



Universiteit
Leiden
The Netherlands

Knowledge discovery from patient forums: gaining novel medical insights from patient experiences

Dirkson, A.R.

Citation

Dirkson, A. R. (2022, December 6). *Knowledge discovery from patient forums: gaining novel medical insights from patient experiences*. SIKS Dissertation Series. Retrieved from <https://hdl.handle.net/1887/3492655>

Version: Publisher's Version

License: [Licence agreement concerning inclusion of doctoral thesis in the Institutional Repository of the University of Leiden](#)

Downloaded from: <https://hdl.handle.net/1887/3492655>

Note: To cite this publication please use the final published version (if applicable).

11

ASSESSING SAMPLE BIAS

Edited from: **Anne Dirkson**, Dide den Hollander, Suzan Verberne, Ingrid Desar, Olga Husson, Winette T.A. van der Graaf, Astrid Oosten, An Reyners, Neeltje Steeghs, Wouter van Loon, Hans Gelderblom and Wessel Kraaij. Sample bias in online patient-reported outcomes of Gastrointestinal Stromal Tumor patients: Survey study.

Although representativeness of the online patient population is an often noted as a concern, studies in this field are limited. In this chapter, we investigate the sample bias of patient-centered social media in Dutch Gastrointestinal Stromal Tumor (GIST) patients through a population-based survey amongst 328 patients. We specifically examine peer-to-peer digital communication. We use logistic regression analysis to analyze clinical and demographic differences between forum users and non-users.

Eighteen percent of survey respondents report having contact with fellow patients via social media. 78% of forum users made use of GIST patient forums. We found no statistically significant differences for age, sex, socioeconomic status and time since diagnosis between forum users (n=46) and non-users (n=273). Patient forum users did differ significantly in (self-reported) treatment phase from non-users ($P = .001$). The odds of being on a patient forum were 2.8 times as high for a patient that is being monitored, compared with a patient that is considered cured. The odds of being on a patient forum were 1.9 times as high for patients that were on curative (adjuvant) treatment and 10 times as high for patients that were in the palliative phase compared to patients that were considered cured.. Forum users also reported a lower level of social functioning (84.8 of 100) than non-users (93.8 of 100) ($P = .008$).

In conclusion, forum users amongst Dutch GIST patients show no particular bias on the most important demographic variables of age, sex, socio-economic status and time since diagnosis. Nonetheless, our results warrant further investigation of the sample bias in other online patient populations as well as research into methods for bias mitigation

11.1. INTRODUCTION

Online patient forums provide patients with both emotional and informational support [324]. In recent years, social media has also been investigated as a potential complementary information source for patient generated health data, for example for pharmacovigilance [13, 55, 115, 171, 266]. The main advantage of social media is that it offers uncensored information [128] in large quantities [42]. Moreover, patients are more likely to share information with fellow patients than with their physicians [75]. Thus, social media may contain information that is not collected in clinical trials or reported in spontaneous reporting systems.

Post-market surveillance is necessary as clinical trials are of limited duration and suffer from sample bias; they often exclude elderly, patients with comorbidities, and pregnant women [274, 289]. Current post-market medication surveillance systems rely mostly on spontaneous reports of adverse events, medical literature, and observational databases. The majority of these spontaneous reports are made by health professionals. In fact, in the Dutch surveillance system Lareb, only 26.3% of all reports between 2010 and 2015 were made by patients [320].

Reliance on spontaneous reports alone results in a severe under-reporting of adverse drug responses (ADRs) [130]. According to work by Lopez-Gonzalez et al. [189], the under-reporting is associated with reporting of severe ADRs only, fear of ridicule for reporting suspected ADRs, lethargy, and indifference and complacency by professionals (i.e. the idea that only safe drugs are allowed onto the market). Although previous work has shown that the ADRs reported on social media are often less serious than those reported via official channels, they do affect the quality of life of the patient [13]. In fact, social media would be able to provide a more patient-centric view of which ADRs are most salient to patients on a day-to-day basis [197].

Yet, researchers as well as patients have expressed concern about sample bias on social media [13, 23, 32, 44, 58, 276, 287, 301]. Previous research on social media usage in general shows that young people, women, and people of a higher socioeconomic class are generally highly represented [34, 125, 126, 162]. Although there has been some work that shows that these differences persist over time [127, 162], other work indicates that some factors such as age are becoming less influential as the overall adoption of social media is growing. According to a recent report of the Pew Research Center, in 2021 72% of all Americans were using social media including 45% of adults over 65 [10].

Based on studies of the general population of social media users [34, 125–127, 162], it appears that those demographic groups that consume more medication (i.e. the elderly, people of low socioeconomic status, and patients with chronic conditions) are generally not highly represented on social media platforms [189]. However, it remains unclear whether these findings generalize to the specific case of online patient-to-patient communication.

