



# Role of 5-aminosalicylic acid in ulcerative colitis management in 8 Asian territories: a physician survey

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Clinical guidelines typically endorse conventional therapies such as 5-aminosalicylic acid (5-ASA) as the mainstay of ulcerative colitis management. However, the degree of adoption and application of guideline recommendations by physicians within Asia remains unclear. This study aims to understand the prescribing patterns of 5-ASA and implementation of current guideline recommendations across Asian clinical practice. A physician survey was conducted among inflammatory bowel disease specialists in 8 Asian territories to understand practices and preferences in ulcerative colitis management, focusing on the use of 5-ASA and concordance with guideline recommendations. Survey findings were validated by country experts in diverse healthcare settings. Subgroup analyses stratified data by income levels and treatment reimbursement status. Ninety-eight valid responses were received from inflammatory bowel disease specialists or gastroenterologists among 8 economic entities. Significant differences were found in clinical practices and treatment preferences for ulcerative colitis management among different income-level and government-subsidy groups. Survey results are summarized in 8 findings that illustrate trends in 5-ASA use and guideline implementation across Asian territories. This study emphasizes socioeconomic factors that impact the adoption of guideline recommendations in real-world practice. Our findings indicate an eclectic approach to guideline implementation across Asia, based on resource availability and feasibility of treatment goals. (**Intest Res 2025;23:117-128**)

**Key Words:** Ulcerative colitis; Guidelines; 5-Aminosalicylates; Mesalamine; Inflammatory bowel diseases

## INTRODUCTION

Ulcerative colitis (UC) is a form of inflammatory bowel dis-

ease (IBD) characterized by chronic inflammation of the colon. The site of disease usually begins from the rectum and extends to more proximal parts of the colon as the disease progresses. Treatment for UC usually comprises anti-inflammatory medications including 5-aminosalicylic acid (5-ASA; also known as mesalazine or mesalamine), corticosteroids, immunomodulators, and biologics, depending on the extent and severity of the disease. 5-ASA remains the cornerstone therapy

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for both active and quiescent diseases, particularly for mild-to-moderate disease.<sup>1-5</sup>

In mild-to-moderate UC, locally acting 5-ASA is recommended as first-line therapy.<sup>1-4</sup> 5-ASA of various formulations via the oral or rectal route may be used to facilitate efficient drug delivery and therefore, effective disease control.<sup>6</sup> For induction of remission, a once-daily dose of higher than 3 g/day is usually recommended<sup>7</sup>; for maintenance of remission, a lower dose—no more than 2 g once daily—may be considered sufficient.<sup>5</sup> While continuous use of 5-ASA in UC patients at any stage is strongly recommended for sustained disease control, with minimal adverse effects observed in the long-term,<sup>5</sup> physician prescribing habits, patient preferences, medication adherence, and healthcare resources, especially treatment costs, all play crucial roles in decision-making in disease management. Real-world data, however, suggest that adherence to oral 5-ASA is low, greatly increasing the risk of relapse,<sup>8</sup> while rectal formulations are underused for patients owing to perceived inconvenience.<sup>9</sup>

In 2015, the concept of treat-to-target (T2T) was first introduced into IBD care by the International Organization for the Study of Inflammatory Bowel Diseases.<sup>10</sup> The group later published the Selecting Therapeutic Targets in Inflammatory Bowel Disease (STRIDE) II guidelines<sup>11</sup> and identified clinical remission as the short-term target for UC patients; clinical response, normalization of C-reactive protein (CRP)/erythrocyte sedimentation rate, and normalization of fecal calprotectin (FC) level as the intermediate treatment targets; and endoscopic healing and quality of life as the long-term treatment goals. Superior disease outcomes have been associated with achieving the nominated targets.<sup>11</sup> However, clinical uptake of the T2T approach remains a challenge, with limited adoption observed in practice.<sup>12</sup>

As UC incidence rates rise sharply in Asia,<sup>1</sup> it becomes imperative that disease management in practice is optimized in alignment with current guidelines in effort to slow disease progression, reduce morbidity, and minimize cost burden. Healthcare resources such as access to diagnostic testing and treatment, as well as the ability to pay for medications and essential procedures in IBD care (e.g., colonoscopy and lab tests), vary considerably across the region. Data on 5-ASA prescribing patterns for UC in Asia are scarce, and it remains unclear as to what extent the T2T concept is embraced by Asian IBD specialists. This study aims to understand the way in which 5-ASA is used to manage UC patients within clinical practices across Asia, and identify barriers and possible facili-

tators to guideline implementation. Although physicians have been previously surveyed to determine trends in IBD care across Asia,<sup>13</sup> to our knowledge this is the first survey among IBD specialists and/or gastroenterologists in Asia to ascertain practice patterns for UC management specifically, and to explore the impact of economic burden on treatment strategies, especially in chronic disease management.

