

COVID-19

Where Are We Now 675 Days (or so) Later?



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Prime Minister Boris Johnson's stark words to the nation on March 23, 2020: *"I urge you at this time of national emergency: stay at home"* to very many working in health care seems like only yesterday's news.¹ It feels as if very little has changed in the course of the pandemic and increasingly poorly patients continue to land on the doorsteps of hospitals up and down the country. However, it's important to reflect on what developments we have seen and what has changed since as a united healthcare service we first donned FFP3 masks, gowns, gloves and visors, and entered into the unknown.

For many, the face of their first COVID-19 patient will be forever etched into their mind. Since December 2019, COVID-19 and its subsequent variants have spread to infect more than 330 million people worldwide, with officially reported deaths now in excess of 5.5 million.² The impact on healthcare has been significant with NHS services running at, or in excess of, their maximum capacity, to the point this has become the 'new normal'.³ This new way of working has resulted in multiple critical incidences being declared at many hospital trusts throughout the UK.⁴ As part of its efforts an extra 8,000 beds and 1,200 ventilators were sourced while the NHS' staff worked tirelessly to overcome increased patient numbers and reductions in staffing because of increased rates of illness and burnout.^{5, 6} The true health impacts of the pandemic are impossible to track as a result of delayed

presentation, investigation or treatment.⁷ The reasons for these are multifactorial, be that lacking hospital beds, appointments, or individuals too scared to leave the safety of self-isolation. There is likely still to come a presentation of increasingly sick individuals as a result. Mental health impacts are similarly likely to be impacted. Early data suggests there has been a 22% reduction in psychiatric presentations, but those presenting had increased severity of symptoms and more likely to require sectioning.⁸ Despite frequent media and parliamentary reports on the nation's mental health to prompt ends to national lockdowns, there is no firm data yet to suggest rates of self-harm or suicide have increased, but the long-lasting impacts on mental and physical health are under investigation.⁹⁻¹¹ If that wasn't enough, the NHS is preparing to manage the effects of Long-Covid.

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The preparations taken by critical care units (CCU) to ready themselves for the initial onset of the pandemic, and data on demographics and three-month follow-up of patients admitted to a single CCU during the first wave, have been previously documented.^{12, 13} Since then, the largest surge in COVID-19 admissions was seen with the Delta variant, with entire CCUs dedicated solely to caring for COVID-19 patients. While CCU admissions with COVID-19 have remained below that seen during the April 2021 peak, they continue to occupy beds across the NHS and adversely impact upon other patient care.

Reasons for post-Delta reduced CCU admissions are likely to be multi-factorial. Firstly, the medical understanding of pathophysiology has progressed. COVID-19 is the disease caused by the virus Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). SARS-CoV-2 contains spike proteins which project outwards from its surface. These spike proteins bind with angiotensin-converting enzyme 2 (ACE2). ACE2 is an essential enzyme with vital roles in many biochemical pathways including the renin-angiotensinogen-aldosterone pathway, which controls elevation of blood volume and arterial tone. ACE 2 is found on the surface of many of the body's cells and helps control the actions of another protein, angiotensinogen II (ANG2). ANG2 helps regulate blood pressure, inflammation, and wound healing. ACE2 converts ANG2 to other molecules which counteract the effects of ANG2. The binding of SARS-CoV-2 to ACE2 results in down regulation of ACE2 and increased ANG2 levels which increases blood pressure and inflammation, resulting in cell death, most notably the alveoli of the lungs. As inflammatory cells are activated, pro-inflammatory cytokines (IL-1, IL-6, TNF-a) are released – a cytokine storm – which results in the shutdown of the fibrinolysis pathway which can cause further organ dysfunction due to blood clots which can further damage the lungs in addition to heart and kidneys.

The pathophysiology has led to numerous trials and now treatments in management of COVID-19. One of the first advancements was the use of dexamethasone. Dexamethasone is a glucocorticoid which is immunosuppressive and anti-inflammatory and inhibits the coding for the cytokine storm, thus reduces inflammation. The RECOVERY trial found the use of dexamethasone in hospitalised patients reduced 28-day mortality from

25.7% to 22.9% ($p < 0.001$). For those mechanically ventilated, mortality was reduced from 41.4% to 29.3% (CI 0.51-0.81), while those receiving oxygen without mechanical ventilation had mortality reduced from 26.2% to 23.3% (CI 0.72-0.75). No significant difference was found for those not receiving any respiratory support (17.8% v 14.0%, CI 0.92-1.55).¹⁴ The World Health Organization (WHO) have since recommended the use of dexamethasone as a treatment option in hospitalised patients needing supplementary oxygen.¹⁵

The immunosuppressive tocilizumab has also demonstrated beneficial effects.¹⁶ Tocilizumab can selectively compete with cells displaying IL-6 receptors, thus blocking the IL-6 mechanism and reducing the body's immune response to SARS-CoV-2. Results found patients who were not mechanically ventilated and received tocilizumab had their likelihood of mechanical ventilation or death at day 28 reduced from 19.3% to 12.0% ($p = 0.04$). Death from any cause within 28-days was found to be insignificant (10.4% v 8.6%, CI -5.2-7.8).