Although there is a large literature base on patient communication forums and the extraction of adverse drug effects, to date the work on sample bias in online patient-to-patient communication is limited to two studies. Prior work on American breast cancer patients [122, 123] using action logs of forum activity in an artificial setting, has shown that users are relatively more likely to be Caucasian than African American. No other significant demographic differences were found between users and non-users. A more

comprehensive overview of literature on patient communication forums for GIST patients on broader topics than bias can be found in the recent work of den Hollander et al. [82] and our own prior work presented in Chapter 9.

Other studies addressed another bias that is relevant when mining social media for patient generated health data: so-called activity bias [323] or the fact that only some users actively post messages. We will use the term “passive users” for forum users that do not post messages and “active users” for forum users that do post messages. Passive users are also commonly referred to as “lurkers” in previous research. Amongst breast cancer patients, Han et al. [123] found that active users were more likely to be younger, Caucasian, living alone and have a greater information need than passive users. Another study [323] specifically compared passive to active community members to posters for breast cancer, arthritis and fibromyalgia and corroborated that posters are younger on average. They also found that active users had a longer disease history and a higher self-reported mental well-being than passive users. In this article, we do not compare active and passive users due to the small sample size.

As Baeza-Yates [16] noted “any remedy of bias starts with awareness of its existence” (p. 54). Thus, to provide a starting point for mitigating bias for the use of patient generated health data from social media in the future, we conducted a survey to investigate sample bias in social media usage amongst Gastrointestinal Stromal Tumor (GIST) patients in the Netherlands relative to the survey sample. GIST is a rare form of cancer which often has a long palliative care trajectory in which patients are treated with chronic, oral medication (tyrosine kinase inhibitors or TKIs) for many years. If caught early, GIST can be cured. Treatment with TKIs can improve survival for GIST patients both in adjuvant and palliative setting, but often also lead to adverse drug events [82]. Patient reports from social media may be especially valuable for rare disorders where patients are sparse and spread out geographically.

In this chapter, we investigated (1) what proportion of patients have contact with fellow patients on social media, (2) why patients abstain from engaging with online patient communities, and (3) to what extent there are significant demographic and clinical differences between those that use social media to converse with patients and those that do not. This study did not assess general social media usage but focused specifically on online communication with other patients. We defined social media as an online communication channel where information and messages are exchanged. When referring to ‘online patient communities’, we mean online groups on social media where the main purpose of the group is for (certain) patients (e.g., breast cancer patients) to communicate with one another. We use the term online patient communities and patient forums interchangeably.

Based on general social media, we hypothesized that forum users will differ in demographic factors including age, sex and socioeconomic status from non-users. We also hypothesized that forum users will differ in marital status and have a lower level of social functioning than non-users, in line with the social compensation model [199] (i.e. those who have less real life (offline) social support make more use of online digital communities). We also expect that forum users will differ from non-users in their treatment status and that their symptom burden may be higher while their global health scale may be lower. Overall, we expect patients with worse outcomes to be online more

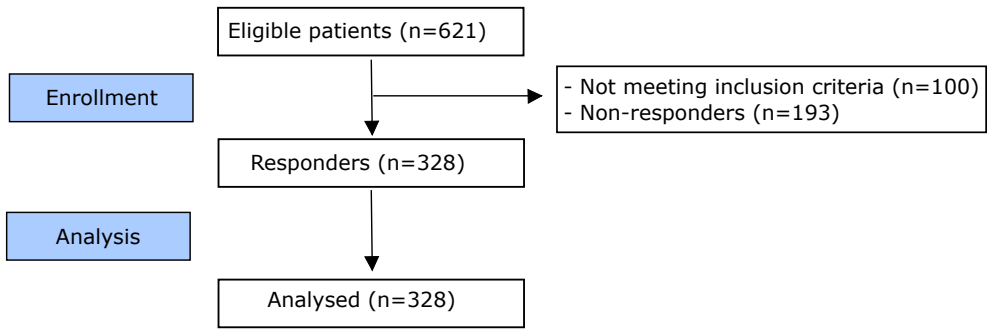


Figure 11.1: CONSORT flow diagram of response rate

often to ask for and receive advice than their peers with better health outcomes.