## METHODS

### 1. Study Design

For this descriptive analysis, we developed a questionnaire that consists of 12 questions to poll gastroenterologists from 8 economic entities in Asia (Hong Kong, Indonesia, Malaysia, the Philippines, Singapore, Taiwan, Thailand, and Vietnam) on management approaches and prescription preferences when treating UC. Input from regional experts in UC management was sought during survey piloting. We performed snowball sampling owing to its practicality: The online questionnaire was distributed to 12 local experts in the 8 economies, who in turn circulated the survey among local teams or communities of gastroenterologists that are involved in UC management. Polling results were collected between June and August 2021, and then presented during 2 expert sessions where 11 experts discussed, elaborated and validated the findings on T2T adoption.

### 2. Statistical Analysis

Questionnaire responses that provided answers to at least 1 of the 12 survey questions were included for analysis. Survey data were summarized using percentages, and weighted scores were used for ranking treatment goals. The chi-square or Fisher exact test were used to assess intergroup differences, where *P*-values of less than 0.05 were indicative of statistical significance. Microsoft Excel (Microsoft Corp., Redmond, WA, USA) and RStudio (version 1.4.1717; RStudio, Boston, MA, USA) were used to perform data analyses.

### 3. Subgroup Analysis

To evaluate the impact of gross domestic production per capita and the reimbursement statuses of treatment options on disease management strategies, we conducted 2 sets of subgroup analyses. The 8 economic entities were first categorized by income groups as assigned by the World Bank in 2021,<sup>14</sup> where the survey was conducted: the high-income group (Hong Kong, Singapore, and Taiwan), the upper-middle-income group (Malaysia and Thailand), and the lower-middle-income group (In-

donesia, the Philippines, and Vietnam) (Table 1). Next, we stratified the 8 economies by reimbursement statuses of relevant treatment options at the time of the survey (Table 2).

SURVEY FINDINGS AND DISCUSSION

1. Survey Participants

There were 98 valid responses to the survey: 41 from the high-income group (Hong Kong, Singapore, and Taiwan), 22 from the upper-middle-income group (Malaysia and Thailand), and 31 from the lower-middle-income group (Indonesia, the Philippines, and Vietnam). Among the 98 responses, 4 entries did not answer the question on “country of practice” and were excluded from the subgroup analyses.

2. Treatment Strategies in UC Management

**Finding 1**  
Sustainable symptom control with affordable solutions is the most preferred treatment goal in UC patients.

Among all 6 T2T approach treatment goals suggested in STRIDE II,<sup>11</sup> IBD experts in Asia opined that “sustainable symptom control with affordable solutions” was the most important for UC patients (n = 72, 77%) (Fig. 1). Good quality-of-life (n = 65, 70%) and avoidance of long-term use of systemic steroids (n = 63, 68%) are also highly regarded goals by over two-thirds of polled clinicians. Only one-third of participating gastroenterologists considered “rapid symptom control, even with short-term biologics” an important treatment goal (n = 35, 38%), and the fewest number of votes was for long-term cost saving (n = 24, 26%). The results underscore that long-term sustainable chronic disease management is prioritized over instant symptom relief in IBD patient care.

The survey also revealed the impact of treatment costs on clinical outcomes. In the subgroup analysis, trends for “sustainable symptom control with affordable solutions,” “good quality-of-life,” and “rapid symptom control, even with short-term biologics” were comparable across all income groups ( $P = 0.774$ ,  $P = 0.962$ , and  $P = 0.916$ , respectively), but illustrated a diverging pattern among other treatment goals. On one

