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REGULAR ARTICLE

Illness Perceptions in Chronic Lymphocytic Leukemia: Testing Leventhal's Self-regulatory Model

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Abstract

Background Leventhal's Self-regulatory Model proposes that somatic characteristics of a health threat (e.g., symptom severity), and prior experience with the threat (e.g., unsuccessful treatment), are determinants of illness perceptions. Chronic lymphocytic leukemia (CLL) is appropriate for test of these postulates, having three phases differing in symptom severity and prior treatment experiences: indolent disease requiring no treatment (active surveillance; AS), symptomatic disease requiring a first treatment (FT), and highly symptomatic disease in those who have relapsed and/or failed to respond to prior treatments (relapsed/refractory; RR).

Purpose To test symptom severity and prior treatment experiences as determinants of illness perceptions, illness perceptions were characterized and contrasted between CLL groups.

Methods Three hundred and thirty CLL patients (AS, n = 100; FT, n = 78; RR, n = 152) provided illness perception data on one occasion during a surveillance visit (AS) or prior to beginning treatment (FT, RR).

Results Analysis of variance with planned comparisons revealed that consequences, identity, and concern were least favorable among RR patients, followed by FT, then AS (ps < .01). AS patients endorsed the lowest levels of coherence (ps < .01), and the most chronic illness timeline (ps < .01). FT patients endorsed the highest levels of personal and treatment control (ps < .01).

Conclusions Data provide preliminary empirical support for Self-regulatory Model postulates that symptom severity and prior disease experiences influence illness perceptions. Unique knowledge needs for AS patients and elevated psychological/physical symptoms for later-stage CLL patients may warrant clinical attention.

Keywords Illness perceptions • Chronic lymphocytic leukemia • Active surveillance • Relapsed refractory disease

Introduction

A goal of health psychology is to understand how individual differences in responses (e.g., behavioral, psychological) to chronic illness arise. Leventhal's Self-regulatory Model of Illness Behavior [1] (Fig. 1) is widely used and highlights mental representations of health threats, or *illness perceptions*, as central to how individuals understand, cope with, and ultimately respond to disease. According to the model, illness perceptions are generated in response to health threats, such as a new physical symptom or disease diagnosis, and reflect emotional responses to and beliefs about the threat (e.g., consequences, controllability, chronicity) that guide coping and influence psychological and physical health outcomes.

Limited empirical research has focused on better understanding *determinants* of illness perceptions [2, 3]. That is, what sources of information do individuals use when forming their perception of a symptom or illness? Although complex, theoretical work of Leventhal et al. [1, 4, 5] highlighted factors such as somatic characteristics of the threat or illness (e.g., symptom severity) and

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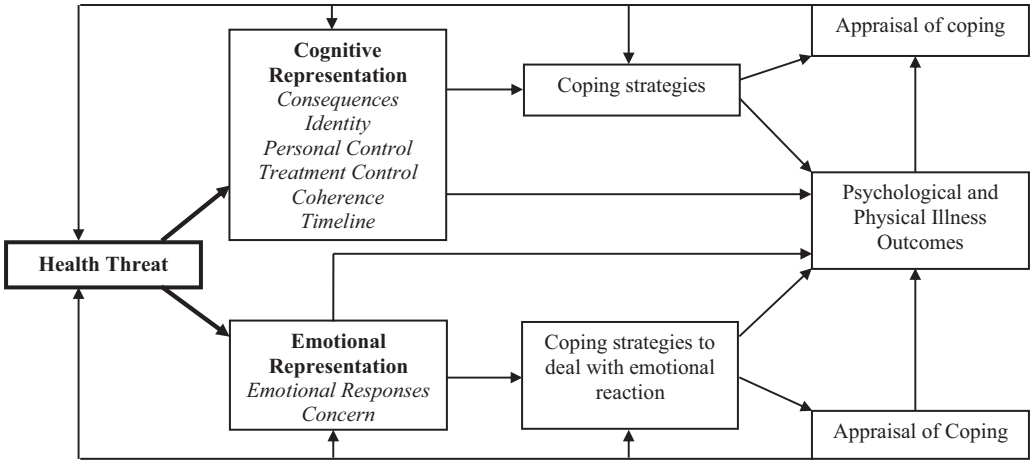

