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Dietetic-led nutrition interventions in patients with COVID-19 during intensive care and ward-based rehabilitation: singlecentre observational study

Ella Terblanche 1,2,*, Jessica Hills 1, Edie Russell 1, Rhiannon Lewis 1 and Louise Rose 2,3

- ¹ Dietetics Department, St Georges University Hospitals NHS Foundation Trust, London, UK; jessica.hills@uon.edu.au(J.H.), edie.russell@stgeorges.nhs.uk(E.R.), r.lewis3@rbht.nhs.uk(R.L.)
 ² Florence Nightingale Faculty of Nursing, Midwifery and Palliative Care, King's College London;
 - louise.rose@kcl.ac.uk
- Adult Critical Care. Guy's and St Thomas' NHS Foundation Trust
- * Correspondence: ella.terblanche@kcl.ac.uk

Abstract: Background: This study described dietitian-led nutrition interventions for patients with 12 COVID-19 during ICU and ward-based rehabilitation. As knowledge of COVID-19 and its medical 13 treatments were evolving, dietetic-led interventionsbetween surge 1 (S1) and surge 2 (S2) were com-14 pared. Methods: A prospective observational study was conducted of patients admitted to the ICU 15 service in a large academic hospital (London, UK). Clinical and nutrition data were collected during 16 1st (March-June 2020) N= 200 and 2nd (November 2020-March 2021) N= 253 COVID-19 surges. Re-17 sults: 453 patients were recruited. All required individualized dietetic-led interventions during ICU 18 admission as the ICU nutrition protocol didn't meet nutritional needs. Feed adjustments for de-19 ranged renal function (p=0.001) and propofol calories (p=0.001) were more common in S1 whereas 20 adjustment for gastrointestinal dysfunction was more common in S2 (p=0.001). One third of all pa-21 tients were malnourished on ICU admission, all lost weight in ICU; mean (SD) total percentage loss 22 of 8.8% (6.9%) Further weight loss was prevented over the remaining hospital stay with continued 23 dietetic-led interventions. Conclusions: COVID-19 patients have complex nutritional needs due to 24 malnutrition on admission and ongoing weight loss. Disease complexity and evolving nature of 25 medical management required multifaceted dietetic-led nutritional strategies which differed be-26 tween surges. 27

Keywords: COVID-19; Intensive Care; Dietitian/Dietician; Nutrition; Malnutrition; weight loss

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1. Introduction

In March 2020, the exponential increase in intensive care unit (ICU) admissions in 31 the United Kingdom (UK) due to the COVID-19 pandemic required significant planning 32 and restructuring of dietetic services to ensure safe and effective nutrition provision [1]. 33 ICU dietitians were faced with multiple challenges including how to best provide nutri-34 tion support for patients with an unknown disease; rapidly train redeployed dietitians 35 inexperienced in ICU nutrition; prioritize dietetic-led nutrition interventions; and manage 36 the logistics of shortages of enteral feed, feed pumps, and ancillaries. Critically ill patients 37 with COVID-19 appeared nutritionally complex with no international consensus on opti-38 mal nutritional management. 39

COVID-19 patients frequently present with malnutrition [2, 3]. This is due to preexisting chronic disease associated with underlying poor nutritional intake, combined with further decline due to common COVID-19 symptoms including gastrointestinal dysfunction and loss of taste and smell [2]. Patients with severe COVID-19 pneumonia exhibit a marked hyperdynamic state with persistent pyrexia leading to hypermetabolism and 44

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protein catabolism [4, 5]. Furthermore, enteral nutrition (EN) intolerance was reported 45 due to gastrointestinal symptoms, refractory hypoxemia requiring prone positioning, hy-46 potension or shock requiring the use of vasopressors, and the progression of multiple or-47 gan failure [1, 6-8]. 48

Nutritional guidelines were written rapidly based on experiential learning and 49 knowledge gained from dietitians in other countries managing critically ill patients with 50 COVID-19 in addition to prior dietetic knowledge of managing patients with severe res-51 piratory failure [1, 6-8]. Feeding protocols were devised to simplify nutrition delivery and 52 ensure consistency of nutrition interventions [6-9] at a time when EN was perceived dif-53 ficult to achieve and not a medical priority [9]. 54

