

ORIGINAL REPORT

IDENTIFYING CLINICALLY IMPORTANT FUNCTIONAL IMPAIRMENTS AND REHABILITATION NEEDS IN CANCER SURVIVORS AND A PILOT VALIDATION OF THE CANCER REHABILITATION QUESTIONNAIRE

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Objectives: Despite the availability of cancer rehabilitation, utilization at our institution was low. We designed the Cancer Rehabilitation Questionnaire (CRQ) to investigate the prevalence of functional impairments amongst cancer survivors and attitudes towards rehabilitation participation. We evaluated the performance of CRQ as a screening tool for detecting clinically important physical dysfunction.

Design: A cross-sectional study was performed, recruiting cancer survivors at a university outpatient oncology clinic. Cancer survivors completed the CRQ and European Organization for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire – Core 30 Questionnaires. Descriptive statistical analysis and receiver operator characteristics analysis were performed to assess the ability of the CRQ to detect clinically important physical dysfunction, as measured by the EORTC QLQ-C30.

Results: Of 204 participants, 87.3% reported impairments in at least 1 CRQ domain. Pain and weakness were most common. The number of positive items correlated with EORTC global health status and functional scales. A cut-off of ≥ 4 on the CRQ predicted clinically important physical dysfunction (sensitivity 61.8%, specificity 75.5%). Of those with impairments, 53.9% were unwilling to participate in rehabilitation. Transportation, need for caregivers, and cost were the main barriers.

Conclusion: Our findings will guide resource allocation to overcome barriers to participation. The CRQ can help to stratify cancer survivors requiring further rehabilitation interventions.

Key words: functional impairments in cancer survivors; cancer rehabilitation; screening tool; rehabilitation needs; quality of life.

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LAY ABSTRACT

Functional impairments due to cancer and its treatment are common, and can be effectively addressed with rehabilitation. To better provide cancer rehabilitation, the Cancer Rehabilitation Questionnaire was designed to investigate what functional problems cancer survivors have and their attitudes towards participation in rehabilitation. We compared the cancer rehabilitation questionnaire with the European Organization for Research and Treatment of Cancer (EORTC QLQ-C30) to see if it could be used as a screening tool for rehabilitation needs. Of 204 participants, 87.3% reported functional impairments in at least 1 Cancer Rehabilitation Questionnaire domain. Pain and weakness were most common. The number of positive Cancer Rehabilitation Questionnaire items correlated with EORTC scales: ≥ 4 positive items in the Cancer Rehabilitation Questionnaire indicated that the number of physical impairments was clinically significant. Among participants with impairments, 53.9% were unwilling to participate in rehabilitation. Transportation, need for caregivers, and cost were cited as barriers. A simple screening tool, such as the Cancer Rehabilitation Questionnaire can help to stratify cancer patients requiring further rehabilitation and intervention.

Advancements in cancer therapeutics have led to more effective treatments and increased cancer survival (1, 2). However, cancer survivors may experience cancer-related disabilities and adverse consequences of cancer treatment (3, 4). Rehabilitation and exercise are effective for treating physical functional decline and addressing symptoms across multiple domains and at multiple points along the cancer disease continuum (5–7). A recent systematic review of functional outcomes after a variety of rehabilitative interventions for cancer survivors at any point in the continuum of care showed statistically significant improvements in function in 71% of studies, particularly in the domains of health-related quality

of life (HRQoL), performing activities of daily living (ADL) and instrumental ADL, cancer-related fatigue and functional mobility, amongst other benefits (8). These interventions ranged from exercise-based interventions to cognitive behavioural therapy and cognitive therapy (8).

In Singapore, the prevalence of functionally significant cancer-related impairments remains unknown. The uptake of cancer rehabilitation programmes is also low despite its availability in most public hospitals.

There is currently no universally accepted multi-dimensional screening tool to assess rehabilitation needs in cancer survivors. Validated screening tools for specific impairments, such as fatigue (Brief Fatigue Inventory, Functional Assessment of Cancer Therapy-Fatigue scales) and general physical functioning and HRQoL, such as the Functional Assessment of Cancer Therapy-General (FACT-G) and European Organization for Research and Treatment of Cancer Quality of Life Questionnaire – Core 30 (EORTC QLQ-C30) (version 3) exist, but do not specifically identify rehabilitation needs.

