

Article

Manifestations of Post-COVID Syndrome in Healthcare Workers in Northeast England

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Abstract: Post-COVID-19 syndrome (PCS) is a common outcome of severe COVID-19 infection; however, less is known about PCS following mild COVID-19. Healthcare workers (HCWs) are more susceptible to acquiring COVID-19 and potentially suffering physical and psychological morbidity secondary to their role. We surveyed HCWs at four hospitals in northeast England at two timepoints during the pandemic, assessing physical and psychophysiological symptoms of PCS, alongside associated factors, whilst also testing for COVID-19 status by SARS-CoV-2 serology and reviewing evidence of infection from previous PCR nasopharyngeal swabs. Of the 379 participants at baseline and 250 HCWs recruited 18 months later, 46% and 64% (respectively) had evidence of previous COVID-19, with no significant associations between COVID-19 status or demographics and symptom scores or self-described PCS. Depression and fatigue were more common later in the pandemic. Furthermore, 20% self-described having PCS, 34% of whom had no evidence of previous COVID-19. Scores for fatigue, pain, mobility, anxiety, and depression were significantly worse in the PCS group compared to those without ongoing symptoms. Significant proportions of HCWs continued to suffer debilitating symptoms during the later pandemic period, although a significant minority had no evidence of previous COVID-19 infection, suggesting that other factors may be involved in their symptomatology.

Keywords: COVID-19; SARS-CoV-2; healthcare workers; psychological impact; mental health; sleep; wellbeing; chronic fatigue; Long-COVID; Post-COVID Syndrome



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1. Introduction

Since the onset of the COVID-19 pandemic in early 2020, it has become clear that SARS-CoV-2 infection may be complicated by prolonged ongoing symptoms, which can persist for many months, particularly in those with severe disease [1–3]. The most recent UK government Office for National Statistics (ONS) survey in April 2024 found that over 2 million of the UK adult population (4% aged >16 years old) were suffering from self-reported post-COVID-19 Syndrome (PCS)—also known as ‘Long-COVID’ [4]. This is defined as symptoms persisting for more than 12 weeks following SARS-CoV-2 infection [5]. An earlier analysis of 10 UK longitudinal studies in 2021 identified 7–18% of participants suffering with PCS using the same definition [6]. The largest UK study of outcomes of COVID-19, the REACT study, surveying nearly 278,000 participants, identified

7.5% as having symptoms continuing beyond 12 weeks, with 32% of these having very severe symptoms leading to major reductions in daily activities [7]. Various other studies, reviews, and metaanalyses have reported a wide prevalence of PCS internationally and have highlighted fatigue, insomnia, dyspnoea, impaired cognition, memory problems, visual changes, anxiety, and depression as the most frequently identified symptoms [1–3,8–11].

Healthcare workers (HCWs) have a unique vulnerability to COVID-19 [12,13]; however, they may also have been subjected to different pressures and anxieties due to this risk. PCS has been described in several studies in this group. One UK study found that working in healthcare was an independent risk factor for developing PCS [8]. A Swiss study of HCWs including controls (PCR/antibody negative) identified fatigue, depression, and neurocognitive impairment as more common in HCWs with COVID-19 after 2 or more months [13]. A study of Swedish HCWs reported 15% (versus 3% of seronegative controls) as having PCS more than 8 weeks following infection, with anosmia, ageusia, and fatigue being the most common symptoms described [14]. A systematic review and metaanalysis of 47 studies of psychological symptoms in HCWs during the early pandemic identified depression (37%), anxiety (36%), and insomnia (25%) as particularly common [15]. More severe cases of anxiety and depression have also been associated with thoughts of self-harm and suicidal ideation [16,17].

Risk factors for the psychological sequelae of COVID-19 in HCWs have been widely reported in the literature. Female gender [17,18], younger age [19], the presence of pre-existing poor health [17], and having children or elderly family members [20] have been associated with higher rates of anxiety and depression in HCWs throughout the pandemic. External factors relating to working environment, job role, and the provision of training also contributed to the development of psychological symptoms. This included working in direct contact with COVID-19 patients [21] and being in hospitals with a higher number of COVID-19 cases [17] or where there had been shortages or concerns about Personal Protective Equipment (PPE) and safety at work [17]. Job role was also important, with studies persistently describing nurses as most vulnerable to anxiety and depression [10,18].

