

Article

Quality of Life and Eligibility for Specific Financial Assistance for Medical Expenses: A Cross-Sectional Web-Based Survey among Patients with Inflammatory Bowel Disease in Japan

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Abstract: Specific financial assistance for people with rare and intractable diseases is part of Japan's public health system. This survey aimed to clarify the relationship between eligibility for this specific financial assistance and quality of life (QOL) among individuals with inflammatory bowel disease (IBD) in Japan. A nationwide, web-based survey was conducted in Japan among 300 people with IBD. Questionnaire items covered socioeconomic characteristics and QOL, assessed with the five-dimension, five-level EuroQol (EQ-5D-5L). The percentage of respondents who were ineligible for specific financial assistance was 11.0% among those with Crohn's disease (CD) and 34.0% among those with ulcerative colitis (UC). For those with CD, the median EQ-5D-5L utility weight did not differ significantly between the non-assistance and assistance groups ($p = 0.2222$). For those with UC, the median EQ-5D-5L utility weight was significantly higher in the non-assistance group than in the assistance group ($p = 0.0034$). The present study demonstrated that the revision of the law on intractable and rare diseases has not had a negative influence on the QOL of patients with IBD in Japan. Based on our findings, further research on patient-reported outcomes among individuals with IBD may be necessary to inform health policy makers.

Keywords: inflammatory bowel disease; specific financial assistance; quality of life; utility; web-based survey

1. Introduction

Inflammatory bowel disease (IBD) is a chronic disease of the gastrointestinal tract comprising of two main diseases, Crohn's disease (CD) and ulcerative colitis (UC). The predominant clinical manifestations of CD are abdominal pain and diarrhea, whereas rectal bleeding is the predominant symptom of UC. Both diseases can affect patients' lives, including school, work, social activities, and family life, especially because the disease occurs during patients' most productive time of life [1].

It is well known that the incidence and prevalence of IBD are increasing worldwide. Molodecky et al. reported that, globally, the highest prevalence rates of IBD were in Europe (UC: 505 per 100,000; CD: 322 per 100,000 persons) and North America (UC: 249 per 100,000; CD: 319 per 100,000 persons) [2]. In Japan, the number of patients with IBD is increasing rapidly, with estimates of 140,000 patients with UC and 40,000 with CD in 2016, according to the Ministry of Health, Labour and Welfare [3]. The

etiopathogenesis of IBD has been thought to be driven by the mutual reactions among host susceptibility genes, environmental factors including intestinal flora and food antigens, and abnormal immune balance. Relevant environmental factors include: westernized, high-calorie, high-fat foods; smoking; and public hygiene. The Japanese government has conducted an IBD research project—a geographic and sequential study on the incidence of IBD—to clarify the disease's etiopathogenesis. In addition, the Japanese government supports patients with IBD financially under the law described below.

Both CD and UC are chronic diseases with repeated cycles of remission and relapse. Disease relapse is a crucial factor affecting the quality of life (QOL) of patients with IBD. Although the etiology of IBD is unknown, the therapeutic goal is not only to improve symptoms but also to improve the QOL of patients with IBD. In Japan, therapies for IBD have evolved over the past decade, and many patients with IBD have been able to sustain long-term remission because of several biological drugs that are covered by health insurance. There is increasing interest in measuring patient-reported outcomes such as QOL among those with IBD, as well as the treatment patterns of IBD therapies [4–8].

Patients with IBD need to receive suitable therapy rapidly to improve their clinical condition and QOL. Patients with IBD can be classified according to the severity of clinical disease activity. In Japan, about 70% of patients with UC have mild disease activity requiring minimal/inexpensive therapy. In contrast, most patients with CD have moderate-to-severe disease activity and need intensive/expensive treatment. Public support to assist patients with IBD with their medical expenses is essential because IBD therapy may include not only medication, but also chemotherapy, hospitalization, or surgery, depending on the patient's condition. In Japan, the Medical Care for Patients with Intractable/Rare Diseases Act has established a public support system to provide assistance with medical expenses for patients with IBD and other intractable or rare diseases. This act, which revised the law on intractable and rare diseases, was introduced into the Japanese healthcare system on 1 January 2015. The public support system was changed under this act to exclude patients with mild diseases who were not receiving very expensive long-term therapy, designating these individuals as ineligible for specific financial assistance. In contrast, patients with IBD who have moderate-to-severe disease activity are treated with intensive long-term therapy that is quite expensive; therefore, they are designated as eligible for assistance [9]. Concerns have been raised about potential declines in the QOL of patients who are excluded from financial support because of inequity in this financial assistance.

