

Nutrient depletions from common medications

And how we can help

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Today's Speaker

Lorraine Nicole

**MSc (Nutr.), PGCHE, BA (hons),
Dip. CIM, Dip. BCNH**

- Education Lead, Pharma Nord UK
- Registered Nutritionist (MBANT) and Nutritional Therapist (CNHC)
- Functional Medicine and Healthy Ageing Specialist
- In clinical practice for 23 years
- Higher education teacher (nutrition science & practice)
- Author/editor of several nutrition books
- Accredited clinical supervisor and mentor for nutrition practitioners

- 1 Top 10 most commonly prescribed meds in England, and some common OTC meds
- 2 Possible nutrient depletions for these
- 3 A brief look at hormone replacement and OCP; and GLP-1 agonists
- 4 Points to consider when assessing the evidence for depletions
- 5 Action points in each section

**Learning
outcomes
for today**

Top 10 most commonly prescribed meds in England, and some common OTC meds

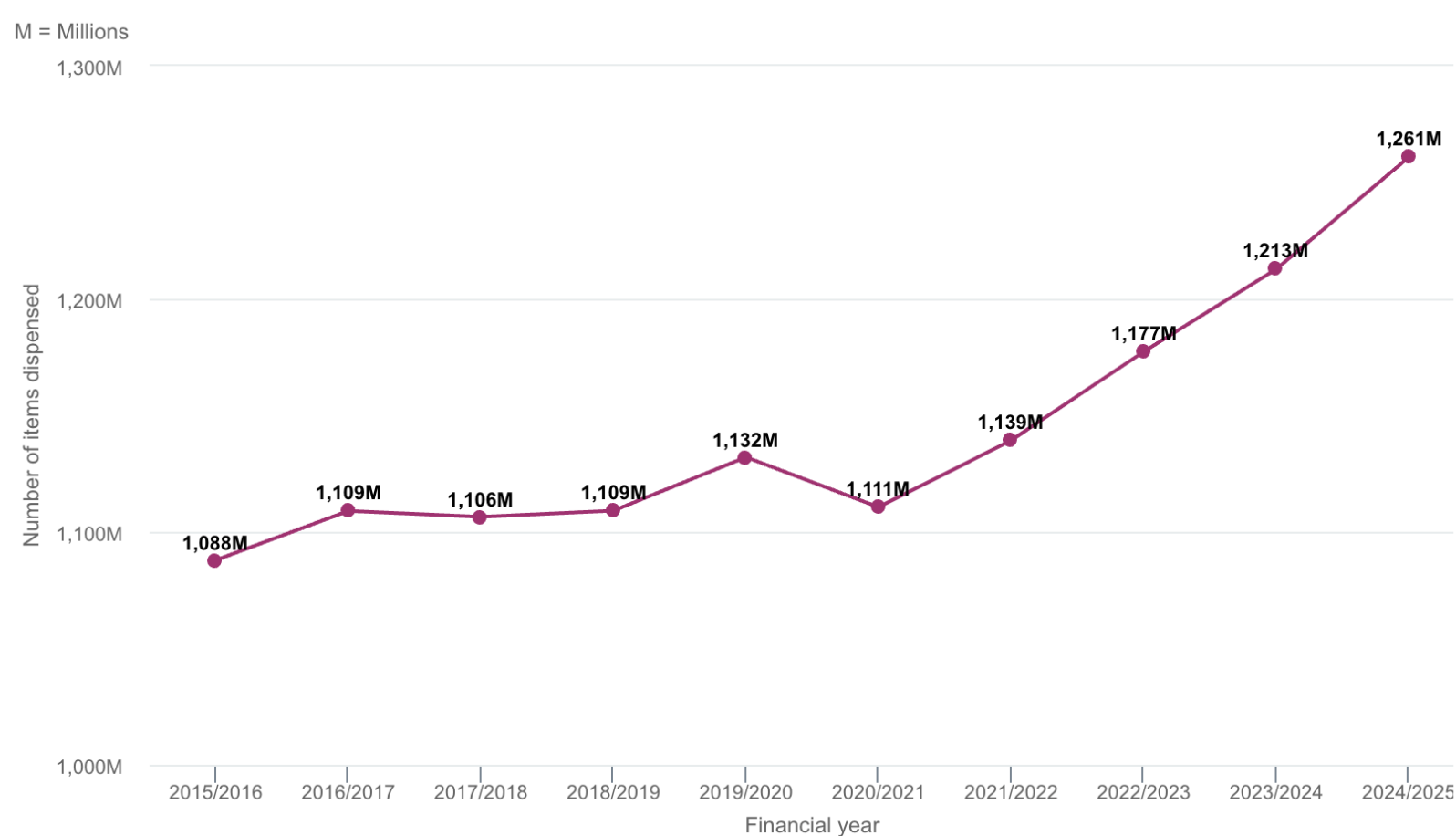


NHS prescriptions in England 2024/5



- 1.26 billion prescription items were dispensed in the community at a cost of £11.2 billion – see graph on next slide
- The number of items dispensed in the community increased by 4% from 2023/24
 - And by 16% from 2015/16, an increase of 170 million items
- The most dispensed medication was Atorvastatin, with 73 million items
- Cardiovascular drugs accounted for 30% of all items dispensed
- Community figures do not include in-patient hospital prescriptions, nor private prescriptions

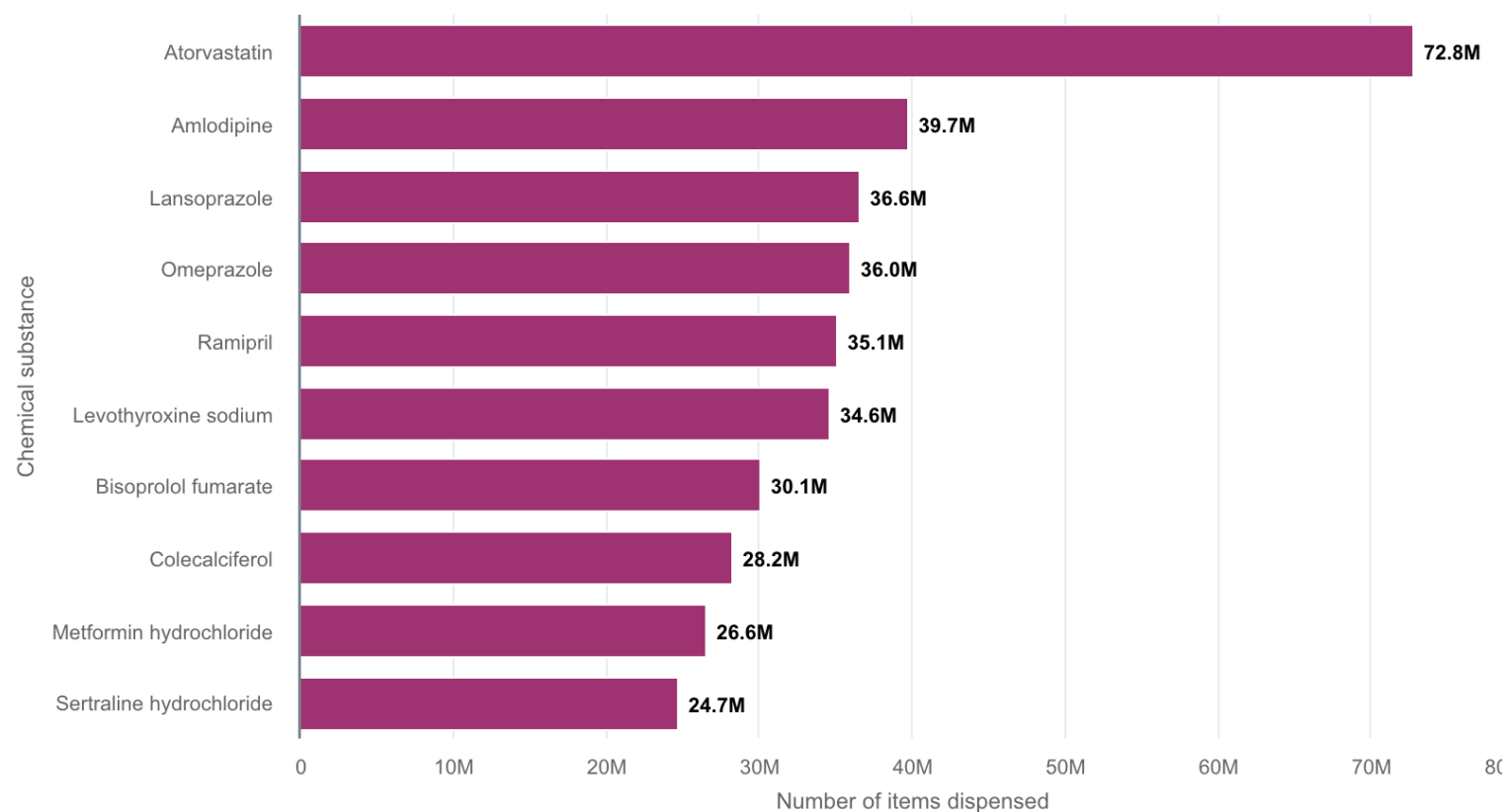
The number of prescription items has been sharply increasing



NHS Business Services Authority.
Prescription cost analysis 2024-4.
Available from: https://nhsbsa-opendata.s3.eu-west-2.amazonaws.com/pca/pca_summary_narrative_2024_25_v001.html.
Accessed 9 Jan 25

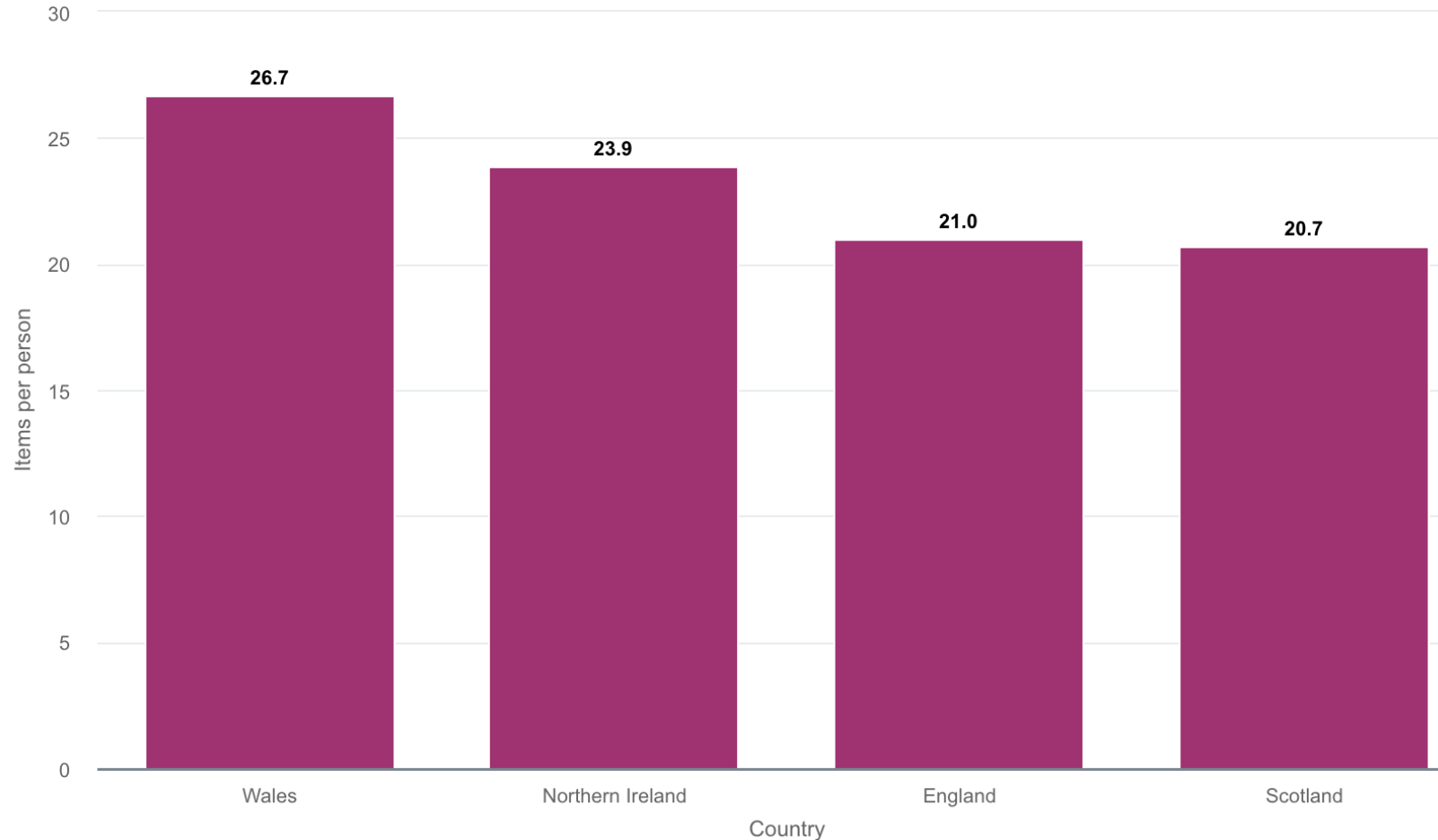
The top 10 most dispensed prescription medications in 2024-5