Whilst there appears to be a significant ongoing burden of PCS, particularly in HCWs, there are several difficulties in interpreting the myriad of studies that have reported its prevalence and different manifestations. First, there is no standardised definition of PCS in terms of time period and symptomatology. Second, many studies have not included control populations, namely people without PCR or antibody evidence of COVID-19. This reduces their ability to attribute the causality of symptoms to COVID-19 as opposed to alternative factors during the pandemic [22]. Third, relatively few studies have examined the psychophysiological manifestations of PCS, including depression, anxiety, cognitive and memory problems, and insomnia. Finally, hardly any studies surveyed populations prior to SARS-CoV-2 infection to determine whether the symptoms described preceded their illness. One exception, the Lifelines Corona Research Initiative, studied participants in the Netherlands and obtained prospective data prior to their infection [23]. This study found that anosmia, dyspnoea, chest pains, myalgia, ageusia, and fatigue were more commonly described 3 months after infection, after adjustment for pre-COVID-19 morbidity.

Most information on PCS has been derived from people with more severe COVID-19 who were admitted to hospital; however, the vast majority of those suffering from PCS have had milder illnesses not requiring hospital admission. The COVID-19 in Healthcare Workers Outcome and Immunity Study (CHOIS) was initiated in 2020, with a view to describing PCS in a population of HCWs in four northeast England hospitals. We aimed to analyse both the physical and psychophysiological ongoing symptoms of COVID-19 in HCWs, most of whom were never admitted to hospital, including a control group comparison. This study assessed a sample of HCWs during two stages of the pandemic

with a view to determining the prevalence, symptomatology, and severity of PCS and to investigate relationships with various population characteristics.

2. Methods

2.1. Participants

Healthcare workers (HCWs) from four hospitals in northeast England were invited to participate in the study via staff email. Invites were sent out to 9317 HCWs at two timepoints—baseline (late 2020—the early pandemic group) and 18 months later (the late pandemic group). Some HCWs who partook in the baseline surveys also participated again at the follow-up. Our opportunistic samples comprised 379 (4.1% response) participants who provided full survey data for analysis at baseline and 250 participants (2.7%) who took part 18 months later, with a subset of 173 participants taking part at both timepoints. Participants were categorised according to their COVID-19 test (i.e., rapid PCR) and SARS-CoV-2 nucleocapsid antibody status. In this study, data was collected in the form of electronic surveys. Participants were also asked to provide a sample of blood both at baseline and follow-up, which was analysed for SARS-CoV-2 antibodies.

2.2. Ethical Approval

All participants gave written informed consent, and the Cambridge East Research Ethics Committee approved this study (Ref: 20/EE/0161), which was performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

2.3. Data and Outcome Measures

The following information was collected from HCWs, including a range of validated surveys to explore physical and psychophysiological symptoms of COVID-19.

1. Participant demographics: this included gender, age, ethnicity, BMI, smoking status, and job characteristics (e.g., job title, patient contact).
2. Depression and anxiety: This was captured using the Hospital Anxiety and Depression Scale (HADS) [24], a 14-item questionnaire comprising two subscales, one each for depression and anxiety. Scores (on each scale separately) of 0–7 = normal; 8–10 = borderline abnormal/mild depression/anxiety; 11–21 = abnormal/moderate–severe depression/anxiety.
3. Health status: The EuroQol (EQ-5D-3L) [25] was used to examine 5 elements of general health: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Participants rate each of these dimensions based on the extent to which they feel they have problems in those areas (i.e., ranging from no problem to an inability to perform an activity/a severe problem).
4. Fatigue: The Fatigue Impact Scale (FIS) [26] was used to capture the impact of fatigue on everyday functioning, including cognitive function. Participants ranked themselves as having fatigue that caused them anything from ‘no problem at all’ to ‘extreme problems’, relating to a range of activities, including workload, motivation, and decision-making. Higher scores indicated greater fatigue.
5. Post-COVID syndrome: The presence of PCS was identified using the following method in the later (18 month) cohort. HCWs were asked whether they had or were experiencing long-term COVID-19 symptoms > 12 weeks following COVID-19. For all participants, using the NICE criteria for defining ‘Long-COVID’ [5], symptom duration was categorised as either acute COVID-19 symptoms (ACs) lasting up to 4 weeks post-infection; ongoing symptomatic COVID-19 (OSC) with symptoms lasting up to 12 weeks; or post-COVID-19 syndrome (PCS), when symptoms span beyond 12 weeks—also known as Long-COVID.