Fig. 1. Self-regulatory Model of Illness Behavior (adapted from Hagger and Orbell [46]). Bold emphasis is placed on the pathway of interest for the present study.

information acquired through prior experience with the threat or illness (e.g., receiving treatment) as central to the formation of illness perceptions. For example, severe abdominal pain would theoretically be perceived as more threatening than a stomachache. Similarly, an individual with chronic abdominal pain, who has received a diagnosis and knows it can be controlled by treatment, would, according to the model, perceive the symptom differently than when it occurred for the first time.

Although direct empirical tests of these postulates have not been a focus of prior research, available illness perception literature (e.g., that documenting relationships between symptom severity measures and illness perceptions) can provide insight into the relationship between theorized determinants and illness perceptions. Regarding symptom severity, Pagels et al. [6] compared illness perceptions between patients with mild-to-moderate (Stages 2–3) and severe (Stages 4–5) chronic kidney disease, finding that, consistent with self-regulatory theory, later-stage patients with greater symptom severity perceived more consequences, experienced more severe symptoms (identity), and endorsed more negative emotional responses than those with mild-to-moderate disease. Single group designs in cancer, osteoarthritis, irritable bowel syndrome, chronic pain, and overactive bladder have corroborated these findings, with greater symptom severity being associated with poorer scores on identity, consequences, emotional responses, and concern, as well as personal and treatment control [7–11].

In contrast, perceptions of the timeline of one's illness, such as being acute versus chronic, have been predominantly unrelated to symptom severity [7, 8, 12–14], and, not surprisingly, stable across time for those with chronic (i.e., permanent) illnesses [15–20]. Exceptions have been observed, however, as in the case of asthma in which some patients adopt a chronic illness model only when symptoms are elevated [21], suggesting that relationships between symptom severity and timeline may vary by disease group. Similar to timeline perceptions, the appraisal of one's understanding of his/her illness, or coherence, bears little, if any, relationship to symptom severity [6, 8, 13, 14]. Instead, longitudinal studies have observed improvements in coherence with the passage of time and/or receipt of treatment [18, 20, 22, 23], that is, the accumulation of experiences with the illness. As with symptom severity, prior illness experience has not been tested as a determinant of illness perceptions as the model would suggest.

Empirical tests of fundamental postulates of the self-regulatory model are needed and would be clinically useful. Providing empirical support for theorized determinants of illness perceptions may assist in the identification of those vulnerable to developing maladaptive perceptions of their illness and, by extension, may provide a window to addressing problems posed by the illness such as psychological distress or poor treatment adherence. As such, the present study tests the relationship between symptom severity and prior illness experience to illness perceptions. Chronic lymphocytic leukemia (CLL) provided an advantageous paradigm for these tests, having three subgroups distinguished by their differences in symptom severity and treatment exposure. One group consists of patients with asymptomatic or minimally symptomatic early-stage disease who are only monitored (i.e., active surveillance; AS) until symptoms progress sufficiently to require treatment. The duration of surveillance can range from months to years, with approximately 30% of patients never requiring treatment [24]. The second group consists of intermediate- to high-risk patients who are diagnosed with or have progressed and have significant physical symptoms (e.g., fatigue, fever, night sweats, abdominal pain, enlarged lymph nodes) and signs (e.g., enlarged spleen and/or liver, low red blood cell

and/or platelet counts) and require initiation of a first CLL treatment (i.e., first treatment; FT) [25]. These patients have greater symptom severity relative to AS patients and are in the midst of initiating treatment (e.g., diagnostics, education, treatment selection) for their illness. The third group consists of patients with significant symptoms/signs who, having initiated a first treatment, either failed to respond (treatment refractory), or responded for a time, but eventually relapsed. These relapsed/refractory (RR) patients experience symptoms similar to or more severe than those initiating a first treatment [26] and have had at least one to several cycles of significant symptoms, treatment, relapse, and retreatment [27, 28]. In sum, three CLL patient groups vary in symptom severity and prior experience with the illness, but it is unknown if variations in these theorized determinants result in differing illness perceptions as the model would suggest.

