Incidence, Prognosis, and Risk Factors for Fatigue and Chronic Fatigue Syndrome in Adolescents: A Prospective Community Study
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Incidence, Prognosis, and Risk Factors for Fatigue and Chronic Fatigue Syndrome in Adolescents: A Prospective Community Study

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ABSTRACT

OBJECTIVE. The objective of this study was to describe the incidence, prevalence, risk factors, and prognosis of fatigue, chronic fatigue, and chronic fatigue syndrome in 11- to 15-year-olds.

METHODS. A random general population sample (n = 842) of British adolescents and their parents were assessed at baseline and 4 to 6 months later. The main outcomes were fatigue, chronic fatigue, and chronic fatigue syndrome, operationally defined.

RESULTS. The incidence over 4 to 6 months was 30.3% for fatigue, 1.1% for chronic fatigue, and 0.5% for chronic fatigue syndrome. The point prevalence was 34.1% and 38.1% for fatigue, 0.4% and 1.1% for chronic fatigue, and 0.1% and 0.5% for chronic fatigue syndrome at time 1 and time 2, respectively. Of participants who were fatigued at time 1, 53% remained fatigued at time 2. The 3 cases of chronic fatigue and 1 case of chronic fatigue syndrome at time 1 had recovered by time 2. Higher risk for development of chronic fatigue at time 2 was associated with time 1 anxiety or depression, conduct disorder, and maternal distress; in multivariate analysis, baseline anxiety or depression remained a significant predictor of chronic fatigue. Increased risk for development of fatigue at time 2 was associated with time 1 anxiety or depression, conduct disorder, and older age; in multivariate analyses, these factors and female gender all were significant predictors of fatigue.

CONCLUSIONS. The incidence rates for chronic fatigue and chronic fatigue syndrome in this adolescent sample were relatively high, but the prognosis for these conditions was good. This prospective study provides evidence for an association between emotional/behavioral problems and subsequent onset of fatigue/chronic fatigue.
Chronic fatigue syndrome (CFS) is characterized by disabling physical and mental fatigue that lasts at least 6 months, with a number of accompanying symptoms. The term “chronic fatigue” (CF) has no widely agreed-on definition but is used variously to describe excessive, persistent fatigue that is associated with less impairment than CFS; fatigue that has fewer accompanying symptoms; or fatigue that has lasted <6 months. There is an extensive empirical literature on many aspects of CF and CFS, but nearly all relates to adults.

Estimates of prevalence in adults vary widely, ranging from ~1.8% to 9% for CF and ~0.075% to 0.42% for CFS in community studies, depending on the setting, methods, and definitions used. Using data from the British Child and Adolescent Mental Health Survey 1999 conducted by the Office for National Statistics, we reported that in 5- to 15-year-olds, CF was present in 0.57% of the sample and CFS according to Centers for Disease Control and Prevention (CDC) criteria was present in 0.19%. A previous incidence study in adults reported an annual incidence of 50 per 1000 per year for CF and 3.7 per 1000 per year for CFS. Incidence rates for fatigue, CF, and CFS in adolescents are not known. The present study involves the longitudinal follow-up of a subgroup of those participants.

**METHODS**

**Design and Participants**

This study was part of a larger Office for National Statistics study of mental health in children who were aged 5 to 15 years. The sample frame consisted of families who lived in private households in England, Scotland, and Wales. The sample was taken from child benefit records. The original sampling frame excluded cases for which “administrative action” such as death or change of address was indicated. The sampling frame was stratified by Regional Health Authority and within that by sociodemographic groupings. Postal sectors were randomly selected within that frame with a probability proportional to the size of the sector. In each of the 475 postal sectors, 30 children were randomly selected and targeted. The Child Benefit Centre sent information to parents about the survey, giving them the opportunity to opt out. Those who agreed to participate were interviewed at home.

