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Multifactorial Determinants Guiding the Choice of Vitamin B12 Therapy

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Abstract

Vitamin B12 (cobalamin) deficiency is a common yet underdiagnosed condition with heterogeneous clinical presentations and diverse etiologies. Its management requires an individualized approach that considers not only the biochemical severity but also patient-specific and contextual factors influencing therapeutic response. This narrative review explores the personal, epidemiological, etiological, clinical, biological, and hematological determinants—as well as comorbidities—that guide the choice of vitamin B12 therapy, including formulation, dosage, route of administration, duration, and treatment regimen. The choice of vitamin B12 replacement therapy depends on multiple interrelated factors: patient age, comorbidities, severity of anemia or neurological involvement, and underlying etiology. Parenteral administration remains the standard in cases of severe deficiency, neurological symptoms, or malabsorption, while high-dose oral therapy is effective and safe in mild to moderate cases. Treatment duration and maintenance regimens must be tailored to disease chronicity and recurrence risk. Personalized approaches integrating biomarkers such as holotranscobalamin and methylmalonic acid, together with genetic and metabolic profiling, may further refine management strategies. Optimal management of vitamin B12 deficiency requires a personalized driven approach. Understanding individual determinants enables clinicians to select the most appropriate formulation, dosage, and regimen, improving therapeutic efficacy, patient adherence, and long-term outcomes.

Keywords: Vitamin B12; Cobalamin; Deficiency; Treatment; Personalized medicine; Etiology; Hematology; Neurology; Clinical management.

Introduction

Vitamin B12 (cobalamin) deficiency represents a frequent yet heterogeneous condition influenced by multiple determinants—genetic, metabolic, environmental, and individual. Its prevalence rises with age and is particularly high among vegetarians, older adults, and patients with gastrointestinal disorders or those receiving long-term metformin or proton pump inhibitor therapy [1,2]. The underlying etiologies encompass pernicious anemia, food-cobalamin malabsorption, dietary insufficiency, and iatrogenic or post-surgical causes [3]. Clinically, vitamin B12 deficiency exhibits a broad and variable spectrum, ranging from asymptomatic biochemical abnormalities to overt hematological, neurological, and psychiatric disorders [4]. This heterogeneity underscores the necessity of a personalized therapeutic approach—one that integrates biological and clinical parameters with personal determinants such as medical history, comorbidities, lifestyle, dietary practices, and psychological or behavioral profiles. These individual factors often influence treatment adherence, tolerance, and ultimately therapeutic outcomes.

From a biochemical standpoint, serum cobalamin, holotranscobalamin, Methylmalonic Acid (MMA), and homocysteine remain the cornerstone biomarkers for diagnosis and therapeutic monitoring [1,5]. However, each marker has limitations that must be interpreted in the context of comorbid conditions and metabolic status.

Therapeutically, the choice of vitamin B12 formulation—cyanocobalamin, hydroxocobalamin, methylcobalamin, or adenosylcobalamin—along with dosage, route of administration (oral, intramuscular, sublingual, or intranasal), and treatment duration should be guided by the underlying etiology, severity of deficiency, absorption capacity, comorbidities, and patient preferences. Randomized controlled trials have demonstrated that high-dose oral therapy (1,000-2,000 µg/day) can be as ef-

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fective as intramuscular injection in many patients with intact absorption [3,6,7].

Importantly, therapeutic decisions should also consider safety, efficacy, and individual response. For instance, intramuscular administration ensures rapid correction in severe deficiency or neurological involvement but may be less acceptable to needle-averse patients or those on anticoagulants. Conversely, oral and sublingual routes improve convenience and adherence, particularly in long-term maintenance therapy, provided absorption mechanisms are preserved.

In this review, we explore the epidemiological, clinical, biochemical, molecular, and therapeutic determinants that shape the selection of optimal cobalamin replacement strategies. Emphasis is placed on a personalized, patient-centered approach, integrating medical, biological, and behavioral factors to maximize treatment efficacy, ensure safety, and enhance long-term adherence in individuals with vitamin B12 deficiency.

Epidemiological and etiological determinants

Vitamin B12 deficiency is a global health concern affecting populations across all age groups, though prevalence varies widely depending on dietary habits, geographic region, and socioeconomic conditions. In high-income countries, prevalence ranges from 5% to 20% among adults, whereas in low- and middle-income settings—particularly South Asia and Africa—it may exceed 40%, especially among women of reproductive age [8,9]. Age-related decline in gastric acid secretion, frequent use of acid-suppressive medications, and intestinal disorders such as celiac disease or inflammatory bowel disease contribute significantly to this burden [2].