Several studies have attempted to assess the QOL of patients with IBD [4–8]. However, it is unclear whether status regarding specific financial assistance for medical expenses affects the QOL of patients with IBD in Japan. This study aimed to examine the difference in QOL between specific financial assistance status groups and to estimate the health-related utility of treatment patterns among patients with IBD in Japan.

2. Results

2.1. The Status of Specific Financial Assistance

We obtained responses from 300 subjects with IBD (100 respondents with CD and 200 respondents with UC), and we included all data in the analyses. Table 1 presents comparisons of the demographic characteristics of respondents with CD and UC by specific financial assistance status. The percentage of respondents who were ineligible for specific financial assistance was 11% (11/100) for patients with CD and 34% (68/200) for patients with UC.

Table 1. Demographic characteristics and utility weight of survey respondents.

Respondent Characteristic	CD				P-Value	UC				P-Value	
	Eligible for Financial Assistance (n = 89)		Ineligible for Financial Assistance (n = 11)			Number or Median	% or IQR	Eligible for Financial Assistance (n = 132)		P-Value	
	Number or Median	% or IQR	Number or Median	% or IQR				Number or Median	% or IQR		
Age (in years)											
20–29	4	4.5%	0	0.0%	0.682	7	5.3%	2	2.9%	0.558	
30–39	20	22.5%	2	18.2%		22	16.7%	7	10.3%		
40–49	29	32.6%	5	45.5%		30	22.7%	14	20.6%		
50–59	28	31.5%	2	18.2%		41	31.1%	28	41.2%		
≥ 60	8	9.0%	2	18.2%		32	24.2%	17	25.0%		
Sex											
Male	64	71.9%	8	72.7%	1.000	90	68.2%	47	69.1%	0.513	
Female	25	28.1%	3	27.3%		42	31.8%	21	30.9%		
Annual income (in Japanese yen)											
Low (<300 million)	51	57.3%	7	63.6%	0.400	79	59.8%	34	50.0%	0.333	
Middle (≥300 million and <500 million)	14	15.7%	3	27.3%		22	16.7%	12	17.6%		
High (≥500 million)	24	27.0%	1	9.1%		31	23.5%	22	32.4%		
Marital status											
Single	44	49.4%	4	36.4%	0.529	38	28.8%	16	23.5%	0.502	
Married *	45	50.6%	7	63.6%		94	71.2%	52	76.5%		
Age at diagnosis (in years)											
Disease duration (in years)	27	20–34	30	21–35	0.494	38	26.5–50	38.5	27.5–52.5	0.457	
Previous surgery for IBD	17	11–24	17	1–27	0.632	10	5–18	9.5	3.5–19.5	0.555	
Hospitalization for IBD in the past year											
Yes	66	74.2%	7	63.6%	0.482	13	9.8%	4	5.9%	0.429	
No	23	25.8%	4	36.4%		119	90.2%	64	94.1%		
IQR: interquartile range; IBD: inflammatory bowel disease; CD: Crohn's disease; UC: ulcerative colitis; * "Married" includes those who were widowed or divorced.											
Yes	23	25.8%	2	18.2%	0.726	19	14.4%	4	5.9%	0.101	
No	66	74.2%	9	81.8%		113	85.6%	64	94.1%		

2.2. Quality of Life Indices

Figure 1 presents the distribution of the five-level EuroQol (EQ-5D-5L) utility weight as boxplots. Among respondents with CD, the median (interquartile range; IQR) EQ-5D-5L utility weight was 0.823 (0.753–0.895) for those who were eligible for assistance and 0.867 (0.784–1) for those who were ineligible for assistance. There was no significant difference in the EQ-5D-5L utility weight between these two groups ($P = 0.2222$). Among patients with UC, the median (IQR) EQ-5D-5L utility weight was 0.895 (0.780–1) for those who were eligible for assistance and 0.895 (0.867–1) for those who were ineligible for assistance, and the median score was significantly higher for the ineligible group than for the group that was eligible to receive specific financial assistance ($P = 0.0034$). The points displayed in Figure 1 are the outliers in the utility data for each group.