The aim of this study was to describe dietitian-led nutrition interventions for patients 55 with COVID-19 during ICU admission and ward-based rehabilitation in a large tertiary 56 ICU service in a single center. As our knowledge of COVID-19 and its medical treatments 57 were evolving, we compared dietetic-led nutrition interventions between surge one (S1) 58 and surge two (S2) in the UK. 59

2. Materials and Methods

2.1. Study design, setting and sample

A prospective observational study was conducted enrolling critically ill patients with 62 COVID-19 admitted to an ICU (66 beds outside of pandemic conditions, 148 maximum 63 bed number during pandemic) in a large academic hospital in London, UK. Data were 64 collected during S1 (March-June 2020) and S2 (November 2020-March 2021). 65

All adult (>16 years) patients with COVID-19 were included who received advanced 66 respiratory support defined as invasive ventilation via endotracheal or tracheostomy tube 67 and required EN or parenteral nutrition (PN) for longer than 48 hours in ICU. Data were collected from ICU admission to hospital discharge. 69

2.2. Nutritional Interventions

To support increased ICU patient numbers, dietitians were redeployed from other clinical areas, equating to one dietitian to 25 ICU patients. The primary treatment aim was to commence nutrition using the newly devised local hospital COVID-19 ICU feeding protocol with EN within 48 hours of admission. The protocol advised feeding to start with a high protein EN product, at 30ml/hr. for six hours. After which time a gastric residual volume (GRV) should be obtained. If the volume is less than 500ml (or 300ml if in the prone position), the rate of feeding is increased to meet a target rate based on the patient's weight, (Actual or ideal if $BMI > 25kg/m^2$). Ideal body weight (IBW) was based on the patient's height calculated to BMI of 25kg/m^2 [10]. If EN was not tolerated sufficiently as defined in the protocol, PN was commenced. As per usual practice prior to COVID-19, all patients were screened by a dietitian each morning and only patients whose nutritional needs were not met using the ICU feeding protocol underwent dietetic assessment within 48 hours of commencing nutrition. Treating dietitians set energy and protein targets as per European Society for Parenteral and Enteral Nutrition (ESPEN) guidelines [7, 10], with target energy recommended at 20kcal/kg/day to avoid overfeeding in the early phase and increased to 30kcal/kg/day or more to facilitate rehabilitation after the acute phase of critical illness. Actual weight was used for patients with a BMI less than 25 kg/m^2 , IBW for those BMI 25-30 kg/m² and an adjusted body weight for those with BMI more than 30kg / m². Indirect calorimetry was used where appropriate to aid prediction of energy needs during the recovery phase on ICU. Nutritional data was collected on type of EN, use of protein supplementation, reasons for dietetic-led nutrition interventions during the ICU admission, on ICU discharge, during ward admission and at hospital discharge. 2.3. Data Collection

Baseline demographics were collected from the medical record including pre-exist-92 ing comorbidities, severity of illness using the Acute Physiology and Chronic Health Eval-93 uation (APACHE) II score, anthropometric measurements, and malnutrition risk as 94

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defined by Global Leadership Initiative on Malnutrition [11] and European ICU criteria 95 [10]. Outcome data included ICU mortality, and length of stay in ICU and hospital. 96

Anthropometric measurements included Body Mass Index (BMI) calculated using 97 ICU admission body weight (kg) and height (m). When a recent accurate weight was not 98 available from medical records, we measured patient weight using a hoist or patient trans-99 fer scales or obtained a reported weight from a family member. When height was not 100 available, it was estimated from ulnar length measurement and converted into an esti-101 mated height [12]. ICU survivors were weighed at ICU and hospital discharge using sit-102 ting, standing or hoist scales. Change in weight during ICU and hospital stay was deter-103 mined in kilograms and percentage total weight loss. Percentage weight loss \geq 5% was 104 considered clinically significant and was used to diagnose malnutrition [11]. 105

2.4. Data Analysis

Categorical data is presented as frequencies and proportions and continuous data as 107 means and standard deviations (SD). Proportions were compared using chi-squared or 108 Fishers exact tests (depending on cell size) and continuous data using 2-sample independ-109 ent t-test or the Wilcoxon rank-sum (Mann-Whitney) test. All tests were 2-tailed with p≤ 110 0.05 considered statistically significant. Statistical analyses were done using Stata version 111 17. The STROBE reporting guidelines for observational studies were followed 112

