

**Specific Question:** In patients that are vitamin B12 deficient is oral vitamin B12 supplementation as effective as intramuscular B12 injection?

### **Clinical bottom line**

Administration of vitamin B12 via IM injection is common, however the results of this literature review suggested that oral vitamin B12 may be as effective as IM for some patients. Use of oral B12 may reduce practice nurse time and is less invasive than IM treatment.

**(See implications for practice)**

### **Why is this important?**

Patients with a B12 deficiency are generally treated with the B12 IM injection, but an alternative treatment is for patients to receive the oral vitamin B12 supplement.

Providing patients with the oral vitamin B12 treatment costs more initially than the B12 injection. However, administration via the oral route frees up nurse time and avoids patient discomfort associated with the injections.

It is unclear which method of administration is more clinically effective than the other or if they are equivalent.

**\*In view of the 2019/20 COVID-19 pandemic this question has become of greater importance to general practice, as surgeries look to reduce the number of face-to-face appointments. For this reason, we have put greater emphasis on our implications for practice section of this CAT.**

### **Search timeframe**

From each databases inception to September 2019.

### **Inclusion criteria**

	<b>Description</b>	<b>Search terms</b>
<b>Population and setting</b>	Adult patients with a B12 deficiency treated in primary care	adults adult primary care family practice B12 deficiency B12 deficiencies B12 deficient pernicious anaemia pernicious anaemia folate deficiency anaemia folate deficiency anaemia

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<b>Intervention or Exposure</b>		oral B12 B12 supplement B12 tablet B12 oral vitamin Folic acid tablet (Cobalamin is the medical name for vit B12)
<b>Comparison, if any</b>		B12 injection B12 shot B12 intramuscular injection B12 intramuscular shot B12 IM injection B12 IM shot (Cobalamin is the medical name for vit B12)
<b>Outcomes of interest</b>		reduced symptoms reduce symptoms increased haemoglobin increased haemoglobin fatigue
<b>Types of studies</b>		SR and RCTs

**Routine databases searched**

Cochrane systematic reviews, Clinical Evidence, DARE/HTA/NHSNEED, Medline, CINAHL, Cochrane Central, Web of Science, British Nursing Index, Joanna Briggs Institute, TRIP< AHMED, Psychinfo, IBSS (BIDS)

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**Results of the search**

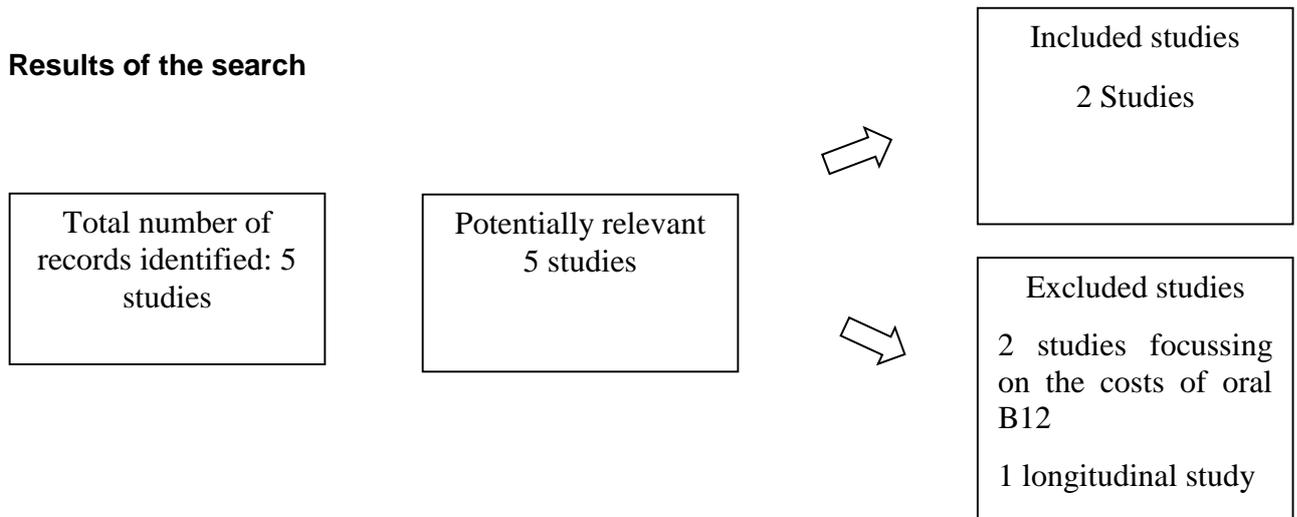


Table 1 – Details of included studies

No studies identified.

