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Optimising Vitamin B12 Supplementation in Older Adults: Evidence-Based Strategies for General Practitioners in Residential Aged-Care Facilities

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Abstract

Vitamin B12 (cobalamin) deficiency is prevalent, often unrecognised and readily treatable in older people, but is a complex condition in residential aged-care facilities (RACFs) due to polypharmacy, cognitive impairment, difficulty with swallowing and differences in laboratory practice. This narrative review aims to summarise the relevant literature published from 2020–2025 to provide a general practitioner (GP) with a practical, evidence-informed tool to recognise, treat and monitor B12 deficiency in residents of residential aged care facilities (RACFs). Causes of deficiency are primarily food-cobalamin malabsorption, autoimmune gastritis and pernicious anaemia, and long-term medication, including acid-suppressing agents; for a few residents, inadequate intake is an additional cause. There is no single biomarker: the typical initial test is serum B12; equivocal results are clarified by using other markers (such as holotranscobalamin, MMA and homocysteine) with renal function, inflammation and clinical context. In most other residents, high-dose oral and sublingual therapy are equally effective in producing a biochemical response and may decrease injection burden; parenteral therapy is preferred for severe presentations and neurological or malabsorptive presentations. There is no evidence for using empirical B12 supplementation to enhance cognition or mood in non-B12 deficient older adults. We suggest a six-step model of admission risk screening, medication review, test interpretation, route selection, monitoring and communication and point to areas of need in aged care research.

Keywords: *vitamin B12; cobalamin; older adults; residential aged care; general practice; supplementation; deprescribing*

Abbreviations: *B12, vitamin B12; GP, general practitioner; Hcy, homocysteine; holoTC, holotranscobalamin; IF, intrinsic factor; IM, intramuscular; MMA, methylmalonic acid; PPI, proton pump inhibitor; RACF, residential aged-care facility.*

1. Introduction

Vitamin B12 (cobalamin) is a water-soluble B complex vitamin that is a cofactor in DNA synthesis and neurological activity. The prevalence of deficiency increases as age increases, and it is especially common among frail older people and those in institutional care [1]. The prevalence of deficiency has been estimated to be 6.9% in adults aged 51-70 years and 15% in adults over 70 years old based on survey data in the United States [2]. The severity of presentation varies from none to macrocytic anaemia, neuropathy, cognitive failure and mood disturbance. These are non-specific features and can be attributed to ageing alone, and if a delayed response occurs, irreversible neurological damage may occur [1,3].

Many risk factors are focused in residential aged-care facilities (RACFs). A cross-sectional study in the

Australian population of 303 people found they had an average of 10.3 regular medicines each, with 92% having polypharmacy and 72% dementia [4]. The results of a national study of health services using electronic medication charts in 287 facilities indicated that 78% of residents were given more than five routine medications [5]. The GP in this context is thus faced with regular questions about who should be tested, what to do with "borderline" results, what other methods of replacement should be used, and when supplements are not indicated. The routes, schedules and doses in international practice differ [6].

This review brings together evidence from the past five years (2020-2025) relevant to these decisions and suggests a pragmatic approach to be taken by GPs caring for residents of RACFs.

2. Review methodology

A targeted search of PubMed, Google Scholar and publisher platforms was conducted for English-language publications from January 2020 to December 2025. The search was performed on **10 October 2026**. Search terms included combinations of the following *keywords: vitamin B12, cobalamin, older adults, aged care, nursing home, long-term care, diagnosis, holotranscobalamin, supplementation route, metformin, proton pump inhibitors, deprescribing, and cognition.*

Eligible Systematic reviews, meta-analyses, randomised trials, consensus statements and guidelines were included, and observational studies were included when these were not available. Twenty-six publications were retained as they were relevant to RACF practice. There was no formal protocol or risk-of-bias appraisal, and conclusions are therefore considered to be an expert synthesis and not a systematic estimate.

