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Article

Subjective Cognitive Decline as a Preclinical Marker of Dementia: A Theoretical Review and Conceptual Framework of Longitudinal Studies in Older Adults

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ABSTRACT

Subjective cognitive decline (SCD) refers to a persistent self-perception of deteriorating cognitive function, particularly in memory, despite normal performance on standardized neuropsychological assessments. Increasing evidence supports its role as a potential preclinical marker of the Alzheimer's disease (AD) continuum. In recent years, the field has witnessed substantial growth, prompting the development of novel research frameworks and methodological approaches. This theoretical study synthesizes recent advances and key findings from longitudinal studies, which offer critical insights into the temporal relationship between SCD and progression to clinically defined stages of cognitive impairment. The literature consistently reports associations between SCD and subtle declines in objective cognitive performance, as well as the influence of sociodemographic and psychosocial factors, including differences related to sex and ethnicity. Additionally, emerging data link SCD with alterations in neurobiological biomarkers assessed through neuroimaging and fluid-based analyses, reinforcing its relevance as an early indicator of pathological aging. Based on this body of evidence, a preliminary comprehensive evaluation framework for clinical practice is proposed to improve early detection. Together, these findings underscore the need for standardized diagnostic criteria and integrative models that encompass the clinical, biological, cognitive, and psychosocial domains to enhance the predictive and diagnostic value of SCD in the context of neurodegenerative disease.

Deterioro Cognitivo Subjetivo como Marcador Preclínico de Demencia: una Revisión Teórica y Marco Conceptual de Estudios Longitudinales en Adultos Mayores

Palabras clave
Envejecimiento
Adultos mayores
Deterioro cognitivo subjetivo
Estudios longitudinales

RESUMEN

El deterioro cognitivo subjetivo (DCS) es la percepción persistente de un declive cognitivo, particularmente de la memoria, en ausencia de déficits objetivos. La evidencia respalda su papel como posible marcador preclínico dentro del continuo de la enfermedad de Alzheimer (EA). En los últimos años, el campo ha crecido e impulsado el desarrollo de nuevos marcos de investigación y enfoques metodológicos. Esta revisión teórica sintetiza los avances más recientes y las principales contribuciones en áreas clave. Se incluyeron exclusivamente estudios longitudinales, lo que permite establecer relaciones temporales entre la presencia de DCS y la progresión hacia deterioro cognitivo. Se destacan investigaciones que analizan la asociación entre el DCS y el rendimiento en pruebas cognitivas objetivas, así como variables sociodemográficas y psicosociales, incluyendo diferencias por sexo y grupo étnico. Asimismo, se revisan hallazgos recientes que exploran la relación del DCS con biomarcadores neurobiológicos obtenidos mediante técnicas de neuroimagen y análisis de fluidos biológicos. A partir de esta evidencia, se propone una guía preliminar de evaluación integral orientada a la práctica profesional con el objetivo de mejorar la detección temprana. En conjunto, estos hallazgos perfilan el DCS como un marcador temprano de riesgo dentro del continuo de la EA. Así, resulta crucial avanzar hacia criterios más homogéneos y enfoques integradores que consideren variables clínicas, biológicas, cognitivas y psicosociales, con el fin de mejorar su valor diagnóstico y pronóstico.

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Population Aging and Early Detection of SCD: Criteria, Controversies, and Updates

Currently, more than 55 million people worldwide live with dementia. This figure could triple by 2050 as a result of anticipated changes in the global demographic structure (WHO, 2021). Since there is currently no effective treatment, efforts are focused on slowing the progression of the disease and improving the quality of life for those living with this condition. In this context, subjective cognitive decline (SCD) has gained prominence as a potential early marker of mild cognitive impairment (MCI), with key implications for early detection and preventive intervention (Marafioti et al., 2025).

SCD is characterized by a self-perceived and persistent decline in cognitive ability compared to a previously normal cognitive state (Jessen et al., 2020). Standardized criteria for SCD were established in 2014 by the *Iniciativa de Deterioro Cognitivo Subjetivo* [Subjective Cognitive Decline Initiative] group, highlighting a personal perception of decline in cognitive ability spanning various cognitive domains beyond memory, along with normal performance on standardized tests used to diagnose MCI (Jessen et al., 2014). Since then, improvements to these criteria have been proposed, such as the inclusion of self-report and informant questionnaires, as well as greater attention to SCD in individuals with high cognitive reserve, taking into account variables such as educational level (Molinuevo et al., 2017).