Of the 14,250 families contacted, 931 (6.5%) opted out by calling the Child Benefit Register and 790 (5.5%) addresses were found to be incorrect. This left a sample of 12,529 eligible children, and 10,438 of these were interviewed. Failed interviews were attributed to either non-contact (2%) or refusal (15%). Of those interviewed, 4,240 were 11- to 15-year-olds and were included in the original epidemiologic study that was reported in the previous article. From this first time point, 1,096 adolescents were selected to be reassessed 4 to 6 months later for the present study. Follow-ups were restricted to participants who had been assessed in the early stages of the study because of budgetary constraints and because this permitted a 4- to 6-month follow-up before the end of the school year. Follow-up questionnaires were returned by 77% (n = 842) of this sample.

**Measures and Interviews**

At time 1, the Development and Well-being Assessment was administered by nonclinical, trained interviewers. Classification according to the International Classification of Disease, Tenth Revision, Classification of Mental and Behavioral Disorders with strict impairment criteria was ascertained by a combination of interviews and rating techniques that were designed to generate psychiatric diagnoses on this age group. The Development and Well-being Assessment has been shown to discriminate well between community and clinic samples in rates of diagnosed disorders. The adolescents were asked whether they had been feeling more tired and worn out than usual. When they answered affirmatively, the interviewer asked supplementary and open-ended questions related to duration, effect of fatigue on various aspects of their life, and number and severity of symptoms, including questions to assess CDC criteria for CFS (Appendix E, questions C3D1–C3D199). These supplementary questions included 4 items concerning impairment: “Has feeling tired and worn-out . . . interfered with (1) how well you get on with the rest of your family, (2) making and keeping friends, (3) learning or class work, (4) playing, hobbies, sports or other leisure activities?” For each of the 4 domains, the participant could choose from among the responses “not at all,” “only a little,” “quite a bit,” and “a great deal.” The responses “quite a bit” and “a great deal” were coded as significant impairment and received scores of 1 and 2, respectively. The total impairment score was the sum of these 4 items and therefore ranged from 0 to 8. Mothers completed the 12-item General Health Questionnaire (GHQ) to assess maternal psychological well-being. The British Picture Vocabulary Scale was used to assess the adolescent’s IQ. Follow-up was conducted by mail and included the same questions that were related to fatigue and asked at time 1.

**Outcomes**

The adolescent was classified as fatigued when he or she answered “yes” to the question, “Over the last month, have you been feeling much more tired and worn out than usual?” CF was defined operationally as severe fatigue that was of at least 6 months’ duration, was not helped by rest, and was associated with significant im-
Impairment in at least 1 domain (see previous section). CFS was defined according to the CDC criteria.¹

**Analysis**
Statistical analysis was conducted without adjustment for stratification and clustering because previous experience has shown that prevalence figures are minimally affected by these processes in this sample.² Logistic regression (also with no adjustment for stratification and clustering) was used to calculate odds ratios between independent variables at time 1 and dependent fatigue variables at time 2. A final multivariate model was used to determine which factors were associated independently with fatigue status at time 2, in which all variables that were shown to be associated significantly (P < .05) were entered simultaneously, together with gender and age, because these were known confounders.

**RESULTS**

**Characteristics of Participants**
Characteristics of participants who took part in the study at both times 1 and 2 were compared with those for the rest of the 11- to 15-year-old participants at time 1. T tests indicated that time 2 participants had a significantly higher IQ score on the British Picture Vocabulary Scale than those who only took part in the first part of the study (mean: 102.02 vs 98.72; t₄₁₇₄ = 4.7; P < .0005). Time 2 participants were more likely to come from a higher social class (58.1% vs 53.4%; χ² = 5.7, P = .017), to have a mother educated to at least “A” levels (advanced level exams) or equivalent (34.4% vs 30.6%; χ² = 4.4, P = .037), and to have a mother who had a partner (82.3% vs 75.6%; χ² = 17.1, P < .0005) but were less likely to report nonwhite ethnicity (7.0% vs 9.5%; χ² = 5.0, P = .026) or to have a psychiatric diagnosis at time 1 (7.5% vs 10.5%; χ² = 6.8, P = .009) than the other participants. There were no significant differences between the 2 groups with regard to age (t₄₂₃₈ = 1.5), gender (χ² = 0.02), maternal GHQ score (t₄₁₅₂ = 0.5), or whether the participant reported being tired at time 1 (χ² = 2.2).