We tested three hypotheses. First, we hypothesized that identity, consequences, emotional responses, concern, and personal control would covary with symptom severity, such that AS patients report the least threatening perception of CLL along these dimensions, followed by FT, and then RR. Second, we hypothesized that among those initiating treatment (FT and RR groups), treatment control will be higher among those with less severe symptoms, such that FT endorse higher treatment control than RR. AS patients were not administered the treatment control item. Third, we hypothesized that coherence scores will be higher among those with more prior "experience" with CLL (e.g., interaction with medical system, receipt of treatment), such that AS patients report the lowest scores on this dimension, followed by FT, and then RR. Finally, with limited evidence linking symptom severity to timeline perceptions and their stability across time in those with chronic illness [7, 8, 12–20], we did not anticipate group differences for this dimension.

Methods

Design and Participants

A cross-sectional design was used. Three hundred and thirty patients with CLL participated from three intact groups: active surveillance (AS; n = 100), initiating a first treatment (FT; n = 78), and initiating treatment for relapsed/refractory disease (RR; n = 152). Overall, the majority was male (63%), and Caucasian (98%), with a mean age of 62.2 years. Most were partnered (86%) and reported some college education or beyond (70%), with 43.8% reporting an annual household income exceeding $100,000.

Procedures

The Institutional Review Board of a university-affiliated, National Cancer Institute-designated comprehensive cancer center granted ethical approval for all procedures. Eligible patients were adults 18 or older with a physician-confirmed diagnosis of CLL and an Eastern Cooperative Oncology Group performance status of 0–2. Medical inclusion criteria (e.g., normal organ function) were required for patients beginning a treatment. Patients with systemic, life-threatening medical comorbidities, recent major surgery or medical procedures, active or secondary cancers, or severe psychiatric illness were excluded.

AS patients were recruited during routine surveillance appointments, with 126 consented. Of them, 3 were subsequently found to be ineligible, 11 did not participate due to loss of interest, and 12 did not provide illness perception data, resulting in 100 AS participants. Each completed a packet of self-report questionnaires over the telephone with research staff, as described previously [29].

Patients about to receive their first or subsequent treatment were screened for entry into investigational trials (NCT01589302, NCT02296918, NCT02427451, and NCT02518555) of targeted CLL therapies. As they were enrolled, patients completed questionnaire assessments immediately or within the next 2 weeks prior to treatment. A total of 261 were consented with 31 later excluded, resulting in 230 patients initiating a first or subsequent treatment.

Measure

Illness perceptions

The Brief Illness Perception Questionnaire (BIPQ [30]) is a nine-item self-report measure used to assess mental representations of illness. The BIPQ uses a single-item scale approach to assess perceptions on a continuous linear 0- to 10-point scale. Five items assess cognitive illness representations: consequences ("How much does your illness affect your life?"), timeline ("How long do you think your illness will last?"), personal control ("How much control do you feel you have over your illness?"), treatment control ("How much do you think your treatment can help your illness?"), and identity ("How much do you experience symptoms from your illness?"). Two items assess emotional representation of illness: concern ("How concerned are you about your illness?") and emotional responses ("How much does your illness affect you emotionally?"). One item assesses illness coherence, a metacognitive dimension reflecting how well an individual feels they understand their illness. As treatment was not indicated for AS patients at the time of data collection, the treatment control dimension for this group was excluded. Six-week

test–retest reliability for the items ranges from 0.42 to 0.75 [30]. Concurrent validity with relevant psychological and biological measures, discriminant validity across illnesses, and predictive validity in different disease groups have been reported [30, 31].

