

Biomarker-Based Dementia Risk Disclosure in Asymptomatic Individuals: An Ethical and Evidence-Based Framework

Andrea Horta-Barba^{1,2}, Sònia Abilleira-Castells^{1,2}, Ana Fernández-Arcos^{1,2}, Natalia Soldevila-Domenech^{1,2}, Gonzalo Sánchez-Benavides^{1,2}, David López-Martos^{3,2}, Marc Suárez-Calvet^{1,4}, Oriol Grau-Rivera^{1,4}

¹Barcelona Brain Health Center (BBHC) at the BarcelonaBeta Brain Research Center (BBRC), Pasqual Maragall Foundation (FPM), Barcelona, Spain · ²Hospital del Mar Research Institute (IMIM), Barcelona, Spain · ³BarcelonaBeta Research Center (BBRC), Barcelona, Spain · ⁴Neurology Department, Hospital del Mar, Barcelona, Spain

ahorta@barcelonabeta.org
www.barcelonabeta.org

Background

- Two complementary sources of information are now available before symptoms appear: Alzheimer's Disease (AD) biomarkers (PET, CSF, plasma p-tau217), which detect Alzheimer's-related pathology, and genetic risk factors (APOE genotype), which reflect susceptibility to AD.
- In asymptomatic individuals, biomarker testing yields heterogeneous profiles linked to a probabilistic risk of cognitive impairment; within the A/T(N) framework, these profiles carry different prognostic trajectories.
- Cognitively unimpaired individuals with abnormal biomarkers show increased risk of cognitive decline at the group level, yet many remain stable for years, reflecting marked interindividual variability.
- As demand for testing grows, standardized approaches for responsibly communicating biomarker-based risk in asymptomatic populations remain limited, a gap relevant across research and specialized clinical settings such as Brain Health Services.

Aim

To establish minimum standards for communicating biomarker- and genetic-based dementia risk in cognitively unimpaired individuals, ensuring respect for autonomy, transparency about uncertainty, and protection from harm.

Methods

Standard Operating Procedure (SOP) → We developed an SOP integrating biomarker and genetic risk factors within a clinical framework for communicating dementia risk in cognitively unimpaired individuals.

Scope → It is intended for specialized neurology-led or multidisciplinary settings and research contexts, not for routine primary care, individuals with cognitive symptoms, or carriers of deterministic autosomal-dominant mutations.

Sources & development → Built through interdisciplinary expert consensus and informed by disclosure practices from analogous predictive contexts (cancer and other neurodegenerative diseases). It defines professional roles, ethical safeguards, and a structured multi-visit pathway.

Results (The SOP)

The SOP conceptualizes disclosure as a voluntary, longitudinal process rather than a single act. Findings are framed as probabilistic indicators rather than diagnoses and situated within an integrated clinical-biological context and the individual's own perspective on their brain health.

Guiding principles

Disclosure of probabilistic risk of future (not current) disease must rest on principled standards. Five principles frame it as a protective, deliberative, bidirectional process (Figure 1).

Autonomy	Both the decision to test and to receive results must be freely chosen and shared; the right to know is balanced with the equally valid right not to know.
Non-maleficence	Risk information is never shared as an isolated data point; deliberate pacing and reflection protect against anxiety, distress, stigma, and medicalization.
Beneficence	Benefit extends beyond therapy to informed decision-making, prevention engagement, and future planning, or may lie in choosing not to know; it is context- and person-dependent.
Confidentiality	Biomarker and genetic data are sensitive health information with implications for insurance, employment, and family, and must remain under the individual's control.
Equity	Access to counseling, communication, and follow-up should not depend on socioeconomic status, education, or location.

Figure 1. Principles guiding biomarker- and genetic-based risk communication.

References

[1] Jack CR Jr, et al. Revised criteria for diagnosis and staging of Alzheimer's disease. *Alzheimers Dement*. 2024;20(8):5143–5169; [2] Ossenkoppele R, et al. Amyloid and tau PET-positive cognitively unimpaired individuals are at high risk for future cognitive decline. *Nat Med*. 2022;28(11):2381–2387; [3] Largent EA, et al. Testing for Alzheimer disease biomarkers and disclosing results across the disease continuum. *Neurology*. 2023;100(22):1010–1019; [4] Baile WF, et al. SPIKES: a six-step protocol for delivering bad news. *Oncologist*. 2000;5(4):302–311; [5] MacLeod R, et al. Recommendations for the predictive genetic test in Huntington's disease. *Clin Genet*. 2013;83(3):221–231; [6] Visser LNC, et al. Dementia risk communication. *A user manual for Brain Health Services, part 3 of 6*. *Alzheimers Res Ther*. 2021;13(1):170; [7] Livingston G, et al. Dementia prevention, intervention, and care: 2024 report of the Lancet standing Commission. *Lancet*. 2024;404(10452):572–628.

The disclosure pathway

The process follows a structured sequence: exploring motivation and assessing readiness, a reflection period, and result communication only if the wish to know is freely re-confirmed, usually across more than one visit (Figure 2).

