

Objective

To utilize real-world effectiveness and cost data to assess the progression and cost-effectiveness of Ustekinumab-based therapies (UST group) compared to existing non-biologic therapies (conventional group) in the context of disease advancement

Methodology

Model design

- All patients were assumed to begin in the state of induction therapy and the starting age of the patient cohort was set at 36 years, which was aligned with the real-world cohort data. After receiving induction therapy, patients would enter a state of disease remission or active disease. Patients who were in the state of disease remission may continue to receive maintenance therapy, moved into the active disease state or death. After entering the active disease state, patients may enter into the next round of induction therapy or death, and a few patients may experience surgery, entering the post-surgery treatment cycle.

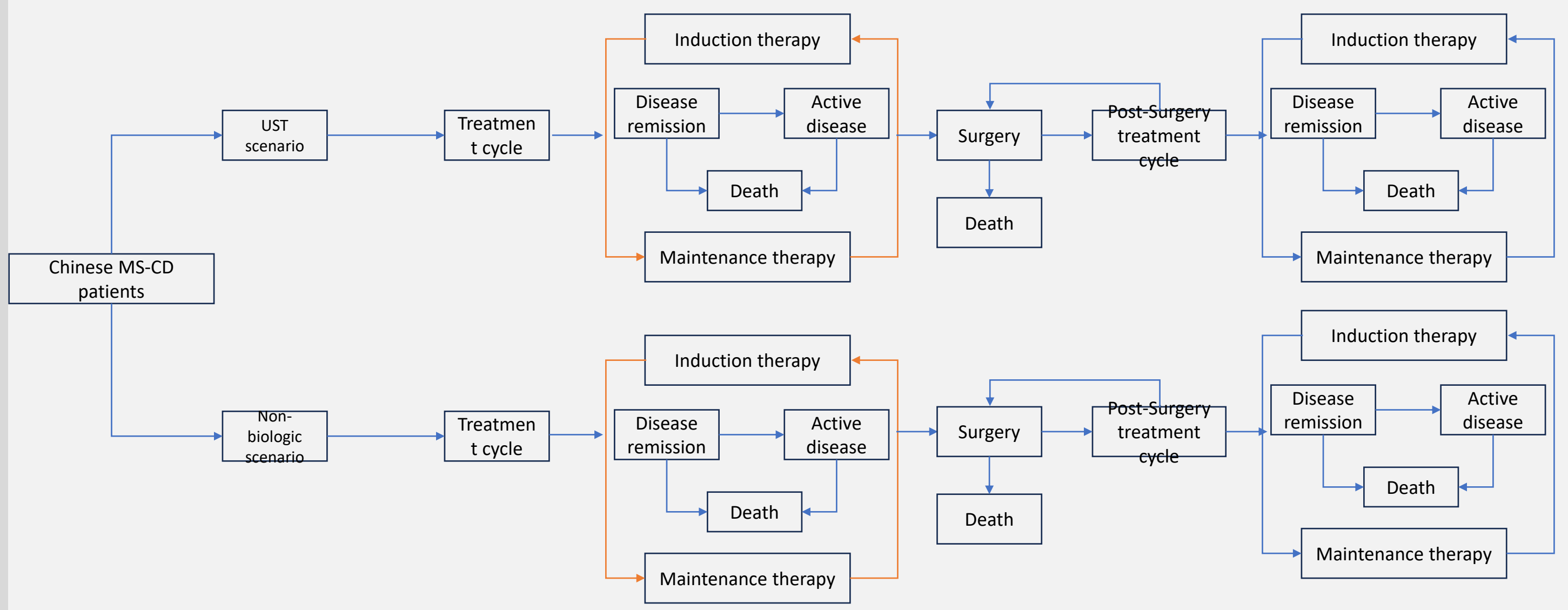


Figure 1 A: Markov Model for Crohn's disease

Real world data

- We extracted comprehensive baseline data on MS-CD patients, along with medication follow-up records spanning from 2020 to 2022 from the hospital’s Crohn’s disease registry, which was put into operation since 2010. Demographic details include age, gender, race, marital status, lifestyle habits (smoking and drinking), disease location, family history of inflammatory bowel disease (IBD), prior Crohn’s disease-related surgeries, and existing comorbidities.