Analytic strategy

First, sociodemographic differences between groups were tested using one-way analysis of variance (ANOVA) for continuous variables (i.e., age) and chi-square tests for nominal variables (i.e., gender, marital status, education level, and household income). Intercorrelations of the illness perception items are reported as well as means, *SD*, and ranges of all items. Primary analyses testing for group differences in illness perceptions used one-way ANOVA or analysis of covariance as appropriate. Normality and homogeneity of group variances were assessed. Skewed data were log-transformed, and Welch's ANOVAs were conducted for heteroscedastic variables.

For the six illness perception dimensions for which group differences were hypothesized (i.e., consequences, identity, concern, emotional responses, coherence, and personal control), a priori planned comparisons were used. The first compared AS with FT, and the second compared FT with RR. As the treatment control item was administered to FT and RR groups only, this comparison was made using an independent samples *t*-test. As there was no a priori expectation of group differences for the timeline dimension, ANOVA followed by the Games–Howell post hoc procedure [32, 33] was used. As timeline comparisons were done post hoc, a Bonferroni corrected *p*-value of .017 (.05/3) was also established. All analyses were performed using IBM SPSS 20.0 for Windows.

We considered sociodemographic characteristics (age, gender, marital status, education level, and household income) as control variables in group difference analyses. Race was not considered due to lack of variability in the sample. Potential control variables were correlated with each illness perception item, collapsing across groups. Variables significantly associated with an illness perception dimension were included in the respective analyses.

Results

Preliminary, Descriptive, and Correlational Data

Sociodemographic and descriptive characteristics by CLL group are displayed in Table 1 along with results of the ANOVA tests contrasting sociodemographic information between groups. As shown, group differences were found for age, $F(2, 323) = 6.615$, $p = .002$, and gender, $\chi^2(2) = 7.69$, $p = .021$, Cramer's $V = .15$, with the RR group being significantly older and having a higher percentage of males in comparison to the other groups.

Distributions for all illness perception dimensions were non-normal; thus, analyses were conducted on log-transformed variables. Results did not differ on the basis of transformation, so untransformed results are presented for ease of interpretation. All dimensions met assumptions for homogeneity of variance between groups except for identity, coherence, and timeline. For these exceptions, group differences were confirmed with Welch's test. Regarding potential covariates, age

Table 1 Sociodemographic and descriptive characteristics by chronic lymphocytic leukemia treatment group ($N = 330$)

	Active surveillance ($n = 100$)	First treatment ($n = 78$)	Relapsed/refractory ($n = 152$)
Age (years), *M* (*SD*)	61.88 (8.33)[a]	59.03 (10.38)[a]	64.08 (10.79)[b]
Gender (% male)	50 (50%)[a]	47 (60%)[a]	107 (70%)[b]
Married (yes)	84 (84%)[a]	66 (85%)[a]	129 (85%)[a]
Race			
Caucasian	100 (100%)	76 (97%)	147 (97%)
African American	0 (0%)	1 (1%)	5 (3%)
Education			
High school/technical school or below	21 (21%)	21 (27%)	44 (29%)
Some college/college graduate	40 (40%)	32 (41%)	58 (38%)
Some graduate school/graduate degree	30 (30%)	25 (32%)	46 (30%)
Household income (k)			
≤100	41 (41%)	39 (50%)	79 (52%)
>100	44 (44%)	34 (44%)	46 (30%)
Prefers not to answer/unknown	15 (15%)	5 (6%)	27 (17%)

Variables with group differences are denoted by superscripts. Similar superscripts denote no difference between groups. Dissimilar superscripts indicate significant group differences ($p < .05$).

was significantly associated and was so only with the emotional responses item ($r = -.172$, $p = .002$). Thus, age was included as a covariate in the analyses for the latter.

Intercorrelations between illness perception dimensions are displayed in Table 2. Consequences and emotional responses were correlated with the greatest number of other illness perceptions (i.e., five dimensions each). In addition to being positively associated with each other ($p < .01$), endorsement of greater consequences and negative emotions were both associated with perception of greater symptoms (identity), greater illness concern, lower levels of treatment control, and a more acute illness timeline ($ps < .05$). The coherence and personal control dimensions displayed the fewest correlations with other illness perceptions (i.e., two dimensions each), each being positively correlated with one other as well as treatment control ($ps < .05$).