Further study has shown the use of the anti-viral Remdesivir as a therapeutic agent due to its ability to inhibit RNA dependent RNA polymerase, thus reducing the potential consequences of SARS-CoV-2.¹⁷ Recovery time in those with evidence of lower respiratory tract infection with Remdesivir was reduced from a median of 15 days to 10 ($p < 0.001$) and a reduction in mortality from 11.9% to 6.7% (CI 0.52-1.03).

The dominant community-transmitted COVID-19 strain has now progressed to the Omicron variant, and although hospital admissions may be down, infection rates have soared to record breaking highs.¹⁸ The combination of the above treatments alongside arguably the biggest medical advancement to treat COVID-19 – vaccines – have contributed to reduced rates of hospitalisation and lower likelihood of CCU admission.¹⁹⁻²¹ The first vaccine to be introduced was the Pfizer-BioNTech vaccine. Studies have demonstrated an acceptable adverse-event profile (CI 89.0-93.2) and an efficacy of 96.7% (CI 80.3-99.9) in severe disease.²² The majority of those admitted to the CCU remain unvaccinated, despite high rates of vaccination being one of the key routes out of the pandemic.²³ Despite perceived benefits, there is still a large hesitancy around vaccination because of concerns of immediate and future side effects, in addition to misinformation and mistrust

in official guidance.²⁴ There is likely no single solution to vaccine hesitancy, but to address the indirect and direct threats to public health, communities must be engaged in wider conversations to address their concerns and minimise their risk of becoming critically unwell, thus reduce pressures on healthcare systems.

As with all critically ill patients, nutrition support is essential in overall management. Known symptoms of COVID-19 include loss of sense of smell and taste, leading to many presenting patients having experienced days of poor intake pre-admission.²⁵ As the medical understanding of COVID-19 has improved, gastrointestinal implications have been further investigated and associations established, including diarrhoea and loss of appetite which could potentially further contribute to the risk of malnutrition.²⁶

Malnutrition screening is a vital part of nutritional management and will direct patients to a suitable pathway to minimise risk. Obesity is common within the COVID-19 population, and as a result may be screened out of need for dietetic input.²⁷ These patients may require a more sensitive screening tool to highlight nutritional support needs. The demand on workforces from the pandemic, staff illness and redeployment has adversely impacted upon patient care throughout the NHS and may mean previously standard care is not performed as routine. Similarly, patients are now presenting who appear younger and fitter than what was seen during the first wave and assumptions may be made that they require no input without adequate screening. Dietetic teams have needed to alter, and optimise, their work pattern and may not be getting as much face-to-face time with patients due to infection prevention guidelines. This may involve taking on a greater role in screening, and incorporating screening as part of the CCU walk around, to minimise risk and ensure appropriate action is taken.

CCU admission directly from COVID-19 is usually the result of acute respiratory distress syndrome and patients requiring high levels of supplementary oxygen, be that nasal high flow, CPAP mask/hood or mechanical ventilation. Incidental COVID-19 cases are similarly rising meaning patients are requiring multiple treatments.²⁸ CPAP presents obvious physical barriers to oral intake, and a patient's ability to take on sufficient dietary intake will be largely dependent on the time the patient is able to manage while they are off CPAP. While nasal high flow is a lesser restrictive

option in terms of feeding orally, this can contribute to dry mouth.²⁹ Breathing difficulties can produce short, shallow breaths that make it difficult to coordinate chewing and swallowing, similar to that seen in a heavy cold. As is the case with all nutrition support, food first should be the first line approach, but the practicalities of this in the hospital setting, even pre-pandemic, was difficult. These patients may benefit from increased prescription and a variety of oral nutritional supplements (ONS) that can provide hydration and essential nutrition to patients. Education and training of the wider multidisciplinary team (MDT) on the appropriate use of ONS, to optimise and promote patient compliance is equally essential so alternative flavours/styles can be offered to those who find they struggle with taste fatigue. Regular monitoring and screening of patients is needed to monitor intake and disease progression status to ensure nutritional plans remain appropriate. Enteral tube feeding should be implemented when nutritional needs cannot be met via the oral route and food fortification and oral nutritional supplements have been used. Those on mechanical ventilation will need appropriate feed prescriptions to meet raised calorie/protein needs. As mentioned previously, patient presentation may make medical teams hesitant regarding feeding tube insertions and fear of further suppressing appetite by introducing feed, despite there being limited evidence to support this and the known clinical proved benefits of using the gut.³⁰ The above combinations may result in greater use of both ONS and feeds. Close working with the housekeeping team will also be needed to ensure sufficient stock is maintained.

