



# Quality of life of nasopharyngeal cancer survivors in China

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## ABSTRACT

**Purpose** We assessed the quality of life (QOL) of nasopharyngeal carcinoma (NPC) survivors with a survival time of more than 2 years in Fujian, China, and we analyzed factors influencing QOL.

**Methods** We calculated the prevalence of psychological distress and radiotherapy (RT)-induced symptoms in 216 NPC survivors who participated in a cross-sectional survey. The European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire (version 3.0) was used to assess the QOL of NPC survivors. Multiple linear regression was applied to analyze the factors influencing QOL.

**Results** The prevalence rates of RT-induced symptoms and psychological problems were 11.58% (95% CI: 7.21% to 15.58%) for difficulty in swallowing, 17.59% (95% CI: 12.51% to 22.67%) for mouth dryness or sores, 13.89% (95% CI: 9.28% to 18.50%) for nasal dryness or congestion, 18.52% (95% CI: 13.34% to 23.70%) for fatigue, 11.11% (95% CI: 6.92% to 15.30%) for frequent dizziness, 18.06% (95% CI: 12.93% to 23.19%) for decline in hearing, 14.81% (95% CI: 10.07% to 19.55%) for poor sleep quality, 18.52% (95% CI: 13.34% to 23.70%) for worry about disease recurrence, 18.98% (95% CI: 13.75% to 24.21%) for anxiety, and 25.00% (95% CI: 19.23% to 30.77%) for depression. Mean survival times were  $4.32 \pm 2.63$  years in patients with mouth dryness or sores,  $4.26 \pm 2.90$  years in patients with fatigue, and  $5.60 \pm 2.94$  years in patients with a decline in hearing. The mean global QOL score was 74.21 (95% CI: 72.22 to 76.20). At a significance level of  $\alpha = 0.05$ , the factors influencing QOL were age ( $p = 0.032$ ), education level ( $p = 0.001$ ), anxiety score ( $p < 0.001$ ), depression score ( $p < 0.001$ ), mouth dryness or sores ( $p < 0.001$ ), fatigue ( $p = 0.027$ ), and disease stage ( $p = 0.044$ ).

**Conclusions** The prevalence rates of mouth dryness or sores, fatigue, decline in hearing, depression, and anxiety were high in NPC survivors with a survival time of more than 2 years. These RT-induced symptoms and psychological problems can last for many years after RT. The QOL of the NPC survivors was good. Factors influencing QOL were age, education level, anxiety, depression, mouth dryness or sores, fatigue, and disease stage. Our results suggest that during clinical treatment, doctors should minimize the radiation dose to the ears of patients. In addition, our results emphasize the importance of providing oral and ear nursing and psychological care to NPC survivors.

**Key Words** Nasopharyngeal cancer, quality of life, depression, anxiety, side effects

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## INTRODUCTION

Nasopharyngeal carcinoma (NPC) is a common cancer in southern China and accounts for 1.58% of new cancer cases yearly<sup>1</sup>. Fujian Province has a high incidence of NPC; the reported crude incidence of NPC ranged from 15 to 30 per 100,000 during 2003–2007<sup>2</sup>. Improvements in diagnosis and treatment have greatly increased the survival rate for NPC patients<sup>3,4</sup>, and the 5-year rate is about 70% in Fujian<sup>4,5</sup>. The 5-year survival rate for patients with early-stage NPC is as high as 93%–100%<sup>6</sup>. The number of long-term NPC survivors

is increasing significantly and gradually forming a large special population<sup>7</sup>. Thus, well-being and improvement in quality of life (QOL) for this population are important concerns in cancer nursing and health care.

Quality of life and its assessment have become increasingly important in health care, especially in the field of chronic and terminal diseases. Conventionally, medical care for cancer patients has focused on the survival rate. However, survival rate assessments provide no knowledge and understanding of the patient's mental and emotional well-being. Evaluations of treatment effect in

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chronic diseases have therefore been changed to depend not only on survival duration, but also on patient QoL<sup>8</sup>. An individual's QoL encompasses personal feelings in the domains of physiology, psychology, and society<sup>9</sup>. The QoL of cancer patients reflects not only treatment effect, but also rehabilitation effect<sup>10</sup>. Few studies have reported the QoL of NPC survivors with a survival time of more than 2 years. The QoL in this population should not be ignored, because NPC affects young people, and NPC survivors can have problems with swallowing, speech, and hearing, as well as psychological effects from loss of function.

