Table 2: Randomised controlled trials and controlled observational studies of selenium

Source: Karen Pilkington, CAM-Cancer Consortium. Selenium [online document]. http://cam-cancer.org/en/selenium. August 18, 2020.

First author, year, ref	Study design	Participants (number, diagnosis)	Interventions (experimental treatments, control)	Main outcome measures	Main results	Comments
Anti-tumour therapy						
Asfour 2007	RCT	50 non-Hodgkin's lymphoma patients	Sodium selenite 200 mcg per day for 30 plus chemotherapy or chemotherapy alone	*Expression of Bcl-2* Survival	Overall survival time in months was significantly longer in complete remission patients in selenium group (21.87±1.41) compared to control (19.70± 1.95) (p=0.01).	Randomisation method not reported Allocation concealment not reported Blinding not reported Power, intention to treat and attrition not reported
Karp 2013	RCT	1,561 resected non–small-cell lung cancer (NSCLC) patients	Selenized yeast 200 micg versus placebo daily for 48 months	*Incidence of lung second primary tumours* *Qualitative and quantitative toxicity* *Incidence of specific cancers* Mortality from cancer and overall survival	The 5-year overall survival rate was 76.8% (SE, 1.6%) in the selenium arm and 79.9% (SE, 2.1%) in the placebo arm (p=0.154)..	Randomisation and allocation concealment appropriate Blinding appropriate Power reported but interim analysis conducted. Intention-to –treat analysis applied and attrition reported.

Mix 2015	RCT	18 patients with Stage III or IV head and neck squamous cell cancer (HNSCC)	Selenium 3600 mcg/m2 or placebo twice daily for 7 days prior to chemoradiation (CRT), once daily during CRT, and daily for 3 wk following CRT.	*Adverse effects including mucositis* *Quality of life (see above)* Survival	Addition of selenium to CRT for HNSCC was well-tolerated but did not *lower the incidence of severe mucositis or* improve *quality of life or* survival outcomes (no p values reported)	Randomisation, allocation concealment and blinding appear appropriate. Power calculated but interim analysis carried out and sample size too small for significant findings
Muecke (also cited as Mücke) 2014*	6 year follow-up of RCT	81 Selenium-deficient cervical and uterine cancer patients	Selenium or no supplement (500 mcg Se (as inorganic sodium selenite; Selenase) orally on days of RT; 300 mcg Se on non-treatment days until the last day of radiotherapy)	Effectiveness of radiation therapy Survival	10-year disease-free survival rate in the Selenium group was 80.1% compared to 83.2% in the control (P = 0.65); 10-year overall survival rate was 55.3% versus 42.7% (P = 0.09).	Randomisation method not reported. Blinding not possible. Power not reported (subgroup analysis of main trial). *Follow-up of Buentzel (also cited as Büntzel) 2010
Supportive cancer care						
Buentzel (also cited as Büntzel) 2010a*	Randomised observational study	121 radiotherapy (RT) patients (81 gynaecological tumours, 40 head and neck tumours).	Selenium or no supplement (500 mcg sodium selenite on RT days, 300 mcg at the weekend)	Selenium blood concentration	Supplemental selenium corrected deficiency during radiotherapy. Difference in levels at end of RT ($p<0.001$); 6 weeks after RT ($p=0.183$)	No details on randomisation. Groups well balanced on age, tumour localization and stage Blinding not possible Power and intention-to-treat not reported **Note: Buentzel 2010b reports HNT patients only; Muecke 2010 reports gynae patients only (update Muecke 2013)*

Daeian et al. 2014	RCT	77 AML and ALL patients undergoing hematopoietic stem cell transplantation (HSCT)	Selenium or placebo (400 mcg daily from first day of chemotherapy to 14 days after HSCT)	Plasma concentrations of TNF-α, IL-1β and IL-6	Plasma levels of TNF-α were not significantly different between Se and control group (P = 0.13); no significant differences in IL-1 levels (P = 0.88) or IL-6 levels (P = 0.96)	Used balanced blocked randomization Researchers, patients and clinical staff were blinded Trial may have been underpowered 3 patients discontinued; no reasons given
Evans 2019	RCT	24 proven chronic lymphocytic leukemia (CLL) patients (and peripheral blood lymphocyte count > 10 × 109/l) or metastatic solid cancers	Selenium (three forms) (400 mcg/day of elemental Se daily for 8 weeks as sodium selenite (SS), Se-methylselenocysteine (MSC) or seleno-l-methionine (SLM))	Safety, tolerability and pharmacokinetic profiles	23 of 24 completed treatment; 1 patient discontinued due to grade 2 constipation, possibly linked to selenium. 2 episodes of ≥ grade 2 toxicity were attributable to other causes	Randomisation and allocation appropriate Blinding appears appropriate as doses given in capsules prepared by manufacturer. Power and intention-to-treat not reported but may be underpowered
Evans 2020	RCT	As above (24 proven CLL patients (and peripheral blood lymphocyte count > 10 × 109/l) or metastatic solid cancers)	As above (400 mcg/day of elemental Se)	Pharmacodynamic (PD) profile(dose and form of selenium most safe and effective with cancer therapies)	No substantial changes in PD parameters. Dose was too low to achieve the Se plasma concentration (≥ 5 μM) expected to elicit significant PD effects	As above Randomisation and allocation appropriate Blinding appears appropriate as doses given in capsules prepared by manufacturer. Power and intention-to-treat not reported but may be underpowered
Ghorbani 2013	RCT	122 cancer patients	Selenium or placebo (400 mcg selenium tablet the day before chemotherapy)	Cisplatin induced renal injury	Acute kidney failure occurred in seven patients in control group none in selenium group (p =0.013).	Randomisation, allocation and blinding appear appropriate. Power not reported 11 (8%) discontinued; intention-to treat not applied Outcome only measured to day 5