2.4. Analysis

Statistical analysis was conducted using JASp v0.18.1.0.27 [27]. Scores for the various psychological/wellbeing measures and the two sets of serology were compared between those with and without a prior history of COVID-19/long-term COVID-19 symptoms and between the two testing periods at baseline and 18 months. The role of risk factors such as age, gender, and ethnicity were also considered. The effects of having had COVID-19 and time were investigated separately for each variable using a series of 2×2 (time \times COVID status) analyses of covariance (ANCOVAs), with age and gender entered as covariates. The effects of symptom duration were investigated separately for each variable using a series of ANCOVAs, with age and gender entered as covariates. Any significant main effects were followed up by Tukey's HSD-corrected post hoc tests and a comparison of corrected group means (95% CI calculated robustly by 1000 bootstrapped bias-corrected accelerated samples correcting for age and gender variance).

3. Results

At baseline, 379 HCWs responded to the invitation, completed the survey, and provided blood samples. At 18 months, 250 HCWs did likewise. The characteristics of each cohort, categorised by COVID-19 status, are shown in Table 1. Data collection issues (principally, the irretrievable corruption of the survey database) for the 18-month cohort meant it was impossible to collect sufficient demographic data to provide reliable figures; however, as 173 (69%) patients from this cohort also took part in the baseline sample, it is likely that the values were similar. The participant HCWs were predominantly female (89%) and Caucasian (96%), with most participants being nurses and around 46 years old. Less than 1% of each cohort had required admission to hospital for COVID-19. The proportion of participants having had COVID-19 increased from 46% at baseline to 64% at 18 months. In the late pandemic sample, 14% reported ongoing symptoms consistent with PCS. There was no association of gender with COVID-19 status at either the early or late pandemic testing point and no significant difference between the ages of the cohorts. For the other variables, those with patient contact at baseline (i.e., the early pandemic group) reported more fatigue than those without ($[F(1.373) = 4.17, p = 0.042]$) at that timepoint. There were no effects of age, gender, time of testing, or having COVID-19 and no interactions between these variables for the variables of EQ5DL anxiety/depression, HADS anxiety, pain, or self-care. Only 95 people responded to the 'Usual Activities' item of the EQ5DL questionnaire at baseline, and 112 responded to it at follow-up. As less than 50% of the cohort responded to this item, we did not include this data in the analysis.

Table 1. Participant characteristics according to COVID-19 status.

		Early Pandemic Cohort (Baseline)			Late Pandemic Cohort (18 mth)		
		COVID-19 Negative (n = 205)	COVID-19 Positive (n = 174)	Total (n = 379)	COVID-19 Negative (n = 90)	COVID-19 Positive (n = 160)	Total (n = 250)
Mean age (SD)		46.19 (10.84)	46.08 (11.60)	46.14 (11.18)	45.54 (16.61)	47.66 (10.53)	46.9 (13.06)
Gender	Female (%)	88.8	83.3	86.2	83.3	88.1	86.4
	Male (%)	11.2	16.7	13.8	16.7	11.9	13.6
Mean BMI (SD)		26.9 (5.5) n = 17	27.2 (5.7) n = 63	27.1 (5.6)	-	-	-
Ethnicity	White (%)	190 (93%)	166 (96%)	357 (95%)	-	-	-
	Non-white (%)	15 (7%)	9 (4%)	22 (5%)	-	-	-
Smoker (%)		No 148 (72%) Yes 44 (21%)	No 133 (76%) Yes 40 (23%)	No 281 (74%) Yes 84 (22%)	-	-	-

Table 1. Cont.