The primary treatment for NPC is radiotherapy (RT)<sup>11</sup>. Given that such tumours are located in close proximity to the base of the skull, most of the important vital structures in that area—such as the optic nerves, optic chiasma, brain, ears, and major salivary glands—are included within or in close proximity to the RT field. Radiotherapy produces many side effects: xerostomia, trismus, swallowing difficulties, neck stiffness, hearing problems, and neuroendocrine dysfunction. Some symptoms can last a long time after treatment<sup>12</sup> and can lead to deterioration in a survivor's QoL<sup>7</sup>.

The cross-sectional survey in the present study set out to describe QoL in NPC survivors with a survival time of more than 2 years in Fujian, China. The prevalence rates of anxiety, depression, and some treatment-related symptoms among NPC survivors were estimated. The factors influencing QoL in this cohort were also analyzed.

## METHODS

### Participants

The study subjects were NPC survivors in the communities of Fuzhou who were surveyed between June 2011 and December 2013. Subjects were included if they had been diagnosed with NPC and had completed cancer treatment more than 2 years earlier, if they had no history of mental or psychological disease, if they were between 18 and 70 years of age, and if they were knowledgeable about their cancer diagnosis. Subjects with tumour metastasis or recurrence were excluded.

All participants provided written informed consent, and the study was approved by the relevant institutional review boards for human research of Fujian Medical University.

### Measures

The European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire (QLQ-C30, version 3.0) is used to determine QoL in cancer patients<sup>13</sup>. This thirty-item questionnaire includes twenty-eight items scored 1–4, and two items scored 1–7. The Chinese version of the questionnaire has been confirmed to be suitable for Chinese cancer patients<sup>13</sup>. In the present study, the sum of the scores for items 1–5 and items 8–19 represented the physical aspect of QoL (QoL-Physical); the sum of the scores for items 20–25 represented the mental aspect of QoL (QoL-Mental); and the sum of the scores for items 6, 7, 26, and 27 represented the social aspect of QoL (QoL-Social). All scores were transformed into values in the 0–100 range. A high total score indicates good QoL.

The anxiety and depression of participants were measured using the Hospital Anxiety and Depression Scale

(HADS)<sup>14</sup>. The HADS is a 14-item questionnaire (7 items each in the Anxiety and Depression subscales). Participants scored each item from 0 to 3 based on their current situation. The total scores for the Anxiety and Depression subscales, which range from 0 to 21, are classified as follows: 0–7, asymptomatic; 8–10, suspicious symptoms; and 11–21, definite symptoms<sup>14</sup>. The Chinese version of the HADS has been confirmed to be suitable for Chinese patients<sup>15</sup>. In the present study, patients with Depression and Anxiety subscale scores exceeding 11 were considered depressed and anxious.

In addition to completing the QoL and HADS, each participant was also investigated for certain symptoms and psychological problems arising from treatment—namely, difficulty swallowing, mouth dryness or sores, nasal dryness or congestion, fatigue, frequent dizziness, decline in hearing, poor sleep quality, and frequent worry about disease recurrence.

### Statistical Analysis

The levels of anxiety, depression, and 8 side effects or problems arising from treatment measured in NPC survivors are presented as percentages with 95% confidence intervals (CIs). Means with standard deviations and 95% CIs are used to describe the QoL of the NPC survivors. Multiple linear regression was applied to analyze factors influencing QoL. The significance level was set at 0.05.

## RESULTS

Of the 216 NPC survivors eligible for the study, 150 were men (69.44%), and 66 (30.55%) were women. Mean age of the survivors was  $47.81 \pm 10.75$  years. The proportions of participants with low, middle, and high levels of education were 19.44%, 62.03%, and 18.52% respectively. The proportions of participants with disease stages I, II, III, and IV were 1.85%, 11.11%, 58.33%, and 28.70% respectively. Mean survival time for the participants was  $4.39 \pm 2.69$  years (range: 2–10 years). The proportions of participants with 2-, 3-, 4-, and 5-year survival durations were 43.06%, 14.35%, 9.72%, and 32.87% respectively.