3. Aetiology and risk factors in residential aged care

3.1 Absorption physiology and why deficiency is silent

Dietary B12 is released from food proteins by gastric acid and pepsin, bound to haptocorrin, transferred to intrinsic factor (IF) in the duodenum and absorbed in the terminal ileum [2]. Deficiency takes years to develop and is insidious, with stores of around 2–3 mg, meaning that long-stay residents may be clinically normal, but their stores are depleted over the years.

3.2 Principal contributors

In older people, the most important mechanism is food-cobalamin malabsorption caused by atrophic gastritis and hypochlorhydria, and autoimmune gastritis; drugs that affect absorption are also a factor [1]. Autoimmune atrophic gastritis is a more advanced form of the disease, in which the production of IF is lost, resulting in severe malabsorption [7]. In RACFs, medicines are a key issue (Table 1). Long-term, high-dose metformin therapy is associated with impaired B12 status [8], and a 2024 mini-systematic review of 21 studies suggested routine screening, prioritising the higher-risk patients [9], while other pathogenetic recommendations have been mooted [10]; definite screening guidelines are still to be provided [8]. With the acid-suppressing agents, there is ongoing uncertainty about whether long-term use of proton pump inhibitors (PPIs) results in clinically significant deficiency [11]. PPIs are, however, often still prescribed for an undue length of time, and as a result there is a high risk of up to 20-80% of the population using them inappropriately [12]; therefore, deprescribing review has a safety and nutrition aim.

Poor intake is not always the only cause but is important for vegetarians and vegans, since plant foods are not a good B12 source unless fortified [13] and for persons with chewing or swallowing problems or lack of appetite [2]. The micronutrient status of older persons, particularly B12 status, has been investigated in relation to frailty, sarcopenia and disability [14,15]. Table 1 shows the main causes of B12 deficiency amongst RACF residents and what this means for GP practice.

Table 1. Principal contributors to vitamin B12 deficiency in RACF residents and practical implications for GPs.

Contributor	Mechanism/evidence	Practical implication	Ref.
Food-cobalamin malabsorption (atrophic gastritis)	Reduced gastric acid and pepsin impair release of B12 from food proteins	A leading mechanism in older adults; consider when no other cause is evident	[1,2]
Autoimmune gastritis / pernicious anaemia	Loss of intrinsic factor in later-stage autoimmune atrophic gastritis	Parenteral therapy with long-term maintenance generally favoured	[7,16]

Contributor	Mechanism/evidence	Practical implication	Ref.
Metformin	Long-term, high-dose therapy impairs B12 status	Periodic B12 monitoring, prioritising higher-risk residents; no definitive screening guideline	[8–10]
Proton pump inhibitors / acid suppression	Proposed reduced release of B12 from food; evidence conflicting	Review indication and consider deprescribing; test if symptoms or other risks present	[11,12]
Inadequate intake	Unfortified vegetarian or vegan diets; poor appetite; chewing or swallowing difficulty	Dietitian review; fortified foods or supplement	[2,13]
Frailty and multiple micronutrient deficits	B12 and other vitamin deficits examined in relation to frailty, sarcopenia and disability	Broader nutritional assessment rather than B12 testing alone	[14,15]