To identify the gaps and inform the development of cancer rehabilitation programmes at National University Hospital Singapore, we developed the Cancer Rehabilitation Questionnaire (CRQ) (Appendix S1) with the aims of: (i) identifying the prevalence of different domains of functional impairments across a broad spectrum of cancer survivors in an outpatient setting; (ii) assessing awareness of rehabilitation as a treatment modality and as an available service for management of functional impairments; and (iii) assessing willingness and barriers to accessing these services, and attitudes towards cancer rehabilitation. Secondly, this study investigated the reliability and validity of the CRQ as a screening tool to identify clinically important impairments in physical functioning. This information will be valuable in developing an impairment-based patient-centric cancer rehabilitation programme.

METHODS

To design the CRQ, a panel of domain experts experienced in the rehabilitation of cancer patients, comprising physiotherapists, occupational therapist, social worker and rehabilitation physician, identified the domains and functional impairment items based on the prevalence in clinical practice, literature review and rehabilitation interventions available to address the issues (9–11). Feasibility and face validity were assessed through feedback from 8 senior therapists and a pilot performed with feedback from 10 patients. The number of functional impairments was rationalized from 30 to 12 common cancer-associated functional issues and simplified from continuous rating scales for

each item, to binary yes/no answers. CRQ score was calculated as the total number of symptoms/impairments reported in item 1 of the CRQ.

The CRQ was validated against the EORTC QLQ-C30 (12), which comprises 30 items for 15 dimensions/scales, including a global health status scale, 5 functional scales (physical, role, cognitive, social, and emotional functioning), 3 symptom scales (fatigue, nausea/vomiting, and pain), 5 single-item symptom scales (dyspnoea, sleep disturbances, appetite loss, constipation, and diarrhoea), and a single-item scale for the financial difficulties from the disease and treatment. The EORTC QLQ-C30 was chosen as it is a validated measure of HRQoL in cancer survivors with good correlation with aspects of physical function, activity limitation and participation on the International Classification of Functioning, Disability and Health (ICF) relevant to rehabilitation interventions (13, 14).

The 2 questionnaires were administered by 3 trained student volunteers from the National University of Singapore in a cross-sectional study of cancer survivors at the oncology specialist outpatient clinics of the National University Cancer Institute, Singapore (NCIS), from May 2014 to July 2014. Ethics approval was obtained from the National Healthcare Group Domain Specific Review Board in Singapore (DSRB 2014/00357). Participants included all patients diagnosed with cancer, more than 21 years old. Those who were unable to answer questions for any reason (e.g. cognitive impairment) were excluded from the study.

Statistical analyses were carried out using SPSS version 19 software (SPSS Inc., WA, USA). Patient characteristics was analysed descriptively. The Mann–Whitney *U* was used for comparing differences in EORTC variables between groups, and the χ^2 test was used for categorical ones. Spearman's correlation between the number of functional impairments, with the functional scales of the EORTC was calculated. The level of significance for all tests was $p < 0.05$, with no adjustment for multiple comparisons. The threshold for clinically important functional limitation for EORTC physical functioning domain was previously determined to be 83 points with a sensitivity of 0.87 and specificity of 0.68 (15). To assess the discriminatory power of the CRQ score to detect clinically important functional limitation as defined by this threshold, the effect sizes (Cohen's *d*) for the CRQ score were calculated for participants whose EORTC physical functioning was ≥ 83 and those < 83 . Internal consistency of the number of CRQ items was assessed using the Cronbach alpha coefficient. Receiver operating characteristic (ROC) and area under the curve (AUC) analyses were performed to evaluate the sensitivity and specificity of the CRQ

to detect clinically important functional limitation, as described by the EORTC physical functioning domain (15–17).

RESULTS

Of 207 participants screened, 3 did not meet the inclusion criteria. Responses from 204 participants were included. The characteristics of the participants are described in Table I. Of 204 participants, 87.3% (178) reported some functional impairment following cancer diagnosis, 83.7% (149) reported impairment in 2 or more domains, 59.3% (121/204) in 3 or more domains, 44.6% (91) in 4 or more domains in the CRQ form. The 4 most frequently reported domains were pain, weakness, difficulty with ADL and numbness/tingling (Table II).