Most of the survivors (163, 75.46%) received intensity-modulated RT; the remaining 53 survivors (24.54%) received conventional RT. The RT was delivered using an electron linear accelerator and was prescribed as 66–78 Gy in 30–39 fractions over 6–7.4 weeks. Of the 216 survivors, 211 (97.68%) also received chemotherapy, with 138 (65.40%) receiving concurrent radiochemotherapy, and 73 (34.60%) receiving induction chemotherapy sequenced with RT. In 32 survivors (14.81%) treatment breaks were required because of acute grade II or III oral mucositis.

Table I shows the prevalence rates of anxiety, depression, and problems arising from treatment among these 216 NPC survivors with a survival time of more than 2 years. The prevalences of depression and anxiety were high (25% for depression and 18.98% for anxiety). Disease recurrence was a frequent worry for 18.52% of the survivors. The prevalence rates of the RT-induced side effects of mouth dryness or sores, fatigue, and decline in hearing remained high, even though the survivors had ended RT more than 2 years earlier. Table II shows the mean survival durations in

**TABLE I** Prevalence of anxiety, depression, and symptoms and psychological problems arising from the side effects of treatment in 216 nasopharyngeal carcinoma survivors

| Symptom or problem             | Affected |     | Prevalence (%) | 95% CI (%)     |
|--------------------------------|----------|-----|----------------|----------------|
|                                | No       | Yes |                |                |
| Difficulty swallowing          | 191      | 25  | 11.58          | 7.31 to 15.58  |
| Mouth dryness or sores         | 178      | 38  | 17.59          | 12.51 to 22.67 |
| Nasal dryness or congestion    | 186      | 30  | 13.89          | 9.28 to 18.50  |
| Fatigue                        | 176      | 40  | 18.52          | 13.34 to 23.70 |
| Frequent dizziness             | 192      | 24  | 11.11          | 6.92 to 15.30  |
| Decline in hearing             | 177      | 39  | 18.06          | 12.93 to 23.19 |
| Poor sleep quality             | 184      | 32  | 14.81          | 10.07 to 19.55 |
| Often worried about recurrence | 176      | 40  | 18.52          | 13.34 to 23.70 |
| Anxiety                        | 175      | 41  | 18.98          | 13.75 to 24.21 |
| Depression                     | 162      | 54  | 25.00          | 19.23 to 30.77 |

CI = confidence interval.

**TABLE II** Mean survival among nasopharyngeal carcinoma patients with and without anxiety, depression, and symptoms and psychological problems arising from the side effects of treatment

| Symptom or problem             | Survival (years) |              | p Value <sup>a</sup> |
|--------------------------------|------------------|--------------|----------------------|
|                                | Affected         | Not affected |                      |
| Difficulty in swallowing       | 5.62±3.23        | 4.28±2.61    | 0.042                |
| Mouth dryness or sores         | 5.51±3.40        | 4.32±2.63    | 0.124                |
| Nasal dryness or congestion    | 4.50±3.09        | 4.30±2.61    | 0.194                |
| Fatigue                        | 4.42±2.65        | 4.26±2.90    | 0.723                |
| Frequent dizziness             | 4.36±2.61        | 4.63±3.24    | 0.641                |
| Decline in hearing             | 4.14±2.56        | 5.60±2.94    | 0.002                |
| Poor sleep quality             | 4.35±2.68        | 4.62±2.75    | 0.610                |
| Often worried about recurrence | 4.40±2.67        | 4.37±2.81    | 0.957                |
| Anxiety                        | 4.25±2.61        | 5.01±2.94    | 0.099                |
| Depression                     | 4.33±2.67        | 4.58±2.75    | 0.541                |

<sup>a</sup> By 2-sample t-test.

participants with and without RT-induced symptoms and psychological problems. Except for difficulty in swallowing and decline in hearing, the differences in mean survival duration between the two groups were not statistically significant. That finding suggests that RT-induced symptoms and psychological problems can last for many years after RT.

