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Quality of life, risk behaviors and depression among carriers of hepatitis C virus and human T-cell lymphotropic virus type 1: a comparative study



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ABSTRACT

Human T-cell lymphotropic virus type 1 (HTLV-1) has low prevalence rates, but is endemic in some regions of the world. It is usually a chronic asymptomatic infection, but it can be associated with serious neurologic and urinary conditions. Hepatitis C virus (HCV) is broadly spread out worldwide. The majority of these infections have a chronic course that may progress to cirrhosis and hepatocellular carcinoma.

Objectives: To compare sociodemographic and mental health (risk behaviors, depression, and suicide) aspects, and quality of life among patients with HCV or HTLV-1.

Methods: Observational, comparative and cross-sectional study involving outpatients with HCV or HTLV-1 infection. Sociodemographic characteristics, risk behaviors and quality of life were assessed through the questionnaires *Mini International Neuropsychiatric Interview – MINI Plus* (depression and suicide) and *Medical Outcomes Study 36-Item Short-Form Health Survey* (quality of life). Univariate and multivariate statistical analyses (hierarchical logistic regression) were conducted.

Results: 143 individuals with HCV and 113 individuals with HTLV-1 infection were included. Males were predominant in the HCV group (68.8%) and females in the HTLV-1 group (71.7%). The frequency of risk behaviors (sexual and drug use) was greater in those with HCV ($p < 0.05$). A past depressive episode was more common in the HTLV-1 group ($p = 0.037$).

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Quality of life was significantly worse in the physical functioning, vitality, mental health, and social functioning domains in those with HTLV-1 ($p < 0.05$). HTLV-1 infection remained independently associated with worse quality of life in multivariate analysis.

Conclusions: Risk behaviors are frequent among those infected with HCV. Additionally, despite HTLV-1 being considered an infection with low morbidity, issues related to mental health (depressive episode) and decreased quality of life are relevant.

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Introduction

Human T-cell lymphotropic type 1 virus (HTLV-1) is an endemic virus in some regions of the world, including some states of Brazil. In the city of Salvador, the prevalence is 1.35–1.76%.^{1–3}

HTLV-1 is transmitted by routes such as sexual relations, vertical transmission (primarily by breastfeeding), blood transfusion, and sharing needles by intravenous drug users (IVDU).^{2,3} It is an infection of low morbidity, as at least 90% of the infected individuals remain asymptomatic. Two to three percent of patients develop symptoms of HTLV-1 associated myelopathy/tropical spastic paraparesis (HAM/TSP),⁴ which include muscle weakness, gait disturbances, lower back pain, paresthesia and hyperreflexia in the lower limbs, intestinal constipation, urinary retention or incontinence and erectile dysfunction. HAM/TSP has a poor prognosis and adversely impacts survival and financial and social costs due to its prolonged and progressive course and absence of an effective treatment.³

Many aspects of the disease have been poorly explored, and there is a lack of health policies and care directed at preventing silent transmission (through asymptomatic individuals who are unaware of their seropositivity) as well as a scarcity of effective treatments for those who develop morbidities.³

It is estimated that more than 70 million people are chronically infected by hepatitis C virus (HCV) worldwide, and close to 400 thousand die each year due to complications of the infection.⁵ It is considered a public health problem, because HCV is an important cause of cirrhosis and hepatocellular carcinoma, leading to liver transplantation.⁶ In Brazil, the prevalence of chronic infection is estimated at 1.38%,⁷ with a higher prevalence in males and a sex ratio of 1.3:1.⁸

In addition to manifestations involving the liver, many extrahepatic manifestations can occur, including neuropsychiatric disorders. This infection is associated with risk behaviors such as use of injected or inhaled drugs, unprotected sex, multiple sexual partners, and sexual activity with sex workers.⁹ Currently, treatments are available with a high rates of sustained virologic response.¹⁰

Health related quality of life (QoL) is an individual assessment of a range of conditions and aspects that affect a personal perception of a health condition.¹¹ QoL is an important measure associated with health and can deteriorate among HTLV-1 and HCV carriers, especially when they develop symptomatic stages of these infections. The existence of emotional, behavioral or social adversities also predisposes those infected to worse QoL measures.^{11–17}