Table I. Participants' characteristics

Characteristics	<i>n</i>	%
Sex		
Male	76	37.3
Female	128	62.7
Age range		
20–30 years	10	4.9
30–40 years	10	4.9
40–50 years	28	13.7
50–60 years	64	31.4
60–70 years	60	29.4
70–80 years	27	13.2
80–90 years	4	2.0
Not known	1	0.5
Cancer type		
Breast	67	32.8
Genitourinary	31	15.2
Colorectal	26	12.7
Leukaemia	22	10.8
Lung	15	7.4
Lymphoma	13	6.4
Other gastrointestinal	12	5.9
Head and neck	11	5.4
Others	7	3.4
Cancer stage		
I	16	7.8
II	44	21.6
III	42	20.6
IV	50	24.5
Not known	52	25.5
Time from diagnosis		
< 1 year	82	40.2
≥ 1 years, < 5 years	75	36.8
≥ 5 years	35	17.2
Not known	12	5.9
Treatment status		
Pre-treatment	3	1.5
On-going	141	69.1
Completed	57	27.9
Not known	3	1.5
Treatment type*		
Chemotherapy	180	88.2
Surgery	76	37.3
Radiotherapy	71	34.8
Stem cell transplant	6	2.9
Hormone therapy	1	0.5
Not known	3	1.5

*Data referring to treatment types total 337 as some participants had > 1 treatment.

Table II. Prevalence of reported symptoms and impairments on the Cancer Rehabilitation Questionnaire

	Participants who answered "Yes", <i>n</i> N = 178	% (out of 204 participants) 87.3%
Pain/aching	102	50.0
Numbness and tingling sensation	82	40.2
Persistent fatigue	78	38.2
Easily breathless	57	27.9
Stiffness	49	24.0
Swelling	38	18.6
Change in posture	26	12.7
Weakness	92	45.1
Less able to perform everyday activities	89	43.6
Unsteady gait	54	26.5
Having falls/near falls in the last year	25	12.3
Difficulty in opening mouth, swallowing or chewing	25	12.3

Characteristics of cancer survivors with functional impairments

Age, cancer stage, cancer duration and treatment status were significantly associated with the presence of functional impairments, as screened by the CRQ and EORTC QLQ-C30 functioning scales (Table III). Cancer survivors ≥ 70 years old were more likely to report limitations in ADL (61.3% vs 40.7%, $p=0.033$), unsteady gait (41.9% vs 23.8%, $p=0.036$), swelling (16.3% vs 32.3%, $p=0.036$), and decline in cognitive function (83.9 ± 19.1 vs 73.1 ± 22.2 , $p=0.005$) compared with younger cancer survivors. Those with more advanced stage cancer (stage 3+4) reported significantly higher percentage of symptoms (93.5% vs 81.7%, $p=0.024$) and worse EORTC-global health score (55.0 ± 20.8 vs 62.9 ± 19.0 , $p=0.019$). Those with cancer diagnosed less than 1 year ago had worse EORTC-physical functioning (73.7 ± 20.9 vs 80.6 ± 18.2 , $p=0.015$) and role functioning scores (66.5 ± 30.6 vs 76.2 ± 29.0 , $p=0.026$), compared with those diagnosed ≥ 1 year ago. Those who had completed treatment had better EORTC-global health score (63.9 ± 23.0 vs 56.4 ± 18.2 , $p=0.016$), physical functioning (83.5 ± 18.9 vs 74.1 ± 21.2 , $p=0.004$), role functioning (81.0 ± 26.8 vs 67.6 ± 30.7 , $p=0.004$), emotional functioning (84.4 ± 20.8 vs 75.8 ± 22.9 , $p=0.016$) and social functioning (86.8 ± 23.7 vs 74.5 ± 28.2 , $p=0.004$) compared with those on treatment. They also reported fewer symptoms (fatigue, nausea, pain, appetite loss) compared with those on treatment.