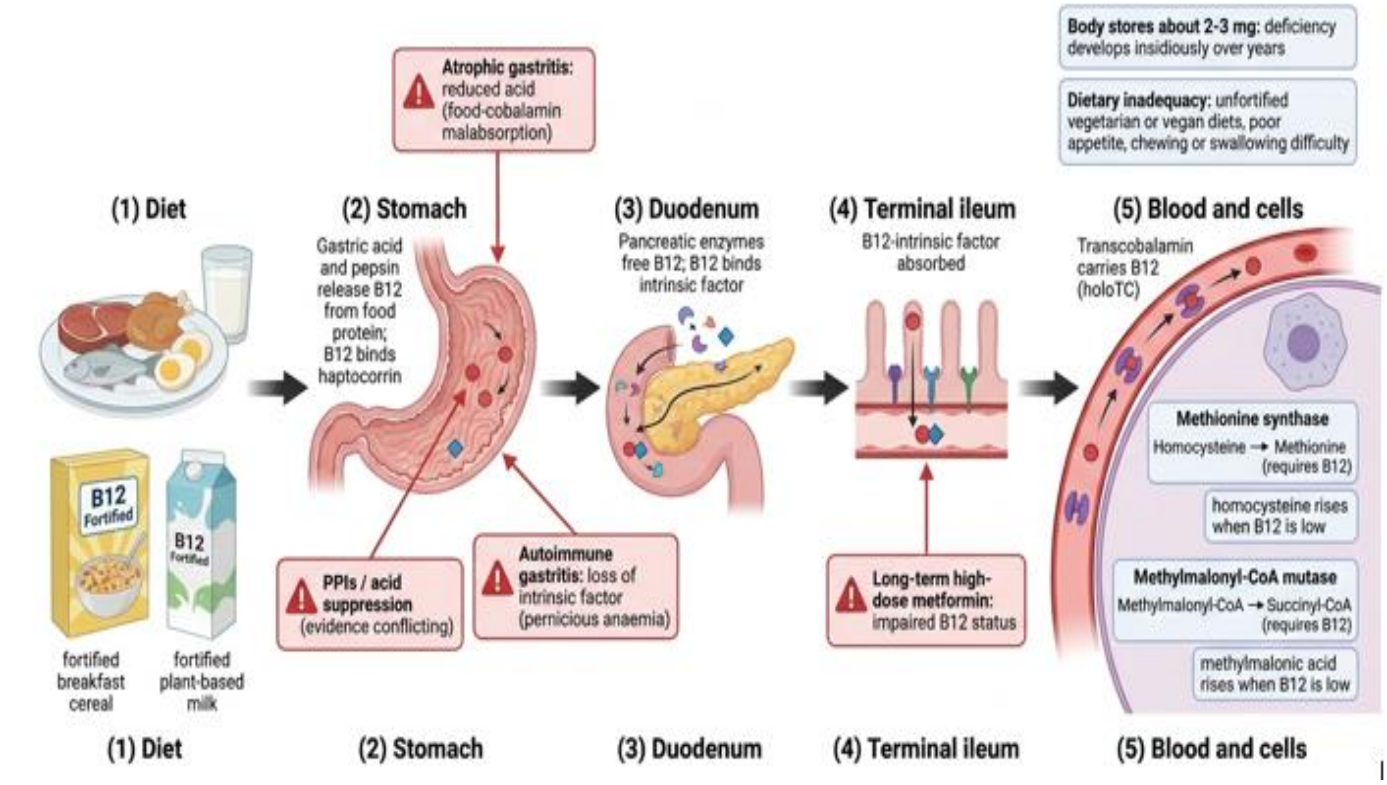

Figure 1. Vitamin B12 absorption pathway and points of failure in older adults, including atrophic gastritis, intrinsic factor loss, medicines and dietary inadequacy.

Sources: Adapted from references [1,2,7,8,11].

4. Diagnosis in the RACF setting

No single test is definitive. Diagnosis should integrate history, clinical features and combined biochemical and haematological indicators, because serum B12 can be falsely normal in conditions such as chronic liver disease and myeloproliferative disorders [1]. Serum B12 remains the usual first-line marker, and a concentration below 148 pmol/L (200 pg/mL) commonly defines deficiency [2], but laboratory cut-offs vary, and intermediate results are frequent.

Functional and active-fraction markers are used to help resolve equivocal results (Table 2). When 11,833 samples were analysed for B12, holoTC, MMA and Hcy in parallel, holoTC was found to have the highest area under the curve for the detection of subclinical B12 deficiency (0.92) and in women 50 years of age and over, holoTC was superior to total B12 (0.92 versus 0.89) [17].

Where results are equivocal, a pragmatic approach combines a second marker with a supervised therapeutic trial and documented response (Figure 2) [1]. Identifying deficiency is clinically worthwhile: in the US NHANES cohort, serum B12 below 140 pmol/L was associated with higher all-cause mortality (hazard ratio 1.39), although association does not establish causation [18]. Table 2 presents the Pathological and clinical tests to help identify B12 deficiency in seniors. Figure 2 gives the possible diagnostic route in suspected B12 deficiency in RACF residents.