The etiologies of vitamin B12 deficiency are multifactorial. Autoimmune pernicious anemia (Biermer's disease) remains one of the leading causes in Western populations, characterized by intrinsic factor antibodies and associated with immune atrophic gastritis [10]. Food-cobalamin malabsorption is another highly prevalent cause, resulting from gastric atrophy, long-term use of metformin or proton-pump inhibitors, or *Helicobacter pylori* infection [11-13]. Nutritional deficiency is frequent among strict vegetarians, vegans, and individuals with restrictive or unbalanced diets [13]. Surgical causes—particularly bariatric procedures—can also impair absorption and lead to long-term dependency on supplementation [14].

Genetic and metabolic factors further contribute to the heterogeneity of B12 deficiency. Mutations in genes encoding cobalamin transport or intracellular processing proteins—such as TCN2, MTR, MMACHC, and CUBAM—can lead to inherited or functional forms of cobalamin deficiency [5]. Likewise, interactions between folate and cobalamin metabolism, notably in carriers of MTHFR polymorphisms, may exacerbate metabolic disturbances and clinical manifestations [15].

Together, these determinants (Table 1) emphasize that vitamin B12 deficiency is not a single disease but a syndrome of diverse origins, requiring individualized diagnostic and therapeutic strategies that integrate personal, epidemiological, and etiological factors. In this context, the choice of vitamin B12 treatment—including formulation, dosage, route of administration, duration, and therapeutic regimen—must account for these determinants to ensure optimal safety, efficacy, and clinical response in each patient.

Table 1: Personalized therapeutic considerations and determinants of B12 treatment.

Determinant	Considerations	Impact on therapy choice
Age	Older adults, physiological decline in gastric acid, comorbidities	May require parenteral therapy; increased monitoring; adherence support
Etiology of deficiency	Pernicious anemia, malabsorption, dietary, post-surgical	Determines formulation (hydroxocobalamin vs cyanocobalamin), route (oral vs parenteral)
Hematological severity	Macrocytosis, anemia, cytopenias	Guides urgency, initial dosage, frequency
Neurological involvement	Paresthesia, gait disturbance, subacute combined degeneration	Favors rapid parenteral correction; higher doses
Comorbidities	CKD, COPD, heart failure, iron deficiency, autoimmune disorders	May mask lab markers; influence route, dose, monitoring
Medication use	Metformin, PPIs, H2 blockers, antiplatelets	Can impair absorption; may require parenteral or higher oral doses
Psychosocial factors	Needle phobia, anxiety, cognitive status, adherence behavior	Oral/sublingual preferred for needle phobia; supervised therapy for impaired patients
Allergic history	Reaction to cobalamin or excipients	Formulation selection, possible allergist referral
Patient preferences & lifestyle	Oral vs injectable, frequency convenience	Improves adherence, satisfaction, long-term outcomes

Clinical, biological, and hematological determinants

Vitamin B12 deficiency exhibits a remarkably heterogeneous clinical spectrum, ranging from subtle, nonspecific symptoms to severe hematological and neurological complications. This variability reflects the complex interplay between the duration and severity of deficiency, underlying etiology, comorbid conditions, and individual host factors such as age, genetic background, and personal characteristics [1,4].

Hematological manifestations are among the earliest and most recognized features. Megaloblastic anemia remains the classic presentation, characterized by macrocytosis, hypersegmented neutrophils, and ineffective erythropoiesis. However, anemia may be absent in up to one-third of patients, particularly in early or subclinical deficiency [16]. Peripheral blood findings often include macrocytosis (MCV>100 fL), anisopoikilocytosis, and hypersegmented neutrophils, although these may be masked by concomitant microcytic conditions such as iron deficiency or thalassemia. Bone marrow morphology, when assessed, typically demonstrates hypercellularity, giant metamyelocytes, and megaloblastic erythropoiesis, though such features may be absent in mild cases. Elevated Lactate Dehydrogenase (LDH), increased indirect bilirubin, and decreased

haptoglobin levels further indicate intramedullary hemolysis due to ineffective erythropoiesis [16]. Cytopenias beyond anemia, including leukopenia and thrombocytopenia, may also occur, occasionally mimicking bone marrow failure syndromes such as myelodysplastic syndromes; rapid hematologic recovery following cobalamin replacement typically confirms the diagnosis [1,16].