M = Millions



NHS Business Services Authority. Prescription cost analysis 2024-4. Available from: https://nhsbsa-opendata.s3.eu-west-2.amazonaws.com/pca/pca_summary_narrative_2024_25_v001.html. Accessed 9 Jan 25

Comparison with other UK nations: prescription items per person 2024-5



NHS Business Services Authority.
Prescription cost analysis 2024-4.
Available from: https://nhsbsa-opendata.s3.eu-west-2.amazonaws.com/pca/pca_summary_narrative_2024_25_v001.html.
Accessed 9 Jan 25

The most prescribed drugs reflect the dxs that dominate today

- **CVD:** atorvastatin, amlodipine, ramipril, bisoprolol, losartan, clopidogrel for: hypertension, high cholesterol and post-heart-attack care
- **GI disorders:** Omeprazole and lansoprazole for acid reflux, peptic ulcers, and GERD.
- **Endocrine:** Levothyroxine for hypothyroidism. Metformin for metabolic syndrome
- **Mental health:** sertraline, citalopram, mirtazapine, and amitriptyline for depression, anxiety, and neuropathic pain
- **Pain and inflammation:** Paracetamol, aspirin, and co-codamol
- **Respiratory:** Beclometasone dipropionate (a steroid inhaler used for asthma and COPD) is also in the top 20



Over-the-counter drugs

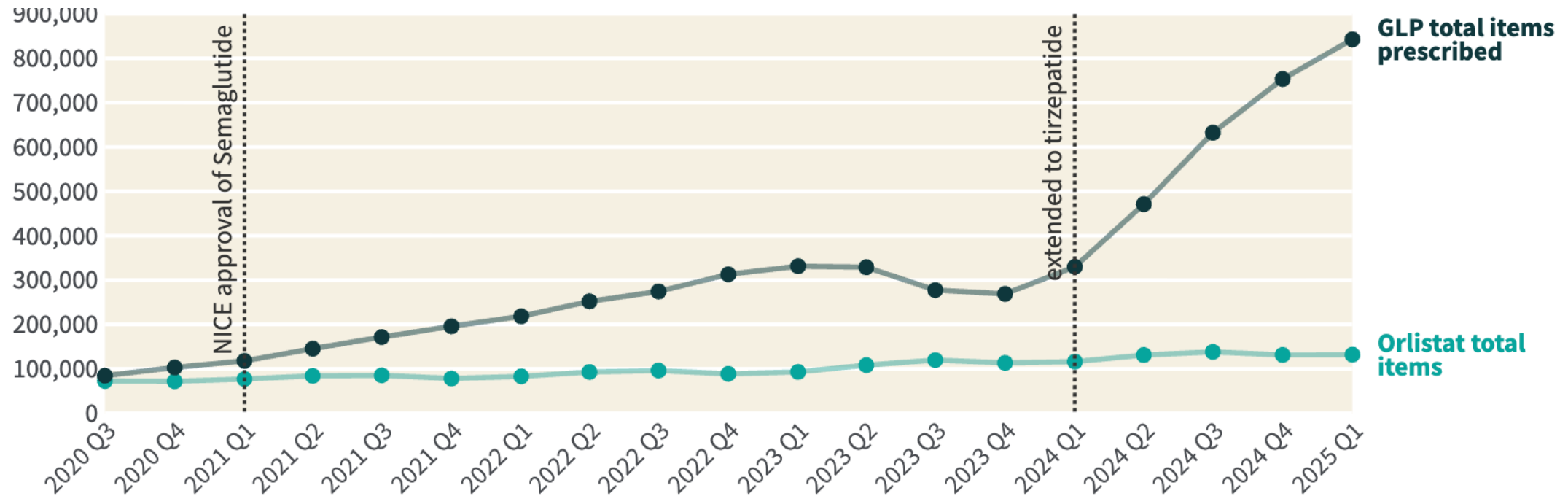
- No such hard data is available, as OTCs are supplied by so many different sources
- Common meds include (GP and pharmacy publicity material):
 - Paracetamol
 - Ibuprofen
 - Aspirin
 - Anti-histamines
 - Antacids
 - Cough and cold remedies
 - Laxatives

2 other increasingly common meds

(NHS data only)

- Oestrogen/progesterone HRT and/or OCP
 - 14.7 million items prescribed in 2024/5 (11% increase in the year)
 - 2.8 million patients
 - Prescription numbers have almost tripled since 2015/16
- GLP-1 receptor agonists:
 - Semaglutide (Ozempic, Wegovy), tirzepatide (Mounjaro)
 - Glucagon-like peptide inhibits gastric emptying, reduces appetite, increases insulin and adiponectin, promotes lipolysis
 - Mostly **privately prescribed** as NHS requires BMI of >40 co-morbidities

GLP-1 agonist prescription increases (NHS only)



Source: [OpenPrescribing.net](https://openprescribing.net), [Bennett Institute for Applied Data Science](https://www.bennettinstitute.com), [University of Oxford](https://www.universityofoxford.ac.uk), 2025 • This time series shows the surge in NHS England prescriptions for semaglutide and tirzepatide (GLP-1 receptor agonists) since 2020, plotted against prescribing levels of Orlistat, a traditional anti-obesity medication. Following the NICE approval of semaglutide in 2021 and tirzepatide guidance in early 2024, GLP-1 prescribing surpassed Orlistat by a wide margin, growing by over 700% from 2020 to 2025.

Data ranges from May 2020 - June 2025

Things to consider when assessing potential nutrient depletions from drugs

- There is some variability across databases and across literature reviews in the specific micronutrients that are proposed to be depleted by specific drugs
- Thus some sources will make claims that are not mentioned here because, having looked at the available evidence, I had not been able to find studies that prove the claim for the nutrient depletion
- Also worth noting that many nutrient deficiencies are pre-existing in populations on certain drugs. The reason is:
 - Certain nutrient deficiencies are associated with disease states (e.g. folate in depression), which then trigger the drug to be prescribed (e.g. SSRI)
 - This is not evidence that the drug (e.g. the SSRI) has caused the nutrient depletion (e.g. folate)
 - But still the patient would likely benefit from improving folate status

Atorvastatin: #1 most dispensed drug

Prescribing purpose: lower cholesterol (esp. LDL-c and apoB) to reduce the risk of cardiovascular events

Listed potential side effects include (NHS and other sources):

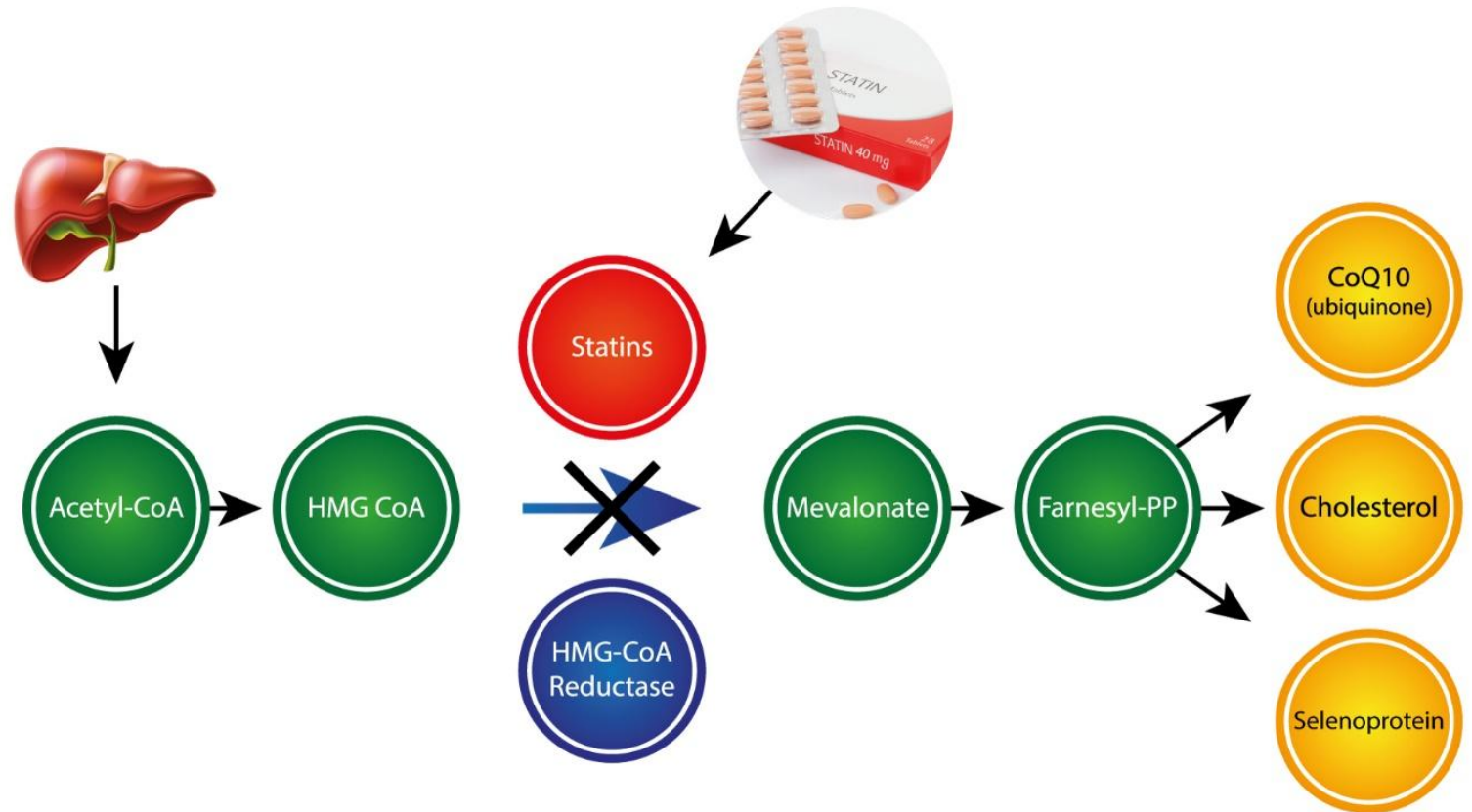
- **Common:** Nausea, headaches, nosebleeds, sore throat, cold-like symptoms, GI gas and constipation and/or diarrhoea
- **Less common but more serious:**
 - Muscle pain, tenderness, weakness or cramps
 - Jaundice or elevated liver enzymes
 - Worsening of pre-existing Metabolic Syndrome
 - Skin rash (erythema multiforme)

Some cross-over
with Q10 deficiency
sxs: fatigue,
weakness, exercise
intolerance, muscle
pain, cramping, poor
memory and
concentration

Statin-associated Q10 depletion

Statin medication **downregulates products of the mevalonate pathway** including:

- Cholesterol
- Ubiquinone (Q10)
- Selenoproteins



Moosmann B, Behl C. Selenoproteins, cholesterol-lowering drugs, and the consequences: revisiting of the mevalonate pathway. Trends Cardiovasc Med. 2004 Oct;14(7):273-81. doi: 10.1016/j.tcm.2004.08.003. PMID: 15542379.

Arch. Neurol. 2004 Jun;61(6): 889-92.