Primary Tests of Group Differences

Identity

The effect of treatment group on endorsement of CLL symptoms (identity) was significant (see Fig. 2), $F(2, 327) = 28.87$, $p < .001$, $\eta^2_p = .150$, as were planned comparisons of AS versus FT, $t(327) = 2.93$, $p < .01$, and FT versus RR, $t(327) = 3.78$, $p < .01$ groups. Consistent with hypotheses, AS patients reported the fewest symptoms ($M = 1.96$, $SD = 2.05$), followed by FT ($M = 3.10$, $SD = 2.74$), and then RR ($M = 4.46$, $SD = 2.81$). In other respects, these data also provide a "validity check" and confirm the assumption that the groups differed in CLL symptoms.

Consequences

The effect of treatment group on consequences of CLL was also significant, $F(2, 326) = 16.93$, $p < .001$, $\eta^2_p = .094$, as were planned comparisons of AS versus FT, $t(326) = 3.04$, $p < .01$, and FT versus RR, $t(326) = 2.09$, $p < .05$ groups. Consistent with hypotheses, AS patients reported the fewest consequences ($M = 2.74$, $SD = 2.56$), followed by FT ($M = 4.03$, $SD = 2.92$), and then RR ($M = 4.84$, $SD = 2.89$).

Concern

The effect of treatment group on concern about CLL was also significant, $F(2, 326) = 14.31$, $p < .001$, $\eta^2_p = .081$, as were planned comparisons of AS versus FT, $t(326) = 2.65$, $p < .01$, and FT versus RR, $t(326) = 2.08$, $p < .05$ groups. Consistent with hypotheses, AS patients reported the lowest levels of concern ($M = 5.38$, $SD = 3.16$), followed by FT ($M = 6.58$, $SD = 3.12$), and then RR ($M = 7.44$, $SD = 2.78$).

Coherence

The effect of treatment group on coherence was also significant, $F(2, 327) = 8.46$, $p < .001$, $\eta^2_p = .049$. Consistent with hypotheses, planned comparisons indicated that AS patients reported lower understanding of CLL ($M = 7.31$, $SD = 2.26$) than FT ($M = 8.23$, $SD = 1.77$), $t(327) = 3.10$, $p < .01$. Contrary to hypotheses, FT ($M = 8.23$, $SD = 1.77$) and RR groups ($M = 8.30$, $SD = 1.86$) did not differ ($p = .793$).

Personal control

The effect of treatment group on personal control was also significant, $F(2, 323) = 7.49$, $p = .001$, $\eta^2_p = .045$. Contrary to hypotheses, planned comparisons indicated that personal control was highest for FT patients ($M = 5.01$, $SD = 3.36$) relative to AS ($M = 3.32$, $SD = 3.10$), $t(323) = 3.67$, $p < .01$, and RR groups ($M = 3.65$, $SD = 2.77$), $t(323) = -3.22$, $p < .01$.

Table 2 Intercorrelations between illness perception dimensions across chronic lymphocytic leukemia groups ($N = 330$)

Illness perception	1.	2.	3.	4.	5.	6.	7.	8.
1. Consequences	1	.664**	.390**	.034	.039	−.194**	−.208**	.531**
2. Identity		1	.290**	.063	.066	−.198**	−.090	.392**
3. Concern			1	.009	−.005	−.159**	−.018	.405**
4. Coherence				1	.136*	−.015	.201**	−.005
5. Personal control					1	−.107	.249**	.069
6. Timeline						1	−.110	−.133*
7. Treatment control							1	−.144*
8. Emotional responses								1

*Correlation is significant at the 0.05 level (two tailed).

