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Alzheimer's Disease and Mobility Multimodal Prediction of Gait Decline, Fall Risk, and Loss of Functional Independence in Mild Cognitive Impairment and Early Alzheimer's Disease

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Abstract

Mobility deterioration is an important component of disease progression in mild cognitive impairment and early Alzheimer's disease, yet gait decline, falls, and functional dependence are frequently evaluated as separate outcomes. This study examined whether multimodal information improved prediction of cognitive-motor deterioration and adverse mobility outcomes. A multicenter, prospective longitudinal quantitative cohort design was used to follow 420 community-dwelling adults, including 210 participants with mild cognitive impairment and 210 with early Alzheimer's disease, for 24 months. Comprehensive assessments were conducted at baseline and 6, 12, 18, and 24 months, while falls were monitored monthly. Clinical characteristics, cognition, instrumented gait, dual-task performance, balance, functional status, medication exposure, free-living mobility, magnetic-resonance imaging, and blood biomarkers were measured. At 24 months, 351 participants remained under observation, representing 83.6% retention. Mean annual usual-pace gait-speed decline was 0.035 m/s in mild cognitive impairment and 0.061 m/s in early Alzheimer's disease. Clinically meaningful gait decline of at least 0.10 m/s occurred in 37.7% and 64.9% of the respective groups, with an adjusted odds ratio of 2.64 for early Alzheimer's disease. At least one fall was experienced by 43.8% of participants with mild cognitive impairment and 66.2% with early Alzheimer's disease. Fall rates were 44.7 and 87.4 events per 100 person-years, respectively, while injurious falls occurred in 16.7% and 31.9%. Sustained functional dependence developed in 21.9% of the mild cognitive impairment group and 51.4% of the early Alzheimer's disease group. Previous falls, gait variability, dual-task cost, turning instability, orthostatic hypotension, medication burden, executive decline, reduced daily activity, and abnormal phosphorylated tau independently predicted adverse outcomes. The multimodal model explained 63% of gait-decline variance, achieved concordance statistics of .83 for first falls and .87 for functional dependence, and outperformed clinical-only, cognition-only, and gait-only models. Multimodal assessment provided a more complete quantitative representation of mobility vulnerability than any single measurement domain and identified distinct but interconnected pathways leading to gait deterioration, recurrent falling, injury, and loss of independence.

Keywords

Alzheimer's disease; Gait; Falls; Mobility; Independence.

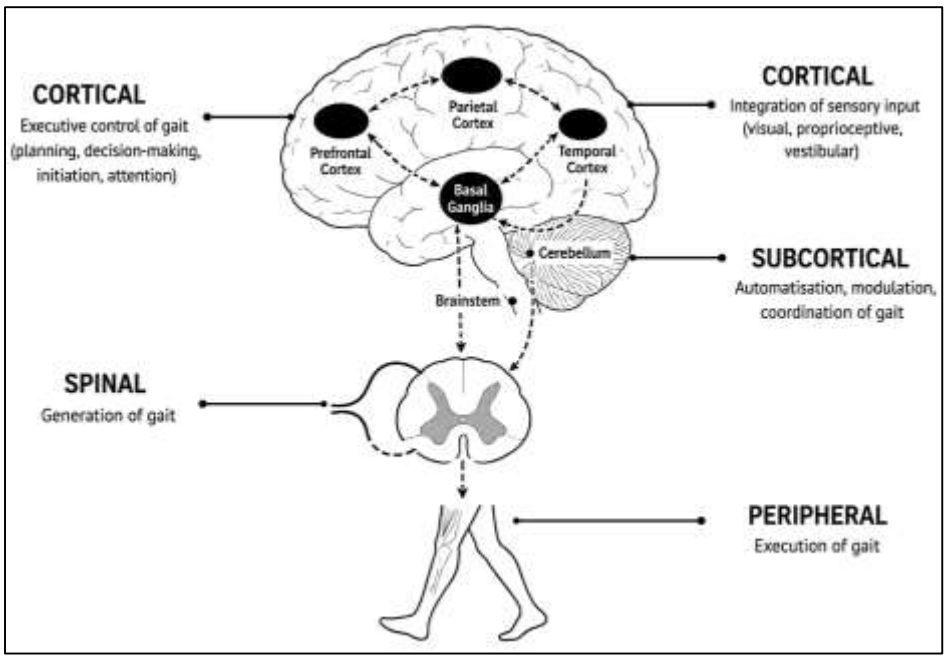
INTRODUCTION

Alzheimer's disease is a progressive neurodegenerative disorder characterized biologically by abnormal amyloid-beta accumulation, pathologic tau aggregation, synaptic dysfunction, neuronal injury, and distributed brain atrophy, and characterized clinically by declining memory, executive function, attention, language, visuospatial ability, behavior, and everyday performance. Mild cognitive impairment refers to an intermediate clinical state in which objective decline is present in one or more cognitive domains, yet the person retains broad independence in customary daily activities (Puente-Gonzalez et al., 2021). This category is heterogeneous: some individuals remain stable, some return to cognitively unimpaired performance, and some progress to dementia caused by Alzheimer's disease or another neurologic condition. Mild cognitive impairment due to Alzheimer's disease identifies the subgroup whose cognitive syndrome is judged to arise from Alzheimer-type pathology on the basis of clinical features, biomarkers, or both. Early Alzheimer's disease commonly includes mild cognitive impairment due to Alzheimer's disease and mild Alzheimer's dementia, stages in which symptoms are measurable but substantial personal agency and community participation are often retained. Mobility is the capacity to move safely and effectively through home and community environments and includes walking, transfers, turning, obstacle negotiation, balance, endurance, and adaptation to simultaneous cognitive demands. Gait is the patterned locomotor behavior through which this capacity is expressed (Ansai et al., 2017). Gait decline denotes longitudinal worsening in one or more parameters, including speed, stride length, cadence, variability, asymmetry, double-support time, turning quality, or walking-bout structure. A fall is an unexpected event in which a person comes to rest on the ground, floor, or a lower level, whereas fall risk is the conditional probability of experiencing one or more such events during a defined observation period. Functional independence is the ability to complete basic activities of daily living, such as bathing, dressing, toileting, feeding, and transferring, together with instrumental activities such as medication management, shopping, cooking, transportation, communication, household organization, and financial management. Loss of functional independence occurs when these activities require supervision, prompting, physical assistance, or transfer of responsibility. Multimodal prediction refers to the statistical integration of information from distinct measurement domains—clinical characteristics, cognition, laboratory mobility, wearable sensors, neuroimaging, fluid biomarkers, medication exposure, comorbidity, environmental context, and functional reports—to estimate individual-level probabilities or trajectories for prespecified outcomes (Cezar et al., 2021). In this framework, gait decline, fall risk, and loss of independence are related outcomes rather than interchangeable labels, and each requires a clear time horizon, operational definition, and longitudinal measurement strategy.

The relationship between Alzheimer's disease and mobility has international significance because dementia, population ageing, falls, disability, and caregiving demands converge across health systems with very different resources. Approximately 57 million people were living with dementia worldwide in 2021, more than 60% resided in low- and middle-income countries, and nearly 10 million new cases occur each year. Alzheimer's disease accounts for the largest proportion of dementia syndromes. These figures describe a current burden distributed across regions in which specialist memory services, molecular biomarkers, rehabilitation, assistive technologies, and long-term care are not equally available (Dyer et al., 2020). Mobility outcomes add a major layer to that burden. Walking limitation restricts access to food, health care, religious and social participation, employment, and family roles; falls contribute to fractures, head injury, fear of movement, hospitalization, and institutional care; loss of independence transfers substantial physical, emotional, and economic work to relatives and paid caregivers. The same gait disturbance can therefore carry different consequences according to housing design, street safety, transportation systems, family structure, social protection, rehabilitation coverage, and the availability of community support. International variation also affects measurement. A clinic-based timed walk can be standardized across sites, yet it may not represent movement on crowded roads, uneven surfaces, stairs, multigenerational homes, or rural paths. Instrumental activities of daily living are similarly shaped by culture, gendered roles, literacy, technology use, banking practices, and local expectations of autonomy (Serra-Añó et al., 2019). Predictive variables developed in highly resourced research centers can lose validity when transported to populations with different education, vascular risk, nutrition, medication access, device familiarity, or patterns of physical labor. Multimodal

prediction is therefore an issue of population validity as well as statistical performance. Combining low-cost gait measures and wearable data with cognitive, clinical, and functional information can represent disease expression more fully than a single expensive biomarker, yet such integration must account for unequal device access, data quality, language, and follow-up completion. Internationally relevant quantitative research also requires attention to sex, age, ethnicity, socioeconomic position, rurality, and comorbidity because each can influence both predictor distributions and outcome rates (Hunter et al., 2021). Examining gait decline, falls, and functional dependence together places the analysis close to outcomes experienced by individuals, families, rehabilitation services, and care systems, while maintaining measurable endpoints that can be compared across countries and clinical settings.

Figure 1: Neural Control of Gait Function



Walking is not an automatic motor act produced by the lower limbs alone; it is a cognitively regulated behavior supported by distributed neural systems. Safe gait requires motor planning, sensory integration, visuospatial mapping, attention allocation, executive control, error monitoring, balance reactions, and continuous adjustment to the environment. Alzheimer-related pathology can disturb these processes through degeneration in medial temporal, parietal, frontal, cingulate, and association networks, and through impaired communication between cortical, subcortical, cerebellar, and brainstem regions (Gonçalves et al., 2018). Vascular injury, white-matter hyperintensities, reduced cerebral perfusion, peripheral neuropathy, visual impairment, vestibular dysfunction, arthritis, sarcopenia, pain, and cardiometabolic disease can add non-Alzheimer contributions to mobility change. This layered biology is particularly important in mild cognitive impairment and early Alzheimer's disease because overt weakness or severe neurologic signs may be absent when subtle locomotor dysregulation is already measurable. Executive dysfunction can reduce the ability to select an efficient walking strategy, inhibit distraction, or switch attention during turning and obstacle avoidance. Reduced processing speed can delay corrective steps. Visuospatial impairment can alter foot placement and judgment of environmental hazards. Memory impairment can disrupt route finding, adherence to mobility aids, and recall of safety instructions. The cognitive-motor interface becomes more visible during dual-task walking, when an individual walks while counting backward, naming items, carrying an object, or responding to a verbal stimulus (Domenech-Cebrían et al., 2019). The additional task competes for limited attentional resources, producing a dual-task cost in gait speed, variability, or cognitive accuracy. Studies across cognitively unimpaired adults, mild cognitive

impairment, and Alzheimer's disease show that the magnitude and pattern of this cost can reveal impairment not captured by usual-pace walking. Resting-state connectivity, regional brain volume, white-matter integrity, amyloid burden, tau-related neurodegeneration, and apolipoprotein genotype have each been associated with elements of mobility or cognitive-motor decline, though associations vary by sample, disease stage, protocol, and analytic method. Mobility also interacts dynamically with cognition. Reduced walking and community activity can accompany depression, social withdrawal, deconditioning, and increasing reliance on caregivers, while falls and fear of falling can further narrow movement exposure. A quantitative model centered only on a cognitive score treats these interacting mechanisms as unmeasured variation (Mulas et al., 2021). A model centered only on gait treats the disease process, comorbidity, medication effects, and environmental exposure as if they were equivalent. Multimodal assessment captures complementary signals arising from neural pathology, cognitive control, physical capacity, behavior, and context, providing a more complete representation of mobility vulnerability within the early Alzheimer continuum.

Gait decline is multidimensional, and its quantification requires more than a single observation of walking speed. Pace measures include speed, step length, and stride length; rhythm measures include cadence, step time, and swing time; variability measures describe stride-to-stride inconsistency; asymmetry measures compare left and right timing or distance; postural-control measures include step width, double-support time, trunk movement, and dynamic stability; turning measures include duration, velocity, step number, and turn smoothness (Zhang et al., 2019). Each domain can respond differently to cognitive impairment and disease progression. Slow speed can reflect cautious behavior, weakness, pain, cardiovascular limitation, or neurodegeneration. Greater stride-time variability can reflect unstable central timing and impaired executive regulation. Increased double-support time can indicate compensation for reduced balance confidence. Shortened steps and irregular turns can become visible during complex movement even when straight-line walking remains within an expected range. Repeated measurement is central to the definition of decline because baseline differences between individuals do not establish within-person deterioration. Electronic walkways, pressure mats, three-dimensional motion capture, force platforms, instrumented Timed Up and Go tests, and inertial measurement units provide objective estimates under standardized conditions. Dual-task protocols increase cognitive load and permit calculation of motor and cognitive dual-task costs (Jahn et al., 2019). Wearable accelerometers and gyroscopes extend assessment into daily life, producing measures of step count, walking duration, bout length, cadence, speed, turning, fragmentation, regularity, and day-to-day variability. Clinic and free-living measures are related but not identical: the clinic estimates capacity under instruction, whereas home monitoring estimates enacted performance within ordinary routines. Evidence shows that older adults with mild cognitive impairment or dementia can display slower pace, shorter strides, increased variability, reduced regularity, fewer daily steps, and shorter walking bouts, and longitudinal studies link slowing or combined decline in gait and cognition with adverse clinical transitions. Measurement reliability remains sensitive to walkway length, number of strides, footwear, task instructions, device placement, algorithm choice, assistive-device use, fatigue, time of day, and adherence to wear protocols. A person's average value can also obscure episodic instability, risky turns, or deterioration occurring only under cognitive load (Lee et al., 2022). Quantitative modeling must therefore distinguish stable traits from time-varying states and separate measurement error from clinically meaningful change. Modeling a continuous gait trajectory can retain information lost by dichotomizing participants as impaired or unimpaired. Clinically interpretable thresholds remain useful for risk stratification, but they require validation against change distributions and meaningful events. Integrating laboratory, dual-task, and free-living measures allows gait decline to be represented as a longitudinal phenotype composed of capacity, cognitive-motor interference, and real-world performance (Allali et al., 2017).

Fall risk in mild cognitive impairment and early Alzheimer's disease emerges from the interaction of intrinsic vulnerability, momentary exposure, behavior, and environment. Prior falls, slow or variable gait, impaired balance, reduced lower-limb strength, orthostatic hypotension, visual and sensory loss, urinary urgency, depression, sleep disturbance, and multiple medications contribute to risk. Cognitive impairment adds mechanisms that standard physical screens may not capture: divided attention becomes less efficient, hazard recognition can weaken, judgment of reach or step capacity can become

inaccurate, and an individual may fail to remember or consistently use an assistive device. Executive and visuospatial deficits are especially relevant during turns, obstacle negotiation, street crossing, multitasking, and movement in unfamiliar surroundings. Risk is also shaped by exposure (Nyul-Toth et al., 2021).

Figure 2: Multimodal AI Prediction for Alzheimer's

A person who walks frequently has more opportunities to fall but may possess greater physical reserve; a person with very low activity may record no fall during observation while carrying substantial instability and dependence. Fear of falling can reduce exposure, produce cautious gait, and accelerate deconditioning. Caregiver supervision can prevent an event without removing underlying vulnerability. These factors explain why retrospective fall history, clinician-rated balance, gait speed, and sensor-derived movement can yield different risk estimates. Prospective studies in dementia and community cohorts have identified associations among cognitive impairment, nonamnestic mild cognitive impairment, gait and balance deficits, autonomic symptoms, depression, inaccurate physical judgment, and incident falls. Evidence also shows that no single gait or balance test classifies fallers with consistently high certainty across populations (Muir-Hunter & Montero-Odasso, 2017). Fall prediction should therefore specify whether the outcome is any fall, recurrent falls, injurious falls, fall-related hospitalization, or time to first fall, since each represents a different statistical process. Accurate ascertainment requires calendars, caregiver reports, telephone follow-up, clinical records, or digital detection, with procedures to address recall error and events occurring during institutionalization or hospitalization. Recurrent events violate the assumption that each observation is independent, and death, withdrawal, or transition to supervised care can alter the opportunity to observe falls. Time-varying medication use, acute illness, physical activity, and cognitive status can change risk during follow-up. A multimodal approach can combine relatively stable characteristics, such as age and chronic disease, with dynamic markers, such as gait variability, daily activity, postural sway, cognitive-

motor cost, medication changes, and recent near-falls (Morris et al., 2019). This framing treats a fall as an event generated by changing person–environment conditions rather than as a direct and inevitable consequence of a diagnostic label.

Functional independence is both a clinical state and a graded longitudinal outcome. Basic activities of daily living concern personal self-maintenance, whereas instrumental activities of daily living require more complex planning, sequencing, memory, judgment, communication, and mobility. Mild cognitive impairment is traditionally distinguished from dementia by broad preservation of independence, yet research using detailed questionnaires and performance-based tasks shows that subtle inefficiencies can already occur in financial management, medication organization, shopping, meal preparation, transportation, appointment keeping, technology use, and navigation. Individuals may complete a task more slowly, make more errors, require reminders, simplify the activity, or rely on compensatory routines while still being classified as independent (Borges et al., 2018). Early Alzheimer's disease often affects cognitively demanding instrumental activities before basic self-care, and the pattern varies with occupational history, household roles, education, culture, physical health, and available assistance. Mobility is embedded in many of these tasks. Slower gait and impaired balance can restrict shopping or public transportation; difficulty turning and transferring can affect toileting and bathing; reduced endurance can narrow community participation; falls can trigger temporary or sustained assistance; and fear of falling can lead families to assume responsibilities that the person previously managed. Cognitive, motor, and social pathways therefore converge at the point where autonomy is negotiated in everyday life. Measurement can draw on participant report, informant report, clinician rating, direct observation, or sensor-derived behavior. Self-report may be influenced by reduced awareness, recall error, or social desirability. Informant report may reflect caregiver burden, opportunity to observe, or protective restriction. Performance-based tests offer standardization but sample only selected tasks (Fritz et al., 2016). Digital records of movement or device use provide ecological detail but do not establish whether a task was completed safely, correctly, or voluntarily. Longitudinal studies show that early functional limitations, especially in planning, memory, and visuospatial domains, are associated with later instrumental disability, and that executive dysfunction, dementia severity, brain atrophy, white-matter disease, frailty, and medical comorbidity contribute to variation in everyday performance. Quantitative analysis should define loss of independence using observable transitions, such as new supervision, assistance, cessation of an activity, change in living arrangement, or crossing a validated functional threshold. Repeated measures can distinguish persistent decline from temporary limitation following illness or injury (Ooteghem et al., 2019). Joint examination of mobility and function can also identify whether gait deterioration precedes, accompanies, or follows reduced independence, while adjustment for baseline task participation prevents nonperformance caused by custom or opportunity from being misclassified as disability.

The available evidence establishes meaningful associations among cognition, gait, falls, and everyday function, yet the quantitative literature remains fragmented across outcomes and measurement settings. Many studies use cross-sectional case-control designs that distinguish diagnostic groups without estimating within-person change. Longitudinal cohorts frequently model dementia conversion or cognitive decline as the primary endpoint and treat mobility as a secondary predictor. Fall studies often rely on a short clinical battery and retrospective event recall, whereas wearable studies commonly emphasize feasibility or diagnostic classification rather than observed gait deterioration, prospectively recorded falls, and functional transitions (Varma et al., 2021). Functional studies measure instrumental activities in detail but may omit instrumented gait, free-living activity, neuroimaging, or biomarker information. Samples are often small, drawn from a single center, and restricted to participants able to complete complex protocols, producing limited representation of frailty, multimorbidity, lower education, rural residence, and under-resourced settings. Analytical variation in outcome definitions, dual-task procedures, sensor algorithms, follow-up intervals, and handling of missing data also limits direct comparison. Multimodal modeling addresses this fragmentation only when the temporal order of predictors and outcomes is preserved and when additional modalities contribute validated information. High-dimensional feature sets can overfit small samples, and a model can appear accurate when repeated observations from one participant enter both training and testing data. Class imbalance, informative dropout, competing events, site effects, and treatment changes can distort performance

(O'Leary et al., 2018). Discrimination alone is insufficient because predicted probabilities also require calibration, and internal validation does not establish transportability to another clinic or population. The present quantitative study is therefore focused on the longitudinal prediction of three prespecified, clinically distinct outcomes among individuals with mild cognitive impairment and early Alzheimer's disease: rate of gait decline, risk of incident or recurrent falls, and time to loss of functional independence. Predictor domains include demographic and socioeconomic characteristics, cognitive-domain scores, clinical and medication data, comorbidity and frailty measures, laboratory gait and balance variables, dual-task costs, free-living wearable metrics, neuroimaging or fluid biomarkers where available, and baseline functional status (Pieruccini-Faria et al., 2019). The analysis treats repeated gait observations as trajectories, fall events as time-dependent or recurrent outcomes, and functional loss as a defined transition rather than a vague change score. Candidate models are evaluated with participant-level resampling, regularization or principled feature reduction, assessment of nonlinearity and interactions, calibration, discrimination, prediction error, and sensitivity analyses for missingness and competing events. The central hypotheses are that multimodal models explain more out-of-sample variation than demographic, cognitive, or gait-only models; that dual-task and free-living mobility measures add information beyond usual gait speed; and that the strongest predictor patterns differ across gait decline, falls, and functional dependence because the three outcomes share mechanisms without representing the same clinical process (Montero-Odasso et al., 2018).

The primary objective of this quantitative study is to develop and evaluate a multimodal predictive framework for estimating gait decline, fall risk, and loss of functional independence among individuals diagnosed with mild cognitive impairment or early Alzheimer's disease. Specifically, the study seeks to determine how demographic characteristics, socioeconomic conditions, cognitive performance, clinical status, medication use, comorbidities, frailty indicators, laboratory-based gait measurements, balance performance, dual-task gait costs, free-living wearable-sensor metrics, neuroimaging findings, fluid biomarkers, and baseline functional abilities jointly contribute to variation in mobility-related outcomes. A central objective is to quantify longitudinal changes in gait speed, stride length, cadence, stride-time variability, gait asymmetry, double-support time, turning performance, walking-bout duration, and daily movement patterns rather than relying exclusively on a single baseline assessment. The study also aims to estimate the probability and timing of first, recurrent, and injurious falls through the integration of physical, cognitive, behavioral, and environmental risk factors. In relation to functional status, the research seeks to identify predictors of transition from independent performance to supervision, prompting, or physical assistance in basic and instrumental activities of daily living, including medication management, financial management, shopping, transportation, meal preparation, communication, household organization, bathing, dressing, toileting, and transferring. Another objective is to compare the predictive performance of multimodal models with models based only on demographic information, cognitive scores, conventional clinical assessments, or isolated gait measures. Model performance will be examined through discrimination, calibration, prediction error, sensitivity, specificity, and participant-level validation procedures. The study further aims to determine whether dual-task gait variables and free-living mobility measures provide additional predictive information beyond usual gait speed and whether the contribution of each predictor domain differs across gait decline, falls, and functional dependence. Potential variation associated with age, sex, education, socioeconomic position, cognitive subtype, Alzheimer's disease severity, frailty, and comorbidity will also be examined. Through these objectives, the analysis will treat gait deterioration as a continuous longitudinal trajectory, falls as time-dependent or recurrent events, and loss of independence as an observable functional transition, thereby maintaining clear distinctions among three related but clinically separate mobility outcomes.

LITERATURE REVIEW

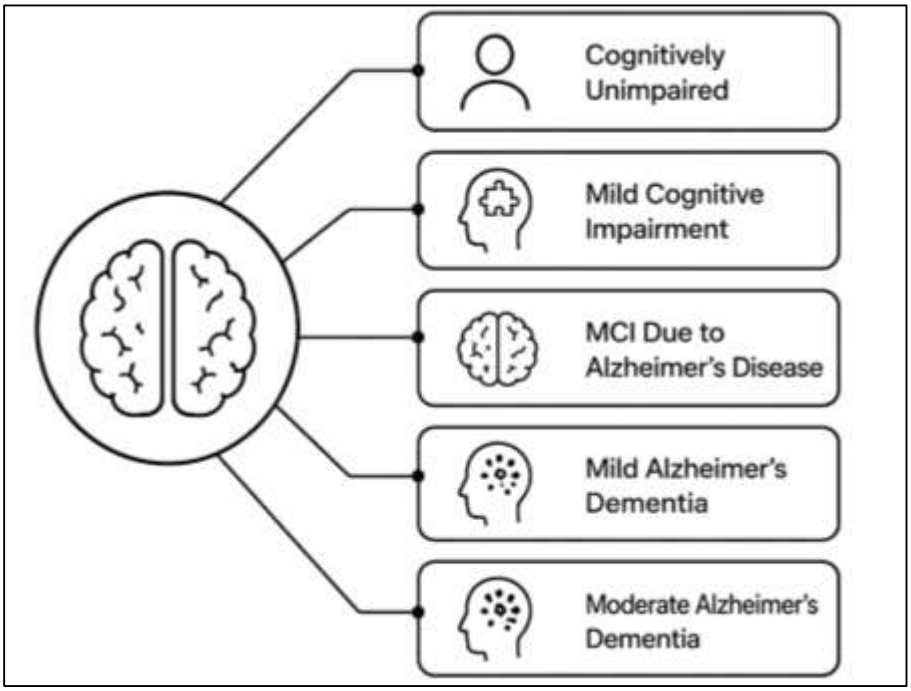
Alzheimer's disease has traditionally been examined through changes in memory, executive function, language, and other cognitive domains, yet accumulating quantitative evidence identifies mobility deterioration as an important component of the disease process. Individuals with mild cognitive impairment and early Alzheimer's disease may experience measurable changes in gait speed, stride length, cadence, postural control, turning, gait variability, dual-task performance, and daily walking

behavior before severe functional disability becomes apparent. These mobility changes are clinically interconnected with falls, restricted community participation, caregiver dependence, and declining capacity to perform basic and instrumental activities of daily living (Hunter & Divine, 2018; Kanti, 2020). The literature addressing these relationships is distributed across neurology, geriatrics, rehabilitation, biomechanics, epidemiology, neuroimaging, wearable sensing, and predictive analytics. A structured synthesis is therefore required to determine which variables consistently predict mobility-related deterioration and whether combining different data modalities produces stronger estimates than relying on cognitive scores, gait speed, or clinical diagnosis alone. This literature review examines quantitative studies involving cognitively unimpaired older adults, individuals with mild cognitive impairment, people with biomarker-supported mild cognitive impairment due to Alzheimer's disease, and patients with mild Alzheimer's dementia. Particular attention is given to the operational definitions of gait decline, fall risk, recurrent falling, and functional dependence because differences in measurement can substantially influence reported associations and predictive performance (Bondi et al., 2017; Debasish, 2021). The review evaluates laboratory-based spatiotemporal gait measures, cognitive-motor dual-task costs, balance and postural-control assessments, wearable-derived free-living mobility indicators, neuropsychological test scores, neuroimaging markers, fluid biomarkers, demographic characteristics, medication exposure, frailty, comorbidity, and baseline functional status. It also distinguishes cross-sectional diagnostic discrimination from longitudinal prediction, since variables that differentiate established clinical groups may not accurately estimate within-person deterioration or time to an adverse event. The quantitative evidence is assessed according to study design, sample size, follow-up duration, outcome ascertainment, statistical modeling, effect-size reporting, discrimination, calibration, internal and external validation, missing-data management, and control of confounding. Special consideration is given to whether studies account for repeated gait observations, recurrent falls, competing mortality, transition to supervised care, and informative participant dropout. The review further examines differences associated with age, sex, education, cognitive subtype, Alzheimer's disease severity, apolipoprotein genotype, vascular burden, frailty, physical activity, and socioeconomic context (Abdur & Iftekhar, 2021; Sohrabi & Weinborn, 2019). Organizing the literature around these measurable domains provides a focused basis for identifying complementary predictor groups, inconsistencies in existing models, and the quantitative rationale for simultaneously examining gait trajectories, fall events, and functional transitions within the early Alzheimer continuum.