11.2. METHODS

11.2.1. STUDY DESIGN & PARTICIPANTS

A cross-sectional study was conducted among Dutch GIST patients aged ≥ 18 years at diagnosis, diagnosed between January 1, 2008 and December 31, 2018 in five GIST reference centers. Patients were selected from the Netherlands Cancer Registry (NCR), a population-based registry which is maintained by the Netherlands Comprehensive Cancer Organization (IKNL) and collects patient and tumor characteristics on all newly diagnosed cancer patients in the Netherlands. Exclusion criteria were: cognitive impairment or being too ill at time of the study, according to advice from the (former) treating specialist. Eligible patients were invited by their (ex-)treating physician by letter. Upon consent of the patient, including permission to link the survey data with National Cancer Registry (NCR) data, patients could complete the survey online or on paper upon request. Survey administration was done within the Patient Reported Outcomes Following Initial treatment and Long term Evaluation of Survivorship (PROFILES) registry [317], a data management system set up for the study of the physical and psycho-social impact of cancer and its treatment. PROFILES contains a large web-based component and is linked directly to clinical data from the NCR. Data was collected from September 2020 through June 2021. Ethical approval for the cross-sectional study was provided by the medical ethical committee of the Radboud University Medical Center (2019-5888). According to the Dutch law, approval of one ethical committee for questionnaire research is valid for all participating centers.

11.2.2. SURVEY

Participants completed questions regarding their participation in social media and online patient communities. These questions were developed by the authors. Respondents were asked whether and how patients use digital platforms to have contact with other patients. Possible answers (translated to English) were: “Generic social media (like Facebook or Twitter)”, “General forum or discussion group”, “Specific online patient forum”, “Other, namely” or “I do not use digital communication”. Patients were

provided with the following definition for a digital medium (translated to English): an online communication channel where information and messages are exchanged between participants. Patients were allowed to give multiple answers.

Respondents having contact with other patients online were subsequently asked about their motivations for going online and about their frequency of posting messages. Both questions were adapted from a Dutch survey designed by van Uden-Kraan et al. [323] in collaboration with medical experts and patient representatives. Survey respondents were allowed to provide multiple reasons for engaging with online forums as well as additional reasons in an open text field. Respondents that did not have contact with other patients on specific online patient forums were asked for their reasons for not doing so. Survey respondents were allowed to provide multiple reasons for abstaining from forum use as well as additional reasons in an open text field.

Demographic variables (i.e., age, sex, and socioeconomic status) as well as clinical variables (i.e., tumor type, tumor stage, time since diagnosis, and whether surgery and/or targeted therapy was part of treatment) of survey respondents were collected from the NCR. Survey respondents were additionally asked about their marital status, their current treatment phase, whether they presently use medication, their most recent medication (if any), and the presence of the fourteen possible comorbid conditions measured in the Charlson comorbidity index [61] (heart condition, stroke, high blood pressure, asthma, chronic bronchitis, COPD, diabetes, stomach ulcer, liver disorder, blood disorder, thyroid disease, depression, arthritis, and back pain). Patients were allowed to fill in “Other” for the most recent targeted medication received for treating GIST. This option was intended for new or experimental TKIs, but because patients frequently used this option for other type of medication such as antacids, it was removed for post hoc analysis.

The options patients can choose for self-reported treatment phase are defined as follows: “Cured and not monitored” (“I am cured and no longer need to be monitored”) refers to patients that are considered cured after surgery with or without adjuvant imatinib; “On curative treatment” (“I am being treated and can still be cured”) refers to patients that are undergoing adjuvant imatinib treatment; “Follow-up after treatment” (“I am not being treated but am only being monitored”) refers to patients that are being monitored after surgery with or without adjuvant imatinib and are not undergoing treatment at this time; “On palliative treatment” (“I am being treated but cannot be cured”) refers to patients undergoing palliative treatment with thyroid kinase inhibitors and “Best supportive care” (“I cannot be cured but am not being treated”) refers to patients that are palliative but are not receiving thyroid kinase inhibitors.

To measure overall health-related quality of life (HRQoL), social functioning and symptom burden, participants completed the EORTC QLQ-C30 version 3.0 [1, 106]. HRQoL was measured with 2 items on a scale of 1 to 7 (from “Very poor” to “Excellent”). Social functioning was measured with 2 items on a scale of 1 to 4 (1- “not at all”, 2- “a little”, 3- “quite a bit” and 4- “very much”). Eight symptom-specific items were evaluated on the same scale (i.e. dyspnea, pain, insomnia, appetite loss, nausea, constipation, diarrhea, fatigue). Each symptom was measured with 1 to 3 items. The scores for a single symptom from multiple items were averaged. Symptom burden was measured by averaging the eight symptom scales. For 17 respondents symptom burden was not assessed, as there was missing data for at least one symptom. All scales were linearly transformed to a “0-

100” scale in line with the standard scoring manual [100]. A higher score on global QoL or on the scales measuring the level of functioning translates to a higher level of functioning and QoL, whereas a higher score on the symptom scales means the patient experiences more complaints.

Any questions that were not previously validated were pre-tested with patients and changed according to their feedback (cognitive debriefing). The questionnaires cannot be shared due to copyright restrictions.