2.5. Ethical Considerations

The study was approved as a service evaluation by the National Health Service 114 Health Research Authority and the Research and Development Service at St George's Uni-115 versity Hospitals NHS Foundation Trust, London, UK. Registration number AUDI000637. Consent was waived as the project was approved as a service evaluation. 117

3. Results

There were 453 critically ill patients with COVID-19 included 200 patients were admitted during S1 (March-June 2020) and 253 during S2 (November 2020-March 2021). 120 Baseline characteristics are shown in Table 1. Figure 1 presents patient numbers from ad-121 mission to discharge. 122

Table 1. Baseline characteristics and clinical outcomes (whole cohort and comparison between pa-123 tients in S1 and S2). 124

Patient characteristics	All patients N = 453	S1 n = 200	S2 n = 253	p value
Age (years), mean (SD)	61 (12.4)	57.9 (12.7)	62.5 (12.0)	0.001
Male gender, n (%)	315 (70)	135 (67)	180 (71)	0.44
Weight (kg), mean (SD)	84 (20)	86 (21)	84 (19.4)	0.32
BMI (kg/m ²), mean (SD)	29 (6.3)	29 (6.5)	29 (6.1)	0.82
Ethnicity, n (%)				
White	114 (25)	46 (23)	68 (27)	0.34
Asian	96 (21)	41 (21)	55 (21)	0.85
Black	71 (16)	36 (18)	35 (14)	0.22
Other ethnic groups	48 (11)	23 (12)	25 (10)	0.57
Not stated	124 (27)	54 (27)	70 (28)	0.87
Comorbidities, n (%)				
Nil or 1	90 (20)	50 (25)	40 (16)	0.02
More than 2	362 (80)	150 (75)	212 (84)	
APACHE II, mean (SD)	15.1 (6.8)	15.5 (7.3)	14.8 (6.5)	0.32
ICU mortality, n (%)	253 (55)	107 (54)	146 (57)	0.37
ICU length of stay (days), mean (SD)	20 (18)	18.1 (14.4)	22.3 (21.2)	0.02

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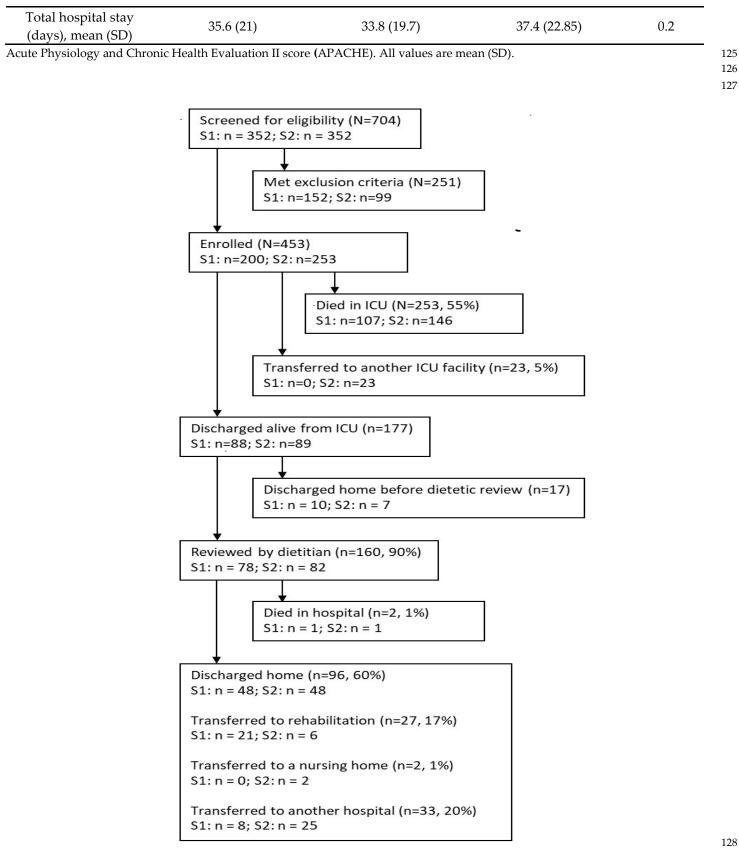


Figure 1. Patient flow diagram Key- S1 = surge one, S2 = surge two.