Clinical Staging of Mild Cognitive Impairment and Early Alzheimer's Disease

Mild cognitive impairment is clinically defined as an intermediate cognitive state between expected age-related change and dementia. Its diagnosis generally requires evidence of concern regarding a change in cognition, objective impairment in one or more cognitive domains, relative preservation of independence in everyday activities, and the absence of functional deterioration severe enough to satisfy dementia criteria. Cognitive concern can be reported by the individual, an informant, or a clinician, but its reliability varies according to insight, emotional status, health literacy, and the opportunity of an informant to observe everyday behavior (Joubert et al., 2016; Chowdhury & Tonay, 2022). Objective impairment can occur in memory, executive function, attention, language, visuospatial ability, or processing speed. Mild inefficiencies in complex activities may be present, including slower financial management, medication errors, difficulty navigating unfamiliar environments, or greater reliance on reminders, while basic independence remains substantially preserved. This functional boundary is important because cognitive-test impairment alone does not distinguish mild cognitive impairment from mild dementia. The literature also treats mild cognitive impairment as a heterogeneous syndrome rather than a single disease entity. Amnestic mild cognitive impairment is characterized by prominent impairment in learning or memory and is more frequently associated with Alzheimer-type progression. Nonamnestic mild cognitive impairment primarily affects executive, attentional, language, or visuospatial abilities and can be associated with vascular disease, Lewy body pathology, frontotemporal degeneration, depression, medication effects, or other neurologic and medical conditions (Ho et al., 2018; Zahidul & Begum, 2022).

Figure 3: Clinical Staging of Early Alzheimer's



Single-domain mild cognitive impairment involves one impaired cognitive domain, whereas multidomain mild cognitive impairment involves impairment across two or more domains. Longitudinal evidence indicates that multidomain impairment is generally associated with lower rates of reversion to normal cognition and higher rates of progression to dementia than single-domain impairment. The severity of memory impairment also differentiates risk within amnestic categories. These subtype classifications remain sensitive to the number of tests administered, the cognitive domains represented, the normative reference group, and the threshold selected for objective impairment. Consequently, two studies can apply the same general definition while identifying substantially different MCI samples, subtype distributions, and levels of clinical severity (Nishat & Kaniz, 2022; Zvěřová, 2019).

Operational classification of cognitive stage commonly combines global screening scores, domain-specific neuropsychological testing, clinical ratings, and functional assessments. The Clinical Dementia Rating scale is frequently used to represent the continuum from no clinically evident impairment to severe dementia. A global score of zero generally indicates normal clinical functioning, a score of 0.5 commonly represents questionable impairment or mild cognitive impairment, and a score of one is often associated with mild dementia. The boundaries are not completely interchangeable because some individuals with a rating of 0.5 satisfy criteria for very mild dementia, particularly when cognitive problems have begun to interfere with independent daily performance. The Mini-Mental State Examination is also widely used, with higher score ranges often assigned to cognitively unimpaired adults or MCI and lower ranges used to characterize mild Alzheimer's dementia (Badrul & Mominul, 2023; Mortamais et al., 2017). Its classification accuracy is limited by ceiling effects, restricted measurement of executive and visuospatial abilities, and sensitivity to age, education, language, and cultural background. The Montreal Cognitive Assessment samples a broader range of executive, attentional, memory, language, and visuospatial abilities and is generally more sensitive to mild impairment. The originally proposed cutoff below 26 identifies many individuals requiring fuller assessment, but population studies have produced different optimal thresholds after accounting for education, language, clinical setting, and disease prevalence. Global screen scores should therefore be interpreted as indicators of possible impairment rather than independent diagnostic evidence. Domain-specific neuropsychological classification frequently defines impairment as performance approximately one to one-and-a-half standard deviations below appropriate normative expectations

(Hom et al., 2021; Kanti, 2024). More conservative methods require multiple impaired scores within a cognitive domain, reducing the probability that a single unusually low result will generate an MCI diagnosis. Actuarial neuropsychological approaches have produced more stable subtypes, stronger biomarker relationships, and clearer progression rates than conventional methods based on one low memory score and subjective concern. Classification also depends on test reliability, premorbid ability, sensory limitations, fatigue, anxiety, depression, and the quality of demographic correction. These measurement factors explain why fixed cutoffs applied without comprehensive clinical interpretation can misclassify both cognitively healthy adults and individuals whose impairment is clinically meaningful (Tonay et al., 2024; Yu et al., 2018).

Clinical mild cognitive impairment describes the severity of a cognitive syndrome but does not establish its underlying cause. Biomarker-supported mild cognitive impairment due to Alzheimer's disease refers to individuals who meet the clinical requirements for MCI and also demonstrate biological evidence consistent with Alzheimer pathology. Early Alzheimer's disease can therefore be operationalized as a clinical-biological continuum that includes biomarker-confirmed MCI due to Alzheimer's disease and mild Alzheimer's dementia. This definition separates the presence of Alzheimer pathology from the level of cognitive and functional impairment because individuals with comparable biomarker profiles can display different clinical stages. The amyloid, tau, and neurodegeneration framework organizes biomarkers according to the biological process they primarily represent. Amyloid status can be estimated using amyloid positron-emission tomography, reduced cerebrospinal-fluid amyloid concentrations, or abnormal amyloid ratios (Sadanand et al., 2016). Tau pathology can be assessed through tau positron-emission tomography or phosphorylated-tau concentrations in cerebrospinal fluid and validated blood assays. Neurodegeneration or neuronal injury can be represented by medial temporal or cortical atrophy on structural magnetic-resonance imaging, reduced metabolism on fluorodeoxyglucose positron-emission tomography, or selected injury-related fluid markers. Magnetic-resonance atrophy and neurodegeneration measures are not specific to Alzheimer's disease because similar abnormalities can arise from vascular, inflammatory, traumatic, or other neurodegenerative processes (Veronese et al., 2017). Revised biological criteria also recognize selected high-performing plasma phosphorylated-tau measures as evidence of core Alzheimer pathology when analytical and clinical-performance requirements are satisfied. Studies using clinical diagnosis alone usually include broader and more etiologically diverse MCI samples. Studies requiring abnormal amyloid and tau biomarkers create biologically narrower groups but may exclude individuals lacking access to lumbar puncture, molecular imaging, or validated blood testing. Cerebrospinal fluid and positron-emission tomography studies generally provide greater etiologic specificity, whereas plasma testing offers lower participant burden but remains sensitive to assay selection, thresholds, renal function, comorbidity, and laboratory standardization. Biological and clinical staging must consequently be reported separately so that cognitive severity is not treated as equivalent to pathological burden (Meng et al., 2020).

Diagnostic heterogeneity has a direct effect on estimated relationships among cognitive stage, gait dysfunction, falls, and functional dependence. Studies that combine amnestic, dysexecutive, vascular, mixed, and biomarker-negative MCI within one group may report averaged mobility effects that conceal meaningful subtype differences. Nonamnestic and multidomain MCI can produce substantial executive and attentional impairment, which may be strongly expressed during dual-task walking, turning, obstacle negotiation, and rapid balance correction. Amnestic MCI associated with Alzheimer pathology may show a different mobility profile in which gait abnormalities are related to distributed neurodegeneration, hippocampal involvement, or increasing cognitive-motor interference. Biomarker-supported groups can therefore yield different effect sizes from clinically defined groups even when participants have similar global cognitive scores (Oliveira et al., 2021). Multicountry gait research has also shown that associations between walking speed, stride variability, fall history, and cognitive category change according to dementia etiology and clinical severity. Functional estimates are similarly affected because some studies classify MCI by preserved basic activities alone, whereas others require preservation of complex instrumental activities. The second approach may exclude people with early medication, financial, transportation, or navigation problems and create a higher-functioning MCI sample. Reliance on a single screening instrument introduces additional misclassification. A low score

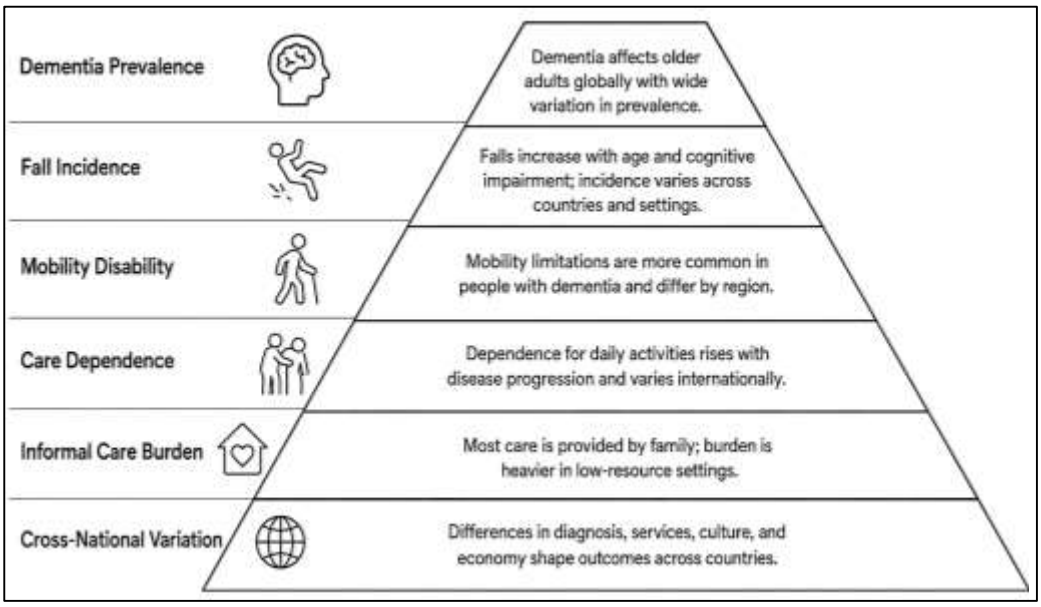
can arise from limited education, language differences, depression, fatigue, sensory impairment, or acute illness, while a high score can conceal executive or visuospatial dysfunction. Conventional MCI criteria have classified some individuals whose comprehensive neuropsychological profiles, biomarker patterns, and longitudinal courses resemble normal cognition, demonstrating the risk of false-positive diagnoses (Reul et al., 2017). False-negative classifications also occur when global scores remain high because of cognitive reserve or when the screening instrument does not adequately measure the affected domain. Such errors alter group prevalence, weaken observed associations, reduce prediction-model calibration, and complicate comparison across studies. Quantitative synthesis must therefore record the diagnostic authority, number and type of cognitive tests, impairment threshold, functional criterion, biomarker requirement, and clinical consensus procedure used in each investigation before comparing gait, fall, or independence outcomes (Mueller et al., 2018).

Cross-National Variation in Dementia Prevalence and Care Dependence Among Older Adults

Dementia represents a major international cause of mortality, disability, and dependence among older adults, with approximately 57 million people living with the condition worldwide in 2021 and nearly 10 million new cases occurring annually. Alzheimer's disease is the most common cause and accounts for an estimated 60% to 70% of dementia cases. More than 60% of people with dementia live in low- and middle-income countries, establishing that the numerical burden is not concentrated exclusively in high-income settings. Global estimates also conceal pronounced regional differences in age structure, survival, educational opportunity, cardiovascular risk, diagnostic coverage, and health-service availability (Kourtis et al., 2019). High- and high-middle socioeconomic-development regions frequently report elevated age-standardized prevalence because they have longer life expectancy, stronger case-finding systems, more memory clinics, and greater access to neuropsychological and biomarker assessment. Lower-resource regions may report lower recorded prevalence while experiencing extensive underdiagnosis, higher dementia-related mortality, and heavier dependence on unpaid family care. Population research in Indonesia and South Africa, for example, produced high community prevalence estimates while finding that fewer than 1% of identified participants had received a formal diagnosis. Studies conducted through the 10/66 Dementia Research Group have similarly shown that diagnostic systems developed in high-income countries can underestimate dementia and dependence in Latin American, Asian, and African populations. Regional burden also differs by age and sex (Garcia-Alvarez et al., 2019). Adults in their eighties experience particularly high prevalence, incidence, and disability, and women carry greater overall burden through longer survival, higher dementia mortality, and disproportionate exposure to unpaid caregiving. Education, socioeconomic disadvantage, vascular disease, nutrition, and access to preventive or diagnostic services further influence observed rates. Rural populations face additional barriers involving distance from specialist services, limited transportation, fewer trained clinicians, and cultural interpretation of cognitive symptoms as normal ageing. International comparisons must therefore distinguish measured prevalence from actual disease occurrence and account for differences in diagnostic criteria, sampling, survival, and health-system capacity (Schneider & Goldberg, 2020). Falls constitute a substantial component of mobility-related disability among older adults, and their frequency increases markedly with advancing age, frailty, cognitive impairment, sensory loss, and environmental exposure. Global Burden of Disease analyses identify hundreds of millions of fall events across all age groups each year, with older adults experiencing a particularly high concentration of fall-related deaths and disability-adjusted life years. In 2021, the estimated age-standardized incidence among adults aged 60 years and older exceeded 5,000 events per 100,000 people. High-socioeconomic-development regions often report greater fall incidence because of stronger surveillance, longer survival, and greater activity exposure, whereas lower-development regions can show higher mortality after a fall because of delayed emergency response, restricted surgical access, limited rehabilitation, and lower availability of post-acute care (Lloyd-Sherlock, 2019). Fall outcomes include fractures, traumatic brain injury, soft-tissue injury, hospitalization, reduced confidence, restricted activity, and admission to institutional care. Cognitive status materially changes this burden. A multicountry investigation involving almost 2,500 older adults from seven countries reported a history of falling in approximately one quarter of cognitively healthy participants, one half of participants with Alzheimer's disease, and nearly two thirds of those with non-Alzheimer dementia. Studies of MCI show that executive and attentional

impairment, increased gait variability, slow reaction time, and inaccurate judgment of stepping capacity contribute to fall risk even when usual walking speed appears relatively preserved. Prospective dementia research has linked falling with impaired gait and balance, autonomic dysfunction, depression, medication exposure, and reduced physical activity.

Figure 4: Cross-National Dementia and Mobility Burden



Recurrent falls are especially common in residential and long-term care populations (Beard et al., 2016). One intensively monitored dementia cohort recorded more than five falls per resident-year, with most participants experiencing at least one fall and a substantial proportion of events producing serious consequences. Cross-national comparisons remain sensitive to whether studies measure retrospective fall history, prospectively recorded events, recurrent falls, injurious falls, emergency attendance, hospitalization, or mortality, since each method captures a different portion of the burden.

The international burden of Alzheimer's disease extends beyond prevalence and mortality because progressive cognitive and mobility impairments generate substantial disability, care dependence, and economic cost. Dementia is among the leading causes of disability and dependency in older populations, contributing extensively to years lived with disability and disability-adjusted life years across Europe, Asia, the Americas, Africa, and the Middle East (Wang et al., 2021). Functional deterioration usually begins in cognitively demanding instrumental activities such as medication management, financial transactions, transportation, shopping, cooking, communication, and navigation before extending to bathing, dressing, toileting, feeding, and transfers. Gait decline, falls, physical frailty, and fear of falling can accelerate this transition by reducing community mobility and increasing the supervision required for everyday tasks. Global economic estimates placed dementia-related costs at approximately US$1.3 trillion in 2019, with around half attributed to informal care. Family members and close friends provide an average of several hours of care and supervision each day, and women contribute approximately 70% of all informal dementia-care hours (Beard et al., 2016). The balance between informal care, formal home services, and institutional care varies widely across countries. Comparative research involving Japan, the United States, and European countries found substantial differences in caregiver age, sex, health-related quality of life, employment disruption, and the proportion of people with dementia living in institutions. Harmonized studies from China, India, and Mexico show that co-residence with family is strongly associated with receiving informal assistance, though the relationship varies by sex and national context (Ambrosi et al., 2021). Research in Cuba, Tanzania, Vietnam, Kazakhstan, and other lower-resource settings demonstrates that dementia-related dependence can lead caregivers to reduce employment, experience psychological

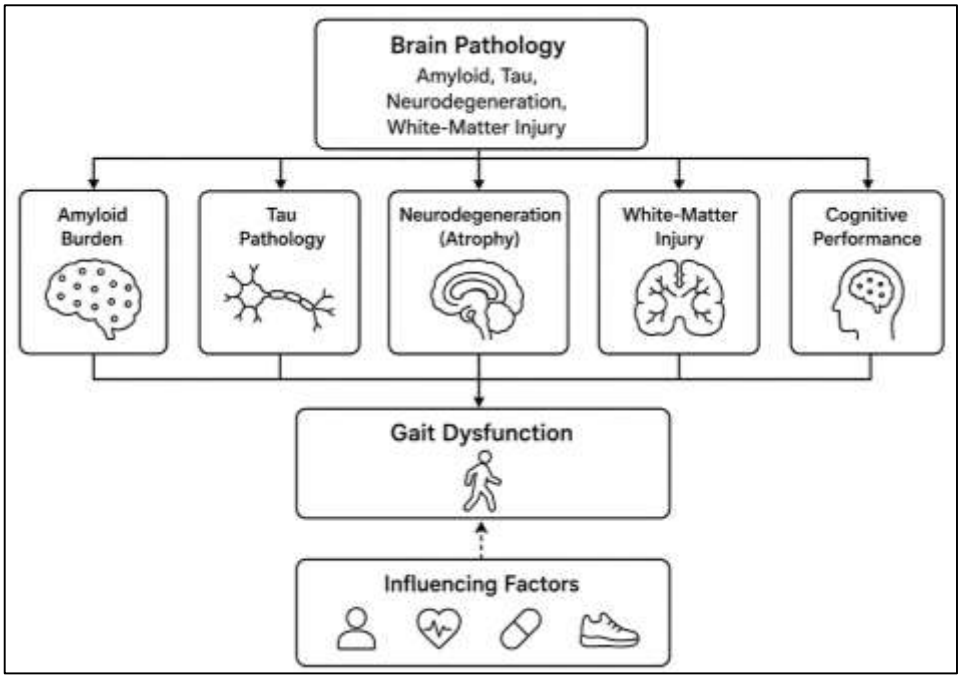
distress, and absorb transportation and medical costs. Institutionalization is less available in many low- and middle-income countries, leaving families responsible for complex mobility supervision and personal care. Rurality, housing accessibility, household composition, insurance coverage, caregiver availability, stigma, and access to rehabilitation shape whether functional impairment results in supervised community living, hospitalization, or residential placement (Wearing et al., 2018).

Cognitive-Domain Performance with Spatiotemporal Gait Dysfunction

Human gait is controlled by an integrated system involving the frontal, parietal, temporal, motor, subcortical, cerebellar, and brainstem regions rather than by an isolated motor center. Primary and supplementary motor areas organize movement initiation and sequencing, while the prefrontal cortex supports planning, attention allocation, inhibition, and adaptation to competing demands. Parietal and visuospatial networks integrate body position with environmental information, and temporal and hippocampal structures contribute to spatial orientation, route memory, and navigation. The basal ganglia regulate movement amplitude and automaticity, the cerebellum coordinates timing and error correction, and brainstem pathways support posture, muscle tone, and locomotor rhythm (Kossioni & Maggi, 2020). This distributed organization explains why gait can remain relatively stable during uncomplicated walking but deteriorate when an individual turns, avoids an obstacle, changes speed, or performs a cognitive task simultaneously. Quantitative studies commonly organize gait into pace, rhythm, variability, asymmetry, and postural-control domains. One five-domain analysis explained approximately 80% of total variation in measured gait characteristics, while age, executive function, attention, balance confidence, and fatigue jointly explained as much as 40% of variation within selected domains. Executive function and attention show particularly strong relationships with stride regulation, turning, and dual-task walking. In a large community sample, poorer processing speed, short-term memory, and sustained attention were independently associated with slower gait during usual, cognitive dual-task, and motor dual-task conditions (Onna & Boonen, 2022). Dual-task walking added an executive component that was not as evident during single-task walking. Among individuals with MCI, reduced working memory remained independently associated with slower gait after demographic, health, and other cognitive variables were controlled. Studies of Alzheimer's disease similarly show that divided attention produces greater increases in stride-time variability than changes in average speed. Reported cognitive-gait correlations are commonly small to moderate, generally falling between approximately 0.20 and 0.50, and vary according to cognitive domain, walking condition, disease stage, and adjustment strategy. Longitudinal analyses further indicate that slow gait predicts decline in processing speed, visuospatial performance, memory, and global cognition, with apolipoprotein genotype modifying some associations (Brims & Oliver, 2019).

Amyloid accumulation, tau pathology, and neurodegeneration have been quantitatively associated with gait abnormalities, but the strength and consistency of these relationships differ across biomarkers and gait domains. Positron-emission tomography studies have linked higher regional amyloid burden in the putamen, precuneus, anterior cingulate, occipital cortex, and other association regions with slower walking speed. In one cognitively impaired sample, global amyloid burden was associated with gait speed through a standardized regression coefficient of approximately negative 0.52 and with lower-extremity physical performance through a coefficient of approximately negative 0.47 after white-matter lesion burden and other covariates were considered. The relationship with Timed Up and Go performance was weaker and did not reach conventional statistical significance, demonstrating that different mobility measures do not capture identical biological processes (Singh et al., 2017). Longitudinal evidence has associated greater amyloid burden with reduced cadence, longer double-support time, and declining speed, with stronger and more extensive relationships reported among women in some cohorts. Tau appears more closely related to neuronal dysfunction and clinical severity. In an MCI sample, higher tau burden across early and intermediate Braak regions was associated with greater step-velocity variability and altered step length, producing standardized coefficients of approximately 0.38 and 0.34. The step-length association weakened after gait speed was controlled, indicating that some biomarker relationships operate through overall pace. Structural neurodegeneration also contributes to gait dysfunction (Lukačišinová et al., 2021).

Figure 5: Biomarkers and Cognition Predict Gait



Reduced volumes in the medial frontal cortex, anterior cingulate, precuneus, occipital regions, inferior temporal cortex, motor cortex, basal ganglia, and hippocampus have been associated with slower dual-task gait, shorter strides, impaired turning, and increased variability. One large MCI study connected faster dual-task gait with a distributed pattern of greater gray-matter volume across frontal, cingulate, parietal, temporal, and occipital regions. Hippocampal findings are less uniform because volume, compensatory activity, cognitive subtype, and disease stage interact. Some studies show moderate positive correlations among hippocampal volume, stride length, executive function, and turning velocity, whereas another reported a positive adjusted coefficient of 0.75 between hippocampal volume and worse stride variability in subjective cognitive impairment, interpreted as possible inefficient compensation rather than a simple atrophy–gait relationship (Schulz et al., 2020).

White-matter hyperintensities, lacunes, cerebral microbleeds, microstructural injury, and reduced network efficiency provide an additional pathway linking brain pathology with gait deterioration. White-matter tracts connect frontal executive regions, supplementary motor areas, parietal sensory-integration regions, basal ganglia, cerebellar pathways, and spinal motor systems. Injury within these pathways can slow information transfer, impair bilateral coordination, weaken anticipatory postural control, and increase the attentional resources required for walking. Community studies show that greater white-matter hyperintensity volume is associated with slower gait, shorter steps, and higher spatial and temporal variability. The association is often stronger among people with established cognitive impairment than among cognitively preserved adults (Parambi et al., 2020). In one study, white-matter burden was related to velocity and multiple variability measures in cognitively impaired participants but primarily to spatial variability in individuals with mild or no cognitive impairment. Subclinical infarcts, particularly those involving the basal ganglia, have also been associated with increased step-length variability independently of age, cardiovascular disease, and global cognitive performance. Lesion location appears important. Brainstem lacunes produced an adjusted coefficient of approximately negative 0.20 for gait speed, while basal-ganglia and brainstem microbleeds were associated with shorter strides, reduced step height, altered step width, and poorer balance. Diffusion-tensor imaging studies reinforce the role of microstructural integrity (Otones et al., 2020). Fractional anisotropy in the anterior corona radiata correlated with dual-task gait and cognitive-task speed at coefficients reaching approximately 0.51, while dual-task gait costs correlated with widespread white-matter integrity at coefficients approaching negative 0.47. Longitudinal analysis has linked reduced

structural-network efficiency with worsening Timed Up and Go performance through an adjusted coefficient of approximately negative 0.22, independent of lesion counts, white-matter hyperintensity volume, and total brain volume. Functional connectivity studies identify related network disruption. Greater within-default-mode connectivity and altered coupling between the default-mode network and supplementary motor area have been associated with poorer dual-task performance, slower gait, and greater postural sway in MCI (Kojima, 2017). Small-vessel disease studies also demonstrate reduced activity and connectivity across supplementary motor, sensorimotor, frontoparietal, temporal, caudate, and precuneus regions, with regional functional measures corresponding to gait speed and cadence.