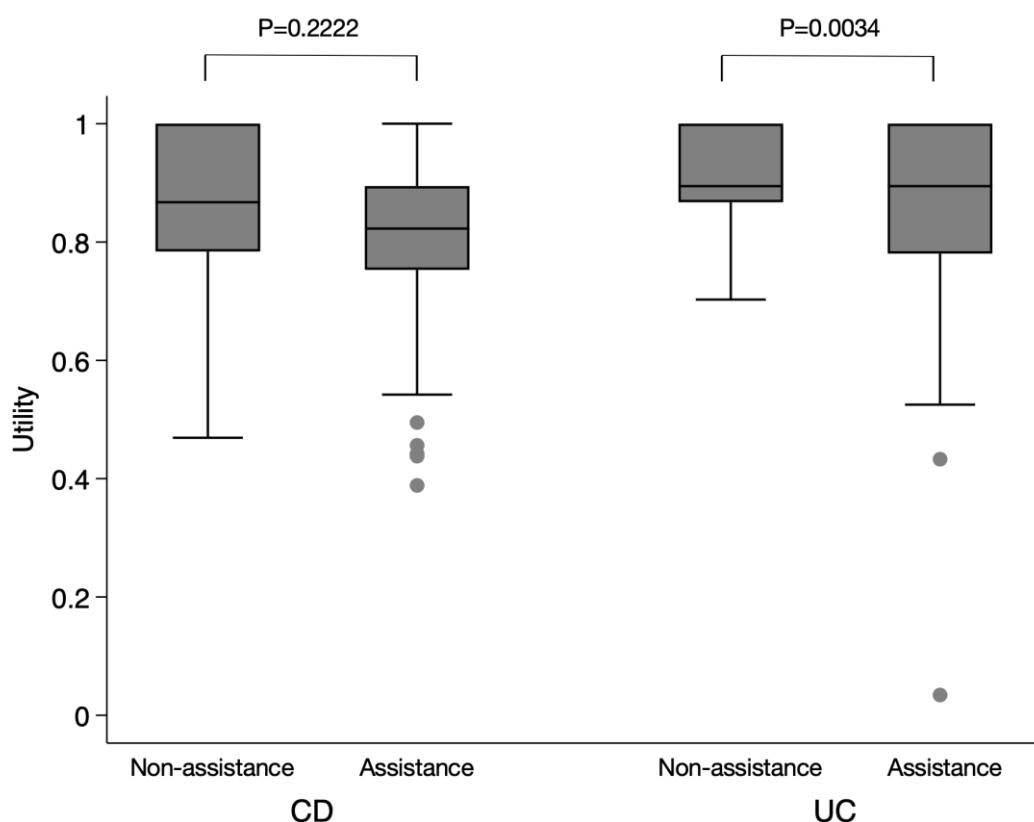


Figure 1. Box plots of EQ-5D-5L utility weight. (EQ-5D-5L: five-dimension, five-level EuroQol instrument).

Figure 2 shows the distribution of respondents' EQ-5D-5L level on each dimension as bar charts. The health-related dimensions most affected by IBD were anxiety/depression and pain/discomfort. The dimensions that were least associated with IBD were self-care and mobility. For both respondents with CD and those with UC, the percentage reporting "no problems" were higher among the non-assistance group than among the assistance group for the dimensions of pain/discomfort and usual activities. For the dimension of anxiety/depression, the percentage of respondents with CD who reported "moderate problems" or worse was almost identical in the assistance and non-assistance groups.