	Early Pandemic Cohort (Baseline)			Late Pandemic Cohort (18 mth)		
	COVID-19 Negative (n = 205)	COVID-19 Positive (n = 174)	Total (n = 379)	COVID-19 Negative (n = 90)	COVID-19 Positive (n = 160)	Total (n = 250)
Post-COVID syndrome # (%)	-	-	-	15 (17%)	20 (12.5%)	35 (14%)
Patient contact ~ (%)	Yes 171 (83%) No 34 (17%)	Yes 134 (77%) No 40 (23%)	Yes 305 (81%) No 74 (19%)	-	-	-
EQ-5D	1.55 (0.77)	1.48 (0.74)	1.51 (0.75)	1.46 (0.67)	1.47 (0.86)	1.46 (0.81)
HADS Anxiety	5.51 (3.65)	5.33 (3.76)	5.43 (3.70)	6.18 (3.59)	5.81 (4.35)	5.94 (4.09)
HADS Depression	5.44 (2.77)	5.45 (2.86)	5.45 (2.81)	3.49 (3.48)	3.51 (3.79)	3.50 (3.67)
Fatigue	3.90 (5.10)	4.98 (5.94)	4.40 (5.52)	4.53 (5.83)	5.83 (6.45)	5.36 (6.25)
Mobility	1.12 (0.41)	1.14 (0.42)	1.13 (0.41)	1.22 (0.54)	1.23 (0.67)	1.23 (0.62)
Pain	1.52 (0.70)	1.36 (0.64)	1.45 (0.67)	1.51 (0.69)	1.50 (0.90)	1.50 (0.83)
Self-care	1.02 (0.14)	1.02 (0.13)	1.02 (0.13)	1.02 (0.15)	1.00 (0.28)	1.01 (0.24)

COVID-19 status defined by having positive PCR (swab) any time prior to the survey and/or testing positive for SARS-CoV-2 nucleocapsid antibody. BMI—body mass index. Clinical—contact with patients as part of role. # Post-COVID Syndrome—self-described persistent symptoms >12 weeks after COVID-19, which was only included in the survey for the late pandemic cohort. ~ Contact with patients through job role.

Participants were significantly less depressed (i.e., indicated by HADS) at 18 months, than at baseline ([F(1.623) = 54.00, $p < 0.001$]) and participants reported significantly more problems with mobility at follow-up than at baseline ([F(1.623) = 4.98, $p = 0.026$]) in both cases, regardless of having had COVID-19. Those HCWs with COVID-19 experienced significantly more fatigue than those without ([F(1.623) = 5.91, $p = 0.015$]). Analyses looking at participants in the 18-month survey through the duration of symptoms following COVID-19 are summarised in Table 2. Only 173/250 (69.2%) provided complete survey data regarding ongoing symptoms, and of these, 35 (20.2%) had PCS and 27 (15.6%) had ongoing symptoms between 4 and 12 weeks. There were no significant associations between the length of symptoms and gender. It was evident that in the PCS group, a significant proportion were suffering clinically significant depression (48.6% vs. 12.6% in those whose symptoms had resolved) and moderate-to-severe fatigue (11.4% vs. 3.6% in those whose symptoms had resolved). Table 3 shows a breakdown of the severity of symptoms across each of the surveys by COVID-19 status and symptom duration.

Table 2. Health outcomes in the late pandemic sample according to duration of symptoms: for age and scores, mean (SD) values are shown.

	No Prolonged Symptoms (n = 111)	Ongoing Symptoms—5–12 Weeks (n = 27)	Post-COVID Syndrome (n = 35)
Gender (% Female)	84.7%	100%	80%
Age (Years)	48.82 (11.95)	47.78 (10.78)	49.03 (11.49)
COVID-19-positive (%)	62.2%	70.4%	65.7%
EQ-5D Anxiety and Depression Score	1.41 (0.82)	1.44 (0.80)	1.71 (0.89)
HADS Anxiety	5.55 (4.30)	6.59 (4.36)	6.91 (2.78)
HADS Depression	2.95 (3.41)	3.56 (3.02)	7.20 (4.05)
Fatigue score	4.15 (5.58)	5.96 (5.47)	11.51 (8.29)
Mobility score	1.14 (0.56)	1.22 (0.58)	1.63 (0.84)

Table 2. Cont.