**Correlation is significant at the 0.01 level (two tailed).

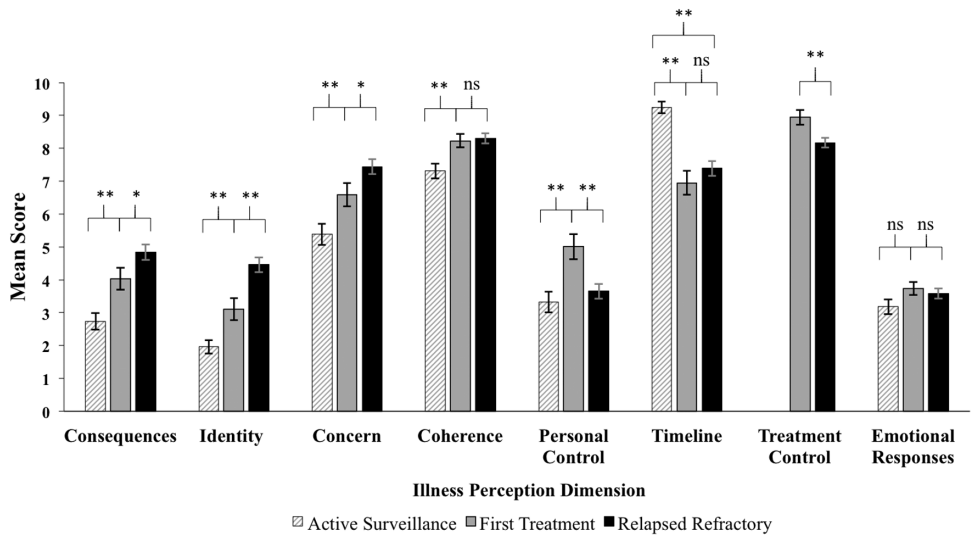

Fig. 2. Mean illness perception scores by chronic lymphocytic leukemia treatment group. Error bars denote standard errors of the group mean. The treatment control item was not administered to active surveillance patients. *$p < .05$, **$p < .01$.

Timeline

Contrary to expectations, the effect of treatment group on timeline perceptions was significant, $F(2, 321) = 20.24$, $p < .001$, $\eta^2_p = .112$, with AS patients believing that CLL would last the longest ($M = 9.24$, $SD = 1.82$), followed by RR ($M = 7.39$, $SD = 2.78$), and then FT ($M = 6.95$, $SD = 3.26$). Post hoc comparisons indicated that timeline perceptions for AS patients were higher relative to RR ($SE = 0.293$, $p < .001$) and FT ($SE = 0.414$, $p < .001$); the latter two groups did not differ ($SE = 0.436$, $p = .566$).

Treatment control

The effect of treatment group on treatment control perceptions was significant, $t(228) = 2.90$, $p = .004$, $d = 0.403$. Consistent with hypotheses, FT patients believed more strongly that treatment would be helpful ($M = 8.94$, $SD = 1.96$) than RR patients ($M = 8.14$, $SD = 1.87$).

Emotional responses

Contrary to hypotheses, groups did not differ in the extent to which they felt CLL affected them emotionally ($p = .225$).

Discussion

Foundational work in self-regulatory theory [1] highlighted symptoms and prior experiences with health threats as central to the formation of illness perceptions. In an empirical test of this postulate, the present study contrasted illness perceptions between three groups of patients with CLL: active surveillance (AS), initiating a first treatment (FT), and initiating treatment for relapsed/refractory disease (RR). Differing in symptoms and prior disease experiences, these groups provided an ideal context for better understanding factors relevant to patients' mental representations of illness. Although consequences, identity, and concern were significantly poorer among patients at each successive phase of treatment, personal and treatment control were highest among FT patients. AS patients reported the lowest levels of coherence and the most chronic illness timeline. Despite these differences, groups reported equivalent emotional responses to CLL.

