

APPENDIX 1. Primary Health Prevention — Evidence for Vitamin and Mineral Supplementation*

| Disease/Condition | Supplement | Evidence of Benefit and Risk |
|---|------------------------------------|---|
| Women of Child Bearing Age – Birth Defects | Folic Acid | Benefit: strong evidence to reduce risk of fetal neural tube defects, multivitamin with folic acid 0.4–1** mg/day if low or moderate risk; start three months prior to conception until 4–6 weeks postpartum or until end of breastfeeding, (4–5 mg)** for high risk patients started three months prior to conception and until 12 weeks gestation ⁵⁹ [High Evidence]. Risk: no evidence of augmented cancer risk for fertile women. ^{86,87} |
| Cardiovascular Disease | Vitamin D and Omega-3 fatty acids | Benefit: vitamin D unlikely, omega-3 fatty acid supplements questionable ⁸⁸ , to be determined in upcoming trials. ³⁷ |
| | Vitamin B (Folic acid, B6 and B12) | Benefit: uncertain. Observational studies raise the possibility that supplementation might prevent cardiovascular disease by lowering homocysteine, but not consistently supported by randomized trials or meta-analysis. ^{31,89,90} |
| Antioxidants Benefit: the hypothesis that extra vitamin E, C and beta-carotene and selenium prevent cardiovascular disease and cancer has not been supported by the results of randomized trials. ^{23,25,91,92} Risk: beta-carotene, vitamin E and high doses of vitamin A appear to increase mortality [Moderate Evidence]. ^{25,91,92} | | |
| Cancer | Vitamin D Calcium and Vitamin D | Benefit: uncertain, conflicting results. Additional studies needed before routinely recommended, including colon cancer. ^{20,93} Benefit: questionable benefit for colon cancer prevention, more studies required before routinely recommended. ²⁰ |
| | Vitamin B (Folic Acid, B6 and 12) | Benefit: none, including colon or breast cancer. Risk: conflicting evidence (RCTs, observational studies); small increased prostate cancer risk for folic acid, but no overall increased risk of cancer. ⁸⁶ |
| | Beta-Carotene | Benefit: none. Risk: increased risk of gastric and lung cancer, doses of 20–30 mg/day and at any dose in patients at high risk (smokers, asbestos exposure). ^{23,94} |
| | Vitamin E and Selenium | Benefit: none for long-term vitamin E or selenium supplementation. ^{23,95-97} Risk: Vitamin E supplementation increases risk of prostate cancer (17% by third year of supplementation). ⁹⁷ Limit/avoid supplementation, especially those at high risk (e.g., smokers) and males > 60 years. |
| Bone Health and Fracture Prevention | Vitamin D | Benefit: uncertain for lower risk groups/general prevention (community dwelling). Evidence in higher risk groups only (elderly, frail, institutionalized, deficiency) doses 700–800 IU/day, majority of trials use concomitant calcium supplement. ³² |
| | Calcium | Benefit: alone, none [Low Evidence]. Risk: mixed results concerning increased risk of cardiac events (MI) if excess calcium supplementation used with or without vitamin D. ⁹⁸⁻¹⁰⁰ Intake > 2 g per day (dietary or supplement) may increase risk of prostate cancer. ⁷⁸ |



APPENDIX 1. Primary Health Prevention — Evidence for Vitamin and Mineral Supplementation* cont'd

| Disease/Condition | Supplement | Evidence of Benefit and Risk |
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| Cognitive Decline | Vitamin B (Folic Acid, B6, B12) and Antioxidants | Benefit: none [Low Evidence]. ^{101,102} Risk: Avoid high dose vitamin B and antioxidant supplementation (see antioxidants above). |
| | Omega-3 fatty acids/fish oils | Benefit: insufficient data to recommend for supplements [Low Evidence], possible lowered risk with fish consumption. ¹⁰² |
| Age-related Macular Degeneration (AMD) | Antioxidants (Vitamins C,E, beta-carotene and Zinc) | Benefit: no evidence for primary prevention. May be beneficial to reduce risk of progression of dry AMD. ^{57,58} Risk: beta-carotene containing formulations no longer recommended for prevention of AMD progression. ¹⁰³ |
| Multiple Sclerosis (MS) | Vitamin D | Benefit: none. Low vitamin D status associated with risk of MS. ^{38,104} However, no randomized controlled trials have confirmed efficacy or safety of vitamin D supplementation to prevent MS. ³⁹ |
| Common Cold | Vitamin C | Benefit: none to reduce the incidence of colds in the general population [Low Evidence]. ¹⁰⁵ Risk: high dose (> 2 g per day) may cause nausea/vomiting, heartburn/diarrhea; long term use may induce nephrolithiasis. ⁷⁹ |
| Headache (migraine) | Omega-3 fatty acids /Fish oils | Benefit: unknown if supplementation result in similar outcomes as reported dietary intervention of increased n-3EPA and DHA and decreased n-6 LA intake, which have been shown to reduce the number and intensity of chronic headaches and increased quality of life [Low Evidence]. ^{38,106} |
| | Coenzyme Q10, B Vitamins (Riboflavin), Magnesium citrate | Benefit: controversial, uncertain [Low Evidence]. ¹⁰⁷ |

NOTES: *Does not include benefits/risk from vitamins & minerals obtained from daily diet (vegetable and fruits); **Folic acid available as 1 or 5 mg tablets. Sources: **1)** Gutschi LM. Nutritional Supplements. 2015. Compendium of Pharmaceuticals. www.e-therapeutics.ca ; **2)** Jensen B, Regier L et al. Over-the-counter products. Vitamins & Minerals. Drug Comparison Chart. 2014. www.rxfiles.ca; **3)** Fairfield KM. Vitamin Supplementation in Disease Prevention. In: UpToDate. 2015. www.uptodate.com