Despite these advances, the term SCD is often used inconsistently across different studies, with various terms being employed such as subjective memory complaints, subjective cognitive complaints, or subjective memory impairment (Jessen et al., 2020; Molinuevo et al., 2017). Although some debate persists in the scientific literature regarding whether SCD constitutes a prodromal state of MCI or dementia, recent research has identified clinical and neurobiological correlates that support this hypothesis (for a review, see Pérez-Blanco et al., 2022). This controversy stems, in part, from the cross-sectional nature of many studies, which limits the ability to establish causal relationships. In this regard, longitudinal studies are essential for establishing temporal relationships between the presence of SCD and progression toward clinical stages of impairment, thereby allowing for a more precise evaluation of its value as an early marker (An et al., 2024).

From this perspective, a systematic review analyzing 32 longitudinal studies in cognitively healthy older adults found that both the combination of symptoms and the intensity of SCD, measured by the frequency or number of complaints, were more strongly associated with the risk of clinical progression than individual symptoms, regardless of the instrument used for assessment (Robertson & Jacova, 2023). Similarly, another review that included 46 longitudinal studies with over 74,000 participants concluded that SCD represents a significant risk factor for the development of MCI and Alzheimer's disease (AD) (Pike et al., 2022).

This study aims to synthesize the most recent evidence from longitudinal studies that have evaluated the relationship between SCD and the risk of progression to dementia. To this end, we review research that has incorporated objective measures of neuropsychological performance, psychosocial factors, biomarkers, and neuroimaging findings. This multidimensional approach allows us to examine the predictive value of SCD from different perspectives and assess its potential role as an early manifestation within the AD continuum.

Neuropsychological Factors and Risk of Deterioration in People With SCD

Several studies have analyzed how certain neuropsychological factors influence the progression of cognitive decline in individuals with SCD, identifying risk profiles. In this context, the longitudinal study by Pereiro et al. (2021), conducted with 253 individuals aged 50 to 87, showed that older adults with more severe SCD were more likely to progress to MCI or to experience a general worsening of cognitive status. The predictive analysis, based on machine learning, indicated that a low cut-off point was more effective in distinguishing the risk of progression. The most relevant predictive variables were memory performance, cognitive reserve, general health status, and diagnostic stability over time.

Similarly, Brundage and Holtzer (2023) assessed 454 individuals with a mean age of 75.6 years via bimonthly telephone interviews. They classified SCD as persistent (more than two reported complaints) or non-persistent (one or two complaints). Both types were significantly associated with a higher risk of developing MCI compared to those who reported no complaints. These findings are reinforced by the study by Numbers et al. (2021), who, in a cohort of 873 individuals with a mean age of 78.6 years, found that a progressive increase in SCD over six years was linked to greater deterioration in global cognition, even after controlling for age, mood, and personality. An annual one-point increase in SCD was associated with a nearly fourfold higher risk of developing dementia within ten years. Expanding on this evidence, Li et al. (2022) analyzed a combined sample of 1,010 adults with SCD and 535 without SCD with a mean age of 70 years. In the cross-sectional analysis, participants with SCD showed lower cognitive performance, particularly in memory and executive functions. Longitudinally, baseline SCD was associated with a higher risk of objective cognitive decline, even after controlling for sociodemographic and emotional variables.

In another study, Liu et al. (2024) investigated the impact of informant-reported memory impairment in adults with SCD with a mean age of 69.5 years over a seven-year follow-up period. At baseline, 41% of the 90 participants exhibited informant-reported memory impairment. This group showed greater depressive symptoms and poorer performance on various cognitive tests, including the Montreal Cognitive Assessment (MoCA), Digit Span Forward, the Visual Matching and Reasoling Tests, and the Picture Completion subtest of the WAIS-PC. Over the course of follow-up, 54% of the group with informant-reported memory impairment progressed to MCI or dementia, compared with 22.6% of the group without informant reports.