**Incidence of Fatigue, CF, and CFS**
There were 166 new cases of fatigue at time 2 (30.3%; 95% confidence interval [CI]: 26.4–34.2) and 9 new cases of CF (1.1%; 95% CI: 0.0–1.8) and 4 new cases of CFS (0.5%; 95% CI: 0.0–0.9) in the 4- to 6-month period (Table 1).

**Point Prevalence of Fatigue, CF, and CFS**
The point prevalence of fatigue was 34.1% (95% CI: 30.9–37.3) at time 1 and 38.1% (95% CI: 34.8–41.5) at time 2. For CF, the point prevalence was 0.4% (95% CI: 0.0–0.8) at time 1 and 1.1% (95% CI: 0.04–1.8) at time 2. For CFS, the point prevalence was 0.1% (95% CI: 0.0–0.4) for time 1 and 0.5% (95% CI: 0.01–0.9) for time 2 (Table 1).

**Prognosis of Fatigue, CF, and CFS**
Of the 283 participants who reported that they were tired at time 1, 151 (53.3%; 95% CI: 47.5–59.2) were still tired at time 2. All 3 participants with CF and the 1 participant with CFS at time 1 had recovered by time 2 (Table 1).

**Impairment That Was Associated With Fatigue, CF, and CFS**
Of the participants with fatigue at time 1, 22.6% (95% CI: 17.7–27.5) reported significant impairment in at least

**TABLE 1**

<table>
<thead>
<tr>
<th>Total Classifications at Time 1</th>
<th>Classification at Time 2 Divided According to Classification at Time 1</th>
<th>Total Classifications at Time 2 (4–6 mo Later)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fatigue</td>
<td></td>
<td></td>
</tr>
<tr>
<td>283 (34.1%) fatigued</td>
<td>151 (53.4%) fatigued</td>
<td>317 (38.1%) fatigued</td>
</tr>
<tr>
<td>548 (65.9%) not fatigued</td>
<td>132 (46.6%) not fatigued</td>
<td>514 (61.9%) not fatigued</td>
</tr>
<tr>
<td>CFb</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3 (0.4%) CF</td>
<td>0 (0%) CF</td>
<td>9 (1.1%) CF</td>
</tr>
<tr>
<td>839 (99.6%) no CF</td>
<td>3 (100%) no CF</td>
<td>833 (98.9%) no CF</td>
</tr>
<tr>
<td>CFSc</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 (0.1%) CFS</td>
<td>0 (0%) CFS</td>
<td>4 (0.5%) CFS</td>
</tr>
<tr>
<td>841 (99.9%) no CFS</td>
<td>1 (100%) No CFS</td>
<td>838 (99.5%) no CFS</td>
</tr>
</tbody>
</table>

* New cases.

* Defined as severe fatigue of 6 months’ duration with nonrestorative rest and functional impairment.

* According to CDC criteria.
1 domain, and of the participants who reported fatigue at time 2, 24.0% (95% CI: 16.3–31.7) reported impairment. The mean impairment scores were 0.36 (95% CI: 0.27–0.46) for those with time 1 fatigue and 0.7 (95% CI: 0.55–0.85) for time 2 fatigue. The 3 participants meeting criteria for CF at time 1 CF all had an impairment score of 1, and for participants with time 2 CF, the mean score was 2.67 (95% CI: 1.18–4.16). The participant with CFS at time 1 had an impairment score of 1, and for participants with CFS at time 2, the mean score was 3.25 (95% CI: 0.53–5.97).

**Time 1 Factors That Were Associated With New Fatigue at Time 2**

To investigate which factors at time 1 were associated with new-onset fatigue at time 2, hypothesized risk factors were entered into a logistic regression model (see Table 2 for details). In univariate analyses, older age, anxiety or depressive disorder, and conduct disorder at time 1 were associated significantly with fatigue at time 2. When these variables were entered into a multivariate model together with gender, the results indicated that age, female gender, conduct disorder, and anxiety or depression were significant independent predictors of fatigue.

