

Aevum BioAI Cognitive Health and Longevity Scores: Scientific Rationale and Development of a Multidomain Biomarker Framework for Precision Healthy Ageing

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Abstract

Background: Population ageing is increasing the prevalence of cognitive impairment, cardiovascular disease, metabolic dysfunction, frailty and multimorbidity. Conventional healthcare is predominantly organised around the diagnosis and treatment of established disease, whereas contemporary geroscience increasingly emphasises earlier identification of biological vulnerability and preservation of healthspan. Ageing is multidimensional and involves interacting inflammatory, metabolic, vascular, nutritional, endocrine, neurological and lifestyle determinants. No single biomarker adequately captures these processes.

Objective: This review describes the scientific rationale, scoring architecture and proposed clinical applications of two complementary artificial-intelligence-assisted health-assessment systems developed by Aevum BioAI: the Aevum BioAI Cognitive Health Score (ABCHS) and the Aevum BioAI Longevity Score (ABLS).

Methods: A narrative review was conducted integrating evidence from geroscience, cognitive ageing, dementia prevention, cardiovascular medicine, metabolic health, biological-age research and lifestyle medicine. Particular attention was given to biomarkers incorporated into the current Aevum BioAI scoring algorithms. The scoring structure was derived from the current ABCHS and ABLS clinical reports.

Results: The ABCHS is a 40-point risk-stratification system, in which increasing scores represent increasing biological risk associated with future cognitive decline. It incorporates age, haematological variables, inflammation, renal and hepatic function, electrolytes, thyroid function, vitamin D, urinary beta-amyloid status and family history. The current risk bands are low (0–7), mild (8–15), moderate (16–23), high (24–31) and very high (32–40). The ABLs uses a complementary 100-point biological-resilience model, in which higher scores indicate more favourable biological and lifestyle profiles. Six domains contribute to the overall score: inflammation (20 points), metabolic health (20), organ function (20), nutrition and endocrine health (15), brain health (15), and lifestyle and clinical factors (10).

Conclusions: The Aevum BioAI framework represents a clinically accessible approach to integrating multidisystem biological and behavioral information into interpretable health scores. Its conceptual basis is consistent with geroscience, cardiovascular-health frameworks, multidomain dementia prevention and biological-age research. However, ABCHS and ABLs should currently be considered investigational risk-stratification and biological-health tools rather than diagnostic or prognostic instruments. Prospective longitudinal validation, external validation, calibration and comparison against established clinical models are required before individual disease or lifespan prediction can be claimed.

Keywords

Aevum BioAI; Artificial intelligence; Longevity; Cognitive health; Biomarkers; Biological ageing; Healthspan; Dementia prevention; Precision medicine; Risk stratification.

Introduction

Life expectancy has increased markedly over the past century, but improvements in lifespan have not necessarily produced proportional increases in healthy lifespan. Longer survival has therefore been accompanied by increasing prevalence of cardiovascular disease, diabetes, chronic kidney disease, neurodegeneration, frailty and multimorbidity.

The distinction between lifespan and healthspan is increasingly important. Lifespan represents the duration of life, whereas healthspan reflects the period during which an individual retains functional, cognitive and physiological capacity.

The World Health Organization conceptualizes healthy ageing around the maintenance of functional ability and intrinsic capacity rather than simply the absence of diagnosed disease [1]. Geroscience similarly proposes that apparently distinct chronic diseases frequently arise from shared biological mechanisms of ageing.

The expanded hallmarks of ageing describe 12 interacting processes: genomic instability, telomere attrition, epigenetic alteration, loss of proteostasis, disabled macro autophagy, deregulated nutrient sensing, mitochondrial dysfunction, cellular senescence, stem-cell exhaustion, altered intercellular communication, chronic inflammation and dysbiosis [2].

These mechanisms operate across multiple organ systems. Consequently, ageing cannot be adequately represented by chronological age or a single laboratory measurement.

Cognitive decline illustrates this multidimensional biology particularly well. Dementia risk reflects interactions among age, genetic susceptibility, vascular disease, metabolic health, inflammation, sensory function and lifestyle. The 2024 Lancet Commission emphasized the potential importance of modifiable risk factors across the life course and reinforced the concept that dementia prevention begins considerably before overt cognitive impairment develops [3].