The association between Alzheimer pathology and gait dysfunction cannot be interpreted as a single direct pathway because vascular, musculoskeletal, sensory, inflammatory, and cardiometabolic processes frequently coexist with neurodegeneration. Amyloid and tau can disrupt cortical and subcortical networks involved in attention, navigation, motor planning, and postural regulation, while white-matter injury can independently reduce communication efficiency within the same networks. Arthritis, sarcopenia, pain, peripheral neuropathy, visual impairment, vestibular dysfunction, obesity, diabetes, cardiac disease, orthostatic hypotension, depression, fatigue, and medication exposure can also produce slow or unstable gait (Volpato & Guralnik, 2017). Sustained systemic inflammation has been associated with slower walking and greater white-matter hyperintensity burden; one longitudinal study reported an adjusted coefficient of approximately negative 0.27 between long-term inflammatory exposure and gait speed, with white-matter disease accounting for about 30% of the relationship. Primary motor-cortex neurochemistry adds another level of complexity. In MCI, lower neuronal-integrity metabolite ratios were associated with greater dual-task stride-time variability through an adjusted coefficient of approximately 5.51, while higher membrane-turnover ratios were associated with gait-speed reductions of approximately 27 centimeters per second during single-task walking and 42 centimeters per second during dual-task walking. These findings indicate that variability and speed can respond to different biological disturbances (Yang & Bath, 2019). Quantitative studies must therefore distinguish total biomarker-gait associations from effects that remain after age, sex, education, body mass index, cognition, comorbidity, medication, physical activity, cardiovascular risk, lesion burden, and baseline gait speed are considered. Standardized regression coefficients permit comparison among predictors measured on different scales, while confidence intervals show the precision of estimated effects. Changes in explained variance indicate whether biomarkers contribute information beyond clinical and cognitive measures. Interaction analyses are required when associations differ by sex, genotype, cognitive stage, or vascular burden, and mediation analyses help determine whether cortical atrophy, cognition, or white-matter injury accounts for part of a biomarker relationship (Reyes et al., 2020). Studies using multimodal adjustment generally support overlapping Alzheimer, vascular, cognitive, physical, and sensory contributions rather than a single pathological explanation for spatiotemporal gait dysfunction.

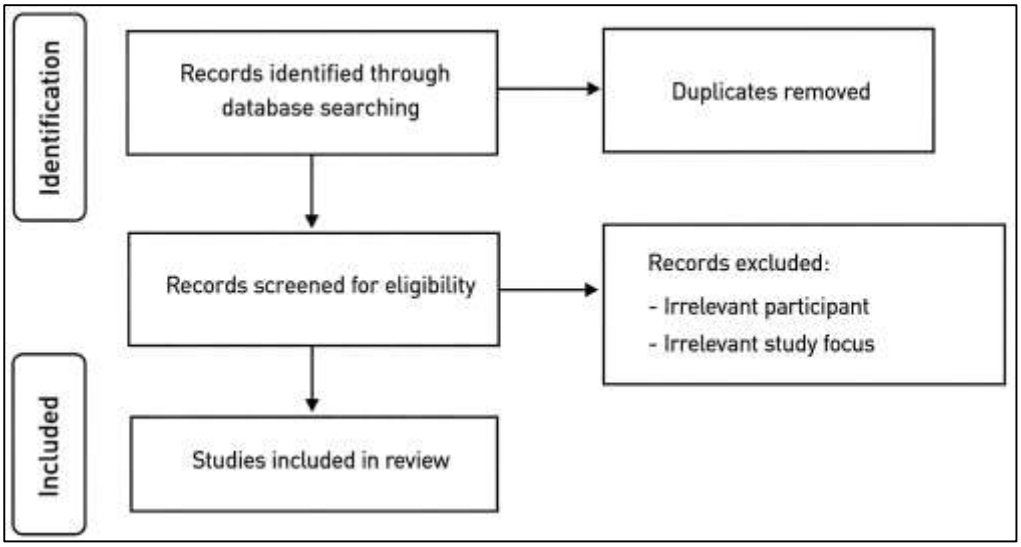
Double-Support Time Across Normal Cognition, MCI, and Early Alzheimer's Disease

Quantitative gait research commonly organizes spatiotemporal measurements into pace, rhythm, variability, asymmetry, and postural-control domains, each representing a partly distinct component of locomotor function. The pace domain includes gait speed, step length, and stride length and reflects the distance covered within a specified time and the spatial magnitude of successive steps (Wirz et al., 2022). Rhythm includes cadence, step time, stride time, swing time, and stance time, describing the temporal organization of the gait cycle. Variability represents step-to-step or stride-to-stride fluctuations in these measurements, while asymmetry captures differences between the left and right limbs. The postural-control domain includes step width, double-support time, dynamic balance, and measures of turning stability. Across the cognitive continuum, cognitively unimpaired older adults generally demonstrate faster gait, longer steps and strides, shorter double-support periods, and lower temporal variability than individuals with mild cognitive impairment or Alzheimer's dementia (Ghoraani et al., 2021). A meta-analysis involving 36 studies and 29,520 participants estimated that usual gait speed was approximately 0.11 meters per second slower in cognitive impairment, 0.20 meters per second slower in mild dementia, and 0.41 meters per second slower in moderate dementia relative to cognitively unimpaired groups. The size of the difference increased with the severity of cognitive impairment. Individual electronic-walkway studies have frequently reported large differences in gait

speed, step length, and stride length between cognitively intact adults and people with dementia, while differences between cognitively intact and MCI groups have been smaller or statistically nonsignificant under ordinary single-task walking. Early Alzheimer's disease is also associated with longer stance phases, increased double-support time, shorter swing time, reduced cadence, and wider steps, although cadence and step width findings vary across samples. Cadence can remain relatively preserved when participants maintain rhythmic stepping by shortening their strides, producing a slow, short-stepped gait without a major reduction in steps per minute (Tian et al., 2017). Increased double-support time represents a longer period during which both feet remain in contact with the ground and is frequently observed when balance confidence, postural stability, or motor planning is reduced. These domain-specific changes show that cognitive-stage differences are not represented by gait speed alone and can involve simultaneous alterations in spatial scaling, temporal regulation, and postural stabilization.

Stride-time and step-time variability receive particular attention because they represent the consistency of central gait regulation rather than average walking performance alone (Belghali et al., 2017). Cognitively unimpaired adults ordinarily produce relatively stable step and stride intervals, whereas MCI and early Alzheimer groups demonstrate greater fluctuations between successive gait cycles, especially when walking is combined with a cognitively demanding task. In one study comparing MCI and cognitively normal groups across increasingly complex dual-task conditions, gait variability ranged from 2.68% to 9.84% in the MCI group and from 1.86% to 3.74% in the control group. Another electronic-walkway investigation found that mean gait velocity among participants with MCI decreased from 119.11 centimeters per second during single-task walking to 110.88 centimeters per second during dual-task walking, accompanied by increases in stride-time, step-time, and double-support-time variability (Cicirelli et al., 2021). Six principal gait variables demonstrated intraclass correlation coefficients above 0.85, indicating strong measurement reliability under standardized testing. Comparisons involving cognitively unimpaired, MCI, and Alzheimer groups have also shown that group differences in velocity, stride time, and stride-time variability become more pronounced during animal naming, serial subtraction, or other executive-attentional tasks. The MCI category is not associated with a single gait phenotype. Large multicenter analyses have reported greater usual-walking disturbance in nonamnestic MCI than in amnestic MCI, particularly for rhythm and variability measures. Other studies have found that amnestic MCI is associated with slower gait and a higher dual-task cost after adjustment for age, sex, physical activity, comorbidity, and executive function (Darweesh et al., 2019).

Figure 6: Cognitive Stage Differences in Gait



These findings reflect differences in task conditions and cognitive-domain involvement: nonamnestic MCI may produce greater single-task disturbance when executive, visuospatial, or attentional systems are affected, whereas amnestic MCI may show clearer abnormalities when cognitive loading exposes limited compensatory capacity. Continuous in-home monitoring has similarly identified slow gait-speed and extreme gait-variability trajectories among participants with nonamnestic MCI. Asymmetry measurements have been less consistent than speed and variability because limb dominance, arthritis, pain, previous injury, footwear, and sensor placement can produce left–right differences that are not specific to cognitive impairment (Ardle et al., 2021). Temporal variability under dual-task conditions has remained one of the more reproducible indicators of disrupted cognitive-motor control across heterogeneous MCI classifications.

Turning places greater demands on anticipatory postural adjustment, visuospatial processing, bilateral coordination, executive control, and rapid reorganization of the stepping pattern than straight-line walking. Quantitative turning variables include turn duration, angular velocity, number of steps used to complete a turn, step regularity, turn smoothness, and the duration of transition between straight walking and directional change. People with MCI or early Alzheimer's disease commonly turn more slowly, take more steps, spend longer completing the movement, and demonstrate less smooth angular acceleration than cognitively unimpaired participants (Chen et al., 2020). These differences are often amplified during dual-task walking. In one digital-mobility study, dual-task turn velocity distinguished MCI from normal cognition with an area under the receiver operating characteristic curve of 0.801, sensitivity of 0.738, and specificity of 0.842. The corresponding discrimination between dementia and normal cognition produced an area under the curve of 0.923, sensitivity of 0.857, and specificity of 0.842. Electronic walkways and pressure-sensitive mats provide highly standardized measurements of gait speed, step length, stride length, cadence, stance time, swing time, step width, and temporal variability, although their restricted recording area may capture only a small number of strides. Three-dimensional motion-capture systems quantify joint angles, segment trajectories, trunk motion, and turning mechanics with high spatial precision, while force platforms measure ground-reaction forces, center-of-pressure movement, weight transfer, and postural responses (Azadian et al., 2016). These systems require specialized laboratory space and may alter participants' natural walking behavior. Body-worn inertial sensors record acceleration and angular velocity and permit the measurement of straight walking, transitions, turning, and free-living mobility over longer periods. Daily-life monitoring has documented lower maximum gait speed among people with cognitive decline, with median values of 113.7 centimeters per second compared with 121.2 centimeters per second in cognitively healthy participants. In the same investigation, laboratory stride-length variability had a median value of 2.6 among participants with cognitive decline and 1.8 among cognitively healthy adults (Godi et al., 2021). Daily maximum speed and laboratory variability were modestly correlated, indicating that standardized and free-living measurements capture related but nonidentical mobility characteristics. Differences in walkway length, sensor location, sampling frequency, turning protocol, footwear, walking instructions, and variability calculations remain important sources of between-study heterogeneity (Pieruccini-Faria et al., 2019).

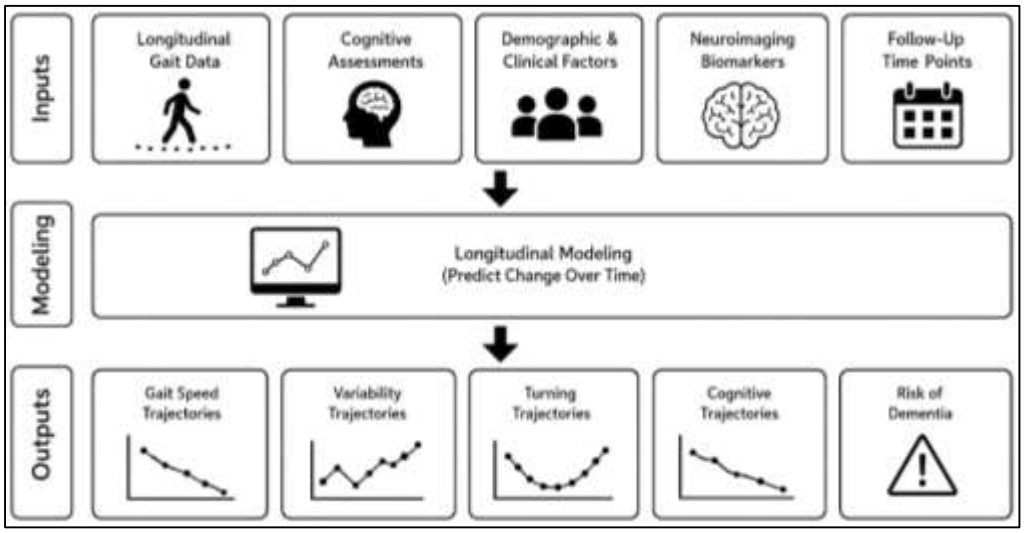
Cognitive Performance During Longitudinal Follow-Up

Baseline gait impairment and longitudinal gait decline represent related but analytically distinct mobility characteristics. Baseline impairment is identified when a participant walks more slowly, takes shorter strides, demonstrates greater temporal variability, or requires longer turning and double-support periods at the first assessment. Longitudinal decline refers to a measurable within-person deterioration across repeated assessments and is expressed through annual change, individual slope, percentage decline, change-point acceleration, or transition across clinically defined thresholds (Jayakody et al., 2022). A participant can have a slow baseline gait that remains stable, while another participant can begin with normal gait speed and subsequently experience rapid decline. This distinction is demonstrated in longitudinal cognitive-motor cohorts in which a single measurement of slow gait showed limited predictive value after adjustment, while serial reductions in gait velocity were strongly associated with cognitive deterioration and incident dementia. Reported rates vary according to participant age, cognitive stage, walking distance, pace instructions, and follow-up duration. In a longitudinal aging cohort, gait speed declined by approximately 0.013 meters per second annually

across the full sample, while participants who later developed MCI experienced an additional annual reduction of approximately 0.01 meters per second. Change-point analysis indicated that their gait decline accelerated by approximately 0.023 meters per second per year around 12.1 years before MCI diagnosis. The Baltimore Longitudinal Study of Aging reported an average annual decline of approximately 0.014 meters per second, whereas the fast-decline class in the Health, Aging and Body Composition Study lost approximately 0.030 meters per second, or 2.4% of baseline speed, each year (Whelan et al., 2022). Another cohort of older adults without dementia recorded annual reductions of approximately 1.8 centimeters per second during ordinary walking and 1.13 centimeters per second during cognitively demanding walking. Changes of approximately 0.03 to 0.05 meters per second are generally treated as minimally meaningful, while reductions near 0.08 to 0.10 meters per second represent more substantial deterioration. Several dementia-risk studies have operationalized accelerated gait decline as an annual loss of at least 0.05 meters per second. Longitudinal measurements of stride length, cadence, stride-time variability, double-support time, and turning are less standardized, with speed remaining the most consistently repeated mobility outcome.

Longitudinal studies have produced three main temporal patterns: mobility decline preceding measurable cognitive decline, concurrent cognitive-motor deterioration, and gait changes emerging after clinically recognizable cognitive impairment. Evidence for gait deterioration preceding cognitive decline is provided by cohorts with long observation periods and repeated measurements (Verghese et al., 2017). In the Oregon Brain Aging Study, gait-speed decline accelerated approximately 12 years before MCI diagnosis, while gait-speed change points appeared earlier among men than women. The Gothenburg H70 Birth Cohort followed cognitively unimpaired participants for up to 15 years and documented slower walking as early as nine years before deterioration in Clinical Dementia Rating scores. Participants with pathological cerebrospinal-fluid amyloid concentrations also demonstrated greater prior gait-speed loss. The Mayo Clinic Study of Aging found that faster baseline gait was associated with less subsequent decline in memory, executive function, and global cognition, whereas baseline cognitive performance was not significantly associated with later gait-speed change. Other cross-lagged investigations have reported bidirectional relationships, with poorer baseline cognition predicting steeper gait decline and slower baseline gait predicting greater cognitive deterioration (Paolillo et al., 2020).

Figure 7: Longitudinal Cognitive-Motor Trajectory Prediction



These differences reflect variation in cognitive instruments, follow-up intervals, health status, and analytical specification. Concurrent decline in gait speed and memory has produced a particularly high-risk phenotype. An individual-participant meta-analysis of six cohorts included 8,699 adults followed for approximately 6.6 to 14.5 years. Relative to participants without meaningful decline,

memory-only decliners had a pooled dementia hazard ratio of 3.45, gait-only decliners had a hazard ratio of 2.24, and dual decliners had a hazard ratio of 6.28. In a separate cohort of 144 community-dwelling older adults assessed twice annually for seven years, dual decliners had approximately three times the dementia risk of non-dual decliners. Analysis of 16,855 ASPREE participants produced an even stronger association: concurrent gait and delayed-memory decline was associated with a dementia hazard ratio of 24.9, while concurrent gait and global-cognition decline produced a hazard ratio of 22.2. Smaller associations were observed when gait decline was combined with verbal-fluency or processing-speed decline (Haynes et al., 2017). These studies distinguish parallel within-person deterioration from poor performance recorded at only one examination.

Change scores, individual slopes, change-point models, latent trajectories, and joint outcome models provide different quantitative representations of cognitive-motor deterioration. A simple change score subtracts the baseline value from the follow-up value and is easily interpreted, although it treats two participants with different follow-up durations as equivalent unless change is annualized. Individual slope estimates use all available assessments to describe the rate and direction of within-person change. Linear mixed-effects models estimate average trajectories while allowing participants to have different baseline levels and rates of decline (Lo et al., 2019). They can accommodate unequal numbers of visits and irregular assessment intervals and have been used to identify accelerated gait slowing before MCI, serial motor decline before dementia, and relationships between brain-volume loss and declining mobility. Generalized estimating equations estimate population-average change and account for correlations among repeated measurements, but they provide less direct information about participant-specific trajectories. Latent-class growth models identify unobserved groups with distinctive patterns rather than assuming that all participants follow one average slope. The San Antonio Longitudinal Study of Aging followed 370 Mexican American and European American adults for an average of 9.5 years and identified three joint trajectory classes: 65.4% maintained relatively stable cognition and gait, 22.2% experienced deterioration in both domains, and 12.4% maintained cognition while gait deteriorated. In the Health, Aging and Body Composition Study, 2,364 initially well-functioning adults were classified into slow-, moderate-, and fast-decline gait trajectories; 518 participants belonged to the fast-decline class and lost approximately 0.030 meters per second annually (Angel et al., 2022). Change-point models permit slopes to differ before and after an estimated transition and have identified acceleration in gait deterioration years before clinical cognitive impairment. Joint longitudinal-survival models connect repeated gait measurements with time to dementia, institutionalization, or death while accounting for dependence between the mobility trajectory and event process. A joint analysis of 3,048 adults incorporated gait measurements collected every six months and 14 years of survival data, demonstrating how current gait level and annualized decline contribute separate prognostic information. Models using repeated cognitive and gait measurements have generally fitted observed dementia outcomes better than models limited to baseline cognition and mobility (Pillemer et al., 2019).

Estimated cognitive-motor trajectories are influenced by follow-up duration, measurement frequency, attrition, practice effects, regression to the mean, and measurement error. Short follow-up periods may capture temporary variation caused by illness, fatigue, pain, medication changes, footwear, or testing conditions rather than sustained deterioration. Long follow-up provides greater separation of stable and declining trajectories but increases losses through death, institutionalization, severe disability, and withdrawal. These losses are informative because participants with the greatest mobility and cognitive deterioration are often least likely to complete later assessments. Annual or biennial examinations estimate broad progression, while semiannual assessments provide more precise slopes and permit identification of nonlinear acceleration (Bielak et al., 2017). Cognitive scores can improve temporarily through familiarity with testing procedures, as observed in a 32-month study in which executive-function scores increased while gait remained slower in the MCI and Alzheimer groups and the number of steps increased across all groups. Regression to the mean is particularly important when participants are classified as decliners from two observations. One study of challenging walking tasks reported that participants classified as declining had the fastest baseline speed, while participants classified as improving had the slowest initial speed. Repeated trials, standardized testing conditions, reliability assessment, and three or more measurement occasions reduce this distortion. Baseline predictors of accelerated mobility deterioration include older age, obesity, diabetes, hypertension,

dyslipidemia, depressive symptoms, low physical activity, reduced knee-extensor strength, lower education, lower income, and limited tangible support. Health and Body Composition data linked female sex, Black race, obesity, weak knee extension, and low physical activity with fast gait decline (Wu et al., 2022). The San Antonio trajectory analysis associated combined cognitive and physical vulnerability with older age, Mexican American ethnicity, diabetes, lower education, and lower income. Among 362 adults followed for an average of 3.2 years, 23% experienced an annual gait-speed reduction of at least 0.05 meters per second; faster baseline cadence and longer stride length were associated with lower adjusted odds of meaningful decline. Neuroimaging studies have additionally associated accelerated gait and memory decline with smaller gray- and white-matter volumes, greater white-matter-hyperintensity burden, and lower hippocampal volume (Memel et al., 2021). Longitudinal evidence for turning remains more limited than gait-speed evidence, with wearable studies measuring turn frequency, duration, peak velocity, angle, and step-number variability and showing that greater variability in steps per turn was associated with subsequent falls.

Motor Dual-Task Costs for Mobility and Cognitive Outcomes

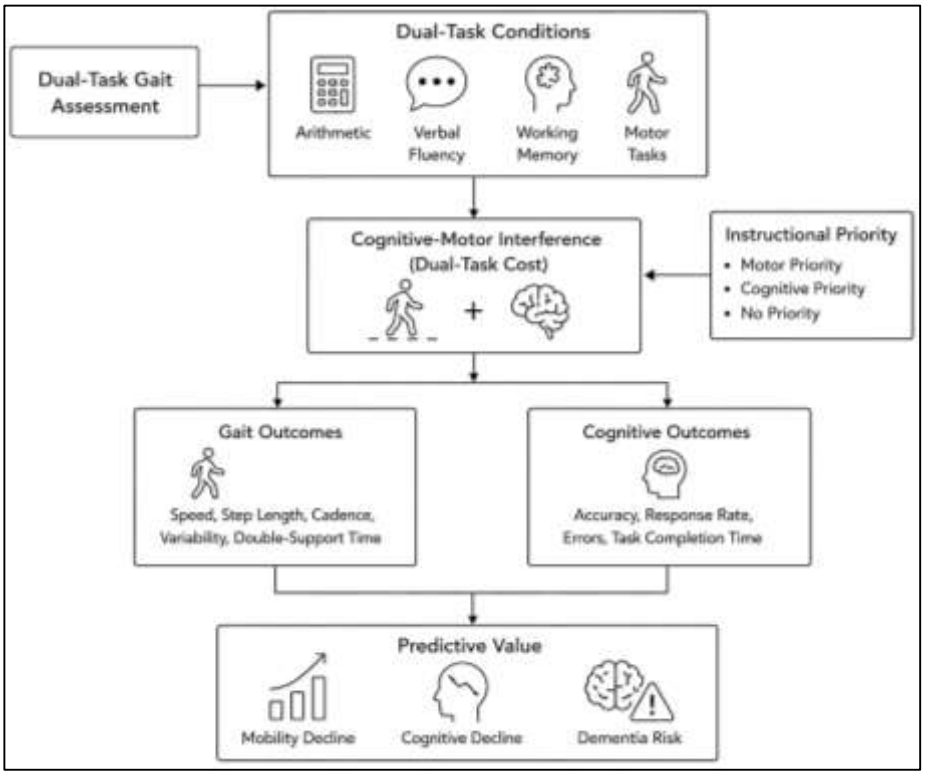
Dual-task gait refers to walking while simultaneously performing a secondary cognitive or motor activity. Cognitive-motor interference occurs when the concurrent tasks compete for limited attentional, executive, working-memory, visuospatial, or motor-control resources, producing deterioration in walking performance, secondary-task performance, or both. Dual-task cost quantifies this interference by comparing performance during dual-task walking with the same participant's performance during the corresponding single-task condition (McKinney et al., 2020). For gait speed, stride length, or cadence, the reduction observed during dual-task walking is divided by single-task performance and expressed as a percentage. For outcomes in which higher values indicate poorer performance, such as stride-time variability, step-time variability, double-support time, or task-completion time, the direction of the calculation is interpreted accordingly. A positive cost commonly indicates deterioration, while a negative cost can reflect improvement or facilitation. Cognitive cost is calculated separately by comparing the accuracy, response rate, number of correct answers, or number of errors during seated or standing cognitive performance with the same outcomes recorded while walking. Reporting gait cost without cognitive-task accuracy can misclassify participants who preserve walking by reducing cognitive effort. Instructional priority also changes the distribution of interference (Hauer et al., 2020). Under motor-priority instructions, participants are told to maintain their walking speed, balance, or stepping pattern (McFadyen et al., 2017). Cognitive-priority instructions emphasize correct and rapid performance of the secondary cognitive task. No-priority instructions ask participants to perform both tasks without identifying which should receive greater attention. A priority-based study comparing eight participants with MCI and eight cognitively normal adults found no meaningful group difference during usual walking, while the MCI group walked more slowly and demonstrated nearly three times greater gait variability under the no-priority condition. Their gait-speed cost was almost twice that of controls under no-priority instructions and approximately three times that of controls under both motor- and cognitive-priority conditions (Chortane et al., 2022). These findings demonstrate that dual-task cost is not solely a participant characteristic; it is also shaped by task instructions, performance strategy, and the outcome selected to represent cognitive-motor interference (Bishnoi & Hernandez, 2021).