3.1. Patient characteristics

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S1 patients were younger than in S2: mean (SD) 57.9 (12.7) compared to 62.5 (12.0) 131 years (p=0.001) and had fewer comorbidities (p=0.02). Length of ICU stay was longer in 132 S2 (p=0.019) (Table 1). Of the 453 patients, 167 (37%) were malnourished on ICU admission; 64 (32%) in S1 and 103 (40%) in S2. 134

3.2. Dietitian-led nutrition interventions

Individualized dietetic-led nutrition interventions were required by all 453 (100%) 136 patients during ICU admission as nutritional needs were not met using the standardized 137 ICU nutrition protocol. Mean (SD) time to first dietetic-led nutrition interventions was 2.3 138 (1.2) days in S1 and 2.9 (2.3) days in S2. Patients received a mean (SD) of 5.2 (4.5) dietetic 139 interventions during the ICU stay. Patients had a similar number of dietetic-led nutrition 140 interventions during their ICU stay in S1 and S2 (mean 5.2 (4.2) compared to 5.3 (4.8) 141 times). PN was only required for six (1%) patients during S2 and none in S1. 142

More patients required feed adjustment for calories derived from propofol, impaired 143 renal function or changes in fluid or electrolyte status in S1 whereas more patients needed 144 adjustments for gastrointestinal dysfunction in S2 (Table 2). 145

Intervention	N = 453 n (%)	S1 N = 200 n (%)	S2 N = 253 n (%)	p value
Feed adjustment to meet energy needs for the different metabolic phases	337 (74)	141 (71)	196 (78)	0.09
Feed adjustment to account for calories derived from propofol sedation >15ml/hr (360kCals/24hrs)	248 (55)	144 (72)	104 (41)	0.001
Feed adjustment for gastrointestinal dysfunction	154 (34)	47 (24)	107 (42)	0.001
Transition from EN to oral diet	146 (32)	62 (31)	84 (33)	0.62
Feed adjustment due to changes in renal function, fluid status, or electrolyte balance	120 (26)	73 (37)	47 (19)	0.001
Feed adjustment to allow feed interruption for drug absorption of medication given via the enteral route	18 (4)	6 (3)	12 (5)	0.34

Table 2. Percentage of patients requiring specific dietetic-led nutrition interventions in ICU.

All values are patient numbers and (%).

Most patients required high-protein enteral feeds during ICU admission; with simi-149 lar proportions in S1 and S2 (184, 92% vs 236, 93%). There was no difference in the pro-150 portion of patients requiring concentrated feeds (39, 20% in S1 vs 45, 18% in S2). More 151 peptide feeds were used in S1 (26, 13%) compared to S2 (17, 7%) (p=0.03). Protein supple-152 mentation also increased from S1 (98, 49%) to S2 (174, 69%) (p=0.001). During S1, first 153 choice of feed was not available due to supplier production shortages in 61 (30%) patients, 154 shortages were not experienced during S2. 155

3.3. Weight loss

Mean (SD) weight loss over the ICU admission was 7.9kg (6.8kg), equivalent to a 157 mean (SD) total percentage loss of 8.8% (6.9%) indicating clinically significant malnutri-158 tion. Mean (SD) weight loss over the total hospital stay was 7.5kg (6.6kg) suggesting no 159 further weight loss occurred after ICU discharge. Details of weight loss according to surge 160 are shown in Table 3. 161

Table 3. Weight loss.

	All N = 160	S1 N = 78	S2 N = 82	p value
ICU admission weight (kg)	85 (20.1)	86 (21)	84 (19.4)	0.32
ICU admission BMI (kg/m ²)	29 (6.3)	29 (6.5)	29 (6.1)	0.82
ICU weight loss (kg)	7.9kg (6.8)	7.8 (7.8)	8.1 (5.9)	0.80
ICU weight loss %	8.8 (6.9)	8.5 (7.7)	9.0 (6.3)	0.65
Percentage ICU weight loss				
N (%)				
< 5 %	58 (35)	30 (41)	36 (40)	0.22
5-10%	57 (34)	27 (36)	27 (30)	
> 10%	53 (32)	22 (30)	26 (29)	
Total weight loss (kg) from ICU admission to hospital discharge	7.5 (6.6)	8.0 (7.4)	7.3 (6.1)	0.70

All values are mean (SD).