Statin-associated Q10 depletion

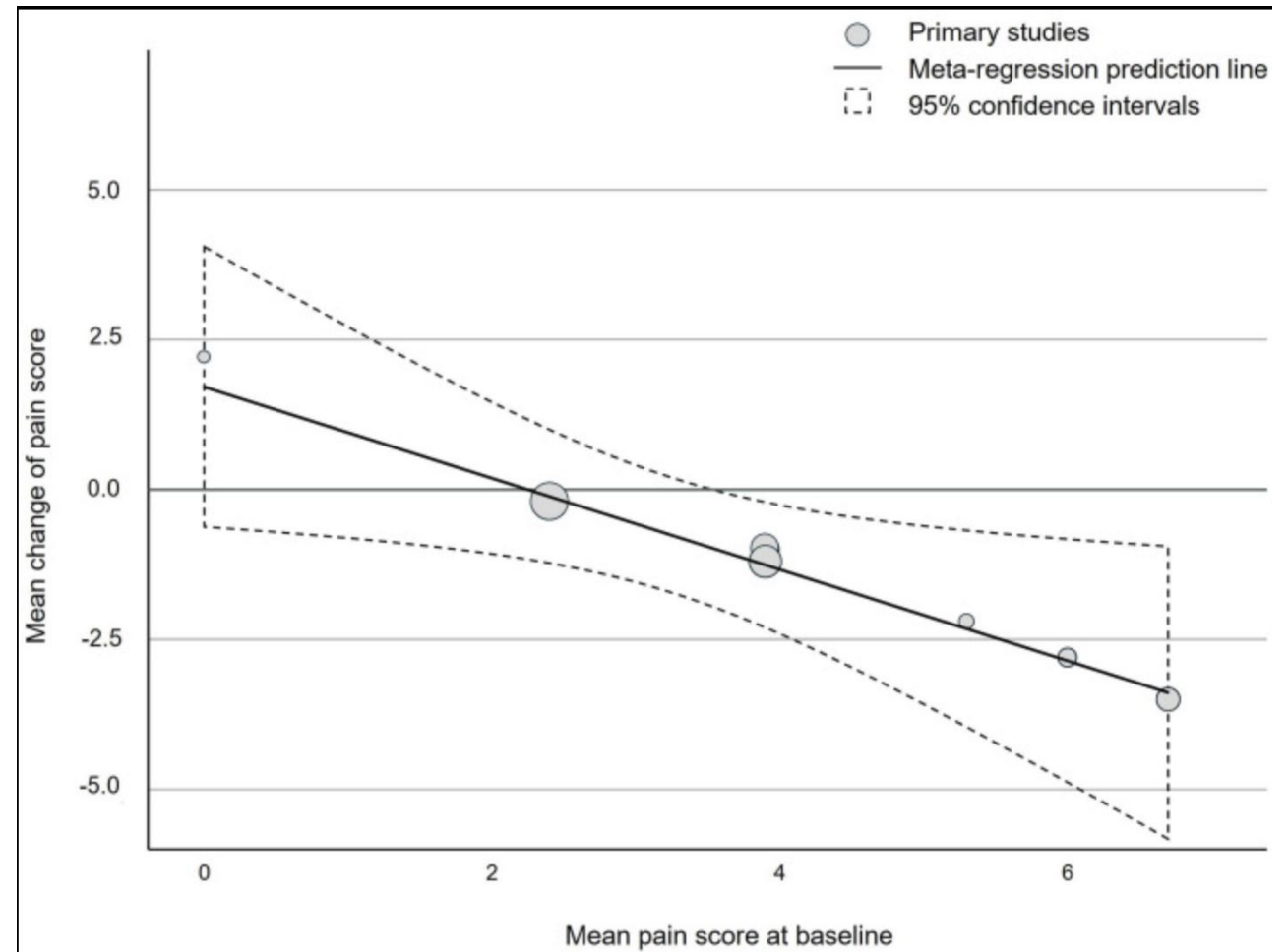
- A systematic review and meta-analysis (2018) of 12 RCTs (N = 1776)
- Compared with placebo, statins → a reduction of circulating CoQ10
- This was not associated with the duration of statin treatment
- Both lipophilic and hydrophilic statins had the same effect on Q10
- Both low-middle and high intensity statins reduced circulating CoQ10
- Concluded this could be a potential mechanism for **statin-associated muscle symptoms** (SAMS): fatigue, muscle weakness, muscle aches and/or cramps
- And suggest that *‘CoQ10 supplementation may be a promising complementary approach for SAMS’*
- More examples of studies on the next slide



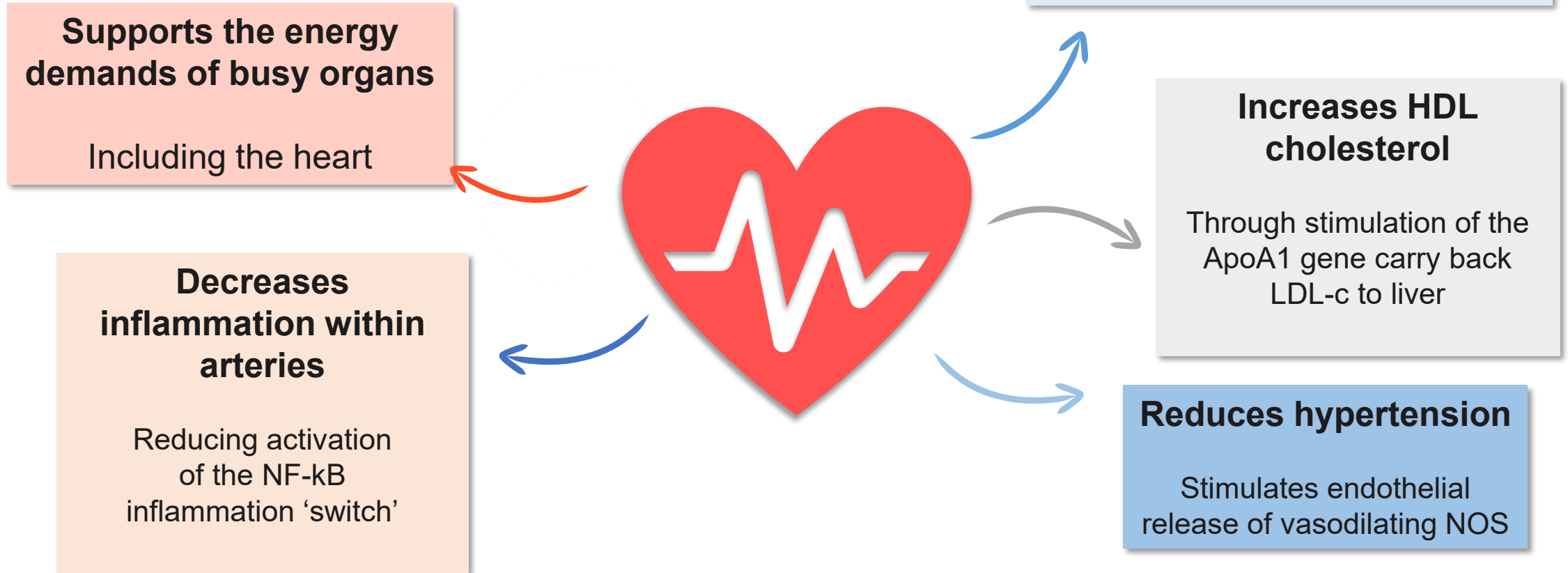
Statins	Coenzyme Q10						
	Chitose et al. (2014) 29	Prospective, randomized, open-label, clinical trial	Total (<i>n</i> = 75) Rosuvastatin (<i>n</i> = 38) Atorvastatin (<i>n</i> = 37)	Compare the effects of hydrophilic (rosuvastatin) and hydrophobic (atorvastatin) statins on patients with ST-elevated myocardial infarction (STEMI) who had received emergency reperfusion therapy.	Mean age: Rosuvastatin group = 64 Atorvastatin group = 65 <i>P</i> = 0.54	6 months treatment of: Rosuvastatin (5 mg/day) Atorvastatin (10 mg/day)	Serum CoQ10 levels significantly lower after 6 months treatment with rosuvastatin and atorvastatin <i>P</i> < 0.001
	McMurray et al. (2010) 30	Clinical trial	1191	To determine whether CoQ10 is an independent predictor of prognosis in heart failure in patients with ischemic systolic heart failure enrolled in CORONA (Controlled Rosuvastatin Multinational Study in Heart Failure)	Mean age = 73 (≥ 60 years were included in this study)	3 months of: Rosuvastatin (10 mg/d) or placebo	Rosuvastatin significantly reduced serum CoQ10 concentration (but no interaction was found between CoQ10 and the effects of rosuvastatin) <i>P</i> < 0.0001
	Mabuchi et al. (2005) 31	Clinical trial	14	Japanese hypercholesterolemic (≥ 220 mg/dL) patients	Mean age = 66	8 weeks of: Atorvastatin (10 mg/d)	Atorvastatin significantly reduced the total CoQ10 levels in all patients. <i>P</i> < 0.0001
	Rundek et al. (2004) 32	Prospective double-blinded, placebo control study	34	To test the hypothesis that i) short-term exposure of atorvastatin for 30 days might significantly decrease plasma CoQ10 levels compared with pre-treatment levels. ii) decrease plasma CoQ10 levels might be rapid and already detectable 2 weeks after initiation of treatment in patients with hypercholesterolemic	Mean age = 70 (≥ 45 years were included in this study)	14 days and 30 days of: Atorvastatin calcium (80 mg/d)	Atorvastatin significantly reduced plasma CoQ10 concentration at 14 days and 30 days 14 days: <i>P</i> < 0.001 30 days: <i>p</i> < 0.001
	Oranje et al. (2001) 109	Double-blind randomized placebo-controlled study	19	To investigate whether atorvastatin has a favourable effect on LDL oxidation in normocholesterolemic in patients with type 2 diabetes	Atorvastatin group = 64 Placebo group = 63	3 months of: Atorvastatin (10 mg/d)	Atorvastatin significantly reduced plasma CoQ10 <i>P</i> = 0.009

Q10 in SAMS

- Systematic review and meta-analysis of 7 RCTs (N = 389) in 2025
- Concluded Q10 can reduce muscle pain in patients with statin-associated muscle sx
- 30 to 90 days duration
- 100 to 600 mg/day
- But some previous reviews found null effect



Q10 is also cardio-supportive in its own right

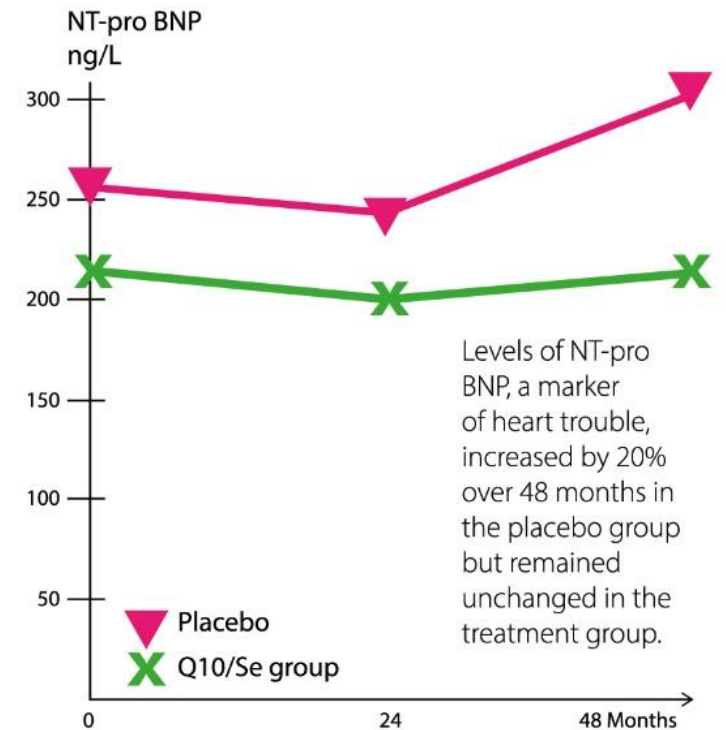


Q10 with selenium may reduce CVD risk within an ageing population

RCT of 443 participants aged 70-88 followed for 5 years

Q10 (200 mg) + Se (200 mcg) →

- A **54%** risk reduction of mortality
- Stable levels of **NT-ProBNP**
- Improved **cardiac function** in Q10 & Se group (via echocardiography)
- Reduction of **pro-inflammatory** biomarkers
- Decreased **oxidative stress** biomarkers



NT-pro BNP should ordinarily rise with age, though the treatment group found this remained stable throughout

Alehagen U, Lindahl T, Aaseth J, Svensson E, Johansson P. Levels of sP-selectin and hs-CRP Decrease with Dietary Intervention with Selenium and Coenzyme Q10 Combined: A Secondary Analysis of a Randomized Clinical Trial. PLOS ONE. 2015;10(9):e0137680.