This creates a rationale for systems capable of combining multiple clinical signals into interpretable measures of health risk. The Aevum BioAI Cognitive Health Score (ABCHS) and Aevum BioAI Longevity Score (ABLS) were developed within this paradigm.

The two systems assess related but different dimensions:

- **ABCHS:** biological vulnerability associated with cognitive decline.
- **ABLS:** systemic biological resilience and modifiable determinants of healthy longevity.

Rather than attempting to replace clinical assessment, their intended function is to identify abnormalities, stratify biological risk, facilitate preventive intervention and monitor change longitudinally.

Conceptual Architecture of Aevum BioAI

The underlying premise of Aevum BioAI is that an individual's health trajectory is more informative than chronological age alone. Two individuals aged 60 years may have profoundly different inflammatory profiles, metabolic health, renal reserve, cardiovascular risk, physical activity, sleep quality and neurological biomarkers.

A multidimensional scoring model attempts to capture part of this heterogeneity. Importantly, the scoring directions of ABCHS and ABLS are opposite.

ABCHS

Higher score = greater biological cognitive-health risk.

Range = 0–40 points.

ABLS

Higher score = more favourable biological resilience.

Range = 0–100 points.

The ABCHS report describes the score as integrating routine laboratory biomarkers with inflammatory, metabolic and neurodegenerative markers while explicitly stating that it does not diagnose Alzheimer's disease or dementia.

Likewise, the ABLS report describes the longevity score as an integration of inflammatory, metabolic, organ-function, nutritional, brain-health and lifestyle biomarkers. Importantly, the report states that it estimates healthy ageing and biological resilience rather than predicting actual lifespan. This distinction is critical scientifically.

Aevum BioAI Cognitive Health Score

Scoring architecture

The current ABCHS contains ten biological domains:

Domain	Maximum risk score
Age	3
Haematology	8
Inflammation	3
Kidney function	3
Liver function	3
Electrolytes	2
Thyroid function	3
Vitamin D	3
Neurodegeneration	8
Family history	4
Maximum ABCHS	40

This structure is directly reflected in the current report.

The score therefore gives relatively greater weighting to haematological/systemic markers and neurodegenerative signals, while retaining smaller contributions from systemic organ-function and potentially reversible abnormalities.

ABCHS Risk Stratification

The current ABCHS categories individuals into five bands:

Score	Risk classification
0–7	Low
8–15	Mild
16–23	Moderate
24–31	High
32–40	Very High

The clinical descriptions become progressively more concerned with the number and severity of biomarker abnormalities. A score of 0–7 indicates no major abnormalities associated with increased cognitive-health risk, whereas scores of 32–40 represent an extensive burden of biological abnormalities associated with cognitive impairment.

These boundaries should currently be regarded as Aevum algorithmic classification thresholds, rather

than epidemiologically validated probabilities of future dementia.

Age Domain: Maximum 3 Points

Chronological age remains the most powerful non-modifiable population-level risk factor for dementia.

Nevertheless, chronological ageing demonstrates substantial biological heterogeneity. Some individuals retain excellent cognitive and functional capacity into advanced age, while others develop vascular, metabolic or neurodegenerative abnormalities decades earlier.

Assigning age only 3 of 40 ABCHS points prevents chronological age from overwhelming potentially modifiable biological information.

This approach is broadly consistent with contemporary geroscience, where chronological age establishes background risk while biological markers help characterise heterogeneity in ageing [2-4].

Haematological Domain: Maximum 8 Points

The ABCHS haematological component contains:

Biomarker	Maximum points
Haemoglobin	2
MCV	1
RDW	2
NLR	3
Total	8

Haemoglobin

Anaemia can influence cognitive function through impaired oxygen delivery, systemic disease and vascular mechanisms. Observational evidence has associated anaemia with increased dementia risk [5-6].

However, haemoglobin is nonspecific. Its principal value within ABCHS is therefore as an indicator of systemic physiological status rather than neurodegeneration.

Mean corpuscular volume

Abnormal MCV may suggest nutritional deficiency, haematological disease, hepatic disease, alcohol exposure or other systemic abnormalities. Its relatively small weighting appropriately reflects its nonspecific nature.