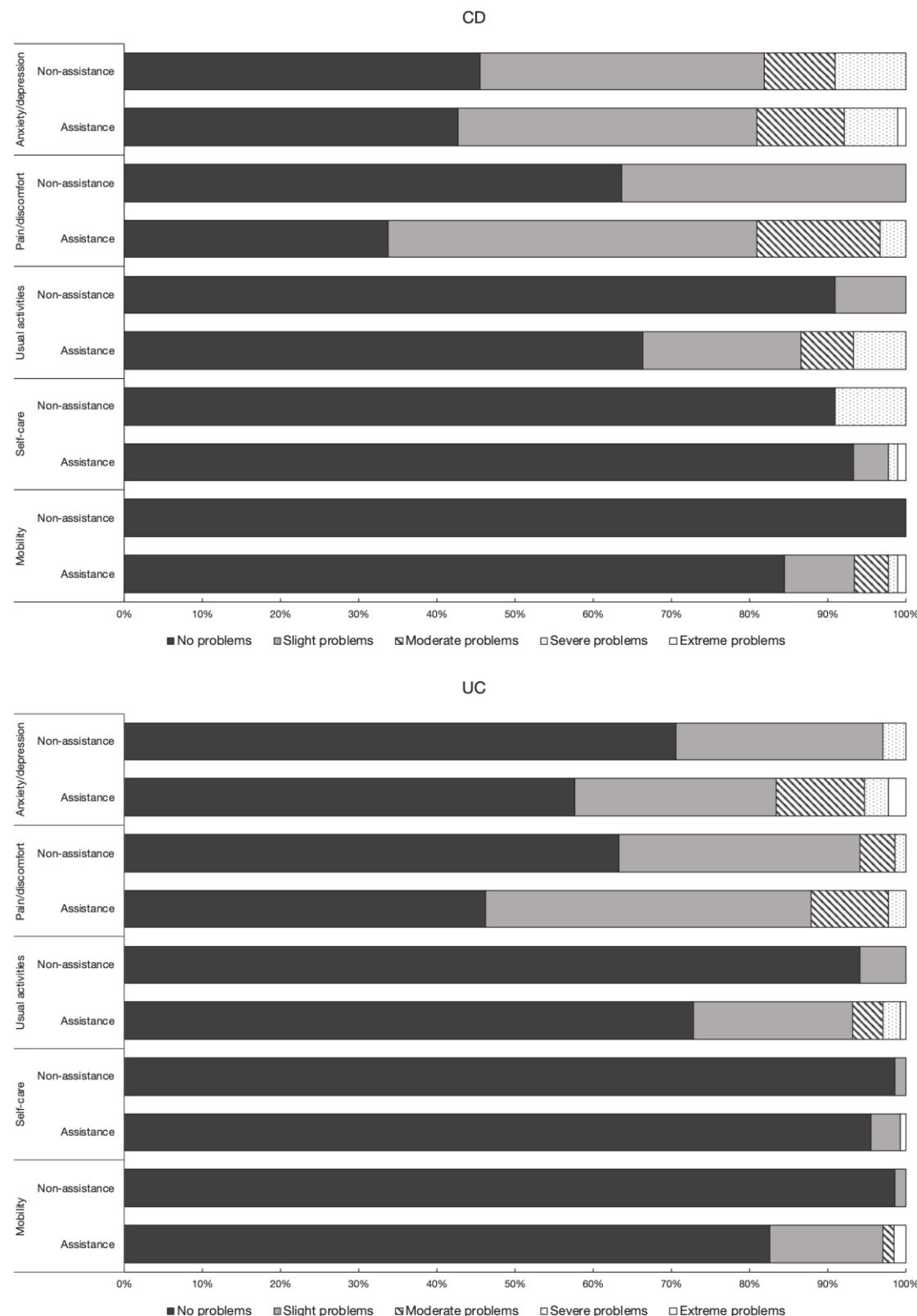


Figure 2. Distributions of responses on the five domains of the EQ-5D-5L. (EQ-5D-5L: five-dimension, five-level EuroQol instrument).

Finally, we calculated the percentage of respondents who had received each type of treatment and the EQ-5D-5L utility weight by treatment subgroup (Table 2). The percentage of patients who had

received biological therapy was much higher in the CD group (60.0%) than in the UC group (6.5%). The percentage of patients who had received steroids was only approximately 10% in both the CD group and the UC group. Our results demonstrated that the median EQ-5D-5L utility weight ranged from 0.469 for patients with CD treated with cytaphereses to 0.895 for patients with UC treated with 5-aminosalicylates who were not treated with steroids or immunomodulators.

Table 2. Treatment status and utility weight.

Treatment	CD (N = 100)				UC (N = 200)			
	Number	%	Median EQ-5D-5L Score	IQR	Number	%	Median EQ-5D-5L Score	IQR
Treated with 5-ASA								
Yes	76	76.0%	0.823	0.751–0.895	164	82.0%	0.895	0.823–1
No	24	24.0%	0.867	0.788–0.895	36	18.0%	0.883	0.780–1
Treated with elemental diet								
Yes	52	52.0%	0.823	0.722–0.880	5	2.5%	0.670	0.629–0.685
No	48	48.0%	0.867	0.810–1	195	97.5%	0.895	0.823–1
Treated with steroids								
Yes	12	12.0%	0.823	0.741–0.849	18	9.0%	0.823	0.676–0.867
No	88	88.0%	0.833	0.772–0.895	182	91.0%	0.895	0.823–1
Treated with immunomodulators								
Yes	30	30.0%	0.792	0.710–0.895	29	14.5%	0.825	0.734–0.895
No	70	70.0%	0.867	0.799–0.895	171	85.5%	0.895	0.823–1
Treated with CAP								
Yes	1	1.0%	0.469	0.469–0.469	2	1.0%	0.657	0.629–0.685
No	99	99.0%	0.823	0.771–0.895	198	99.0%	0.895	0.823–1
Treated with biological drugs								
Yes	60	60.0%	0.823	0.751–0.895	13	6.5%	0.799	0.734–0.895
No	40	40.0%	0.849	0.772–0.947	187	93.5%	0.895	0.823–1