Awareness of cancer rehabilitation

Of 204 participants, 131 (64.2%) knew how to access rehabilitation services for treatment of their functional impairments, but only 85 (41.7%) had undergone or were seeking treatment. More than half who had reported functional impairments (96/178 or 53.9%) were not willing to undergo rehabilitation. The most

Table III. Comparing functioning as measured by the Cancer Rehabilitation Questionnaire (CRQ) and European Organization for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire – Core 30 (EORTC QLQ C30) across ages, cancer stages, cancer duration and treatment status

	Age			Cancer stage			Cancer duration			Treatment status		
	<70 years	≥70 years	p-value	Stage 1+2	Stage 3+4	p-value	<1 year	≥1 year	p-value	On-going	Completed	p-value
CRQ, %												
Having symptoms	85.5	96.8	>0.05	81.7	93.5	0.024*	85.4	89.1	>0.05	89.4	82.5	>0.05
Pain/aching	48.3	58.1	>0.05	51.7	54.3	>0.05	42.7	54.5	>0.05	54.6	42.1	>0.05
Numbness/tingling sensation	41.3	32.3	>0.05	33.3	46.7	>0.05	39.0	40.0	>0.05	43.3	33.3	>0.05
Persistent fatigue	37.8	41.9	>0.05	41.7	39.1	>0.05	42.7	35.5	>0.05	39.0	38.6	>0.05
Easily breathless	29.1	22.6	>0.05	20.0	30.4	>0.05	29.3	28.2	>0.05	30.5	24.6	>0.05
Stiffness	24.4	22.6	>0.05	25.0	25.0	>0.05	18.3	27.3	>0.05	22.0	29.8	>0.05
Swelling	16.3	32.3	0.036*	21.7	15.2	>0.05	18.3	19.1	>0.05	19.9	15.8	>0.05
Change in posture	12.2	16.1	>0.05	15.0	12.0	>0.05	9.8	13.6	>0.05	13.5	12.3	>0.05
Weakness	45.3	45.2	>0.05	43.3	44.6	>0.05	45.1	45.5	>0.05	49.6	36.8	>0.05
Affected daily activities	40.7	61.3	0.033*	36.7	50.0	>0.05	48.8	41.8	>0.05	45.4	36.8	>0.05
Unsteady gait	23.8	41.9	0.036*	28.3	27.2	>0.05	23.2	29.1	>0.05	29.1	22.8	>0.05
Recent falls	12.2	12.9	>0.05	10.0	15.2	>0.05	11.0	13.6	>0.05	13.5	10.5	>0.05
Dysphagia	14.0	3.2	>0.05	11.7	15.2	>0.05	13.4	10.9	>0.05	13.5	12.3	>0.05
EORTC,												
Global health status	59.3±20.3	55.4±16.6	>0.05	62.9±19.0	55±20.8	0.019*	57.9±18.7	59.1±20.6	>0.05	56.4±18.2	63.9±23.0	0.016*
Physical functioning.	77.9±20.9	71.0±21.8	>0.05	79.3±18.0	76.1±23.4	>0.05	73.7±20.9	80.6±18.2	0.015*	74.1±21.2	83.5±18.9	0.004*
Role functioning.	70.6±30.7	74.7±27.5	>0.05	74.2±27.2	71.6±31.0	>0.05	66.5±30.6	76.2±29.0	0.026*	67.6±30.7	81.0±26.8	0.004*
Emotional functioning.	78.0±22.8	78.8±21.5	>0.05	80.1±21.7	76.3±22.9	>0.05	74.7±24.7	80.1±20.3	>0.05	75.8±22.9	84.4±20.8	0.016*
Cognitive functioning.	83.9±19.1	73.1±22.2	0.005*	84.2±19.3	80.8±19.4	>0.05	81.9±19.8	83.5±19.6	>0.05	81.0±20.3	85.4±19.2	>0.05
Social functioning.	77.5±27.4	78.0±29.0	>0.05	83.6±24.1	75.9±27.4	>0.05	73.6±29.6	81.1±25.4	>0.05	74.5±28.2	86.8±23.7	0.004*

CRQ data shows the percentage of participants having the symptom and impairment, χ^2 test was used to analyse the differences in CRQ scores between groups. EORTC data shows Mean±SD of the scores, Mann-Whitney U test was used to analyse the differences in EORTC scores between groups. *indicates results that meet significance.

frequently reported reasons included difficulties with transport arrangements (43.2%), lack of accompanying caregivers (39.0%) and cost of rehabilitation (31.4%). Disease-related fatigue or feeling unwell (23.7%), as well as time commitment for the rehabilitation programme (16.1%) were also cited as reasons. Of the remaining 94 participants who were willing to participate, 43 were willing to attend weekly sessions, 18 preferred fortnightly sessions, and 33 preferred monthly sessions.