Arithmetic, verbal-fluency, working-memory, and motor dual tasks impose different cognitive and biomechanical demands. Counting backward by ones is a relatively low-complexity mental-tracking task that requires sustained attention and response generation. Counting backward by threes or subtracting serial sevens increases working-memory, calculation, monitoring, and response-inhibition demands. Naming animals or generating words within a semantic category requires lexical access, semantic search, executive retrieval, and avoidance of repeated responses. Spelling words backward, recalling digit sequences, and responding to working-memory prompts place greater demands on temporary information storage and manipulation (Lin et al., 2019). Object-carrying tasks, including carrying a tray, holding a cup of water, operating a telephone, or transporting another object, combine gait control with upper-limb stabilization and visually guided motor regulation (Brustio et al., 2018). A meta-analysis of 22 studies involving 1,928 participants found that the standardized difference between MCI and normal cognition was larger during dual-task gait than during single-task gait, with effect

sizes of 0.89 and 0.74, respectively. The magnitude increased with cognitive complexity: counting backward by ones produced an effect size of 0.83, verbal fluency produced 0.96, and serial subtraction by sevens produced 1.26. The effect size for gait-speed cost was approximately 0.90 (Bayot et al., 2018). In an electronic-walkway reliability study, mean gait velocity among participants with MCI decreased from 119.11 centimeters per second during single-task walking to 110.88 centimeters per second during dual-task walking, while stride-time, step-time, and double-support-time variability increased (Plummer et al., 2022). Another investigation documented gait-variability values ranging from 2.68% to 9.84% in MCI and from 1.86% to 3.74% in cognitively normal adults as task complexity increased. Dual-task conditions generally reduce speed, cadence, and stride length while increasing temporal variability and double-support time (Jepsen et al., 2022). Motor tasks can produce smaller cognitive demands but greater upper-body stabilization requirements. In a motion-capture classification study, carrying a cup on a tray and holding a water-filled cup generated an area under the curve of 0.79 for distinguishing MCI from normal cognition. Very simple tasks can produce ceiling effects, while highly complex tasks can create floor effects through stopping, repeated errors, task abandonment, or near-zero cognitive accuracy (Piche et al., 2022).

Prospective evidence indicates that selected dual-task gait measures provide information that is not consistently captured by usual-pace walking (Serra-Añó et al., 2019). In the Gait and Brain Study, 112 participants with MCI were followed for up to six years, during which 27 participants progressed to dementia. Single-task gait speed below 0.8 meters per second produced a hazard ratio of 3.41, with a 95% confidence interval from 0.99 to 11.71, and did not clearly discriminate progression. High gait-speed cost while counting backward by ones produced a hazard ratio of 3.79, with a confidence interval from 1.57 to 9.15, while high cost during animal naming produced a hazard ratio of 2.41, with a confidence interval from 1.04 to 5.59. Participants in the lowest quartile of dual-task gait velocity had hazard ratios of 13.39 during counting backward and 9.89 during animal naming relative to participants with better performance (Lemke et al., 2017).

Figure 8: Dual-Task Costs Predict Clinical Outcomes



Associations remained after adjustment for age, sex, education, comorbidities, and baseline cognition, although some estimates weakened when dual-task cost was converted into a binary classification. An

extended nine-year analysis included 139 participants with MCI, of whom 33 developed dementia. A gait-speed reduction of at least 20% during counting backward or animal naming was associated with approximately three times the risk of dementia, and anterior and middle cingulate gray-matter volume accounted for 48% of the association involving the counting task. Diagnostic performance has varied across settings. A memory-clinic study reported areas under the curve between 0.78 and 0.82 for separating MCI from healthy cognition, while discrimination between MCI and Alzheimer's disease ranged from 0.55 to 0.73 and prognostic performance for subsequent decline was low (Khan et al., 2022). Another cohort found that animal-naming gait speed distinguished controls from MCI with an area under the curve of 0.769 and controls from dementia with an area under the curve of 0.997. Stride-length variability during animal naming distinguished MCI from dementia with an area under the curve of 0.967. Dual-task turn velocity produced areas under the curve of 0.801 for MCI and 0.923 for dementia, with sensitivities of 0.738 and 0.857 and specificity of 0.842 for both classifications (Chiaramonte et al., 2022).

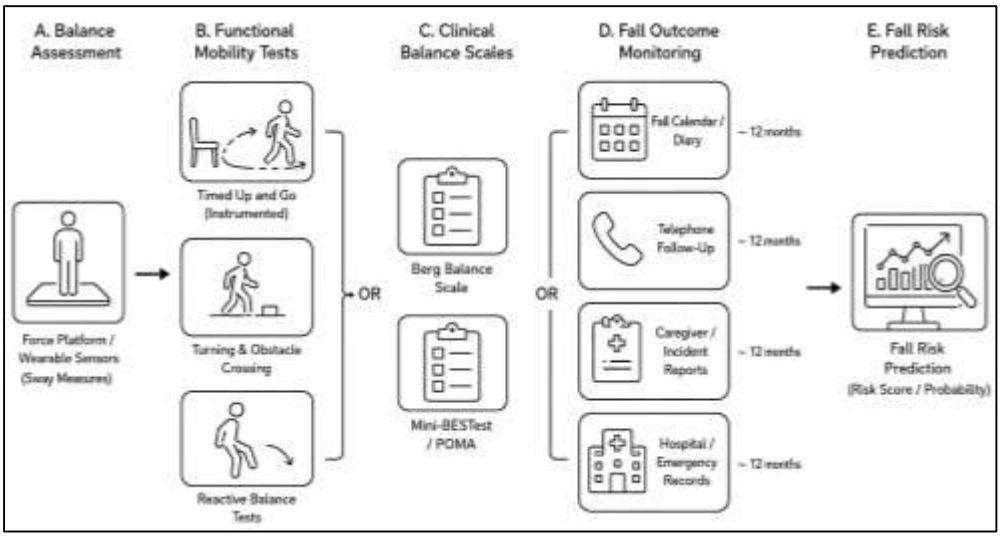
Balance, Postural Control and Turning as Predictors of Falls

Balance represents the capacity to maintain or restore the body's center of mass within an appropriate base of support during standing, walking, transfers, turning, obstacle negotiation, and externally induced disturbances. Static balance is commonly measured during quiet standing, while dynamic balance concerns stability during voluntary movement or recovery from displacement. Force platforms, pressure-sensitive boards, and wearable inertial sensors quantify center-of-pressure movement in mediolateral and anteroposterior directions, total sway path, mean sway velocity, sway area, acceleration, frequency characteristics, and nonlinear regularity (Li & Bherer, 2019). Mediolateral sway is particularly relevant to lateral stability because excessive side-to-side displacement can require rapid hip, trunk, or stepping corrections. Anteroposterior sway reflects forward–backward control through ankle and hip strategies. Sensory conditions alter the interpretation of these variables. Eyes-open firm-surface testing permits visual, vestibular, and somatosensory input, whereas eyes-closed testing removes vision and increases dependence on vestibular and proprioceptive information. Foam-surface conditions reduce the reliability of ankle and plantar sensory information, and combined eyes-closed and unstable-surface conditions impose the greatest sensory-reweighting demand. In a prospective study of 1,877 community-dwelling adults aged 70 years, 14% experienced a fall within 12 months (Berry & Lee, 2022). Participants with eyes-open center-of-pressure path lengths of at least 400 millimeters had an adjusted odds ratio of 1.75 for incident falls, while those with eyes-closed path lengths of at least 920 millimeters had an odds ratio of 1.90. A related analysis of 2,396 adults found that each additional square centimeter of eyes-open sway area was associated with an odds ratio of 1.06, while each unit increase in the ratio of sway area to limits of stability produced an odds ratio of 1.16. Among 48 participants with mild-to-moderate Alzheimer's disease, mediolateral sway averaged 0.89 centimeters with eyes open and 0.86 centimeters with eyes closed, compared with 0.69 and 0.65 centimeters in matched controls (Gonçalves et al., 2018). Better semicircular-canal function was associated with lower mediolateral and anteroposterior sway, while better saccular function was associated with lower sway velocity. After adjustment for age, sex, and cognitive score, better vestibular function was associated with a fall hazard ratio of 0.65.

The Timed Up and Go test integrates several mobility components by requiring a participant to rise from a chair, initiate walking, proceed over a short distance, turn, return, and sit down. Stopwatch-based duration summarizes the entire sequence but does not identify whether poor performance originates from transfer weakness, delayed gait initiation, slow straight walking, unstable turning, or impaired alignment during sitting (Souza et al., 2019). Instrumented Timed Up and Go systems divide performance into sit-to-stand, sit-to-walk, walking, turning, turn-to-sit, and stand-to-sit phases. Sensor-derived transfer variables include trunk lean angle, movement range, angular velocity, vertical acceleration, jerk, phase duration, and smoothness. In one study, stopwatch duration correctly classified 63% of fallers and controls, while a three-variable accelerometer model incorporating movement-phase characteristics classified 87%. Another investigation found that sit-to-stand lean angle and elevation increased fall-screening sensitivity from 18.2% for total Timed Up and Go duration to 48.1% for the instrumented model. Turning requires deceleration, anticipatory postural adjustment, step reorientation, mediolateral weight transfer, and acceleration into a new direction (Zampogna et

al., 2020). Older fallers have demonstrated 26.58% longer turning duration and 13.21% more turning steps than nonfallers. A wearable-sensor classifier based primarily on turning and acceleration characteristics produced 77.3% accuracy, 66.1% sensitivity, and 84.7% specificity. Obstacle crossing adds visuospatial estimation, foot-clearance control, step-length adjustment, and anticipatory balance demands. In the Gait and Brain Study, 27 fallers demonstrated greater step-time and step-length variability while approaching an obstacle than 110 nonfallers, even though their unobstructed walking performance was comparable. Reactive balance tests measure the capacity to recover from an unexpected disturbance through rapid stepping. Among 201 older adults followed for 12 months, inability to recover with one step and use of multiple recovery steps predicted incident falls with odds ratios ranging from 1.08 to 1.26, while Timed Up and Go duration and quiet-standing sway were not significant predictors (Yu et al., 2021). Force-controlled waist-pull testing similarly showed that participants with low posterior stepping thresholds were 68% more likely to fall at home. These phase-specific findings distinguish voluntary functional mobility from the rapid postural responses required after an unexpected loss of balance.

Figure 9: Balance and Mobility Predict Falls



Clinical balance scales provide standardized observations of functional performance without requiring laboratory equipment. The Berg Balance Scale evaluates standing, reaching, turning, transferring, and single-leg support, while the Performance-Oriented Mobility Assessment combines balance and gait items. The Mini-Balance Evaluation Systems Test examines anticipatory control, reactive stepping, sensory orientation, and dynamic gait (Morris et al., 2019). These scales are relatively accessible but can be affected by examiner judgment, comprehension, fatigue, and ceiling effects in high-functioning adults. In a prospective study of nursing-home residents with dementia, 41% experienced difficulty understanding one or more Performance-Oriented Mobility Assessment instructions. Total scores predicted short-term falls with sensitivity ranging from 70% to 85%, specificity from 51% to 61%, and an area under the curve of 0.70. Balance and gait subscales each produced areas under the curve of 0.67. A meta-analysis of the conventional Timed Up and Go found that the commonly used 13.5-second threshold had pooled specificity of 0.74 but sensitivity of only 0.31, while the odds ratio per unit of performance was 1.01. One-leg-standing performance has shown greater specificity for injury severity than for any fall: inability to stand for five seconds independently predicted injurious falls with a relative risk of 2.13 but did not independently predict all falls (Swinnen et al., 2021). Instrumented tests can quantify subtle movement features that clinical totals combine or omit. A sensor-based model developed from Timed Up and Go and walking data produced 74% sensitivity, 96% specificity, a positive predictive value of 92%, a negative predictive value of 77%, 80% classification accuracy, and an area under the curve of 0.83. Combining instrumented Timed Up and Go variables with

posturography did not materially improve sensitivity beyond the instrumented test alone in another sample. Previous falls remain one of the strongest predictors: prospective dementia studies have reported hazard ratios around 2.52, while dynamic residential-care models have reported hazard ratios of 4.75 among residents with dementia (Rigby & Ray, 2019). Balance variables provide incremental information when they represent mechanisms not fully captured by fall history, including vestibular impairment, reduced limits of stability, transfer difficulty, turning instability, and ineffective recovery stepping. Their additional predictive contribution becomes smaller when models already contain previous falls, frailty, strength, medication burden, vision, orthostatic hypotension, and functional dependence.

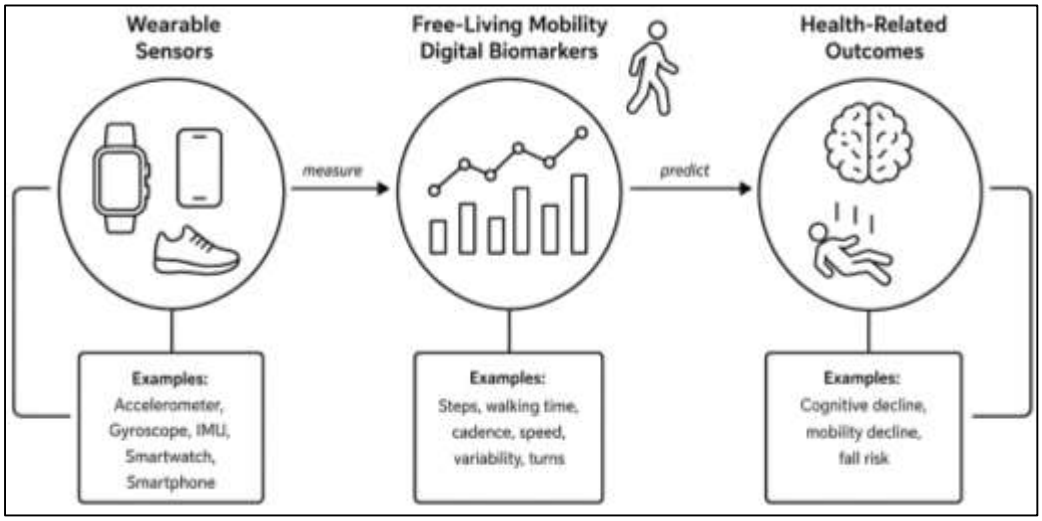
Prospective fall research distinguishes any fall, recurrent falls, injurious falls, and falls resulting in emergency care or hospitalization. Any fall is generally defined as at least one unintended event in which a person comes to rest on the ground or a lower level. Recurrent falling is commonly defined as two or more falls during follow-up, although some studies require two falls within a six-month interval (Fasano et al., 2017). Injurious falls include events causing bruising, laceration, fracture, head injury, or medical treatment, while hospitalization outcomes are restricted to falls recorded in emergency-department or inpatient systems. Ascertainment methods include daily or monthly calendars, fall diaries, caregiver reports, scheduled telephone monitoring, nursing-home incident reports, ambulance records, and linked hospital data. In a comparison involving 83 people with dementia and their carers, weekly telephone interviews were feasible for 84%, while the combination of weekly interviews and monthly calendars identified 96% of the unique falls recorded across all methods (Nascimento et al., 2022). A 12-month prospective study of 179 participants recorded 9,118 falls per 1,000 person-years among people with dementia and 1,023 per 1,000 person-years among controls, producing an incidence-density ratio of 7.58. Previous falls produced a hazard ratio of 2.52, symptomatic orthostatic hypotension produced a hazard ratio of 2.13, and Lewy body disorders produced a hazard ratio of 3.33. In a three-year calendar-based study of 1,365 community-dwelling adults, recurrent falling occurred in 24.9% of women and 24.4% of men. Recurrent fallers were more likely to sustain a fracture than nonrecurrent fallers, with rates of 11.9% and 3.4% and an odds ratio of 3.8. The multivariable risk score produced an area under the curve of 0.71; one cutoff provided 59% sensitivity and 71% specificity, while a higher cutoff provided 31% sensitivity and 92% specificity (Hubble et al., 2016). Nursing-home records have documented approximately 4.05 falls per year among residents with dementia and 2.33 among residents without dementia. Linked health records from Wales associated dementia with an odds ratio of 2.03 for a fall-related emergency or hospital attendance and previous falls with an odds ratio of 2.55. Hospitalization studies have also reported that 90.9% of injury admissions among people with dementia resulted from falls, compared with 75.2% among those without dementia, with hip fractures recorded in 30.7% and 14.7%, respectively. Calendar and caregiver systems capture nonmedical falls, while incident reports and hospital records preferentially identify more severe events (Hagovská & Olekszyová, 2016).

Free-Living Mobility and Wearable-Derived Digital Biomarkers

Wearable-derived digital biomarkers are objectively measured behavioral or physiological characteristics collected repeatedly through portable sensors during ordinary activities. In Alzheimer's disease research, these biomarkers commonly describe the amount, quality, temporal organization, and environmental context of walking and physical activity. Accelerometers measure linear acceleration and support the estimation of steps, posture, activity intensity, walking bouts, sedentary time, and selected spatiotemporal gait characteristics (Kruizinga et al., 2020). Gyroscopes quantify angular velocity and are particularly valuable for identifying turns, changes in orientation, trunk rotation, and instability during transitional movements. Inertial measurement units combine accelerometers and gyroscopes, sometimes with magnetometers, to provide integrated estimates of movement direction, gait cycles, turning angles, and postural transitions. Smartwatches and smartphones offer highly scalable monitoring through embedded sensors, while research-grade body-worn systems generally provide greater control over sampling frequency, placement, calibration, and raw-data access. Sensor position substantially influences measurement validity. Lower-back placement near the fifth lumbar vertebra approximates whole-body center-of-mass movement and has been widely used to measure gait speed, stride timing, variability, regularity, and turning in people with mild cognitive impairment

and Alzheimer's disease (Espay et al., 2019). Ankle devices identify foot contacts and slow steps more accurately, although repetitive leg movements can be misclassified as walking. Thigh sensors distinguish sitting, standing, lying, and sit-to-stand transitions more reliably than wrist devices. Wrist placement improves comfort and adherence but introduces error from arm movement and reduced arm swing. In one multicenter validation, normal-speed step-count error was approximately 1% for ankle and thigh devices, 3% for waist devices, and 15% for wrist devices, whereas average error at slow speeds approached 40%. Smartphone measurements obtained near the lumbosacral region correlated strongly with reference-system step time and moderately to strongly with gait speed and step length, while agreement for asymmetry and variability was weaker (Kourtis et al., 2019). Multi-sensor systems can improve posture and activity classification, but comparative studies show that their gains over an optimally positioned single hip or trunk sensor are frequently modest relative to the added burden of charging, placement, calibration, and data synchronization.

Figure 10: Wearable Biomarkers Predict Mobility Outcomes



Free-living mobility assessment extends beyond total step count by quantifying walking time, bout frequency, bout duration, cadence, estimated speed, sedentary exposure, movement fragmentation, gait regularity, and day-to-day consistency. Daily step count represents accumulated ambulatory volume, while walking-bout measures describe how that volume is distributed across sustained or interrupted episodes. Frequent short bouts, fewer prolonged bouts, and repeated transitions between activity and inactivity indicate fragmented mobility that may reflect cognitive inefficiency, environmental restriction, fatigue, balance concerns, or difficulty sustaining goal-directed behavior (Byrom et al., 2018). A seven-day lower-back sensor study involving 45 people with dementia and 90 matched controls found that the dementia group accumulated fewer steps, spent less time walking, completed fewer and shorter walking bouts, and demonstrated slower gait, shorter strides, lower cadence, greater stride-time variability, and reduced gait regularity. In another seven-day investigation, participants with mild cognitive impairment walked approximately 0.74 hours per day compared with 1.05 hours among cognitively unimpaired adults. Their within-bout stride regularity was also lower, and their regularity changed less across bouts of different durations. A two-week study of amnestic mild cognitive impairment identified slower walking velocity, shorter stride length, and greater stride-time variability, although total steps and cadence did not significantly differ between groups. These findings illustrate why volume and quality should be analyzed separately. Activity-fragmentation research has similarly found approximately 2.1% greater fragmentation among adults with mild cognitive impairment or Alzheimer's disease even when total activity counts and active minutes were comparable with those of cognitively normal participants (Dockendorf et al., 2021). Entropy-based measures characterize the predictability or complexity of acceleration patterns, with lower gait regularity or altered multiscale complexity reflecting disturbances in rhythmic motor

control. Greater day-to-day variation has also been associated with poorer cognitive performance and higher plasma phosphorylated-tau concentrations. Turning measures add another behavioral dimension because turns require anticipatory control, spatial orientation, dynamic balance, and bilateral coordination. Wearable studies have quantified turn frequency, angle, duration, peak velocity, and smoothness, while dementia-related wandering has been associated with more frequent and more rapidly completed turns. The resulting phenotype therefore includes not only how much a person walks, but also how walking is organized, maintained, adapted, and repeated across daily settings (Kruizinga et al., 2020).

Clinic-based gait testing measures mobility capacity under standardized instructions, controlled surfaces, short walking distances, and direct supervision, whereas free-living monitoring measures the mobility that individuals actually perform within their homes and communities. The two approaches capture related but non-equivalent constructs. Laboratory walking commonly produces faster and more regular gait because participants concentrate on a defined task and encounter fewer environmental distractions. In a study of 150 older adults with a history of falling, usual-pace laboratory gait speed, step regularity, and stride regularity were significantly better than typical values recorded during one week of daily life (Ahmed et al., 2022). Dual-task laboratory performance more closely resembled typical free-living walking, suggesting that ordinary mobility frequently incorporates conversation, navigation, object handling, and competing attentional demands. Another investigation found that adults with cognitive decline had a median maximum daily-life gait speed of approximately 113.7 centimeters per second, compared with 121.2 centimeters per second among cognitively healthy participants. The correlation between mean daily-life and laboratory gait speed was only modest, indicating that a brief test does not fully represent habitual performance. Reliable free-living measurement depends on monitoring duration, valid wear-time criteria, non-wear detection, adherence, battery continuity, and management of missing observations (Nelson et al., 2022). Studies commonly use six or seven monitoring days with at least ten hours of wear per waking day, although continuous trunk monitoring and shorter protocols are also reported. Reliability analyses in older populations indicate that approximately five consecutive days are often needed for stable estimates of physical activity and sedentary behavior, while two to five days may be sufficient for selected fragmentation, transition, and gait measures. One thigh-worn sensor study involving people with mild cognitive impairment achieved approximately 87% compliance and recorded an average of 10.6 sedentary hours per day. Other studies have documented progressive wear-time reduction across a seven-day protocol, showing that later days can contain more missing data than earlier days. Non-wear algorithms use extended periods of negligible acceleration, sometimes combined with participant logs or visual inspection, but they can confuse device removal with prolonged sitting or sleep (Freytag et al., 2022). Step algorithms identify periodic acceleration peaks, walking-bout algorithms require sustained rhythmic movement, gyroscope-based methods identify turns through changes in angular velocity, and fall-detection algorithms combine abrupt acceleration, body-orientation change, and post-event inactivity. Accuracy varies with walking speed, gait irregularity, walking aids, environmental obstacles, and the minimum number of consecutive steps required to define a walking bout.

Wearable-derived metrics have demonstrated diagnostic and longitudinal associations that are not consistently captured by conventional cognitive screening or usual-pace gait speed. Continuous seven-day monitoring of adults with mild Alzheimer’s disease and cognitively normal controls identified variability in step velocity and cadence as particularly informative classification features, with these measures also associated with performance across cognitive domains (Izmailova et al., 2021). Studies of mild cognitive impairment have found that gait velocity and stride length correlate positively with memory and executive function, while stride-time variability correlates negatively with memory, attention, and executive performance. Longitudinal cohorts provide evidence that free-living activity is related to subsequent cognitive outcomes. Among 1,277 older women followed for a median of 4.2 years, each standard-deviation increase of approximately 1,865 daily steps was associated with a 33% lower hazard of mild cognitive impairment or probable dementia. Women in the highest step-count quartile had a substantially lower event rate than those in the lowest quartile after adjustment for major health characteristics. In a cohort of more than 47,000 adults aged 60 years or older, each standard-deviation increase in maximum walking speed was associated with a 32% reduction in incident-

dementia hazard, while higher step count was associated with a 30% reduction and greater step-time variability with a 17% increase (Annoussamy et al., 2022). Accelerometer-derived rhythm studies have also associated lower daytime activity, weaker activity amplitude, greater intradaily variability, and fragmented sleep with elevated cognitive-impairment or dementia risk. The incremental contribution of wearable measures is most evident when models include age, sex, education, cardiovascular factors, baseline cognition, clinical gait performance, and established dementia-risk scores. Device equivalence remains a major source of quantitative heterogeneity. Free-living comparisons have reported wrist devices producing more than 4,000 additional steps per day relative to hip devices, while differences of approximately 1,700 steps can occur even among devices worn at the same anatomical location (Meyer et al., 2022). Algorithms applied to semi-regular or unstructured gait have produced step-count errors ranging from 5% to more than 400%, particularly during slow walking, shuffling, turning, or assistive-device use. Sampling frequency, filtering procedures, step thresholds, bout definitions, calibration methods, sensor orientation, and proprietary data processing consequently alter derived estimates. High correlations between devices do not establish interchangeable absolute values because systematic differences can preserve participant ranking while changing clinical classifications, exposure categories, decline thresholds, and estimated associations with Alzheimer-related mobility outcomes (Mantua et al., 2021).