Studies have reported many aspects of these infections; however, HTLV-1 still remains an under-studied infection around the world. There has not been a real-world study comparing QoL and the frequency of depression, suicide, and risk behaviors among HTLV-1 and HCV infected patients. This study aimed to compare these aspects in these two groups of infected individuals. Although the two infections are viral and have a chronic course, it is important to compare quality of life, behavioral aspects and outcomes related to mental health as they may be different, and thus call for specific considerations and treatment settings. Bearing in mind that HCV receives noticeably greater attention from the standpoint of public policies and investments in general, and that HTLV-1 is a commonly neglected infection for its low morbidity and mortality, the results of these study may flag up the need for changing this scenario of disregard from the health care system and from the academic community regarding HTLV-1.

Material and methods

Study design

This was a quantitative, observational and comparative cross-sectional study of HCV or HTLV-1 infected individuals who were receiving care in the multidisciplinary outpatient clinic at the University Hospital Complex Professor Edgard Santos - Com-HUPES (Federal University of Bahia) from 2010 to 2014.

Ethics aspects

This research was submitted to and approved by the Research Ethics Committee of the Maternity Hospital Climério de Oliveira at the Federal University of Bahia (MCO-UFBA - process number 14/2002) before the start of the interviews and data collection. All participating patients read and signed the informed consent form. The study was conducted according to the principles expressed in the Declaration of Helsinki, version 2013.

Subjects

All study participants were diagnosed with HCV or HTLV-1 infection by the health services team as well as the research group. During their regular medical appointments, patients receiving outpatient care at the participating centers of Com-HUPES diagnosed with HCV or HTLV-1 infection were invited to participate in the study.

A convenience sample of 171 HCV infected individuals and 119 HTLV-1 infected individuals signed the informed consent form and met the eligibility criteria were included in the study.

Group 1: HCV infected individuals

To be included, HCV infected patients had to be aged 18 years or more, have a chronic infection, as determined by a positive anti-HCV test by enzyme-linked immunosorbent assay III and confirmed by qualitative determination of HCV RNA. Those coinfecting with hepatitis B virus (HBV) (eight patients), human immunodeficiency virus (HIV) (two patients), or HTLV-1 (one patient) were excluded. In addition, current treatment with interferon alfa (17 patients), with missing data (two patients) were also excluded. After exclusions, 141 patients remained in the study. In this group, 89 (63.1%) patients were on the waiting list for liver transplantation and 52 (36.9%) had no indication for hepatic transplantation (controlled infection without expressive damage or having a contraindication for this procedure; of these, only 14.3% presented, upon liver biopsy, absence of inflammatory activity and no fibrosis according to the METAVIR classification, besides showing transaminases at slightly elevated levels) at the time of the interview.

Group 2: HTLV-1 infected individuals

The inclusion criteria were age over 18 years and infection by HTLV-1, as determined by serological diagnosis performed by ELISA (Cambridge Biotech Corp., Worcester, MA, USA) and confirmed by Western blot (HTLV blot 2.4, Genelabs, Singapore). Were excluded those with HCV (five patients), HBV (one patient), or HIV (no patient) coinfection, as well as those with missing data (no patient). After exclusions, 113 patients remained in the study. In this group, there were 43 (38.1%) asymptomatic patients, 36 (31.9%) with overactive bladder, and 34 (30.1%) with HAM/TSP. Symptomatic patients comprised 62% of the sample.

The sample size of both groups was considered suitable for the task of conducting the statistical analyses used in this study.

Instruments

Sociodemographic questionnaire

Included data such as age, sex, marital status and risk behaviors throughout life (sex with sex worker, more than three sex partners in the previous year, use of inhaled or injected drugs).

Mini International neuropsychiatric interview - M.I.N.I. plus 5.0.0 (MINI plus)

Brazilian version of the psychiatric interview (hetero-evaluation questionnaire)¹⁸ to explore the main mental disorders listed in Diagnostic and Statistical Manual of Mental Disorders, fourth edition, text revision (DSM-IV-TR) and International Classification of Diseases, tenth revision (ICD-10).¹⁹

Medical outcomes study 36-Item short-form health survey (SF-36)

Brazilian version of the validated instrument,²⁰ which measures eight domains of QoL: physical functioning, role-physical, role-emotional vitality, mental health, social functioning, pain, and general health.²¹

Interviews were carried out by researchers with an academic background in Psychology or Medicine/Psychiatry (properly trained for the application of the instruments). The patients were identified by the outpatient clinic staff and referred to the research group for evaluation by the same researcher until the end of the interviews. Considering that MINI Plus is a hetero-evaluation instrument and it was applied first and that SF-36 is an auto-evaluation scale, it was not necessary for the interviewer to be blinded to the mental status of the subjects.