Neurological and neuropsychiatric symptoms may precede hematologic manifestations or occur in isolation. They include paresthesia, gait disturbances, memory loss, cognitive impairment, mood disorders, and, in severe cases, subacute combined degeneration of the spinal cord. These deficits result from demyelination secondary to impaired methylation and accumulation of neurotoxic metabolites such as methylmalonic acid and homocysteine. Prompt recognition and treatment are critical, as neurological damage may become irreversible if intervention is delayed [5,17].

Biochemical markers play a central role in diagnosis and in guiding therapeutic decisions. Serum cobalamin remains the most widely used screening test, but its sensitivity is limited, particularly in functional deficiency. Holotranscobalamin (holoTC), the active transport form of cobalamin, better reflects cellular bioavailability, while elevated plasma Methylmalonic Acid (MMA) and homocysteine levels indicate intracellular deficiency [18]. These biomarkers also serve to monitor treatment efficacy and metabolic recovery.

However, the clinical and biological heterogeneity of vitamin B12 deficiency extends beyond diagnostic complexity to therapeutic response (Table 1). Variability in hematologic recovery or manifestation, neurological improvement—also presentation, and biomarker normalization depends on multiple determinants—such as the underlying cause of deficiency, age, comorbidities, inflammation, and concurrent medication use.

Comorbidities and systemic modifiers

Comorbidities significantly influence both the clinical expression and the therapeutic response in vitamin B12 deficiency, often complicating diagnosis and management decisions. Age is one of the most decisive determinants: older adults are particularly vulnerable owing to the physiological decline in gastric acid secretion, frequent atrophic gastritis, and polypharmacy—all contributing to impaired cobalamin absorption. Pernicious anemia remain the leading causes of severe deficiency in Western populations and frequently coexist with autoimmune thyroid disease, Sjögren syndrome, type 1 diabetes, and vitiligo [19,20].

Gastrointestinal disorders—including atrophic gastritis, Helicobacter pylori infection, celiac disease, inflammatory bowel disease, and post-bariatric surgery—further interfere with vitamin B12 absorption through mucosal injury, bacterial overgrowth, or loss of intrinsic factor production. These conditions often necessitate parenteral rather than oral supplementation to ensure adequate repletion [1-3].

Metabolic and systemic conditions such as chronic kidney disease, Chronic Obstructive Pulmonary Disease (COPD), and heart failure can alter cobalamin metabolism via chronic inflammation, tissue hypoxia, or dysregulated transport proteins. Moreover, concurrent iron deficiency may obscure macrocytosis, delaying recognition of cobalamin deficiency and appropriate treatment initiation [18].

Medication exposure represents another pivotal determinant. Long-term therapy with metformin, proton pump inhibitors, H_2 receptor antagonists, and certain antiepileptic or antiplatelet agents has been shown to impair vitamin B12 absorption or utilization, sometimes leading to functional deficiency despite normal serum concentrations [12,13]. Chronic inflammatory states further confound biochemical monitoring by increasing homocysteine levels and altering holotranscobalamin kinetics.

The coexistence of multiple comorbidities and concurrent medication use (Table 1) results in heterogeneous therapeutic responses. Some patients experience incomplete hematologic recovery or persistently abnormal biomarkers despite adequate supplementation. Consequently, the choice of vitamin B12 formulation, route of administration, dosage, and treatment duration must be carefully individualized according to etiology, comorbidity burden, age, tolerance, and expected adherence. Such a personalized, integrative approach optimizes treatment efficacy, reduces relapse risk, and minimizes the likelihood of irreversible neurological damage.

Patient characteristics and personalized therapeutic considerations

Beyond biological and etiological determinants, individual patient characteristics and personality traits play a pivotal role in determining both the choice and success of vitamin B12 therapy. Treatment adherence, tolerance, and clinical outcomes are influenced not only by physiological parameters but also by behavioral, cognitive, and psychological dimensions—underscoring the importance of a personalized and holistic therapeutic approach [1,21].

