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Ulcerative colitis outcomes research in Japan: protocol for an observational prospective cohort study of YOURS (YOu and Ulcerative colitis: Registry and Social network)

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ABSTRACT

Introduction Ulcerative colitis (UC) is a chronic inflammatory disease that mainly affects the colon in young patients. Typical symptoms of UC are bloody diarrhoea and faecal urgency, which disturb the quality of life (QOL) of patients, and intractable UC leads to hospitalisation and colectomy. To improve relevant outcomes such as symptoms, QOL and colectomy, many clinical questions need to be resolved regarding what the ideal lifestyle, psychosocial burden and optimal practice patterns are. In this YOu and Ulcerative colitis: Registry and Social network (YOURS) study, we will investigate the effect of lifestyle, psychosocial factors and practice patterns on patient-reported outcomes (PRO), hospitalisation rate and colectomy rate in Japanese patients with UC.

Methods and analysis For this prospective cohort study, we recruited 2006 patients from five hospitals (Tokyo and Chiba; May 2018–January 2019). Patients will be able to access their own data and compare them with summarised data from all patients on the website beyond the YOURS study. At baseline, patients will answer a questionnaire regarding lifestyle (diet, exercise, sleep and work), psychosocial factors (stress, depression and social support) and PRO (symptoms and QOL). Information on practice patterns (eg, medications, endoscopy frequency) will be collected from electronic medical records. Gaps between patients’ needs and healthcare professionals’ practice will be identified. Follow-up surveys will be conducted periodically for approximately 3 years. Research questions suggested by patients and healthcare professionals may be used in subsequent surveys. Results from the YOURS study will demonstrate optimal UC management strategies to improve relevant outcomes.

ETHICS AND DISSEMINATION

The study was approved by the ethics committees of five investigational sites before starting the study. The results will be submitted to journals.

TRIAL REGISTRATION NUMBER UMIN000031995.

INTRODUCTION

Ulcerative colitis (UC) is a chronic inflammatory disease with no curative treatment. It mainly affects the colon and is associated with bloody diarrhoea and faecal urgency as typical symptoms.¹ Aberrant immunity in the gut is considered to be involved in the pathogenesis of UC;² however, the aetiology of UC is not fully understood. UC is increasing around the world, especially in Asia, including Japan.³–⁵ The prevalence of UC has been reported to range from 5.3 to 63.6 per 100 000 people in Asia and from 37.5 to 238 per 100 000 people in North America,¹ and differs between regions, with the prevalence in Japan reported as approximately 100 per 100 000 people in 2013.³ The onset of UC often has a major influence on patients’ quality of life (QOL), and...
Factors and outcomes assessed in the YOURS study. All four factors can contribute to all four outcomes. HCP, healthcare professional; YOURS, YOu and Ulcerative colitis: Registry and Social network.

Figure 1

Factors

1. Lifestyle
2. Psychosocial burden
3. Practice patterns
4. Gaps between patients’ needs and HCPs’ practice

Outcome

1. Relapse/exacerbation
2. Hospitalisation
3. Colectomy
4. Patient-reported outcomes

Optimal disease monitoring and treatment need to be clarified.

Intractable UC can lead to hospitalisation and colectomy. Patients need to manage UC throughout their lives with both self-management and support from healthcare professionals (HCPs) to avoid unwanted clinical outcomes, including relapse/exacerbation, hospitalisation, and colectomy, as well as to improve patient-reported outcomes such as QOL.

In this YOURS (YOu and Ulcerative colitis: Registry and Social network) study, we identified four main factors/challenges to the improvement of patient outcomes: (1) lifestyle, (2) psychosocial factors, (3) practice patterns and (4) gaps between patients’ needs and HCPs’ practice (figure 1).

First, there has been much discussion and debate about the optimal lifestyle (diet, exercise, sleep and work) for UC management. In particular, diet is a critical issue for both patients and their HCPs. Although a large-scale study has reported that the relationship between diet and relapse is of major interest to patients with inflammatory bowel disease (IBD) and their HCPs, only two exploratory studies have examined the relationship. However, the results from these studies were not consistent.

Second, psychosocial factors including stress, depression and social support may affect clinical outcomes in UC. Approximately half of patients with IBD have low QOL and depression, and one-third of patients are reported to feel stigmatised. It remains unknown how these psychosocial factors affect disease course.