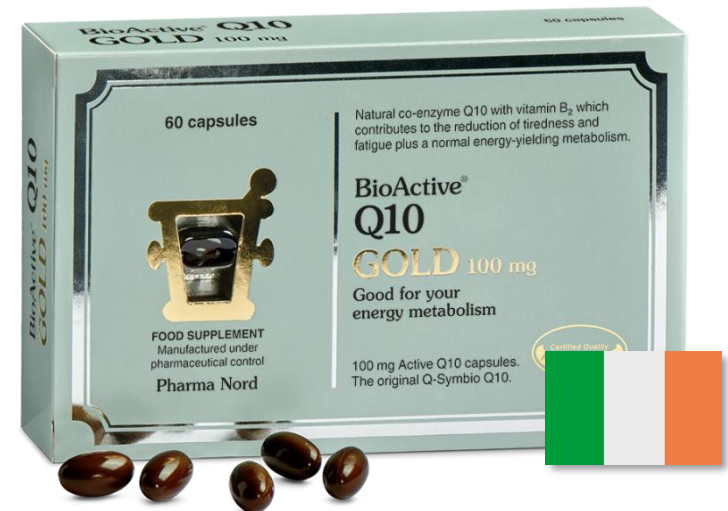
Pharma Nord Formulations

Coenzyme Q10

- Used in 100+ clinical trials, 30+ years
- Reference product of the International Coenzyme Q10 Association
- Documented bioavailability, proven in human clinical trials
- Manufactured under pharmaceutical control



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Statin-associated Mg depletion

- An early trial of 23 non-insulin-dependent diabetics found that administering Simvastatin at 10 mg a day for 4 months (a low dose) reduced serum magnesium levels by 0.02 mmol/litre, after which a 17% increase in serum glucose concentration was observed
- Symptoms of magnesium deficiency cross over with some of the side effects people experience with statins:
 - E.g. fatigue, weakness, muscle weakness, muscle spasms, confusion, tremors, convulsions, arrhythmia, ventricular tachycardia, loss of appetite, nausea, vomiting

Haenni A, Ohrvall M, Lithell H. Serum magnesium status during lipid-lowering drug treatment in non-insulin-dependent diabetic patients. *Metabolism*. 2001 Oct;50(10):1147-51. Nartea R, Mitoiu BI, Gheorghiu I. The Link between Magnesium Supplements and Statin Medication in Dyslipidemic Patients. *Curr Issues Mol Biol*. 2023 Apr 5;45(4):3146-3167. El-Haggar SM, Mostafa TM. Role of Magnesium Supplement on Hyperlipidemia and L-CAT Level in Patient on Atorvastatin Therapy. *British Journal of Pharmaceutical Research*. 2014 Jun 15;4(12):1521-34

Statin-associated Mg depletion

- 10 years later another study found that patients treated for 12 months with atorvastatin plus magnesium showed lower (but non-significant) creatine kinase levels than those on atorvastatin only
- This, combined with previous findings that statins can raise liver enzymes, led the researchers to propose that Mg supplements could provide some protection against statin induced muscle symptoms
- But still a lack of RCTs to evidence this
- Action point: hard to assess deficiency due to crossover of sxs – therefore, trial increasing intake and monitor sxs changes



Pharma Nord Formulations

Magnesium

- Contains a complex of three forms of Mg, offering high bioavailability
- Each tablet contains 200 mg of elemental Mg
- Dissolves in water
- Used in clinical research
- Manufactured to pharmaceutical standards



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Statin-associated Zinc depletion

Clinical studies have found that the administration of statins (Simvastatin, Atorvastatin, or Fluvastatin) was associated with a significant reduction in mean serum or plasma Zinc

- **Action point:** check for sxs of Zinc deficiency: skin lesions, hair loss, taste disturbance, delayed wound healing
- **Action point:** can also measure in blood test and/or organic acids testing



Antioxidant complex

Selenium + Zinc

- A powerful combination of selected antioxidants optimized from over 30 years of research
- Unique complex of selenium, zinc and vitamins B6, C and E
- With SelenoPrecise – the selenium formulation with the highest recorded absorption and 30+ se-based compounds
- Manufactured under pharmaceutical control



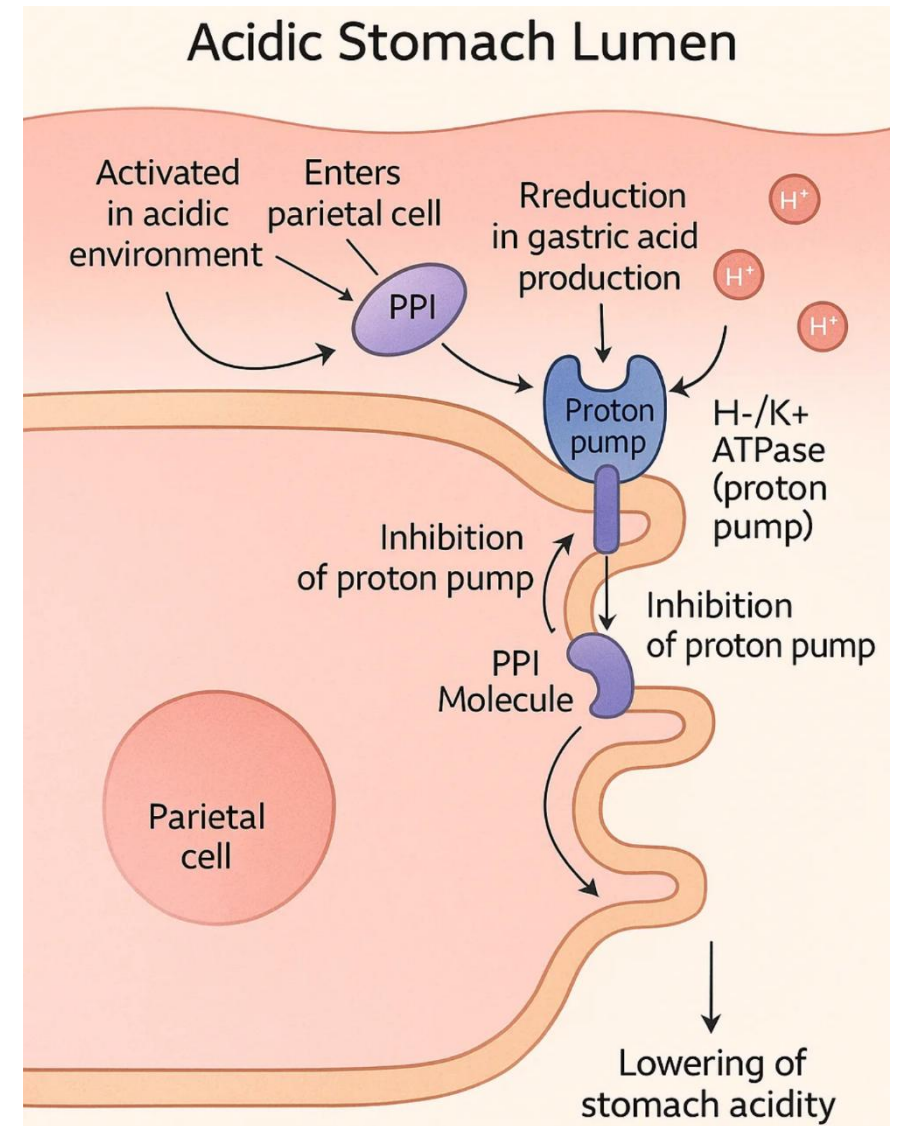
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Proton pump inhibitors: # 3 + 4

- The **number 2** most prescribed category when you add **omeprazole + lansoprazole** (72.6 million prescriptions in England)
- Irreversibly block the proton pump (hydrogen-potassium ATPase enzyme) in the gastric parietal cells, which is the final step in HCl production
- Other types of PPIs are H₂ blockers e.g. ranitidine (not so commonly prescribed)

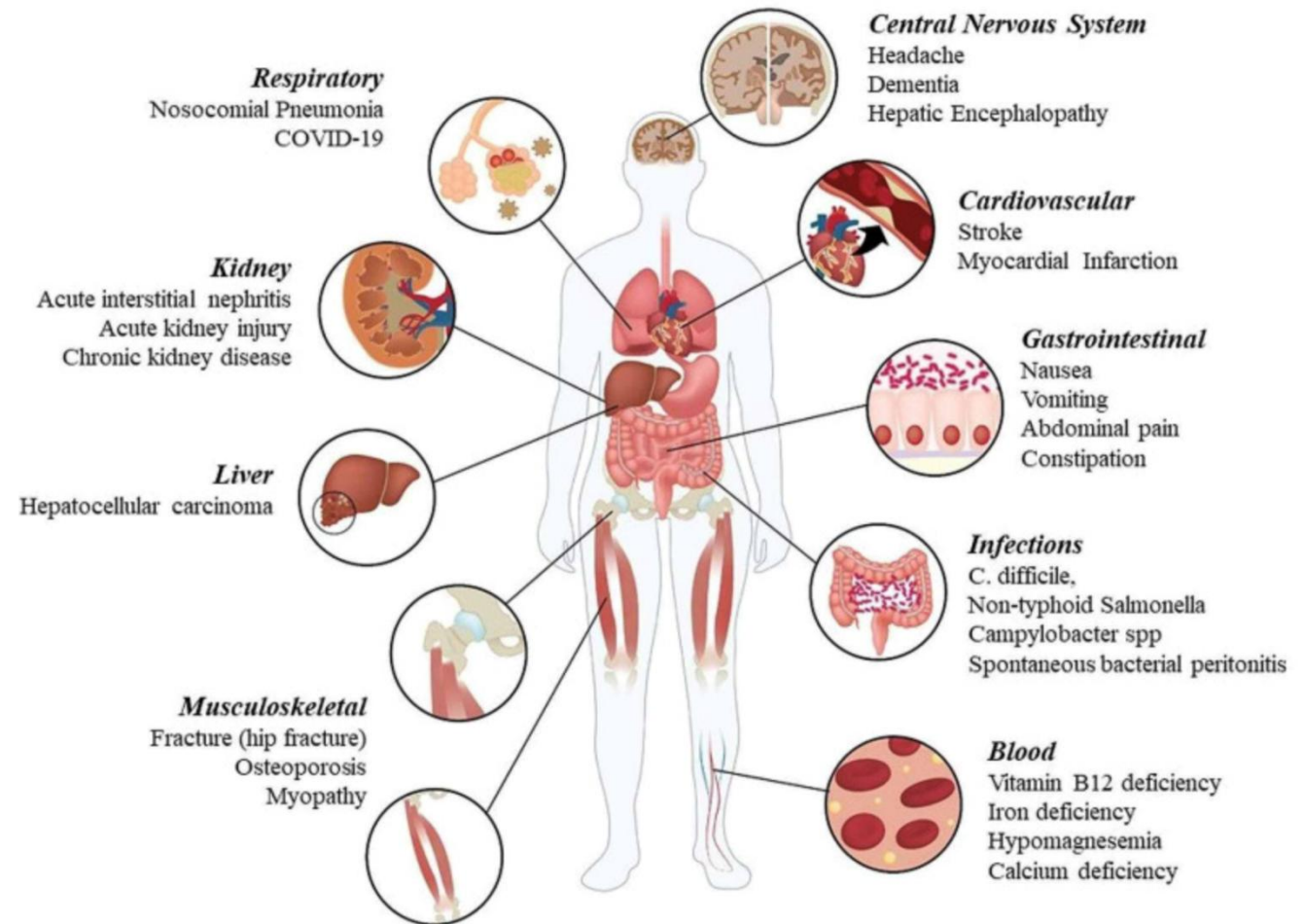


Side effects of PPIs

Prescribed for gastroesophageal reflux disease, peptic ulcer, *Helicobacter pylori* and as a prevention against bleeding from GI tract...

...Including from other prescribed drugs (e.g. NSAIDs, steroids)

Potential side effects also include SIBO, dysbiosis and increased risk of *C. Diff*



Yibirin M, De Oliveira D, Valera R, Plitt AE, Lutgen S. Adverse Effects Associated with Proton Pump Inhibitor Use. Cureus. 2021 Jan 18;13(1):e12759

Well-established to deplete B12

- Several human studies show PPI use to be associated with decreased B12 levels and B12 deficiency (esp. with longer term use)
- Mainly affects B12 absorption from food, rather than from supplements, because HCl is needed to cleave B12 from dietary proteins
- Most B12 supplements do not require HCl for absorption
- B12 supplements have been found to prevent PPI-induced depletion, especially those that by-pass the GI tract (nasal spray / intramuscular)



Miller JW. Proton Pump Inhibitors, H2-Receptor Antagonists, Metformin, and Vitamin B-12 Deficiency: Clinical Implications. Adv Nutr. 2018 Jul 1;9(4):511S-518S, Mohn ES, Kern HJ, Saltzman E, Mitmesser SH, McKay DL. Evidence of Drug-Nutrient Interactions with Chronic Use of Commonly Prescribed Medications: An Update. Pharmaceutics. 2018 Mar 20;10(1):36, Damodharan S, Raj GM, Sakthibalan M, et al. Effect of long-term acid suppression therapy with proton pump inhibitors or H2 receptor blockers on serum vitamin B12 levels in elderly population. Ir J Med Sci. 2021 Aug;190(3):1213-1217, Lam JR, Schneider JL, Zhao W, et al. Proton pump inhibitor and histamine 2 receptor antagonist use and vitamin B12 deficiency. JAMA. 2013 Dec 11;310(22):2435-42, Rozgonyi NR, Fang C, Kuczmarski MF, et al. Vitamin B(12) deficiency is linked with long-term use of proton pump inhibitors in institutionalized older adults: could a cyanocobalamin nasal spray be beneficial? J Nutr Elder. 2010 Jan;29(1):87-99, Bellou A, Aimone-Gastin I, De Korwin JD, et al. Cobalamin deficiency with megaloblastic anaemia in one patient under long-term omeprazole therapy. J Intern Med. 1996 Sep;240(3):161-4, Ruscin JM, Page RL 2nd, Valuck RJ. Vitamin B(12) deficiency associated with histamine(2)-receptor antagonists and a proton-pump inhibitor. Ann Pharmacother. 2002 May;36(5):812-6.