Adherence and patient behavior represent central determinants of therapeutic efficacy. Some patients display high motivation and self-discipline, ensuring consistent supplementation and follow-up, while others demonstrate irregular compliance due to low perceived benefit, lack of understanding, or lifestyle constraints. Early identification of these behavioral patterns enables clinicians to tailor communication, monitoring intensity, and follow-up frequency—thereby reducing the risk of relapse or incomplete biochemical correction [1].

Psychological and personality traits also shape treatment preferences and tolerance. Individuals with needle phobia or anxiety disorders may experience significant distress with intramuscular injections. For such patients, high-dose oral or sublingual cobalamin offers a well-tolerated and equally effective alternative, provided gastrointestinal absorption is adequate [2,3,22]. Conversely, patients with obsessive or perfectionist tendencies may prefer parenteral administration due to its perceived reliability, medical supervision, or reassurance of adherence control—even when oral therapy could be clinically sufficient.

Comorbidities and concurrent medications must also guide therapeutic decisions. Patients receiving anticoagulant or antiplatelet therapy face a higher risk of injection-site hematoma, favoring oral or intranasal administration routes [3]. Similarly, individuals with a history of hypersensitivity reactions to cobalamin preparations—particularly to cobalt or preservatives such as benzyl alcohol—require careful formulation selection, sometimes necessitating allergological evaluation).

Functional and cognitive status further influence therapeutic planning. Elderly or cognitively impaired patients may have

difficulty maintaining oral adherence, making supervised or parenteral regimens more appropriate. In contrast, younger, health-literate, and motivated individuals can often manage self-administered oral therapy, particularly when biochemical monitoring is feasible and reliable [3,20].

A patient-centered strategy thus integrates both medical and psychosocial determinants—biological efficacy, safety profile, behavioral factors, and psychological comfort (Table 1). By considering personal preferences, personality traits, comorbidities, and potential risks, clinicians can optimize adherence, clinical response, and quality of life. This individualized framework exemplifies the evolution of modern precision medicine, in which management of vitamin B12 deficiency extends beyond correcting biochemical abnormalities to addressing the patient's broader clinical, emotional, and lifestyle context.

Therapeutic modalities and personalized decision-making

Therapeutic response depends on deficiency severity, administration route, comorbidities, and genetic background. Hematologic recovery is generally rapid, while neurological improvement may take months and remains incomplete in 20–30% of delayed cases [23]. Persistent metabolic abnormalities (MMA, homocysteine) indicate suboptimal response. Hence, in practice, clinical and biochemical monitoring are essential to adjust therapy over time.

The choice of vitamin B12 therapy must be individualized, taking into account the etiology of deficiency, severity of clinical and biochemical manifestations, comorbidities, and patient-specific factors such as age, cognitive status, adherence potential, and personality traits [1,3] (Table 2). Effective management requires careful selection of formulation, dosage, route of administration, treatment duration, and regimen, all of which can significantly impact therapeutic outcomes and patient satisfaction.

Table 2: Personalized treatment choice for vitamin B12 deficiency.

Determinant	Therapeutic consideration	Impact of treatment choice
Etiology	Pernicious anemia, food-cobalamin malabsorption, surgical causes	Parenteral or high-dose oral therapy may be required for malabsorption; oral therapy sufficient for dietary deficiency
Age	Older adults with gastric atrophy or polypharmacy	IM injections often preferred due to impaired absorption; oral therapy may be less reliable
Hematological status	Presence of severe anemia or cytopenias	Rapid correction may require parenteral therapy; mild deficiency may respond to oral supplementation
Neurological involvement	Peripheral neuropathy, cognitive impairment, subacute combined degeneration	Early parenteral therapy recommended for neurological protection; delayed treatment risks irreversible damage
Comorbidities	CKD, GI disorders, iron deficiency, chronic inflammation	Malabsorption conditions favor IM therapy; oral therapy may suffice in absence of absorption defects
Medication exposure	Long-term metformin, PPIs, H_2 blockers, antiepileptics	IM or high-dose oral therapy preferred; monitor serum B12 and metabolites during treatment
Behavioral/psychological factors	Needle phobia, adherence, cognitive ability	Oral or sublingual therapy preferred for needle-sensitive or cognitively intact patients; supervised IM for those with poor adherence
Formulation tolerance	Hypersensitivity to preservatives or cobalamin preparations	Selection of preservative-free formulations; consider allergology consult if necessary
Lifestyle & personal preference	Willingness to self-administer, convenience	Oral therapy increases autonomy and adherence; parenteral therapy may offer reassurance in highly anxious or perfectionist individuals
Monitoring feasibility	Access to lab testing for cobalamin, holoTC, MMA	Oral therapy requires reliable follow-up; IM therapy may be safer in settings with limited monitoring

Cobalamin is available as cyanocobalamin, hydroxocobalamin, methylcobalamin, or adenosylcobalamin. Cyanocobalamin remains widely used due to its cost-effectiveness and stability, whereas hydroxocobalamin offers superior tissue retention and is preferred for severe or autoimmune forms [1,3]. Bioactive coenzyme forms such as methylcobalamin or adenosylcobalamin may have theoretical neurological benefits, though robust evidence remains limited [13,24].