- We systematically collected and analyzed medical resource utilization data for patients. We use the patient's first complete inpatient or outpatient record at the facility as the index date to collect information about the patient's costs in the coming year. This data encompassed outpatient visits, hospital admissions, and the length of hospital stays. Additionally, we examined direct medical costs, which included expenses related to medications, administrative fees for hospitalizations and outpatient visits, as well as treatment costs incurred during surgical procedures for the patients.

Table 1. one-year health resource utilization

Outcome measure	UST, n = 133		Non-biologic, n = 133		P value
	Mean/%	SD	Mean/%	SD	
Clinical outcomes					
Surgery rate	18.5%		36.1%		0.001
Disease remission rate	56.1%		44.1%		0.043
Health resource utilization					
Outpatient clinic visits	8.32	7.22	4.76	4.42	P<0.001
Outpatient injections of ustekinumab frequency	1.21	1.95			
Hospital admissions	3.55	2.03	1.52	1.01	P<0.001
Hospital stay days	3.20	2.15	7.42	3.14	P<0.001
Total outpatient costs	120	137	179	239	P<0.001
Direct medical costs for hospitalizations					
Hospital costs related to administration	3195	4991	9459	8309	P<0.001
Drug acquisition costs	4460	3151	3994	4986	0.375
Total Hospital costs	7656	7086	13454	12891	P<0.001
Annual Outpatient Total Cost	879	1137	655	949	1
	8877	14294			0.086
Annual drug costs for hospitalization	15067	13861	7045	10469	P<0.001
Annual administration costs for hospitalization	9107	11413	14888	16829	1
Annual Inpatient Total Cost	24174	20962	21933	26324	0.002
Total Direct Medical Expenses	33930		22588		0.454

- Utility values include preoperative relief phase, utility values during active phases, and utility values during postoperative relief and active phases. Patient utility values were derived from our previous research conducted at the same hospital[9].

Table 2. Utility value from previous reserach

Phase	Utility Value
UST group	
Disease remission before surgery	0.917
Active disease before surgery	0.885
Disease remission before surgery	0.872
Active disease before surgery	0.680
Non-biologic	
Disease remission before surgery	0.795
Active disease before surgery	9.771
Disease remission before surgery	0.767
Active disease before surgery	0.682

Results

The Ustekinumab group incurred an incremental cost of 55,848 RMB and gained an additional 1.47 QALYs. The incremental cost-effectiveness ratio (ICER) was 38,011 RMB per QALY, which is below the one-time per capita GDP of China in 2022. The probability that UST is cost-effective across increasing willingness-to-pay (WTP) thresholds per QALY gained. The results showed that, compared with Non-biologic group, the likelihood of UST being cost-effective was 98.51% using 1 times per capita GDP of China as the cost-effectiveness threshold (Figure 2).

Table 3. Base case results (cost: CNY, utility: QALY)

Regimen	Total cost	Incremental cost	Total QALYs	Incremental QALYs	ICER
Non-biologic	¥253,301	-	7.78	-	-
UST	¥197,453	¥55,848	9.25	1.47	38,011