Red-cell distribution width

RDW reflects heterogeneity in erythrocyte size but is increasingly recognised as a marker associated with systemic inflammation, frailty, cardiovascular disease and mortality [7]. Its inclusion may therefore contribute information concerning systemic biological resilience.

Neutrophil-to-lymphocyte ratio

NLR provides an inexpensive measure of peripheral inflammatory balance. A 2024 systematic review and meta-analysis involving 1,309 individuals with Alzheimer's disease, 1,929 with mild cognitive impairment and 2,064 healthy controls found progressively higher mean NLR from healthy controls to MCI and Alzheimer's disease [8].

Recent evidence continues to investigate peripheral immune indices as potential correlates of cognitive disease, although they remain nonspecific and should not be interpreted diagnostically.

Inflammation Domain: Maximum 3 Points

High-sensitivity CRP is used within the ABCHS inflammatory component. Chronic systemic inflammation represents one of the expanded hallmarks of ageing.

Inflammatory processes potentially influence cognitive health through endothelial dysfunction, cerebrovascular injury, insulin resistance, microglial activation and altered blood-brain-barrier integrity.

Meta-analysis of prospective population studies found that higher CRP was associated with increased all-cause dementia risk, although inflammatory markers were considerably less specific for Alzheimer's disease [9]. This distinction supports the ABCHS approach: CRP should serve as a risk modifier, not an Alzheimer's biomarker.

More recent systematic evidence in 2026 continues to support associations between inflammatory biomarkers and dementia while emphasising substantial biological heterogeneity [10].

Renal Function: Maximum 3 Points

Renal health is assessed through:

- eGFR: maximum 2 points;
- creatinine: maximum 1 point.

Kidney and brain health share several pathological pathways, including small-vessel injury, diabetes, hypertension, inflammation and endothelial dysfunction.

A 2025 systematic review and meta-analysis of 17 studies involving 32,141 participants demonstrated increasing cognitive-impairment prevalence with declining renal function: approximately 10% among participants with eGFR ≥ 60 , 47.3% with eGFR 30–60 and 60.6% below 30 mL/min/1.73 m² [11]. These associations provide support for incorporating renal reserve into multidomain cognitive-risk assessment.

Hepatic Function: Maximum 3 Points

The liver component includes:

Variable	Maximum points
ALT/AST/GGT	2

Albumin	1
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Hepatic biomarkers do not directly measure neurodegeneration. They provide information concerning metabolic health, inflammation, hepatic synthetic function and alcohol or medication exposure.

Metabolic dysfunction-associated steatotic liver disease has been associated with cognitive impairment.

A 2026 systematic review and meta-analysis of 13 studies involving 15,545 participants found significantly poorer cognitive performance among individuals with MASLD; higher BMI and increased AST, ALT and GGT were important moderators [12]. This evidence illustrates why hepatic status may add systemic context to cognitive-health assessment.

Electrolytes: Maximum 2 Points

Sodium and calcium each contribute up to one point. Electrolyte abnormalities represent potentially reversible causes of neurological dysfunction.

Hyponatraemia can produce attention impairment, confusion, falls, seizures and altered consciousness, while abnormalities in calcium homeostasis may influence neurological and neuromuscular function [13].

Their inclusion therefore improves clinical safety by recognizing systemic disturbances capable of mimicking or exacerbating cognitive abnormalities.

Thyroid Function: Maximum 3 Points

TSH with or without free T4 contributes up to three points. Thyroid hormones influence cerebral metabolism, cardiovascular function and neurotransmission. Both hyperthyroidism and hypothyroidism can present with neuropsychiatric and cognitive manifestations.

A 2023 systematic review and meta-analysis found hypothyroidism significantly more prevalent among individuals with Alzheimer's disease than controls, although the causal relationship remains uncertain [14].

Thyroid assessment is especially useful because dysfunction can represent a treatable contributor to cognitive symptoms.

Vitamin D: Maximum 3 Points

A 2024 meta-analysis of prospective studies found vitamin D deficiency associated with approximately 42% greater dementia risk, 57% greater Alzheimer's disease risk and 34% greater cognitive-impairment risk [15].