Table 1. Income Levels of the 8 Economic Entities Surveyed

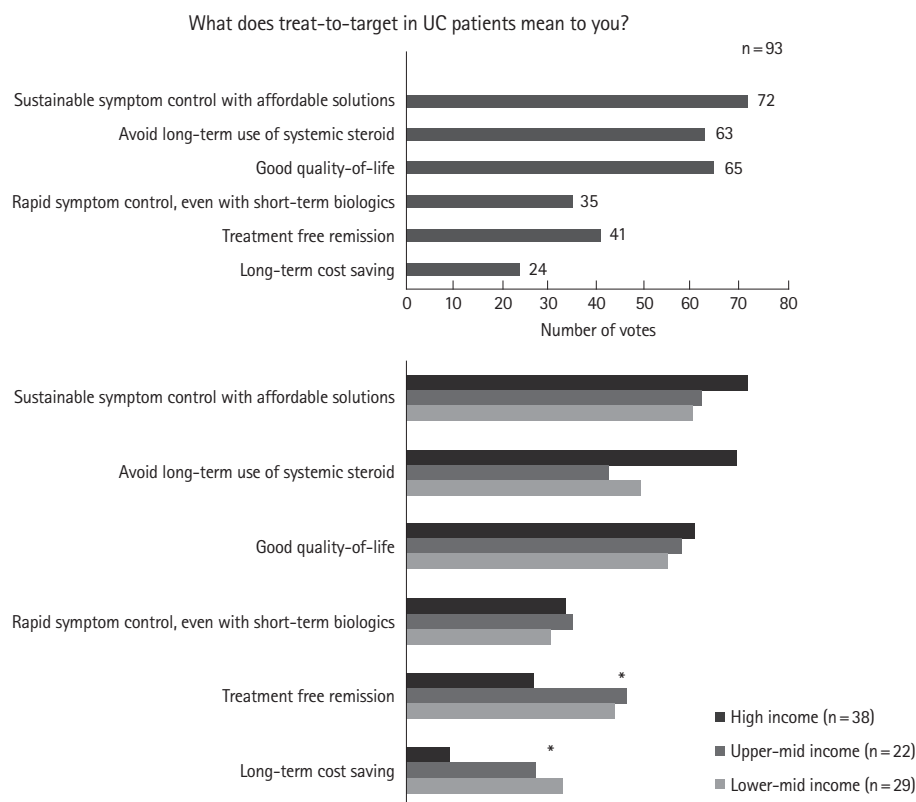
Income level <sup>15</sup>	GDP per capita (USD), 2024
High income	Singapore (88,450), Hong Kong (53,610), Taiwan (34,430)
Upper-middle income	Malaysia (13,310), Thailand (7,810)
Lower-middle income	Indonesia (5,270), Vietnam (4,620), Philippines (4,130)

GDP, gross domestic product; USD, United States dollar.

Table 2. Reimbursement Status of Inflammatory Bowel Disease Treatment Options in August 2021

Variable		Hong Kong	Taiwan	Singapore	Thailand	Malaysia	Philippines	Vietnam	Indonesia
Oral 5-ASA	pH dependent	R	R	R	R	R	R	R	R
	Time dependent	R	R	R	R	R	NR	R	NR
	MMX	R	R	NR	R	NR	NA	NA	NA
Rectal 5-ASA	5-ASA suppository	R	R	R	R	R	NR	R	NR
	5-ASA enema	R	R	R	R	R	NR	R	NR
Steroid	Systemic	R	R	R	R	R	NR	R	NR
	Topical	R	R	NR	NR	NR	NR	NA	NR
Immunomodulators		R	R	R	R	NR	NR	R	NR
Advanced therapies		R	R	R	NR	R	NR	R	NR
Medical consultation		R	R	R	R	R	R	R	R
Colonoscopy and histopathological exams		R	R	R	R	R	R	R	R
Surrogate markers	FC test	NR	NR	NR	NR	NR	NR	NR	NR
	CRP	R	R	R	R	R	R	R	R

5-ASA, 5-aminosalicylic acid; MMX, multi-matrix system; FC, fecal calprotectin; CRP, C-reactive protein test; R, reimbursed; NR, not reimbursed; NA, not available.



**Fig. 1.** Preferred treat-to-target approach treatment goals for ulcerative colitis (UC) patients. (A) Total votes of all surveyed participants. (B) Votes of survey participants from income-level subgroups, standardized against total votes from within the subgroup. \* $P < 0.05$ .

hand, achieving “treatment free remission” and “long-term cost saving” appeared to be significantly more important for clinicians from upper- and lower-middle-income countries than for those from high-income countries ( $P = 0.037$  and  $P = 0.007$ , respectively). On the other hand, clinicians in Hong Kong and Taiwan, where topical steroid (budesonide MMX) is reimbursed, are significantly more likely to “avoid long-term use of systemic steroid” (which is cheaper than topical steroids) than those clinicians in the 6 other countries ( $P = 0.003$ ).

Our survey finding emphasizes the importance of long-term treatment-cost considerations, even in Singapore. Effective implementation of the T2T strategy might be compromised if the treatment options were to impose considerable financial burdens on the payers.

### Finding 2

Endoscopic findings are the most indicative when adjusting treatment in UC patients.

Participating gastroenterologists ranked the importance of 5 clinical reports commonly used in disease assessment in con-

sideration of medication adjustment for UC patients, including endoscopic findings, clinical symptoms, FC level, histopathological report, and CRP level (Supplementary Fig. 1). We found the most indicative measures of management effectiveness to be endoscopic findings and clinical symptoms. This finding validates the accessibility of reimbursed colonoscopies and medical consultations.

Across all polled economies is an increasing trend to take reference from FC instead of CRP level as biomarker for disease-activity monitoring. CRP is not specific to IBD<sup>16</sup> and less sensitive to inflammatory activity than FC.<sup>17</sup> Therefore, the FC test is becoming the preferred option where it is available or reimbursed.