**Time 1 Factors That Were Associated With Persistence of Fatigue at Time 2**

Logistic regression analyses were performed using participants who were fatigued at time 1 to investigate which factors were associated with either persistent fatigue or recovery (see Table 2 for details). Individuals who still reported being much more tired or worn out than usual in the past month at time 2 were regarded as having persistent fatigue, whereas those who did not report fatigue at time 2 were regarded as having recovered. Time 1 factors that were associated with remaining fatigued were older age, female gender, higher IQ, higher maternal GHQ score, and the mother’s being educated to at least A levels or equivalent. When these variables were entered together in a multivariate analysis, older age, female gender, higher IQ, and maternal GHQ score were significant independent predictors of persistent fatigue.

**Time 1 Factors That Were Associated With Chronic Fatigue at Time 2**

Maternal GHQ score, conduct disorder, and anxiety or depression at time 1 all were significantly associated with new-onset CF at time 2 (Table 2). When these variables were entered into a multivariate analysis together with age and gender, only the presence of an anxiety or depressive disorder remained a significant predictor of new-onset CF.

**Characteristics of Individuals With Recent-Onset CFS**

There were only 4 new cases of CFS at time 2, so the numbers were too small to analyze risk factors statistically. Three of the 4 new cases of CFS were in girls. Three of the 4 had at least 1 psychiatric diagnosis at baseline. Three of them had reported being “much more tired and worn out than usual over the last month” at time 1. Two of the participants had frequent headaches at time 1; 1 of them also had sleep problems and postexertional malaise at this point.

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### TABLE 2  Associations Between Factors at Time 1 and New-Onset Fatigue, Persistent Fatigue, and New-Onset CF at Time 2

<table>
<thead>
<tr>
<th>Factors Assessed at Time 1</th>
<th>New Cases of Fatigue at Time 2 (n/N = 166/548)</th>
<th>Participants With Fatigue at Time 1: Prognosis of Fatigue at Time 2 (n/N = 151/283)</th>
<th>New Cases of Chronic, Severe Fatigue With Disability at Time 2a (n/N = 9/839)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Univariate OR (95% CI)</td>
<td>Multivariate OR (95% CI)</td>
<td>Univariate OR (95% CI)</td>
</tr>
<tr>
<td>Age</td>
<td>1.30 (1.14–1.49)</td>
<td>1.34 (1.16–1.54)</td>
<td>1.33 (1.11–1.58)</td>
</tr>
<tr>
<td>Female gender</td>
<td>1.43 (0.99–2.07)</td>
<td>1.77 (1.20–2.61)</td>
<td>1.82 (1.13–2.93)</td>
</tr>
<tr>
<td>Social class (I, II, III versus IIIM, IV, V)</td>
<td>1.04 (0.72–1.51)</td>
<td>0.74 (0.46–1.19)</td>
<td>0.46 (0.09–2.92)</td>
</tr>
<tr>
<td>Ethnicity (white versus nonwhite)</td>
<td>1.16 (0.57–2.38)</td>
<td>1.98 (0.73–5.36)</td>
<td>1.02 (0.95–1.03)</td>
</tr>
<tr>
<td>IQ</td>
<td>1.00 (0.99–1.01)</td>
<td>1.02 (1.01–1.04)</td>
<td>1.03 (1.01–1.05)</td>
</tr>
<tr>
<td>Any anxiety or depressive disorder</td>
<td>4.88 (1.80–13.2)</td>
<td>4.33 (1.49–12.6)</td>
<td>1.99 (0.73–5.36)</td>
</tr>
<tr>
<td>Any conduct disorder</td>
<td>3.16 (1.36–7.6)</td>
<td>3.01 (1.18–7.68)</td>
<td>2.40 (0.63–9.26)</td>
</tr>
<tr>
<td>Hyperkinetic disorder</td>
<td>0.57 (0.06–5.16)</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Tired at time 1</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Mother’s GHQ score</td>
<td>1.05 (1.00–1.12)</td>
<td>1.09 (1.00–1.17)</td>
<td>1.11 (1.02–1.21)</td>
</tr>
<tr>
<td>Mother educated “A” level or above</td>
<td>1.05 (0.71–1.55)</td>
<td>1.80 (1.11–2.92)</td>
<td>1.31 (0.75–2.28)</td>
</tr>
<tr>
<td>Mother: single (partner)</td>
<td>1.53 (0.97–2.41)</td>
<td>1.82 (0.96–3.46)</td>
<td>—</td>
</tr>
</tbody>
</table>