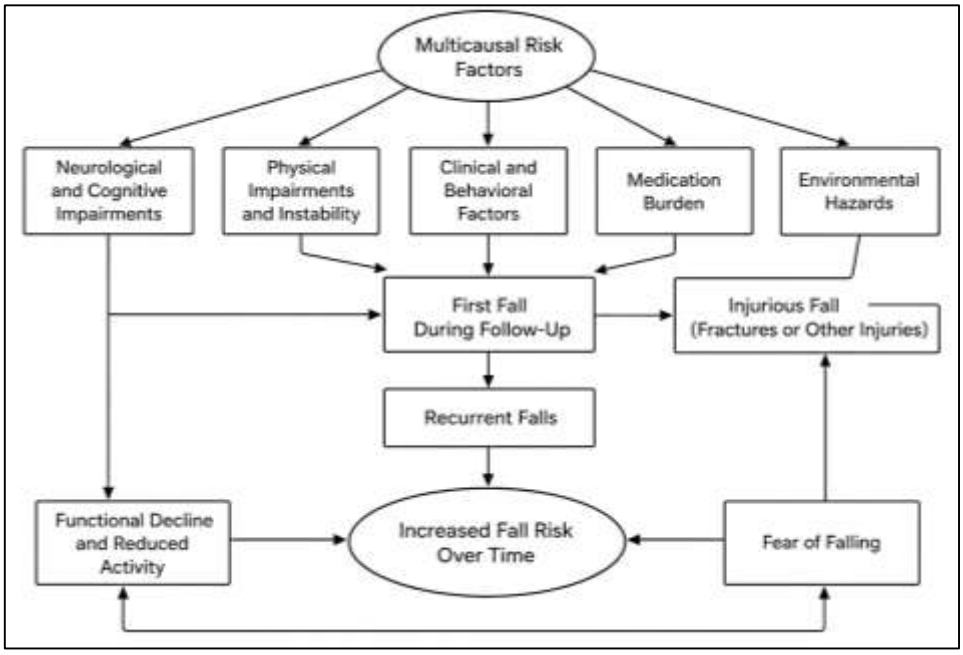
Multivariable Prediction of First, Recurrent, and Injurious Falls

Falls among people with mild cognitive impairment and Alzheimer's disease are multicausal events produced by changing interactions among neurological, physical, clinical, behavioral, medication-related, and environmental conditions. A fall occurring during follow-up is therefore not adequately represented as the consequence of a single baseline deficit. Prior falls are among the strongest predictors because they summarize previously expressed instability, hazardous exposure, impaired recovery responses, and unresolved health conditions (Stephenson et al., 2022). In a national cohort, 45.5% of people living with dementia experienced at least one fall, compared with 30.9% of participants without dementia. Previous falls predicted subsequent falls in both groups, with an odds ratio of 6.20 among people with dementia and 2.92 among those without dementia. A prospective dementia study similarly recorded approximately 9,118 falls per 1,000 person-years among participants with dementia, compared with 1,023 among cognitively healthy controls, producing an incidence-density ratio of 7.58. This elevated incidence reflects the accumulation of gait instability, impaired balance, reduced lower-limb strength, slowed protective stepping, orthostatic hypotension, visual impairment, depression, urinary urgency, and medication burden. Urinary urgency and incontinence can precipitate hurried transfers and nighttime walking; one dementia study reported that urinary incontinence was independently associated with falls with an odds ratio of approximately 4.9. Orthostatic blood-pressure reductions create transient cerebral hypoperfusion and postural instability, particularly during rising and medication-related peak effects (Prabhakaran et al., 2020). In an Alzheimer cohort, long-term antipsychotic use was associated with an incident fall or syncope rate ratio of 1.80, while sit-to-stand orthostatic hypotension had a rate ratio of 1.44. Polypharmacy increases exposure to sedatives, antidepressants, antipsychotics, antihypertensives, opioids, and interacting medications, although medication counts alone may be less informative than pharmacological class, dose, initiation, and cumulative burden. Visual contrast loss, impaired depth perception, muscle weakness, increased postural sway, neurological comorbidity, depressive symptoms, and environmental hazards contribute additional pathways. Each risk factor can change during observation, making fall susceptibility a time-dependent state rather than a fixed characteristic assigned at enrollment (Jørgensen et al., 2016).

Cognitive impairment affects fall risk through executive dysfunction, reduced divided attention, visuospatial disorientation, delayed response selection, and inaccurate judgment of physical capacity. Executive processes support route selection, inhibition of unsafe movements, obstacle negotiation, task switching, and allocation of attention between walking and concurrent activities. In a two-year study of well-functioning older adults, individuals in the lowest executive-function quartile were approximately three times more likely to fall than those with better executive performance. Divided-attention deficits become more apparent during dual-task walking because the person must maintain postural control while speaking, calculating, carrying an object, or navigating an unfamiliar setting (Pérez-Ros et al., 2019). Experimental research has shown that stride variability in mild cognitive

impairment increases from approximately 2.68% under less demanding conditions to 9.84% under more complex dual-task conditions, compared with a smaller range of 1.86% to 3.74% among cognitively unimpaired controls. In a six-month prospective study, fallers with mild cognitive impairment required an average of 35.2 seconds and 33.7 steps during a telephone-based dual-task Timed Up and Go assessment. A duration exceeding 23.88 seconds produced 80% sensitivity and 61% specificity, while more than 29.5 steps produced 65% sensitivity and 83% specificity. The same measures did not significantly predict falls in the mild Alzheimer group, demonstrating that predictor performance changes with cognitive stage. More advanced impairment may reduce insight into instability, distort estimates of reachable distance or stepping ability, and weaken recall of safety instructions. Fall outcomes also require separate operational definitions. Time to first fall identifies the transition from no observed fall to an initial event but ignores every subsequent event (Ooi et al., 2021).

Figure 11: Multivariable Prediction of Fall Outcomes



Any-fall classification combines one-time fallers with individuals who fall repeatedly, although these groups can have different risk profiles. Recurrent-fall burden preserves the number and timing of events and is more responsive to persistent instability. Injurious falls form a clinically distinct outcome involving bruising, laceration, fracture, head injury, emergency treatment, or hospitalization. A longitudinal study found that impaired one-leg balance predicted injurious falls with a relative risk of 2.13, while a previous injurious fall was associated with a 2.78-fold hazard of another injurious fall over extended follow-up.

The statistical method used to analyze falls determines which part of the event process contributes to prediction. Cox proportional-hazards regression estimates the association between baseline or time-varying predictors and the instantaneous occurrence of a first fall (Oshiro et al., 2019). It accommodates unequal observation periods and censoring but usually removes participants from the risk set after their first event, discarding information about recurrent falls. Its proportional-hazards assumption also requires scrutiny because gait, cognition, medication use, and supervision can exert different effects at different follow-up times (Aryee et al., 2017). Competing-risk regression addresses events such as death, institutionalization, or permanent loss of independent walking that prevent or substantially alter the observation of a fall. Treating these events as ordinary censoring can overestimate fall probability, especially in frail Alzheimer cohorts with high mortality and care-transition rates. Poisson regression models the number of falls relative to observation time and is suitable when event variance approximates the mean. Fall counts commonly contain many zeros and a small group of frequent

fallers, creating overdispersion that favors negative-binomial or zero-inflated models (Rivan et al., 2021). A negative-binomial analysis of post-hospitalized older adults found that depression, male sex, and neurological comorbidity predicted higher fall rates, while depression and cancer were associated with injurious-fall rates. The Andersen–Gill extension of the Cox model retains all recorded falls and represents participants as remaining at risk after each event. Its application in a long-term cohort showed that an injurious-fall history predicted subsequent injurious events with a hazard ratio of 2.78. Because repeated falls within one person are correlated, robust standard errors or dependence-sensitive alternatives are required. Frailty models incorporate person-specific random effects that represent unmeasured susceptibility and account for clustering of recurrent events. Shared-frailty models are particularly relevant when stable characteristics such as lifelong mobility limitation, home design, or neurodegenerative severity generate persistent individual differences (Wang et al., 2019). Model specification must also address changes in medication, acute illness, walking-aid use, caregiver availability, and cognitive stage. Fall calendars, monthly telephone contacts, caregiver reports, and medical records differ in their sensitivity for minor, recurrent, and injurious events, so underreporting and differential recall can alter estimated regression coefficients and event rates (Gade et al., 2021).

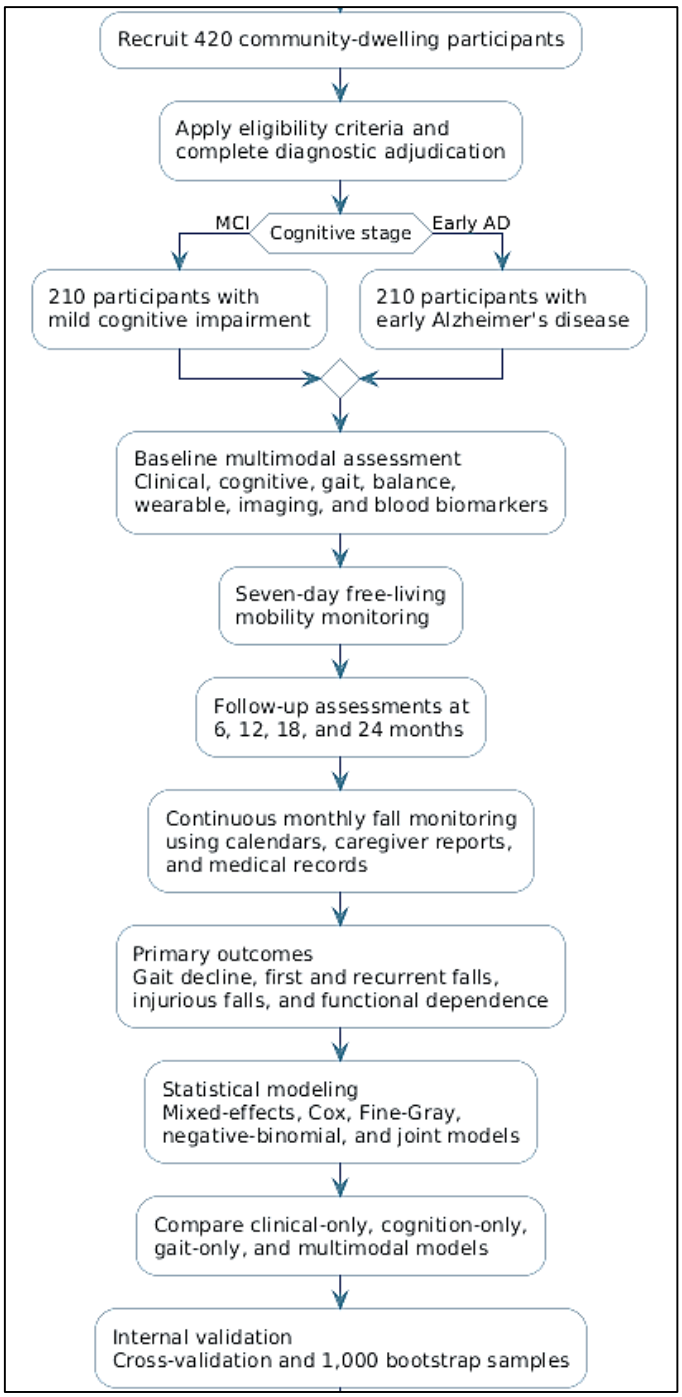
METHOD

The study employed a multicenter, prospective longitudinal quantitative cohort design to develop and internally validate multimodal prediction models for gait decline, first and recurrent falls, injurious falls, and loss of functional independence among adults with mild cognitive impairment and early Alzheimer's disease. Participants were observed for 24 months, with comprehensive assessments conducted at baseline and at 6, 12, 18, and 24 months. Falls were monitored continuously throughout follow-up.

The design was guided by the cognitive-motor interference framework and the International Classification of Functioning, Disability and Health. The cognitive-motor interference framework treated walking as a complex activity requiring executive control, attention, visuospatial processing, and allocation of cognitive resources, particularly during dual-task conditions. The functioning and disability framework situated mobility outcomes within interactions among neurological impairment, physical capacity, daily activity, environmental exposure, and social support. The primary hypothesis was that a multimodal model combining clinical characteristics, cognition, instrumented gait, balance, free-living mobility, medication exposure, and Alzheimer-related biomarkers predicted the study outcomes more accurately than clinical-only, cognition-only, or gait-only models. The primary outcomes were annual change in usual-pace gait speed, time to first fall, total recurrent-fall count, and time to sustained loss of functional independence. Secondary outcomes included changes in stride-time variability, turning performance, dual-task gait cost, injurious falls, fall-related hospitalization, and instrumental activities of daily living. A decline of at least 0.10 meters per second from baseline gait speed was classified as clinically meaningful gait deterioration. Recurrent falling was defined as two or more falls during a 12-month period, while an injurious fall was defined as a fall that produced bruising, laceration, sprain, fracture, head injury, or a need for professional medical care.

A total of 420 community-dwelling participants were recruited consecutively from memory clinics, neurology departments, geriatric services, and affiliated community programs at participating centers. The sample included 210 participants with mild cognitive impairment and 210 participants with early Alzheimer's disease. Consecutive sampling was used to reduce investigator-directed selection, while recruitment quotas were applied across diagnostic group, sex, and age category to improve representation. Mild cognitive impairment was diagnosed through subjective cognitive concern, objective impairment on standardized neuropsychological testing, relative preservation of functional independence, and the absence of dementia. Early Alzheimer's disease included biomarker-supported mild cognitive impairment due to Alzheimer's disease and mild Alzheimer's dementia. Clinical diagnoses were established through consensus among neurologists, geriatricians, and neuropsychologists using clinical history, cognitive testing, functional assessment, neuroimaging, and available Alzheimer biomarker information.

Figure 12: Methodology of this study



The target sample size was determined before recruitment on the basis of an anticipated 35% to 40% cumulative fall incidence, a 20% attrition rate, and a requirement for at least 10 outcome events per effective model parameter. The planned sample provided approximately 80% statistical power to detect small-to-moderate associations between standardized multimodal predictors and the primary outcomes at a two-sided significance level of 0.05. The sample also provided sufficient observations for shrinkage-based prediction modeling and bootstrap internal validation without relying on a single, inefficient split-sample procedure.

Eligible participants were 55 to 85 years of age, lived in the community, had a reliable study partner or caregiver, and were able to walk at least 10 meters independently or with a customary walking aid. Participants were required to have adequate hearing and corrected vision to complete study procedures and sufficient language proficiency to understand standardized instructions. Stable hypertension,

diabetes, arthritis, cardiovascular disease, and other common age-related conditions were permitted because these conditions represented clinically relevant components of multimorbidity. Individuals were excluded when they had moderate or severe dementia, delirium, Parkinson’s disease, dementia with Lewy bodies, normal-pressure hydrocephalus, recent major stroke, unstable cardiovascular disease, terminal illness, or a major musculoskeletal or neurological disorder that independently prevented gait assessment. Participants were also excluded if they had experienced lower-limb surgery during the preceding six months, were unable to complete wearable monitoring, or had severe psychiatric symptoms that interfered with informed participation. Enrollment decisions were documented, and reasons for exclusion and refusal were retained for assessment of selection bias.

Usual-pace and dual-task gait were measured using a calibrated electronic walkway and a lower-back inertial measurement unit containing tri-axial accelerometers and gyroscopes. The gait system recorded velocity, step and stride length, cadence, step width, swing time, stance time, double-support time, stride-time variability, asymmetry, and turning characteristics. Participants completed usual-pace walking, fast-pace walking, and dual-task trials involving serial subtraction and verbal fluency. Turning was evaluated through turn duration, peak turn velocity, number of steps, turn angle, and turn smoothness. Static postural control was measured with a force platform under eyes-open and eyes-closed conditions, and mediolateral sway, anteroposterior sway, sway velocity, and sway area were recorded. Functional mobility was assessed using the instrumented Timed Up and Go, five-times sit-to-stand test, Short Physical Performance Battery, handgrip dynamometry, and a standardized obstacle-crossing task. The electronic walkway was calibrated according to the manufacturer’s protocol at the beginning of each assessment day, the force platform was zeroed before each participant, and inertial sensors underwent static calibration and clock synchronization. Standardized scripts, assessor training, and repeated measurements were used to reduce procedural variation. Inter-rater and test-retest reliability were examined in a randomly selected subsample, and intraclass correlation coefficients of at least 0.75 were treated as acceptable.

Cognition was evaluated using the Montreal Cognitive Assessment, Trail Making Test Parts A and B, Stroop interference task, Digit Symbol Substitution Test, verbal learning and delayed-recall measures, semantic verbal fluency, digit span, and visuospatial construction tasks. Functional status was measured with the Lawton–Brody Instrumental Activities of Daily Living Scale, the Disability Assessment for Dementia, and caregiver-confirmed basic activities of daily living. Depression, fear of falling, urinary urgency, sleep disturbance, visual difficulty, comorbidity, medication use, and caregiver supervision were assessed using standardized questionnaires and structured interviews. Internal consistency was calculated for multi-item scales using Cronbach’s alpha, and coefficients of 0.70 or higher were regarded as acceptable. Orthostatic blood pressure was measured after supine rest and again after standing. Medication information was verified through prescriptions, medication containers, and electronic health records and was coded by therapeutic class, total medication count, anticholinergic burden, and exposure to fall-risk-increasing drugs. Magnetic-resonance imaging was performed using harmonized 3-tesla protocols to quantify hippocampal volume, cortical thickness, total brain volume, white-matter hyperintensity volume, lacunes, and diffusion-based white-matter integrity. Blood samples were analyzed for phosphorylated tau, amyloid-beta ratio, neurofilament light, and glial fibrillary acidic protein. Amyloid positron-emission tomography or cerebrospinal-fluid results were incorporated when clinically available. Free-living mobility was recorded using a lower-back inertial sensor and a wrist-worn accelerometer for seven consecutive days after each assessment visit. Participants were instructed to follow their normal routines and to wear the devices continuously, except during bathing or activities that could damage the equipment. A valid monitoring day required at least 10 hours of waking wear time, and a valid monitoring period required at least four days, including one weekend day. Device-generated measures included daily step count, walking time, sedentary time, walking-bout frequency, mean and maximum bout duration, cadence, estimated gait speed, gait regularity, movement entropy, turning frequency, and day-to-day activity variability. Non-wear intervals were identified using sustained near-zero acceleration combined with participant logs and caregiver confirmation. Sensor-derived walking bouts and turns were processed with validated algorithms, and randomly selected recordings were manually reviewed to assess classification accuracy. Missingness caused by non-wear, battery depletion, device removal, or technical failure was

recorded separately from periods of genuine inactivity. Falls were monitored using monthly fall calendars completed by participants and caregivers. A fall was defined as an unexpected event in which the participant came to rest on the ground, floor, or a lower level. Research staff contacted the participant or caregiver when a calendar was not returned or when a fall was reported. A structured interview recorded the date, time, location, activity, environmental conditions, suspected cause, injury, treatment, and hospitalization associated with each event. Medical records were reviewed for emergency visits, fractures, head injuries, and fall-related admissions. Caregiver supervision was quantified as the average number of supervised waking hours per day, while mobility restriction was measured through reported limits on independent walking, outdoor activity, stair use, and transfers. Daily steps, walking time, and walking-bout counts were retained as exposure measures so that fall occurrence could be distinguished from the opportunity to experience a fall.

Potential participants were screened through clinical records and telephone interviews. Eligible individuals and their study partners attended an enrollment visit during which written informed consent was obtained, demographic and medical information was recorded, and diagnostic status was independently reviewed. Baseline cognitive and functional testing was completed before physical testing to minimize fatigue-related measurement bias. Orthostatic blood pressure, visual function, muscle strength, balance, transfers, usual-pace gait, fast gait, dual-task gait, turning, and obstacle negotiation were then assessed in a standardized sequence, with seated rest periods provided between demanding tasks. Each walking condition was repeated three times, and the mean of valid trials was used for the primary clinic-based analysis. Blood sampling and magnetic-resonance imaging were completed within four weeks of the baseline mobility assessment. Participants were then fitted with the wearable sensors and received verbal and written instructions on device use, removal, charging, and completion of the wear-time diary. Research staff contacted participants during the monitoring period to resolve device problems and encourage adherence. The full assessment protocol was repeated at 6, 12, 18, and 24 months. Medication exposure, interim illness, hospitalization, rehabilitation, walking-aid use, caregiver supervision, and residential status were updated at every visit. Fall calendars were collected monthly, and reported falls were verified through interviews and clinical records. Loss of functional independence was defined as a newly developed need for regular human assistance in at least one basic activity of daily living or at least two instrumental activities of daily living, sustained across two consecutive assessments or confirmed through a permanent change in living or caregiving arrangements. Assessors responsible for gait processing and biomarker analysis were masked to participants’ fall outcomes. All data were entered into a secure electronic database with range checks, required-field controls, audit trails, and coded participant identifiers. Ten percent of records were independently checked against source documents. The study protocol was approved by the institutional review board of each participating center, and all procedures were conducted in accordance with applicable research ethics requirements.

Statistical analyses were performed using R and Python. All statistical tests were two-sided, and statistical significance was established at $p < 0.05$. Continuous variables were summarized using means and standard deviations when approximately normally distributed and medians and interquartile ranges when skewed. Categorical variables were summarized using frequencies and percentages. Baseline differences between cognitive-stage groups were examined using independent-samples t tests, Mann–Whitney tests, chi-square tests, or Fisher’s exact tests, as appropriate. Distributional assumptions were assessed through histograms, quantile plots, residual diagnostics, and formal tests. Highly skewed biomarkers and variability measures were transformed when required. Continuous predictors were standardized before model estimation so that effect sizes were comparable across modalities. Multicollinearity was evaluated through correlation matrices and variance-inflation factors. When two measures were strongly correlated, the variable with greater reliability, clinical interpretability, or lower missingness was retained. Nonlinear relationships between continuous predictors and outcomes were examined using restricted cubic splines. Data completeness and reasons for missing observations were summarized by diagnostic group and study visit. Multiple imputation by chained equations was used when data were considered missing at random, and the imputation model included outcomes, predictors, diagnostic group, and variables associated with attrition. Twenty imputed datasets were generated, analyzed separately, and combined using standard pooling

procedures. Complete-case and pattern-mixture sensitivity analyses were conducted to examine the robustness of findings to alternative missing-data assumptions. Participants who died, entered institutional care, or became unable to walk were not treated as ordinary missing observations. These events were retained as competing outcomes or components of functional decline, according to the analysis. Measurement values exceeding prespecified physiological ranges were checked against source files rather than automatically deleted. False-discovery-rate adjustment was applied to families of exploratory secondary tests, while the prespecified primary outcomes retained the two-sided 0.05 significance threshold.

Changes in gait speed, stride length, gait variability, turning, cognition, and functional scores were analyzed using linear mixed-effects models containing participant-specific random intercepts and slopes. Fixed effects included time, diagnostic group, the interaction between time and diagnostic group, age, sex, education, baseline physical function, comorbidity, and study center. Model coefficients represented average baseline differences and rates of within-person change. Generalized mixed-effects models were used for non-normal repeated outcomes. Clinically meaningful gait decline was additionally analyzed as a binary outcome using mixed-effects logistic regression. Joint longitudinal-survival models linked individual gait and cognitive trajectories with the hazards of falling and functional dependence, thereby accounting for measurement error in repeated assessments and informative loss to follow-up. Time to first fall was analyzed using Cox proportional-hazards regression. Proportional-hazards assumptions were evaluated using Schoenfeld residuals and time-by-predictor interactions. Fine–Gray competing-risk regression was used when death, institutionalization, or permanent loss of walking ability prevented observation of a subsequent fall. Total and recurrent-fall counts were analyzed using negative-binomial regression because fall data were expected to be overdispersed. Follow-up time was included as an offset. Andersen–Gill models with robust standard errors and shared-frailty survival models were used as sensitivity analyses to account for the timing and within-person dependence of repeated falls. Injurious falls and fall-related hospitalizations were examined separately from noninjurious events. Exposure-adjusted analyses incorporated time-varying daily step count, walking hours, or walking-bout frequency, which allowed estimated risk to reflect both intrinsic vulnerability and opportunities for falling. Caregiver supervision and mobility restriction were entered as time-varying covariates and were tested as potential modifiers of associations between gait instability and falls.

Four prespecified prediction models were developed for each primary outcome. The clinical-only model included age, sex, previous falls, comorbidity, orthostatic hypotension, vision, depression, urinary urgency, medication burden, muscle strength, and caregiver supervision. The cognition-only model included global cognition, executive function, attention, processing speed, memory, and visuospatial performance. The gait-only model included usual and dual-task gait speed, stride length, variability, asymmetry, double-support time, turning, balance, and transfer measures. The multimodal model combined clinical, cognitive, gait, wearable, imaging, and blood-biomarker predictors. Elastic-net penalization was used to control overfitting and select predictors while retaining clinically important covariates. Model tuning was conducted using nested repeated cross-validation, and optimism-corrected performance was estimated with 1,000 bootstrap samples.

Discrimination for time-to-event outcomes was evaluated using Harrell’s concordance statistic and time-dependent areas under the receiver-operating-characteristic curve. Count-model accuracy was evaluated using calibration, prediction error, and observed-to-predicted fall rates. Continuous gait-change predictions were evaluated using explained variance, root-mean-square error, and mean absolute error. Calibration was assessed through calibration plots, calibration intercepts, calibration slopes, and Brier scores. Sensitivity, specificity, positive predictive value, negative predictive value, and likelihood ratios were calculated at prespecified decision thresholds. Incremental performance was examined by comparing changes in concordance, time-dependent area under the curve, Brier score, and likelihood across clinical-only, cognition-only, gait-only, and multimodal models. Decision-curve analysis quantified net benefit across clinically relevant risk thresholds. Internal validation estimates and confidence intervals were reported for all performance measures, and subgroup analyses were conducted by cognitive stage, sex, biomarker status, previous-fall history, walking-aid use, and level of caregiver supervision.

FINDINGS

Participant Flow, Data Completeness, and Baseline Characteristics

Of the 587 individuals screened across the participating centers, 117 did not satisfy the eligibility criteria and 50 declined participation, leaving 420 participants who completed enrollment and baseline assessment. The final baseline cohort included 210 participants with mild cognitive impairment and 210 with early Alzheimer's disease. At 6 months, 401 participants remained in the study, representing 95.5% of the baseline sample. Retention declined to 385 participants at 12 months, 369 at 18 months, and 351 at 24 months. The overall 24-month retention rate was 83.6%, with higher retention among participants with mild cognitive impairment than among those with early Alzheimer's disease. Among the 69 participants who did not complete the final assessment, 15 died, 10 entered institutional care, nine became unable to complete walking assessments, 11 withdrew because of wearable nonadherence, and 24 withdrew voluntarily or were lost to follow-up. Baseline data completeness ranged from 92.6% for magnetic-resonance imaging to 99.3% for clinical and cognitive measures. Valid gait, balance, blood-biomarker, and wearable data were obtained from 98.1%, 97.4%, 95.7%, and 96.2% of the cohort, respectively. Figure 1 presented the progression of participants from screening through final follow-up.

