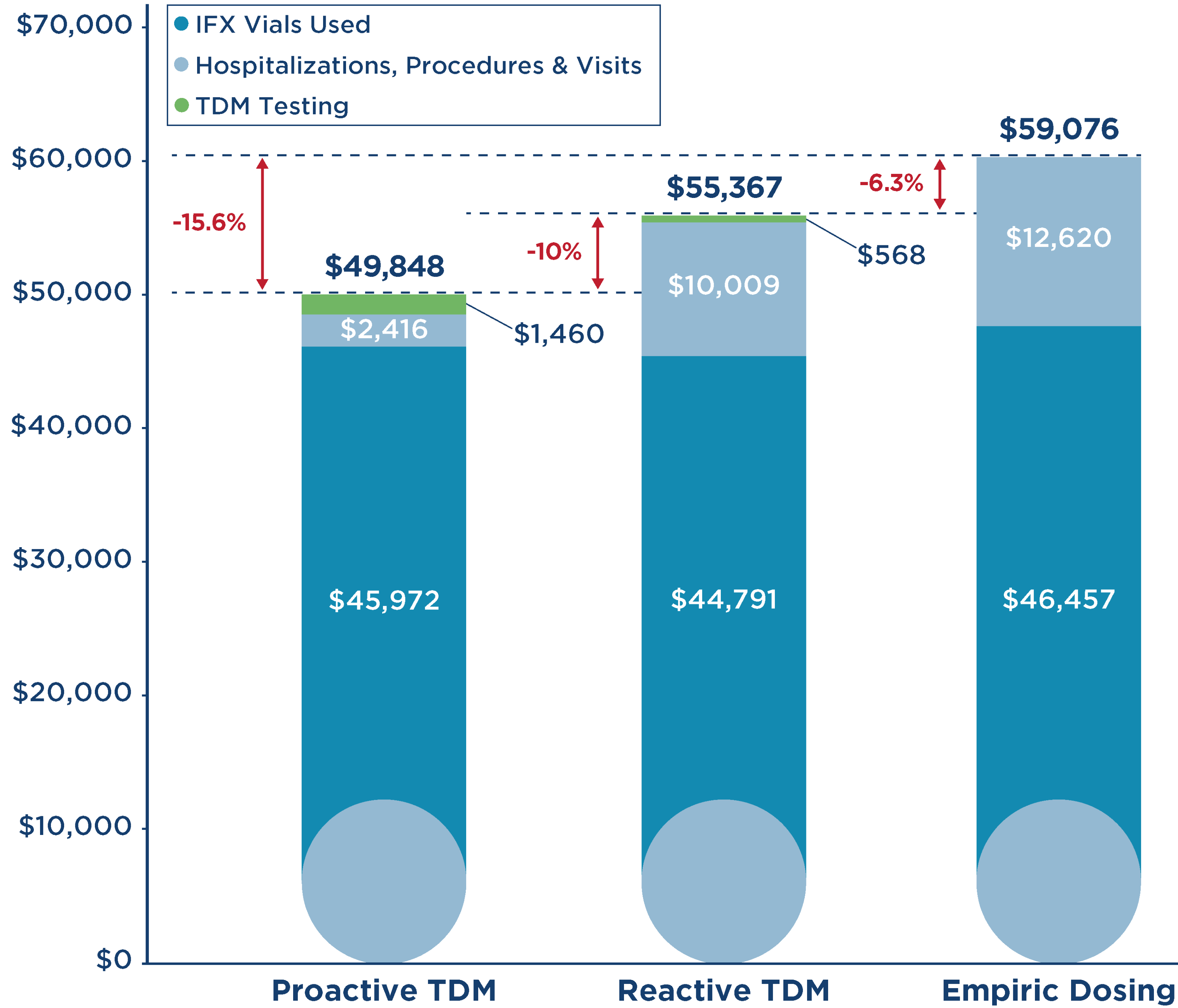|	Proactive TDM	Reactive TDM	Empiric Dosing
All HCRU	$2,416	$10,009	$12,620
IBD related hospitalizations	$726	$4,155	$5,797
IBD related surgeries	$408	$3,806	$4,960
Procedures*	$1,017	$1,708	$1,591
ER visits	$23	$46	$28
Office visits	$240	$294	$242
IFX Vials Used	$45,972	$44,791	$46,457
Successful therapy	$41,738	$32,883	$33,621
Failed Therapy	$4,234	$11,908	$12,836
Monitoring Tests	$1,460	$568	- - -
Total	**$49,848**	**$55,367**	**$59,076**
Proactive TDM PMPY Savings	- - -	**$5,520**	**$9,229**

*CT Scan, Colonoscopy, Surgical Pathology

Fig. 3 - Distribution of IFX dosed patient cohort (modeling based on clinical IBD expertise)

Out-patient (90%)

Patient A — 50%
Induction
- Weeks: 0, 2 & 6
- Dose: 5 mg/kg

Maintenance
- Weeks: 14 - 104
- Dose: 7.5 mg/kg

Patient B — 35%
Induction
- Weeks: 0, 2 & 6
- Dose: 5 mg/kg

Maintenance
- Weeks: 14 - 104
- Dose: 5 mg/kg

Patient C — 15%
Induction
- Weeks: 0, 2 & 6
- Dose: 5 mg/kg

Maintenance
- Weeks: 14 - 46
- Dose: 5 mg/kg

Maintenance
- Weeks: 46 - 104
- Dose: 7.5 mg/kg

In-patient (10%)

Patient D — 75%
Induction
- Weeks: 0, 2 & 6
- Dose: 10 mg/kg

Maintenance
- Weeks: 14 - 104
- Dose: 10 mg/kg

Patient E — 25%
Induction
- Weeks: 0 & 2
- Dose: 10 mg/kg

Maintenance
- Weeks: 6 - 104
- Dose: 5 mg/kg

*Unused drug, if any, is assumed to be rounded up at the time of infusion

Per Member Per Year (PMPY) Costs

Legend:
- IFX Vials Used
- Hospitalizations, Procedures & Visits
- TDM Testing

Proactive TDM: $49,848 (TDM Testing $2,416 / $1,460; Hospitalizations, Procedures & Visits; IFX Vials Used $45,972)
-15.6%
-10%
Reactive TDM: $55,367 ($10,009; $568; IFX Vials Used $44,791)
-6.3%
Empiric Dosing: $59,076 ($12,620; IFX Vials Used $46,457)

References: 1. Syed et al. *Crohns Colitis 360*. 2020; 2:otaa050. **2.** Afzali et al. *J Med Econ*. 2017; 20:409-422. **3.** Negoescu et al. *Inflamm Bowel Dis*. 2020; 26:103-111. **4.** Xu et al. *Appl Health Econ Health Policy*. 2019; 17:77-91. **5.** U.S. Bureau of Labor Statistics, Consumer Price Index Historical Tables for U.S. City Average. https://bit.ly/3KW5gRE