Histological remission, though difficult to achieve in clinical practice, has been shown to improve long-term outcomes, including sustained remission and reduced colorectal cancer.<sup>11</sup> It has been proposed to be the ultimate endpoint when considering treatment de-escalation or cessation. Nevertheless, together with CRP level, histological reports of intestinal biopsies were the 2 least referred to considerations when adjusting management plans for UC patients. This finding corroborates

the recent STRIDE II consensus,<sup>11</sup> where histological healing is positioned as a supplementary long-term treatment target. Our survey reveals a diverse picture among income groups, where the lower-middle-income group clinicians rely more on histopathological reports than biomarkers when compared with their peers in the other 2 groups. This finding may reflect limited accessibility of FC tests in lower-middle-income countries, rendering invasive examinations indispensable in disease-activity monitoring.

### 3. Role of 5-ASA in UC Management

#### Finding 3

5-ASA suppository is preferred for treating proctitis.

Proctitis is considered the most common phenotype of UC. In patients with mild-to-moderate proctitis, rectal 5-ASA is recommended by multiple clinical guidelines.<sup>1,2,4</sup> A Cochrane analysis of 38 studies concluded that rectal 5-ASA should be considered as the first-line therapy for patients with mild-to-moderate active distal UC.<sup>18</sup>

Our survey results (Supplementary Fig. 2) are consistent with guideline recommendations: Most gastroenterologists prefer rectal 5-ASA monotherapy, more often with a 5-ASA suppository ( $n=53$ , 60.2%) than with a 5-ASA enema ( $n=10$ , 11.4%). Approximately 20% of physicians ( $n=18$ ), most of whom were from the high-income group, stated their preference for a combined oral and rectal therapy for proctitis.

In real-world practice, however, physicians often encounter patient reluctance in relation to the use of rectal drugs, owing to inconvenience or hygiene reasons. The expert panel discussed the use of an oral 5-ASA multi-matrix system (MMX) as an alternative, which allows distal drug release; however, evidence supporting its use in proctitis is lacking.

#### Finding 4

Oral high-dose 5-ASA should be higher than 3 g per day.

In mild-to-moderate UC management, 5-ASA remains the mainstay of treatment. Meta-analysis shows that standard doses (2–3 g) and high doses (>3 g) are significantly better than low doses (<2 g) for inducing remission in mild-to-moderate UC, and high-dose 5-ASA may be superior to the standard dose in moderately severe disease.<sup>19</sup>

We asked gastroenterologists to identify “high dose” in our survey, and most ( $n=87$ , 90%) agreed that when using oral

5-ASA to induce remission in UC patients, a >3 g per day “high-dose” should be given (Supplementary Fig. 3). Notably, 60%–70% of respondents from high- to upper-middle-income groups more aggressively opted for at least 4 g per day, whereas 60% in the lower-middle-income group stated that >3 g per day would be a sufficiently high dose for induction of remission ( $P<0.05$ ).

Approximately 10% of all survey participants, especially in the lower-middle-income group (16%), considered  $\leq 3$  g/day adequately “high-dose.” Assuming that all respondents were physicians involved in specialty care for UC patients, our survey results suggest a knowledge gap in the medical treatment of UC in addition to potential concerns over the high cost for high dose, and highlight the need for education in managing the rare but emerging disease of IBD in Asia.

#### Finding 5

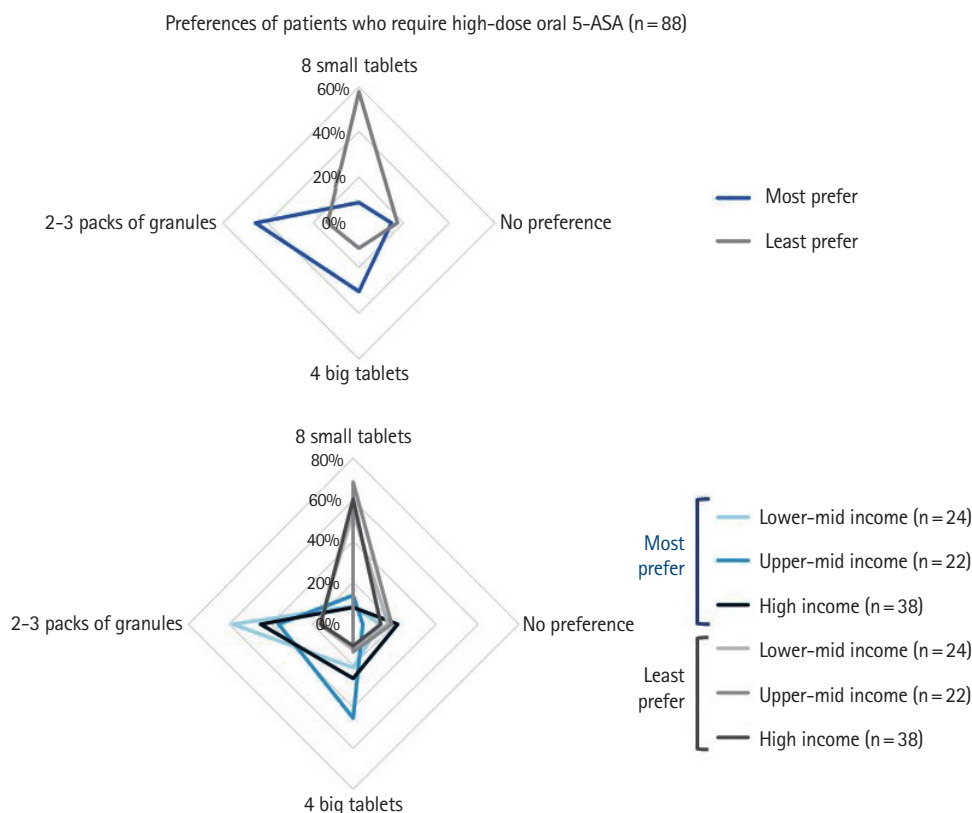
Most physicians stated variations in preferences for 5-ASA preparation.