However, observational associations cannot prove causation. A separate meta-analysis of 24 randomised trials involving 7,557 participants found a small improvement in global cognition with vitamin D supplementation, with larger effects observed among vitamin-D-deficient populations [16]. Vitamin D is therefore appropriately regarded as a modifiable health marker rather than a disease-specific biomarker.

Neurodegeneration Domain: Maximum 8 Points

The neurodegeneration component currently contains urinary beta-amyloid testing.

In the example report: Positive urine beta-amyloid = 8/8 risk points.

This is one of the highest-weighted ABCHS components. Amyloid- β pathology is central to the biological definition of Alzheimer's disease and can now be assessed through PET, cerebrospinal-fluid assays and increasingly blood biomarkers¹⁷⁻²⁰.

However, the evidence base for urinary beta-amyloid is substantially less mature. Therefore: a positive urinary beta-amyloid result should not be equated with Alzheimer's disease. Aevum's own report appropriately states that ABCHS is not a diagnostic test for Alzheimer's disease, dementia or other neurological disease.

This component should therefore be described in publications as an investigational neurodegenerative-risk marker pending analytical and clinical validation.

A particularly valuable validation study would compare urine results with:

- plasma p-tau₂₁₇;
- p-tau₁₈₁;
- A β ₄₂/A β ₄₀;
- GFAP;
- neurofilament light;
- amyloid PET; and
- longitudinal cognitive outcomes.

Family History: Maximum 4 Points

Family history contributes up to 10% of the ABCHS. Family history represents both inherited predisposition and shared environmental exposures. APOE ϵ 4 remains the most important common genetic susceptibility factor for sporadic late-onset Alzheimer's disease [21].

However, inherited susceptibility is probabilistic rather than deterministic. Future versions of ABCHS could investigate the incremental predictive value of APOE genotype or polygenic-risk scores compared with family history alone.

Aevum BioAI Longevity Score

The ABLS approaches ageing from the opposite direction. Whereas ABCHS awards increasing points for risk, ABLS awards higher points for biological resilience.

The total possible score is 100.

The ABLS combines six major domains.

ABLS domain	Maximum points	Weight
Inflammation	20	20%
Metabolic health	20	20%
Organ function	20	20%
Nutrition & endocrine	15	15%
Brain health	15	15%
Lifestyle & clinical factors	10	10%
Total	100	100%

ABLS Inflammation Score: 20 Points

The domain consists of:

- **hs-CRP: 8 points**
- **NLR: 6 points**
- **RDW: 6 points**

The example report demonstrates this architecture directly.

This combination attempts to capture chronic systemic inflammatory status through readily accessible measurements. The biological rationale corresponds to inflammageing, a persistent age-associated pro-inflammatory state associated with cardiovascular disease, metabolic disorders, sarcopenia, frailty and neurodegeneration [22].

Metabolic Health: 20 Points

The ABLS metabolic domain is particularly clinically actionable:

Parameter	Maximum score
HbA1c	8
LDL	2
HDL	2
Triglycerides	2
Total cholesterol	2
BMI/Waist	4
Total	20

The relatively high HbA1c weighting reflects the central importance of glycaemic health. Insulin resistance

and diabetes contribute to cardiovascular disease, chronic kidney disease, microvascular injury and premature mortality [23-24].

Adiposity, particularly central adiposity, is closely linked with metabolic disease and systemic inflammation. The inclusion of lipids, glycaemic status and adiposity also has conceptual similarities with the American Heart Association's Life's Essential 8, which integrates blood glucose, cholesterol, blood pressure, body weight and health behaviours into a multidimensional cardiovascular-health framework [25].

Organ Function: 20 Points

The ABLS organ-function domain consists of:

Parameter	Maximum score
eGFR	6
Creatinine	4
ALT/AST/GGT	6
Albumin	4
Total	20

Rather than considering renal and hepatic measurements purely as disease markers, ABLS treats preservation of organ function as an indicator of systemic biological resilience. This philosophy parallels biological-age models that integrate multiple organ-system biomarkers to distinguish biological ageing from chronological time.

Nutrition and Endocrine Health: 15 Points

The domain allocates:

- Vitamin D: 5 points
- Vitamin B12: 4 points
- TSH ± free T4: 6 points.