Table 2. Laboratory and clinical tools for diagnosing B12 deficiency in older residents.

Tool	Role in RACF practice	Limitations/confounders	Ref.
Serum total B12	Usual first-line screening marker	Limited sensitivity and specificity; can be falsely normal (e.g. chronic liver disease, myeloproliferative disorders); cut-offs vary between laboratories	[1,2,16]
Holotranscobalamin (holoTC)	Active fraction; second-line test for equivocal serum B12	Highest AUC (0.92) for subclinical deficiency in a large mixed cohort and superior to B12 in women aged 50 years or older; availability and cost vary	[17]
Methylmalonic acid (MMA)	Functional marker supporting the diagnosis	Influenced by renal impairment; not universally available	[1,16]
Homocysteine (Hcy)	Sensitive functional marker	Less specific: raised by folate or B6 deficiency, hypothyroidism and reduced GFR	[1,16]
Full blood count and film	Detects macrocytosis or anaemia	Absence of anaemia or macrocytosis does not exclude deficiency; presence is not specific	[1]
Inflammation markers / context	Aid interpretation of micronutrient results	Inflammation alters circulating micronutrient concentrations	[19]
Supervised therapeutic trial	Supports diagnosis when tests are equivocal	Requires documented clinical and laboratory response and a review date	[1]

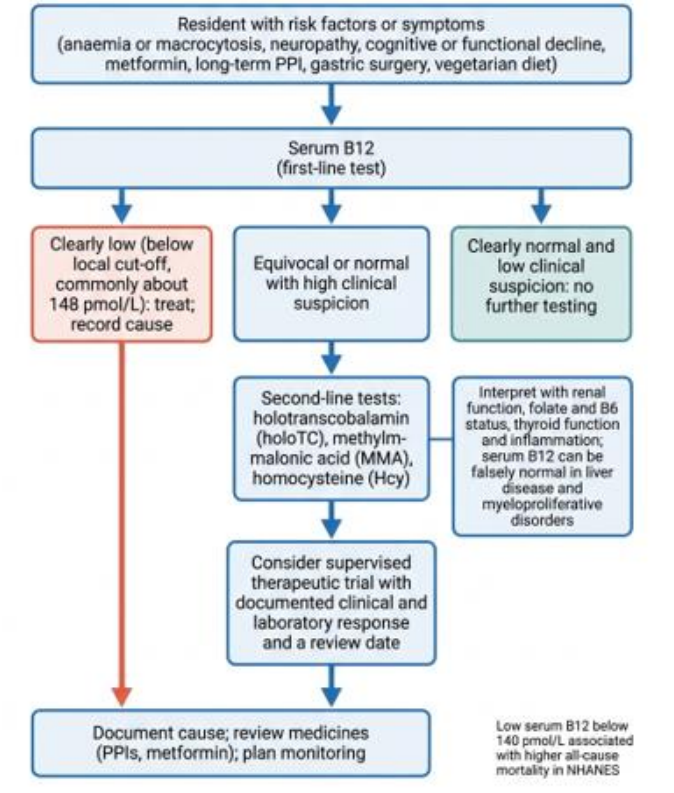

Figure 2. Possible diagnostic route in suspected B12 deficiency in RACF residents.

Sources: Adapted from references [1,16–19].

5. Treatment: choosing the route, dose and duration

The route and dose depend on the severity of the symptoms, cause and treatment objectives [16]. The Delphi panel expressed a consensus that parenteral therapy is the preferred treatment for the acute and severe manifestation, whereas high-dose oral therapy with different dosing frequency can be used for long-term and/or prophylactic therapy in certain high-risk groups [16]. In Australia, the most commonly used parenteral forms are hydroxocobalamin and cyanocobalamin, with alternatives including mecobalamin and adenosylcobalamin and administration under the skin is under-researched [3].