Notably, consequences, identity (symptoms), and concern were significantly poorer among patients at each successive phase of treatment. Mapping onto a clinical picture of increasing symptom severity as CLL patients transition from surveillance to an FT and beyond [26, 34, 35], these findings support Leventhal's postulate that greater symptom severity influences more negative illness perceptions. Although the illness concern finding is consistent with the self-regulatory model, it is noteworthy that emotional responses, an additional dimension of emotional representations (Fig. 1), did not differ between groups. The concern item in the BIPQ captures worry [31], which is not an emotional response per se, but a chain of thoughts and images, which are laden with negative affect [36]. It could be that worry increases throughout the course of CLL treatment, but not overall rates of negative emotions such as sadness or anger. Van den Broek et al. [35] provide support for this hypothesis, observing differences between CLL treatment groups (surveillance vs. on treatment) on several domains of cancer-specific worry (e.g., personal health, future, cancer recurrence), but no group differences in anxiety or depression. Future work in this population may benefit

from use of cancer-specific worry scales when evaluating and monitoring psychological functioning.

Also, consistent with the self-regulatory model, group differences in treatment control mapped onto increasing symptom severity across CLL groups, with FT patients believing more strongly that treatment would be helpful than RR. Although also in line with prior research linking symptom severity and treatment control [7, 9, 10, 12, 13], the treatment history of RR patients is important to consider. Average number of previous CLL therapies for RR patients was 3.5 (*SD* = 2.6), with some relapsing and/or failing to respond to upwards of 16 prior therapies. Thus, patients conceivably learned that treatment effects do not remain (i.e., relapse) and may be aware that subsequent treatments are less effective in controlling CLL. Nevertheless, treatment control perceptions were high for both groups (FT = 8.9/10; RR = 8.1/10), reflecting that, despite ultimately being incurable, patients in this context had high levels of confidence in the ability of treatment to be helpful for at least some period of time.

Contrary to treatment control findings, personal control did not vary across groups in a manner that would be expected based on symptom severity alone. We hypothesized that personal control would be highest among those with less severe symptoms (i.e., AS patients). Instead, personal control was highest among FT patients, followed by RR and AS groups. It could be that entering a phase of active attempts at managing their disease provides FT patients with more opportunities (or a first opportunity) to mobilize coping behaviors and request information from medical providers about how to best control their symptoms. AS patients are frequently told that their disease requires no immediate action [37]. RR patients, at the other end of the spectrum, may feel less personal control over CLL as a result of their cycling of treatment and relapse. Future longitudinal research documenting changes in personal control as patients' transition from surveillance to a first treatment and beyond may help clarify the nature of these relationships.

Coherence also differed between groups, with FT and RR patients endorsing greater understanding of CLL than AS. These findings are largely consistent with expectations of self-regulatory theory that those with greater prior experience with a condition would learn from their experiences and thus endorse greater understanding of their condition. Findings are also consistent with prior research [18, 20, 22, 23] and may reflect a general tendency across illnesses to learn more about one's condition through continued interactions with physicians and treatment experiences.

We anticipated that the timeline dimension would not differ by CLL group. Group differences emerged, however, with AS patients endorsing their illness would last the longest, followed by both treatment groups that did not differ. This finding may be more readily understood in the context of prior research [38–40] criticizing the construct validity of the acute/chronic timeline item ("How long do you think your illness will last?"). The authors have provided evidence that, particularly among older patients and those with advanced disease, the timeline item may elicit responses related to perceived life expectancy rather than permanence of the condition per se. Thus, CLL patients requiring a first or subsequent treatment may have believed that their disease will continue for the rest of their lives but that this will be a shorter period of time. Intercorrelations between illness perception dimensions (Table 2) support this rationale, showing that endorsement of a less chronic illness timeline was associated with greater consequences, symptoms, concern, and negative emotions related to CLL ($ps < .05$).

