

“Seeing a trend”- increasing vitamin A levels on Elexacaftor/ Tezacaftor/ Ivacaftor therapy (Poster Number 160)

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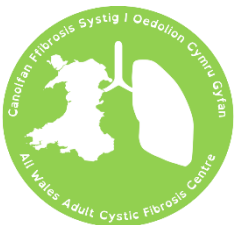
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Declaration of Interest

Presenter: David Proud

Vertex Pharmaceuticals: Consultancy fee educational video 2021



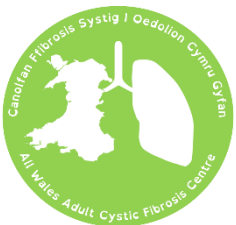
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Content

- Background
- Method
- Results
- Discussion and hypothesis



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Background: Vitamin A

- Available as
 - Preformed vitamin A (animal source), Provitamin A Beta-Carotene (plant source)
 - Most multi-functional vitamin in the body¹
 - Embryogenesis to adulthood
 - Vision, Immune system, epithelial cells, anti-oxidant, reproduction, embryonic development
 - Deficiency
 - $<0.7\mu\text{mol/L}$ Severe deficiency $<0.35\mu\text{mol/L}$
 - Night blindness, xerophthalmia, infection risk
 - Toxicity
 - Acute: Single excessively high dose
 - N&V, anorexia, abdominal pain, blurred vision, headaches, irritability, intracranial swelling
 - Chronic: $>25,000\text{iu}$ daily²
 - Headaches, muscle and bone pain, fracture risk, ataxia, skin disorders, alopecia, liver toxicity, dyslipidaemia, intracranial swelling

1 Timoneda et al. *Nutrients*. 2018. 10. 1132

2 Hathcock et al. 1990. *Am J Clin Nutr*. 52(2)183-202.



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Background & Aim

- Risk of fat soluble vitamin deficiencies in patients with CF³
 - Supplementation common but risk of hypervitaminosis
 - CFTR modulators dramatically improving health landscape⁴
 - Case studies: Elexacaftor/ Tezacaftor/ Ivacaftor (ETI) therapy may increase risk of hypervitaminosis A⁵
-
- Assess fat soluble vitamin levels before and after ETI commencement in adult CF population

3 CF Trust. Nutritional Management of Cystic Fibrosis 2nd edn. 2016

4 Zaher A et al. *Cureus*. 2021. 13(7): e16144.

5 Miller MJ & Foroozan R. *Can J Ophthalmol*. 2021 May 28:S0008-4182(21)00162-9.



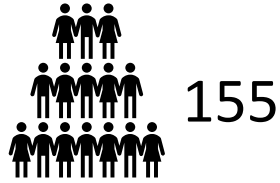
Method

- Annual vitamin levels pre-post ETI therapy
- Welsh Gov: Sweat chloride pre-post ETI (post ETI 6, 12 months then annually)
- Age, pancreatic status, genetic mutation
- SPSS, paired t test, Statistical sig $p < 0.05$.

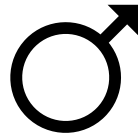
Results



2020-2021



155



88



67



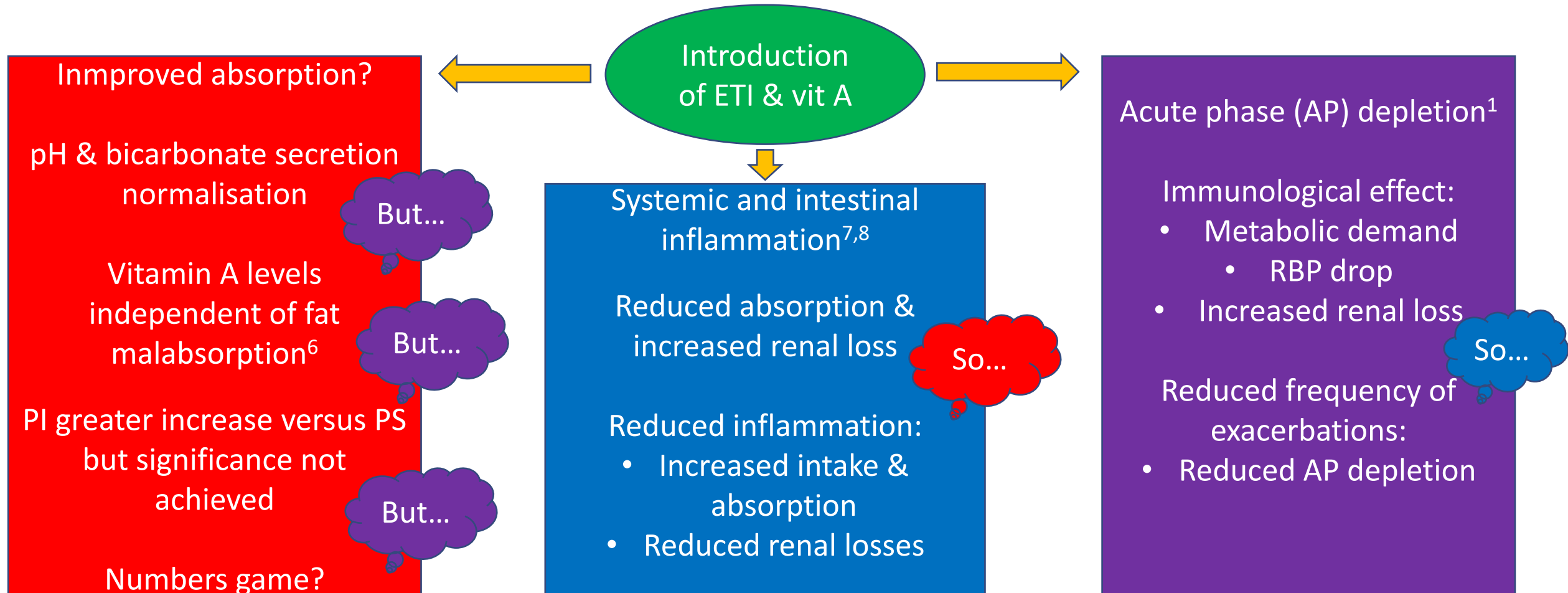
PI: 142 (92%)

PS: 13 (8%)

	Normal range	Change (mean)	<i>p</i> value
Sweat Chloride (nmol/L)	0-40	-46.1	<0.001
Vitamin A (umol/L)	1.10-2.60	0.37	<0.001
Vitamin E/Ratio	>4.4	-0.25	0.23
Vitamin D (nmol/L)	>50	-0.74	0.70

	PI (Mean increase)	PS (Mean increase)	<i>p</i> value
Vitamin A (umol/L)	0.39	0.15	0.11
Vitamin E/ratio			0.18
Vitamin D (nmol/L)			0.78

Discussion & Hypothesis



6 Ahmed et al. *Arch Dis Child*. 1990;65(6):589–93

7 Colombo et al. *Expert Rev Respir Med*. 2019;13(6):533–44

8 Ruben et al. *ASN*. 2017. 8:197–212

Safety & future:

- Supplementation source?
- Limitations and future studies....



Thank you for listening

Any Questions?

Poster Number: 160

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