For oral 5-ASA to reach the inflamed colons of UC patients, 3 types of coatings offering distinct delivery mechanisms are currently available, namely, the MMX for controlled pH-dependent release, Eudragit (Evonik Industries AG, Essen, Germany) for gastric-resistant release, and ethyl-cellulose for prolonged release. Yet, the European Crohn’s and Colitis Organisation UC guideline mentions that all kinds of oral 5-ASA preparations effectively maintain remission.<sup>20</sup> Recent meta-analyses show no significant difference in efficacy in both induction and maintaining remission among different 5-ASA formulations.<sup>21</sup> Despite the lack of evidence to differentiate the 3, experiences of individual physicians may differ.

We surveyed physician preference with respect to oral 5-ASA (Supplementary Fig. 4). Approximately one-third of respondents stated no preference for one preparation over the rest ( $n=28$ , 31.46%), while others mostly preferred a 5-ASA that is either MMX-based or time-dependent ( $n=26$  for both, 29.21%). Eudragit-coated pH-dependent 5-ASA was only preferred by 10% of the polled physicians.

In the subgroup analysis, preferences among the 3 income groups varied significantly ( $P=0.007$ ). Gastroenterologists from high-income economies expressed a high preference for MMX-based 5-ASA compared with the other 2 groups ( $P=0.010$ ) but significantly lower interest in time-dependent 5-ASA ( $P=0.009$ ). As 5-ASA with MMX was only recently introduced to several Asian markets, the discrepancy in preferences across the 8





**Fig. 2.** Preferences of patients who require high-dose oral 5-aminosalicylic acid (5-ASA).

polled economies could imply that accessibility and reimbursement status play important roles in decision-making for drug use.

#### Finding 6

Physicians reported that patients prefer 5-ASA granules over large numbers of tablets, due to pill burden.

Owing to the relatively high dosage required for 5-ASA to be effective in managing UC, pharmaceutical companies have developed tablets of different sizes, usually ranging from 12 mm (approximately 0.47 in) to 20 mm (approximately 0.79 in) in length, as well as sachets, to accommodate patient needs. In this survey, the gastroenterologists were asked to report their patients' most and least preferred formulations of 5-ASA, according to their clinical experiences.

Most physicians reported high dose granules in 2 or 3 sachets taken at one sitting to be the regimen most preferred by patients, and large numbers of small tablets (i.e., 8 tablets per dosing) were the least preferred ( $P < 0.05$ ); this indicates that high volume pill burden is a major factor in prescription pref-