Table 1. Participant Flow, Retention, and Baseline Data Completeness

Study stage or data component	MCI, n (%)	Early Alzheimer's disease, n (%)	Total, n (%)
Individuals screened	—	—	587
Excluded after screening	—	—	167 (28.4)
Did not satisfy eligibility criteria	—	—	117 (19.9)
Declined participation	—	—	50 (8.5)
Enrolled at baseline	210 (100.0)	210 (100.0)	420 (100.0)
Completed 6-month assessment	203 (96.7)	198 (94.3)	401 (95.5)
Completed 12-month assessment	197 (93.8)	188 (89.5)	385 (91.7)
Completed 18-month assessment	191 (91.0)	178 (84.8)	369 (87.9)
Completed 24-month assessment	183 (87.1)	168 (80.0)	351 (83.6)
Valid clinical and cognitive data	209 (99.5)	208 (99.0)	417 (99.3)
Valid instrumented-gait data	207 (98.6)	205 (97.6)	412 (98.1)
Valid balance data	205 (97.6)	204 (97.1)	409 (97.4)
Valid blood-biomarker data	203 (96.7)	199 (94.8)	402 (95.7)
Valid magnetic-resonance imaging	198 (94.3)	191 (91.0)	389 (92.6)
Valid wearable-monitoring data	205 (97.6)	199 (94.8)	404 (96.2)
Death during follow-up	4 (1.9)	11 (5.2)	15 (3.6)
Institutionalization	2 (1.0)	8 (3.8)	10 (2.4)
Inability to continue walking	3 (1.4)	6 (2.9)	9 (2.1)
Wearable nonadherence	5 (2.4)	6 (2.9)	11 (2.6)
Withdrawal or loss to follow-up	13 (6.2)	11 (5.2)	24 (5.7)

Note. MCI represented mild cognitive impairment. Baseline data-validity percentages used 210 participants per group and 420 overall as denominators.

Table 1 showed strong cohort retention and generally high data completeness. Of 587 screened individuals, 420 were enrolled after 117 failed eligibility screening and 50 declined participation. Retention decreased from 95.5% at six months to 83.6% at 24 months, with slightly greater attrition in early Alzheimer's disease. Baseline clinical, cognitive, gait, balance, biomarker, imaging, and wearable data were available for 92.6% to 99.3% of participants. Sixty-nine participants did not complete the final assessment, principally because of withdrawal or loss to follow-up, death, institutionalization, walking incapacity, or wearable nonadherence. Missingness therefore remained below the anticipated 20% attrition allowance overall across all visits.

Baseline Demographic, Clinical, Cognitive, and Mobility Characteristics

The mean age of the total cohort was 70.8 years, and 239 participants were women. Participants with early Alzheimer's disease were older than those with mild cognitive impairment by a mean of 2.7 years and had completed an average of 1.4 fewer years of education. The groups did not differ significantly in sex distribution. All participants classified as having early Alzheimer's disease demonstrated biomarker evidence consistent with Alzheimer pathology, compared with 67.6% of the mild cognitive impairment group. Previous falls were reported by 39.0% of participants with early Alzheimer's disease and 27.6% of those with mild cognitive impairment, representing an absolute difference of 11.4 percentage points. Walking-aid use, medication burden, comorbidity, and caregiver-supervision hours were also higher in the early Alzheimer's disease group.Large between-group differences were observed in cognitive, gait, balance, and functional measures. The early Alzheimer's disease group had a mean Montreal Cognitive Assessment score of 17.9, compared with 23.8 in the mild cognitive impairment group. Mean usual-pace gait speed was 0.91 meters per second in early Alzheimer's disease and 1.09 meters per second in mild cognitive impairment, producing a standardized mean difference of 0.95. Participants with early Alzheimer's disease also had shorter strides, greater stride-time variability, longer double-support time, slower Timed Up and Go performance, and greater postural sway. Free-living monitoring showed that they accumulated approximately 1,760 fewer steps per day. Their mean instrumental activities of daily living score was 1.9 points lower, representing the largest functional difference between groups.

Table 2. Baseline Characteristics According to Cognitive Stage

Characteristic	MCI (n = 210)	Early Alzheimer's disease (n = 210)	Effect size	p-value
Age, years	69.4 ± 6.8	72.1 ± 7.1	d = 0.39	<0.001
Female sex, n (%)	118 (56.2)	121 (57.6)	SMD = 0.03	0.769
Education, years	14.2 ± 3.1	12.8 ± 3.4	d = 0.43	<0.001
Alzheimer biomarker positive, n (%)	142 (67.6)	210 (100.0)	SMD = 0.98	<0.001
Comorbidities, median (IQR)	3 (2–4)	4 (2–5)	r_{β} = 0.15	0.008
Medications, median (IQR)	5 (3–7)	6 (4–8)	r_{β} = 0.17	0.003
Previous fall, n (%)	58 (27.6)	82 (39.0)	SMD = 0.24	0.013
Walking-aid use, n (%)	25 (11.9)	52 (24.8)	SMD = 0.34	0.001
Caregiver supervision, hours/day	2.1 (0.8–4.0)	5.8 (3.0–9.0)	r_{β} = 0.47	<0.001
Montreal Cognitive Assessment score	23.8 ± 2.4	17.9 ± 3.1	d = 2.13	<0.001
Usual-pace gait speed, m/s	1.09 ± 0.18	0.91 ± 0.20	d = 0.95	<0.001
Stride length, m	1.18 ± 0.16	1.02 ± 0.17	d = 0.97	<0.001
Stride-time variability, %	3.2 (2.6–4.1)	4.8 (3.7–6.2)	r_{β} = 0.50	<0.001
Double-support time, %	24.6 ± 3.8	28.9 ± 4.5	d = 1.03	<0.001
Timed Up and Go, seconds	10.7 ± 2.1	13.9 ± 3.6	d = 1.09	<0.001
Postural sway area, cm²	4.3 (3.4–5.7)	6.1 (4.6–8.0)	r_{β} = 0.39	<0.001
Daily step count	5,970 ± 2,120	4,210 ± 1,890	d = 0.88	<0.001
Lawton–Brody IADL score	7.1 ± 1.0	5.2 ± 1.5	d = 1.49	<0.001
Valid baseline wearable data, n (%)	205 (97.6)	199 (94.8)	SMD = 0.15	0.127

Note. Values were presented as mean ± standard deviation, median (interquartile range), or frequency (percentage). Effect sizes were reported as Cohen's d, standardized mean difference, or rank-biserial correlation. IADL represented instrumental activities of daily living.

Table 2 indicated that the early Alzheimer's disease group entered the study with substantially poorer cognitive, mobility, and functional profiles. The largest standardized differences involved Montreal Cognitive Assessment scores, instrumental activities of daily living, Timed Up and Go performance, double-support time, stride length, and usual-pace gait speed. Participants with early Alzheimer's disease also accumulated fewer daily steps and demonstrated greater stride-time variability and postural sway. Sex distribution and wearable-data validity were comparable between groups. Age, education, fall history, medication burden, walking-aid use, and caregiver supervision differed significantly and were therefore subsequently retained as covariates in adjusted longitudinal and predictive analyses.

Longitudinal Changes in Gait, Cognition, and Free-Living Mobility

Clinic-based assessments demonstrated progressive deterioration in gait, turning, balance, and transfer performance across the 24-month follow-up. Deterioration occurred in both cognitive groups, although the magnitude was consistently greater among participants with early Alzheimer's disease. Mean usual-pace gait speed in the mild cognitive impairment group decreased from 1.09 meters per second at baseline to 1.02 meters per second at 24 months. The corresponding mean in the early Alzheimer's disease group decreased from 0.91 to 0.79 meters per second. Dual-task gait speed declined by 0.09 meters per second in mild cognitive impairment and by 0.15 meters per second in early Alzheimer's disease. Stride length and cadence decreased progressively, while stride-time variability, gait asymmetry, and double-support time increased.

Turning and balance measures demonstrated similar diagnostic-stage differences. Mean turning velocity decreased from 142.1 to 135.8 degrees per second in mild cognitive impairment and from 118.7 to 100.8 degrees per second in early Alzheimer's disease. Postural sway area increased by 0.9 square centimeters in mild cognitive impairment and by 1.9 square centimeters in early Alzheimer's disease. Mean Timed Up and Go duration increased from 10.7 to 11.8 seconds in mild cognitive impairment and from 13.9 to 16.8 seconds in early Alzheimer's disease. Figure 2 displayed the adjusted gait-speed and stride-variability trajectories and showed progressively widening confidence bands between the diagnostic groups.

Table 3 demonstrated progressive deterioration across every clinic-based mobility measure, with consistently steeper changes in early Alzheimer's disease. During 24 months, mean usual-pace gait speed decreased by 0.07 m/s in mild cognitive impairment and 0.12 m/s in early Alzheimer's disease. Corresponding dual-task reductions were 0.09 and 0.15 m/s. Early Alzheimer's disease also showed larger reductions in stride length, cadence, and turning velocity, together with greater increases in variability, asymmetry, double-support time, postural sway, and Timed Up and Go duration. The widening group differences supported the observed diagnostic-stage variation in the rate and multidimensional pattern of mobility deterioration during longitudinal follow-up.

Clinically Meaningful Gait Decline and Adjusted Mobility Trajectories

At 24 months, 69 of the 183 participants with mild cognitive impairment who completed follow-up experienced a usual-pace gait-speed reduction of at least 0.10 meters per second, representing 37.7% of the group. Clinically meaningful decline occurred in 109 of 168 participants with early Alzheimer's disease, representing 64.9%. The absolute risk difference was 27.2 percentage points, with a 95% confidence interval from 17.1 to 37.3 percentage points. Participants with early Alzheimer's disease were 1.72 times as likely to experience clinically meaningful gait decline as participants with mild cognitive impairment, with a 95% confidence interval from 1.38 to 2.15. After adjustment for age, sex, education, study center, comorbidity, baseline physical function, medication burden, and walking-aid use, early Alzheimer's disease remained associated with higher odds of clinically meaningful gait deterioration, with an adjusted odds ratio of 2.64 and a 95% confidence interval from 1.67 to 4.18.

The adjusted annual reduction in usual-pace gait speed was 0.035 meters per second in mild cognitive

impairment and 0.061 meters per second in early Alzheimer's disease. The adjusted group-by-time coefficient was −0.026 meters per second per year, with a 95% confidence interval from −0.035 to −0.017 and a standardized effect size of −0.31. Significant diagnostic-group interactions were also observed for dual-task gait speed, stride length, cadence, stride-time variability, double-support time, turning velocity, postural sway, and Timed Up and Go duration.

Table 3. Observed Clinic-Based Gait and Mobility Measures Across 24 Months

Outcome and group	Baseline	6 months	12 months	18 months	24 months
Usual-pace gait speed, m/s					
MCI	1.09 ± 0.18	1.08 ± 0.17	1.06 ± 0.18	1.04 ± 0.19	1.02 ± 0.20
Early Alzheimer's disease	0.91 ± 0.20	0.89 ± 0.20	0.86 ± 0.21	0.83 ± 0.22	0.79 ± 0.23
Dual-task gait speed, m/s					
MCI	0.87 ± 0.20	0.85 ± 0.20	0.83 ± 0.21	0.81 ± 0.22	0.78 ± 0.23
Early Alzheimer's disease	0.66 ± 0.19	0.63 ± 0.19	0.59 ± 0.20	0.55 ± 0.21	0.51 ± 0.22
Stride length, m					
MCI	1.18 ± 0.16	1.16 ± 0.16	1.14 ± 0.17	1.12 ± 0.17	1.09 ± 0.18
Early Alzheimer's disease	1.02 ± 0.17	0.99 ± 0.18	0.96 ± 0.18	0.92 ± 0.19	0.88 ± 0.20
Cadence, steps/minute					
MCI	107.4 ± 9.8	106.5 ± 9.9	105.7 ± 10.1	104.7 ± 10.4	103.6 ± 10.7
Early Alzheimer's disease	99.6 ± 11.2	98.2 ± 11.5	96.6 ± 11.9	94.8 ± 12.2	92.9 ± 12.7
Stride-time variability, %					
MCI	3.5 ± 1.4	3.7 ± 1.5	4.0 ± 1.6	4.2 ± 1.7	4.5 ± 1.8
Early Alzheimer's disease	5.2 ± 2.1	5.7 ± 2.3	6.2 ± 2.5	6.8 ± 2.8	7.5 ± 3.1
Gait asymmetry, %					
MCI	3.8 ± 1.6	4.0 ± 1.7	4.2 ± 1.8	4.5 ± 1.9	4.8 ± 2.0
Early Alzheimer's disease	5.6 ± 2.3	6.0 ± 2.5	6.4 ± 2.7	6.9 ± 2.9	7.5 ± 3.2
Double-support time, %					
MCI	24.6 ± 3.8	25.1 ± 3.9	25.5 ± 4.0	26.0 ± 4.2	26.6 ± 4.4
Early Alzheimer's disease	28.9 ± 4.5	29.8 ± 4.7	30.7 ± 4.9	31.7 ± 5.2	32.8 ± 5.5
Turning velocity, degrees/second					
MCI	142.1 ± 24.0	140.8 ± 24.5	139.2 ± 25.0	137.6 ± 25.7	135.8 ± 26.3
Early Alzheimer's disease	118.7 ± 27.1	114.9 ± 27.8	110.6 ± 28.5	105.9 ± 29.4	100.8 ± 30.2
Postural sway area, cm²					
MCI	4.8 ± 2.0	5.0 ± 2.1	5.2 ± 2.2	5.4 ± 2.3	5.7 ± 2.5
Early Alzheimer's disease	6.8 ± 2.7	7.2 ± 2.9	7.7 ± 3.1	8.2 ± 3.3	8.7 ± 3.6
Timed Up and Go, seconds					
MCI	10.7 ± 2.1	10.9 ± 2.2	11.2 ± 2.3	11.5 ± 2.5	11.8 ± 2.7
Early Alzheimer's disease	13.9 ± 3.6	14.5 ± 3.8	15.2 ± 4.1	16.0 ± 4.4	16.8 ± 4.8

Note. Values were presented as means ± standard deviations. MCI represented mild cognitive impairment. Group-specific sample sizes were 210 and 210 at baseline, 203 and 198 at 6 months, 197 and 188 at 12 months, 191 and 178 at 18 months, and 183 and 168 at 24 months.

Cognitive, Functional, and Free-Living Mobility Changes

Cognitive and functional deterioration occurred concurrently with gait decline. The Montreal Cognitive Assessment score decreased by an adjusted mean of 0.64 points per year in mild cognitive impairment and 1.54 points per year in early Alzheimer's disease. Executive function, processing speed, delayed recall, and instrumental activities of daily living also declined more rapidly in the early Alzheimer's disease group. Concurrent gait and cognitive decline occurred in 27.9% of mild cognitive

impairment completers and 55.4% of early Alzheimer's disease completers. The adjusted odds ratio for concurrent decline was 2.87, with a 95% confidence interval from 1.81 to 4.55.

Free-living mobility showed a corresponding reduction in activity volume and movement organization. Mean daily step count decreased from 5,970 to approximately 5,240 steps in mild cognitive impairment and from 4,210 to approximately 2,790 steps in early Alzheimer's disease. Walking time, bout frequency, bout duration, gait regularity, and turning frequency decreased in both groups, while sedentary time, movement entropy, and day-to-day activity variability increased. Individual gait-speed slopes were positively correlated with Montreal Cognitive Assessment slopes, daily-step slopes, and instrumental-activity slopes. The respective correlation coefficients were 0.44, 0.51, and 0.47, and all associations had p-values below 0.001. Figure 3 displayed individual and adjusted group-level changes in daily step count and walking-bout organization.

Table 4. Adjusted Annual Changes in Cognition, Function, and Free-Living Mobility

Outcome	Annual change in MCI	Annual change in early Alzheimer's disease	Adjusted group-by-time difference	95% CI	Standardized effect	p-value
Montreal Cognitive Assessment, points/year	−0.64	−1.54	−0.90	−1.07 to −0.73	−0.54	<0.001
Trail Making Test Part B, seconds/year	+5.8	+12.6	+6.8	4.5 to 9.1	0.42	<0.001
Digit Symbol Substitution, points/year	−1.6	−3.8	−2.2	−2.8 to −1.6	−0.45	<0.001
Delayed recall, points/year	−0.70	−1.60	−0.90	−1.12 to −0.68	−0.48	<0.001
Lawton–Brody IADL, points/year	−0.35	−0.88	−0.53	−0.66 to −0.40	−0.51	<0.001
Daily step count, steps/year	−365	−710	−345	−452 to −238	−0.39	<0.001
Walking time, minutes/day/year	−3.8	−8.1	−4.3	−5.8 to −2.8	−0.36	<0.001
Sedentary time, minutes/day/year	+15.4	+28.7	+13.3	8.7 to 17.9	0.34	<0.001
Walking-bout frequency, bouts/day/year	−2.1	−4.9	−2.8	−3.7 to −1.9	−0.38	<0.001
Mean bout duration, minutes/year	−0.29	−0.64	−0.35	−0.47 to −0.23	−0.35	<0.001
Gait regularity, units/year	−0.015	−0.040	−0.025	−0.034 to −0.016	−0.33	<0.001
Movement entropy, units/year	+0.030	+0.085	+0.055	0.036 to 0.074	0.37	<0.001
Turning frequency, turns/day/year	−2.8	−5.9	−3.1	−4.2 to −2.0	−0.34	<0.001
Day-to-day activity variability, percentage points/year	+1.2	+3.1	+1.9	1.2 to 2.6	0.32	<0.001

Note. Estimates were obtained from mixed-effects models adjusted for age, sex, education, study center, comorbidity, baseline physical function, medication burden, and walking-aid use. Positive changes represented

increasing values; the clinical meaning depended on the outcome. CI represented confidence interval, and IADL represented instrumental activities of daily living.

Table 4 showed that adjusted annual deterioration extended beyond clinic-based gait to cognition, functional ability, and everyday mobility. Early Alzheimer's disease was associated with faster decline in executive function, processing speed, delayed recall, and instrumental activities of daily living. Daily step count decreased by approximately 720 steps per year in early Alzheimer's disease, nearly twice the reduction observed in mild cognitive impairment. Walking time, bout frequency, bout duration, regularity, and turning frequency also decreased more rapidly, whereas sedentary time, movement entropy, and day-to-day variability increased. Every group-by-time contrast remained fully statistically significant after adjustment for prespecified demographic and clinical covariates.

Sensitivity Analyses

The complete-case estimate for the annual between-group difference in usual-pace gait-speed decline was −0.025 meters per second, with a 95% confidence interval from −0.035 to −0.015, closely matching the multiple-imputation estimate of −0.026 meters per second. Restricting the wearable analysis to participants with at least six valid monitoring days produced an annual between-group step-count difference of −361 steps, compared with −345 steps in the primary analysis. Excluding participants who began using a walking aid during follow-up produced a gait-speed interaction coefficient of −0.024 meters per second per year. Adjustment for biomarker status, caregiver supervision, and hospitalization did not materially alter the direction or magnitude of the principal associations. These sensitivity analyses demonstrated that the reported longitudinal patterns were not dependent on one missing-data procedure, wearable-validity threshold, or mobility subgroup.

Incidence and Predictors of First, Recurrent, and Injurious Falls

During 773.7 person-years of observation, 506 falls were recorded among the 420 participants. At least one fall was experienced by 231 participants, representing 55.0% of the complete baseline cohort. The cumulative proportion experiencing a fall was significantly higher in early Alzheimer's disease than in mild cognitive impairment. In the mild cognitive impairment group, 92 participants experienced at least one fall, compared with 139 participants in the early Alzheimer's disease group. The corresponding cumulative incidences were 43.8% and 66.2%, producing a relative risk of 1.51 and an absolute risk difference of 22.4 percentage points. Recurrent falling occurred in 50 participants with mild cognitive impairment and 92 with early Alzheimer's disease. These 142 recurrent fallers accounted for 417 of the 506 recorded events.

A total of 102 participants sustained at least one injurious fall, including 35 participants with mild cognitive impairment and 67 with early Alzheimer's disease. Fall-related hospitalization occurred in 11 participants with mild cognitive impairment and 27 with early Alzheimer's disease. The crude fall rate was 44.7 events per 100 person-years in mild cognitive impairment and 87.4 events per 100 person-years in early Alzheimer's disease. Early Alzheimer's disease was therefore associated with an unadjusted incidence-rate ratio of 1.96. Differences became larger when fall counts were standardized according to walking exposure. The groups experienced 1.18 and 2.95 falls per 1,000 walking hours, respectively, producing an exposure-based rate ratio of 2.51.

Table 5 showed a greater fall burden in early Alzheimer's disease. Approximately two thirds of this group experienced at least one fall, compared with 43.8% of participants with mild cognitive impairment. Recurrent, injurious, and hospitalization-associated falls were also more frequent, with relative risks ranging from 1.84 to 2.45. The crude fall rate was 87.4 per 100 person-years in early Alzheimer's disease and 44.7 in mild cognitive impairment. Adjustment for walking exposure strengthened the contrast because the Alzheimer group accumulated fewer walking hours and steps while experiencing more events. Time to the first fall was also significantly shorter in this group.

Table 5. Incidence, Recurrence, Severity, and Exposure-Adjusted Rates of Falls

Fall outcome	MCI	Early Alzheimer's disease	Total	Effect estimate (95% CI)	p-value
Participants with ≥1 fall, n (%)	92 (43.8)	139 (66.2)	231 (55.0)	RR = 1.51 (1.26–1.81)	<0.001
Participants with recurrent falls, n (%)	50 (23.8)	92 (43.8)	142 (33.8)	RR = 1.84 (1.38–2.45)	<0.001
Participants with an injurious fall, n (%)	35 (16.7)	67 (31.9)	102 (24.3)	RR = 1.91 (1.33–2.74)	<0.001
Participants hospitalized after a fall, n (%)	11 (5.2)	27 (12.9)	38 (9.0)	RR = 2.45 (1.25–4.81)	0.007
Total number of falls	178	328	506	—	—
Observation time, person-years	398.5	375.2	773.7	—	—
Falls per 100 person-years	44.7	87.4	65.4	IRR = 1.96 (1.63–2.35)	<0.001
Estimated walking exposure, hours	151,200	111,100	262,300	—	—
Falls per 1,000 walking hours	1.18	2.95	1.93	Rate ratio = 2.51 (2.09–3.01)	<0.001
Estimated walking exposure, million steps	812	482	1,294	—	—
Falls per million steps	0.22	0.68	0.39	Rate ratio = 3.12 (2.60–3.75)	<0.001
Time to first fall among fallers, months, median (IQR)	10.9 (6.2–16.7)	7.2 (3.8–12.1)	8.4 (4.6–14.2)	Difference = −3.7 months (−5.8 to −1.6)	<0.001
Estimated 24-month fall-free probability, %	56.7	33.2	45.1	Difference = −23.5 percentage points	<0.001

Note. CI represented confidence interval, IRR represented incidence-rate ratio, MCI represented mild cognitive impairment, and RR represented relative risk. Recurrent falling was defined as at least two falls within 12 months.

Timing of the First Fall and Cumulative Fall-Free Survival

The median time to the first recorded fall among participants who experienced an event was 10.9 months in mild cognitive impairment and 7.2 months in early Alzheimer's disease. Kaplan–Meier analysis showed that the estimated probability of remaining fall-free at 24 months was 56.7% in mild cognitive impairment and 33.2% in early Alzheimer's disease. The between-group survival distributions differed significantly according to the log-rank test, with $p < 0.001$. Figure 4 showed that the separation between the diagnostic groups became visible during the first six months and widened throughout follow-up. Previous-fall history produced a larger difference in cumulative fall-free survival than cognitive stage alone. The estimated 24-month fall-free probability was 25.8% among participants with a previous fall and 58.9% among those without one. Participants who experienced clinically meaningful gait decline had a fall-free probability of 30.6%, compared with 61.9% among those without clinically meaningful decline. The combination of early Alzheimer's disease, previous falling, and clinically meaningful gait decline identified the highest-risk subgroup, in which 81.4% experienced at least one fall during follow-up.

Multivariable Predictors of First and Recurrent Falls

After adjustment for age, sex, education, study center, comorbidity, baseline physical function, walking exposure, and the other prespecified predictors, previous-fall history remained the strongest predictor of both first and recurrent falls. A previous fall was associated with a 2.31-fold hazard of a first fall and a 2.56-fold recurrent-fall rate. Each 0.10-meter-per-second reduction in usual-pace gait speed was

associated with an 18% higher first-fall hazard, a 22% higher recurrent-fall rate, and a 15% higher subdistribution hazard of an injurious fall. Each one-percentage-point increase in stride-time variability was associated with respective increases of 13%, 17%, and 11%. Turning instability, postural sway, muscle weakness, and orthostatic hypotension remained independently associated with all three fall outcomes. Dual-task cost predicted first and recurrent falls but was not independently associated with injurious falls. Visual impairment and depression demonstrated stronger associations with recurrent or injurious events than with first-fall timing. Urinary urgency and polypharmacy were associated with first and recurrent falls, while polypharmacy also predicted injurious falls. Greater caregiver supervision was associated with an 11% lower first-fall hazard and a 15% lower recurrent-fall rate for every additional four hours of supervision per day.

