

**Supplementary Table 1. Adverse Vitamin-Drug Interactions**

VITAMINS	RDA MG /DAY	TUL /DAY (MG)	TOXICITY/SIDE EFFECTS	INTERACTIONS
<b>Vitamin C</b>	Male: 90 Female: 75	2000	<i>Mega doses (&gt;2000 mg):</i> Nausea, diarrhea, GI disturbances, <sup>1</sup> calcium oxalate calculi, <sup>2</sup> ↑ hemolysis in patients with glucose-6-phosphate dehydrogenase deficiency, <sup>3</sup> interference with certain laboratory results (serum bilirubin, creatinine, urinalysis) guaiac positive assay for occult blood <sup>4</sup>	↑ iron absorption and should be avoided in patients with hemochromatosis <sup>5</sup> or conditions requiring frequent blood transfusions (thalassemia, sickle cell disease) <sup>6</sup> ↑ aluminum absorption and may cause aluminum toxicity (personality changes, seizures, coma) <sup>7</sup> ↑ free radicals by interaction with free metal ions ↓ plasma concentration of protease inhibitor (indinavir) <sup>8,9</sup> ↓ protective effects of simvastatin-niacin combination on coronary stenosis <sup>10</sup> ↓ copper and vitamin B12 levels <sup>11</sup> ↓ blood lead levels by increased vitamin C levels <sup>12</sup>
<b>Riboflavin (B1)</b>	Male: 1.3 Female: 1.1	None	<i>Mega doses:</i> Itching, numbness, yellow/orange urine (flavinuria), ↑ sensitivity to light	<u><i>Medications that decrease riboflavin levels or increase riboflavin loss</i></u> Anticholinergics, antidepressants, antipsychotics, antiepileptics, anticancer (doxorubicin), antigout (probenecid), thiazide diuretics, tetracycline <sup>13,14</sup> chronic alcohol use.
<b>Niacin (B3)</b>	Male: 16 Female: 14	35	Flushing, itching, rash, headache, blurred vision, dry skin, nausea, vomiting, hypotension, hepatitis, <sup>15</sup> impaired glucose tolerance, <sup>16</sup> hyperuricemia, gout, <sup>17</sup> ↑ risk of arrhythmia with (mega doses), may make allergies worse by ↑ in histamine release	↑ bleeding with anticoagulants ↑ hypotension with antihypertensives (alpha-blockers) ↑ rhabdomyolysis with statins <sup>18</sup> ↑ flushing with use of nicotine patches ↓ uricosuric effect of sulfipyrazone <sup>19</sup> ↓ effectiveness of bile-acid binding resins ↓ absorption with tetracycline ↓ niacin-induced flushing with aspirin Carbamazepine and primidone ↑ niacin levels in the body  <u><i>Medications lowering the levels of niacin in the body</i></u> Azathioprine, chloramphenicol, cycloserine, isoniazid, 5-fluorouracil, levodopa, carbidopa, mercaptopurine, phenytoin, valproic acid
<b>Pyridoxine (B6)</b>	Male: 1.7 Female: 1.5	10	Sensory neuropathy, photosensitivity, headache, nausea, anorexia, heart burn, abdominal pain <sup>20, 21</sup>	↑ amiodarone-induced photosensitivity ↓ blood levels of pyridoxine with ↓ efficacy of phenytoin, phenobarbital and levodopa → suboptimal control of seizures or Parkinson's disease <sup>22-24</sup> Antiepileptic drugs (valproic acid, phenytoin, carbamazepine) ↓ pyridoxine levels and cause hyperhomocystenemia → ↑ risk of epileptic seizures and systemic vascular events (stroke) <sup>25, 26</sup> ↓ methotrexates anticancer effects <sup>27</sup>  <u><i>Medications lowering the levels of B6 in the body</i></u> Cycloserine, hydralazine, isoniazid, monoamine oxidase inhibitors, oral contraceptives,