	No Prolonged Symptoms (n = 111)	Ongoing Symptoms—5–12 Weeks (n = 27)	Post-COVID Syndrome (n = 35)
Pain score	1.40 (0.81)	1.52 (0.89)	2.09 (0.95)
Self-care score	0.98 (0.19)	0.93 (0.27)	1.43 (0.43)

Table 3. Severity of health outcomes in relation to duration of symptoms.

	No Prolonged Symptoms (n = 111)	Ongoing Symptoms—5–12 Weeks (n = 27)	Post-COVID Syndrome (n = 35)
Gender (% Female)	84.70%	100%	80%
Age (Years)	48.82 (11.95)	47.78 (10.78)	49.03 (11.49)
COVID-19-Positive (%)	62.20%	70.40%	65.70%
EQ-5D Anxiety and Depression			
No Problem	79 (71%)	16 (59%)	18 (51%)
Slight Problem	20 (18%)	8 (30%)	11 (31%)
Moderate Problem	9 (8%)	3 (11%)	4 (11%)
Severe Problem	2 (2%)	0 (0%)	2 (6%)
Extreme Problem	1 (1%)	0 (0%)	0 (0%)
HADS Anxiety			
Normal	80 (72%)	15 (56%)	21 (60%)
Mild	16 (14%)	4 (15%)	11 (31%)
Moderate/Severe	15 (14%)	8 (30%)	3 (9%)
HADS Depression			
Normal	97 (87%)	24 (89%)	18 (51%)
Mild	10 (9%)	2 (7%)	9 (26%)
Moderate/Severe	4 (4%)	1 (4%)	9 (23%)
Fatigue Score			
Normal	107 (96%)	27 (100%)	31 (89%)
Mild to Moderate	4 (4%)	0 (0%)	4 (11%)
Severe	0 (0%)	0 (0%)	0 (0%)
Mobility Score			
No Problem	100 (90%)	19 (70%)	21 (60%)
Slight Problem	5 (4.5%)	8 (30%)	6 (17%)
Moderate Problem	5 (4.5%)	0 (0%)	8 (23%)
Severe Problem	1 (1%)	0 (0%)	0 (0%)
Extreme Problem	0 (0%)	0 (0%)	0 (0%)
Pain Score			
No Problem	81 (73%)	16 (59%)	12 (34%)
Slight Problem	16 (14%)	6 (22%)	10 (29%)
Moderate Problem	11 (10%)	5 (19%)	11 (31%)
Severe Problem	3 (3%)	0 (0%)	2 (6%)
Extreme Problem	0 (0%)	0 (0%)	0 (0%)
Self-Care Score			
No Problem	110 (99%)	27 (100%)	31 (89%)
Slight Problem	1 (1%)	0 (0%)	3 (9%)
Moderate Problem	0 (0%)	0 (0%)	1 (3%)
Severe Problem	0 (0%)	0 (0%)	0 (0%)
Extreme Problem	0 (0%)	0 (0%)	0 (0%)

Significant proportions of participants with ongoing COVID-19 symptoms (29.6%) and PCS (34.3%) did not have prior PCR/serological evidence of COVID-19 infection. There was no significant difference in any outcome measure for HCWs with and without confirmed COVID-19 in the PCS group. Participants self-describing themselves as having PCS scored

worse in all health-domain scores than those without PCS. Significantly higher scores were noted in the PCS group compared to other groups for depression ($[F(1.168) = 18.90, p < 0.001]$), fatigue scores ($[F(1.168) = 19.25, p < 0.001]$), mobility scores ($[F(1.168) = 7.64, p < 0.001]$), pain scores ($[F(1.168) = 8.15, p < 0.001]$), and self-care scores [$F(1.168) = 6.19, p = 0.003$].

4. Discussion

This study looked at HCWs at two timepoints in the COVID-19 pandemic. Most participants with COVID-19 had not required admission to hospital with COVID-19. The main differences between these sampling timepoints were, firstly, the circulating SARS-CoV-2 variants (wild-type/alpha at baseline, and mostly delta at 18 months) and, secondly, the fact that most participants had received a SARS-CoV-2 vaccine course by the late pandemic timepoint. Moreover, the proportion of participants with laboratory-confirmed evidence of COVID-19 increased from 46% to 64% between baseline and 18 months. The demographics of the cohorts were different to many other studies examining PCS given that HCWs in northeast England are predominantly female and white. Interestingly, there was very little difference, in terms of symptoms and outcomes, between the early and late pandemic cohorts, despite a higher proportion having had COVID-19 by the time of the 18-month survey.