11.2.3. DATA ANALYSIS

Reasons for abstaining and engaging with online patient-to-patient communication were analyzed manually by the first author. Fifty-two cases (16%) contain missing data. As none of these cases are forum users, the data is not missing completely at random (MCAR). Since we do not observe any other patterns in the missing data that cannot be explained by the variables on which we have full information, the data is missing at random (MAR). Since the missing data occurs in multiple variables, we used Multivariate Imputation by Chained Equations (MICE)[186, 316] to impute these values, which is valid under assumption of MAR. We generated 20 imputed data sets that include all survey respondents (N=328).

We aimed to analyze whether there were statistically significant differences in demographic and clinical characteristics as well as quality of life measures between forum users and non-users. For each imputed data set, a multiple logistic regression analysis was performed with forum use as the dependent and demographic and clinical factors are independent variables (see Section 11.2.2). The effects of one variable on forum use are thus conditional on the other variables in the model. We report the average and standard deviation of the 20 imputed data sets, since this provides a more reliable result than a single run. We use the mean as the average for all variables except the *P*-value where we use the median [94].

For this analysis, the number of variables was restricted by the small size of the user population. We checked for multicollinearity using Variance Inflation Factor (VIF) tests. If the VIF value was larger than 3, we removed one of the collinear explanatory variables. In total, we removed two variables accordingly: the most recent medication, and whether the patient is on systemic treatment currently (“On systemic treatment currently”). Note that whether the patient received targeted therapy at some point in time (“Targeted therapy”) is included. Moreover, two categories of self-reported treatment phase, namely on palliative treatment and on best supportive care needed to be merged into one palliative category, as only one patient was receiving best supportive care. Benjamini-Hochberg correction [29] was used to adjust for multiple testing (controlling the false discovery rate or Type I errors at 0.05). Analyses were conducted using statsmodels (v 0.12.2) and scipy (v 1.4.1) in Python 3.7. Graphs were created with plotly (v 5.3.1) in Python.

11.3. RESULTS

11.3.1. PARTICIPANTS

In total, 328 GIST patients responded to the survey (response rate 64%). The median age of the participants was 67 years (range 28 to 91 years), and 53.8% were male (see Table

11.1). On average, they had been diagnosed with GIST for 5 years ranging from 1 to 12 years since diagnosis. One hundred and sixty-two participants (49%) are in follow-up after treatment with curative intent, 61 (19%) were considered cured and are not in follow-up, and 100 receive systematic treatment, either with curative (34) or palliative intent (67). One patient received best supportive care only.

Nine of the patients did not answer the question about forum usage and their forum use is thus unknown. Consequently, the sum of the reported numbers under forum usage (Y and N) does not equal the number reported for all respondents. The percentages were calculated based on the counts per category, i.e., 55% of non-users are male (150 of the 273 non-users).

		FORUM USER*		
		ALL	N	Y
Count		328	273	46
Age	Median (Range)	67 (28-91)	68 (28- 91)	65 (47 – 83)
Sex	Count (%)			
– Male		174 (53%)	150 (55%)	21 (45%)
– Female		154 (47%)	123 (45%)	25 (54%)
Socio-economic status	Count (%)			
– Low (1-3)		90 (28%)	74 (27%)	13 (28%)
– Intermediate (4-7)		132 (40%)	113 (41%)	16 (35%)
– High (8-10)		106 (32%)	86 (32%)	17 (37%)
Marital status	Count (%)			
– Married or living together		246 (75%)	202 (74%)	38 (83%)
– Single		79 (24%)	68 (25%)	8 (17%)
– Missing		4 (1%)	3 (1%)	0
Time since diagnosis (in years)	Median (Range)	5 (1- 12)	5 (1-12)	5 (2 -11)
Tumor stage	Count (%)			
– I		121 (37%)	109 (40%)	8 (17%)
– II		61 (19%)	51 (19%)	10 (22%)
– III		66 (20%)	53 (19%)	10 (22%)
– IV		55 (17%)	38 (14%)	16 (35%)
– Missing		25 (8%)	22 (8%)	2 (4%)
Surgery	Count (%)			
– Yes		287 (88%)	244 (89%)	36 (78%)
– No		41 (12%)	29 (11%)	10 (22%)
Targeted therapy	Count (%)			
– Yes		214 (65%)	170 (62%)	39 (85%)
– No		114 (35%)	103 (38%)	7 (15%)
Self-reported current treatment status	Count (%)			
– Cured and not monitored		61 (19%)	56 (21%)	2 (4%)
– On curative treatment		34 (10%)	31 (11%)	3 (7%)
– Follow-up after treatment		162 (49%)	139 (51%)	19 (41%)