In addition to providing empirical support for components of Leventhal's model, the patterns of group differences observed here also have clinical implications. As the negative effects of CLL on patients' lives (consequences), physical symptoms (identity), and illness concern were greater among patients at each successive phase of CLL treatment, it may be important to monitor for levels of/changes in psychosocial and physical distress as patients move through treatment phases, and provide referral to psychological and symptom management services as appropriate. Results also indicated that coherence was poorest among AS patients. These findings are consistent with a prior qualitative report from Evan et al. [37] in which surveillance patients commonly expressed a desire for more information and confusion about their illness and the lack of need for immediate treatment. Thus, surveillance may represent a period of heightened uncertainty as patients face an indolent disease with an undetermined course, and care should be taken to insure that the unique knowledge and communication needs for this population are addressed. Also relevant to the clinical management of surveillance patients were their decreased levels of personal control relative to those initiating a first CLL treatment. This finding is particularly important in light of prior research linking personal control to medication adherence and other self-management behaviors such as appointment attendance, diet, and exercise [41–44]. Although there is no conclusive evidence that positive health behaviors delay progression in CLL, education regarding modifiable lifestyle factors may enhance personal control and reduce risk for development of medical comorbidities (e.g., secondary cancers, cardiovascular disease, diabetes) that may complicate CLL treatment.

A primary strength of the present study is its theory-based analysis of the CLL patient experience, which is particularly appropriate given the unique disease trajectory and limited psychosocial study of

CLL relative to other cancers. Furthermore, patients initiating a first or subsequent treatment completed the illness perception assessment before treatment began, preventing the potential confounding physical side effects of anti-cancer therapy (e.g., nausea, fatigue). The group comparison design is an additional strength, as it did not require self-report of symptom severity. Self-regulatory theory indicates that type and severity of symptoms are critical determinants of illness perceptions, yet when considering this question, studies reliant on patients' self-report encounter methodological issues of common measurement and conceptual overlap. Individuals who perceive more severe symptoms (identity) are likely to report more severe symptoms, complicating inferences about the relationship between severity and illness perceptions. One way to circumvent this is to contrast illness perceptions among groups known or presumed on the basis of prior literature to differ on symptom severity as done here (and corroborated by group differences on the identity item). An additional option for future studies would be to include use of objective disease severity markers (e.g., lymph node volume or hemoglobin counts in CLL) akin to that done previously in a select group of studies from other disease groups [7, 13, 45].

Limitations are also considered. Although the present study focused on symptom severity and prior illness experience as determinants of illness perceptions, additional factors are probably relevant and warrant future study, including social communication (e.g., that from friends, family, media, etc.), history of serious illness in close others, personality, and cultural background [1, 5, 46]. In addition, patients initiating treatment were doing so in the context of clinical trials, which often underrepresent minorities and older adults [47, 48]. Thus, our sample was younger (mean age = 62.2 years) and more likely to be Caucasian (98%) than rates recorded in national CLL samples (median age at diagnosis = 71; 90% Caucasian) [49, 50]. Furthermore, as a low incidence disease, CLL patients are often treated at regional centers, which may produce expectancy effects that differ from those of a community treatment setting. Last, although the cross-sectional design provides a first step in the context of a disease where several years may pass between treatment phases, a longitudinal design, perhaps targeting critical change periods (e.g., patients transitioning from surveillance to a first treatment), would help clarify mechanisms giving rise to group differences.

In conclusion, novel data contrasting illness perceptions from three phases of CLL treatment provided preliminary empirical support for theoretical postulates that symptoms and prior disease experiences influence illness perceptions. Although certain dimensions appeared to map closely onto symptom experiences (i.e., consequences, identity, concern, treatment control), others may have been more influenced by factors such as knowledge acquired through prior experience with the illness (i.e., coherence) or the context of treatment itself (i.e., personal control). Future work is needed, particularly in the form of longitudinal studies and those that examine the influence of multiple theorized determinants (e.g., personality, culture, severe illness in close others) to continue to garner a better understanding of the formation of mental representations of illness.

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Compliance with Ethical Standards

Conflict of Interest K.M. has received research funding from Pharmacyclics. J.W. has received research funding from Morphosys, Karyopharm, Abbvie, Acerta, and served as a consultant for Janssen. J.B. has received research funding from Genentech, Janssen, Acerta, and Pharmacyclics.

Authors' Contributions All authors were involved in the preparation of this manuscript and read and approved the final version.

Ethical Approval All procedures performed were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed Consent Informed consent was obtained from all individual participants included in the study.

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