Table III shows mean scores, with 95% CIs, for survivor QOL. The mean score for global QOL was 74.21 (95% CI: 72.22 to 76.20). Of the three functional scales, QOL-Social showed the highest scores (mean: 78.32; 95% CI: 75.93 to 80.71), and QOL-Physical showed the lowest scores (mean: 72.36; 95% CI: 71.36 to 73.36). Compared with the highest possible QOL score of 100, the mean QOL score of 74.21 was high, which suggests that the QOL of our NPC survivors was good.

Table IV shows the frequency distributions for the global QOL score and the QOL-Physical and -Social scores. The mean global QOL scores for participants with 2-, 3, 4-,

**TABLE III** Mean scores for global quality-of-life (QOL) and QOL subscales in 216 nasopharyngeal carcinoma survivors

| Variable     | Range        | Mean±SD     | 95% CI         |
|--------------|--------------|-------------|----------------|
| Global QOL   | 27.50–99.11  | 74.21±14.92 | 72.22 to 76.20 |
| QOL-Physical | 47.06–82.35  | 72.36±7.49  | 71.36 to 73.36 |
| QOL-Mental   | 37.50–87.50  | 74.22±9.78  | 72.92 to 75.52 |
| QOL-Social   | 25.00–100.00 | 78.32±17.95 | 75.93 to 80.71 |

SD = standard deviation; CI = confidence interval.

**TABLE IV** Frequency distributions of scores for global quality-of-life (QOL) and QOL subscales in 216 nasopharyngeal carcinoma survivors

| Score group | Quality-of-life domain |       |          |       |        |       |        |       |
|-------------|------------------------|-------|----------|-------|--------|-------|--------|-------|
|             | Global                 |       | Physical |       | Mental |       | Social |       |
|             | (n)                    | (%)   | (n)      | (%)   | (n)    | (%)   | (n)    | (%)   |
| <40         | 1                      | 0.46  | 1        | 0.46  | 2      | 0.93  | 4      | 1.85  |
| 40–49       | 12                     | 5.56  | 2        | 0.93  | 3      | 1.39  | 8      | 3.70  |
| 50–59       | 26                     | 12.04 | 12       | 5.56  | 15     | 6.94  | 21     | 9.72  |
| 60–69       | 45                     | 20.83 | 50       | 23.15 | 36     | 16.67 | 31     | 14.35 |
| 70–79       | 51                     | 23.61 | 122      | 56.48 | 105    | 48.61 | 46     | 21.30 |
| ≥80         | 81                     | 37.50 | 29       | 13.42 | 55     | 25.46 | 106    | 49.07 |

and 5-year survival durations were 76.40 (95% CI: 73.66 to 79.14), 72.17 (95% CI: 65.97 to 78.36), 75.61 (95% CI: 70.32 to 80.90), and 71.83 (95% CI: 68.12 to 75.54) respectively. The differences in mean global QOL score for the survivors with 2-, 3-, 4-, and 5-year survival durations were not statistically significant ( $p = 0.206$ ). In addition, the correlation coefficient between years of survival and QOL score was not statistically significant ( $r = 0.081$ ,  $p = 0.236$ ). Those findings suggest that the QOL of NPC survivors did not improve with greater survival duration.

Stepwise regression was used to detect factors influencing the global QOL of our NPC survivors. The factors analyzed in the regression model were age, sex, education level (low, medium, high), disease stage, depression, anxiety, difficulty in swallowing (no, yes), mouth dryness or sores (no, yes), nasal dryness or congestion (no, yes), fatigue (no, yes), frequent dizziness (no, yes), decline in hearing (no, yes), poor sleep quality (no, yes), and frequent worry about disease (no, yes). Table V shows the results.

At a significance level of  $\alpha = 0.05$ , the factors influencing QOL were age ( $p = 0.032$ ), education level ( $p = 0.001$ ), Anxiety score ( $p < 0.001$ ), Depression score ( $p < 0.001$ ), mouth dryness or sores ( $p < 0.001$ ), fatigue ( $p = 0.027$ ), and disease stage ( $p = 0.044$ ). The linear regression model containing those seven factors explained 70.10% of the variation in global QOL (adjusted  $R^2 = 0.701$ ). The results suggest that younger NPC survivors had worse QOL than older survivors, that NPC survivors with higher education levels had better QOL than those with a low education level, and that disease stage was negatively correlated with QOL (Table V). The results also suggest that RT-induced symptoms (including