IQR: interquartile range; 5-ASA: 5-aminosalicylate; CAP: cytaphereses; CD: Crohn's disease; UC: ulcerative colitis; EQ-5D-5L: five-dimension, five-level EuroQol instrument.

3. Discussion

In Japan, before 2015, all patients with intractable or rare diseases were able to receive specific financial assistance to help pay for their medical expenses. These patients' deductibles and copayments were decided on the basis of their family income, and most patients had to pay only a fixed fee of approximately 10,000 Japanese yen per month, regardless of the total amount of their medical fees. However, at the beginning of 2015, the law on intractable and rare diseases was revised to ensure sufficient funds to assist patients with certain intractable or rare diseases. This revised law extended the target diseases to cover 333 diseases, but it excludes patients with mild diseases who do not need aggressive therapy, making them ineligible for specific financial assistance.

Therefore, patients with IBD who are in good clinical condition and not receiving aggressive treatment are excluded from specific financial assistance. This has raised concerns that many patients with IBD who became ineligible for this financial assistance under the revised law may have experienced a decline in their QOL. We conducted a nationwide investigation using a web-based questionnaire to clarify the relationship between specific financial assistance status and QOL among patients with IBD in Japan.

The same tendencies in utility score were observed for both patients with CD and patients with UC. However, because the number of patients with ineligible status was much smaller among those with CD than among those with UC, there was a statistically significant difference only for patients with UC. Our results suggest that patients with UC who are ineligible for specific financial assistance do not have worse QOL compared with those who are eligible for this assistance, possibly because their clinical condition can be controlled with only mild treatment. However, the percentage of respondents who are ineligible for specific financial assistance is lower among those with CD than among those with UC. This finding may be explained by the possibility that many patients with CD are able to achieve remission or a mild condition through continued biological therapy. In the revised law on

intractable and rare diseases, patients who need long-term, expensive treatment are designated as eligible for financial assistance, regardless of their clinical condition.

The health status of patients with IBD should be measured not only with the EQ-5D-5L but also with a disease-specific scale such as the Inflammatory Bowel Disease Questionnaire [10,11]. However, we were unable to use a disease-specific scale in this self-reported web-based study because these scales include clinical factors that should be assessed by a physician or contain a much larger number of questions compared with the EQ-5D-5L. As we were unable to include such a scale, we could not analyze the data with stratification by degree of symptoms or disease activity. Among the patients with IBD that were ineligible for specific financial assistance, the level of anxiety/depression was better for those with UC than for those with CD.

Web-based surveys are a reliable method for epidemiological research [12–14]. Nevertheless, this study had several limitations. First, the sex and age distributions of the research participants, who had IBD, differed from these distributions in the Japanese population. Compared with recent data on the Japanese population reported by the Japan Intractable Diseases Information Center [3], the survey sample in the present study included somewhat fewer individuals from younger age groups (i.e., those in their 20s and 30s), and women also appear to be underrepresented in the survey sample. However, we believe that such selection bias had minimal impact on our results because there were no significant differences in background factors between the non-assistance and assistance groups. Second, we were unable to use a second approach to verify the respondents' clinical history or financial support status because of the anonymous and self-reported nature of the survey. Finally, because our study design was cross-sectional, we could not verify the causal effect of the revision of the law on intractable and rare diseases, and we could not examine changes in QOL scores over time following the revision to the law among patients who became ineligible for specific financial assistance after this revision. Despite these limitations, the statistical analysis presented in this study can serve as important information for future health policies related to IBD.