These results align with other research highlighting the prognostic value of neuropsychological and psychosocial factors. For example, Yun et al. (2021) conducted a comprehensive neuropsychological assessment of 107 healthy older adults over five years. Of these, 61 developed dementia. Better performance on memory tasks was associated with a lower risk of conversion. Furthermore, lower social engagement was also linked to a higher risk of dementia. In contrast to these findings, Sabatini et al. (2022)

analyzed 1,531 older adults with a mean age of 73 years and found that higher SCD did not predict objective changes in global cognition or in remote or recent memory, but was associated with lower scores on learning tasks.

The reviewed studies agree that, in older adults with SCD, certain neuropsychological and psychosocial factors play a significant role in predicting progression to MCI. Among the variables with the greatest predictive power are poor performance on memory tasks, lower cognitive reserve, the presence of depressive symptoms, and the persistence or external validation of cognitive complaints. These findings reinforce the need to incorporate longitudinal assessments and multifactorial approaches that allow for more accurate and earlier identification of risk profiles. However, the evidence is not entirely consistent. For example, Sabatini et al. (2022) reported no association between the presence of SCD and objective cognitive decline, highlighting the clinical heterogeneity of the SCD construct. These discrepancies highlight the need for more sensitive neuropsychological instruments, as well as longer follow-up periods, to detect subtle cognitive changes not captured by global cognitive assessments.

In this vein, the study by Elkana et al. (2015) provides relevant empirical evidence by demonstrating that, even in older adults with a high level of education, certain neuropsychological instruments such as the Rey Auditory-Verbal Learning Test, Semantic Verbal Fluency, the Rey Complex Figure Copy Test, and the MoCA cognitive assessment test are more sensitive than other general tests for detecting incipient cognitive decline over a 12-month follow-up period. The authors emphasize the importance of selecting tests with high sensitivity and of considering cognitive reserve when interpreting results, given that highly educated individuals may maintain performance within normal ranges despite underlying neurodegenerative changes.

Taken together, the reviewed data support the importance of a comprehensive characterization of the neuropsychological profile, longitudinal monitoring of SCD, and the inclusion of psychosocial factors to optimize diagnostic and prognostic accuracy. These approaches are essential for the early detection of individuals at higher risk of conversion to MCI or dementia, and for the design of personalized preventive strategies in early clinical stages.

Sociodemographic and Psychosocial Factors Associated With SCD

Various sociodemographic factors (e.g., family history of dementia, sex, ethnicity) and psychosocial factors (e.g., perceived social status, personality traits, depression, anxiety), as well as clinical characteristics such as the persistence of SCD symptoms over time, have been shown to influence the relationship between SCD and the risk of developing MCI or dementia.

An example of this is provided by a study that conducted a cross-sectional and longitudinal analysis in a population sample of 3,256 participants with a mean age of 79.6 years, over a follow-up period of up to 13 years. In the cross-sectional analysis, participants with SCD were more likely to report a family history of dementia. On the other hand, the longitudinal analysis revealed that such a family history was significantly associated with the subsequent development of dementia, but only in the group with SCD, and not in those without SCD (Heser et al., 2023). Complementing this evidence, Liew (2020a) conducted a longitudinal study with 5,661 participants with a mean age of 75 years and identified three SCD trajectories based on four annual visits. No SCD (those who did not report SCD at any of the 4 annual visits), intermittent SCD (those who reported SCD at approximately 1 to 2 annual visits), and persistent SCD (those who reported SCD at approximately 3 to 4 annual visits). Compared with those without SCD, intermittent SCD was associated with a higher risk of MCI and dementia, while persistent SCD presented the highest risk of all groups.

Regarding sex, a study of 3,019 healthy older adults assessed cognitive trajectories and conversion to MCI or dementia during a 4.5-year follow-up. Individuals with SCD had a higher rate of conversion to MCI or dementia, with this association being more pronounced in women. In women, SCD was associated with a significant decline in cognitive domains such as memory, language, and executive functions. Furthermore, women with SCD showed a higher risk of clinical progression than men, even after controlling for genetic and psychological factors (Oliver et al., 2022).