The third challenge is practice patterns. The Selecting Therapeutic Targets in Inflammatory Bowel Disease programme, published in 2015 by IBD specialists, recommends setting concrete treatment goals as part of a ‘Treat to Target’ strategy. The agreed treatment goals for UC were clinical remission (defined as resolution of rectal bleeding and diarrhoea/altered bowel habit) and endoscopic remission (based on endoscopic findings). However, achievement of these treatment goals may be accompanied by decreased QOL due to frequent colonoscopies or side effects caused by immune suppression.

The last challenge is gaps between patients’ needs and HCPs’ practice. A previous survey has identified important differences between patients and HCPs in their perception of the impact of UC symptoms on patients’ lives, suggesting that HCPs may underestimate the effect of UC symptoms on patients. However, the effect of perception gaps on patient outcomes is unknown.

The YOURS study is an observational prospective cohort study in patients with UC in Japan that aims to clarify how these four challenges affect relapse/exacerbation, hospitalisation, colectomy and patient-reported outcomes such as QOL.

METHODS AND ANALYSIS

Study design

The YOURS study is an observational prospective cohort study with a 3-year follow-up being conducted at five investigational sites in Japan. Patient registration started in May 2018 and ended in January 2019. As of 11 January 2019, 2006 patients have been enrolled.

The study is being conducted in compliance with the Declaration of Helsinki, Ethical Guidelines for Medical Research on Humans, Ministry of Education, Culture, Sports, Science and Technology of Japan and Ministry of Health, Labour and Welfare of Japan and all applicable laws and guidelines. Written informed consent will be obtained from all patients. The study is registered at the University hospital Medical Information Network (UMIN) Center.

Study population and sample size

Patients diagnosed with UC, as defined by the ‘Evidence-based Clinical Practice Guidelines for Inflammatory Bowel Disease’, who are ≥16 years of age at informed consent and are attending the investigational sites are eligible for enrolment.
The sample size was determined by considering the feasibility of enrolling patients.

**Outcome measures and survey items**

Relapse/exacerbation, hospitalisation, colectomy and patient-reported outcomes such as QOL will be assessed as main outcomes. Lifestyle, psychosocial factors, practice patterns and gaps between patients’ needs and HCPs’ practice will be evaluated as exposures. All surveys will be conducted in Japanese and will include standard, validated questionnaires for most measures of lifestyle, psychosocial factors and symptoms.

At the initial survey, patients will complete written questionnaires with demographic, lifestyle, psychosocial and symptom questions (table 1, figure 2). Following the initial survey, patients will complete a three-item brief symptom survey including psychosocial and symptom questions by smartphone application, email, phone or written questionnaire every 3 months, and a follow-up

<table>
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<tr>
<th>Table 1 Survey items/questionnaires</th>
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<tr>
<td><strong>Category</strong></td>
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<td><strong>By patients</strong></td>
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<td>Initial survey</td>
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<tr>
<td>Special survey (in patients in remission for at least 90 days, at 3 months from the time of initial survey)</td>
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<tr>
<td>Symptom survey (every 3 months)</td>
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<tr>
<td>Follow-up survey (every year)</td>
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<td></td>
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<tr>
<td><strong>By HCP</strong></td>
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<tr>
<td>HCP survey (initial)</td>
</tr>
<tr>
<td>Medical record survey (initial only)</td>
</tr>
<tr>
<td>Medical record survey (initial, 3 months from the initial survey, every year)</td>
</tr>
</tbody>
</table>

ASK-12,15–18 Adherence Starts with Knowledge-12; BDHQ,19 20 Brief-type self-administered Diet History Questionnaire; FACIT-F,21–23 Functional Assessment of Chronic Illness Therapy-Fatigue; HADS,24–27 Hospital Anxiety and Depression Scale; HCP, healthcare professional; IPAQ,28 29 International Physical Activities Questionnaire; JPSS,30 31 Japanese version of the Perceived Stress Scale; mMOS-SS,32–34 modified Medical Outcomes Study Social Support Survey; NRS,35 36 Numerical Rating Scale; PRO-2,37 two-item patient-reported outcomes; PSQI,36 37 Pittsburgh Sleep Quality Index; QDIS,38 Quality of life Disease-specific Impact Scale; QGEN,39 Quality of life GENeral; QOL, quality of life; SIBDQ,40–42 Short version of Inflammatory Bowel Disease Questionnaire; UC, ulcerative colitis; WPAI,43 44 Work Productivity and Activity Impairment questionnaire.
Study design. Surveys on the left side are for patients, and surveys on the right side are for HCPs. All surveys were completed by written questionnaires, except for the symptom survey, which could be completed by smartphone application, email, phone or written questionnaire. The special survey at 3 months from the time of initial survey was only completed by patients who maintained remission for at least 90 days. HCP, healthcare professional.
The brief symptom survey every 3 months from the time of the initial survey, which includes lifestyle questions focusing on diet, exercise and stress management as strategies to prevent relapse (table 1, figure 2). Remission is defined as a stool frequency score of 0 or 1 and a rectal bleeding score of 0 (two-item patient-reported outcome; table 2). Patients will have the opportunity to provide their own research questions at the initial survey and all follow-up surveys. We plan to categorise and create a ranking of the research questions. The members of the steering committee will review the ranking of these research questions. If the research questions are feasible for this study, they will be included in the subsequent surveys within the YOURS study. The three-item brief symptom survey will provide the most important information for this study because the survey evaluates relapse or exacerbation of UC. In cases where patients are reluctant to complete the follow-up survey, for reasons such as changing hospitals, we will offer to continue with only the brief symptom survey every 3 months to reduce the number of dropouts.