A network meta-analysis of 13 studies (4275 patients) showed that IM therapy was most effective at increasing serum B12 compared to oral therapy (mean difference 94.09 pg/mL) and sublingual therapy (43.31 pg/mL), but neither difference was statistically significant [20]. A meta-analysis published in 2025 revealed that there were significant pooled increases in cobalamin on all routes (mean +402.6 pg/mL) and no significant differences between the oral, sublingual and IM routes for cobalamin or Hcy, even stratified by age and clinical condition [21]. Non-parenteral routes have the potential to enhance compliance and lower cost [6]. These data are mostly biochemical and from heterogeneous populations not RACF residents and do not provide equivalence for neurological outcomes in advanced disease. If malabsorption is profound, parenteral therapy is still the best choice, regardless of the cause [20].

Table 3 and Figure 3 make the link between this evidence and RACF practice. People with neurological symptoms, severe anaemia and pernicious anaemia should be given parenteral loading and maintenance doses, the latter given every 1-3 months (consensus) [16]. High dose (oral) therapy is considered for those with mild to moderate or subclinical deficiency due to food-cobalamin malabsorption or medicines, and the dose is typically in the order of 1000 mcg daily in published regimens, but can vary considerably [6,21]; response should not be taken for granted. For individuals who are unable to swallow or who do not want injection therapies, sublingual products may be a viable option [20,21]. Local guidelines and product information are to be adhered to. Regardless of the route, medication administration should be documented on the medication chart and care plan, and should be taken into consideration with the number of regular medications the resident is taking [4,5]. Table 3 shows the differences between the various B12 replacement methods for older residents of RACFs. Figure 3 presents the decision pathway for selection of the B12 replacement route in residents of RACFs based on severity, cause and practical constraints.

Table 3. Comparison of B12 replacement routes for older RACF residents.

Route	Evidence summary	Suitable residents	RACF considerations	Ref.
Intramuscular (hydroxocobalamin or cyanocobalamin)	Ranked highest for raising serum B12 in network meta-analysis; no significant difference between routes overall	Severe or neurological presentations; pernicious anaemia; severe malabsorption	Requires trained staff and scheduling; maintenance intervals per local protocol	[3,16,20]
High-dose oral	Comparable pooled biochemical response to IM; doses and schedules vary widely	Mild to moderate or subclinical deficiency; long-term maintenance when appropriate	Adherence via medication rounds; pill burden; swallowing ability	[6,16,21]
Sublingual	Comparable efficacy to IM and oral in meta-analyses	Dysphagia or injection refusal	Product availability varies; confirm local supply	[20,21]
Subcutaneous / intranasal	Described as emerging routes; subcutaneous use not well studied	Case-by-case, specialist advice	Limited evidence; not first-line	[3,6]

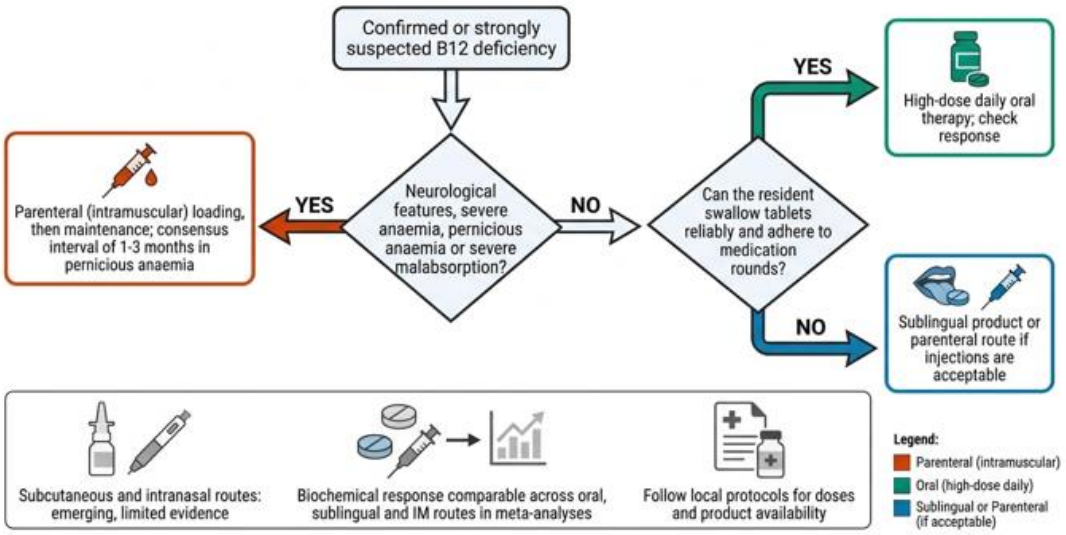

Figure 3. Decision pathway for selecting the route of B12 replacement in RACF residents according to severity, cause and practical constraints.