These variables were selected because nutritional and endocrine disturbances can influence multiple physiological systems while remaining potentially modifiable.

Vitamin B12 deficiency is particularly important because neurological manifestations can occur independently of severe anaemia [26]. Thyroid status affects cardiovascular, neurological and metabolic function, while vitamin D is associated with skeletal, immune and metabolic health.

Brain Health: 15 Points

The current domain contains:

Variable	Maximum
Urine beta-amyloid	10
Age	5
Total	15

The high weighting acknowledges the importance of neurological health to overall healthspan. However, as discussed above, urinary beta-amyloid requires prospective validation before being interpreted as an established measure of neurodegenerative disease burden.

Lifestyle and Clinical Factors: 10 Points

ABLS explicitly integrates behavior:

Factor	Maximum points
Smoking status	2
Blood pressure	2
Physical activity	2
Sleep quality	2
Alcohol	1
Perceived stress	1
Total	10

This is a particularly important aspect of the system because it connects measurement directly with intervention.

- **Smoking:** Smoking increases cardiovascular, oncological, respiratory and dementia risk [3,27].
- **Blood pressure:** Hypertension contributes substantially to stroke, cardiovascular disease, kidney disease and cognitive decline. Midlife hypertension is also recognised as a modifiable dementia-risk factor [3,28].
- **Physical activity:** Regular physical activity improves cardiorespiratory fitness, glucose regulation, cardiovascular health, muscle function and psychological wellbeing and is associated with reduced premature mortality [29].
- **Sleep:** Sleep duration and quality influence cardiometabolic function, immune regulation and cognitive health. Both inadequate and excessive sleep duration have been associated with adverse health outcomes [30,31].
- **Alcohol:** Alcohol-related risk is dose-dependent and varies by outcome. High or hazardous alcohol consumption increases hepatic, cardiovascular, cancer and neurological disease burden [32].
- **Stress:** Chronic psychological stress may influence autonomic regulation, inflammation, sleep and cardiovascular health [33].

ABLS Categories

The current scoring system divides ABLS into six categories:

ABLS	Classification
90–100	Exceptional Longevity Profile
80–89	Healthy Longevity
70–79	Good – Optimisation Recommended
60–69	Moderate Risk
50–59	High Risk
0–49	Very High Risk

These classifications are useful for communicating biological status. Nevertheless, the associated bands should presently be considered internal score categories rather than validated actuarial predictions.

This distinction is especially important regarding the "modelled lifespan ranges" appearing within the report. The report itself states that these are population score-band research estimates and not individual predictions of actual lifespan.

Comparison of ABCHS and ABLS

The two models measure different dimensions.

Feature	ABCHS	ABLS
Purpose	Cognitive-health risk	Biological resilience/healthy ageing
Range	0–40	0–100
Direction	Higher = worse	Higher = better
Main emphasis	Cognitive vulnerability	Multisystem resilience
Biomarkers	Biological/clinical	Biological + lifestyle
Neurodegeneration	Strong weighting	Incorporated within brain health
Lifestyle	Indirect	Explicit
Intended use	Risk stratification	Health optimisation
Diagnostic?	No	No
Longitudinal use	Yes	Yes

The most interesting clinical application may therefore arise from combining, rather than merging, both scores.

Proposed Aevum BioAI Phenotypes

A two-dimensional framework produces four broad health phenotypes.

Phenotype I: Low ABCHS + High ABLS

Cognitively favourable / biologically resilient

This represents the most favourable profile.

Phenotype II: High ABCHS + High ABLS

Cognitive vulnerability despite systemic resilience

This phenotype could suggest a relatively neurological-specific signal requiring further assessment.

Phenotype III: Low ABCHS + Low ABLS

Low current cognitive risk but impaired systemic resilience

This patient may have an important opportunity for cardiometabolic and lifestyle intervention before cognitive risk develops.

Phenotype IV: High ABCHS + Low ABLS

Combined cognitive and systemic vulnerability

This potentially represents the group requiring the greatest intensity of preventive assessment.

This two-axis approach deserves formal prospective evaluation.

Relationship With Multidomain Dementia Prevention

The conceptual rationale of Aevum BioAI is supported by multidomain intervention research.