With regard to ethnicity, Chapman et al. (2023) conducted a longitudinal study involving 1,237 healthy older adults with an average age of 69 years from diverse ethnic backgrounds. During the follow-up period, they found that SCD was associated with a higher risk of developing MCI or dementia, even after adjusting for sociodemographic factors, the presence of the APOE ε4 allele, medical comorbidities, and depressive symptoms. This association was consistent across all ethnic groups in the study (non-Hispanic whites, non-Hispanic Blacks, and Hispanics). Furthermore, SCD was associated with objective cognitive decline over time, especially when reported persistently over time. Similarly, Boza-Calvo et al. (2024) assessed the progression from SCD to MCI in 188 Hispanic and non-Hispanic white adults at two time points: at baseline and after two years. Hispanic individuals showed a higher risk of developing MCI, along with more depressive symptoms from the outset, which intensified over time. They also reported more SCD, particularly in concentration, past memory, and daily functioning. Regarding objective cognitive performance, Hispanic ethnicity was associated with greater decline on tests such as the Mini-Mental State Examination (MMSE), MoCA, Trail Making Test A and B, and the Guild Paragraph Recall.

Regarding psychosocial factors, Hopper et al. (2023), in a study with 12,694 participants, found that factors such as depression, perceived social status, and personality traits are significantly associated with SCD. The study suggests that SCD reflects not only cognitive changes but also aspects of mental health. Higher negative affect was associated with a more negative perception of one's own cognitive functioning. Furthermore, those who perceived a higher social status reported lower SCD, indicating a possible protective effect of the psychosocial environment. Regarding personality, the Big Five traits were associated with a lower risk of SCD, with conscientiousness and emotional stability being the factors most strongly linked to a lower prevalence.

Anxiety has also been linked to SCD in older adults. In a study of 14,066 healthy individuals over the age of 50, Liew (2020b) found that both anxiety and SCD were independently associated with a higher risk of developing MCI or dementia. The risk was particularly high among those with both coexisting factors (anxiety and SCD), as they increased the probability of progression to MCI

or dementia to 25% over an average of 3.1 years, compared to 8.2 years among those with neither.

The reviewed findings indicate that SCD constitutes a relevant clinical marker of the risk of progression to MCI and dementia, especially when it occurs in combination with certain individual factors. Among these, a family history of dementia, the persistence of SCD over time, female sex, and belonging to ethnic minority groups stand out. The latter face additional challenges related to SCD, possibly influenced by external stressors, cultural barriers, and inequalities in access to health services, which could limit early detection and intervention.

Furthermore, mental health conditions such as depression and anxiety are consistently associated with an increased risk of clinical conversion. Likewise, psychosocial factors such as perceived social status and certain personality traits like conscientiousness and emotional stability appear to modulate the expression and progression of SCD, suggesting the existence of an underlying affective-cognitive component in its manifestation.

In summary, these results underscore the importance of considering SCD from a multidimensional perspective, integrating biological, psychological, social, and cultural factors, to enable a more accurate identification of risk profiles. Early identification, especially in vulnerable populations, coupled with culturally sensitive prevention strategies, represents a key pathway to mitigating the risk of progression to dementia.

Plasma, Genetic, and Neuroimaging Biomarkers in SCD Progression

A study by Hong et al. (2022) analyzed cognitive trajectories over 24 months in older adults with SCD, comparing those with positive amyloid burden (Aβ+) to those with negative burden (Aβ-). The study included 47 participants aged 50 or older, who underwent neuropsychological testing, magnetic resonance imaging, and positron emission tomography (PET) to measure amyloid burden and regional brain volumes. The results showed that the Aβ+SCD group exhibited a more rapid decline in verbal memory compared to the Aβ-SCD group, even after adjusting for age. Although differences in the decline in MMSE scores were not statistically significant, the trend was more pronounced in the Aβ+SCD group. Furthermore, both amyloid burden and baseline memory performance were associated with greater cognitive decline. Expanding the evidence on the role of biomarkers in the progression of SCD, Hong et al. (2023) conducted a longitudinal study involving 120 adults aged 60 years or older, with a 24-month follow-up. Of the participants, 107 completed the follow-up assessments, and a subgroup (18.5%) was Aβ+. This subgroup was significantly larger and had a higher proportion of APOE ε4 carriers compared to Aβ- participants. Although no cognitive differences were observed at baseline, the Aβ+ group showed lower scores on the Seoul Verbal Learning Test. After two years, this group exhibited elevated plasma levels of p-tau181 and volume reductions in key brain regions, including the hippocampus, entorhinal cortex, and globus pallidus, which were associated with greater declines in verbal memory and executive functions.