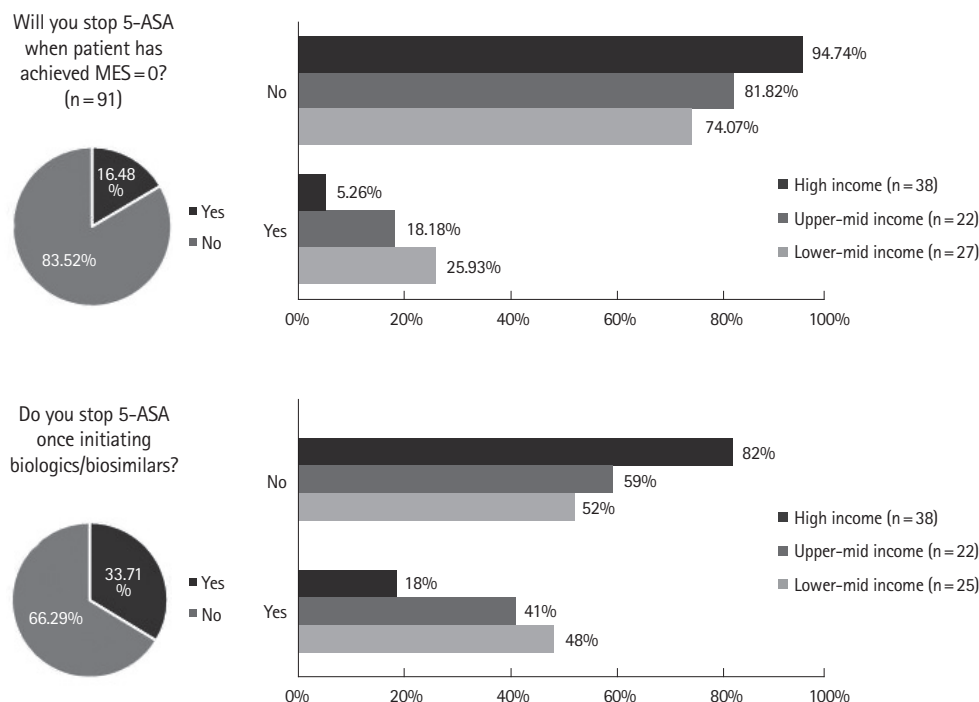
erence. The expert panel also recognized that granule sachets were the most preferred oral regimen among younger patients (<45 years) for being "stylish," easy to use, and suitable for once-daily high doses. Nevertheless, experts also pointed out a potential disconnect between real patient preference and physician perception, as shown in a survey conducted in Europe.<sup>22</sup> Efforts to reveal actual patient preferences in patients with IBD in Asia are required.

In further analysis (Fig. 2), the 3 income groups reported comparable results except in preference for 4 big tablets (45%) over granules (36%) by the patients from upper-middle-income countries. The disinclination to granules might have been driven by the absence of governmental subsidy and higher medical costs of using 5-ASA sachets in these countries.

#### Finding 7

Once-daily dosing is preferred by most UC patients, but pill burden might hinder implementation.

In patients with mild-to-moderate UC, once-daily dosing of 5-ASA has been shown to have non-inferior efficacy to twice-



**Fig. 3.** Whether there is maintenance or withdrawal of 5-ASA when ulcerative colitis patients have achieved endoscopic healing. 5-ASA, 5-aminosalicylic acid; MES, Mayo endoscopic subscore.

daily doses in induction of remission<sup>23</sup> and is subsequently recommended in multiple guidelines.<sup>1,4,20</sup> The convenient dosing regimen has also been associated with improved treatment adherence.<sup>24,25</sup> In the current survey (Supplementary Fig. 5), gastroenterologists reported that patients mostly prefer once-daily dosing (n = 54, 62.07%). In the lower-middle-income group, however, significantly fewer patients were reported to prefer once-daily dosing ( $P = 0.009$ ), while approximately 30% of patients would prefer twice- or thrice-daily dosing or more. The willingness towards multiple dosing times per day may have stemmed from limited access and greater financial burden of high-dose formulations, for instance, 2-g granules. The expert panel commented that patients might have to take multiple tablets to adequately achieve daily high dose, thus making twice-daily dosing more appealing. However, the impact on patient adherence and long-term outcomes remains unknown.

#### Finding 8

Most will continue to prescribe 5-ASA to their patients when their patients have achieved Mayo endoscopic subscore 0.

Among patients who have achieved remission with 5-ASA monotherapy, long-term maintenance treatment is recom-

mended for almost all, and intermittent therapy is acceptable in some who have proctitis.<sup>2</sup> A systematic review in 2020 reported high relapse rates among patients who discontinued 5-ASA, of 29%–60.3% at 6 months and 26%–49% at 12 months, whereas the corresponding values in those who continued 5-ASA are 12.1%–41.2% at 6 months and 18%–23% at 12 months.<sup>26</sup> Most physicians in our survey (83.5%) agreed with these data and chose to maintain 5-ASA for their UC patients after having attained complete endoscopic mucosal healing (Mayo endoscopic subscore = 0). This trend is consistent across all 3 income groups.

Although evidence from large observational cohorts and *post hoc* analysis of randomized controlled trials have revealed no benefit of 5-ASA for both clinical and endoscopic remission when use of biologics has commenced,<sup>19,27,28</sup> the majority of participating IBD experts (n = 59, 66%) (Fig. 3) preferred not to discontinue 5-ASA treatment for patients requiring advanced therapies. Our experts suggested that long-term 5-ASA use has a favorable safety profile, may help achieve and maintain mucosal healing, and acts as a chemopreventive agent in colorectal cancer.<sup>29</sup> Nevertheless, burden from medication cost appears to be a predictor of treatment discontinuation. Over 80% of physicians from the high-income group

stated that they would continue 5-ASA treatment after having initiated advanced therapies, whereas only approximately half of those from upper- or lower-middle-income groups were reported to have retained first-line therapy ( $P=0.033$ ).