– On palliative treatment		66 (20%)	42 (15%)	22 (48%)
– Best supportive care		1 (0.3%)	1 (0.4%)	0
– Missing		4 (1%)	4 (1%)	0
On systemic treatment currently	Count (%)			
– Yes		208 (63%) **	181 (66%)	25 (54%)
– No		108 (33%)	83 (30%)	21 (46%)
– Missing		12 (4%)	9 (3%)	0
Most recent medication	Count (%)			
– Imatinib		178 (54%)	140 (51%)	31 (67%)
– Sunitinib		9 (3%)	7 (3%)	2 (4%)
– Regorafenib		6 (2%)	4 (1%)	2 (4%)
– Other		15 (5%)	8 (3%)	4 (9%)
– No therapy		114 (35%)	103 (38%)	7 (15%)
– Missing		14 (4%)	11 (4%)	0
Number of comorbid conditions	Count (%)			
– 0		109 (33%)	92 (34%)	14 (30%)
– 1		71 (22%)	59 (22%)	10 (22%)
– 2 +		146 (45%)	120 (44%)	22 (48%)
– Missing		2 (0.6%)	2 (0.7%)	0
Global health scale (0-100)	Mean (SD)	78.6 (18.1)	79.0 (17.7)	76.1 (20.1)
Symptom burden (0-100)	Mean (SD)	12.1 (12.8)	11.4 (12.6)	15.6 (13.0)
Social functioning (0-100)	Mean (SD)	92.4 (18.9)	93.8 (17.1)	84.8 (26.0)

Table 11.1: Demographic characteristics of survey respondents. *Nine participants did not answer this question. **It appears patients that are currently being monitored may have misunderstood this question, inflating the number of patients that are currently on targeted medication for GIST

11.3.2. SOCIAL MEDIA USAGE

As shown in Table 11.2, 81% of GIST patients do not have contact with other patients via any social media platform. We distinguished between specific social media, such as patient forums, and general social media such as Twitter or Facebook¹. Of the patients to communicate with peers via social media, the majority (46 of 59) make use of specific online patient forums focused on GIST. Only 6 respondents make use of general social media platforms to communicate with other GIST patients and only 7 use more general cancer-related forums or discussion groups for this purpose.

11.3.3. REASONS FOR ABSTAINING FROM ONLINE COMMUNICATION WITH PEERS

Table 11.3 shows the reasons the 265 non-users report for not using any digital medium to communicate with fellow patients. Patients were allowed to report multiple reasons.

¹Although it is possible for patient communities to exist as groups on general social media platforms (in fact: the biggest GIST forum is a Facebook group), general social media refers to communication with peers outside of GIST-specific communities on these general social media platforms.

Which of the following digital media do you use to have contact with other patients? (Indicate all that apply)	Frequency
General social media (like Facebook or Twitter)	6 (2%)
General cancer-related forum or discussion group	7 (2%)
GIST specific online patient forum	46 (14%)
Any social medium	59 (18%)
None or via another medium than social media	265 (81%)
Missing	4 (1%)
TOTAL	328

Table 11.2: Descriptive statistics for usage of social media to have contact with other patients. Respondents can give multiple answers to this question.

Twenty patients did not fill in the question. The most common reason reported for abstaining from using a digital medium to communicate with peers was that they felt no need to do so (31.8%), followed by finding it too confronting (13.5%) and not knowing where to find online communities (12.2%). Only eight participants reported not using social media to communicate with other patients because they lack the skills or access to do so.

11.3.4. REASONS FOR ENGAGING WITH PATIENT FORUMS

Survey respondents most frequently used patient forums to communicate with other patients. The number of survey respondents that use other online platforms was too small to analyze how they compare to non-users. Thus, we will focus on analyzing the sample bias of GIST-specific patient forums. Hereafter, when we refer to ‘forum users we mean users of GIST-specific patient forums.

Table 11.4 shows the reasons users reported for engaging with a disease-specific patient forum. The most prevalent reasons were having a question on or having heard new information about their illness (both 40%) and being curious how the other members are doing (36%). Another prevalent trigger was experiencing new symptoms (31%).

11.3.5. CHARACTERISTICS OF THE PATIENT FORUM USERS

In total, 85.8% (273) of the participants were not making use of specialized GIST patient forums (see Table 1). The difference in model fit between the multiple logistic regression model and the null model was found to be statistically significant in all 20 imputed data sets ($LR = 47.0 \pm 1.48$, $df = 20$, $P < .001 \pm 0.0004$). Likelihood ratio tests between the full model and the full model without the variable were used to test the significance of individual variables.