Consistent with these findings, Ebenau et al. (2022) conducted a longitudinal cohort study involving 401 individuals with SCD, with a mean follow-up of 4 ± 3 years. These researchers highlighted the value of integrating molecular biomarkers with structural measures obtained through neuroimaging to improve the prediction of clinical course in individuals with SCD. In their analysis of five biomarkers (t-tau in cerebrospinal fluid, medial temporal lobe atrophy, hippocampal volume, neurofilament light chain [NfL], and glial fibrillary acidic protein [GFAP]), all demonstrated predictive ability, although only hippocampal volume, NfL, and GFAP provided additional value beyond the classic amyloid and tau markers. Specifically, higher baseline levels of NfL and GFAP, as well as a reduction in hippocampal volume, were associated with an increased risk of conversion to MCI or dementia. Complementing this evidence, another study focused on structural biomarkers developed a predictive model to estimate the risk of progression from SCD to MCI over a seven-year follow-up period. The study included 76 older adults, of whom 24 progressed to MCI while 52 remained cognitively stable. The multivariate model incorporated clinical variables, cognitive test scores, and neuroimaging measures, including hippocampal volume and cortical thickness in key regions. The strongest predictors of progression to MCI were low educational attainment, a low baseline MoCA score, a reduced left amygdala, and increased white matter at the margins of the right superior temporal sulcus (Yue et al., 2021).

The reviewed studies reinforce the importance of integrating plasma biomarkers with neuroimaging techniques for a more precise characterization of neurodegenerative processes in SCD. This approach allows for more sensitive detection of structural, functional, and molecular alterations and constitutes a promising strategy for improving the prediction of clinical progression toward more advanced stages of cognitive decline.

In addition to findings from studies using neuroimaging and cerebrospinal fluid biomarkers, recent research has highlighted the importance of plasma biomarkers and genetic factors for improving risk stratification and predicting clinical progression in individuals with SCD. In this vein, Perna et al. (2023) conducted a large-scale longitudinal study that followed 6,357 adults with a mean age of 62 years over 17 years. The results indicated that the presence of persistent SCD, along with elevated blood GFAP levels and the presence of the APOE ε4 allele, was associated with an increased risk of developing dementia from any cause.

The accumulation of Aβ in the brain, when it coexists with SCD, has also been linked to accelerated progression toward cognitive decline. In a multinational study, Shao et al. (2024) evaluated 821 participants from German and Chinese cohorts, finding that individuals with SCD and Aβ+ experienced faster decline than those without Aβ accumulation, regardless of the assessment tool or cultural context. Along the same lines, Stockmann et al. (2020) analyzed plasma samples from 203 individuals with SCD with a mean age of 61 years and observed that misfolding of the Aβ protein predicted progression to MCI or dementia highly accurately. This is a process in which the protein adopts a pathological conformation that promotes its aggregation into plaques. In combination with the Aβ42/40 ratio—an indicator whose decrease is associated with greater cerebral amyloid deposition—greater predictive power was achieved. This result highlights the utility of combining structural and quantitative properties of amyloid in blood as predictive markers.

Several studies have highlighted the modulatory role of genetic factors in the risk associated with SCD. Kang et al. (2024), in a community-based cohort of 3,585 older adults with a mean age of

68 years followed for 12 years, found that SCD preceded MCI by an average of 4.4 years, AD by 6.8 years, and dementia by 6.9 years. Multivariate analyses showed significant associations between SCD and progression to MCI, AD, and dementia, even after adjusting for the APOE ε4 allele and polygenic risk score. Complementarily, Liew (2022) analyzed data from a cohort of 16,221 individuals with a mean age of 71 years and concluded that the combination of SCD and the presence of the APOE ε4 allele significantly increased the risk of conversion to MCI or dementia, especially in women over 70 years of age.

