

completed encounter mortality between no flag (9.97% [37/371]); medium-risk (28.5% [68/239]); high-risk (51.2% [105/205]); and suspected thromboembolism (52.4% [65/124]), Kruskal Wallis  $p < 0.0001$ . 173 of 535 consecutive COVID-19 positive patients whose hospital encounter completed before real-time introduction died (32.3% [95% confidence intervals 28.0, 36.0]), compared to 46 of 200 (23.0% [95% CI 17.1, 28.9]) admitted after implementation of real-time traffic light flags ( $p = 0.013$ ). The real-time cohort were older (median age 72ys compared to 67ys,  $p = 0.037$ ), and were more likely to flag at risk of thromboembolism on admission. However, adjusted for age/sex, the probability of death was 0.33 (95% confidence intervals 0.30, 0.37) before real-time implementation, and 0.22 (0.17, 0.27) after real-time implementation ( $p < 0.001$ ). In subgroup analyses, older patients, males, and patients with hypertension ( $p \leq 0.01$ ) and/or diabetes ( $p = 0.05$ ) derived the greatest benefit from admission under the real-time traffic light system.

**Conclusion** Personalised early interventions were associated with a reduction in mortality. We suggest benefit predominantly resulted from early triggers to review/enhance anticoagulation management, without exposing lower-risk patients to potential risks of full anticoagulation therapy.

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#### THE ROLE OF ANTICOAGULATION THERAPY IN MANAGEMENT OF COVID-19 PATIENTS

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**Introduction** Hypoxemia, acute respiratory distress syndrome and coagulopathy are common issues experienced by pts with severe COVID-19 disease.<sup>1</sup> The aim of this study was to evaluate the efficacy of anticoagulation therapy in COVID-19 patients.

**Methods** This is a retrospective observational study for patients admitted to a busy district hospital during the peak period of the COVID-19 pandemic. All patients aged  $> 18$  with suspected or confirmed RT-PCR COVID-19 and raised D-Dimer were included in this study. Data including demographics, comorbidities, and effects of anticoagulation on mortality were examined.

**Results** A total of 628 pts with more males ( $n = 365$ ; 58.1%), and 48.7%  $> 75$  years were included in the study. 27.9% were obese ( $BMI \geq 30$ ); and 25% were overweight ( $BMI 25 - 29.9$ ). 448/628 (71.3%) had a positive swab for coronavirus and a further 70 patients (11.1%) had probable infection based on clinic-radiological suspicion. Nearly half ( $n = 311$ ; 49.5%) of the patients had hypertension and a quarter ( $n = 166$ ; 26.4%) had diabetes. A total of 226 (36%) pts died of which 85.8% ( $n = 194$ ) had a positive swab compared to 12.8% ( $n = 29$ ) with negative swab. This was statistically significant with a  $p$ -value of 0.001. Patients with a raised D-dimer 150/628 (23.8%) received therapeutic dose anticoagulation and 408/628 (64.9%) received prophylaxis or no anticoagulation. 53 patients (22.5%) of those who received treatment dose died compared to 183 (77.5%) who received

**Abstract S99 Table 1** Association of swab PCR with Anticoagulants, D-Dimer in Mortality

Variables	Mortality with SWAB				p-value	
	Positive (n=236)		Negative (n=41)			
	n	%	n	%		
Anticoagulant	Yes	206	87.3	38	92.7	0.32
	No	30	12.7	3	7.3	
Treatment Dose Anticoagulant	Yes	53	22.5	16	39.0	0.02*
	No	183	77.5	25	61.0	

prophylactic dose or no anticoagulation due to comorbidities. This was statistically significant ( $p$  value 0.02).

**Conclusion** Therapeutic anticoagulation significantly reduces mortality in COVID-19 patients with a high D-dimer.

#### REFERENCE

1. Klok F, Kruip M, van der Meer N, *et al.* Incidence of thrombotic complications in critically ill ICU patients with COVID-19. *Thromb Res* 2020 Apr 10. [Epub ahead of print]

## Baby and bathwater: not all lung infections are COVID-19

S100

#### VITAMIN D SUPPLEMENTATION TO PREVENT ACUTE RESPIRATORY INFECTIONS: SYSTEMATIC REVIEW AND META-ANALYSIS OF AGGREGATE DATA FROM RANDOMISED CONTROLLED TRIALS

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**Background** A 2017 meta-analysis of data from 10,933 participants in 25 randomised controlled trials (RCTs) of vitamin D supplementation for prevention of acute respiratory infections (ARI) revealed a protective effect. Since then, data from 15 new RCTs with over 20,000 participants have emerged.

**Methods** Systematic review and meta-analysis of data from RCTs of vitamin D for ARI prevention using a random effects model. Pre-specified sub-group analyses were done to determine whether effects of vitamin D on risk of ARI varied according to baseline 25-hydroxyvitamin D (25[OH]D) concentration or dosing regimen. We searched MEDLINE, EMBASE, the Cochrane Central Register of Controlled Trials (CENTRAL), Web of Science, ClinicalTrials.gov and the International Standard RCT Number (ISRCTN) registry from inception to 1st May 2020.