Table 11.5 reports the average results of twenty runs of multiple logistic regression models of which factors influence forum use. Our analysis shows that self-reported treatment status differs significantly between forum users and non-users for each run ($LR = 10.6$, $P = .001$). The odds of being on a patient forum were 2.8 times as high for a patient that is being monitored, compared with a patient that is considered cured. The odds of being on a patient forum were 1.9 times as high for patients that were on curative

Self-reported reason	Frequency
Feel no need to communicate (digitally) with other patients	78 (29.4%)
I find it too confronting or burdensome	33 (12.5%)
I would not know where to find online communities	30 (11.3%)
There are too many negative comments	26 (9.8%)
I do not have the time	23 (8.7%)
The information shared is useless or less valuable	20 (7.5%)
I communicate with enough patients personally or via another non-digital medium	18 (6.8%)
I do not use social media, lack a computer or digital skills or do not like obtaining information digitally	8 (3.0%)
I obtain sufficient information via my medical specialist or searching online	7 (2.6%)
I no longer have symptoms or do not like to consider myself a patient	5 (1.9%)
I have privacy concerns	3 (1.1%)
They do not exist in my language	2 (0.8%)
No particular reason	1 (0.4%)
Missing	20 (7.5%)'
Total number of users that do not use any digital communication with other patients	265

Table 11.3: The reasons non-users report for not using social media to communicate with other patients. Multiple answers were possible.

Self-reported reason	Frequency
When I have a question about my illness	18 (40%)
When I have heard new information about my illness	18 (40%)
When I am curious how other members are doing	16 (36%)
When I get new symptoms	14 (31%)
When I have a lot of symptoms	6 (13%)
When I feel insecure	5 (11%)
Before making a medical choice	4 (9%)
For the company	4 (9%)
Because other members expect me to be there	2 (4%)
When I feel lonely	1 (2%)
It is part of my daily routine	1 (2%)
I never use the forum anymore	1 (2%)
Total number of users that do communicate via patient forums with other patients	45

Table 11.4: The reasons users report for visiting the patient forum. Multiple answers were possible

(adjuvant) treatment and 10 times as high for patients that were in the palliative phase compared to patients that were considered cured.

We did not find significant differences between forum users and non-users for other disease-related characteristics when they were adjusted for covariates. We also did not find significant differences in key demographic variables such as age, sex, socioeconomic status, and marital status. Yet, we did find a significant difference in the level of social functioning in seven of twenty runs ($LR = 6.8, P = .008$). Forum users on average reported a lower level of social functioning than non-users (84.8 vs 93.8 of 100). These scores were normalized according to the scoring manual[100]. Converting the normalized values back to the mean raw score gives a 1.19 for forum users and a 1.46 for non-users, where 1 translates to the highest possible value for self-reported social functioning on the survey items.

	COEF	SE	df	LR	P	ODDS RATIO		
						5%	95%	
Intercept	-2.795 (0.541)	2.081 (0.034)	-	-	-	-	-	-
Age	-0.020 (0.004)	0.018 (0.0002)	1	1.318 (0.535)	0.264 (0.100)	0.945 (0.004)	0.980 (0.004)	1.015 (0.004)
Sex	0.622 (0.039)	0.371 (0.004)	1	2.858 (0.348)	0.088 (0.021)	0.900 (0.034)	1.863 (0.072)	3.860 (0.161)
Socio-economic status	-	-	2	1.365 (0.485)	0.249 (0.081)	-	-	-
– Low (1-3)	-	-	-	-	-	-	-	-
– Intermediate (4-7)	-0.386 (0.102)	0.441 (0.006)	-	-	-	0.288 (0.027)	0.683 (0.066)	1.622 (0.163)
– High (8-10)	0.048 (0.101)	0.440 (0.005)	-	-	-	0.445 (0.041)	1.055 (0.102)	2.499 (0.255)
Marital status	-0.321 (0.085)	0.468 (0.006)	1	0.517 (0.251)	0.467 (0.114)	0.291 (0.038)	0.728 (0.062)	1.820 (0.062)
Time since diagnosis	0.016 (0.019)	0.073 (0.001)	1	0.118 (0.159)	0.847 (0.152)	0.880 (0.018)	1.017 (0.019)	1.174 (0.022)
Tumor type	0.567 (0.063)	0.377 (0.003)	1	2.292 (0.519)	0.129 (0.042)	0.843 (0.054)	1.766 (0.112)	3.699 (0.237)
Tumor stage	-	-	3	2.602 (0.920)	0.116 (0.071)	-	-	-
– I	-	-	-	-	-	-	-	-
– II	0.506 (0.126)	0.547 (0.009)	-	-	-	0.572 (0.072)	1.671 (0.211)	4.886 (0.632)
– III	0.212 (0.214)	0.6262 (0.013)	-	-	-	0.372 (0.090)	1.266 (0.290)	4.309 (0.942)
– IV	0.863 (0.170)	0.663 (0.013)	-	-	-	0.655 (0.119)	2.405 (0.433)	8.834 (1.613)
Surgery	0.039 (0.124)	0.574 (0.012)	1	0.053 (0.103)	0.887 (0.103)	0.339 (0.036)	1.048 (0.123)	3.237 (0.421)
Targeted therapy	0.120 (0.099)	0.573 (0.010)	1	0.073 (0.080)	0.826 (0.097)	0.368 (0.032)	1.133 (0.111)	3.490 (0.383)
Self-reported current treatment status	-	-	3	10.673 (1.096)	0.001** (0.0006)	-	-	-
– Cured and not monitored	-	-	-	-	-	-	-	-
– On curative treatment	0.590 (0.264)	1.071 (0.050)	-	-	-	0.225 (0.040)	1.863 (0.446)	15.559 (4.651)