B12 depletion: action points

- **Check for depletion sx's:**
 - Fatigue, headaches, pale skin, shortness of breath, tingling, numbness, confusion, memory loss, depression, irritability
- Monitor serum B12, methylmalonic acid and/or homocysteine
- PPIs may also lead to deficiencies of other B vitamins
- Hence it may be better to supplement the B12 in a B complex
- If B12 is overtly deficient, consider short-term sublingual delivery that by-passes the gut
 - *Long-term* higher doses (e.g. 400-500mcg) are unlikely necessary



B Vitamins

B-Complex

A comprehensive B-Complex

- Supports energy-yielding metabolism
- One-a-day formula
- Suitable for vegetarians & vegans
- Manufactured to pharmaceutical standards



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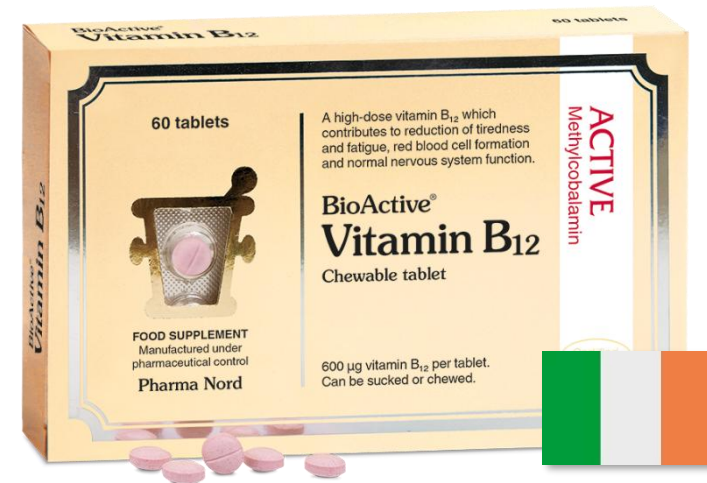
Pharma Nord Formulations

Vitamin B12

- Highly bioavailable lozenges / chewable tablets (peppermint flavour)
- Methylcobalamin - 'Active' form of B12, found in nature
- Suitable for vegetarians and vegans
- Manufactured under Danish pharmaceutical control



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Vitamin C and PPIs

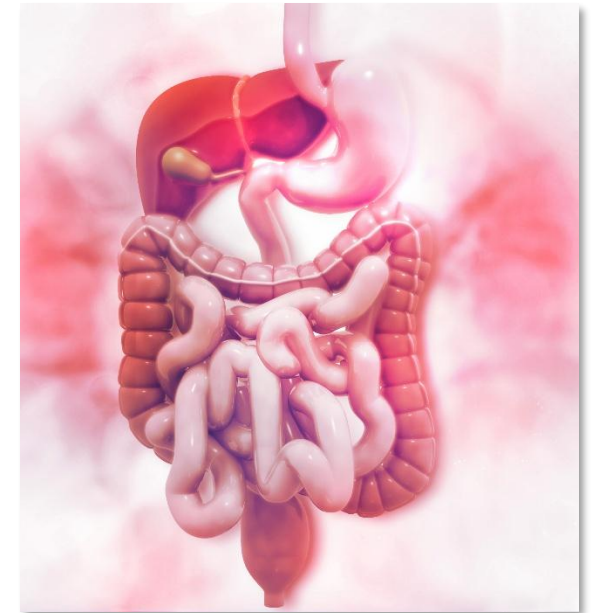
- PPIs are associated with increased risk of vit C deficiency (several studies)
 - An alkaline environment may inhibit vitamin C absorption
 - And also promote the one-way conversion of ascorbic acid to an inactive form (2,3-diketo-L-gulonic acid)
- Another review found deficiency to affect mainly *H. pylori*-positive patients
- **Action:** look for sxs of depletion: immune weakness, poor wound healing, bleeding and inflammation in the gums, subcutaneous bleeding, fatigue, irritability, skin disorders, joint and muscle pain
- Measure serum vitamin C levels and/or urinary organic acids



Aditi A, Graham DY. Vitamin C, gastritis, and gastric disease: a historical review and update. Dig Dis Sci. 2012 Oct;57(10):2504-15. Heidelbaugh JJ. Proton pump inhibitors and risk of vitamin and mineral deficiency: evidence and clinical implications. Ther Adv Drug Saf. 2013 Jun;4(3):125-33. Mohn ES, Kern HJ, Saltzman E, Mitmesser SH, McKay DL. Evidence of Drug-Nutrient Interactions with Chronic Use of Commonly Prescribed Medications: An Update. Pharmaceutics. 2018 Mar 20;10(1):36. McColl KE. Effect of proton pump inhibitors on vitamins and iron. Am J Gastroenterol. 2009 Mar;104 Suppl 2:S5-9.

PPIs inhibit mineral absorption

- Several minerals are at risk of depletion with PPIs because they need HCl to be liberated from food
- Studies have found depletions of calcium, magnesium (up to 25% of long-term users) and iron in particular (cohort study data)
 - And contributing to related conditions like microcytic anaemia and low bone density
- Zinc, potassium and chromium depletions have been found in other studies



Wołowicz Ł, Osiak-Gwiazdowska J, Jaśniak A, et al. Pharmacodynamics, pharmacokinetics, interactions with other drugs, toxicity and clinical effectiveness of proton pump inhibitors. *Front Pharmacol*. 2025 Jul 23;16:1507812, Koyyada A. Long-term use of proton pump inhibitors as a risk factor for various adverse manifestations. *Therapie*. 2021 Jan-Feb;76(1):13-21, Mohn ES, Kern HJ, Saltzman E, Mitmesser SH, McKay DL. Evidence of Drug-Nutrient Interactions with Chronic Use of Commonly Prescribed Medications: An Update. *Pharmaceutics*. 2018 Mar 20;10(1):36, Yibirin M, De Oliveira D, Valera R, Plitt AE, Lutgen S. Adverse Effects Associated with Proton Pump Inhibitor Use. *Cureus*. 2021 Jan 18;13(1):e12759

Minerals with PPI use: action points

- Keep an eye on blood levels or other testing (e.g. urinary organic acids)
- Check the diet for good intake
- Check for depletion symptoms
- If in doubt, supplement a low-dose multinutrient with all trace elements
- And the RDA of calcium and magnesium
- Calcium supplementation may not be necessary with good dairy intake
- Be aware that NICE guidelines are that PPIs are for short term use only in most cases (4-8 weeks) and that there should be regular reviews, *not* on repeat prescription, with a view to reducing and stopping when possible
 - There are exceptions e.g. Barratt's Oesophagus

Blood pressure medications

Calcium channel blockers

ACE inhibitors

Beta blockers



Amlodipine: #2 most dispensed drug

Relaxes and widens blood vessels so that the heart can more easily pump blood around the body and increase blood supply to the heart

CALCIUM CHANNEL BLOCKERS

NON-DIHYDROPYRIDINES

DIHYDROPYRIDINES

USED to TREAT



CARDIAC
ARRHYTHMIAS



HYPERTENSION

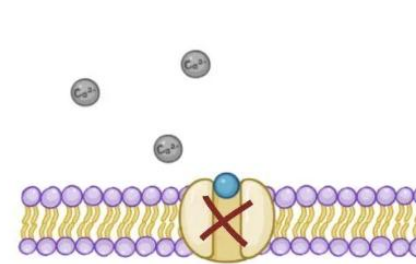


ANGINA
PECTORIS

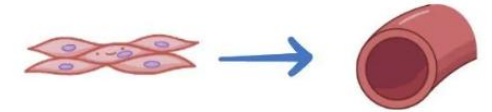


OTHER
CONDITIONS

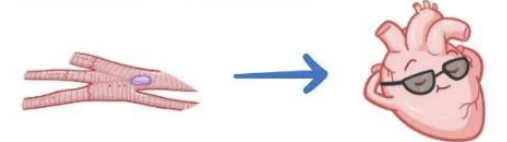
MECHANISM



VASCULAR SMOOTH MUSCLES



CARDIAC MUSCLES



Common side effects

- Headaches
- Dizziness
- Flushing
- Pounding heartbeat
- Palpitations
- Swollen ankles

NHS advises that these most commonly only last for the first week of the medication – seek medical help if they last for longer

Reduce **caffeine and alcohol** and allow for plenty of rest during the first week



Low vitamin D from CCBs

- Calcium-channel blockers have been found to reduce serum vitamin D levels compared with non-use
- Likely due to inhibition of CYP3A4 activity resulting in reduced vitamin D activation in the liver the kidneys (hydroxylation)
- Supplementing vitamin D was able to increase serum levels in patients taking CCBs at 6 months
- And in 2 other trials was found to support better markers of blood pressure and inflammation in CCB-treated hypertension and preeclampsia respectively
- Not all studies have found the same but...
- Action point: it is worth monitoring vit D while on CCBs

Wakeman M. A Literature Review of the Potential Impact of Medication on Vitamin D Status. Risk Manag Healthc Policy. 2021 Aug 14;14:3357-3381., Sohl E, van Schoor NM, de Jongh RT, et al. The impact of medication on vitamin D status in older individuals. Eur J Endocrinol. 2012 Mar;166(3):477-85, Chen WR, Liu ZY, Shi Y, et al. Vitamin D and nifedipine in the treatment of Chinese patients with grades I-II essential hypertension: a randomized placebo-controlled trial. Atherosclerosis. 2014 Jul;235(1):102-9, Shi DD, Wang Y, Guo JJ, et al. Vitamin D Enhances Efficacy of Oral Nifedipine in Treating Preeclampsia with Severe Features: A Double Blinded, Placebo-Controlled and Randomized Clinical Trial. Front Pharmacol. 2017 Nov 24;8:865.

Pharma Nord Formulations

Vitamin D3

- Small, easy to swallow 'pearl' capsules
- Dissolved in cold pressed organic olive oil to enhance absorption
- Available in a range of strengths from 800IU – 20,000 IU
- Documented bioavailability, proven in clinical trials



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CCB-associated iron depletion

- A prospective observational study that included patients with heart failure on various different blood pressure medications found that blood markers of **iron** status were significantly lower in the patients using calcium-channel blockers than those who were not
- **Action point:** look for symptoms of iron deficiency
 - E.g. extreme fatigue, pale skin, weakness, shortness of breath, headaches, and cold hands/feet
- **Action point:** Keep an eye on iron biomarkers
 - Ferritin, serum iron, transferrin, haemoglobin, haematocrit levels

Amlodipine and zinc depletion

Evidence is mixed but a study of 98 subjects on different types of blood pressure medication for 3 months reported CCB → a decrease in erythrocyte zinc concentration (but normal levels in hair and urine)

- **Action point:** look for signs of low zinc status (skin lesions, hair loss, taste disturbance, delayed wound healing)
- **Action point:** measure zinc status if necessary (red cell levels, urinary organic acids)

Note the study also found hypotensive drugs generally to → decreases in catalase and superoxide dismutase serum concentrations – antioxidant enzymes that need iron and zinc respectively to function

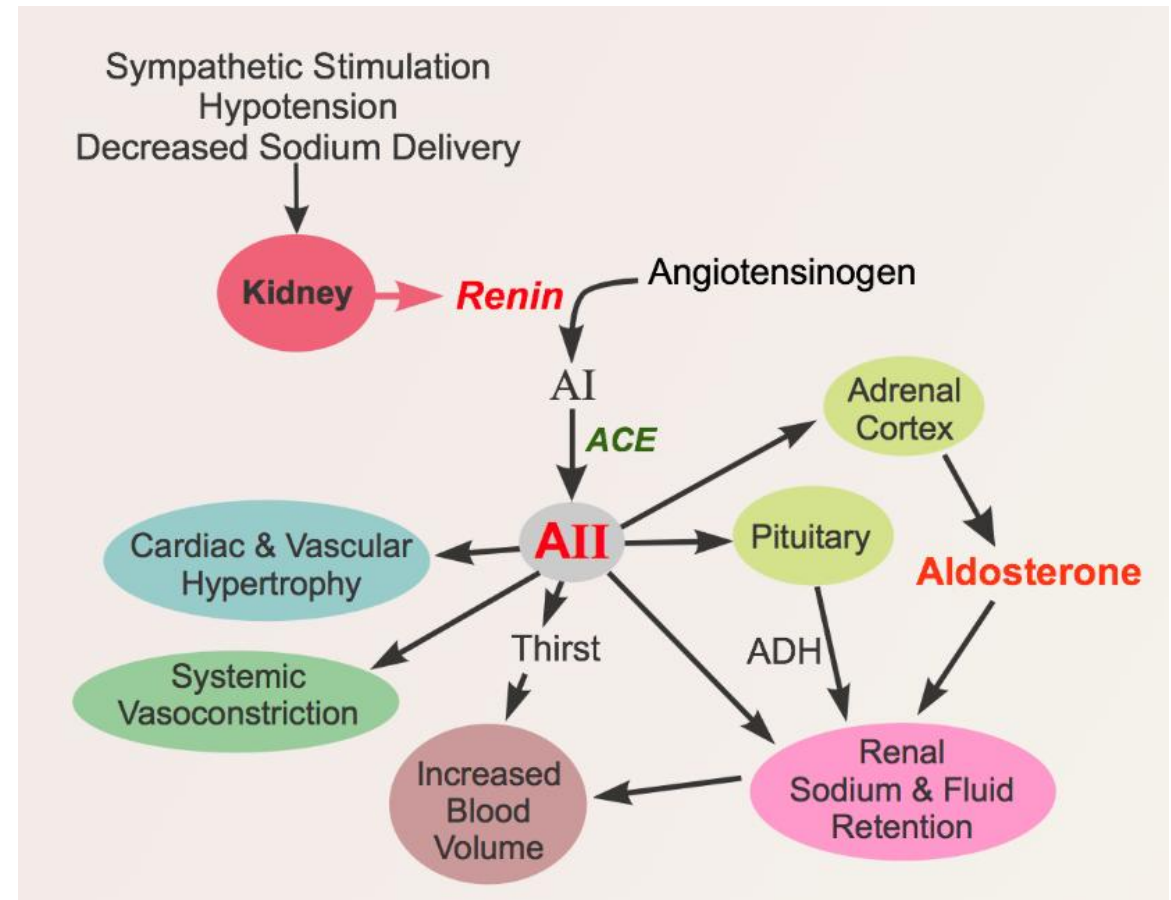
What about folate?