The landmark FINGER trial demonstrated that simultaneous intervention involving diet, exercise, cognitive training and vascular-risk monitoring could maintain or improve cognitive function among older individuals at elevated dementia risk [34].

This finding shifted dementia-prevention research away from assuming that one intervention must target one mechanism. Cognitive health emerges from multiple interacting systems. The 2024 Lancet Commission similarly emphasises the potentially preventable component of dementia risk across multiple exposures.

Thus, a multidomain score potentially offers two functions:

1. **Risk identification**, and
2. **Selection of modifiable intervention targets.**

Relationship With Life's Essential 8

The American Heart Association's Life's Essential 8 provides an important precedent for composite positive-health scoring [25].

It combines:

- diet;
- physical activity;
- nicotine exposure;
- sleep;
- body mass index;
- blood lipids;
- glucose; and
- blood pressure.

The framework uses a 0–100 cardiovascular-health scale. ABLS extends a similar philosophy beyond cardiovascular health by incorporating inflammation, renal and hepatic function, nutritional/endocrine variables and brain-health indicators.

Relationship With Biological-Age Algorithms

Biological-age models attempt to quantify heterogeneity in ageing beyond chronological age. Horvath demonstrated that DNA methylation signatures can estimate age across tissues [35].

Levine and colleagues subsequently developed Phenotypic Age, linking clinical biomarkers with morbidity, healthspan and mortality before translating this phenotype into an epigenetic clock [36].

GrimAge improved mortality and healthspan prediction using methylation surrogates associated with smoking and plasma proteins [37].

DunedinPACE was developed to estimate the pace of biological ageing rather than simply biological age [38]. Aevum BioAI differs conceptually from these approaches.

ABLS is not simply intended to answer:

"How biologically old is this person?"

Instead, it attempts to answer:

"Which biological systems appear resilient, which are deteriorating and what potentially modifiable factors are driving the difference?"

This distinction may make ABLS particularly appropriate for preventive clinical practice.

Longitudinal Scoring May Be More Important Than a Single Score

A single biomarker result represents only one point in time. The more clinically important variable may be change.

For example: **ABLS 58 → 66 → 76 → 84**

following intervention could indicate improvement in several underlying systems.

Similarly: **ABCHS 5 → 8 → 13 → 17**

Could indicate progressive accumulation of risk even before subjective cognitive symptoms appear.

The current Aevum reports already support this longitudinal philosophy.

ABCHS recommends repeat assessment approximately every 12 months.

ABLS recommends repeat assessment approximately every 6–12 months.

Proposed Aevum BioAI Longitudinal Model

Future risk could conceptually be represented as:

$$H_{i,t} = f(B_{i,t}, M_{i,t}, O_{i,t}, N_{i,t}, C_{i,t}, L_{i,t}, F_i)$$

where:

- H = overall health trajectory,
- B = inflammatory/haematological biology,
- M = metabolic health,
- O = organ function,
- N = nutritional/endocrine state,
- C = cognitive/neurological markers,
- L = lifestyle,
- F = familial/genetic susceptibility,
- i = individual,
- and t = time.

The clinically interesting quantity may ultimately be:

$$\Delta H = H_{t2} - H_{t1}$$

rather than H at a single assessment.

Role of Artificial Intelligence

The current score architecture can operate through explicit predefined rules.

However, accumulation of sufficiently large prospective datasets would allow Aevum BioAI to progress toward genuine data-driven prediction.

Potential machine-learning techniques could identify:

- nonlinear relationships;
- biomarker interactions;
- age-specific effects;
- sex-specific associations;
- temporal trajectories;
- clusters of risk;
- differential responses to intervention.

Importantly, AI should not automatically replace the transparent score.

A clinically preferable structure may be:

- Layer 1: Transparent score. Physicians can see exactly which variables contribute points.
- Layer 2: AI risk model. Machine learning analyses interactions among variables.
- Layer 3: Longitudinal model. The platform evaluates direction and rate of change.
- Layer 4: Clinical decision support Interventions are suggested based upon modifiable drivers.

Such an architecture preserves clinical interpretability while taking advantage of AI.