3.4. Dietetic-led nutrition interventions after ICU discharge

Ward dietitians received a dietetic handover for all patients discharged alive from 165 ICU (n = 177). Most patients (160, 90%) received ward-based dietetic-led nutrition interventions with similar numbers in S1 (78, 89%) and S2 (82, 92%). The 17 patients not re-167 viewed were discharged home before the ward dietitians were able to assess. 168

Upon discharge to the ward, patients were reviewed earlier during S1 compared to 169 S2, within a mean (SD) of 1.9 (1.3) vs. 2.4 (1.8) days (p=0.04); but at similar frequencies (2.8 170 (2.5) times over 9.9 (8.0) days vs. 3.3 (2.4) times over 13 (8.5) days). 171

Table 4 details the type of ward-based nutrition support received. Exclusive or sup-172 plementary (to oral diet) EN was prescribed for 106 patients (52 (67%) in S1 and 54 (66%) 173 in S2) for a mean of 6 (5.5) days (similar duration in both surges). More high-protein feed 174 was used on the ward in S2 (33, 61%) compared to S1 (9, 17%) (p=0.0001), whereas more 175 high-energy feed was used in S1 (17, 33% vs. 7, 13%, p=0.007). Of the 106 patients receiving 176 EN, nasogastric feeding was ceased on the ward without prior dietetic review on 58 occa-177 sions (54%). During ward admission, 117 (73%) patients required prescribed ready-to-178 drink oral nutritional supplements; 52 (66%) in S1 and 65 (79%) in S2. The most commonly 179 prescribed product was a compact high-protein milkshake-style; 32 (62%) in S1 and 40 180 (62%) in S2. 181

Table 4. Nutrition support	received on ward admission.
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Nutrition intervention	N = 160	S1 N =78	S2 N = 82	p value

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	n (%)	n (%)	n (%)	
Exclusive EN	36 (23)	14 (18)	22 (27)	0.17
Supplementary EN	70 (44)	38 (49)	32 (39)	0.21
Exclusive and supplemen- tary EN combined	106 (66)	52 (67)	54 (66)	0.91
ONS	68 (43)	34 (44)	34 (42)	0.78
Texture modification	34 (21)	23 (29)	11 (13)	0.01
Diet alone	33 (21)	21 (27)	12 (14)	0.05

All values are patient numbers and (%). Enteral Nutrition (EN), Oral Nutrition Supplement Drinks (ONS).

Of the 453 patients, 175 (39%) survived to hospital discharge, of which 128 (73%)186needed community dietetic follow-up. This was consistent across both surges with 63187(72%) respectively in S1 vs. 65 (74%) in S2. Community referrals reasons for each surge188were continued EN (15, 12%), oral nutritional supplements (70, 55%), and healthy eating189advice (43, 34%).190

4. Discussion

In this large cohort of patients with COVID-19, a standardized feeding protocol was 192 insufficient to meet nutritional needs with individualized dietetic-led nutrition interven-193 tions required for all patients during ICU admission. Significant differences were ob-194 served in dietetic-led nutrition interventions in S1 and S2. More patients required feed 195 adjustment for calories derived from propofol, impaired renal function, and fluid and 196 electrolyte adjustments in S1, whereas patients more commonly needed adjustments for 197 gastrointestinal dysfunction in S2. Over one third of patients were malnourished on ICU 198 admission and patients lost an average of 7.9kg over the ICU stay. Further weight loss 199 was prevented over the remaining hospital stay with continued dietetic-led nutrition in-200 terventions. Only 39% of the cohort survived to hospital discharge, with 73% of these re-201 quiring further dietetic interventions in the community. 202