Intramuscular injections are traditionally used in cases of severe deficiency, pernicious anemia, or malabsorption syndromes, ensuring rapid correction of hematologic and neurologic deficits [6]. High-dose oral therapy (typically 1,000-2,000 µg/day) is effective in patients with intact absorption capacity and is particularly advantageous for needle-phobic or non-compliant individuals [3,22]. Sublingual and intranasal formulations offer additional alternatives, improving convenience and adherence, especially in ambulatory or elderly populations.

Historically, parenteral replacement was considered essential. However, randomized controlled trials demonstrated comparable efficacy between oral and intramuscular therapy for most non-pernicious etiologies [25]. Oral methylcobalamin or cyanocobalamin (≥1,000 µg/day) normalizes serum and metabolic markers in >90% of mild cases [26]. In contrast, parenteral therapy remains mandatory for intrinsic-factor deficiency, severe neurological involvement, or profound malabsorption. Sublingual and intranasal forms serve as maintenance options. A pragmatic algorithm recommends oral therapy for mild nutritional forms, IM therapy for autoimmune or neurologic cases, and periodic reevaluation based on biological response.

Initial replacement strategies vary depending on severity: severe deficiency or neurological involvement often requires daily parenteral administration for 1-2 weeks, followed by weekly injections or high-dose oral therapy until biochemical and clinical normalization [3,13]. Lifelong therapy is warranted for irreversible causes such as pernicious anemia or post-gastrectomy states, whereas shorter courses (3-6 months) suffice for nutritional or iatrogenic deficiencies once the cause is corrected.

As we see below, several cobalamin formulations are available (Table 3). summarizes their main characteristics, indications, and dosing strategies.

Table 3: Therapeutic molecules, doses, and routes of administration.

Molecule / Formulation	Typical indication	Recommended dose and route	Advantages	Limitations
Hydroxocobalamin (IM)	Pernicious anemia, severe neuropsychological deficiency	1 mg IM every 2-3 days × 2 weeks, then monthly	Long tissue half-life; strong binding	Requires injections; rare hypersensitivity
Cyanocobalamin (IM/PO)	Nutritional deficiency, mild malabsorption, food-cobalamin malabsorption	1 mg IM weekly × 1 month → monthly; 1-2 mg/day PO	Inexpensive; stable oral absorption	Shorter retention; less active in IF deficiency
Methylcobalamin (PO/ sublingual)	Neurological symptoms, diabetic neuropathy	1500-2000 µg/day PO	Neuroprotective; convenient oral form	Cost; limited trial data
Adenosylcobalamin (PO)	Mitochondrial/metabolic disorders	1-3 mg/day PO	Active coenzyme form	Limited stability; sparse data
Intranasal cobalamin	Maintenance or poor adherence	500 µg weekly spray	Bypasses GI tract; noninvasive	Unsuitable for severe deficiency

Clinical and biochemical monitoring is essential—reticulocyte counts rise within 1-2 weeks, hematologic normalization follows within 2 months, and neurological recovery may require several months [3,13]. Persistent abnormalities suggest poor adherence, continued malabsorption, or coexisting deficiencies such as iron or folate [22].

Treatment duration and regimen must be personalized. Oral therapy requires patient education and regular biochemical follow-up (serum B12, holoTC, MMA, and homocysteine) to ensure efficacy [3,13,22]. Patients with comorbidities such as chronic kidney disease, gastrointestinal malabsorption, or concurrent medications (e.g., metformin, proton pump inhibitors, anticoagulants) may require parenteral therapy or dose adjustments to achieve therapeutic goals. Allergic history or sensitivity to excipients may also dictate formulation choice.