Han 2019	RCT	26 participants with clinical stage II to III breast cancer related lymphoedema	Selenium or saline (500 mcg sodium selenite (Selenase) IV injections 5 doses within 2 weeks)	Lymphoedema and oxidative markers	Improvement in lymphodema with selenium: at 2 wks 75.0% vs no change; at follow-up, 83.3% vs 10.0% (p = 0.002) No changes in biomarkers	No details of randomisation or allocation. Blinding appears possible. Power not reported. 3 discontinued and not included in analysis
Jahangard-Rafsanjani 2013	RCT	77 patients with AML or ALL undergoing allogeneic hematopoietic stem cell transplantation (HSCT)	Selenium or placebo (400 mcg per day from first day of chemotherapy to 14 days after transplantation)	Oral mucositis	Incidence of severe OM (grades 3–4) was significantly lower in the selenium group (10.8% vs 35.1%, P<0.05). Duration of OM (grades 2–4), significantly shorter in the selenium group (P=0.014).	Randomisation unclear Allocation concealment not reported. Blinding appears appropriate. Power calculated but intention to treat analysis not used; 3 patients discontinued with reasons reported.
Mix 2015	RCT	18 patients with Stage III or IV head and neck squamous cell cancer (HNSCC)	Selenium or placebo (3600 mcg/m2 twice daily for 7 days prior to CRT, once daily during CRT, and daily for 3 wk following CRT)	Adverse effects including mucositis Quality of life *Survival (see below)*	*Incidence of grades 3-4 mucositis reduced from 37.5% to 20% in the experimental group but numbers to too small for significance.* *Effect on quality of life non-significant (p values not reported)*	Randomisation, allocation concealment and blinding appear appropriate. Power calculated but interim analysis carried out and sample size too small for significant findings
Muecke 2013 (update of results of Buentzel et al. 2010 trial in Cochrane review)	RCT (subgroup analysis)	81 Se-deficient cervical and uterine cancer patients	Selenium or no supplement (500 mcg Se (as inorganic sodium selenite; Selenase) orally on days of RT; 300 mcg Se on non-treatment days until the last day of radiotherapy)	Diarrhoea	Se supplementation during RT improved Se-deficiency Radiation-induced diarrhoea in the SeG 20.5% compared to 44.5% (p=0.04).	Randomisation method not reported. Blinding not possible. Power not reported (subgroup analysis of main trial).

Son 2017	RCT	16 patients with differentiated thyroid cancer	Selenium or placebo (300 mcg of selenium orally for 10 days, from 3 days before to 6 days after treatment)	Radio-protective effect on salivary glands	Based on various measures of salivary gland function using scintography, selenium supplementation during treatment reduced salivary gland damage ($p<0.05$ for most measures taken)	Randomisation and allocation not reported Power and intention to treat not reported
Prevention of cancer						
Chatterjee 2019 (long term follow up of study included in Cochrane review)	Case-control (17 year follow up)	155,000 participants	-	Incidence of prostate cancer	Serum selenium was not associated with prostate cancer risk (OR: 0.66; 0.32-1.37).	Original study design evaluated in Cochrane systematic review. Control matched with cases by age (±5 year), sex, race, and date of blood sample
Rayman 2018	RCT	491 male and female volunteers	Selenium or placebo (100, 200, or 300 mcg selenium/d as selenium-enriched-yeast) for 5 years	All-cause mortality	Selenium 300 mcg/d d taken for 5 years in a country with moderately-low selenium status increased all-cause mortality 10 years later (Hazard ratio 1.62 95% CI 0.66, 3.96 after 5 years of treatment and 1.59 95% CI 1.02, 2.46 at end of follow-up)	Randomisation was appropriate, allocation unclear Blinding appears appropriate Power calculated and intention to treat analysis carried out
Terry 2017	Case-control	406 ovarian cancer cases and 632 age- and site-matched controls of African-American descent	Selenium or no supplement (Highest intakes of supplemental selenium (>20 mg/d))	Risk of ovarian cancer in African-American women	Risk of ovarian cancer significantly lower with the highest intakes of supplemental selenium compared with no supplemental intake (OR: 0.67; 95% CI: 0.46, 0.97; P = 0.035). There was no association with dietary selenium.	Observational study in a random sample.

ALL = acute myeloid leukemia
AML = acute lymphocytic leukemia
CI = confidence interval

OR = odds ratio
QOL= quality of life
RCT = randomised controlled trial
SE = standard error