– Follow-up after treatment	1.026 (0.262)	0.865 (0.061)	-	-	0.519 (0.080)	2.881 (0.685)	16.179 (5.095)
– Palliative	2.288 (0.232)	0.965 (0.057)	-	-	1.503 (0.229)	10.111 (2.208)	68.678 (19.838)
Number of comorbid conditions	-	-	2	0.419 (0.259)	0.532 (0.144)	-	-
– 0	-	-	-	-	-	-	-
– 1	0.275 (0.108)	0.497 (0.007)	-	-	0.501 (0.057)	1.325 (0.143)	3.505 (0.362)
– 2 +	0.207 (0.077)	0.451 (0.005)	-	-	0.510 (0.036)	1.234 (0.093)	2.987 (0.240)
Global health scale/ QoL	0.029 (0.002)	0.014 (0.0001)	1	4.382 (0.686)	0.036 (0.016)	1.001 (0.002)	1.039 (0.002)
Symptom burden	-0.0003 (0.005)	0.018 (0.0004)	1	0.088 (0.096)	0.830 (0.114)	0.964 (0.006)	1.000 (0.005)
Social functioning	-0.025 (0.002)	0.009 (0.0002)	1	6.865 (0.900)	0.008* (0.005)	0.958 (0.002)	0.975 (0.001)

Table 11.5: Average results (with SD) of a logistic regression of demographic and clinical characteristics of patient forum users and non-users using MICE with 20 runs. For the p-value, the median is reported. *Significant after Benjamini-Hochberg correction in some runs **Significant after Benjamini-Hochberg correction in all runs.

11.4. DISCUSSION

11.4.1. SUMMARY OF FINDINGS

A survey was conducted amongst 328 GIST patients in the Netherlands. Our results show that the majority of survey respondents do not have contact with other patients via social media. They indicate a large heterogeneity of reasons of why they abstain from doing so with the most prevalent being they feel no need, find it too confronting, or do not know where to find such online communities. Of the minority that do use social media for this purpose, most use disease-specific patient forums. The most prevalent reasons for accessing a patient forum are i) having a question about their illness, ii) having heard new information, iii) experiencing new symptoms, or iv) wondering how other patients are doing. Patient forum users differ significantly in their (self-reported) treatment phase from non-users. Patients in the palliative phase are 10 times more likely to be forum users than patients that are cured. Patients that are monitored approximately 3 times and patients undergoing curative treatment approximately 2 times more likely to be users than cured patients. For seven of the twenty data imputations, forum users also have a significantly lower level of social functioning.

11.4.2. COMPARISON WITH EXISTING LITERATURE

In contrast to the general population of social media users, patient forum users do not appear to differ in age, sex and socioeconomic status from non-users. On the one hand,

this may be an effect of the increasingly more widespread adoption of social media. This idea is supported by the small number of patients that indicate they lack the skills or access to be on social media (3.3%). On the other hand, it is also possible that there is less demographic bias on patient forums than in general social media. This may be related to the widely different goals that users have with their participation. Although a feeling of community and social support may overlap, patients report motivations such as questions around their illness, and the experience of new symptoms that normal social media users are unlikely to share.

Prior work [122] on forum usage amongst breast cancer patients did not find significant differences between forum users and non-users in terms of clinical characteristics, i.e. stage of cancer and quality of life. We similarly did not find any significant differences for these characteristics, although we did find significant differences for clinical characteristics that prior work did not investigate i.e. treatment phase. Prior work also found that amongst breast cancer patients, non-users and passive users had greater offline social support than posters. Their results supported the social compensation model [199] i.e. those who have less real life (offline) social support use and engage online with digital communities. The lower offline support of forum users compared to non-users in our data also supports this theory. However, passive users appear to have a lower offline support than active users amongst GIST patients. This would support the competing theory: the social engagement model [163] i.e. those that have more social resources will use and benefit from online social communities more. Consequently, our data offers support for the social compensation model for those who use a forum (i.e. those with less real-life support are more likely to be using a forum) and social engagement theory for those who actually actively engage with the forum community (i.e. users with sufficient social resources will be active and benefit more). Demographic differences in terms of age, marital status (i.e. living alone or not) and disease duration between passive and active users that were found in previous work were not evident from our data.