Data analysis

Collected data were stored using the Statistical Package for Social Sciences (SPSS win, version 21) and analyzed using the statistical software R (R Development Core Team, 2011). Quantitative variables were represented by their means and standard deviations when their distributions were normal and by medians and interquartile ranges when not normal. The definition of normality was made through graphical analysis and the Shapiro-Wilk test. Categorical variables were represented by frequencies and percentages. Univariate comparisons between groups were made using Student's t-test for normally distributed variables and the Mann-Whitney test for non-normally distributed variables. For categorical variables, the chi square test or Fisher's exact test were used when necessary. The tests were performed with a significance level of $p < 0.05$.

The multivariate analysis was conducted through hierarchical logistic regression, sequentially evaluating the power of the variables that might be considered confounders. The increase of predictive power of the model signals that additional variables have their own predictive power regardless of the formerly added variables.

Results

Considering sociodemographic characteristics, male sex was more common in the HCV group (68.8% HCV vs. 28.3% HTLV-1; $p < 0.001$). The majority of patients from both groups were married or in a stable relationship (58.4% HTLV-1 and 66% HCV). There were no significant differences between the groups regarding age and marital status (Table 1).

We analyzed risk behaviors associated with sex practices and use of drugs. The variables sex with sex worker at least once in a life time, more than three sex partners in the previous year, use of inhaled or injectable drugs at least once were always more prevalent in the HCV group ($p < 0.05$). HTLV-1 patients developed significantly more depressive episodes in the past (26.5% HTLV-1 vs. 17.7% HCV; $p = 0.037$). Risk of suicide tended to be higher in the HTLV-1 group, but the difference was did not reach the level of significance ($p = 0.08$) (Table 2).

Additionally, the HTLV-1 group had a significantly worse QoL in four of the eight domains evaluated by SF-36, as follows: physical functioning ($p = 0.001$), vitality, mental health and social functioning ($p < 0.001$ for these last three domains). The remaining domains (role-physical, role-emotional, pain and general health) were equivalent or non-significantly worse in the two groups (Table 3).

Table 1 – Sociodemographic aspects between the HCV and HTLV-1 infected groups. Salvador, Brazil, 2017.

	Total (n = 254)	HTLV-1 (n = 113)	HCV (n = 141)	p-value
Age ^a	56.0 (49.0–63.0)	55.0 (45.0–64.0)	57.0 (51.0–63.0)	0.165
Male	129 (50.8)	32 (28.3)	97 (68.8)	<0.001
Marital Status				0.132
Single	41 (16.1)	24 (21.2)	17 (12.1)	
Married/stable relationship	159 (62.6)	66 (58.4)	93 (66.0)	
Divorced	33 (13.0)	12 (10.6)	21 (14.9)	
Widower	20 (7.9)	11 (9.7)	9 (6.4)	

Tests used: Mann–Whitney test and Chi square test. The tests were performed with a significance level of $p < 0.05$.
All data are arranged as N (%).

^a Mean \pm standard deviation.

Table 2 – Risk behaviors, depression and suicide risk between the HCV and HTLV-1 groups. Salvador, Brazil, 2017.