Finally, the longitudinal study by Amariglio et al. (2024) followed 1,147 cognitively healthy adults with elevated levels of cerebral Aβ. Subjective perceptions of cognitive functioning were assessed through self-report and caregiver evaluation, along with objective measures such as the Preclinical Alzheimer Cognitive Composite. Both types of reports reflected progressive functional decline; however, the association between subjective reports and objective decline was stronger in caregiver reports, particularly among participants with higher baseline amyloid burden. These results suggest that external observers may be more sensitive to detecting subtle functional changes that might go unnoticed by the individual themselves.

Although plasma biomarkers and structural neuroimaging measures such as amyloid burden, hippocampal atrophy, cortical thickness, and the presence of the APOE ε4 allele have proven to be powerful predictors of progression from SCD to MCI, their high complexity and cost limit their routine implementation in clinical and community settings. In this context, more affordable alternative methods such as electroencephalography (EEG) emerge as promising tools. The use of EEG offers significant benefits as it is non-invasive, portable, low-cost, and capable of detecting functional changes before clinical symptoms appear (Babiloni et al., 2020). However, larger-scale longitudinal studies are needed to support its predictive capacity, as EEG has the potential to become a valuable tool for the early detection of cognitive decline in individuals with SCD, especially if validated in combination with other biomarkers.

Proposed Procedure for the Evaluation of SCD in Professional Practice

Based on the evidence analyzed in this review, and with the aim of providing psychology professionals with diagnostic tools, a preliminary model for comprehensive assessment is proposed. This proposal does not constitute a closed diagnostic protocol, but rather a structured guide for clinical decision-making, based on the integration of evidence from the reviewed longitudinal studies.

Phase 1. Standardized Assessment of Subjective Cognitive Complaints

The assessment should begin by moving beyond the simple open-ended question about memory: "Do you have memory problems?" It is recommended to use standardized psychometric instruments that allow for the quantification of the patient's perception and that of their immediate environment using validated cut-off points. In this vein, we propose the use of the Subjective Cognitive Decline Questionnaire (SCD-Q; Rami et al., 2014), which assesses the decline perceived over the past two years, both by the subject and by a reliable informant. Scores above 7 on the self-report and above 5 on the informant's report indicate a level of risk that warrants clinical follow-up.

In addition, the Memory Failures in Everyday Life Questionnaire (MFE-30), which has been validated in the Spanish population (Lozoya-Delgado et al., 2012), is recommended. A score above 36 indicates a significant functional impact on daily life, helping to distinguish SCD from benign memory impairments associated with aging.

Phase 2. External Validation of Subjective Cognitive Complaints

Given the nature of SCD, the assessment should not be based solely on self-perception. The inclusion of a reliable informant (family member, spouse, or caregiver) is key to validating the persistence, frequency, and functional impact of cognitive complaints. The reviewed evidence indicates that the informant's report provides additional predictive value regarding clinical progression, especially when it confirms the decline perceived by the subject themselves (Jessen et al., 2014; Molinuevo et al., 2017; Rami et al., 2014).

Phase 3. Neuropsychological Assessment Sensitive to Early-Stage Decline

In the presence of clinically relevant SCD, the administration of a sensitive neuropsychological battery is recommended, avoiding the use of global screening tests alone. Priority should be given to instruments capable of detecting subtle changes in episodic memory, executive functions, processing speed, and verbal fluency.

The interpretation of cognitive performance should take into account the individual's cognitive reserve, given its modulatory role in the clinical expression of cognitive decline. In this regard, the use of the Cognitive Reserve Scale (León et al., 2014) is recommended, which assesses the frequency of participation in cognitively stimulating activities throughout life. The scale consists of 24 items distributed across four dimensions: activities of daily living, education/information, leisure/hobbies, and social life. Likewise, the use of the Cognitive Reserve Questionnaire (Rami et al., 2011) is recommended; it consists of eight items that measure various aspects of a person's intellectual activity throughout life. As a complementary measure, proxy measures of cognitive reserve—such as years of schooling and educational attainment—can be incorporated.