- Some sources cite folate as being depleted by amlodipine but no specific studies appear to show this
- But CCB use has been associated with gingival hyperplasia, a common cause of which is folate deficiency
- There is evidence that combining amlodipine with folic acid is more effective than amlodipine alone for treating hypertension
 - (i.e. that folic acid used *with* amlodipine can improve outcomes, rather than being *depleted by* the drug)
 - RCT of 351 hypertensive patients taking either amlodipine alone, or with 400mcg or 800mcg folic acid for 8 weeks
- Folate can be depleted with long term use of *diuretic* hypertension drugs

Bao H, Huang X, Li P, et al. Combined use of amlodipine and folic acid are significantly more efficacious than amlodipine alone in lowering plasma homocysteine and blood pressure among hypertensive patients with hyperhomocysteinemia and intolerance to ACEI: A multicenter, randomized, double-blind, parallel-controlled clinical trial. J Clin Hypertens (Greenwich). 2023 Aug;25(8):689-699, Mohn ES, Kern HJ, Saltzman E, Mitmesser SH, McKay DL. Evidence of Drug-Nutrient Interactions with Chronic Use of Commonly Prescribed Medications: An Update. Pharmaceutics. 2018 Mar 20;10(1):36

Ramipril: #5 prescribed drug

- An angiotensin-converting enzyme inhibitor (ACE-I) used to treat hypertension, heart failure, and to reduce the risk of heart attacks, strokes and kidney problems
- Inhibits the vasoconstrictor angiotensin II (AII)
- AII is formed by renin (released by the kidneys) acting on circulating angiotensinogen to form AI. AI is then converted to AII by angiotensin converting enzyme



ACE inhibitors (ACE-I) and zinc

- Some studies show that serum, red cell and/or triglyceride levels of zinc are depleted after ACE-I therapy
 - Due to the medication binding with zinc and causing more excretion
- But other studies have not found lower levels in people on the medication
- Evidence is strongest for captopril rather than for ramipril
- But still a good idea to monitor zinc dietary intake, and also deficiency symptoms
 - Frequent infections, skin lesions, hair loss, taste disturbance, delayed wound healing
- And test zinc levels if necessary (blood and/or urinary organic acids)

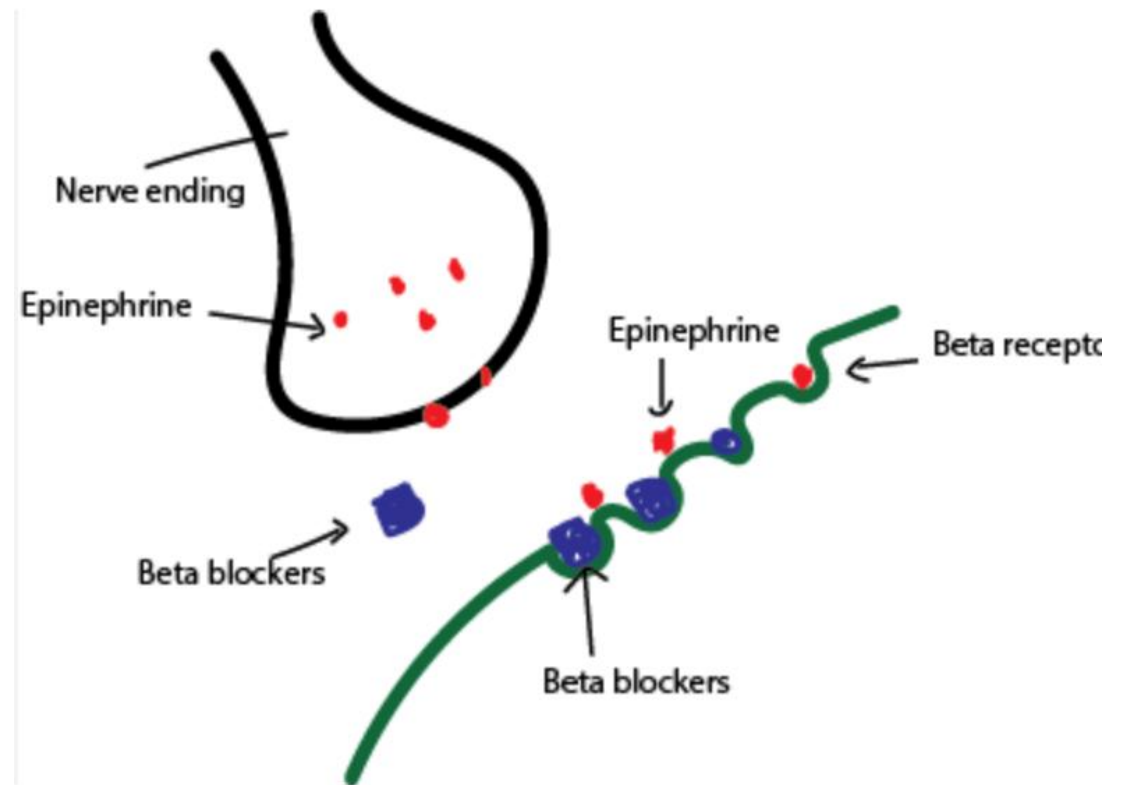
Mohn ES, Kern HJ, Saltzman E, Mitmesser SH, McKay DL. Evidence of Drug-Nutrient Interactions with Chronic Use of Commonly Prescribed Medications: An Update. *Pharmaceutics*. 2018 Mar 20;10(1):36. Suliburska J, Skrypnik K, Szulińska M, Kupsz J, Markuszewski L, Bogdański P. Diuretics, Ca-Antagonists, and Angiotensin-Converting Enzyme Inhibitors Affect Zinc Status in Hypertensive Patients on Monotherapy: A Randomized Trial. *Nutrients*. 2018 Sep 11;10(9):1284.

ACE-I and other micronutrients

- Some sources advise monitoring levels of minerals like calcium, magnesium and potassium; and also vitamin D
- But evidence is so conflicting on whether ramipril depletes these that we cannot *assume* they do
- There is some evidence that potassium levels may *increase*, especially in people with heart failure and/or kidney disease
- **Action:** ensure good dietary intake of all nutrients
- Supplement where dietary intake is difficult
- Periodic vitamin D testing is cost-effective and helpful for most people

Bisoprolol fumarate: #7 prescribed

- Beta blockers compete with noradrenaline and adrenaline to bind to the B1 adrenergic receptor
- This blockage results in:
 - less strong heart muscle contraction
 - and lower blood pressure
- Used in hypertension, angina, heart failure and atrial fibrillation



Bisoprolol and iron

- Although some sources claim that bisoprolol may lead to iron deficiency, this does not seem to be the finding in the prospective observational study used to evidence this
 - Patients with heart failure on various different blood pressure medications had different levels of iron markers in the blood but this wasn't attributed to bisoprolol use
- Action: ensure iron sufficiency through diet
- If symptoms of iron deficiency are present, test ferritin
 - fatigue, pallor, tachycardia, dyspnea on exertion, shortness of breath, cold hands and feet, diffuse hair loss
- If ferritin seems higher than it should relative to intake, consider a full iron panel

Sirbu O, Sorodoc V, Jaba IM, Floria M, Stoica A, Profire L, Tuchilus C, Rusu G, Sorodoc L. The Influence of Cardiovascular Medications on Iron Metabolism in Patients with Heart Failure. Medicina (Kaunas). 2019 Jul 2;55(7):329.

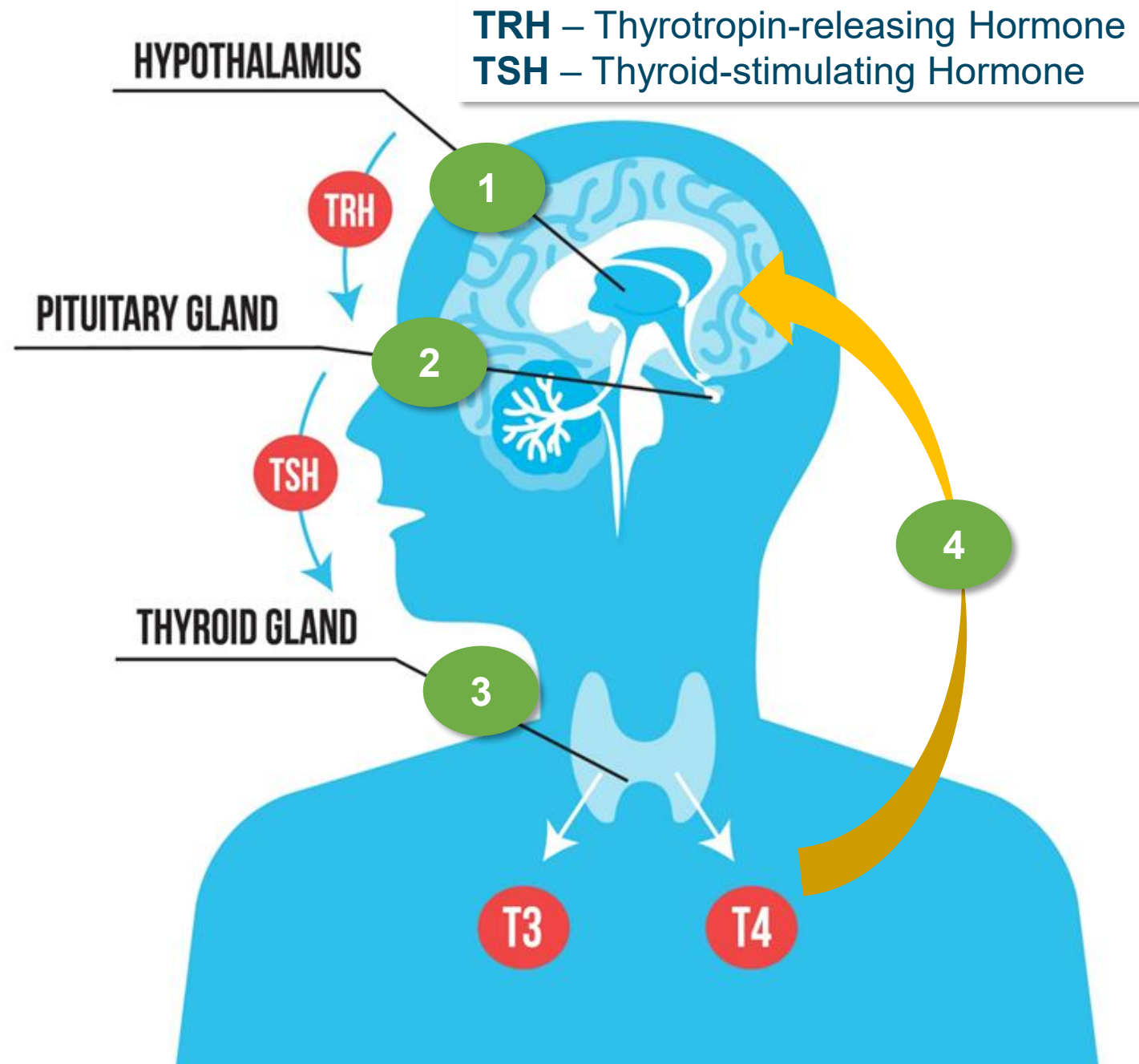
Bisoprolol and zinc

- Evidence is inconsistent and conflicting
- One review reported increased urinary loss of zinc with beta blocker use
- And an earlier study reported lower serum zinc levels
- But some studies show no effect on zinc and suggest that lower zinc may be a result of other hypertensive drugs (like diuretics) sometimes prescribed with the beta blocker
- **Action:** check dietary intake, deficiency symptoms (see earlier) and, if necessary, blood levels and/or urinary organic acids
- **Note:** some sources claim beta blockers deplete CoQ10 but I have not been able to identify any studies on this

Braun LA, Rosenfeldt F. Pharmaco-nutrient interactions - a systematic review of zinc and antihypertensive therapy. Int J Clin Pract. 2013 Aug;67(8):717-25, Suliburska J, Skrypnik K, Szulińska M, et al. Diuretics, Ca-Antagonists, and Angiotensin-Converting Enzyme Inhibitors Affect Zinc Status in Hypertensive Patients on Monotherapy: A Randomized Trial. Nutrients. 2018 Sep 11;10(9):1284.