**TABLE V** Stepwise regression of factors associated with quality of life (dependent variable: global quality-of-life score)

| Factor                 | $\beta$ | SE    | t      | p Value |
|------------------------|---------|-------|--------|---------|
| Age                    | -1.096  | 0.508 | 2.157  | 0.032   |
| Education level        | 7.237   | 2.162 | 3.348  | 0.001   |
| Anxiety                | -1.623  | 0.190 | 8.559  | 0.000   |
| Depression             | -0.777  | 0.191 | 4.075  | 0.000   |
| Mouth dryness or sores | -6.140  | 1.655 | 3.710  | 0.000   |
| Fatigue                | -3.124  | 1.399 | -2.233 | 0.027   |
| Disease stage          | -1.628  | 0.802 | 2.030  | 0.044   |

SE = standard error.

mouth dryness or sores and fatigue) and psychological problems (including anxiety and depression) affect QOL (Table v).

## DISCUSSION

With the emergence of new treatment techniques, NPC patients have a better chance to live cancer-free for an extended period of time. However, some RT-induced side effects are chronic and progressive<sup>16,17</sup>, and those sequelae can lower QOL in survivors<sup>7</sup>. Understanding patient perspectives about QOL and exploring the factors related to QOL are helpful not only for clinicians making treatment decisions, but also for health workers attempting to provide NPC survivors with adequate health services in their communities.

Mouth dryness, mouth sores, and decline in hearing are common side effects in NPC patients who receive RT. Previous studies have suggested that those side effects can be sustained for many years after the end of RT<sup>18,19</sup>. In a study of 336 NPC survivors (survival duration: 5–38 years), researchers reported that 23.51% had serious mouth dryness, 10.71% had mouth sores, and 28.87% experienced a serious decline in hearing<sup>18</sup>. Wu *et al.*<sup>7</sup> reported that prevalence rates of serious decline in hearing and difficulty in swallowing were 51.67% and 52.38% respectively in 192 NPC survivors (survival duration: 2–5 years). Fang *et al.*<sup>19</sup> also reported that the prevalence rates of difficulty in swallowing and decline in hearing were 55.56% and 55.43% respectively in NPC survivors with a survival duration of 2 or more years. In our study, the prevalence rates of mouth dryness or sores, difficulty in swallowing, and decline in hearing were 17.59%, 11.58%, and 18.06% respectively. Our results could not be compared with those from previous reports because the methods used to assess symptoms in those studies differed from ours. However, our results confirm that RT-induced mouth dryness or sores and decline in hearing were the main symptoms in NPC survivors, which accords with the previous reports. Based on the mean survival time shown in Table II, those symptoms can last for many years after RT.

During treatment, doctors should minimize the radiation dose to organs at risk (especially the ears) of patients, and community health care workers should provide oral and ear care to NPC survivors. During clinical treatment, the dose constraints for normal tissue should be fully considered, and newer RT techniques such as intensity-modulated RT, which,

compared with conventional RT, can provide better clinical outcomes and sparing of organs at risk, should be used for NPC patients if possible<sup>20</sup>. In 1991, Emami *et al.*<sup>21</sup> recommended partial organ tolerance doses, which were useful in designing treatment plans, although the recommended doses had some uncertainties and limitations. Today, quantitative correlates of dose–volume with clinical outcome can be obtained because of the use of three-dimensional treatment planning. The QUANTEC (quantitative analysis of normal tissue effects in clinic) articles<sup>22–25</sup> summarized studies since the early 1990s and updated the information provided by Emami *et al.* The dose–volume limits of major organs at risk during treatment for NPC as recommended by QUANTEC are these:

- A 5%–10% risk of symptomatic radiation necrosis is predicted to occur at 72 Gy and 90 Gy in 2-Gy fractions<sup>22</sup>.
- The incidence of radiation-induced optic neuropathy was unusual for a maximum dose of less than 55 Gy, particularly for fraction sizes below 2 Gy<sup>23</sup>.
- To minimize the risk for sensorineural hearing loss, the mean dose to the cochlea should be limited to 45 Gy or less—or more conservatively, to 35 Gy or less with concurrent cisplatin and RT<sup>24</sup>.
- Severe xerostomia can usually be avoided if at least 1 parotid gland has been spared to a mean dose of less than 20 Gy or if both glands have been spared to a mean dose of 25 Gy<sup>25</sup>.