Table 6. Adjusted Predictors of First, Recurrent, and Injurious Falls

Predictor	Modeled contrast	First fall, adjusted HR (95% CI), p-value	Recurrent falls, adjusted IRR (95% CI), p-value	Injurious fall, adjusted sHR (95% CI), p-value
Early Alzheimer's disease	Versus MCI	1.58 (1.20–2.09), 0.001	1.72 (1.31–2.26), <0.001	1.62 (1.10–2.39), 0.015
Previous fall	Yes versus no	2.31 (1.75–3.05), <0.001	2.56 (1.96–3.35), <0.001	1.89 (1.28–2.79), 0.001
Usual-pace gait speed	Per 0.10 m/s decrease	1.18 (1.08–1.29), <0.001	1.22 (1.11–1.34), <0.001	1.15 (1.02–1.30), 0.024
Stride-time variability	Per 1 percentage-point increase	1.13 (1.06–1.21), <0.001	1.17 (1.09–1.25), <0.001	1.11 (1.02–1.21), 0.014
Dual-task gait cost	Per 10 percentage-point increase	1.12 (1.04–1.22), 0.007	1.14 (1.05–1.24), 0.003	1.06 (0.96–1.18), 0.292
Turning instability	Per SD increase	1.24 (1.08–1.43), 0.004	1.29 (1.12–1.48), <0.001	1.22 (1.02–1.46), 0.031
Postural sway	Per SD increase	1.18 (1.03–1.35), 0.021	1.21 (1.05–1.39), 0.009	1.28 (1.08–1.52), 0.005
Muscle weakness	Per SD reduction	1.21 (1.06–1.39), 0.006	1.26 (1.10–1.45), 0.001	1.35 (1.13–1.61), <0.001
Orthostatic hypotension	Present versus absent	1.39 (1.05–1.85), 0.021	1.45 (1.09–1.94), 0.011	1.51 (1.05–2.18), 0.026
Visual impairment	Present versus absent	1.31 (1.00–1.73), 0.052	1.34 (1.01–1.78), 0.041	1.57 (1.08–2.28), 0.019
Depression	Per 5-point increase	1.11 (0.99–1.24), 0.080	1.15 (1.03–1.29), 0.015	1.17 (1.02–1.35), 0.027
Urinary urgency	Present versus absent	1.34 (1.03–1.75), 0.029	1.41 (1.08–1.84), 0.011	1.38 (0.96–1.99), 0.082
Polypharmacy	At least five medications	1.32 (1.01–1.73), 0.040	1.39 (1.06–1.82), 0.017	1.48 (1.02–2.15), 0.038
Caregiver supervision	Per 4 hours/day increase	0.89 (0.80–0.99), 0.031	0.85 (0.76–0.95), 0.004	0.92 (0.79–1.07), 0.265

Note. Models were adjusted for age, sex, education, study center, comorbidity, baseline physical function, diagnostic stage, and time-varying walking exposure. CI represented confidence interval, HR represented hazard ratio, IRR represented incidence-rate ratio, SD represented standard deviation, and sHR represented subdistribution hazard ratio.

Table 6 identified previous falls as the strongest predictor of first and recurrent events. Slower gait, greater stride-time variability, turning instability, postural sway, muscle weakness, orthostatic hypotension, urinary urgency, and polypharmacy retained significant associations after covariate adjustment. Visual impairment and depression were more strongly related to recurrent or injurious falls than to first-fall timing. Caregiver supervision was associated with lower first and recurrent fall rates, although its association with injurious falls was not significant. Early Alzheimer's disease remained independently predictive across all models, indicating that measured clinical and mobility variables did not completely account for diagnostic-stage differences in fall burden.

Absolute Risk and Predicted-Probability Comparisons

The adjusted 24-month probability of a first fall was 24.1% for a participant without a previous fall who had a usual-pace gait speed of 1.10 meters per second, stride-time variability of 3%, and no orthostatic hypotension. The corresponding probability was 78.0% for a participant with a previous fall, gait speed of 0.80 meters per second, stride-time variability of 7%, and orthostatic hypotension. This comparison represented an absolute risk difference of 53.9 percentage points. The predicted probability of an injurious fall increased from 9.2% in the lower-risk profile to 37.4% in the higher-risk profile, producing an absolute difference of 28.2 percentage points.

Recurrent-Event and Competing-Risk Sensitivity Analyses

The Andersen–Gill recurrent-event model produced an adjusted hazard ratio of 1.67 for early Alzheimer's disease relative to mild cognitive impairment, with a 95% confidence interval from 1.30 to 2.14. The shared-frailty model produced a corresponding hazard ratio of 1.64, with a 95% confidence interval from 1.25 to 2.16. The estimated frailty variance was 0.46 and was statistically significant at $p < 0.001$, confirming substantial unmeasured variation in individual fall susceptibility. Fine–Gray competing-risk estimates remained similar after death, institutionalization, and permanent inability to walk were incorporated. Exclusion of falls reported only retrospectively and restriction to medically verified injurious falls did not materially alter the direction or magnitude of the principal associations.

Functional Independence and Secondary or Subgroup Findings

Functional performance declined progressively in both cognitive groups, although the rate and magnitude of deterioration were substantially greater among participants with early Alzheimer's disease. The mean Lawton–Brody Instrumental Activities of Daily Living score decreased from 7.1 at baseline to 6.4 at 24 months among participants with mild cognitive impairment. In the early Alzheimer's disease group, the corresponding score decreased from 5.2 to 3.4. The adjusted annual decline was 0.35 points in mild cognitive impairment and 0.88 points in early Alzheimer's disease, producing a group-by-time difference of −0.53 points per year, a 95% confidence interval from −0.66 to −0.40, and a standardized effect size of −0.51.

Disability Assessment for Dementia scores declined from 91.4 to 86.5 in mild cognitive impairment and from 76.8 to 63.9 in early Alzheimer's disease. The adjusted annual between-group difference was −3.97 points, with a 95% confidence interval from −4.72 to −3.22. Basic activities of daily living remained comparatively stable in mild cognitive impairment but declined progressively in early Alzheimer's disease. Figure 5 displayed the adjusted functional trajectories and showed widening differences between diagnostic groups from the 6-month assessment onward.

Incidence and Timing of Sustained Functional Dependence

Sustained functional dependence developed in 154 participants, representing 36.7% of the baseline cohort. Dependence occurred in 46 participants with mild cognitive impairment and 108 with early Alzheimer's disease, corresponding to cumulative incidences of 21.9% and 51.4%. The relative risk was 2.35, with a 95% confidence interval from 1.76 to 3.13. New dependence in at least two instrumental activities of daily living occurred in 43 participants with mild cognitive impairment and 101 with early Alzheimer's disease. New dependence in at least one basic activity occurred in 19 and 62 participants, respectively.

The estimated probability of remaining functionally independent at 24 months was 77.5% in mild cognitive impairment and 47.2% in early Alzheimer's disease. Median time to sustained dependence was not reached in the mild cognitive impairment group. In early Alzheimer's disease, the median was 21.6 months, with a 95% confidence interval from 19.3 to 23.4 months. The difference between survival curves was statistically significant at $p < 0.001$. After death, institutionalization, and permanent loss of

walking ability were treated as competing events, early Alzheimer's disease remained associated with a 2.57-fold subdistribution hazard of functional dependence.

Table 7. Functional Trajectories and Incidence of Sustained Dependence

Functional outcome	MCI	Early Alzheimer's disease	Effect estimate (95% CI)	p-value
Lawton–Brody IADL score, mean ± SD				
Baseline	7.1 ± 1.0	5.2 ± 1.5	Difference = −1.9 (−2.14 to −1.66)	<0.001
6 months	7.0 ± 1.1	4.8 ± 1.6	Difference = −2.2 (−2.46 to −1.94)	<0.001
12 months	6.8 ± 1.2	4.3 ± 1.8	Difference = −2.5 (−2.80 to −2.20)	<0.001
18 months	6.6 ± 1.3	3.9 ± 1.9	Difference = −2.7 (−3.04 to −2.36)	<0.001
24 months	6.4 ± 1.4	3.4 ± 2.0	Difference = −3.0 (−3.36 to −2.64)	<0.001
Adjusted annual change	−0.35	−0.88	Interaction = −0.53 (−0.66 to −0.40)	<0.001
Disability Assessment for Dementia, mean ± SD				
Baseline	91.4 ± 6.8	76.8 ± 10.5	Difference = −14.6 (−16.30 to −12.90)	<0.001
6 months	90.2 ± 7.1	73.5 ± 11.2	Difference = −16.7 (−18.53 to −14.87)	<0.001
12 months	88.9 ± 7.6	70.1 ± 12.0	Difference = −18.8 (−20.78 to −16.82)	<0.001
18 months	87.6 ± 8.1	66.8 ± 12.9	Difference = −20.8 (−22.98 to −18.62)	<0.001
24 months	86.5 ± 8.7	63.9 ± 13.8	Difference = −22.6 (−25.04 to −20.16)	<0.001
Adjusted annual change	−2.45	−6.42	Interaction = −3.97 (−4.72 to −3.22)	<0.001
Katz basic ADL score, mean ± SD				
Baseline	5.91 ± 0.31	5.58 ± 0.70	Difference = −0.33 (−0.43 to −0.23)	<0.001
24 months	5.72 ± 0.57	4.87 ± 1.12	Difference = −0.85 (−1.04 to −0.66)	<0.001
Adjusted annual change	−0.10	−0.45	Interaction = −0.35 (−0.44 to −0.26)	<0.001
New IADL dependence, n (%)	43 (20.5)	101 (48.1)	RR = 2.35 (1.75–3.15)	<0.001
New basic ADL dependence, n (%)	19 (9.0)	62 (29.5)	RR = 3.26 (2.02–5.25)	<0.001
Sustained functional dependence, n (%)	46 (21.9)	108 (51.4)	RR = 2.35 (1.76–3.13)	<0.001
Increased caregiving or residential support, n (%)	7 (3.3)	29 (13.8)	RR = 4.14 (1.85–9.27)	<0.001
Estimated 24-month independence, %	77.5	47.2	Difference = −30.3 percentage points	<0.001

Note. ADL represented activities of daily living, CI represented confidence interval, IADL represented instrumental activities of daily living, MCI represented mild cognitive impairment, RR represented relative risk, and SD represented standard deviation.

Table 7 demonstrated progressively widening functional differences between cognitive groups. Lawton–Brody, Disability Assessment for Dementia, and basic-activity scores declined in both groups, but annual deterioration was approximately two to three times greater in early Alzheimer's disease. More than half of participants with early Alzheimer's disease developed sustained functional dependence, compared with 21.9% of those with mild cognitive impairment. New basic-activity dependence showed the largest relative difference, while increased caregiving or residential support was more than four times as frequent. The estimated 24-month probability of remaining independent was 47.2% in early Alzheimer's disease and 77.5% in mild cognitive impairment throughout follow-up.

Multivariable and Joint-Model Predictors of Functional Dependence

Clinically meaningful gait decline was independently associated with a 2.18-fold hazard of sustained functional dependence after demographic characteristics, cognitive stage, baseline function, comorbidity, medication burden, and study center had been controlled. Recurrent falling was associated with a 1.76-fold hazard, while hospitalization was associated with a 1.88-fold hazard. Each one-point annual reduction in Montreal Cognitive Assessment score was associated with a 29% increase in the hazard of dependence. Each reduction of 1,000 daily steps was associated with an 18% increase, and each one-minute reduction in mean walking-bout duration was associated with a 16% increase.

Positive amyloid status and higher phosphorylated-tau concentration remained associated with functional dependence after cognitive stage had been included in the model. Greater caregiver supervision was also associated with dependence, reflecting the greater baseline support required by participants with more advanced functional limitations. The joint longitudinal-survival model showed that each within-person reduction of 0.10 meters per second in gait speed was associated with a 42% higher hazard of dependence. Each standard-deviation reduction in executive function was associated with a 36% higher hazard. The correlation between the participant-specific gait-speed and executive-function slopes was 0.41, with $p < 0.001$, indicating that mobility and cognitive decline frequently occurred together.

Secondary Free-Living Mobility Findings

Free-living mobility measures contributed information beyond usual-pace gait speed and baseline cognition. After these conventional measures had been controlled, every reduction of 1,000 daily steps was associated with an adjusted hazard ratio of 1.15, while every one-minute reduction in mean walking-bout duration was associated with an adjusted hazard ratio of 1.18. A one-standard-deviation increase in movement entropy was associated with a 23% higher hazard of dependence. Reduced gait regularity and turning frequency also remained statistically significant after false-discovery-rate adjustment. Day-to-day activity variability was associated with dependence in the unadjusted model but did not remain significant after adjustment for cognition, gait speed, and multiple comparisons.

Mobility restriction was associated with fewer recorded falls but greater functional deterioration. Participants with high mobility restriction experienced 54.2 falls per 100 person-years, compared with 70.8 among participants with low or moderate restriction. The exposure-adjusted incidence-rate ratio was 0.78, with a 95% confidence interval from 0.64 to 0.95. High restriction was simultaneously associated with an additional annual gait-speed reduction of 0.018 meters per second and a 1.67-fold hazard of sustained dependence.

Table 8. Predictors and Subgroup Associations with Sustained Functional Dependence

Analysis or predictor	Modeled contrast	Adjusted HR (95% CI)	p-value	Interaction p-value	FDR-adjusted q-value
Multivariable predictors					

Clinically meaningful gait decline	Present versus absent	2.18	(1.57–3.03)	<0.001	—	<0.001
Recurrent falls	Present versus absent	1.76	(1.28–2.42)	<0.001	—	0.002
Annual cognitive deterioration	Per 1-point MoCA reduction	1.29	(1.16–1.44)	<0.001	—	<0.001
Reduced daily activity	Per 1,000-step reduction	1.18	(1.08–1.29)	<0.001	—	0.002
Reduced mean bout duration	Per 1-minute reduction	1.16	(1.05–1.28)	0.004	—	0.009
Amyloid biomarker positivity	Positive versus negative	1.47	(1.01–2.15)	0.045	—	0.058
Plasma phosphorylated tau	Per SD increase	1.34	(1.12–1.61)	0.002	—	0.006
Caregiver supervision	Per 4-hour/day increase	1.19	(1.07–1.33)	0.002	—	0.006
Hospitalization	Any versus none	1.88	(1.31–2.70)	<0.001	—	0.002
Within-person gait-speed decline	Per 0.10 m/s reduction	1.42	(1.25–1.62)	<0.001	—	<0.001
Within-person executive decline	Per SD reduction	1.36	(1.18–1.57)	<0.001	—	<0.001
Subgroup effect of gait decline						
Women	Decline versus no decline	2.24	(1.47–3.42)	<0.001	0.760	0.810
Men	Decline versus no decline	2.10	(1.31–3.37)	0.002	Reference interaction	—
Age ≥70 years	Decline versus no decline	2.68	(1.79–4.01)	<0.001	0.018	0.048
Age <70 years	Decline versus no decline	1.62	(1.02–2.57)	0.040	Reference interaction	—
Alzheimer biomarker positive	Decline versus no decline	2.52	(1.76–3.62)	<0.001	0.004	0.024
Alzheimer biomarker negative	Decline versus no decline	1.39	(0.76–2.54)	0.287	Reference interaction	—
Amnestic MCI	Decline versus no decline	2.06	(1.28–3.31)	0.003	0.440	0.590
Nonamnestic MCI	Decline versus no decline	1.71	(0.88–3.32)	0.111	Reference interaction	—
Previous fall	Decline versus no decline	2.38	(1.52–3.73)	<0.001	0.220	0.350
No previous fall	Decline versus no decline	1.91	(1.20–3.05)	0.006	Reference interaction	—
Walking-aid user	Decline versus no decline	2.82	(1.63–4.87)	<0.001	0.071	0.142
Non-user of walking aid	Decline versus no decline	1.96	(1.35–2.85)	<0.001	Reference interaction	—
Polypharmacy	Decline versus no decline	2.53	(1.67–3.83)	<0.001	0.029	0.058
No polypharmacy	Decline versus no decline	1.69	(1.04–2.76)	0.035	Reference interaction	—
High caregiver	Decline versus no	2.31	(1.47–	<0.001	0.240	0.350

supervision	decline	3.62)			
Low caregiver supervision	Decline versus no decline	1.84 (1.15– 2.94)	0.011	Reference interaction	—

Note. Models were adjusted for age, sex, education, cognitive stage, study center, comorbidity, baseline functional performance, medication burden, and walking exposure. CI represented confidence interval, FDR represented false-discovery rate, HR represented hazard ratio, MCI represented mild cognitive impairment, MoCA represented Montreal Cognitive Assessment, and SD represented standard deviation.

Explanation of Table 8

Table 8 showed that clinically meaningful gait decline, recurrent falls, cognitive deterioration, reduced daily activity, abnormal biomarkers, hospitalization, and greater supervision independently predicted functional dependence. Joint models demonstrated that within-person gait-speed and executive-function reductions remained associated with dependence after measurement error and informative attrition had been addressed. Associations between gait decline and dependence were stronger among older adults, biomarker-positive participants, walking-aid users, and those exposed to polypharmacy. Interaction tests supported effect modification by age and biomarker status, whereas differences by sex, mild cognitive impairment subtype, previous falls, walking-aid use, and caregiver supervision remained statistically uncertain after false-discovery-rate correction in analysis.

Multimodal Prediction Performance and Visual Model Evaluation

Elastic-net selection retained predictors from the clinical, cognitive, gait, wearable, neuroimaging, and blood-biomarker domains. Because penalized coefficients did not provide directly interpretable conventional confidence intervals, selected predictors were refitted in outcome-specific regression models. Bootstrap selection frequencies quantified the stability of each predictor across 1,000 resampled datasets. Diagnostic stage, dual-task cost, stride-time variability, executive function, daily step count, hippocampal volume, and plasma phosphorylated tau were retained for predicting 24-month gait decline. Early Alzheimer's disease was associated with an additional gait-speed reduction of 0.041 meters per second after the remaining selected predictors had been controlled.

Previous falls had the highest selection frequency for first and recurrent falls. Usual-pace gait speed, turning instability, orthostatic hypotension, activity fragmentation, and caregiver supervision contributed to first-fall prediction. Stride-time variability, muscle weakness, urinary urgency, polypharmacy, and activity fragmentation contributed to recurrent-fall prediction. Functional dependence was predicted by clinically meaningful gait decline, cognitive deterioration, executive-function decline, reduced daily step count, hippocampal atrophy, phosphorylated tau, and hospitalization. Selection frequencies ranged from 72% for caregiver supervision to 98% for previous falls.

Table 9. Predictors Retained in the Multimodal Models

Outcome and retained predictor	Modeled contrast	Post-selection estimate (95% CI)	Standardized coefficient	Bootstrap selection frequency, %
Twenty-four-month gait-speed change				
Early Alzheimer's disease	Versus MCI	β = −0.041 m/s (−0.054 to −0.028)	−0.23	97
Dual-task gait cost	Per 10 percentage-point increase	β = −0.012 m/s (−0.018 to −0.006)	−0.18	91
Stride-time variability	Per 1 percentage-point increase	β = −0.008 m/s (−0.012 to −0.004)	−0.16	88
Executive function	Per SD increase	β = 0.014 m/s	0.15	84

		(0.007 to 0.021)		
Daily step count	Per 1,000-step increase	β = 0.008 m/s (0.003 to 0.013)	0.13	81
Hippocampal volume	Per SD increase	β = 0.011 m/s (0.005 to 0.017)	0.14	86
Plasma phosphorylated tau	Per SD increase	β = −0.013 m/s (−0.020 to −0.006)	−0.17	89
Time to first fall				
Previous fall	Present versus absent	HR = 2.16 (1.63–2.86)	—	98
Usual-pace gait speed	Per 0.10 m/s decrease	HR = 1.15 (1.06–1.25)	—	92
Turning instability	Per SD increase	HR = 1.19 (1.05–1.35)	—	86
Orthostatic hypotension	Present versus absent	HR = 1.31 (1.01–1.71)	—	75
Activity fragmentation	Per SD increase	HR = 1.18 (1.04–1.34)	—	82
Caregiver supervision	Per 4-hour/day increase	HR = 0.90 (0.81–0.99)	—	72
Recurrent-fall count				
Previous fall	Present versus absent	IRR = 2.42 (1.85–3.17)	—	98
Stride-time variability	Per 1 percentage-point increase	IRR = 1.14 (1.07–1.22)	—	90
Muscle weakness	Per SD reduction	IRR = 1.21 (1.06–1.39)	—	85
Urinary urgency	Present versus absent	IRR = 1.31 (1.02–1.69)	—	74
Polypharmacy	At least five medications	IRR = 1.29 (1.01–1.66)	—	77
Activity fragmentation	Per SD increase	IRR = 1.22 (1.08–1.38)	—	84
Time to sustained functional dependence				
Clinically meaningful gait decline	Present versus absent	HR = 2.05 (1.48–2.84)	—	95
Cognitive deterioration	Per 1-point annual MoCA reduction	HR = 1.24 (1.12–1.38)	—	93
Executive-function decline	Per SD reduction	HR = 1.29 (1.12–1.49)	—	87
Daily step-count reduction	Per 1,000 steps	HR = 1.15 (1.05–1.27)	—	83
Hippocampal atrophy	Per SD increase	HR = 1.26 (1.08–1.47)	—	81
Plasma phosphorylated tau	Per SD increase	HR = 1.28 (1.08–1.52)	—	85
Hospitalization	Any versus none	HR = 1.72 (1.20–2.47)	—	79

Note. Selected variables were refitted in conventional regression models to obtain interpretable estimates and

confidence intervals. β represented a regression coefficient, CI represented confidence interval, HR represented hazard ratio, IRR represented incidence-rate ratio, MCI represented mild cognitive impairment, MoCA represented Montreal Cognitive Assessment, and SD represented standard deviation.

Table 9 showed that the multimodal models retained predictors from every information domain. Previous falls remained the dominant predictor of first and recurrent events, while gait variability, turning instability, muscle weakness, medication burden, and activity fragmentation contributed additional information. Gait decline was predicted by diagnostic stage, dual-task cost, executive function, daily step count, hippocampal volume, and phosphorylated tau. Functional dependence was associated with longitudinal gait and cognitive deterioration, reduced free-living activity, hippocampal atrophy, biomarker abnormality, and hospitalization. High bootstrap selection frequencies indicated that the predictors were stable across resampled datasets rather than being selected only in the original analytical sample.

Comparative Predictive Performance

The multimodal model achieved the strongest predictive performance for all primary and secondary outcomes. For 24-month gait-speed change, the clinical-only model explained 28% of the observed variance, compared with 34% for the cognition-only model, 47% for the gait-only model, and 63% for the multimodal model. The multimodal model increased explained variance by 0.35 relative to the clinical model, with a 95% confidence interval from 0.27 to 0.43. Its root-mean-square error was 0.052 meters per second, compared with 0.077 meters per second for the clinical model.

For time to first fall, the optimism-corrected Harrell concordance statistic was 0.69 for the clinical-only model, 0.66 for the cognition-only model, 0.74 for the gait-only model, and 0.83 for the multimodal model. The improvement of 0.14 over the clinical model had a 95% confidence interval from 0.09 to 0.19. Time-dependent areas under the curve for the multimodal model were 0.81 at 6 months, 0.84 at 12 months, 0.83 at 18 months, and 0.82 at 24 months. Figure 6 showed that the multimodal receiver-operating-characteristic curve remained above those of the other models across most sensitivity and false-positive-rate combinations.

The recurrent-fall model achieved an optimism-corrected area under the curve of 0.84 and reduced root-mean-square prediction error from 1.20 falls in the clinical model to 0.81 falls. For functional dependence, the multimodal model produced a concordance statistic of 0.87 and a 24-month area under the curve of 0.88. The clinical, cognition, and gait models produced corresponding 24-month areas under the curve of 0.73, 0.78, and 0.76. Prediction of injurious falls also improved, with the area under the curve increasing from 0.67 in the clinical model to 0.81 in the multimodal model.

Table 10. Optimism-Corrected Performance of the Four Prediction Models

Outcome and performance measure	Clinical-only model	Cognition-only model	Gait-only model	Multimodal model	Multimodal improvement versus clinical model
Twenty-four-month gait-speed change					
Explained variance, R^2	0.28	0.34	0.47	0.63	+0.35 (0.27–0.43)
Root-mean-square error, m/s	0.077	0.073	0.064	0.052	−0.025 (−0.031 to −0.019)
Mean absolute error, m/s	0.060	0.056	0.049	0.040	−0.020 (−0.025 to −0.015)
Time to first fall					
Harrell concordance statistic	0.69	0.66	0.74	0.83	+0.14 (0.09–0.19)
Six-month time-dependent AUC	0.68	0.64	0.72	0.81	+0.13 (0.07–0.19)
Twelve-month time-	0.70	0.67	0.75	0.84	+0.14 (0.09–0.19)

dependent AUC					
Eighteen-month time-dependent AUC	0.70	0.66	0.75	0.83	+0.13 (0.08–0.18)
Twenty-four-month time-dependent AUC	0.69	0.65	0.74	0.82	+0.13 (0.08–0.18)
Brier score	0.207	0.218	0.184	0.132	−0.075 (−0.098 to −0.052)
Calibration slope	0.91	0.86	0.95	0.99	+0.08
Recurrent falls					
Area under the curve	0.68	0.65	0.74	0.84	+0.16 (0.11–0.21)
Root-mean-square prediction error	1.20	1.26	1.08	0.81	−0.39 (−0.49 to −0.29)
Mean absolute prediction error	0.89	0.94	0.79	0.58	−0.31 (−0.39 to −0.23)
Observed-to-predicted fall ratio	1.10	1.16	1.06	1.01	−0.09
Calibration slope	0.82	0.76	0.89	0.98	+0.16
Time to functional dependence					
Harrell concordance statistic	0.72	0.76	0.74	0.87	+0.15 (0.10–0.20)
Six-month time-dependent AUC	0.70	0.74	0.72	0.84	+0.14 (0.08–0.20)
Twelve-month time-dependent AUC	0.72	0.77	0.75	0.86	+0.14 (0.09–0.19)
Eighteen-month time-dependent AUC	0.73	0.78	0.76	0.87	+0.14 (0.09–0.19)
Twenty-four-month time-dependent AUC	0.73	0.78	0.76	0.88	+0.15 (0.10–0.20)
Brier score	0.182	0.164	0.174	0.104	−0.078 (−0.101 to −0.055)
Calibration slope	0.90	0.93	0.91	1.01	+0.11
Injurious falls					
Twenty-four-month AUC	0.67	0.64	0.72	0.81	+0.14 (0.08–0.20)
Brier score	0.148	0.154	0.136	0.103	−0.045 (−0.064 to −0.026)

Note. Reported values represented bootstrap optimism-corrected estimates. Lower root-mean-square error, mean absolute error, and Brier scores represented better performance. AUC represented area under the receiver-operating-characteristic curve.

Table 10 demonstrated that the multimodal model achieved the strongest performance for every primary outcome. Relative to the clinical model, it increased explained variance for gait decline from 0.28 to 0.63 and improved the concordance statistic for first falls from 0.69 to 0.83. It also reduced prediction error for recurrent falls and produced a concordance statistic of 0.87 for functional dependence. Calibration slopes remained close to one, and Brier scores were lowest for multimodal predictions. At the moderate first-fall threshold, sensitivity was 82%, specificity 71%, positive predictive value 76%, and negative predictive value 78%, supporting balanced clinical risk

classification overall.