Levothyroxine

- Sixth most commonly prescribed med
- A synthetic form of thyroid hormone T4 used to treat hypothyroidism (by providing T4 and lowering TSH) and sometimes thyroid cancer (by lowering TSH)
- Side effects can occur if dosing is too high (hyperthyroid sx's)



Levothyroxine and nutrients

- Doesn't directly deplete nutrients
- But important to monitor that blood levels of TSH and T4 remain well within range, as elevated T4 can be catabolic to bone
 - This can then → calcium and magnesium loss in urine
- Interestingly, studies have reported that supplementing vitamin C may increase the absorption of levothyroxine and lower TSH in people who are poor absorbers
 - Studies of patients with elevated TSH levels despite Levothyroxine



Wiesner A, Gajewska D, Paško P. Levothyroxine Interactions with Food and Dietary Supplements-A Systematic Review. *Pharmaceuticals (Basel)*. 2021 Mar 2;14(3):206, Skelin M, Lucijanić T, Amidžić Klarić D, et al. Factors Affecting Gastrointestinal Absorption of Levothyroxine: A Review. *Clin Ther*. 2017 Feb;39(2):378-403, Jubiz W, Ramirez M. Effect of vitamin C on the absorption of levothyroxine in patients with hypothyroidism and gastritis. *J Clin Endocrinol Metab*. 2014 Jun;99(6):E1031-4

Metformin # 9



- Widely prescribed in T2DM and gestational diabetes
- Common side effects are GI sx; rarely can cause hypoglycaemia and/or lactic acidosis

Metformin and CoQ10

- There is speculation that metformin could deplete Q10
- One mechanism could be that metformin affects mitochondrial function, which in turn could reduce Q10 synthesis
 - Inhibits Complex I of the electron transport chain
- I couldn't find any human studies showing a direct reduction in Q10 from metformin
- However, Q10 supports insulin sensitivity and metabolic health and has been found to improve biomarkers of these when supplemented with metformin compared to metformin alone

Metformin and B12

- Systematic reviews and meta-analyses of clinical studies consistently report that metformin use in diabetic patients significantly lowers serum vitamin B12 levels...
- ... and increases the risk of deficiency...
- ... in a dose- and duration-dependent manner
- Metformin suppresses intrinsic factor secretion and impairs calcium-dependent uptake of the B12-intrinsic factor complex in the ileum
- Such strong evidence for depletion that the MHRA (2022) advises monitoring B12 status in metformin users

Stargrove MB, Treasure J, McKee D. L. Herb, Nutrient, and Drug Interactions, Elsevier, 2008, Kakarlapudi Y, Kondabolu SK, Tehseen Z, et al. Effect of Metformin on Vitamin B12 Deficiency in Patients With Type 2 Diabetes Mellitus and Factors Associated With It: A Meta-Analysis. Cureus. 2022 Dec 7;14(12):e32277, Yang W, Cai X, Wu H, et al. Associations between metformin use and vitamin B12 levels, anemia, and neuropathy in patients with diabetes: a meta-analysis. J Diabetes. 2019 Sep;11(9):729-743, Chapman LE, Darling AL, Brown JE. Association between metformin and vitamin B12 deficiency in patients with type 2 diabetes: A systematic review and meta-analysis. Diabetes Metab. 2016 Nov;42(5):316-327, Wulffelé MG, Kooy A, Leher P, Bets D, Ogterop JC, Borger van der Burg B, Donker AJ, Stehouwer CD. Effects of short-term treatment with metformin on serum concentrations of homocysteine, folate and vitamin B12 in type 2 diabetes mellitus: a randomized, placebo-controlled trial. J Intern Med. 2003 Nov;254(5):455-63.

Metformin and folate

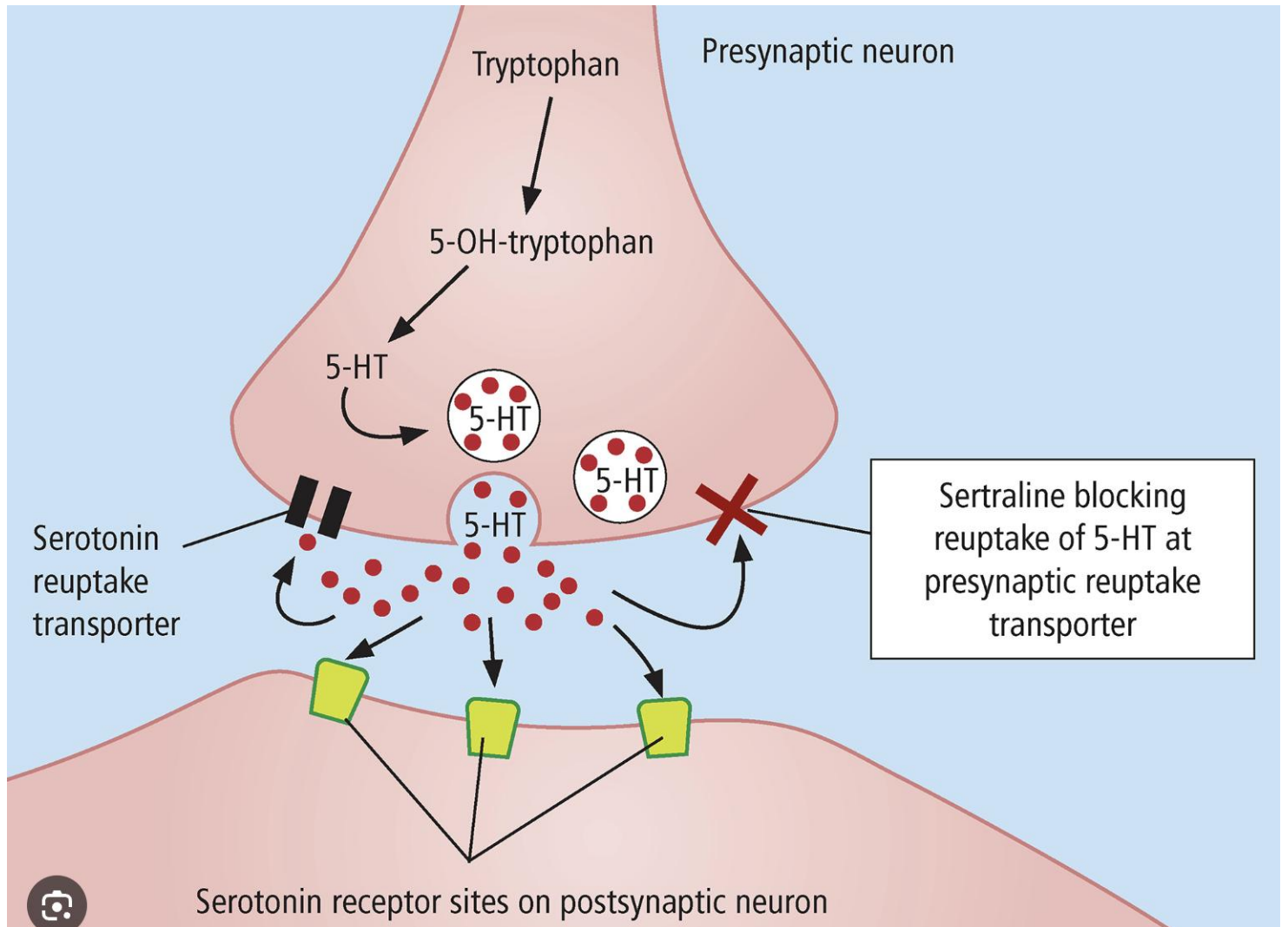
- An RCT found metformin to reduce not only serum B12 (-14% but also folate (-7%) and to increase homocysteine (+4%) over 16 weeks
- Other studies have also found metformin intake to be associated with elevated homocysteine and reduced folate
- And that this could be alleviated when co-administering folic acid
- Action: keep an eye on serum B12 and folate, urinary organic acids (MMA and FiGlu) and homocysteine levels
- Other B vitamins (B1, B6) and vit D may also be depleted but evidence is inconsistent

Li X, Fang Z, Yang X, Pan H, Zhang C, Li X, Bai Y, Wang F. The effect of metformin on homocysteine levels in patients with polycystic ovary syndrome: A systematic review and meta-analysis. J Obstet Gynaecol Res. 2021 May;47(5):1804-1816, Khattab R, Albannawi M, Alhajmohammed D, et al. Metformin-Induced Vitamin B12 Deficiency among Type 2 Diabetes Mellitus' Patients: A Systematic Review. Curr Diabetes Rev. 2023;19(4):1-10, Aghamohammadi V, Gargari BP, Aliasgharzadeh A. Effect of folic acid supplementation on homocysteine, serum total antioxidant capacity, and malondialdehyde in patients with type 2 diabetes mellitus. J Am Coll Nutr. 2011 Jun;30(3):210-5..

Sertraline

10

- A selective serotonin re-uptake inhibitor
- Prescribed for depression and anxiety disorders
- Common side effects: GI sx's; transient increase in anxiety



Sertraline may increase fracture risk

- Several studies within the last 10 years have reported loss of bone density with SSRI use and increased risk of fracture. E.g.:
- A systematic review and meta-analysis of 18 studies (N = 42,656)
- A 2025 study of 1849 women taking SSRI in mid-life
- And a recent retrospective cohort study of 1,611 patients found that those taking SSRI at the time of dental implant surgery had a significantly increased risk for implant failure at 12 months (18.6% failure rate vs 6.7%)

Curio M, de Filippis R, Spina G, De Fazio P, Segura-Garcia C, Galasso O, Gasparini G. The use of antidepressants is linked to bone loss: A systematic review and metanalysis. Orthop Rev (Pavia). 2022 Oct 13;14(6):38564, Block MS, Mercante D. Selective Serotonin Reuptake Inhibitors May Increase Implant Failure. J Oral Maxillofac Surg. 2025 May;83(5):585-591, Solomon DH, Ruppert KM, Lian Y, Neal-Perry G, Cauley JA, Burnett-Bowie SM. The risk of fracture among women starting selective serotonin reuptake inhibitors. J Bone Miner Res. 2025 Oct 28;40(11):1238-1245

Vitamin D depletion as a factor in increased fracture risk?

- Osteoblasts and osteoclasts have serotonin receptors – so their function may alter when serotonin is pharmacologically increased
- But also SSRI has been suggested to deplete serum vitamin D levels (Efficasafe data and recent reviews)
- Somewhat ironically, data also shows that lower vitamin D status is associated with more depression and therefore an increased likelihood of an SSRI like sertraline being prescribed
- Action: ensure sufficient Ca, Mg, vits D + K
- Check BMD and/or bone turnover biomarkers if possible

Antidepressants and sodium

- Case reports and observational studies indicate that sertraline can cause hyponatraemia compared with control groups
 - Low sodium due to excessive water inside cells
- E.g. in a large population cohort study (utilising data from a primary care database of 60,405 patients ≥ 65 years), older patients taking SSRIs had an increased risk of primary hyponatraemia compared to control group
- Incidence is not common but, where it does occur, can be severe
- Nausea, headache, fatigue, dizziness on standing and muscle cramps but can lead to seizures and coma
- People aged 65+ years, female, those with low sodium baseline levels, mild hypokalaemia may be more at risk

Joseph SW, Grant KE, Sousou JM, Qadir N, Reddy P. Severe Hyponatremia Caused by Sertraline-Induced Syndrome of Inappropriate Antidiuretic Hormone Secretion: A Complication With Critical Implications for Patient Safety. *Cureus*. 2024 Oct 12;16(10):e71309, Shubrata KS, Narayanaswamy JC, Viswanath B, Rudhran V, Chandrasekhar CR, Math SB. Sertraline-induced hyponatremia and seizures in old age. *J Neuropsychiatry Clin Neurosci*. 2012 Winter;24(1):E47, Coupland CA, Dhiman P, Barton G, Morriss R, Arthur A, Sach T, Hippisley-Cox J. A study of the safety and harms of antidepressant drugs for older people: a cohort study using a large primary care database. *Health Technol Assess*. 2011 Aug;15(28):1-202, iii-iv..

