

## Supplementary Appendix

### Assessment of treatment compliance

At each follow-up visit, compliance to treatment was assessed by the research team. The participant was asked to bring all remaining capsules which were counted and recorded in a tracking form. Capsule supplies were then replenished and the number of capsules dispensed by the research pharmacy team was recorded on the tracking form. The “expected” number of returned capsules at subsequent visits were calculated by the following:  $[(\# \text{ capsules kept from prior visit}) + (\# \text{ capsules dispensed at prior visit}) - [3 * (\# \text{ of days between prior visit and next visit})]$ .

**Table S1.** Inclusion and exclusion criteria

Inclusion Criteria	Exclusion Criteria
<ul style="list-style-type: none"> <li>● Post-bronchodilator FEV<sub>1</sub>/FVC ratio &lt; 70%</li> <li>● Post-bronchodilator FEV<sub>1</sub> ratio &lt;65 predicted %</li> <li>● Clinical diagnosis of COPD</li> <li>● Stable medical regimen for 30 days prior to enrollment</li> <li>● Age &gt; 40 years</li> <li>● Past history of former cigarette smoking with at least 10 cigarette pack-years</li> </ul>	<ul style="list-style-type: none"> <li>● COPD exacerbation and/or hospitalization for COPD in the past 30 days prior to enrolment</li> <li>● History of physician-diagnosed asthma</li> <li>● History of unrelated pulmonary disease (interstitial lung disease, thromboembolic disease)</li> <li>● Status-post lung transplantation</li> <li>● Status-post lung volume reduction surgery</li> <li>● Active cigarette smoking</li> <li>● Left-sided congestive heart failure</li> <li>● History of coronary artery disease</li> <li>● History of cerebrovascular disease</li> <li>● History of peripheral vascular disease</li> <li>● History of stroke</li> <li>● History of myocardial infarction</li> <li>● Clinical diagnosis of obstructive sleep apnea</li> <li>● Current breastfeeding</li> <li>● Current pregnancy</li> <li>● History of hypersensitivity to fish oil</li> <li>● Allergy to fish oil</li> <li>● Allergy to corn oil</li> <li>● Current use of high-dose fish oil capsules (defined as &gt; 1 gram/day of omega-3 fatty acids)</li> <li>● Current use of Coumadin</li> <li>● Congenital abnormality of the arm or hand</li> <li>● Raynaud's Phenomenon</li> <li>● Alanine aminotransferase &gt; 2 times the upper limit of normal at baseline</li> <li>● History of radical mastectomy</li> <li>● History of removal of axillary lymph nodes</li> <li>● Unstable angina within 30 days prior to enrolment</li> <li>● History of end-stage liver disease</li> <li>● Systolic blood pressure &gt; 170 mmHg or &lt; 100 mmHg at rest</li> <li>● Diastolic blood pressure &gt; 100 mmHg at rest</li> <li>● Heart rate &gt; 120 beats per minute at rest</li> <li>● Body mass index &lt; 35 kg/m<sup>2</sup></li> </ul>

FVC = forced vital capacity; FEV<sub>1</sub> = forced expiratory volume in 1 second; COPD = chronic obstructive lung disease

**Table S2. Outcome Assessments**

<b>Outcome</b>	<b>Time of Assessments</b>
Flow mediated dilation	0 and 6 months
Peripheral arterial tonometry	0 and 4 months
Endothelial microparticles	0 and 6 months
Questionnaires (MMRC, SGRQ)	0, 2, 4, and 6 months
6 minute walk distance	0, 2, 4, and 6 months
Spirometry	0, 2, 4, and 6 months
DL <sub>CO</sub>	0 and 6 months

Abbreviations: DL<sub>CO</sub> = diffusing capacity of carbon monoxide; MMRC = Modified Medical Research Council; SGRQ = St. George's Respiratory Questionnaire

**Table S3. Primary endpoint excluding participants using supplemental oxygen**

<b>End Point</b>	<b>Fish Oil (95% CI)</b>	<b>Placebo (95% CI)</b>	<b>Difference between groups (95% CI)*</b>	<b>P-value</b>
Primary end point: percent change in flow-mediated dilation of the branchial artery from baseline to 6 months	n=13	n=12		
Maximum post-deflation diameter	-2.4 (-6.2 to 01.4)	-1.7 (-5.5 to 2.2)	-0.7 (-5.8 to 4.4)	0.77
55-65 second deflation diameter	-1.4 (-4.1 to 1.3)	-0.7 (-2.7 to 1.2)	-0.7 (-3.9 to 2.6)	0.68

**Table S4.** Serious adverse events

Participant	Description of Event	Follow-up
1	Spontaneous left pneumothorax 9 days after starting study intervention. Hospitalized and discharged as pneumothorax was treated with chest tube.	Pneumothorax determined to be unanticipated and unrelated to study pill or any procedure during participant's study visits.
2	Hospitalized for acute renal insufficiency 1 month after completion of study intervention. Renal insufficiency determined to be secondary to other medication and unrelated to study pill.	Acute renal insufficiency determined to be unrelated to study intervention or procedures.
3	Hospitalized for dyspnea determined to be secondary to acute bronchitis and discharged with course of antibiotics. Participant had completed research study approximately 3 weeks prior to hospitalization.	Determined to be unrelated to study pill or procedures.
4	Participant hospitalized approximately 1 month after starting study intervention for pneumonia and atrial fibrillation. Participant recovered and discharged. Approximately two weeks later was admitted again with worsening mental status, renal failure, and new emboli strokes. During hospitalization developed hypotension secondary to sepsis and underwent cardiac arrest and passed.	Determined to be unrelated to study pill and study procedures.