Early View

Research letter

The high mental health burden of "Long COVID" and its association with on-going physical and respiratory symptoms in all adults discharged from hospital

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Title page

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Background

During previous severe coronavirus outbreaks, 15% of survivors suffered from depression and 33% from post-traumatic stress disorder (PTSD) at a mean follow-up of 22.6 and 32.2 months respectively (1). A recent systematic review identified that whilst physical symptoms receive most attention, the effects of COVID-19 upon mental health may be equally important (2). One meta-analysis estimated the prevalence of depression and PTSD in the general public during this pandemic at 24% and 15% respectively (3). In adults with pre-existing asthma and chronic obstructive pulmonary disease, the prevalence of depression and PTSD was 31.5% and 11.3% respectively (4). For patients with acute COVID-19 infection, this increased to 42% for depression and 96% for symptoms consistent with PTSD (3).

There are little data on psychiatric ill-health in adults recovering from COVID-19, especially in those with symptoms weeks to months after their initial infection or 'Long COVID' (5). One study suggested these adults are more likely to be diagnosed with psychiatric conditions, with an estimated incidence of mood disorders of 9.9%. However, this was suggested to be under-estimated as it relied on reporting via electronic health data rather than active screening of symptoms (6).

Objective

We investigated the mental health burden in adults discharged from hospital with COVID-19 and explored factors that contribute to this.

Methods

We established a virtual follow-up service (methodology and questionnaire previously reported (7)) for all adults discharged from hospital with a clinical diagnosis of COVID-19 (with or without positive swabs). Our cohort included adults treated in the Emergency Department (ED), inpatient wards and intensive care (ICU). We screened for psychological morbidity using the Patient Health Questionnaire 2-item scale

(PHQ-2) for depression and Trauma Screening Questionnaire (TSQ) for PTSD; these are brief but have good diagnostic sensitivity (8, 9). Adults with positive scores (PHQ-2 ≥3/6 and TSQ ≥6/10) were provided a referral link to local psychology services.

We consecutively sampled and included in our analysis all adults who consented to follow up. A power calculation was not undertaken due to the observational nature of the study. In line with national guidance for such work, our research was exempt from the need for institutional review board approval (10). Non-parametric data were compared with Mann-Whitney U test and categorical data with chi-squared test. Logistic regression analysis was performed to review the multi-variate association between different factors. All tests of significance were two-tailed. P-values ≤0.05 were considered statistically significant.

Results and findings

As of 22/05/2020 our hospitals had discharged 1050 adults with COVID-19. After excluding patients who died or were clinically inappropriate for follow-up, 90% (n=946) received virtual follow-up at a median of 65 days (interquartile range [IQR] 37.5-92.5). Efforts to follow-up all patients included using translation services, ensuring results were representative of the hospital population.

760 (80.3%) completed the consultation (mean age 60.7 (standard deviation [SD] ±16.3 years), 60.2% male and 48.4% of black or minority ethnic (BAME) background). Table 1 summarises our follow up outcomes. 47.0% (n=357) of adults had persisting physical and psychiatric symptoms. 105 (13.8%) and 80 (10.5%) adults screened positive for depression and PTSD respectively. Pre-existing depression and anxiety were associated with positive PHQ-2 (18.2% vs. 2.7%; 11.1% vs.1.5%; both p<0.001) and TSQ (11.8% vs. 4.2%, p=0.004; 7.9% vs. 2.5%, p=0.01). No other comorbidity was associated with positive PHQ-2 or TSQ.

Adults with positive PHQ-2 and TSQ were significantly more likely to experience persistent symptoms (PHQ2 80.0% vs. 41.8%, TSQ 88.8% vs. 42.9%; both p<0.001). In particular, they were likely to have ongoing physical symptoms of breathlessness, myalgia, anorexia and confusion (all p<0.001). They were also less likely to have returned to work (PHQ2 36.0% vs. 57.6%, p=0.004; TSQ 37.5% vs. 56.5%, p=0.01).

Positive PHQ-2 and TSQ scores were more common in adults with more physical symptoms on admission (PHQ2: 5 symptoms (IQR 3-6) vs. 4 symptoms (IQR 3-5), p=0.03; TSQ: 5 symptoms (IQR 3-6) vs. 4 symptoms (IQR 3-5), p<0.001; as pre-defined from a list of 14 symptoms) and follow-up (PHQ2: 2 symptoms (IQR 1-3.75) vs. 0 symptoms (IQR 0-1); TSQ: 3 symptoms (IQR 1-4) vs. 0 symptoms (IQR 0-1), both p<0.001; as pre-defined from a list of 10 symptoms).