Sources: Adapted from references [3,6,7,16,20,21].

6. Supplementation without deficiency: what the evidence supports

Although supplementation is widely used for fatigue, low mood, and cognitive decline, the evidence for doing so in residents without a deficiency is limited (Table 4). In a meta-analysis of 16 RCTs, involving 6,276 people, neither B12 alone nor B-complex seemed to affect cognitive function or depressive symptoms in patients without advanced neurological diseases or known B12 deficiency, and B12 prescription rates in a Canadian study were as high as 60% in patients aged 65 years or older with normal or unknown B12 status [22]. However, a systematic review of oral B vitamins in cognitively unimpaired adults found no overall effects on cognitive decline [23]. A 24-month randomised trial of 279 older adults with MCI and elevated homocysteine found that the same 500 µg of methylcobalamin and 400 µg of folic acid per day failed to slow cognitive decline, although greater improvements in depressive symptoms were observed at 12 months, which were not sustained thereafter, and aspirin use appeared to interact with use of the supplementation [24]. A systematic review of vitamin supplementation and dementia found contradictory results for combined vitamin B12 and folic acid [25]. Fortunately, NHANES analyses did not show any negative relationship between B12 supplementation and mortality [18].

The bottom line is that it is a supplement to treat or prevent a known deficiency, not as a yet-to-be-proven cognitive therapy. If there is a mixture of symptoms of deficiency with cognition, treat the deficiency and then re-evaluate cognition. Table 4 gives the evidence on B12 status and supplementation for non-haematological outcomes in older adults.

Table 4. Evidence on B12 status and supplementation for non-haematological outcomes in older adults.

Source	Design / population	Main finding	Implication	Ref.
Markun et al. 2021	Systematic review and meta-analysis; 16 RCTs, 6,276 participants without advanced neurological disease or overt deficiency	No effect of B12 alone or B-complex on cognition or depressive symptoms	Avoid empirical use for cognition or mood	[22]
Behrens et al. 2020	Systematic review and meta-analysis of oral B vitamins in cognitively unimpaired people	No overall effect on cognitive decline (SMD 0.02)	No preventive role demonstrated	[23]
Kwok et al. 2020	RCT; 279 older adults with MCI and elevated Hcy; methylcobalamin 500 µg plus folic acid 400 µg for 24 months	No difference in cognitive decline; transient fall in depressive symptoms at 12 months; negative aspirin interaction	Review concomitant aspirin; no cognitive benefit shown	[24]

Source	Design / population	Main finding	Implication	Ref.
Gil Martínez et al. 2022	Systematic review of vitamin supplementation and dementia	Discrepant results for combined folic acid and B12	Evidence inconsistent	[25]
Wolffenbuttel et al. 2020	NHANES cohort; 24,262 adults; mortality follow-up	Low serum B12 (<140 pmol/L) associated with higher all-cause mortality; supplement intake not associated with adverse mortality	Supports treating deficiency; supplementation appears safe	[18]

7. A practical framework for GPs in RACFs

Figure 4 presents a 6-step process that can be incorporated into the admission and medication-review process.

Step 1: Admission risk screening. Look for risk factors (vegetarian, an autoimmune condition, unexplained cognitive or functional loss, neuropathy, anaemia or macrocytosis, recent B12 result is not available, long-term metformin or acid suppression, advanced age or gastric surgery) and if available, review a recent B12 result [1,3,8].