	Total (n = 254)	HTLV-1 (n = 113)	HCV (n = 141)	p-value
Risk behaviors	96 (37.8)	18 (15.9)	78 (55.3)	<0.001
Sexual				
Sex with sex worker	75 (29.5)	14 (12.4)	61 (43.3)	<0.001
More than 3 sexual partners in the last year	23 (9.1)	4 (3.5)	19 (13.5)	0.011
Drug use				
Injectable drug	20 (7.9)	1 (0.9)	19 (13.5)	0.001
Inhaled drug	27 (10.6)	2 (1.8)	25 (17.7)	<0.001
Major depressive episode (current/past)	69 (27.2)	33 (29.2)	36 (25.5)	0.609
Current major depressive episode				0.361
Absent	227 (89.4)	105 (92.9)	122 (86.5)	
Not specified	18 (7.1)	7 (6.2)	11 (7.8)	
Due to medical condition	1 (0.4)	0 (0.0)	1 (0.7)	
With melancholic characteristics	8 (3.1)	1 (0.9)	7 (5.0)	
Total	27 (10.6)	8 (7.1)	19 (13.5)	
Past major depressive episode				0.037
Absent	199 (78.3)	83 (73.5)	116 (82.3)	
Not specified	39 (15.4)	25 (22.1)	14 (9.9)	
Due to medical condition	3 (1.2)	1 (0.9)	2 (1.4)	
With melancholic characteristics	13 (5.1)	4 (3.5)	9 (6.4)	
Total	55 (21.7)	30 (26.5)	25 (17.7)	
Suicide risk				0.149
Absent	190 (74.8)	78 (69.0)	112 (79.4)	
Low	39 (15.4)	20 (17.7)	19 (13.5)	
Moderate	3 (1.2)	1 (0.9)	2 (1.4)	
High	22 (8.7)	14 (12.4)	8 (5.7)	
Suicide risk (low, moderate or high – reference: absent)	64 (25.2)	35 (31.0)	29 (20.6)	0.08

Tests used: Mann–Whitney test and Chi square test. The tests were performed with a significance level of $p < 0.05$.
All data are arranged as N (%).

Table 3 – Quality of life according to SF-36 among HCV and HTLV-1 groups. Salvador, Brazil, 2017.

	Total (n = 254)	HTLV-1 (n = 113)	HCV (n = 141)	p-value
Physical functioning	70.0 (45.0–90.0)	60.0 (20.0–90.0)	80.0 (52.5–95.0)	0.001
Role-physical	50.0 (0.0–100.0)	50.0 (0.0–100.0)	50.0 (0.0–100.0)	0.554
Role-emotional	100.0 (33.3–100.0)	100.0 (33.3–100.0)	100.0 (33.3–100.0)	0.727
Vitality	55.0 (45.0–70.0)	50.0 (45.0–60.0)	65.0 (45.0–80.0)	<0.001
Mental health	64.0 (56.0–80.0)	60.0 (51.0–64.0)	80.0 (64.0–92.0)	<0.001
Social functioning	50.0 (50.0–75.0)	50.0 (37.5–50.0)	75.0 (50.0–100.0)	<0.001
Pain	77.5 (55.0–100.0)	87.5 (87.5–87.5)	70.0 (55.0–100.0)	0.392
General health	60.0 (45.0–80.0)	60.0 (45.0–70.0)	60.0 (45.0–80.0)	0.817

Tests used: Mann–Whitney test and Chi square test. The tests were performed with a significance level of $p < 0.05$.
All data are arranged as median (25th percentile - 75th percentile).

Table 4 – Multivariate analysis (hierarchical logistic regression) Salvador, Brazil, 2017.

	Group 1 (Risk behavior)	Group 2 (Sex)	Group 3 (Current depressive episode)	Group 4 (Quality of life)
Nagelkerke R ²	0.212	0.256	0.295	0.619
Likelihood-ratio	–	10.2	9.2	109
p value	<0.001	<0.001	0.02	0.01
AIC	309.2	300.9	297.7	205.7
AUROC (95% CI)	0.697 (0.644–0.750)	0.740 (0.682–0.794)	0.766 (0.710–0.821)	0.907 (0.869–0.943)

The multivariate analysis conducted through hierarchical logistic regression showed that the presence of HTLV-1 was considered an independent factor for worse results in QoL. This evidence stems from progressing values of Nagelkerke R² and decreasing Akaike information criterion (AIC), which are measures for model quality, insofar as the variables thought to be confounders were being added to the analysis: risk behaviors, sex, and current depressive episode (Table 4).