In our COVID-19 cohort, all required individualized dietetic-led nutrition interven-203 tions during ICU admission suggesting critically ill patients with COVID-19 are nutri-204 tionally complex. This proportion is markedly higher than non-COVID patients for whom 205 the need for individualized dietetic led nutrition interventions is reported to range from 206 50 to 70% [13, 14]. Differences in dietetic led nutrition interventions required in pandemic 207 S1 and S2 reflect changes in medical management as knowledge of the disease evolved. 208 Furthermore, in our institution, propofol shortages in S2 requiring alternate opioid seda-209 tion agents obviating the need for EN manipulation to avoid overfeeding were experi-210 enced. Fluid restriction commonly employed in S1 was not used in S2 as evidence 211 emerged that it was not beneficial [15]. Increased gastrointestinal dysfunction and EN in-212 tolerance in S2 might be attributed to two changes in clinical practice. Firstly, there was 213 an increased use of prone positioning which can present unique feeding challenges due 214 to large gastric residual volumes, vomiting, and aspiration of gastric contents [16]. Sec-215 ondly, increased use of opioid-based sedation due to propofol shortages observed in this 216 study may have contributed to the cycles of constipation and laxative induced diarrhoea 217 observed [3, 17]. 218

In our patient cohort a mean weight loss of 7.9kg over the ICU stay was identified. 219 Two-thirds of patients lost more than 5% of body weight; one-third lost more than 10% 220 indicating severe malnutrition. Disease severity and prolonged ICU stay were likely contributing factors. Weight loss and malnutrition contribute to worse functional ability following ICU discharge in patients with COVID-19 [2, 3]. A substantial proportion of patients surviving to hospital discharge required further dietetic led nutrition interventions in the community was also found. 225

Despite all patients experiencing weight loss in ICU, no further weight loss occurred 226 before hospital discharge which may be attributed to ongoing dietetic led nutrition 227

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interventions. Of the patients transferred to the ward, 90% received ward-based dietitian-228 prescribed individualized nutrition interventions. Continuity of nutritional interventions 229 can be problematic during transition from ICU to the ward [18]. Structured dietetic hand-230 over between ICU and ward dietitians to improve transfer of nutritional history and meet 231 nutritional needs for recovery were used [1]. Additionally, more patients received high-232 protein feeds on the ward during S2 as ward dietitians became more familiar with treating 233 COVID-19 patients and as guidelines became available. A high protein diet is recom-234 mended due to the catabolism experienced during critical illness and thought to aid re-235 covery [1]. 236

To our knowledge, this is the largest prospective cohort study describing dietetic-led 237 nutritional interventions provided to patients with COVID-19 from ICU admission to 238 ward discharge. Our study has limitations. First, a single-center limits generalizability. 239 Second, the observational design means no assumptions about causality can be made and 240 therefore cannot determine if dietetic led nutrition interveniontsinfluenced clinical out-241 comes. Third, it was not possible to make comparisons to dietetic-led nutritional interven-242 tions for patients without COVID-19 at this time as there were very few patients admitted 243 without COVID-19. Finally, due to pandemic dietetic working conditions data on 244 amounts of energy and protein received could not be captured. 245

5. Conclusions

In this large prospective cohort of patients with COVID-19, all patients required in-247 dividualized dietetic led nutrition interventions during ICU admission as the standard-248 ized ICU nutrition protocol did not meet nutritional needs. The complexity and evolving 249 nature of medical management necessitated multifaceted dietetic led nutrition interven-250 tions which differed between surges. Over one third of patients were malnourished on 251 ICU admission and all patients lost weight in the ICU. Most patients were nutritionally 252 compromised at ICU discharge and required ongoing dietitian-led individualized nutri-253 tion interventions in the ward which prevented further weight loss over the remaining 254hospital stay. Based on our results future studies are needed to determine if individual-255 ized nutrition support provision led by the dietitian, compared to standard care, increases 256 the adequacy of nutritional delivery, and improves clinical outcomes. 257

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Institutional Review Board Statement: The study was approved as a service evaluation by the Na-262 tional Health Service Health Research Authority and the Research and Development Service at St 263 George's University Hospitals NHS Foundation Trust, London, UK. Registration number 264 AUDI000637. 265

Informed Consent Statement: Consent was waived.

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Conflicts of Interest: The authors declare no conflict of interest.

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