Adherence, personality traits, and psychosocial context influence therapy selection. Needle-phobic or anxious patients may prefer non-injectable routes, whereas highly adherent or perfectionist individuals may favor supervised parenteral therapy. Elderly or cognitively impaired patients may require caregiver-assisted administration. Incorporating these factors enhances compliance, optimizes clinical outcomes, and reflects a personalized medicine approach [3,13].

Consensus via delphi methodology on vitamin B12 therapeutic choices

To identify expert consensus on determinants influencing the choice of vitamin B12 therapy, a Delphi survey was conducted among 18 participants comprising clinicians (n=12), researchers (n=4), and patients (n=2) representatives from the *CARE B12* group at the University Hospital of Strasbourg (France) (*personal not-published data*). The objective was to systematically evaluate factors guiding therapy selection, including formulation, route of administration, dosage, and treatment duration, and to integrate both clinical evidence and patient perspectives.

The Delphi process followed three iterative rounds of structured questionnaires. Participants rated the importance of various determinants—including etiology (e.g., pernicious anemia, malabsorption, dietary deficiency), biochemical severity (serum B12, holotranscobalamin, methylmalonic acid, homocysteine), hematological and neurological status, comorbidities, patient adherence, needle tolerance, cognitive function, and psychosocial factors—on a 5-point Likert scale. Items achieving ≥75% agreement were considered consensus recommendations.

Results demonstrated high agreement on several key points:

- Formulation choice should be guided by absorption capacity, patient preference, and underlying etiology. Parenteral hydroxocobalamin or cyanocobalamin is preferred in severe deficiency or malabsorption, whereas high-dose oral or sublingual therapy is acceptable for patients with intact absorption or needle aversion.
- Route of administration must account for patient-specific factors, including anxiety, phobia, cognitive ability, and adherence potential.
- Dosage and duration should be individualized based on severity, neurological involvement, comorbidities, and biochemical monitoring. Maintenance therapy is lifelong in autoimmune or irreversible etiologies, with flexible regimens in dietary or transient deficiencies.
- Patient-centered considerations, including psychosocial context and behavioral traits, were strongly emphasized by both clinicians and patient representatives as determinants of long-term success.

The Delphi process facilitated multidimensional integration of clinical, biochemical, hematological, and psychosocial factors, yielding a structured framework for personalized vitamin B12 therapy. This consensus approach underscores the value of combining expert knowledge with patient input to optimize treatment decisions and adherence in real-world practice.

Conclusion and future perspectives

Vitamin B12 deficiency is a multifactorial syndrome characterized by heterogeneous clinical, hematological, and biochemical manifestations. Its etiology spans autoimmune, gastrointestinal, nutritional, genetic, and iatrogenic causes, while individual patient characteristics—including age, comorbidities, personality traits, and behavioral factors—profoundly influence both presentation and treatment response [1,3].

Effective management requires a personalized medicine approach, integrating laboratory biomarkers (serum B12, holotranscobalamin, methylmalonic acid, homocysteine), hematologic assessment, and clinical evaluation with patient-centered considerations such as adherence, needle tolerance, and psychosocial context. Formulation choice, dosage, route of administration, treatment duration, and monitoring frequency should be tailored to the individual's etiology, comorbid conditions, and lifestyle, ensuring both therapeutic efficacy and neurological preservation.

Emerging evidence highlights the need for precision-guided strategies that combine biochemical, genetic, and behavioral profiling. Future research should focus on: 1) identifying predictors of response to different cobalamin formulations, 2) optimizing dosing regimens for high-risk populations, 3) evaluating long-term outcomes of personalized therapy, and 4) integrating digital adherence tools and patient education into routine care.

Integration of molecular and clinical determinants heralds an era of personalized cobalamin therapy. Pharmacogenomic profiling may guide molecule and dose selection, while artificial-intelligence models combining clinical, biochemical, and metabolomic data are under development to predict treatment response. Population-level fortification and early biomarker-based screening could further reduce subclinical deficiency. Future clinical trials should compare coenzyme forms (methyl- and adenosylcobalamin) for neurocognitive protection and explore optimal strategies for individualized long-term management.

In summary, vitamin B12 deficiency is not a uniform disorder but a syndrome requiring individualized evaluation and therapy. A patient-centered, evidence-based, and precision-guided approach offers the greatest potential to prevent hematologic and neurologic complications, enhance adherence, and improve long-term health outcomes, illustrating the transformative role of personalized medicine in routine clinical practice.

Declarations

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