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a Severe fatigue of at least 6 months’ duration with nonrestorative rest and functional impairment.

b P < .0005
c F < .005
d P < .05

*Not possible to analyze because cell sizes were too small.
DISCUSSION

We have already shown that fatigue is common in adolescents but CF and CFS less so, a finding that since has been replicated elsewhere. In this article, we present the first incidence data, the first prospective epidemiologic data on prognosis, and the first prospective data on preillness risk factors for fatigue, CF, and CFS in adolescents. The use of a community sample ensures that the findings are less open to the selection and referral biases that may operate in clinical samples. The prospective design allows identification of predictor/risk factors and can help in determination of the sequence of causality. This is particularly important for factors such as anxiety or depression, which may occur as a consequence of conditions such as CF or CFS. However, using a prospective design shows that these and other characteristics clearly are vulnerability factors for fatigue conditions.

The incidence rates for CF and CFS were surprisingly high (1.1% for CF and 0.5% for CFS during a 4- to 6-month period), given the relatively low prevalence. Prevalence is a function of incidence and prognosis, and we found that the high incidence was balanced by high remission rates 4 to 6 months later.

Having an anxiety or depressive disorder at time 1 was strongly associated with new onset of fatigue or CF at time 2. Conduct disorder was associated with new-onset fatigue and CF in univariate analyses and remained a significant predictor of new fatigue (but not CF) in multivariate analysis. Three of the 4 adolescents who developed CFS at time 2 had had at least 1 psychiatric diagnosis at time 1. Maternal distress at time 1 was associated with the persistence of fatigue and new-onset CF at time 2. Older age and female gender also were associated with an increased risk for new-onset fatigue and the persistence of fatigue between times 1 and 2. Higher IQ and having a mother who was educated to A levels or beyond were associated with the persistence of fatigue.

Limitations

One limitation is that the participants from time 1 who also completed the questionnaire at time 2 were different from the rest of the time 1 sample in several ways that reflected higher socioeconomic status and better mental health. These differences might influence the results. For example, a strong predictor of fatigue or CF at time 2 was having a psychiatric diagnosis at time 1, and because people were less likely to take part at time 2 when they had a psychiatric diagnosis, it is possible that the incidence and prevalence figures at time 2 are an underestimation of those that would have been found if all of the sample had taken part at follow-up. Another limitation is that the small number of participants with CF in this sample means that we cannot draw firm conclusions from these analyses regarding the factors that were associated with the onset of this condition. (Similarly, the numbers of participants with CFS were too small to undertake statistical analysis to examine factors that were associated with onset.) However, 2 of the factors that were identified as predictors of new-onset of CF—conduct disorder and anxiety/depression—also were identified as being associated with new cases of fatigue that were less chronic or disabling, for which the numbers of cases were much larger. An additional limitation is that the diagnoses at time 2 were made on the basis of questionnaire rather than clinical interview data; it was not possible for logistic reasons to repeat the psychiatric interview at time 2. At neither time point were the adolescents physically examined or investigated to exclude other possible diagnoses. However, the number of cases of fatigue that were caused by defined biomedical diagnoses in this age group is likely to be very small.

Comparison With Others Studies

This is the first study, to our knowledge, that examined the incidence of CF and CFS in adolescents. The incidence was 11 per 1000 for CF and 5 per 1000 for CFS for the 4- to 6-month study period, findings that are broadly comparable to the incidence figures that were reported in an adult community sample (50 per 1000 per year for CF and 3.7 per 1000 per year for CFS), despite the use of different definitions for CF and CFS in that study. The incidence rates for CF and CFS in the present study were higher than those previously reported for a number of other disorders in adolescents, such as asthma (estimated annual incidence of 2.1 per 1000 per year), type 1 diabetes (0.16–0.18 per 1000 per year), and anxiety disorders (6.1 per 1000 per year). However, the CF and CFS incidence figures are lower than those for depression in adolescents (33 per 1000 per year).