The interpretation of results should be based on normative cut-off points adjusted for age and educational level, as well as on the analysis of the overall cognitive profile, prioritizing patterns of functioning and longitudinal changes over isolated deficits.

Phase 4. Assessment of Emotional, Sociodemographic, and Psychosocial Factors

The assessment of SCD should integrate emotional and psychosocial variables, given their modulatory role in the expression of cognitive complaints. It is recommended to assess symptoms of depression and anxiety, level of social participation and perceived loneliness, perceived social status, family history of dementia, and

relevant sociodemographic characteristics (sex, educational level, and cultural context).

Phase 5. Integration of Biomarkers

In clinical settings, and when resources permit, the incorporation of genetic, plasma, or neuroimaging biomarkers can improve the stratification of AD risk. However, given their limited accessibility, these indicators should be considered complementary to, rather than a substitute for, clinical and neuropsychological assessment in the SCD phase.

Outlook and Future Research Directions and Advances in SCD Assessment

SCD is increasingly recognized as a clinically relevant phenomenon within the AD continuum, with a growing body of evidence supporting its role as an early risk marker. Longitudinal studies consistently show that SCD is associated with a higher probability of progression to MCI and dementia, especially when it coexists with factors such as amyloid accumulation, structural brain changes, abnormal plasma biomarkers, and the APOE ε4 genotype (Figure 1).

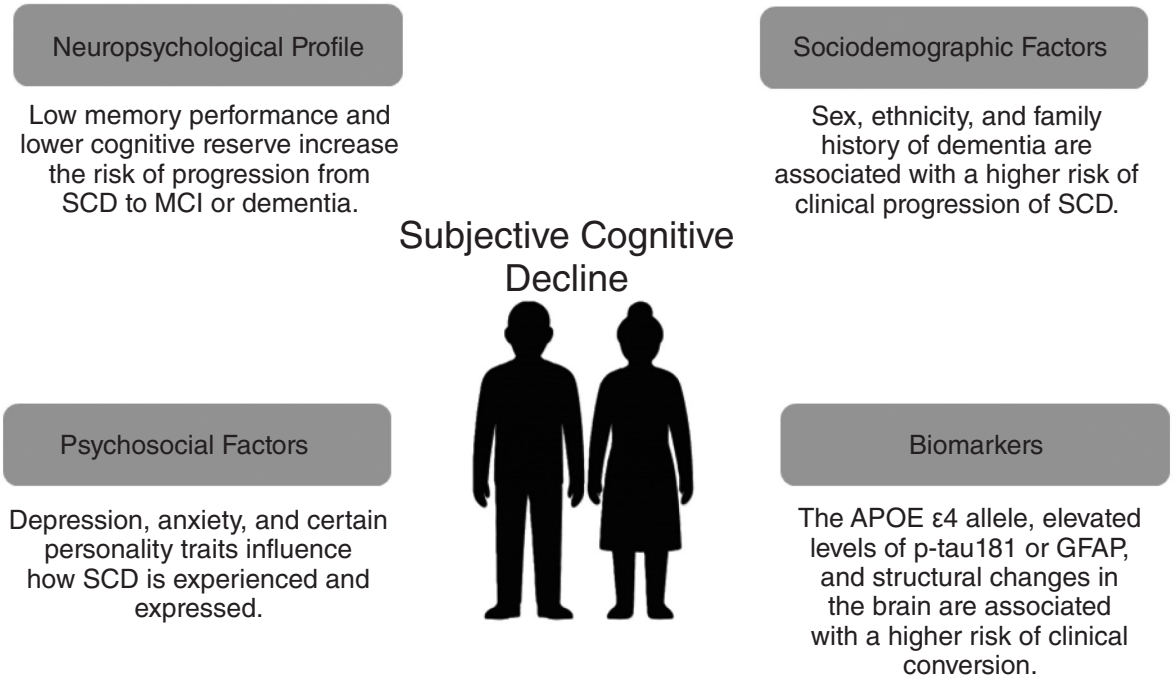
However, several methodological and conceptual challenges remain. Despite notable efforts to establish a standardized definition, particularly those led by the SCD Initiative Working Group (Jessen et al., 2014), there continues to be considerable variability in the diagnostic and operational criteria used across studies. Moving toward a unified conceptual model is essential to improve consistency in characterization and enable meaningful comparisons across studies.