In the HCP survey, HCPs will complete written questionnaires about their guidance to patients with remission regarding diet, exercise and stress management in order to prevent relapse. Answers from patients and HCPs will be compared and any gaps in the perception of the ideal lifestyle to prevent relapses will be identified and explored. In addition, HCPs will collect patients’ medical information such as medication use, blood examinations, stool examinations, endoscopic findings, pathologic findings, hospitalisations, colectomy status and adverse events (throughout the study) from electronic medical records at all surveys (table 1, figure 2).

### Data management

The YOURS study uses an electronic data capture system to register patients, collect survey answers and create a database, which can be accessed securely by only those investigators who have received appropriate training. The principal investigators are responsible for ensuring data quality.

### Feedback to patients

Patients will be provided written feedback on their data compared with the other patients participating in the YOURS study. Moreover, patients can use the website for reviewing their data over time, comparing with others and sharing their data with HCPs via the website, provided the patients have requested access and agreed to the transfer of their data from the database to the website with written informed consent (figure 3).

### Statistical analysis

Analysis groups will be determined for each outcome measure and survey item. The baseline data on demographics, lifestyle, psychosocial factors, practice patterns and gaps between patients’ needs and HCPs’ practice will be summarised. The following statistical analyses to clarify the association of these baseline data with relapse/exacerbation, hospitalisation, colectomy and patient-reported outcomes such as QOL will be conducted.

Logistic regression analysis or Cox proportional hazard model will be used for analysis of binary variables. Linear regression analysis will be used for analysis of continuous variables. Multilevel analysis may be used for considering differences between investigational sites. Confounding factors will be adjusted appropriately for all analyses.

Interim database locks and interim analyses are planned as follows: initial survey, special survey at 3 months from the time of the initial survey, and follow-up surveys at 2 and 3 years after the initial survey.

### Patient and public involvement statement

We will collect research questions from both patients and HCPs from surveys in the YOURS study. If the research questions are feasible for this study, they will be included in the subsequent surveys within the YOURS study.

### ETHICS AND DISSEMINATION

The YOURS study is sponsored by Takeda Pharmaceutical Company Limited (Tokyo, Japan) and advice on the study plan was obtained from the Japanese Society for Inflammatory Bowel Disease. The study is managed by six joint research organisations, including Takeda and five investigational sites: Tokyo Medical and Dental University, Medical Hospital (Tokyo, Japan); Kitasato University Kitasato Institute Hospital (Tokyo, Japan); Kyorin University Hospital (Tokyo, Japan); Tokyo Women’s Medical University Hospital (Tokyo, Japan) and Toho University Sakura Medical Center (Chiba, Japan), and was approved by the ethics committees of five investigational sites before starting the study. The YOURS study has a steering committee consisting of medical experts conducting

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<tr>
<th>Table 2</th>
<th>Definition of stool frequency score and rectal bleeding score in PRO-2</th>
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<tr>
<td><strong>Score</strong></td>
<td><strong>Definition</strong></td>
</tr>
<tr>
<td>Stool frequency</td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>Normal number of stools</td>
</tr>
<tr>
<td>1</td>
<td>1–2 stools more than normal</td>
</tr>
<tr>
<td>2</td>
<td>3–4 stools more than normal</td>
</tr>
<tr>
<td>3</td>
<td>5 or more stools more than normal</td>
</tr>
<tr>
<td>Rectal bleeding</td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>None</td>
</tr>
<tr>
<td>1</td>
<td>Streaks of blood with stool less than half the time</td>
</tr>
<tr>
<td>2</td>
<td>Obvious blood with stool most of the time</td>
</tr>
<tr>
<td>3</td>
<td>Blood alone passed</td>
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</table>