**Findings** We identified 40 eligible RCTs (total 30,956 participants, aged 0 to 95 years). Data were obtained for 29,841 (96.5%) of 30,909 participants in 39 studies. For the primary comparison of vitamin D supplementation vs. placebo, the intervention reduced ARI risk overall (Odds Ratio [OR] 0.89, 95% CI 0.81 to 0.98;  $P$  for heterogeneity 0.009). No statistically significant effect of vitamin D was seen for sub-groups defined by baseline 25(OH)D concentration. However, protective effects were seen for trials using a daily dosing regimen

**Abstract S100 Table 1** Placebo controlled RCTs: Proportion of participants experiencing at least one acute respiratory infection, overall and stratified by potential effect-modifiers

Variables	No of trials	Proportion with $\geq 1$ ARI, intervention group (%)	Proportion with $\geq 1$ ARI, control group (%)	Odds ratio (95% CI)	I <sup>2</sup> %	P for heterogeneity
<b>Overall</b>	34	8307/14155 (58.7)	8196/13660 (60.0)	0.89 (0.81 to 0.98)	40.0	0.009
<b>Baseline 25(OH)D, nmol/L</b>						
<25	19	1348/1798 (75.0)	1388/1819 (76.3)	0.78 (0.53 to 1.16)	47.2	0.012
25 – 49.9	27	3411/4637 (73.6)	3337/4491 (74.3)	1.03 (0.91 to 1.17)	4.1	0.40
50 – 74.9	28	1607/2761 (58.2)	1531/2542 (60.2)	0.90 (0.75 to 1.07)	14.1	0.25
$\geq 75$	24	923/1520 (60.7)	895/1458 (61.4)	0.97 (0.81 to 1.16)	0.0	0.74
<b>Dosing frequency</b>						
Daily	18	1056/2134 (49.5)	1020/1871 (54.5)	0.75 (0.61 to 0.93)	52.5	0.005
Weekly	5	4357/6288 (69.3)	4388/6274 (69.9)	0.97 (0.88 to 1.06)	0.0	0.41
Monthly or less frequently	11	2894/5733 (50.5)	2788/5515 (50.6)	1.00 (0.91 to 1.09)	0.0	0.50
<b>Daily dose equivalent, IU<sup>[a]</sup></b>						
<400	2	482/1175 (41.0)	511/1133 (45.1)	0.65 (0.31 to 1.37)	86.3	0.007
400–1000	10	656/1236 (53.1)	627/1069 (58.7)	0.70 (0.55 to 0.89)	31.2	0.16
1001–2000	14	4693/7885 (59.5)	4712/7817 (60.3)	0.96 (0.87 to 1.06)	8.0	0.37
>2000	7	2291/3462 (66.2)	2250/3444 (65.3)	1.05 (0.84 to 1.31)	37.1	0.15
<b>Trial duration, months</b>						
$\leq 12$	28	1852/4754 (39.0)	1807/4307 (42.0)	0.82 (0.72 to 0.94)	39.9	0.017
>12	6	6455/9401 (68.7)	6389/9353 (68.3)	1.03 (0.95 to 1.11)	0.0	0.97

[a] Data from one trial that included higher-dose, lower-dose and placebo arms<sup>18</sup> are excluded from this sub-group analysis, since the higher-dose and lower-dose arms spanned the 1,000 IU/day cut-off, rendering it unclassifiable

(OR 0.75, 95% CI 0.61 to 0.93); at daily dose equivalents of 400–1000 IU (OR 0.70, 95% CI 0.55 to 0.89); and for a duration of  $\leq 12$  months (OR 0.82, 95% CI 0.72 to 0.94). Vitamin D did not influence the risk of experiencing a serious adverse event. Risk of bias within studies was assessed as being low for all but two trials. A funnel plot showed asymmetry, suggesting that small trials showing non-protective effects of vitamin D may have been omitted from the meta-analysis.

**Interpretation** Vitamin D supplementation was safe and reduced risk of ARI, despite evidence of heterogeneity across trials. The overall effect size may have been over-estimated due to publication bias. Protection was associated with administration of daily doses of 400–1000 IU vitamin D for up to 12 months. The relevance of these findings to COVID-19 is not known and requires investigation.

### S101 PREDICTORS OF AND TIME FRAME FOR READMISSION FOLLOWING HOSPITALISATION WITH COMMUNITY ACQUIRED PNEUMONIA

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**Background** There is a paucity of UK data to aid healthcare professionals in predicting which patients hospitalized with Community Acquired Pneumonia (CAP) are at greatest risk of readmission and to determine which readmissions may occur soonest.

**Methodology** An analysis of CAP cases admitted between 1/1/2017 and 31/3/2019 to 9 hospitals in Northwest England participating in the Advancing Quality Pneumonia program. For entry into the AQ program, patients hospitalised with CAP require the diagnosis to be made by a Consultant Physician along with a chest radiograph compatible with pneumonia

**Results** 12,144 subjects with CAP (mean age 73 years (SD 16)) were admitted during the study period. Mean Charlson Comorbidity Index (CCI) was 9.47 (SD 8.81) and in-hospital mortality was 14.7%. 2691 (26%) were readmitted within 30 days of discharge. Readmission was predicted by severe liver disease (aOR = 2.43), non-metastatic cancer (aOR = 1.72), Diabetes with complications (aOR = 1.64), Chronic Kidney Disease (aOR = 1.25), Congestive Cardiac Failure (aOR = 1.16), Ischaemic Heart Disease (aOR = 1.16) and longer Length of Stay (LOS). 24% of those readmitted had Pneumonia as the principal readmission diagnosis. 41% of readmissions occurred within 7 days of discharge; 25% between day 8–14 and the remaining 34% between 14 to 30 days post discharge. Comparing patients readmitted within 14 days with those readmitted 14–30 post discharge, earlier readmissions were older (72 years (SD 14.72) v 71 years (SD 14.08) p=0.01) and have a diagnosis of metastatic cancer (6.6% v 4.4%; p=0.02). Of the readmitted patients who had a comorbidity, none with Severe Liver Disease had a principal readmission diagnosis of Pneumonia compared with 23% of those with Ischaemic Heart Disease, 20% with Congestive Cardiac Failure, 27% with Metastatic Cancer and 23% with Non-Metastatic Cancer.

**Discussion** A quarter of patients who survive to discharge following hospital admission for CAP are subsequently