Development of the Scoring Algorithm

For a formal methods publication, ABCHS and ABLs should be described as weighted additive composite scores.

For ABCHS: $ABCHS = \sum_{j=1}^{10} R_j$

Where R_j represents the risk contribution from each domain and: $0 \leq ABCHS \leq 40$

For ABLs: $ABLs = \sum_{k=1}^{16} P_k$

Where P_k represents points retained within each biological-resilience domain and: $0 \leq ABLs \leq 100$

The full scoring matrix should eventually be published as supplementary material.

Example of the required ABCHS supplement

Marker	Result range	Risk points
hs-CRP	Optimal range	0
	threshold 2	x

	threshold 3	x
	highest-risk range	3
Vitamin D	Optimal range	0
	intermediate	1
	intermediate	2
	severe abnormality	3

Clinical Actionability

A clinically useful score should not simply classify individuals. It should influence management.

The Aevum reports already link abnormalities with interventions including:

- Mediterranean-style dietary patterns;
- regular aerobic exercise;
- resistance training;
- improvement in sleep;
- smoking cessation;
- alcohol reduction;
- lipid optimisation;
- blood-pressure optimisation;
- vitamin-D correction;
- stress management; and
- repeat biomarker evaluation.

This produces a clinically intuitive sequence:

Measure → Stratify → Identify → Intervene → Reassess

The system therefore shifts emphasis from static laboratory reporting toward longitudinal health optimisation.

Proposed Validation Strategy

The most important next step is prospective validation. A multicenter longitudinal cohort would be preferable.

Study population

- Ideally: **n = 1,000–5,000 participants**
- Age: **40–80 years**
- Follow-up: **minimum 3 years; preferably 5–10 years.**

Recruitment should include participants from different ethnic and socioeconomic backgrounds. A

Malaysian cohort would be particularly valuable because most biological-age and dementia-risk algorithms have historically been developed in Western populations.

ABCHS Validation Endpoints

Baseline evaluation should include:

- ABCHS;
- MoCA;
- MMSE where appropriate;
- subjective cognitive complaints;
- medical history;
- medications;
- depression assessment;
- sleep assessment;
- vascular-risk factors.

A nested subgroup could undergo:

- plasma p-tau217;
- p-tau181;
- A β 42/40;
- NfL;
- GFAP;
- MRI;
- amyloid PET where clinically justified.

Primary endpoints could include:

- **change in MoCA**
- **incident mild cognitive impairment**
- **incident dementia**
- **neurological biomarker progression**
- **structural brain changes.**

ABLS Validation Endpoints

Potential outcomes include:

- cardiovascular events;
- diabetes;
- chronic kidney disease;
- cancer;
- frailty;
- multimorbidity;

- hospitalisation;
- functional impairment;
- major adverse health events;
- all-cause mortality.

Healthspan outcomes may ultimately be more scientifically relevant than crude lifespan.

Statistical Validation

A rigorous validation programme should evaluate four dimensions.

- **Discrimination:** Receiver-operating-characteristic curves and area under the curve.
- **Calibration:** Agreement between predicted and observed outcomes.
- **Reclassification:** Whether ABCHS or ABLs adds meaningful information beyond conventional models.
- **Clinical utility:** Decision-curve analysis to determine whether using the score improves clinical decision-making.

Other analyses should include:

- sensitivity;
- specificity;
- PPV;
- NPV;
- calibration slope;
- Brier score;
- net reclassification improvement;
- test-retest reliability;
- inter-laboratory reproducibility.

Comparison Against Existing Models

ABCHS should eventually be compared with established dementia-risk frameworks and cognitive assessment.

ABLS should be compared with:

- chronological age;
- Life's Essential 8;
- frailty index;
- Phenotypic Age;
- conventional cardiovascular-risk scores;
- metabolic-health indices.

Demonstrating correlation is insufficient. The key question is whether Aevum provides incremental

predictive value.

Avoiding Algorithmic Bias

AI-based health systems require careful evaluation for bias. Age, sex, ethnicity, socioeconomic status, laboratory methodology and underlying disease prevalence can affect biomarker distributions. Models trained predominantly on one population may perform poorly in another.