				penicillamine, NSAIDS, tetracycline, theophylline <sup>28, 29</sup>
<b>Folic Acid (B9)</b>	0.4	None	Nausea, GI upset, seizures, insomnia, can saturate dihydrofolate reductase metabolic capacity with appearance of unmetabolized folic acid in blood <sup>30</sup> causing poor cognition, <sup>31</sup> hematologic abnormalities, <sup>31</sup> and poor immune function <sup>32</sup> May mask symptoms of vitamin B12 deficiency, ↑ risk of colorectal cancers <sup>33</sup>	↑ serum levels of 5-fluorouracil and capecitabine to toxic levels ↓ serum folate levels with phenytoin, carbamazepine and valproic acid, which increases risk of seizures <sup>26, 34</sup> ↓ methotrexate's anticancer effects <sup>27</sup> ↓ antiparasitic effect of pyrimethamine by pharmacodynamic antagonism  <u>Medications lowering the levels of folic acid in the body</u> Anticonvulsants, antacids, histamine-2 blockers, proton pump inhibitors, bile acid sequestrants, cycloserine, pyrimethamine, trimethoprim, methotrexate, anticancer NSAIDS and sulphasalazine <sup>26, 34-36</sup>
<b>Cyanocobalamin (B12)</b>	0.0024	None	Sensory neuropathy (mega doses; 1-6 g/day), <sup>21</sup> dermatological lesions, photosensitivity, nausea, and heartburn <sup>37</sup>	Metformin can ↓ absorption of vitamin B12 <sup>38</sup>  <u>Medications lowering the levels of vitamin B12 in the body</u> Antacids, antiseizure medications (phenytoin, phenobarbital, primidone), methotrexate, colchicine, cholestyramine, cholestipol, colestivelam, omeprazole, lansoprazole, cimetidine, famotidine, ranitidine, metformin, tetracycline <sup>26, 38-42</sup>
<b>Vitamin E</b>	15	1000 (1500 IU)	↑ risk of hemorrhage stroke and all-cause mortality, <sup>43,44</sup> ↑ risk of lung cancer in smokers, <sup>45</sup> ↑ risk of prostate cancer, <sup>46</sup> ↑ progression of retinitis pigmentosa <sup>47</sup>	↑ bleeding risk with NSAIDS, platelet inhibitors, anticoagulants <sup>44, 48</sup> and herbal products such as garlic or Ginkgo biloba <sup>49</sup> ↓ protective effects of simvastatin-niacin combination <sup>10</sup> ↓ effectiveness of cyclosporine <sup>50</sup> ↓ absorption of propranolol, desipramine, and chlorpromazine  <u>Medications lowering the levels of vitamin E in the body</u> Anticonvulsants (phenobarbital, phenytoin, carbamazepine), cholestyramine, cholestipol, isoniazid, orlistat, sucralfate, olestra <sup>51</sup>
<b>Vitamin A</b>	Male: 0.9 Female: 0.7		<u>Acute toxicity:</u> Nausea, anorexia, fatigue, headache, dizziness, dry skin, desquamation, cerebral edema <u>Severe cases:</u> Liver damage, hemorrhage, and coma <u>Chronic toxicity:</u> Dry, itchy skin, desquamation, anorexia, headache, bone and joint pain ↑ risk of lung cancer in high-risk individuals (smokers, asbestos) <sup>52</sup> ↑ risk of osteoporotic fracture in elderly, <sup>53, 54</sup> hematopoietic abnormalities, <sup>55</sup> liver abnormalities,	↑ bleeding risk with antiplatelets and anticoagulants ↑ serum triglycerides ↑ risk of vitamin A toxicity with oral contraceptives ↑ risk of hepatotoxicity when taken in high doses with medications metabolized by liver (acetaminophen, carbamazepine, isoniazid, methotrexate) ↑ risk of pseudotumor cerebri with tetracycline ↓ vitamin A effectiveness with cholestipol Chronic alcohol consumption results in depletion of liver stores of vitamin A, and may contribute to alcohol-induced liver damage <sup>59</sup>  <u>Medications decreasing vitamin A absorption</u> Oral contraceptives, cholesterol-lowering medications, orlistat, olestra <sup>60</sup>

			coagulability disorders, neurotoxicity and birth defects, <sup>56, 57</sup> ↑ risk of mortality <sup>58</sup>	
<b>Vitamin D</b>	51-70 y 0.015 (600 IU)  ≥71 y 0.02 (800 IU)	1 (4,000 IU)	<u>Hypervitaminosis D</u> ; Hypercalcemia, nausea, vomiting, poor appetite, constipation, weakness, weight loss, <sup>61</sup> hyperphosphatemia, hypercalciuria, kidney stones, <sup>62-64</sup> ↑ risk of pancreatic cancer, <sup>65</sup> ↑ risk of falls, <sup>66</sup> fractures, <sup>67, 68</sup> and frailty <sup>69</sup>	Ketoconazole ↓ serum levels of 1,25-hydroxyvitamin D levels <sup>70</sup> Glucocorticoids and HIV drugs (highly active antiretroviral therapy) impair vitamin D metabolism <sup>71</sup> Vitamin D induced hypercalcemia may precipitate cardiac arrhythmia in patients on digitalis <sup>72</sup>  <u>Medications decreasing vitamin D levels</u> Cholestyramine, cholestipol, phenytoin, <sup>73</sup> fosphenytoin, phenobarbital, corticosteroids, carbamazepine, ketoconazole, glucocorticoids, HIV treatment drugs <sup>70, 71, 73-75</sup>  <u>Medications increasing vitamin D absorption and serum levels</u> Isoniazid, thiazide diuretics, estrogen
<b>Vitamin K</b>	Male: 0.12 Female: 0.09	None	Allergic reaction; menadione (vitamin K 2) given by injection can induce hepatotoxicity and hemolytic anemia in infants <sup>76</sup>	↓ anticoagulant effectiveness of warfarin <sup>77</sup> Large doses of vitamin A and vitamin E can antagonize vitamin K  <u>Medications decreasing vitamin K absorption and levels</u> Cholesterol lowering medications, orlistat, olestra, prolonged broad-spectrum antibiotic use (e.g., cephalosporin)

GI indicates gastrointestinal; HIV, human immunodeficiency virus; NSAID, nonsteroidal anti-inflammatory drug; RDA; recommended dietary allowance, TUL; toxic upper limit.

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