Discussion

This study found that HTLV-1 infected individuals have a significantly higher rate of past depression and worse QoL in physical functioning, energy, emotional well-being and social functioning domains of SF-36. These four domains represent not only physical but also psychosocial elements, showing a broad negative repercussion in the life of these subjects. Thus, it was shown that people with HTLV-1 may have a worse health status despite the idea that, due to the low morbidity of the virus, this infection does not need to receive extra attention in health policies. The study compared relevant health aspects (especially mental) of patients with HTLV-1 and those with HCV. This latter infection receives great investments in prevention campaigns, screening, effective treatment, and access to care.

Regarding sex, this sample is consistent with previous reports. There were more males in the HCV group with an M:F ratio (2.2:1) which exceeds the ratio in Brazilian general population (1.3:1).²² Being male is a risk factor for progressing to the symptomatic stage,^{23,24} which might explain the higher rates of diagnoses and follow-up in men, also shown in this study. Among HTLV-1 patients, there were more females (71.7%), in line with other studies (66.6–83%).^{14–16,25–27} Evolution to HAM/TSP has been described to be associated with female sex.⁴

Review studies have reported the relationship between risk behaviors and HCV infection. Giunta et al.²⁸ showed high rates, between 50% and 90%, of positive serology for HCV among IVDU. Cucciare et al.²⁹ found that 58–78% of those with HCV had a current or past history of problematic use of psychoactive substances. Lucaciu and Dumitrascu³⁰ showed a significant presence of risk behaviors among HCV infected subjects (intravenous drug use, alcohol consumption, and risky sexual activities), such as was found in this present study.

Depression rates in the complete sample (27.2%) or in each group separately (29.2% HTLV-1 vs. 25.5% HCV) were higher than Brazilian rates: São Paulo city—16.8% during life and 4.5% in the last month.³¹

Depression prevalence in the HCV group is also consistent with previous studies.^{32–34} Tavakkoli et al.³⁵ reported a higher prevalence of current depression, which is probably explained

by higher rates of intravenous drugs use (53% vs. 13.5%). Another item of interference might have been the evaluation method (self-administered instrument *Patient Health Questionnaire - PHQ-9* – vs. *MINI Plus* self-report psychiatric interview). Even though the PHQ-9 is a validated instrument for this population,³³ assessment by way of psychiatric interviews by an experienced evaluator is the most accurate method.³⁶

In the HTLV-1 group, current depression rate (7.1%) was similar to that found by Gultinan et al.³⁷ (5.4%). Boa-Sorte et al.²⁷ and Galvão-Castro et al.¹⁵ reported 38% and 34.1%, respectively, of recurrent depression, while our research found 29.2% of major depression as a whole (current and/or past episodes). In these studies the rates of depression maybe slightly overestimated as more subjects were affected by HAM/TSP (43.5% and 36.4%, respectively) compared to the current study (30.1%). This reasoning can be upheld according to Gascón et al.¹⁴ who showed an association between presence of HAM/TSP and markedly elevated rates of depression compared to asymptomatic patients (59.3% in HAM/TSP subjects and 22.4% in asymptomatic subjects; $p < 0.001$). It should be noted that the rate of HAM/TSP appears to be insufficient to fully explain the clear difference in current depression rates to other studies,^{15,26,27,38} even when considering that Rocha-Filho and Gonçalves³⁹ found elevated rates of depression in individuals with HTLV-1, with a slight variation among symptomatic (70%) than among asymptomatic patients (60.5%) and in non-infected controls (15.6%), by way of the self-assessment instrument *Hospital Anxiety and Depression Scale—HADS*). Other unidentified factors may have contributed to this divergence.

Past depressive episodes were significantly more frequent in the HTLV-1 group. The frequencies of depression as a whole (past and/or current) were also higher in the HTLV-1 group, although it did not reach statistical significance. The chronic course of the two infections, with changes in the scale of decades, and the cross-section study design made the evaluation of chronology to be adequately ascertained. Therefore, the investigation of the role of the viral infection in causing depression could be firmly established.

All the individuals were receiving multi-professional assistance at the time of the study. This may signal that this type of support is capable of decreasing the incidence of depression (given the lower rates of past and current depression in both groups), mainly in those with HTLV-1 infection (the rates of depression in this group reduced from 26.5% to 7.1%, whereas in the HCV group it only reduced from 17.7% to 13.5%). Suicide risk was generally higher in the HTLV-1 group; however, it did not reach statistical significance, only a trend when considering all the levels of severity together ($p = 0.08$).