## DISCUSSION

The T2T strategy in UC management is poised to modify the disease course of IBD and improve long-term outcomes.<sup>30</sup> The primary goal of treatment has evolved from symptomatic control to sustained control of inflammation with mucosal healing and possibly histological remission. However, this shift in treatment goals may generally lead to prolonged follow-up periods and medication durations, as well as intensive disease monitoring for each episode of active disease. Physician education, healthcare resource allocation, and patient preferences all play important roles in tailoring the T2T strategy. We conducted the current survey study to evaluate the current situation and potential next steps for improving implementation of the T2T strategy in UC management in Asia. We hereby offer the following propositions for major stakeholders to consider, for the better care of UC patients in Asia.

### 1. Implications for Physicians

Observed physician preference for 5-ASA as first-line therapy in patients with mild-to-moderate disease is consistent with findings from a 2023 survey of Asian experts treating patients with UC or Crohn's disease.<sup>13</sup> As 5-ASA is the mainstay first-line therapy for mild-to-moderate UC,<sup>1-4</sup> and earlier diagnosis is generally associated with better outcomes,<sup>31</sup> it is imperative to minimize diagnostic delays and promptly identify patients who will benefit from treatment with conventional therapies such as 5-ASA. Studies have found that longer diagnostic delays were associated with increased need for intestinal surgery and greater rates of anti-tumor necrosis factor- $\alpha$  use.<sup>32,33</sup> Improving awareness of UC in the medical community and the use of validated screening tools may allow timely referral of patients from primary to specialist care.<sup>34</sup>

Ambitious therapy goals make it vital for clinicians to optimize the use of 5-ASA therapy, including appropriate route and evidence-based dosing. A systematic review and meta-analysis revealed that 5-ASA at  $\geq 3.3$  g/day was significantly more effective than lower doses at inducing remission.<sup>35</sup> Accordingly, over 85% of respondents to our survey preferred high-dose ( $> 3$  g) 5-ASA for the induction of remission, which contrasts considerably with real-world data from 2009 that found up to 39% of pa-

tients with UC were taking 5-ASA doses of  $\leq 2.4$  g daily before being subject to treatment escalation.<sup>36</sup> Differences in prescribing trends between the studies could suggest that dose maximization was not uniformly practiced among physicians in the past; however, UC management appears to be undergoing a positive shift, perhaps owing to growing awareness and alignment of practice with the evidence base.

The UC treatment plan, informed by T2T goals, should be dynamic, realistic, and determined jointly by the patient and the physician. Our survey highlights the importance of shared decision-making in designing an effective management plan for optimal targets. This recommendation is consistent with a previous survey of 56 IBD experts (21% of whom were from Asia, the Middle East, or Australia), where physicians also indicated that factors related to educating and empowering patients to understand their disease, its treatment and the goals of therapy were considered of higher priority than other treatment considerations, such as disease history.<sup>37</sup>

It is imperative to promptly identify patients who might benefit from treatment escalation from 5-ASA.<sup>6,38</sup> For these patients, there may be benefit in continuing the 5-ASA treatment regimen as concomitant treatment to accommodate patient preference or to comply with reimbursement policy. Guidance on treatment withdrawal in IBD from the European Crohn's and Colitis Organisation states that the optimal duration of 5-ASA treatment is uncertain and recommends that UC patients maintain 5-ASA treatment, even when they are in remission, owing to its favorable safety profile and chemopreventive effects in patients at risk of colorectal cancer or prolapse.<sup>5,39-41</sup> Treatment discontinuation of 5-ASA should be undertaken with caution. Despite cost-saving considerations, further data are needed to identify patients who might be suitable for treatment withdrawal. Cessation of 5-ASA treatment may be considered in carefully selected patients with limited disease extent, extended duration of remission, a single disease flare only, and no history of systemic corticosteroid use.<sup>5</sup> A reduction of 5-ASA maintenance dose may be an option for patients with satisfactory adherence, mild disease and good biomarker or mucosal healing response.<sup>5</sup>

The long-term goal of treatment suggested by contemporary guidelines is deep remission.<sup>4</sup> It is an evolving concept, but generally defined as the combination of symptomatic remission and endoscopic/histological healing,<sup>4</sup> although a formal definition of this term is lacking.<sup>4,42,43</sup> Treatment advancements have made deep remission a realistic target for some patients with UC.<sup>30</sup> However, achieving deep remission in UC



within local healthcare settings may be limited by several challenges unique to Asia, including lack of reimbursement in certain markets.