Step 2: Medication review. Review and reconcile current B12 products; review indication for PPIs; consider structured deprescribing (preferably with pharmacist involvement) [12]. Use metformin as indicated and add B12 surveillance [8,9].

Step 3: Test and interpret. Renal function and inflammation should be taken into consideration (Figure 2) [1,16,17,19] and serum B12 is administered as a first step followed by holoTC, MMA or Hcy for equivocal results.

Step 4: Treatment – by severity and cause. Apply the route pathway in Figure 3 [16,20,21].

Step 5: Monitor. Analyse clinical response (neurological, haematological and functional) and note the presumed cause and review date; practical tips on micronutrient monitoring are given in the ESPEN short guideline [26].

Step 6: Communicate and maintain. Document the diagnosis, administration route, dosage and next review date in the care plan, short notes for the nursing staff and review the requirement for ongoing medication in the care plan if medicines are changed.

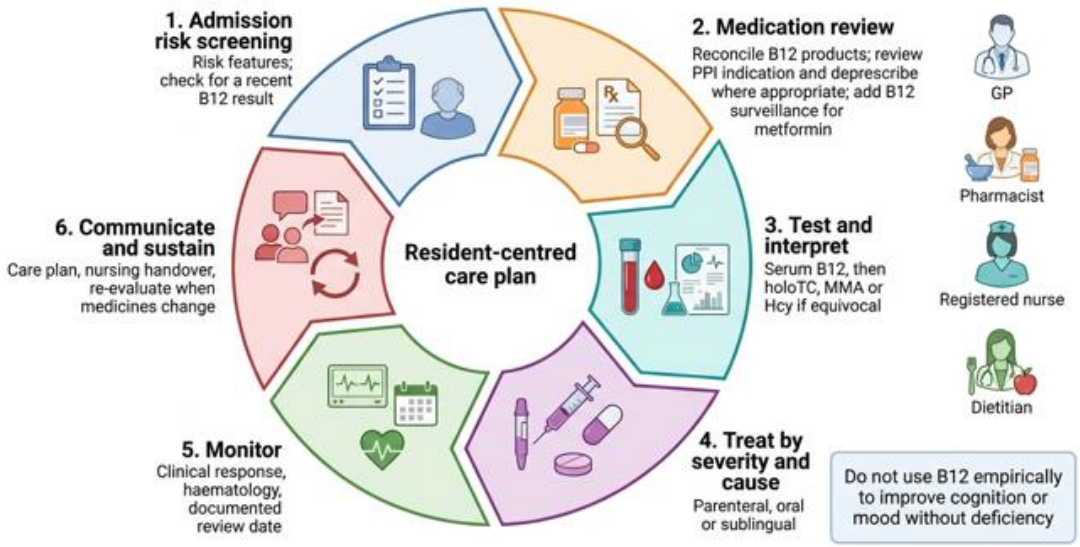

Figure 4. Six-step implementation and monitoring framework for B12 optimisation in residential aged care.

Sources: Adapted concept from references [1,3–5,8,9,12,16,17,19–21,26].

8. Evidence gaps and future directions

Important gaps remain. Few trials have enrolled RACF residents, so route comparisons rely on mixed populations and biochemical endpoints rather than neurological or functional outcomes. Optimal diagnostic thresholds and the role of holoTC or MMA in residents with renal impairment or inflammation are unresolved [1,19]. Screening intervals for people taking metformin are unsettled [8,9], and the effect of PPI deprescribing on B12 status is unclear [11,12]. Our targeted search identified few recent Australian RACF-specific prevalence studies, and cost-effectiveness data for admission screening are lacking.

9. Conclusion

B12 deficiency is a frequent condition among residents of RACFs, and frequently asymptomatic and treatable. To enhance outcomes, GPs should aim to test only those at increased risk, consider renal function and inflammation in interpreting test results, tailor antibiotic therapy to the level of risk and cause, and avoid giving cognitive supplements. Every deficiency workup should be accompanied by a review of medications, especially PPIs and metformin. There is a need for high-quality, RACF specific trials to establish the optimum route, dose and monitoring recommendations.

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Conflict of Interest Statement

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