Several previous studies have examined the QOL of individuals with IBD in Japan and other countries. Matsumoto et al. conducted a web-based survey assessing the QOL of Japanese patients with IBD using the short form-8 instrument. These researchers reported a significant negative correlation between the short form-8 score and the degree of CD and UC symptoms [4]. Ueno et al. found that the lives and social activities of patients with IBD are affected by the deterioration of QOL caused by IBD and its symptoms [6]. In Israel, Greenberg et al. estimated utility among patients with IBD using the short form-36 health survey and the short inflammatory bowel disease questionnaire, based on the degree of IBD symptoms [8]. Although biological therapies have been found to improve disease activity and QOL among patients with IBD, the cost-effectiveness of these agents is a growing concern in Japan because of increasing health care costs [15,16]. Our results on the difference in the frequency of biological therapy between patients with CD and those with UC were similar to the findings reported in a previous claims data-based study in Japan [17]. Therefore, the optimal use of biologics and the introduction of inexpensive biosimilars as substitutes for expensive biologics might substantially reduce the health care costs of IBD.

4. Materials and Methods

4.1. Setting and Participants

This study used data from a cross-sectional survey assessing QOL and socioeconomic status among patients with IBD in Japan. The study participants were extracted from a large database of more than two million candidates administered by the Cross Marketing Corporation, Tokyo, Japan, which specializes in questionnaire research. During the period of 14–21 February 2019, we used the Internet to survey patients with IBD in Japan. Respondents with CD and UC were regarded as having IBD on the basis of their own reports of a CD or UC diagnosis. All respondents were registered in the database before the start of the present study. The target sample sizes for the final analyses were

100 respondents with CD and 200 respondents with UC. These sample sizes were predetermined on the basis of the numbers of inhabitants of Japan with these diseases and the general response rate for web-based surveys. The survey continued until data had been collected from the predetermined numbers of respondents. The responses were anonymous, and personal information was not linked to patient data. The study was approved by the medical ethics committee of Niigata University of Health and Welfare (No. 18151; date: February 18 2019), and it was conducted in accordance with the principles in the 1964 Declaration of Helsinki and its later amendments. This article is based on a web-based survey and does not involve any interventions conducted on human subjects by any of the authors. Informed consent was obtained from all respondents.

4.2. Questionnaire

The survey questions covered several background/socioeconomic characteristics (current age, sex, marital status, and income) and disease and treatment status (age at diagnosis, history of previous surgery and hospitalization, current therapies and medications used to treat IBD, and eligibility for specific financial assistance). We used the five-dimension EQ-5D-5L instrument to assess the respondents' QOL. The EQ-5D-5L consists of five items, namely mobility, self-care, usual activities, pain/discomfort, and anxiety/depression, rated across five levels. The resulting generic preference-based measure reflects subjective values assigned to specific health-related outcomes ranging from -0.025 to 1, with 0 indicating death and 1 indicating perfect health; we call this score the utility weight [18,19]. To assess IBD treatment status, we included items on 5-aminoosalicylates, elemental diet, steroids, immunomodulators, cytaphereses, and biological therapy [20].

4.3. Statistical Analysis

Respondent characteristics are reported as percentages and medians (IQR). Statistical analyses were performed using Fisher's exact test for categorical variables. The two-sample Wilcoxon rank-sum test was used for comparisons of continuous variables and of the difference in EQ-5D-5L utility weight between financial assistance status groups. EQ-5D-5L utility weight is expressed as the median and IQR according to the Japanese value set. We calculated EQ-5D-5L utility weight by treatment patterns and summarized the distributions of responses on the different domains of the EQ-5D-5L separately for respondents with CD and UC. Data analyses were performed using Stata, Version 15 (College Station, TX, USA: StataCorp LP), and statistical significance was defined as p-values less than 0.05 for all analyses.

5. Conclusions

In conclusion, the present study shows that the revision of the law on intractable and rare diseases, which made patients with mild disease activity ineligible for financial assistance, has not had a negative influence on the QOL of patients with IBD in Japan. Our findings suggest that there are many more individuals with UC who are ineligible for specific financial assistance, compared with those with CD who are ineligible for this assistance. We also found that more than half of the patients with CD had received biological therapies. Further studies are required to clarify the relationships between patient outcomes and specific financial assistance status for intractable diseases other than IBD in Japan. Based on our findings, to appropriately inform Japan's government and health policy makers regarding continuing to make fair and cost-effective amendments to the law, more research may be needed to further investigate patient-reported outcomes for health economic evaluations for patients with IBD.

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Conflicts of Interest: The authors declare that they have no conflict of interest.

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