Cancer Rehabilitation Questionnaire as a screening tool to detect clinically significant physical functioning decline

In terms of reliability of CRQ score to detect clinically important physical dysfunction, as defined by the EORTC physical functioning scale, the AUC of the ROC curve was 0.75 (95% confidence level (95% CI) 0.68–0.82) (Fig. 1). Three or more positive responses on the CRQ predicted for clinically important physical dysfunction, with a sensitivity of 74.5% and a specificity of 58.5%. Four or more positive responses resulted in a sensitivity of 61.8% and a specificity of 75.5%.

Internal consistency was acceptable for 13 functional impairments screened on item 1 of the CRQ (Cronbach’s alpha coefficient=0.76).

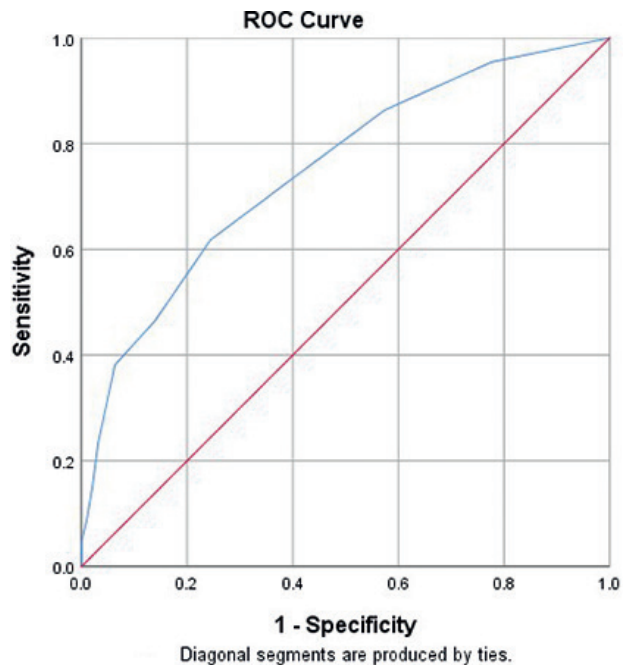


Fig. 1. Receiver operator characteristic (ROC) curve for number of positive items on the Cancer Rehabilitation Questionnaire.

The discriminatory power of the CRQ to differentiate those with clinically significant decline in physical functioning was good. Effect size (Cohen’s d) for the

Table IV. Correlation between the Cancer Rehabilitation Questionnaire (CRQ) and European Organization for Research and Treatment of Cancer Quality of Life Questionnaire–Core 30 (EORTC QLQ C30) functional scales

	Global Status	Physical F.	Role F.	Emotional F.	Cognitive F.	Social F.
Correlation coefficient	-0.37	-0.50	-0.30	-0.39	-0.27	-0.31
<i>p</i> -value	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001

Spearman's correlation analysis was used.
F: Functioning.

mean difference in CRQ score between participants whose EORTC physical functioning was ≥ 83 and those < 83 , was large (0.96) (15).

Participants who reported functional impairments on the CRQ scored significantly lower on the EORTC global health status (57.6 ± 19.8 vs 65.7 ± 18.5 , $p = 0.029$), total functional scale (379.8 ± 7.1 vs 432.1 ± 71.6 , $p = 0.003$), physical functioning (75.1 ± 21.0 vs 89.5 ± 17.3 , $p < 0.001$) and emotional functioning (76.2 ± 22.8 vs 91.4 ± 15.4 , $p < 0.001$). The number of impairments on the CRQ correlated with the EORTC global health status ($r = -0.37$, $p < 0.001$) and all functional scales. Moderate correlation was found between CRQ score and physical functioning ($r = -0.50$, $p < 0.001$), emotional functioning ($r = -0.39$, $p < 0.001$) and social functioning ($r = -0.31$, $p < 0.001$). Weaker correlations were also seen in role functioning ($r = -0.30$, $p < 0.001$) and cognitive functioning ($r = -0.27$, $p \leq 0.001$) (Table IV).