QoL measures should receive special attention, as they broadly evaluate the elements that interfere with and contribute to the personal perception of a specific individual's

health status.¹¹ Among those with HTLV-1, the declining QoL measures highlight the detrimental repercussions of HTLV-1 infection on the patients' physical and psychic health. A high adverse impact on the levels of life satisfaction could be observed, considering that the scores were worse compared to those of individuals with HCV, who also suffer from an infection with many adversities.

Compared to the study by Coutinho et al.,²⁵ in our study the domains physical aspects, functional capacity, and pain of HTLV-1 infected patients had more favorable levels (Coutinho et al. found scores of 24.2, 27.1 and 41.7 respectively). However, in the reported study, all patients had symptoms of HAM/TSP, compared to only 30.1% in our study. Gonçalves et al.⁴⁰ found very similar rates for almost all QoL domains according to SF-36 compared to this study. The rates of individuals with HAM/TSP in either study were reasonably similar (36% and 30.1%). Nonetheless, the authors did not mention whether the rest of the sample was completely asymptomatic or if there were also some urinary symptoms.

Vahidnia et al.⁴¹ conducted a study involving blood donors and found worse levels of QoL among HCV individuals compared with HTLV individuals (the study did not specify whether the study included HTLV-1 alone or if it also included HTLV-2), countering the findings of our study. It should be pointed out that the study sample had different characteristics, since the subjects had no significant symptoms and the infections were diagnosed by chance. This differs from the sample of the current study, which was a clinical sample with many subjects with advanced symptoms. Furthermore, a different instrument was used, the EuroQol Five Dimension (EQ-5D).

Shublaq et al.¹⁶ evaluating a sample exclusively composed of HAM/TSP patients, found scores below 20 for the domains physical functioning, physical aspects and emotional functioning, much lower than the current results. Our study did not evaluate QoL of HTLV-1 infected patients stratified by clinical picture, which does not allow comparisons with these previously published data.

Although the studies by Galvão-Castro et al.¹⁵ and by Gascón et al.¹⁴ evaluated QoL of study participants affected by HTLV-1, these researchers used a different instrument (WHOQOL-Bref), making it difficult to compare results. However, these studies seem to be consistent with the data from our study regarding the unfavorable QoL in HTLV-1 infected patients.

Results of our study suggest that HTLV-1 infected patients, with an adverse prognosis and degrading course of disease, progressively evolve to dysfunctionality.^{3,25,27} The absence of effective viral treatment, with only symptomatic therapy,³ would result in increased stress and hopelessness compared to HCV patients. Future studies that specifically evaluate data such as hopelessness among HTLV-1 carriers, through specific instruments, will be necessary for further clarification of this subject.

Some limitations of this study should be taken into account. This was a cross-sectional study, which hinders the evaluation of causality. A convenience sample was used, making it difficult to extrapolate the results to the general infected population. Due to the limited sample size, it was

impossible to stratify all infected individuals into different levels of clinical impairment severity, for this would compromise statistical power to detect important differences between groups. In addition, there was no control group with other clinical illnesses. Future longitudinal studies, with large probability samples and broader control for confounding variables, will hopefully offer a more comprehensive evaluation of the issues presented in this publication.

In summary, the results of this study show that patients with HTLV-1 had unfavorable outcomes regarding mental health and QoL when compared to those with HCV. Patients with HCV, in turn, had higher frequencies of risk behaviors. In view of this comparative scenario, more investments regarding public health policies to tackle HTLV-1-related problems are necessary so that patients with such compromised health indicators can receive the necessary therapeutic support. One should also be aware of the need for the development of studies to complement the scarce literature on this infection, especially regarding aspects of mental health. Thus, these studies should aim to determine what other health markers of HTLV-1 carriers are negatively affected. In the same way, support and treatment methods must be developed to improve QoL and overall health during the course of the disease, including preventive strategies for these outcomes. This support should be based on specialized care environments with multi-professional teams, involving rehabilitation and physical activity, provision of orthotics and supplies to facilitate motor function, pain management, psychiatric and psychological support, and social support and care.

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Conflicts of interest

The authors declare no conflicts of interest.

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