Anxiety and depression are the psychological problems most commonly seen in cancer patients<sup>26–28</sup>. The reported prevalence of anxiety and depression in cancer patients ranges from 25% to 54%<sup>26,29</sup>. A study using the HADS showed that 51.2% of NPC patients are anxious and that 44.2% are depressed<sup>30</sup>. In a study using the Self-Rating Anxiety Scale and Self-Rating Depression Scale, researchers reported that the prevalence rates of anxiety and depression in 46 NPC survivors (mean survival duration: 5.7 ± 3.1 years) were 82.6% and 78.3% respectively<sup>31</sup>. Those studies indicated that psychological disorders, such as depression and anxiety, are apparent as early as the start of RT and can last long after RT<sup>31,32</sup>. Our study also suggested that anxiety and depression can continue for many years after RT. Psychological problems in cancer survivors should not be ignored, because depression and anxiety can influence cancer survival<sup>33,34</sup> and QOL<sup>35</sup>. Data from several studies indicate that poor psychological status can influence a patient's immune status and illness duration<sup>36,37</sup> and that untreated depression can result in significant morbidity and mortality<sup>38</sup>. Close attention and psychological care should therefore be given to patients not only during the period of RT but also during follow-up.

Fatigue is a common and frequently disabling symptom in cancer survivors<sup>39</sup> that can last for a long time after treatment in some cancer survivors<sup>40</sup>. Fatigue affects the ability to perform daily activities<sup>41</sup>, increases anxiety and depression<sup>42</sup>, and lowers QOL in cancer patients<sup>43</sup>. The prevalence of fatigue in NPC survivors is rarely reported. In a study of head-and-neck cancer survivors, researchers reported a 10% prevalence of fatigue<sup>44</sup>. In our study, the prevalence of self-reported fatigue in NPC survivors

was 18.52%. The higher prevalence of fatigue in our study might be a result of the method used to assess fatigue. The participants might lack the ability to distinguish fatigue from depression. Fatigue and depression are both heterogeneous constructs with physical, cognitive, and emotional dimensions and a high degree of overlap across the dimensions<sup>45</sup>. Further studies with a special scale are needed to measure fatigue.

In the present study, the mean score for global QOL was 74.21 (range: 27.50–99.11). Compared with the highest possible QOL of 100, we believe that 74.21 is not low. A high mean QOL score could suggest that NPC survivors in Fujian experience good QOL. Several studies have reported QOL in NPC survivors<sup>7,19,30,31,46,47</sup>. Among those studies, only the one by Cengiz *et al.*<sup>47</sup> used the QLQ-C30 version 3.0, the same scale used in our study, to measure QOL. In the Cengiz study, the mean global QOL score for 187 NPC survivors with a survival duration of 0.5–24 years was 73.0 (range: 8.3–100.0), a result very similar to ours.

The limitations of our study must be mentioned. Our study used a cross-sectional design. The prevalence of anxiety and depression—and the QLQ-C30 score—described the psychological status and QOL of the NPC survivors at only one time point. A more methodologically sound approach would be to use a longitudinal design in which the same individuals are assessed repeatedly at various time points. The pattern of change in QOL with the passage of time can best be evaluated in longitudinal studies.

## CONCLUSIONS

The prevalence rates of mouth dryness or sores, fatigue, decline in hearing, depression, and anxiety were high in our cohort of NPC survivors with a survival duration of more than 2 years. Those RT-induced symptoms and psychological problems can last for many years after RT. The QOL of the NPC survivors was good. The factors influencing QOL were age, education level, anxiety, depression, mouth dryness or sores, fatigue, and disease stage. Our results suggest that, during clinical treatment, doctors should minimize the radiation dose to the ears of patients. Our results also emphasize the importance of providing oral and ear nursing and psychological care to NPC survivors.

## CONFLICT OF INTEREST DISCLOSURES

We have read and understood *Current Oncology's* policy on disclosing conflicts of interest, and we declare that we have none. This study had no financial relationship with any sponsoring organization. The corresponding author has full control of all primary data and will allow a data review if requested.

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