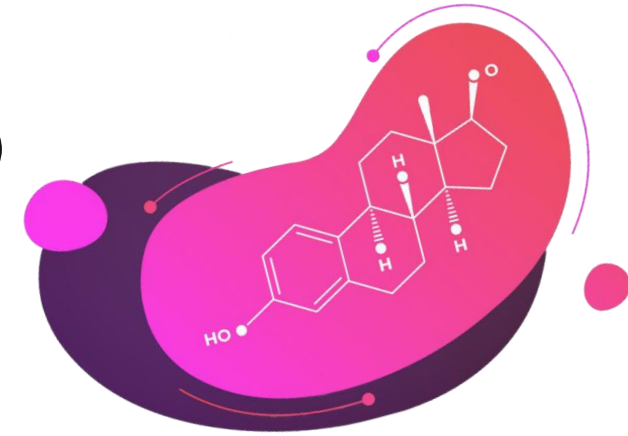
2 other commonly prescribed medication classes



Hormones: OCP and HRT

Studies have found OCP and/or HRT use to be associated with:

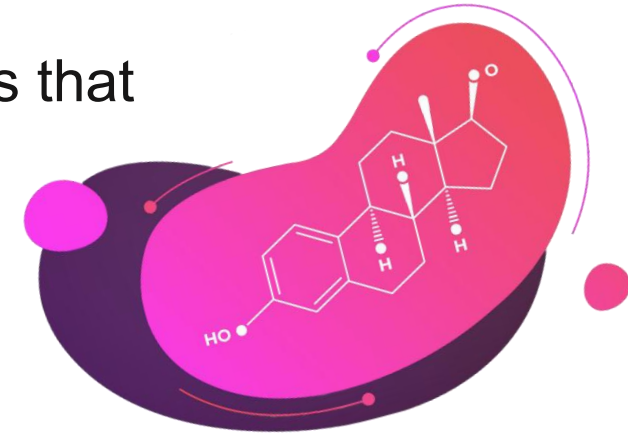
- Reduced serum CoQ10 and vitamin E levels vs. non-users, and higher levels of oxidative stress (lipid peroxidation)
- Lower levels of serum B12, although without necessarily affecting *functional* biomarkers (homocysteine and MMA levels)
- Lower levels of serum magnesium (but possibly better uptake into bone and soft tissues)
- Mixed / contradictory results for depletion of vit B6 and folate



Begum A, Nessa A, Wahed F, Suchi SS, Sadia S, Paul M, Sultana N, Yesmin S. Status of Fasting Serum Glucose and Serum Magnesium among Women Having Low Dose Oral Contraceptive Pill. Mymensingh Med J. 2025 Apr;34(2):319-323 Palan PR, Connell K, Ramirez E, Inegbenijie C, Gavara RY, Ouseph JA, Mikhail MS. Effects of menopause and hormone replacement therapy on serum levels of coenzyme Q10 and other lipid-soluble antioxidants. Biofactors. 2005;25(1-4):61-6, Palan PR, Magneson AT, Castillo M, Dunne J, Mikhail MS. Effects of menstrual cycle and oral contraceptive use on serum levels of lipid-soluble antioxidants. Am J Obstet Gynecol. 2006 May;194(5):e35-8. Mohn ES, Kern HJ, Saltzman E, Mitmesser SH, McKay DL. Evidence of Drug-Nutrient Interactions with Chronic Use of Commonly Prescribed Medications: An Update. Pharmaceutics. 2018 Mar 20;10(1):36.

Hormones: OCP and HRT: action

- Consider dietary intake of all nutrients but in particular Mg and B vitamins
- Consider a broad-based test, such as urinary organic acids
- UOA testing can also be helpful in testing biochemical pathways that may become over-worked due to hormone treatment
 - Methylation
 - Antioxidant systems
- Supplement a MVM, CoQ10 and/or Mg where appropriate
- These same nutrients are reported as helping some side effects of OCP use (mood changes, depression, headaches)



GLP-1 agonists: Mounjaro (tirzepatide)

- Mounjaro is the most commonly used GLP-1 agonist in the UK for weight loss and also contains a GIP agonist to further reduce appetite
- Mostly via private prescription
 - Only on the NHS with a BMI of 40+ (37.5 for certain ethnicities) and 4 co-morbidities (as at June 2025)
- An estimated 4.9 million adults in the UK in Q1 2025 were on a GLP-1
- **Common side effects:** nausea, vomiting, diarrhoea
- **Less common:** pancreatitis
- Also consider muscle and bone loss

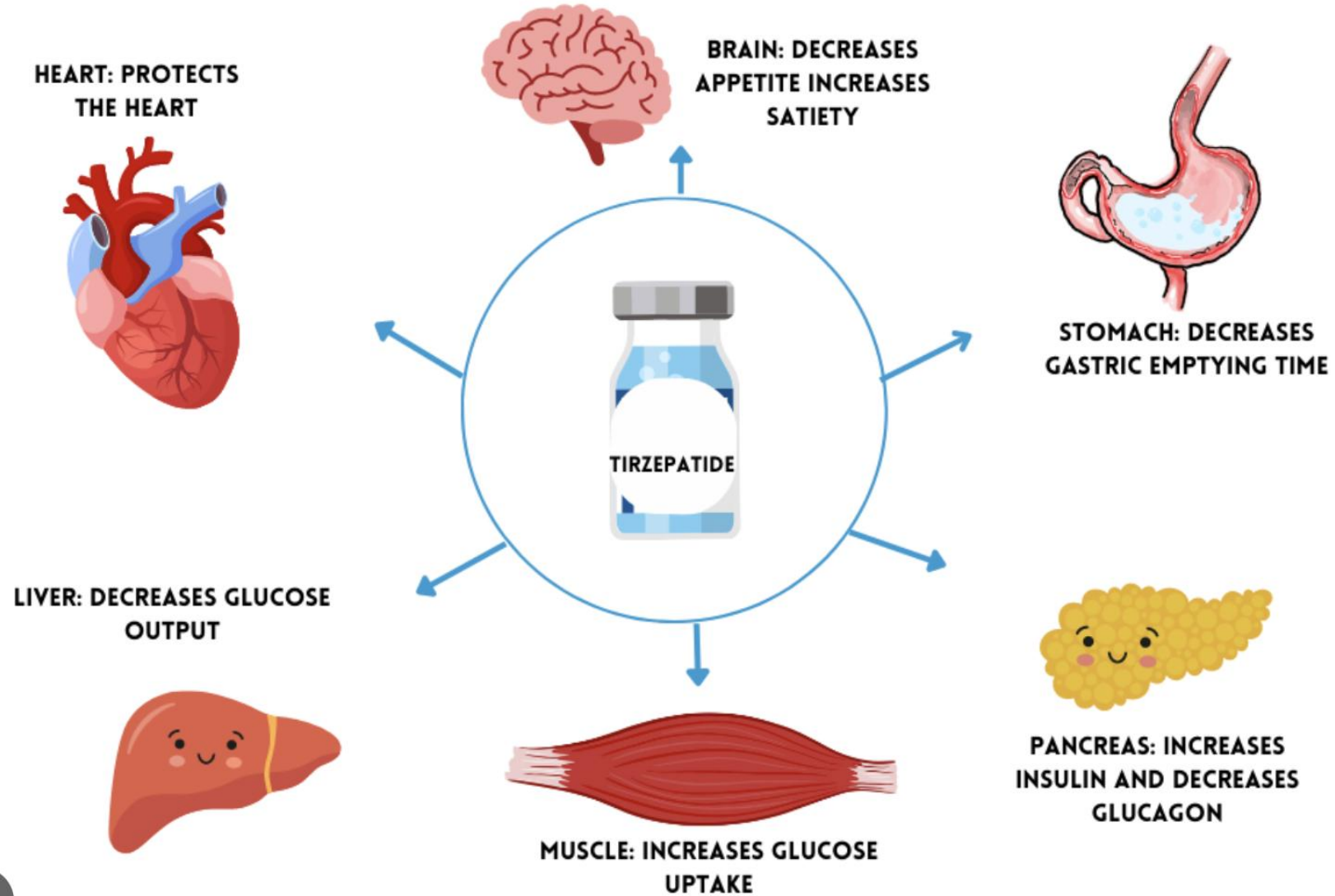


Image:
<https://www.shenhealthacupuncture.com/weightlossmedication>

Mounjaro and nutrient depletions

There is no published evidence that the drug leads to direct depletions of nutrients

- BUT: there is a significant reduction in appetite and therefore food intake
- And can also commonly → GI symptoms
- Thus intake of any nutrient can be far lower; and absorption may be compromised if GI sx's are severe and longer term
- Therefore consider protein intake, a wholefoods diet and supplement a MVM, Mg and Ca if necessary



Pharma Nord Formulations

Antioxidant Multi

- Contains antioxidants that protect tissues against the damaging effects of free radicals
- Manufactured under Danish pharmaceutical control



Available in **UK**



Available in **ROI**

Common OTC meds



Paracetamol

No good evidence for specific vitamin / mineral depletions

- But high dose or longer term use of paracetamol depletes glutathione
 - GSH conjugation is required for paracetamol metabolism
- **Action:** ensure dietary cysteine levels are good
- **Action:** measure glutathione wasting with urinary pyroglutamate
- **Action:** supplement N-acetyl-cysteine (NAC) if necessary as this has been shown to prevent GSH depletion from paracetamol without affecting the drug's pain management effects
- **Note:** no evidence that paracetamol → selenium depletion BUT Se depletion can make it harder to detox paracetamol, causing toxicity

Pickering G, Macian N, Papet I, et al. N-acetylcysteine prevents glutathione decrease and does not interfere with paracetamol antinociceptive effect at therapeutic dosage: a randomized double-blind controlled trial in healthy subjects. *Fundam Clin Pharmacol*. 2019 Jun;33(3):303-311, Li J, Cheng P, Li S, Zhao P, Han B, Ren X, Zhong JL, Lloyd MD, Pourzand C, Holmgren A, Lu J. Selenium Status in Diet Affects Acetaminophen-Induced Hepatotoxicity via Interruption of Redox Environment. *Antioxid Redox Signal*. 2021 Jun 10;34(17):1355-1367.

Ibuprofen: a commonly used NSAID

- A cross-sectional study of rheumatoid arthritis patients found that patients taking COX inhibitors, especially those taking NSAIDs (unspecified) for >6 months had lower circulating B6
- A retrospective study reported ibuprofen to reduce blood iron levels and/or impair its absorption
- Evidence is mixed/conflicting for zinc depletion
- Ibuprofen can → gut lining distress and this may → nutrient absorption
- Hence a good idea to monitor nutrient levels and GI sx's in NSAID users and if necessary take a MVM
- And remember these drugs are for short-term use only unless the use is being monitored by a medical specialist

Points to consider when assessing the evidence for depletions



Polypharmacy in our clients

- Clearly, the number of different medications taken by an individual, the more likely nutrient depletions will occur
- Age UK estimates that nearly 4 million people over 65 take at least 5 prescribed medicines...
- ... and that nearly 2 million people take at least seven
- Polypharmacy rises sharply from age 60 onwards
- Action: refer the patient to their prescribing GP or pharmacy for a medication review, with a view to de-prescribing where possible
- The key question for the patient to ask is: what is the *current* rationale for each of my medications?

Chong RQ, Gelissen I, Chaar B, et al. Do medicines commonly used by older adults impact their nutrient status? Explor Res Clin Soc Pharm. 2021 Sep 3;3:100067, J Clin Pharm Ther. 2013 Oct;38(5):360-72. doi: 10.1111/jcpt.12059. Epub 2013 Apr 2. Application of the STOPP/START criteria: a systematic review of the prevalence of potentially inappropriate prescribing in older adults, and evidence of clinical, humanistic and economic impact. Hill-Taylor B1, Sketris I, Hayden J, Byrne S, O'Sullivan D, Christie R. NHS Digital Health Survey for England – 2016: Prescribed medicines – table 1 <https://files.digital.nhs.uk/excel/4/2/hse2016-pres-med.xlsx>

Which nutrients are the most commonly affected?

- We've seen that almost *any* vitamin and mineral can be depleted with common medications
- Recent reviews (incl. one of 23 studies in older adults) reported the most common drug-induced depletions: Vits B12 & D, Na, Mg, Q10
- And that these were depleted by PPIs, diuretics, statins, insulin sensitizers and/or anti-depressants
- But note that many people being prescribed medications are already at less than optimal nutrient levels before starting
 - This is because these most common meds are prescribed for illnesses that are more likely to take hold in situations of nutrient deficiency

Chong RQ, Gelissen I, Chahr B, Penm J, Cheung JM, Harnett JE. Do medicines commonly used by older adults impact their nutrient status? *Explor Res Clin Soc Pharm.* 2021 Sep 3;3:100067, Bennie M, Santa-Ana-Tellez Y, Galistiani GF, et al. The prevalence of polypharmacy in older Europeans: A multi-national database study of general practitioner prescribing. *Br J Clin Pharmacol.* 2024 Sep;90(9):2124-2136, Woodford HJ. Polypharmacy in Older Patients. *Br J Hosp Med (Lond).* 2024 Oct 30;85(10):1-12, Burrows K (2025). Comprehensive Geriatric Assessment: Medication history and review. The British Geriatrics Society. Avail from www.bgs.org.uk, Wendimere Reilly, Jasminka Ilich (2017). Prescription Drugs and Nutrient Depletion: How Much Is Known? *Advances in Nutrition*, 8 (1): 23

And finally...

- ✓ Consider whether it is **safe** to supplement
- ✓ Check for drug-nutrient contraindications
- ✓ Or even interactions that may either:
 - ✓ Reduce the drug's effects
 - ✓ Or increase unwanted side effects
- ✓ Get medical advice for any interaction for which the clinical outcome is uncertain
- ✓ If supplementing, use the lowest dose that will achieve the desired effect



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through nutrition

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Speaker

Helen Lynam

BSc (Nutr), PGCHE,
Registered Nutritionist
(BANT), Registered Nutritional
Therapist (CNHC)

Thank you!

Please email

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For any queries!