In addition, there are areas that require further exploration, such as the impact of cognitive reserve, cultural differences in the perception and reporting of SCD, and the clinical value of informant observations for detecting early functional decline. These dimensions may prove critical for refining the assessment of older adults with subjective cognitive complaints. The integration of clinical, neuropsychological, genetic, neurobiological, psychosocial, and cultural indicators represents a promising direction to improve diagnostic accuracy and risk stratification. This comprehensive approach not only improves the identification of individuals in preclinical stages of neurodegeneration but also supports the development of more timely and effective preventive interventions.

It is important to note that not all individuals with SCD will develop AD. However, a subgroup is at significantly higher risk of clinical progression. In this context, a comprehensive assessment of SCD allows for a more in-depth analysis of the nature, persistence, and functional impact of the symptoms experienced and, consequently, helps distinguish individuals at risk of transitioning to MCI or dementia from those with cognitive changes attributable to normal aging or changes that may be transient due to depressive states (Figure 2).

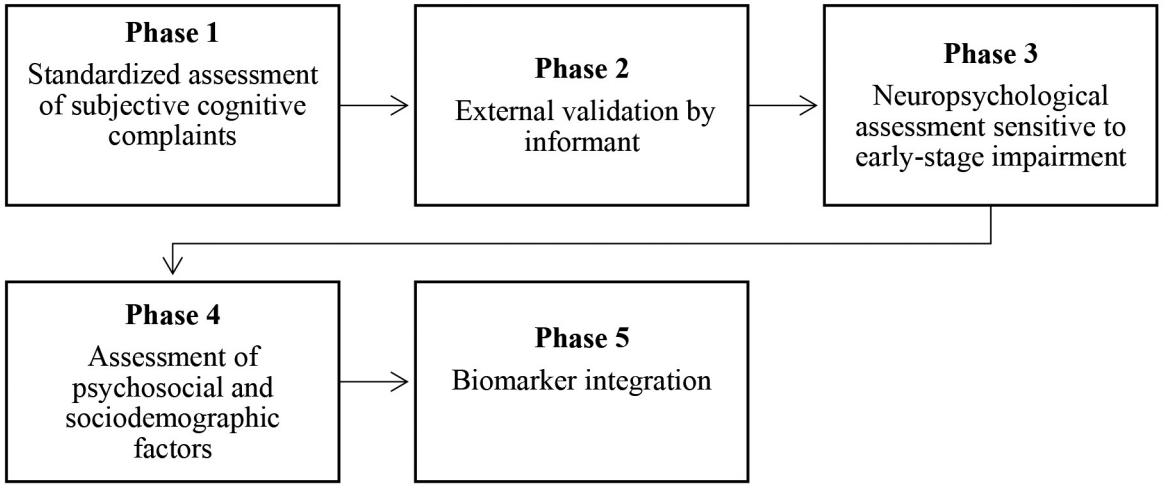
Based on the reviewed longitudinal evidence, a comprehensive assessment model is proposed that pursues a dual objective. First, to identify older adults with a high probability of underlying AD pathology, facilitating timely access to follow-up and early intervention strategies. Second, to provide a technical guide for clinical decision-making, enabling professionals to more rigorously distinguish cognitive concerns typical of healthy aging from those representing a real clinical risk.

Figure 1
Factors Associated With Subjective Cognitive Decline (SCD)



Note: Schematic representation of the main factors involved in the progression of SCD according to current evidence. SCD: Subjective cognitive decline; MCI: mild cognitive impairment; APOE ε4: apolipoprotein E ε4 allele; p-tau181: phosphorylated tau 181; GFAP: glial fibrillary acidic protein.

Figure 2
Comprehensive Assessment Procedure for Subjective Cognitive Decline (SCD)



Note. The diagram represents the five sequential phases of the proposed model for the assessment of SCD in clinical practice.

Taken together, the integration of clinical, neuropsychological, genetic, neurobiological, psychosocial, and cultural indicators represents a particularly promising direction for both future research and professional practice.

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Conflict of Interest

The authors declare that they have no conflicts of interest.

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