Additional material for online data repository

Supplementary Methods

Blood measurements

Baseline and end of trial EDTA plasma samples for each individual were analysed for selenium in the same batch, by dynamic reaction cell-inductively coupled plasma mass spectrometry (DRC ICP-MS) using an Elan 6100 DRC plus (SCIEX Perkin-Elmer). ^{78}Se was measured, employing methane (at 0.5ml/min) as the DRC gas to remove the argon dimer background(1) and butanol to increase the sensitivity of the signal(2). Accuracy was assured by analysis of four internal quality control serum samples (TEQAS, University of Surrey, Guildford) and certified reference materials: Seronorm Serum (Nycomed, Norway) JL4409, mean value (5 determinations) 0.90, SD 0.04 $\mu molL^{-1}$ (certified 0.92, range 0.84 – 1.00) $\mu molL^{-1}$, and NO0371 mean value (5 determinations) 1.76, SD 0.04 (certified 1.72, range 1.61-1.83) $\mu molL^{-1}$. The detection limit was less than 0.01$\mu molL^{-1}$.

Plasma vitamin E (α- and γ-tocopherol, adjusted for serum cholesterol) was measured using reverse phase HPLC with detection at A292nm(3). The lower limit of detection was 0.3µmol/L and the intra- and inter-assay coefficients of variation were 2.1% and 3.9% respectively. Red blood cell GPx activity (standardised for haemoglobin level) was determined from the rate of oxidation of NADPH and was measured spectrophotometrically at 340 nm. One unit of GPx-1 activity was defined as the amount of protein required to oxidize 1.0 µmol NADPH per minute. All samples were stored at –20ºC following collection; samples for vitamin E and GPx assays were stored at -80 ºC prior to analysis.

Sampling probability weighting

We first calculated a propensity score (4) for the event of having missing data ("missingness") for each outcome, using logistic regression, based on characteristics of all randomised participants at baseline. The weights used were specific to the 10 combinations of the 2 treatments and the 5 quintiles of "missingness" propensity score for each outcome, and were used to standardise the effect estimates to the distribution of treatment and "missingness" propensity in all randomised participants. This weighting implicitly imputes the outcomes in those with missing outcome data, based on the outcomes observed in individuals with complete data who had a similar "missingness" propensity score and were allocated the same treatment(5).

Supplementary references

(1) Sloth JJ, Larsen EH. The application of ICP dynamic reaction cell mass spectrometry for measurement of selenium isotopes, isotope ratios and chromatographic detection of selenoamino acids. J Anal At Spectrom 2000;15:669-72.

(2) Sieniawska CE, Mensikov R, Delves HT. Determination of total selenium in serum, whole blood and erythrocytes by ICP-MS. J Anal At Spectrom 1999;(14):109-12.

(3) Kelly FJ, Rodgers W, Handel J, Smith S, Hall MA. Time course of vitamin E repletion in the premature infant. British Journal of Nutrition 63(3):631-8, 1990 May.

(4) Joffe MM, Rosenbaum PR. Invited commentary: propensity scores. Am J Epidemiol 1999 August 15;150(4):327-33.

(5) Rubin DB. Multiple imputation for nonresponse in surveys. Wiley Classic Library Edition ed. Hoboken, NJ: John Wiley and Sons, Inc.; 2004.

Supplementary Tables:

Table E1: Arithmetic mean differences in asthma severity outcomes (end of trial minus baseline), restricted to individuals with complete measured outcome data

Outcome	*N*	*Difference*	*(95%*	*CI)*	*P*
Square root QoL score					
Placebo	78	-0.16	(-0.27,	-0.06)	.0021
Selenium	85	-0.21	(-0.30,	-0.12)	3.2x10-6
Se-placebo difference	**163**	**-0.05**	**(-0.18,**	**0.09)**	**.49**
Mean night-time asthma symptom score					
Placebo	62	-0.20	(-0.37,	-0.02)	.028
Selenium	68	-0.13	(-0.29,	0.02)	.082
Se-placebo difference	**130**	**0.06**	**(-0.17,**	**0.29)**	**.6**
Mean daytime asthma symptom score					
Placebo	59	-0.18	(-0.35,	-0.00)	.05
Selenium	67	-0.10	(-0.26,	0.07)	.25
Se-placebo difference	**126**	**0.08**	**(-0.16,**	**0.32)**	**.52**
Mean bronchodilator dosage (puffs/day)					
Placebo	65	-0.56	(-1.13,	0.01)	.054
Selenium	68	-0.86	(-1.53,	-0.19)	.013
Se-placebo difference	**133**	**-0.30**	**(-1.18,**	**0.58)**	**.5**

Table E2: Odds and odds ratios for additional bronchodilator use and waking at night with asthma symptoms at end of trial, restricted to individuals with complete measured outcome data

Outcome	*N*	*Odds/OR*	*(95%*	*CI)*	*P*
Additional bronchodilator usage					
Placebo	76	0.36	(0.21,	0.60)	.000081
Selenium	83	0.22	(0.13,	0.39)	$1.3x10^{-7}$
Se/placebo ratio	**159**	**0.62**	**(0.29,**	**1.32)**	**.21**
Woken at night with asthma symptoms					
Placebo	78	0.39	(0.24,	0.64)	.00021
Selenium	85	0.33	(0.20,	0.54)	$1.0x10^{-5}$
Se/placebo ratio	**163**	**0.84**	**(0.42,**	**1.68)**	**.61**

Table E3: Arithmetic mean differences in lung function (end of trial minus baseline), restricted to individuals with complete measured outcome data

Outcome	*N*	*Difference*	*(95%*	*CI)*	*P*
FEV_1 (L)					
Placebo	76	-0.05	(-0.10,	0.01)	.086
Selenium	84	-0.04	(-0.12,	0.04)	.33
Se-placebo difference	**160**	**0.01**	**(-0.09,**	**0.10)**	**.89**
FEF_{25-75} (L/s)					
Placebo	76	-0.02	(-0.14,	0.10)	.75
Selenium	84	-0.04	(-0.16,	0.07)	.48
Se-placebo difference	**160**	**-0.02**	**(-0.19,**	**0.15)**	**.8**
FEV_1/FVC ratio					
Placebo	76	0.00	(-0.01,	0.02)	.56
Selenium	84	-0.00	(-0.01,	0.01)	.97
Se-placebo difference	**160**	**-0.00**	**(-0.02,**	**0.01)**	**.6**
FEF_{25-75} /FVC ratio					
Placebo	76	0.01	(-0.03,	0.05)	.66
Selenium	84	-0.00	(-0.03,	0.03)	.8
Se-placebo difference	**160**	**-0.01**	**(-0.06,**	**0.04)**	**.61**

Table E4: Arithmetic mean differences in morning peak flow (end of trial minus baseline) and geometric mean end of trial/baseline ratios for PEFR variability, restricted to individuals with complete measured outcome data

Outcome	*N*	*Difference/GM ratio*	*(95%*	*CI)*	*P*
Mean morning PEF (L/min)					
Placebo	47	-0.93	(-12.91,	11.06)	.88
Selenium	46	3.36	(-12.13,	18.84)	.67
Se-placebo difference	**93**	**4.28**	**(-15.30,**	**23.86)**	**.67**
Mean PEF amplitude (% mean)					
Placebo	47	0.97	(0.88,	1.07)	.58
Selenium	46	0.91	(0.79,	1.04)	.16
Se/placebo ratio	**93**	**0.93**	**(0.79,**	**1.10)**	**.42**