No significant differences were seen in PHQ-2 or TSQ scores for patients discharged from ED versus inpatient wards, or in patients requiring positive-airway pressure or ICU treatment versus general care.

Logistic regression analysis was undertaken to clarify possible confounders between positive PHQ-2 and TSQ and the above factors. When adjusting for demographics, co-morbidities and symptoms, adults with increased symptoms at admission and follow-up remained more likely to have positive PHQ-2 and TSQ; no other significant factors were unmasked. Adults with pre-existing diagnoses of depression and anxiety remained more likely to have positive PHQ-2 but not TSQ.

Discussion

Amongst adults attending hospital services for COVID-19, there is significant mental health burden at follow-up; 13.8% and 10.5% screened positive for depression and PTSD respectively at a median of 9 weeks post discharge. This is not dissimilar to the prevalence derived from electronic health data (6).

An association between ethnicity and COVID-19 infection is reported (11). Our sample had a higher proportion of adults from BAME backgrounds compared to the demography of our local population. Ethnicity was neither associated with prevalence of psychiatric symptoms nor confounded the association of these symptoms with other risks. However, uptake of mental health services by adults of BAME backgrounds may be affected by well-recognised, important factors (11). This has public health implications for the management of adults from BAME backgrounds suffering with 'Long COVID'.

Our data demonstrate adults with pre-existing depression and anxiety were likely to have positive PHQ-2 and TSQ at follow-up. When adjusting for psychiatric comorbidity, there remained an increased likelihood of depression but not PTSD. This may be due to their pre-existing psychiatric disease, however, the association between mental health and COVID-19 is complicated. Psychiatric disease is an independent

risk factor for COVID-19, though the explanation for this remains uncertain (6). In practice, this population is likely to be vulnerable and would certainly benefit from additional support during recovery.

Psychiatric ill-health at follow-up was associated with persistent physical symptoms such as breathlessness and myalgia. This may be bidirectional: ongoing physical symptoms could lead to psychiatric ill-health and conversely increased mental health burden may present as physical symptoms. Additionally, the SARS-CoV-2 virus may directly cause psychiatric morbidity through cerebral infection or hyperinflammation (2). Recovery in Long COVID is multi-faceted and we recommend mental health screening to support patients holistically.

There was no association between severity of acute COVID-19 infection and psychiatric morbidity at follow-up, suggesting all adults, even those with initially limited healthcare interaction, may be at equal risk. Considering the large numbers of adults affected, there is a need to establish robust follow-up and rehabilitation services. Given the association between psychiatric ill-health and inability to return to work, this would support societal and economic recovery through improved functional outcomes.

We believe our data are representative of our patient population as we actively screened for symptoms in all patients. We included a diverse range of patients with different comorbidities and disease severity. Our multi-variate analysis was able to account for possible confounding factors.

Our limitations include not screening for psychiatric ill-health on presentation; thus we cannot directly compare the prevalence of psychiatric disease pre- and post-infection with COVID-19. Our data cannot sufficiently explain the complex interaction between pre-existing psychiatric illness and current mental health burden. Our data focused on identifying psychological morbidity, but adults infected with COVID-19 may experience positive psychological change and post-traumatic growth (12). This may mediate psychological morbidity and is interesting to consider for future work by following up the same patients over time.

In summary, adults with 'Long COVID' are likely to be referred to healthcare professionals specialising in respiratory or rehabilitation medicine. We advocate using brief mental health screening questionnaires to

identify psychological needs and support the recovery of patients who may be far from 'back to normal' physically and mentally.