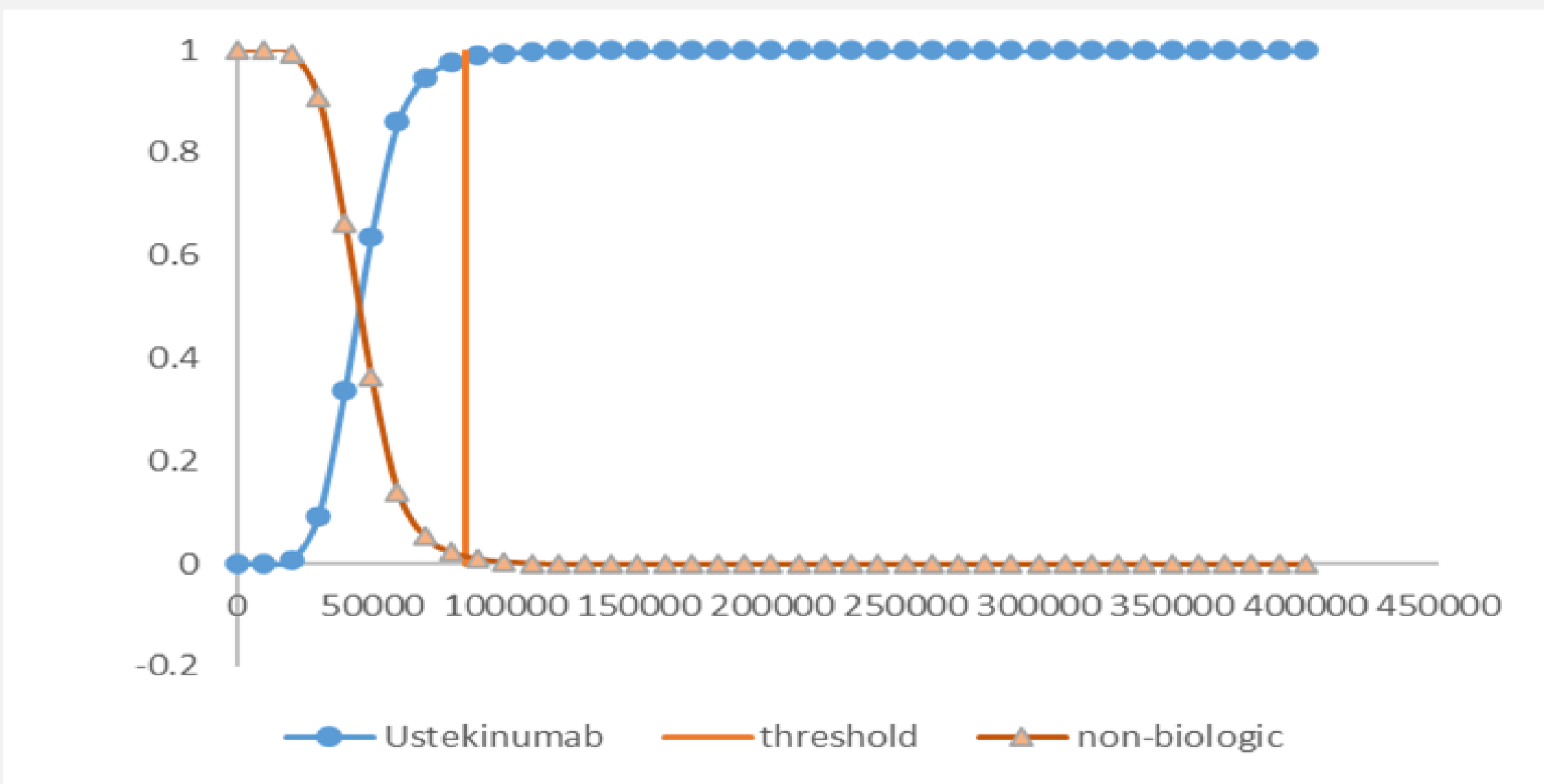


Figure 2. Cost-effectiveness acceptability curves for UST versus Non-biologic

Conclusion

UST significantly improved real-world health outcomes at a cost to the Chinese public healthcare system of less than one-time 2022 Chinese GDP per capita per QALY gained in Chinese MS-CD patients.