11.4.3. LIMITATIONS

First and foremost, we only studied a specific patient population in a single country and thus further research is needed to elucidate to what extent our results are generalizable. Patients in other countries may have lower digital access or skills or may not wish to use social media for patient-to-patient communication for other reasons (e.g. other privacy laws or country-specific customs).

Our choice of GIST patients as a target population may also impact to which disorders our results generalize to. Patients with GIST have a median age of mid 60s [285], meaning that it is on average an older population than the general population that is often studied for social media usage. Our results may consequently also generalize better to conditions that are prevalent in an older population. GIST is also characterized by a long palliative phase in which patients receive treatment. Thus, our results may also generalize better to conditions that similarly have a long treatment duration (e.g. metastasized breast cancer). As GIST is a rare type of cancer, our results may also generalize better to rare than common conditions. Further research into other patient populations should be able to provide more insight into the differences in forum usage between rare and common conditions. The fact that GIST is a rare condition makes it an interesting first case. Patient generated

health data from social media are particularly promising for rare conditions due to their dispersed patient communities and the scarcity of research [15].

A second limitation of this study is the small sample size. Amongst the 328 respondents, only 46 indicate that they use patient forums. Nonetheless, given the low incidence of GIST at 12.7 per million [113], this is a substantial number of participants. A third limitation is the sample bias of the survey itself. There may be two underlying factors, namely selection bias and responder bias. Patients who were too ill or had cognitive impairment were excluded, leading to selection bias. A non-responder analysis was conducted using the database of the Netherlands Cancer Registry to assess the extent of the responder bias. After correcting for multiple testing, no significant differences were found in terms of age, sex, socioeconomic status, time since diagnosis, tumor stage, and primary treatment between respondents and non-respondents. Moreover, it was possible to fill in the survey on paper, which prevents the exclusion of less digitally adept patients on these grounds.

11.4.4. FUTURE WORK AND RECOMMENDATIONS

Based on this work, a number of recommendations can be made. First, out of the possible digital resources that can be used to source complementary real-world evidence, patient forums should be preferred over other social media. Our results reveal that GIST patients strongly prefer disease-specific patient forums over general social media for communicating with fellow patients. Yet, most research in this field currently focuses on general social media such as Twitter [171, 266]. Our results are in line with previous work that estimates ADR reports to be more prevalent in patient forums than on Twitter [114].

Although we find that there is sample bias in patient forum users and thus the sample is not wholly representative for the patient population, sample bias is also a concern for other sources of patient reports. Understanding which patients are over- and under-represented on online forums is the first step to using online patient reports as a complementary resource, for instance for pharmacovigilance. For pharmacovigilance specifically, it is not of great concern that patients that are considered cured and not undergoing treatment currently are under-represented. Future work on comparing the sample bias of clinical trials to that of online patient forums would be beneficial to further explore its complementary value in detail. It would also be valuable to gain more insight into the different types of forum users.

Secondly, it may be beneficial to create awareness amongst medical professionals that patients are more likely to search for information in online patient communities when they have questions, have been given new information, or have new symptoms. Medical professionals could try to aid patients in their information needs by pointing them towards such resources in these cases. This may also take away the barrier mentioned by patients that they do not know where to find such online communities.

Thirdly, future work into the sample bias of patient forums for other patient populations is necessary as this study was limited to a single population in a single country. Nonetheless, our work is a stepping stone towards dissuading the concerns that researchers have expressed regarding the sample bias of social media [13, 23, 32, 44, 58, 276, 287, 301] by unravelling on which characteristics users differ significantly from the overall patient population. Future work could also investigate how compensatory

measures can be implemented to statistically correct for sample bias. As these factors may not be known for the participants of a forum, it would also be worthwhile to consider to what extent correcting for sample bias is possible without this information.

11.5. CONCLUSION

In this chapter, we investigated how representative participants in patient forums are for the general patient population by conducting a survey amongst GIST patients in the Netherlands. We found statistically significant differences in terms of treatment phase and offline social support between forum users and non-users. The consequent over- and under-representation of certain types of patients should be considered when sourcing patient forums for patient generated health data. As our study was limited to a single patient population, a further investigation of sample and activity bias in other online patient populations is warranted as well as research into methods for bias mitigation. Sample bias is inherent to any information source and only through awareness of these biases can these resources be used as a source for complementary real-world evidence in the future.