The prevalence of CF in the adolescents in this sample was slightly lower than that reported for adults in previous community studies and was lower than in a study of children and adolescents in the Netherlands, where 9.6% of girls and 2.3% of boys had severe and chronic fatigue. The latter study used a different definition and assessment of severe fatigue, which, for example, did not require nonrestorative rest or functional impairment, was of 3 months’ duration rather than 6, and included motivational problems. The present study finds higher CFS prevalence rates (0.1% and 0.5%) than the estimated 0.034% in an American adolescent community study, although the figures are within the ranges reported in adult community research. The finding that the adolescents with CF or CFS at time 1 all had recovered by time 2 is consistent with previous tertiary care research indicating that adolescents with CFS have better outcomes than adults.

No previous prospective studies have examined variables that predict the onset of fatigue, CF, and CFS in young people. The demonstration of a relationship be-
tween psychiatric disorder and subsequent fatigue or CF in this study is consistent with previous cross-sectional and retrospective research into fatigue and CFS in adolescents. For example, a study found that two-thirds of young people (aged 10–18) who had CFS and attended a specialist clinic had had a psychiatric disorder in the previous year. In a prospective primary care study in adults, participants with depression had an increased risk for a new episode of unexplained fatigue at 12-month follow-up. An interesting finding in the present study was the association between conduct disorder and CF, a relationship that was not demonstrated previously.

The findings that indicated associations between maternal distress and subsequent new CF and persistent fatigue and between older age and female gender and new-onset fatigue are consistent with previous cross-sectional findings in adolescents. Unlike a prospective study of CFS in adulthood, this study did not find an association between social class and the onset of CFS in adolescence. Prospective research into adult-onset CFS has identified other risk factors, including lower childhood physical fitness, long-standing physical or mental illness in childhood that significantly affected home or school life, certain viruses (eg, mononucleosis), and prolonged convalescence and particular illness beliefs after a virus.

Implications of the Findings
The nature of the relationship between psychological problems and subsequent fatigue states requires additional investigation. Possible explanations for the association included overlapping criteria in the definitions of CFS and some psychiatric conditions, psychological problems playing a contributory role in the development of fatigue syndromes, or psychological conditions and fatigue syndromes sharing common risk factors that account for the association between them. One implication of these results is that when health professionals consider the various factors that may be contributing to a young person’s fatigue, of any severity, they should assess for emotional/behavioral difficulties.

Although this study suggests that the prognosis of CF and CFS in adolescents who are aged 11 to 15 may be relatively good, even a few months’ school absence may have profound effects on an adolescent’s education and peer relationships. Furthermore, evidence from tertiary care suggests that a substantial minority of individuals remain disabled for long periods of time. Therefore, effective treatments are needed to help reduce the length of the illness and improve outcomes. Results from a randomized, controlled trial indicate that cognitive behavior therapy can be effective for adolescents who have CFS and are referred from a pediatrics clinic. This intervention involves components that are tailored to the specific needs of the child, such as the establishment of a baseline level of activity and rest (to prevent bursts of overactivity and subsequent severe fatigue), followed by a gradual, structured increase in physical activity and cognitive work to address unhelpful thinking patterns that might be contributing to functional impairment or emotional problems. There is little evidence regarding primary care interventions for adolescents with CF or CFS, but evidence from this study suggests that emotional factors may need to be addressed in this setting too.

CONCLUSIONS
This is the first prospective community survey of the incidence, prognosis, and risk factors for CF and CFS in adolescents, thus overcoming the problems that are associated with cross-sectional studies that are conducted in specialist settings. The observed incidence rates for CF and CFS in adolescents were relatively high. Anxiety or depressive disorder was associated with an increased risk for fatigue or CF 4 to 6 months later. Assessment of new cases of fatigue therefore should include a review of any possible psychological problems. Future research needs to investigate the nature of the relationship between the identified risk factors and the development of CF or CFS and identify other risk factors. Although the prognosis for CF and CFS in this sample was good, these conditions can be extremely disabling, and effective treatments for young people in primary care settings are needed.

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REFERENCES


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