References

[1].Feuerstein JD, Cheifetz AS. Crohn Disease: Epidemiology, Diagnosis, and Management. Mayo Clin Proc. 2017;92(7):1088-1103.
[2].Ananthakrishnan AN, Kaplan GG, Ng SC. Changing Global Epidemiology of Inflammatory Bowel Diseases: Sustaining Health Care Delivery Into the 21st Century. Clin Gastroenterol Hepatol. 2020;18(6):1252-1260.
[3].APDW2004 Chinese IBD Working Group. Retrospective analysis of 515 cases of Crohn's disease hospitalization in China: nationwide study from 1990 to 2003. J Gastroenterol Hepatol. 2006;21(6):1009-1015.
[4].Chow DK, Leong RW, Lai LH, et al. Changes in Crohn's disease phenotype over time in the Chinese population: validation of the Montreal classification system. Inflamm Bowel Dis. 2008;14(4):536-541.
[5].Ananthakrishnan AN, Kaplan GG, Ng SC. Changing Global Epidemiology of Inflammatory Bowel Diseases: Sustaining Health Care Delivery Into the 21st Century. Clin Gastroenterol Hepatol. 2020;18(6):1252-1260.
[6].Feuerstein JD, Cheifetz AS. Crohn Disease: Epidemiology, Diagnosis, and Management. Mayo Clin Proc. 2017;92(7):1088-1103.
[7].Shao B, Yang W, Cao Q. Corrigendum: Landscape and predictions of inflammatory bowel disease in China: China will enter the Compounding Prevalence stage around 2030. Front Public Health. 2022;10:1083211.
[8].Feagan BG, Sandborn WJ, Gasink C, et al. Ustekinumab as Induction and Maintenance Therapy for Crohn's Disease. N Engl J Med. 2016;375(20):1946-1960.
[9].Shi JH, Luo L, Chen XL, et al. Real-world cost-effectiveness associated with infliximab maintenance therapy for moderate to severe Crohn's disease in China. World J Gastroenterol. 2020;26(41):6455-6474.
[10].Ashton LJ, Gavin J, Beattie RM. Exclusive enteral nutrition in Crohn's disease: Evidence and practicalities. Clin Nutr. 2019;38(1):80-89.
[11].Di Caro S, Fragkos KC, Keetart K, et al. Enteral Nutrition in Adult Crohn's Disease: Toward a Paradigm Shift. Nutrients. 2019;11(9):2222.
[12].Dray X, Marteau P. The use of enteral nutrition in the management of Crohn's disease in adults. JPN J Parenter Enteral Nutr. 2005;29(4 Suppl):S166-S188.
[13].Day A, Wood J, Melton S, Bryant RV. Exclusive enteral nutrition: An optimal care pathway for use in adult patients with active Crohn's disease. JGH Open. 2019 Sep 10;4(2):260-266.
[14].Gomollon F, Dignass A, Annese V, et al. 3rd European Evidence-based Consensus on the Diagnosis and Management of Crohn's Disease 2016: Part 1: Diagnosis and Medical Management. J Crohns Colitis. 2017;11(1):3-25.
[15].Inflammatory Bowel Disease Group, Chinese Society of Gastroenterology, Chinese Medical Association. Chinese consensus on diagnosis and treatment in inflammatory bowel disease (2018, Beijing). J Dig Dis. 2021;22(6):298-317.
[16].Sands BE, Sandborn WJ, Panaccione R, et al. Ustekinumab as Induction and Maintenance Therapy for Ulcerative Colitis. N Engl J Med. 2019;381(13):1201-1214.
[17].Hanauer SB, Sandborn WJ, Feagan BG, et al. IM-UNITI: Three-year Efficacy, Safety, and Immunogenicity of Ustekinumab Treatment of Crohn's Disease. J Crohns Colitis. 2020;14(1):23-32.
[18].Sandborn WJ, Rebuck R, Wang Y, et al. Five-Year Efficacy and Safety of Ustekinumab Treatment in Crohn's Disease: The IM-UNITI Trial. Clin Gastroenterol Hepatol. 2022;20(3):578-590.e4.
[19].Singh S, George J, Boland BS, Vande Castele N, Sandborn WJ. Primary Non-Response to Tumor Necrosis Factor Antagonists is Associated with Inferior Response to Second-line Biologics in Patients with Inflammatory Bowel Diseases: A Systematic Review and Meta-analysis. J Crohns Colitis. 2018;12(6):635-643.
[20].Casanova MJ, Chaparro M, Minguez M, et al. Effectiveness and Safety of the Sequential Use of a Second and Third Anti-TNF Agent in Patients With Inflammatory Bowel Disease: Results From the Eneida Registry. Inflamm Bowel Dis. 2020;26(4):606-616.
[21].Miao Y, Gu J, Zhang L, He R, Sandeep S, Wu J. Improving the performance of social health insurance system through increasing outpatient expenditure reimbursement ratio: a quasi-experimental evaluation study from rural China. Int J Equity Health. 2018;17(1):89. Published 2018 Jun 25.