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Table 1: Demographics and results from virtual follow-up of patients with and without positive PHQ-2 and TSQ scores

Variable	PHQ-2		p - value	TSQ		p-value
	Negative	Positive		Negative	Positive	
N	622	105		680	80	
Demographics						
Age*	60.5 (±16.1)	59.7 (±16.1)	0.65	61.2 (±16.5)	57.0 (±13.2)	**0.03**
Sex – Female (%)	243 (39.1)	48 (45.7)	0.20	259 (38.1)	43 (53.8)	**0.007**
Black, Asian & Minority Ethnic (BAME) (%)	289/606 (47.7)	50/100 (50.0)	0.69	316/657 (48.1)	36/75 (48.0)	0.99
Co-morbidities						
Clinical frailty (Rockwood) score (out of 9)	2 (2-3)	2 (2-4)	0.50	2 (2-4)	2 (2-3)	0.07
Diabetes (%)	144/576 (25.0)	27/97 (27.8)	0.55	161/625 (25.8)	20/76 (26.3)	0.92
Any cardiovascular disease (%)	280/585 (47.9)	47/99 (47.5%)	0.94	314/636 (49.4)	33/76 (43.4)	0.33
Chronic respiratory disease (%)	107/585 (18.3)	26/99 (26.3%)	0.06	120/636 (18.9)	20/76 (26.3)	0.12
Chronic kidney disease (%)	70/579 (12.1)	15/97 (15.5)	0.35	81/630 (12.9)	8/74 (10.8)	0.62
Depression (%)	16/585 (2.7)	18/99 (18.2)	**<0.001**	27/636 (4.2)	9/76 (11.8)	**0.004**
Anxiety (%)	9/584 (1.5)	11/99 (11.1)	**<0.001**	16/635 (2.5)	6/76 (7.9)	**0.01**
Admission data						
Total number of symptoms (of 14)**	4 (3-5)	5 (3-6)	**0.03**	4 (3-5)	5 (3-6)	**<0.001**
Discharged following Emergency Department (ED) assessment (%)	93 (15.0)	16 (15.2)	0.94	100 (14.7%)	11 (13.8%)	0.81
Admitted to Intensive Care Unit (ICU) (%)	72/487 (14.8)	16/83 (19.3)	0.30	78 (11.5%)	12 (15.0%)	0.43
Length of stay (days)	7 (4-11)	7 (3-15)	0.44	7 (4-12)	7 (3-13)	0.70
Follow up data						
Any persistent symptoms	259/620 (41.8%)	84/105 (80.0%)	**<0.001**	286/667 (42.9%)	71/80 (88.8%)	**<0.001**
Non-improved breathlessness (%)	126/567 (22.2)	14/97 (14.4)	0.08	135/603 (22.4)	10/73 (13.7)	0.09

Medical Research Council breathlessness scale	1 (1-2)	3 (2-3.75)	**<0.001**	1 (1-2)	3 (2-3.5)	**<0.001**
Non-improved cough (%)	157/567 (27.7)	32/98 (32.7)	0.31	174/603 (28.9)	19/74 (25.7)	0.57
Non-improved fatigue (%)	90/564 (16.0)	28/97 (28.9)	**0.002**	101/598 (16.9)	19/74 (25.7)	0.06
Non-improved sleep quality (%)	220/559 (39.4)	46/96 (47.9%)	0.12	233/593 (39.3)	37/73 (50.7)	0.06
Myalgia (%)	106/619 (17.1)	49/104 (47.1)	**<0.001**	120/667 (18.0)	40/79 (50.6)	**<0.001**
Anorexia (%)	37/620 (6.0)	22/104 (21.2%)	**<0.001**	40/668 (6.0)	22/79 (27.8)	**<0.001**
Confusion or 'fuzzy head' (%)	57/619 (9.2)	46/104 (44.2)	**<0.001**	65/667 (9.7)	42/79 (53.2)	**<0.001**
Persistent symptom burden (out of 10)*	0 (0-1)	2 (1-3.75)	**<0.001**	0 (0-1)	3 (1-4)	**<0.001**
How close to 100%	90 (80–100)	70 (60-80)	**<0.001**	90.0 (80-100)	70.0 (60-80)	**<0.001**
Back to work (%)	174/302 (57.6)	18/50 (36.0)	**0.004**	174/308 (56.5)	18/48 (37.5)	**0.01**

*Presented as mean with standard deviation. All other data non-parametric and presented as median with IQR.

** Symptoms: cough, dyspnoea, chest pain, sore throat, rhinitis, fever, fatigue, myalgia, headache, anorexia, anosmia, diarrhoea, abdominal pain, confusion

*** Symptoms included: myalgia, anosmia, chest pain, chest tightness, confusion, diarrhoea, abdominal pain, anorexia, peripheral oedema, focal weakness