On CCU discharge, timely and efficient handovers to the ward dietetic team should be performed to ensure ongoing care. A hyperinflammatory response has been demonstrated and how long this continues for in Long-Covid sufferers is yet to be fully understood, but early data suggests this to be lasting from weeks to months.^{31, 32} Those who have lost significant muscle mass will need a prolonged period of increased calorie and protein provision in recovery. Post-CCU discharge oral intake is sub-optimal and patients will struggle to meet nutritional needs via oral diet alone and even patients who are tolerating diet well may need support to meet estimated nutritional needs in the absence of visitors bringing additional meals and snacks.³³

It's important to remember as patients enter the post-ICU phase of their recovery, they will increase their physical activity level and oral intake optimisation is needed to meet increased energy demands. Routine monitoring of intake, and ensuring feeding tubes are not removed or ONS terminated prematurely, will be key to supporting these patients in rehabilitation.

Some individuals may continue to experience symptoms of COVID-19 long after their initial diagnosis. NICE has defined three areas of COVID-19 infection (Table 1).³⁴ Long-Covid has essentially become a collective term, after the acute phase, that includes both ongoing symptomatic COVID-19 and post-COVID-19 syndrome, with NICE describing this as symptoms that continue or develop after acute COVID-19. Symptoms that continue for four weeks post COVID-19 would be termed Long-Covid.

Table 1: NICE definitions on COVID-19

Acute COVID-19	Signs and symptoms of COVID-19 lasting up to four weeks
Ongoing symptomatic COVID-19	Signs and symptoms of COVID-19 from four to 12 weeks
Post-COVID-19 syndrome	Signs and symptoms that develop during, or after, an infection consistent with COVID-19, continue for more than 12 weeks and are not explained by alternative diagnosis. Symptoms of this can change and vary over time

Long-Covid is yet to be fully understood, but an estimated 1.3 million people are thought to be affected.³⁵ Ongoing symptoms include:

- fatigue/reduced mobility,
- reduced sense of taste and smell,
- shortness of breath,
- difficulty concentrating/brain fog,
- anxiety/depression,
- pain,
- loss of appetite,
- weight loss.

Maintaining adequate nutrition is essential to ensure the body can function properly and recover well from illness, but this will be specific. All patients have different needs and present with different symptoms to those listed above. This highlights the need for tailored dietary advice from trained healthcare professionals.

The wide variety of symptoms will likely mean dietetic departments will need vague referral criteria to capture all those needing support with Long-Covid. Individuals may still struggle to meet nutritional needs once back in the community, long after their initial infection and treatment, and therefore require on-going high-energy, high-protein ONS alongside dietetic follow-up. Ready-made ONS are frequently used in the inpatient setting, however many GPs request ONS are the powdered options due to lower prescription costs. Careful consideration needs to be given in selecting appropriate patients for powdered formulations to ensure they can use them correctly and, indeed, have access at home to everything they would need to prepare the powdered ONS for themselves. Team-working between acute and community teams is needed to ensure care continuity and minimise delays that may exacerbate symptoms.

Long-term COVID-19 support groups have been set-up in many regions around the country for those struggling with the long-term effects of having experienced a CCU admission. This allows for open and frank discussions of patient's experiences which are eye-opening from a healthcare professional standpoint. Many report on-going difficulties in transitioning back to their normal lifestyle, and on-going difficulties with appetite and weight loss

because of their loss of taste and smell.³⁶ While these support groups have many benefits, there is a risk of sharing poorly researched treatments and managements. Such diets include the low histamine diet, which is currently poorly evidenced.³⁷ The maintenance of a low histamine diet is also very restrictive and may further exacerbate nutritional losses and inhibit recovery. These patients require individualised nutrition care pathways that could account for all their needs. Despite ongoing weight loss and continued diminished appetite, access to Long-Covid-specific nutrition support remains difficult for some as the medical focus tends to remain focused on their waistline, or other comorbidities, and nutrition support needs are not addressed.

Conclusions

In summary, medical knowledge of COVID-19 continues to expand, however specific nutritional pathways for individuals with COVID-19 remain inconclusive and current best-practice is based largely on prior research regarding respiratory distress within CCU. The biggest advance in care has been the vaccination programme which has demonstrated a clear reduced risk of CCU admission.³⁸ We are likely yet to see the true magnitude, long-term impact of Long-Covid as daily cases of COVID-19 infection continue to remain stubbornly high. Optimal medical and

nutritional management alongside other members of the MDT will be essential to reduce the impact on the NHS. Any services setting up Long-Covid clinics should include all members of the MDT to ensure a holistic approach to care provision. To date there is currently little evidence to support any specific eating patterns, food products or nutritional supplements in the management of Long-Covid. Indeed, the low histamine diet, which has been portrayed as 'curing' Long-Covid has little-to-zero scientific merit and could have negative impacts. Eating a healthy well-balanced diet consisting of sufficient energy and protein alongside sufficient micronutrient, vitamin and minerals has many proven health benefits and has the potential to support a good recovery. Those patients identified at malnutrition risk will require tailored food fortification advice and the assessment of ongoing need for ONS alongside their diet. Individuals who are struggling to optimise their diet, or deal well with their symptoms post-COVID-19, alone or in conjunction with other health conditions, should have access to appropriately trained health care professionals to optimise management. Further research is required in devising a dedicated tool that can capture, assess, and guide the management of the COVID-19 patient cohort with suitable evidence-based interventions.

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