First author, year and type of study	Population and setting	Intervention or exposure tested	Study results	Assessment of quality and comments
Wang <i>et al</i> (2018) Cochrane Review	Participants with a B12 level of <200 pg/ml	Oral B12	In two trials employing 1000 µg/day oral vitamin B12, there was no clinically relevant difference in vitamin B12 levels when compared with IM vitamin B12. One trial used 2000 µg/day vitamin B12 and demonstrated a mean difference of 680 pg/mL (95% confidence interval 392.7 to 967.3) in favour of oral vitamin B12.	All studies included in the review were of low quality
Vidal-Alball <i>et al</i> (2005) Systematic Review	Participants with low serum B12 levels cut off point of 180 pmol/l	Oral B12	The evidence derived from these limited studies suggests that 2000 mg doses of oral vitamin B12 daily and 1000 mg doses initially daily and thereafter weekly and then monthly may be as effective as intramuscular administration in obtaining short-term haematological and neurological responses in vitamin B12-deficient patients.	The authors did not assess the quality of included papers

## **Implications for Practice/research**

The two systematic reviews suggest that the use of oral vitamin B12 may be equivalent to IM B12 in terms of haematological outcomes. However, both reviews reported that the studies included were of low or unclear quality. Caution is therefore needed in interpreting these findings, even though the direction of effect is towards these two methods of administration being equivalent. There was no examination of the costs associated with each method of administration and therefore no conclusions can be drawn as to the cost effectiveness of each method.

Our view is that all newly diagnosed patients with vitamin B12 deficiency (cobalamin) <200pg/ml should have their intrinsic factor checked. If this is negative then oral supplementation is appropriate, with a repeat B12 blood test after 3 months. If this is then >200pg/ml then patients can continue with oral treatment. If the intrinsic factor is positive, then the BNF guidelines for initiating lifelong injectable vitamin B12 therapy should be adhered to.

**\*Patients with Pernicious Anaemia, Crohn's Disease or a Gastric Bypass should remain on IM B12**

### **Updated April 2020**

In view of the COVID-19 pandemic practices have asked if 2 or 3 monthly injection of hydroxocobalamin can be delayed or if an alternative oral preparation can be recommended to reduce patient footfall through practices. The guidance issued by the Medicines Optimisation team for the Stoke-on-Trent and Staffordshire CCG on April 14<sup>th</sup> 2020 states:

1. Hydroxocobalamin is stored in the body for several months and optimal body stores are believed to be enough for 3-4 years. A single 1000 mcg (1mg) IM dose of Hydroxocobalamin is believed to provide vitamin B12 sufficient for 2-10months. It is therefore unlikely that skipping a single 3-monthly dose will result in significant deficiency in a patient whose levels are well within range.
2. If patients are symptomatic or they have only recently commenced B12 therapy, ideally they should be given IM injection. However, if clinicians would prefer to use an oral preparation then Cyanocobalamin 1000 mcg food supplements are available over the counter. The dose is Cyanocobalamin 1000 mcg daily. If clinicians would prefer to prescribe these products, then

they should be prescribed generically as it will help pharmacists source the relevant product more easily. There is some evidence that large doses of Cyanocobalamin may be effective in malabsorption state.

3. Once Covid-19 infection risk has declined and patients can be seen in practices again, they should undergo the usual tests for management of B12 related anaemia. The patient should be transferred to relevant dosing schedule of IM Hydroxocobalamin based on their test results, where appropriate.

### What would you tweet? (140 characters)

Oral vitamin B12 may produce equivalent clinical effects as IM B12.

### Original references

Wang H, Li L, Qin LL, Song Y, Vidal-Alaball J, Liu TH. Oral vitamin B12 versus intramuscular vitamin B12 for vitamin B12 deficiency. Cochrane Database of Systematic Reviews 2018, Issue 3. Art. No.: CD004655. DOI: 10.1002/14651858.CD004655.pub3

Vidal-Alaball J, Butler CC, Cannings-John R, Goringe A, Hood K, McCaddon A, McDowell I, Papaioannou A. Oral vitamin B12 versus intramuscular vitamin B12 for vitamin B12 deficiency. The Cochrane Database of Systematic Reviews 2005, issue 3

### References for 2020 update

Cyanocobalamin 50mcg Tablets <https://www.medicines.org.uk/emc/product/5716/smpc>

Use of Vit B12 in to treat Vit B12 Deficiency. *UKMi* West Midlands Report ref 14337 [04/12/2019]

Anaemia - B12 and folate deficiency NICE: Feb 2019[Accessed 25/3/20] <https://cks.nice.org.uk/anaemia-b12-and-folate-deficiency>

Treatment Vit B12 or Folate Deficiency <https://www.nhs.uk/conditions/vitamin-b12-or-folate-deficiency-tment/> [Accessed 25/3/2020]

BNF.org [accessed 25/3/20] <https://bnf.nice.org.uk/drug/cyanocobalamin.html>

Oral Vit B12 Compared to Intramuscular vitamin B12 for vitamin B12 deficiency <https://www.cochrane.org/oral-vitamin-b12->[accessed 26/3/2020]

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Alternatives to intramuscular administration of hydroxocobalamin: UKMi Report ref 144230  
[26/3/2020]

MedOptimise® Complete Prescribing Analysis Report March  
2020 [www.medoptimise.co.uk](http://www.medoptimise.co.uk) [accessed 27/3/2020]