PRO-2, two-item patient-reported outcomes.
Figure 3 Feedback scheme of the YOURS study. (a) Survey answers and medical records will be collected from patients and HCPs by written questionnaire, smartphone application, email or phone, and stored in the YOURS study database. (b) Patients can use a website for reviewing their own data over time if the patients have requested access and agreed to the transfer of their data to the website. (c) Patients can also use the website for comparing their data with others, and for sharing their data with HCPs via the website. HCP, healthcare professional; YOURS, YOU and Ulcerative colitis: Registry and Social network.
the study, representatives of the joint research organisations and clinical epidemiology experts. The roles of the steering committee are to supervise the overall study operation, provide medical expertise guidance, ensure the scientific quality of the study is at a high level and update the protocol appropriately when needed. The results will be submitted to journals for publication.

DISCUSSION

There are four primary goals of the YOURS study: (1) develop a platform to share clinical knowledge and patient experience, (2) define optimal care for UC, (3) fill gaps between patients’ needs and HCPs’ practice and (4) improve relevant outcomes. To achieve these goals, the YOURS study will investigate how four main challenges (lifestyle, psychosocial factors, practice patterns and gaps between patients’ needs and HCPs’ practice) affect relapse/exacerbation, hospitalisation, colectomy and patient-reported outcomes such as QOL.

Using the YOURS study results, we plan to create a booklet to clarify how challenges such as lifestyle, psychosocial factors, practice patterns and gaps between patients’ needs and HCPs’ practice affect clinical outcomes. Although booklets are a preferred adjunct source of information for patients with IBD and it is important to distribute booklets, the same information will also be disseminated in other ways, such as websites, as needed. The YOURS study booklet will include specific information on diet, exercise, sleep, work, stress, depression and social support. Moreover, if we identify any gaps between patients’ needs and HCPs’ practice regarding lifestyle guidance, we will include that information in the booklet as background information. We anticipate that the booklet will facilitate the sharing of information between patients and HCPs, thereby helping to bridge gaps between patients’ needs and HCPs’ practice.

The YOURS study is a large-scale, long-term, prospective observational study without any prohibited concomitant drugs and therapies, thereby reflecting real clinical settings. However, as all investigational sites are located in Tokyo or Chiba (which is near Tokyo) in Japan, the applicability of the study results to other locations may be affected by lifestyle and psychosocial factors influenced by regional, country and/or cultural differences. The other limitation of this study is the possibility that patients will confuse some of the questions, because various kinds of scales are used in each survey to evaluate lifestyle and psychosocial factors. The YOURS study can potentially be expanded in subsequent surveys within the study because patients and HCPs can ask research questions not otherwise included in the survey.

In conclusion, the YOURS study provides an important opportunity to clarify how challenges such as lifestyle, psychosocial factors, practice patterns and gaps between patients’ needs and HCPs’ practice affect clinical outcomes in patients with UC in Japan. We anticipate that results from the YOURS study will demonstrate optimal UC management strategies to improve relevant outcomes.

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Contributors All authors participated in the interpretation of study results, and in the drafting, critical revision and approval of the final version of the manuscript. HY, KM, JF and SF were involved in the study design, KM, TH, MW and TH are investigators and have collected the data in the study.

Funding Clinical experts, clinical epidemiologists and Takeda Pharmaceutical Company Limited (Takeda) discussed and developed the protocol, and Takeda contracted out the collection of supporting data by clinicians to site management organisations. Takeda will also contract out data analysis to a third organisation. Regarding manuscript preparation, Jovelle Fernandez, an employee of Takeda Japan Medical Office, is one of the authors of this manuscript. She participated in the study design, interpretation of study results, drafting, critical revision and approval of the final version of the manuscript, as stated in the authors’ contributions section. Takeda contracted out medical writing to Yukiko Homma, MPHarm and Rebecca Lew, PhD, CMP of ProScribe: Envision Pharma Group. ProScribe’s services complied with international guidelines for Good Publication Practice (GPP3).

Disclaimer Takeda Pharmaceutical Company Limited has been or will be involved in the study design, data collection, data analysis and preparation of the manuscript.


Patient consent for publication Not required.


REFERENCES