The analyses identified a minority (36%) with symptoms persisting more than 4 weeks after COVID-19, including 20% beyond 12 weeks, hence satisfying the criteria for PCS, in the late pandemic sample. The latter figure is significantly higher than the 7.5% with PCS seen in the REACT study conducted at a similar time to our present study but more similar to the 15% found by Havervall et al. earlier in the pandemic [14]. There were no significant associations between any demographic factors, the level of contact with patients, or COVID-19 status and any of the symptom scores. In the PCS group, it was clear that some participants were suffering clinically significant depression and high levels of fatigue, impaired mobility, and pain. However the rates of moderate or severe anxiety and depression on the HADS scores were lower than those seen in patients with multiple sclerosis (9% and 23% versus 48% and 39%, respectively) [28]. Surprisingly, a higher proportion of these HCWs with PCS were men compared to the group without persisting symptoms, which contrasts with the characteristics of most studies on PCS/Long-COVID; however, the overall numbers with PCS were relatively small. These findings have implications for the provision of treatment services to at-risk groups. This is particularly important in the context of HCWs, who are relied upon to provide care for the public during pandemics.

Of interest in the PCS group was the observation that around one third had no evidence, from SARS-CoV-2 serology or previous PCR tests, to confirm COVID-19 infection. Given that during both sampling periods, HCWs were advised to obtain throat swabs for PCR testing at their workplace if symptomatic and we had access to these results, it is unlikely that many HCWs in this group had COVID-19 confirmed by self-tested lateral flow tests with false-negative SARS-CoV-2 serology. This is the only scenario that might explain such individuals having true PCS. Similar findings, in terms of people self-describing their symptoms as PCS with no evidence of previous infection, have been noted in several other studies [29,30]. In the case of HCWs, one potential explanation for the significant morbidity observed in those with prolonged symptoms and without confirmed COVID-19 infection might be the psychological effect of the pandemic itself. This factor could have been important in the development of both physical and psychophysiological symptoms for a prolonged period after an illness assumed to be COVID-19. It may also be relevant that a very high proportion of our sample were nurses, who appeared to be more prone to anxiety and depression during the pandemic [18,20,31].

One strength of our study is that it examined HCWs with predominantly mild COVID-19 and confirmed previous COVID-19 infection via both serology and PCR data. Our study is relatively unique in doing this, as well as in providing data on quality of life and psychophysiological outcomes. The main limitation of this study is a likely selection bias in that HCWs suffering from prolonged COVID-19 symptoms may have been more likely to respond to the study invitation. Hence, it is possible that the proportion of HCWs with prolonged symptoms or PCS was overestimated, and this would explain the significantly higher levels seen compared to the REACT study. The other limitations of this study included missing data we were unable to collate in the late pandemic cohort, including the proportion of participants who had taken significant time off work or not returned, given the sampling method and technical issues with the survey. Hence, we were unable to determine clearly if our sample was different to the larger population of HCWs in the four hospitals.

5. Conclusions

In conclusion, this study found that a large proportion of HCWs continued to experience symptoms such as anxiety, fatigue, and depression during the later pandemic period, despite many of these participants not having any objective evidence of confirmed SARS-CoV-2 infection. This suggests that other factors, such as the psychological and physical implications of working through a global pandemic, may be contributing factors to the long-term symptomatology experienced by this at-risk group [30].

Author Contributions: D.C., J.R., and R.K.R. designed the study; D.W., S.G. and N.C.E. assisted with data extraction and preliminary analysis. The main statistical analysis was performed by J.R.; D.C. and R.K.R. wrote the first draft of the manuscript and all authors reviewed the final manuscript. All authors have read and agreed to the published version of the manuscript.

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Institutional Review Board Statement: The study was conducted in accordance with the Declaration of Helsinki, and approved by the Cambridge East Research Ethics Committee (Ref: 20/EE/0161), on 28 June 2020.

Informed Consent Statement: Written informed consent was obtained from all subjects involved in the study.

Data Availability Statement: Due to local constraints on the time allowed for retaining data related to the CHOIS study, the original data is not available.

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