DISCUSSION

To our knowledge, this is the first study to describe the extent of self-reported functional issues and cancer rehabilitation needs and attitudes in cancer survivors in Singapore, a multicultural Asian population. The study found a high prevalence of various functional impairments, particularly in those who were older, those on cancer treatment or closer to the time of cancer diagnosis, and those with later stage disease. The presence and number of symptoms and functional impairments reported on the CRQ correlated well with HRQoL, particularly in the domains of total and physical functioning. This information will help to guide the development of holistic screening and tailored interventions for these at-risk patient groups.

Cancer rehabilitation is an interdisciplinary, multi-dimensional and coordinated intervention to minimize the impact of functional impairments and maximize function. Rehabilitation needs vary among cancer survivors. While physical activity and exercise are key modifiers of outcome (5), a process of stratification and further evaluation is required to systematically address the variety of needs while optimizing the use of limited resources.

The current study identified a higher prevalence of functional impairments in older cancer survivors. Rehabilitation of this population can be complex.

Age-related decline in functional organ reserves (18), together with accumulating comorbidities, not only interact with cancer to produce debilitating functional impairments, but can also hamper rehabilitation and limit progress. Social issues also often directly impact delivery of rehabilitation. A geriatric assessment (GA) (19) to assess multiple domains, including comorbidities, functional status, cognition, psychological status, nutritional status, polypharmacy and social support, is useful to identify patients who require complex multidisciplinary interventions, including individually tailored rehabilitation, to address interacting issues. However, GA is resource intensive and challenging to implement at scale. Strategies at multiple levels of the healthcare system are required to address this, which is outside the scope of this discussion (20).

The current study also highlighted low levels of willingness and perceived barriers reported by cancer survivors to participate in cancer rehabilitation programmes. Cancer survivors with functional limitations often rely on caregivers to access care. Repeated lengthy hospital visits can deter participation in rehabilitation. Effectiveness of cancer rehabilitation is not restricted by setting (21). In addition to the traditional hospital setting for rehabilitation, a low-to-moderate-intensity, home-based exercise programme has also been shown to improve mood and anxiety (22). Paper-based or video-based individually tailored unsupervised exercise programmes have also been demonstrated to be feasible in helping cancer survivors maintain physical function during cancer treatment (23). Alternative modes, such as telehealth platforms, can be explored in appropriate patients to improve outreach, facilitate interdisciplinary assessments and treatment, and overcome some of the barriers identified in the current study (25). Alternatively, services can be centralized via multidisciplinary clinics in the hospital setting (24), allowing assessment and prescription of interventions in a single setting. Finally, systematic education to increase awareness of the benefits of rehabilitation to address functional issues could influence participation and improve treatment outcomes.

Screening tools for cancer-related functional issues currently focus on specific symptoms, such as fatigue or numbness, or specific populations, such as frailty screening in the geriatric population (26). There is a lack of simple, validated multidimensional screening tools to identify those with functional impairments

who might benefit from rehabilitative interventions. Functional evaluations are also time-consuming to perform. The CRQ is a simple, multidimensional screening tool with adequate sensitivity and specificity to detect clinically important physical dysfunction in a wide-range of cancer survivors.

Study limitations

This study has several limitations. The CRQ does not assess the severity of each impairment that would impact on treatment decisions. There is significant construct overlap between items. The CRQ does not explore social factors impacting participation restriction, including community and vocational participation, which is another important domain impacting HRQoL. In evaluating the willingness of participants to undergo rehabilitation, an individualized rehabilitation prescription and plan was not provided, which may have contributed to higher-than-expected rates of rejection of rehabilitation.

CONCLUSION

This study identified the extent of functional impairments, willingness to participate and barriers to access cancer rehabilitation among cancer survivors in Singapore. The majority of cancer survivors had multiple functional impairments, which was significantly associated with reduction in HRQoL. This supports the need for holistic screening of functional impairments and to systematically address this gap in cancer survivorship care. This can be done through the use of simple, multidimensional tools, such as the CRQ. This better understanding will help enable future efforts to better allocate and site resources in order to improve access to cancer rehabilitation.

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