## 2. Implications for Payers

Our findings indicate that treatment cost has considerable influence on the feasibility of adopting guideline recommendations. Effective implementation of the T2T strategy, encompassing an optimized treatment regimen, requires several levels of effort, one of which is medication reimbursement. Financing models such as health insurance-based health maintenance organizations can be approached to create a special category for rare diseases, like IBD, which require relatively expensive medication, including generics or biosimilars. In some countries (like the Philippines) where private health maintenance organizations do not reimburse the cost of medicines for outpatients, innovative pricing schemes such as risk-sharing agreements via public-private partnership can be explored to make long-term treatment affordable.

## 3. Implications for IBD Patients

Total healthcare costs and the need for disease control play equally important roles in decision-making by both physicians and patients, particularly in middle-income countries. Effective implementation of the T2T strategy in UC management might be compromised, thus also compromising long-term patient outcomes, if treatment options were to impose financial burdens on the patient in the long run. For active disease, patient education regarding (1) natural history of disease and treatment options, and (2) patient goals and perspectives in management plans, are pre-eminent in shared decision-making with their physicians.<sup>37</sup> Additionally, striking a balance between the overall treatment cost and the desired quality of life, while also considering long-term cost savings of effective disease control, is crucial. A disconnect between gastroenterologist considerations and patient preferences for disease management plans has been observed in IBD management in Europe.<sup>22</sup> Therefore, exploratory studies in Asia, which appraise patient preferences and concerns, including choice of drug route, dosing frequency and dosage regimen, might be beneficial.

## STRENGTHS AND LIMITATIONS

To our knowledge, this is the first physician survey in Asia to assess the use of 5-ASA in clinical practice and identify barriers

to adoption of the T2T concept in long-term outcome management for patients with UC. The strengths of the current study are that (1) we surveyed clinicians involved in IBD specialty care from 8 different economic entities in Asia, ranging from high- to lower-middle-income countries, each presenting unique healthcare systems and reimbursement scenarios. The impact of economic burden and the benefit of government subsidy on chronic disease management were observed across the region, validating the necessity of healthcare resource allocation to treat the emerging-though-rare disease of IBD in Asia; and (2) experts from each of the 8 participating economies were invited to critically interpret the survey results. Findings in this study were validated in the context of challenges unique to Asia.

This study has several limitations. First, snowball sampling may have impaired the generalizability of our survey results, and members of the community with smaller networks may not be included. This sampling bias in turn may limit the extent of generalization.<sup>44</sup> Nevertheless, IBD is still rare in Asian countries, and specialty care for patients with UC is relatively concentrated. Second, the current study focused mainly on the use of 5-ASA because it is the first-line therapy in mild-to-moderate UC. The results may not be generalizable to other treatment options for UC patients. Third, prescribing behavior and patient preferences are subject to availability of medications. As shown in Table 2, the 8 economies do not have the same access to all treatment options.

## CONCLUSION

Medication cost in the management of chronic diseases like IBD is an essential consideration in Asia. This study suggests that sustainable symptom control with affordable solutions can be achieved with government aid, physician and patient education, as well as treatment adherence. Optimizing conventional therapy like 5-ASA was identified as a priority consideration in establishing and maintaining remission in patients with UC. Shared decision-making between patients and physicians in devising treatment plans is a key contributor to improving long-term patient outcomes.

## ADDITIONAL INFORMATION

### Funding Source

This survey was supported by Ferring Pharmaceuticals.

**Conflict of Interest**

Lai AY and Teo MMH are employees of Ferring Pharmaceuticals. Li STH was an employee of Ferring Pharmaceuticals when the survey was conducted and departed during data analysis and manuscript development. Lim WC is on the advisory boards for AbbVie, Pfizer, and Ferring and has received speaker's honoraria from Janssen and AbbVie. Sollano J is on the advisory board for A Menarini and Takeda and a speaker bureau for Celltrion, Takeda, J&J, Ferring, and A Menarini. Wei SC has consulted or served on advisory boards for AbbVie, Bristol Myers Squibb, Celltrion, Ferring Pharmaceuticals, Janssen, Pfizer, Takeda, and Tanabe, and has received lecture fees from AbbVie, Bristol Myers Squibb, Celltrion, Ferring Pharmaceuticals, Janssen, Pfizer, Takeda, and Tanabe. Leung WK has received speaker's fee or honorarium from AbbVie, Astra Zeneca, Ferring and Janssen.

Wei SC and Ali RAR are editorial board members of the journal but were not involved in the peer reviewer selection, evaluation, or decision process of this article. No other potential conflicts of interest relevant to this article were reported.

**Data Availability Statement**

De-identified source data are available upon reasonable request from the Corresponding Author for research purposes.

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**Additional Contributions**

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**Supplementary Material**

Supplementary materials are available at the Intestinal Research website (<https://www.irjournal.org>).

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