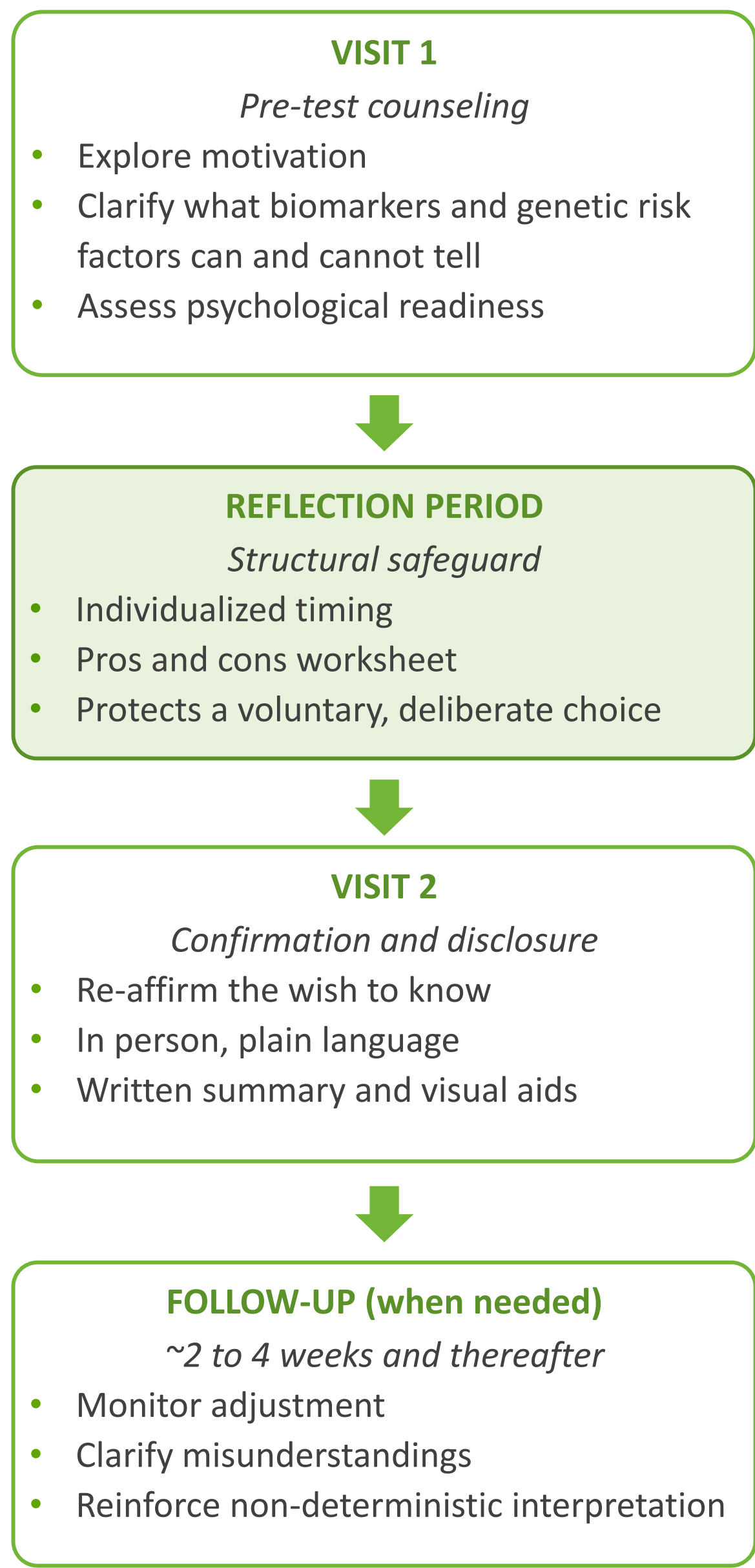


Figure 2. Structured disclosure pathway.

Interpreting & representing risk

Associations with cognitive decline are well established at the group level, yet their predictive value for the individual remains limited. How probabilistic information is framed and presented can substantially change how it is perceived and may be misread as certainty.

Pre-test counseling

A central component of the process is ensuring understanding of the distinction between biological information and clinical diagnosis, communicating possible outcomes and uncertainties, and assessing psychological readiness. Communication may be deferred when conditions are not optimal.

Result communication & follow-up

Results are delivered in person, in plain language and adapted to each individual's needs. Follow-up, when needed, monitors adjustment, clarifies misunderstandings, and reinforces a non-deterministic interpretation.

Contextualizing within brain health

- Multifactorial context**
Biological risk is communicated within a broader discussion of brain health and potentially modifiable dementia risk factors.
- Relevance and uncertainty**
Disclosure should emphasize both the potential value of risk-reduction strategies and the uncertainty of individual clinical outcomes.
- Avoiding stigma**
Attributing outcomes mainly to preventive behaviors oversimplifies disease complexity and risks self-blame.
- Person-dependent choices**
Future planning and disclosure preferences follow each individual's own values and goals.

Conclusions

- ❖ Detection alone is insufficient to warrant disclosure of biological risk information.
- ❖ This SOP provides an ethically grounded and clinically practical framework that conceptualizes disclosure as a preference value-dependent decision.
- ❖ Its structured multi-step pathway offers a framework for implementation across clinical practice, research settings, and Brain Health Services.