Development should therefore include:

- sex-stratified analysis;
- age-stratified analysis;
- ethnicity-stratified validation;
- missing-data analysis;
- calibration across populations;
- external replication.

Explainability should remain central. Clinicians should be able to identify which variables caused an individual's score.

Future Biomarker Expansion

Future ABCHS and ABLs versions could evaluate additional biomarkers, but expansion should be evidence-driven.

Cardiometabolic

- ApoB
- lipoprotein(a)
- fasting insulin
- HOMA-IR
- uric acid

Inflammation

- IL-6
- TNF- α
- GlycA

Neurodegeneration

- p-tau217
- p-tau181
- NfL
- GFAP
- plasma A β 42/40

Cardiovascular function

- pulse-wave velocity
- coronary calcium
- cardiorespiratory fitness

Biological ageing

- epigenetic clocks
- proteomic age
- metabolomic age
- glycomic age

Wearables

- heart-rate variability
- sleep efficiency
- sleep regularity
- resting heart rate
- physical activity
- gait
- continuous glucose profiles

The criterion for inclusion should be:

Does the new biomarker materially improve prediction, intervention selection or monitoring?

Not simply whether it is technologically novel.

Toward the Aevum Digital Health Twin

A longer-term objective could be transformation of ABCHS and ABLs into a dynamic individual health model.

A person's record could integrate:

ABCHS+ABLS+genomics+imaging+wearables+longitudinal biomarkers

A continuously updated model could then estimate:

- **current biological resilience**
- **trajectory of ageing**
- **major risk drivers**
- **response to previous interventions**
- **potentially modifiable targets.**

This can be conceptualised as an **Aevum Digital Health Twin**.

Rather than asking:

"What is my biological age?"

precision longevity medicine could ask: "**Which parts of my biology are ageing unfavorably, how rapidly are they changing, and which interventions are most likely to alter that trajectory?**"

That is arguably the more clinically meaningful application of BioAI.

Limitations

Several limitations of the current framework must be clearly acknowledged.

- First, the score weights and categories presently represent a **proposed clinical algorithm**, not coefficients derived from a published perspective cohort.
- Second, several included biomarkers are nonspecific.
- Third, individual biomarker results can be affected by transient illness, medication, hydration, laboratory methodology and environmental exposures.
- Fourth, the lifestyle domain partly depends upon self-reported information.
- Fifth, the urinary beta-amyloid component requires substantially greater validation.
- Sixth, the biological-age and lifespan projections within ABLS should not be interpreted as individual actuarial predictions.

The current report appropriately acknowledges that the biological-age calculation has not yet been validated against longitudinal disease, frailty, hospitalisation or mortality outcomes. These limitations should be described transparently because doing so strengthens rather than weakens the scientific credibility of the programme.

Conclusion

The Aevum BioAI Cognitive Health Score and Aevum BioAI Longevity Score represent complementary attempts to translate complex biological information into practical measures of health trajectory.

ABCHS is a **40-point cognitive-health risk score** incorporating age, haematology, inflammation, renal and hepatic function, electrolytes, thyroid status, vitamin D, neurodegenerative markers and family history.

ABLS is a **100-point biological-resilience score** incorporating inflammation, metabolic health, organ function, nutrition and endocrine health, brain health, and lifestyle-clinical factors.

Their scientific premise is supported by an increasingly coherent body of evidence showing that ageing and cognitive decline result from interconnected biological and behavioral processes rather than isolated abnormalities.

The principal innovation of Aevum BioAI is therefore not an individual laboratory test.

It is the attempt to integrate: **biomarkers + organ function + brain health + lifestyle + longitudinal change**

At present, both systems should remain investigational and should complement rather than replace clinical judgement. Prospective validation will be necessary to determine their calibration, discrimination, reproducibility and incremental clinical value.

If those studies demonstrate robust predictive performance, Aevum BioAI could evolve from a biomarker scoring platform into a longitudinal precision-health system capable of detecting biological deterioration before the development of established disease. The goal of longevity medicine need not be to predict the exact age at which an individual will die.

A more clinically useful objective is to determine: **where biological vulnerability is developing, whether the trajectory is worsening, and whether intervention can alter it before irreversible disease occurs.**

That represents the central proposition underlying Aevum BioAI.

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