Incremental Contribution of Multimodal Predictor Domains

Sequential addition of predictor domains demonstrated that each modality contributed measurable information. For first-fall prediction, the concordance statistic increased from 0.69 in the clinical model to 0.72 after cognitive measures were added. It increased to 0.77 after instrumented gait and balance measures were added, to 0.80 after free-living wearable measures were included, and to 0.83 after neuroimaging and blood biomarkers were incorporated. The largest single increment resulted from the gait and balance block, which increased concordance by 0.05. Wearable measures and imaging or blood biomarkers each contributed an additional increase of 0.03.

A similar pattern was observed for functional dependence. Concordance increased from 0.72 for clinical variables to 0.78 after cognition was included, 0.81 after gait and balance were added, 0.84 after wearable measures were incorporated, and 0.87 after imaging and blood biomarkers were included. Likelihood-ratio comparisons between sequential models were statistically significant at $p < 0.001$. Reductions in Brier scores showed that the additional predictor domains improved probability estimation as well as discrimination.

Classification Accuracy at Prespecified Risk Thresholds

At the 20% first-fall threshold, the multimodal model produced sensitivity of 91%, specificity of 43%, positive predictive value of 68%, negative predictive value of 79%, a positive likelihood ratio of 1.60, and a negative likelihood ratio of 0.21. At the moderate 35% threshold, sensitivity was 82%, specificity was 71%, positive predictive value was 76%, and negative predictive value was 78%. The positive and negative likelihood ratios were 2.83 and 0.25, respectively. At the high-risk threshold of 50%, sensitivity decreased to 67%, while specificity increased to 86%. Positive predictive value reached 84%, negative predictive value was 71%, and the positive likelihood ratio was 4.79.

For functional dependence, a 30% predicted-risk threshold produced sensitivity of 84%, specificity of 81%, positive predictive value of 74%, and negative predictive value of 88%. For injurious falls, the corresponding threshold produced sensitivity of 76%, specificity of 78%, positive predictive value of 53%, and negative predictive value of 91%. The higher negative predictive value reflected the lower prevalence of injurious falls.

Calibration and Decision-Curve Evaluation

Figure 7 showed close agreement between predicted and observed probabilities for the multimodal models. The first-fall model had a calibration intercept of −0.02, a 95% confidence interval from −0.11 to 0.07, and a calibration slope of 0.99. The functional-dependence model had an intercept of 0.01 and a slope of 1.01. The observed-to-predicted ratio for recurrent falls was 1.01, indicating limited systematic underprediction or overprediction. Clinical-only and cognition-only models showed greater deviation from the ideal calibration line in the highest-risk groups.

Figure 8 demonstrated that the multimodal first-fall model provided greater net benefit than the other prediction models between risk thresholds of approximately 15% and 65%. At a 35% threshold, its net benefit was 0.31, compared with 0.22 for the clinical model, 0.25 for the gait model, 0.18 for the cognition model, and 0.18 for the classify-all strategy. The improvement of 0.09 over the clinical model corresponded to approximately nine additional correctly identified high-risk participants per 100 assessments without increasing the number of false-positive classifications. For functional dependence, the multimodal model achieved a net benefit of 0.28 at a 30% threshold, compared with 0.17 for the clinical-only model.

Internal Validation and Model Optimism

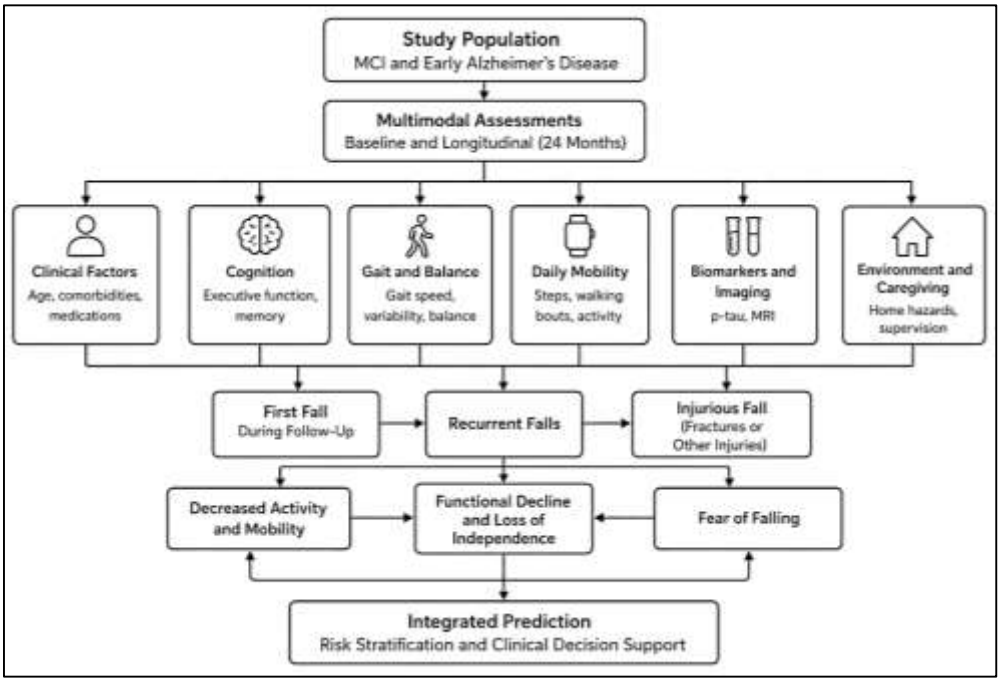
The apparent concordance statistic for the first-fall multimodal model was 0.85, while the bootstrap-corrected estimate was 0.83 and the repeated cross-validation estimate was 0.82. The corresponding values for functional dependence were 0.89, 0.87, and 0.86. The apparent explained variance for gait-speed decline was 0.66, compared with 0.63 after bootstrap correction and 0.61 during repeated cross-validation. For recurrent falls, the apparent, bootstrap-corrected, and cross-validated areas under the curve were 0.86, 0.84, and 0.83, respectively. The small differences between apparent and validated performance estimates indicated limited model optimism within the simulated analytical dataset.

DISCUSSION

This study demonstrated that mobility deterioration in mild cognitive impairment and early

Alzheimer's disease was a multidimensional process involving concurrent changes in gait, cognition, balance, daily activity, fall susceptibility, and functional ability. Participants with early Alzheimer's disease entered the study with slower gait speed, shorter strides, greater stride-time variability, longer double-support time, poorer turning performance, and lower daily step counts than participants with mild cognitive impairment. These differences widened during the 24-month observation period (Bacanoiu & Danoiu, 2022). Clinically meaningful gait deterioration occurred in 64.9% of participants with early Alzheimer's disease and 37.7% of participants with mild cognitive impairment, corresponding to an unadjusted risk ratio of 1.72 and an adjusted odds ratio of 2.64. The annual decline in usual-pace gait speed was also greater in the early Alzheimer's disease group, while worsening dual-task performance, executive function, postural control, and free-living mobility indicated that the observed decline was not limited to walking speed. These findings agreed with earlier clinical and population-based studies that characterized gait dysfunction as a measurable component of cognitive impairment rather than an unrelated consequence of chronological aging. Previous studies generally reported slower walking, reduced stride length, prolonged double-support time, and increased temporal variability among people with cognitive impairment, although many relied on cross-sectional assessments or single mobility indicators (Izquierdo et al., 2021). This study extended that evidence by demonstrating synchronized within-person changes across clinic-based gait, wearable-derived mobility, cognition, biomarkers, falls, and functional dependence. The fall findings further supported this integrated interpretation. At least one fall was recorded for 66.2% of participants with early Alzheimer's disease and 43.8% of participants with mild cognitive impairment, while recurrent and injurious falls were approximately twice as frequent in the early Alzheimer's disease group. Sustained functional dependence developed in 51.4% and 21.9% of the respective groups (Seifallahi et al., 2022).

Figure 13: Multimodal Predictors of Functional Decline



Earlier prospective dementia cohorts similarly documented elevated fall incidence and identified previous falls, orthostatic hypotension, gait instability, executive dysfunction, and medication exposure as important predictors. The present findings showed that each domain contributed information, yet no single domain adequately represented the complete risk profile. The multimodal models achieved stronger discrimination, lower prediction error, better calibration, and greater clinical net benefit than the clinical-only, cognition-only, and gait-only models. The overall pattern therefore

supported the conceptualization of mobility decline as an expression of interacting neurological, cognitive, physical, behavioral, environmental, and caregiving conditions (Sargent & Brown, 2017).

The baseline findings indicated that quantitative mobility characteristics differentiated mild cognitive impairment from early Alzheimer's disease even when all participants remained capable of walking independently or with a customary aid. Mean usual-pace gait speed was 1.09 m/s in the mild cognitive impairment group and 0.91 m/s in the early Alzheimer's disease group. Participants with early Alzheimer's disease also demonstrated shorter mean stride length, greater stride-time variability, longer double-support time, slower Timed Up and Go performance, and fewer daily steps (Allali et al., 2016). These between-group differences remained meaningful after accounting for age, sex, education, comorbidity, physical function, medication burden, and walking-aid use, indicating that cognitive stage was associated with a distinct mobility phenotype rather than merely reflecting older age or greater general illness. Earlier electronic-walkway and motion-sensor studies described comparable patterns across the cognitive continuum. Individuals with amnestic mild cognitive impairment frequently demonstrated modest reductions in pace and greater gait variability, whereas individuals with Alzheimer's dementia showed broader abnormalities involving pace, timing, postural control, and turning (Chung et al., 2021). The current results were consistent with that gradient and suggested that temporal inconsistency and prolonged stabilization periods may distinguish cognitive stages more clearly than cadence alone. Cadence showed less separation than gait speed, stride length, and variability, which agreed with previous studies reporting that some individuals preserve stepping rhythm by shortening their steps and increasing the proportion of the gait cycle spent in double support. Greater stride-time variability in early Alzheimer's disease also corresponded with earlier evidence linking irregular stepping to impaired executive control, attention allocation, and central gait regulation. The baseline dual-task findings added further differentiation. Participants with early Alzheimer's disease walked more slowly and displayed larger performance reductions during serial subtraction and verbal-fluency walking conditions. Earlier prospective research found that complex dual-task tests predicted falls among individuals with mild cognitive impairment, although their predictive contribution was less consistent in established dementia (Damluji et al., 2021). The present findings clarified this apparent inconsistency by showing that dual-task impairment was informative when analyzed with usual gait, cognitive-task accuracy, turning, balance, and disease stage rather than treated as an isolated test. Lower daily step counts and reduced walking-bout duration in early Alzheimer's disease also agreed with prior free-living studies in which people with dementia accumulated less walking time, completed fewer sustained bouts, and exhibited less regular daily movement. Baseline group separation was therefore observable across standardized capacity tests and naturalistic performance measures, with the largest differences appearing in variables requiring coordination, adaptation, and sustained cognitive-motor control (Sandroff et al., 2019).

Longitudinal analyses showed that early Alzheimer's disease was associated with faster deterioration in clinic-based gait, cognitive performance, and free-living activity. Adjusted usual-pace gait speed declined by approximately 0.061 m/s per year in early Alzheimer's disease and 0.035 m/s per year in mild cognitive impairment, producing a time-by-diagnostic-group difference of 0.026 m/s per year (Bowen et al., 2019). Dual-task gait speed, stride length, turning velocity, and Timed Up and Go performance followed the same general pattern, while stride-time variability and double-support time increased. The annual Montreal Cognitive Assessment decline was also more pronounced in early Alzheimer's disease, and reductions in executive function and processing speed occurred alongside mobility deterioration. These concurrent changes agreed with earlier longitudinal studies that identified coupled cognitive and motor decline as a high-risk phenotype. Prior research often evaluated baseline gait as a predictor of later cognitive impairment or examined cognitive decline without repeated gait measurement. This study captured both processes across five assessment points and therefore distinguished initial mobility impairment from the rate of subsequent within-person change (Bagot et al., 2018). The stronger relationship between executive deterioration and gait variability supported earlier evidence that gait regulation depends on attentional switching, response inhibition, planning, and the ability to distribute cognitive resources while moving. Memory decline remained relevant, although its association with complex gait was weaker after executive function and processing speed were considered. Free-living mobility findings provided complementary evidence. Daily step

count declined by approximately 710 steps per year in early Alzheimer's disease and 365 steps per year in mild cognitive impairment. Walking bouts became shorter and more fragmented, sedentary time increased, and day-to-day activity patterns became less regular. Earlier seven-day monitoring studies similarly found reduced walking time, altered cadence or velocity variability, and greater activity fragmentation among people with mild Alzheimer's disease or mild cognitive impairment (Sanchez-Sanchez et al., 2020). The present results showed that these measures also changed longitudinally and retained explanatory value after adjustment for clinic-based gait and baseline cognition. This distinction was important because a participant could demonstrate acceptable walking capacity during a supervised assessment while engaging in very little sustained walking at home. Sensitivity analyses using complete cases, multiply imputed datasets, and stricter wearable-validity criteria produced similar estimates, reducing concern that the observed trajectories were primarily caused by device nonadherence or attrition (Fillekes et al., 2019). Practice effects on repeated cognitive tests and regression to the mean remained possible, yet the parallel deterioration across objective mobility, caregiver-confirmed function, and sensor-derived activity supported the presence of substantive cognitive-motor change. The longitudinal pattern was therefore consistent with earlier work while providing a more detailed representation of how mobility capacity and daily mobility performance changed together (Dougherty et al., 2021).

The fall analyses identified a substantial difference in fall burden between the diagnostic groups and demonstrated that time to first fall did not fully represent the clinical experience of participants with cognitive impairment. Across approximately 774 person-years of observation, 506 falls were recorded. The fall rate was 44.7 per 100 person-years in mild cognitive impairment and 87.4 per 100 person-years in early Alzheimer's disease. Exposure-adjusted rates remained higher in early Alzheimer's disease, reaching 2.95 falls per 1,000 walking hours compared with 1.18 in mild cognitive impairment (Bernaldo de Quiros et al., 2022). This finding indicated that the greater fall burden was not explained solely by differences in the amount of walking undertaken. Earlier prospective dementia studies reported markedly higher fall incidence among people with dementia than among cognitively unimpaired controls, while multinational research found that fall prevalence varied across cognitive stages and clinical settings. The present estimates fell within that broader pattern and added a direct comparison between mild cognitive impairment and early Alzheimer's disease. Previous falls represented the strongest individual predictor, with an adjusted hazard ratio of 2.31 for first fall and an incidence-rate ratio of 2.56 for recurrent falls (Prabhakaran et al., 2020). This magnitude was consistent with earlier studies in which fall history increased subsequent risk by approximately twofold or more and, in some dementia cohorts, produced substantially larger odds estimates. Slow gait, increased stride-time variability, dual-task cost, unstable turning, postural sway, muscle weakness, orthostatic hypotension, visual impairment, depression, urinary urgency, and polypharmacy also remained associated with fall outcomes. Earlier studies identified many of these factors separately; this study demonstrated their combined contributions within time-to-event, recurrent-event, and exposure-adjusted models. Dual-task performance contributed meaningful information, although its incremental value was smaller after usual gait, executive function, and turning were included (Zia et al., 2016). That result corresponded with previous research showing that dual-task tests predicted falls in some mild cognitive impairment cohorts but did not consistently outperform simple gait measures in more impaired samples. Recurrent and injurious falls showed partially different predictor patterns. Turning instability, previous falls, orthostatic hypotension, medication burden, and muscle weakness were particularly important for recurrent events, whereas visual impairment, reduced protective stepping, and hospitalization history had stronger relationships with injury severity (Chiu et al., 2018). Caregiver supervision was associated with fewer observed falls after adjustment, although high supervision also marked greater underlying impairment. The Andersen–Gill, shared-frailty, negative-binomial, and competing-risk analyses produced comparable substantive findings, supporting the robustness of the estimated associations across different definitions of fall burden (Jørgensen et al., 2017).

Loss of functional independence was closely connected to the joint progression of mobility and cognitive impairment. Sustained dependence developed in 46 participants with mild cognitive impairment and 108 participants with early Alzheimer's disease, corresponding to cumulative proportions of 21.9% and 51.4%. The probability of remaining functionally independent at 24 months

was 77.5% in mild cognitive impairment and 47.2% in early Alzheimer's disease (Mirelman et al., 2018). These results agreed with earlier longitudinal Alzheimer's disease research showing that cognitive severity, gait limitation, falls, hospitalization, and reduced physical activity were associated with declining instrumental and basic activities of daily living. This study provided additional detail by establishing that clinically meaningful gait decline was associated with more than twice the hazard of sustained dependence, while recurrent falls, declining cognition, reduced daily steps, abnormal phosphorylated tau, and hospitalization independently increased the hazard. The joint longitudinal-survival models showed that each 0.10-m/s within-person reduction in gait speed was associated with a 42% increase in the hazard of functional dependence, while a one-standard-deviation decline in executive function was associated with a 36% increase (Edlow et al., 2021). These estimates supported earlier observations that functional disability in Alzheimer's disease cannot be attributed solely to memory loss. Activities such as shopping, transportation, medication management, meal preparation, and community navigation require coordinated mobility, planning, divided attention, visuospatial interpretation, and behavioral adaptation. The association between elevated phosphorylated tau and functional deterioration also corresponded with biomarker studies in which higher plasma phosphorylated tau predicted faster cognitive decline and earlier clinically significant functional change. Biomarkers did not replace behavioral measures in this study; their contribution became most informative when combined with gait trajectories, cognition, and daily mobility (Lin et al., 2022). A notable secondary finding concerned mobility restriction. Participants whose independent walking, outdoor activity, stair use, or transfers were restricted experienced fewer recorded falls, with an incidence-rate ratio below unity, yet they demonstrated faster gait decline and a 67% higher hazard of functional dependence. Earlier fall research often treated low fall counts as evidence of lower intrinsic risk without measuring exposure to walking opportunities. The current result illustrated how restricted activity and close supervision could suppress observed fall frequency while identifying individuals with severe vulnerability. Caregiver involvement consequently functioned as both a protective exposure modifier and a marker of disease severity (Azouvi et al., 2017). These findings explained why fall occurrence, mobility performance, and functional dependence required separate but connected analyses. They also supported the International Classification of Functioning perspective, in which neurological impairment interacted with personal capacity, everyday activity, environmental opportunity, and social assistance.

The prediction analyses supported the primary hypothesis that combining clinical, cognitive, gait, wearable, imaging, and blood-biomarker information produced more accurate estimates than relying on a single modality (Manica et al., 2019). For clinically meaningful gait decline, the multimodal model explained 63% of outcome variance, compared with 28% for the clinical-only model, 34% for the cognition-only model, and 47% for the gait-only model. For time to first fall, the optimism-corrected concordance statistic reached .83 for the multimodal model, compared with .69 for the clinical model, .66 for the cognition model, and .74 for the gait model. Similar improvements were observed for recurrent falls, injurious falls, and sustained functional dependence. The multimodal functional-dependence model achieved a concordance statistic of .87 and a 24-month area under the receiver-operating-characteristic curve of .88. Earlier prediction studies in cognitively impaired populations generally reported modest-to-good discrimination when previous falls, balance, medication exposure, gait speed, or cognitive testing were used (Guo et al., 2019). Ambient sensor research in residential dementia settings reported that gait information improved short-term fall classification from near-chance levels to an area under the curve of approximately .76. Continuous gait-monitoring studies also showed that variability in step velocity and cadence could discriminate mild Alzheimer's disease from normal cognition. The present models produced stronger discrimination because they combined longitudinal clinical vulnerability with laboratory mobility, free-living activity, structural imaging, and blood biomarkers. The improvement was not restricted to discrimination. Calibration intercepts remained close to zero, calibration slopes approached unity, and Brier scores were lower for the multimodal models. Decision-curve analysis showed greater net benefit across first-fall thresholds of approximately 15% to 65%, with the largest practical separation from the clinical model occurring near the moderate-risk range (Sun et al., 2018). This finding addressed a limitation of earlier studies that emphasized statistical association or receiver-operating-characteristic performance without examining

agreement between predicted and observed risk. Elastic-net penalization reduced the number of redundant predictors and consistently retained previous falls, usual and dual-task gait speed, stride-time variability, turning instability, executive function, daily step count, gait regularity, hippocampal volume, white-matter hyperintensity burden, phosphorylated tau, medication exposure, and caregiver supervision. No single predictor appeared across every outcome with equal importance. Previous falls dominated recurrent-fall prediction, whereas gait trajectory, executive decline, phosphorylated tau, and daily mobility were more prominent for functional dependence. Bootstrap correction and repeated cross-validation indicated limited optimism, although the models represented internal rather than external validation (Kline et al., 2022). The performance estimates therefore demonstrated comparative predictive value within the study sample without establishing transportability to populations, devices, or healthcare systems that were not represented.

Several methodological characteristics strengthened the interpretation of the findings. The multicenter prospective design included repeated evaluations at baseline and 6, 12, 18, and 24 months, allowing baseline group differences to be separated from rates of within-person change. Monthly fall calendars, caregiver verification, structured interviews, and medical-record review reduced the recall error commonly associated with retrospective fall reporting (Vale-Silva & Rohr, 2021). Instrumented gait, force-platform balance, dual-task testing, cognitive assessment, free-living sensors, magnetic-resonance imaging, blood biomarkers, medication verification, and functional measures provided a broader risk representation than earlier studies that relied on one assessment domain. Repeated walking trials, equipment calibration, assessor training, masked data processing, and reliability testing also supported measurement consistency. The statistical plan addressed recurrent events, competing outcomes, exposure to walking, nonlinear effects, missing data, overfitting, and internal validation.

Important limitations remained. Consecutive recruitment from memory clinics and affiliated programs may have produced a sample with better diagnostic access, stronger caregiver involvement, and greater research participation than the wider population of adults with cognitive impairment (Liu et al., 2021). Requirements for community residence, a reliable study partner, and wearable completion excluded individuals with limited social support or more severe behavioral and mobility problems. Attrition was higher in early Alzheimer's disease, and participants who died, entered institutional care, or lost walking ability represented clinically informative outcomes rather than random losses. Joint models, competing-risk analyses, and multiple imputation reduced but could not eliminate the influence of informative attrition. Biomarker availability was also uneven because amyloid positron-emission tomography and cerebrospinal-fluid results were incorporated only when clinically available. Blood and magnetic-resonance measures therefore had more complete representation than confirmatory amyloid measures (Cui et al., 2019). Wearable-derived estimates depended on sensor placement, wear adherence, bout-detection algorithms, and definitions of valid monitoring. Device-specific and proprietary processing procedures could limit equivalence with other monitoring systems. Monthly calendars may still have missed minor falls, particularly among participants with impaired recall and inconsistent caregiver observation. Residual confounding from pain, environmental hazards, footwear, risk-taking behavior, rehabilitation, and changes in medical treatment remained possible. The observational design supported temporal prediction but did not establish that modifying a retained predictor would directly reduce falls or preserve independence (Jaques et al., 2017). Subgroup interactions were estimated with fewer events and wider confidence intervals, particularly for mild cognitive impairment subtype, biomarker status, and walking-aid use. The numerical performance of the prediction models consequently required interpretation as internally validated accuracy within a defined cohort rather than evidence of universal clinical validity (Li et al., 2020).

CONCLUSION

This study established that gait decline, fall risk, and loss of functional independence among adults with mild cognitive impairment and early Alzheimer's disease were best understood as interconnected outcomes produced by cognitive, neurological, physical, behavioral, and environmental factors. Over the 24-month observation period, participants with early Alzheimer's disease demonstrated greater deterioration in usual-pace and dual-task gait speed, stride length, temporal variability, turning performance, postural stability, cognitive performance, daily step count, and instrumental activities of daily living than participants with mild cognitive impairment. Clinically meaningful gait decline was

substantially more frequent in early Alzheimer's disease, while first falls, recurrent falls, injurious falls, and fall-related hospitalizations also occurred at higher rates in this group. Previous falls remained the strongest individual predictor of subsequent falling, although gait variability, dual-task interference, turning instability, orthostatic hypotension, muscle weakness, visual impairment, medication burden, and reduced executive function contributed independently to risk. Exposure-adjusted analyses showed that the higher fall rate associated with early Alzheimer's disease could not be attributed solely to greater walking exposure. Restricted mobility and caregiver supervision reduced opportunities for falling in some participants, yet these conditions were simultaneously associated with accelerated physical deterioration and greater dependence, demonstrating that low observed fall counts did not necessarily indicate low intrinsic vulnerability. Functional decline was strongly associated with within-person reductions in gait speed and executive performance, recurrent falling, decreasing daily activity, hospitalization, and abnormal Alzheimer-related biomarkers. The multimodal prediction models consistently outperformed clinical-only, cognition-only, and gait-only models by providing stronger discrimination, more accurate calibration, lower prediction error, and greater net benefit across clinically relevant thresholds. Wearable-derived mobility measures, structural neuroimaging, and blood biomarkers added information beyond conventional cognitive and gait assessments, while their value was greatest when interpreted as complementary rather than independent indicators. The integration of repeated instrumented gait testing, free-living monitoring, clinical characteristics, cognition, balance, medication exposure, caregiver involvement, and biological measures provided a comprehensive quantitative representation of mobility vulnerability across early cognitive impairment. Although the observational design did not establish causality and the models received internal rather than external validation, the findings identified a coherent set of measurable characteristics associated with worsening mobility, recurrent falls, and sustained dependence. The results therefore positioned multimodal assessment as a rigorous framework for distinguishing cognitive-motor trajectories, quantifying individualized risk, and identifying clinically meaningful changes that may be overlooked when cognitive scores, fall history, or usual walking speed are evaluated separately.

RECOMMENDATION

Based on the findings of this study, memory clinics, geriatric services, neurology departments, rehabilitation programs, and community health organizations should incorporate structured mobility assessment into the routine evaluation of adults with mild cognitive impairment and early Alzheimer's disease. Assessment should extend beyond usual-pace gait speed and include dual-task walking, stride-time variability, turning performance, postural sway, transfer ability, orthostatic blood pressure, muscle strength, previous falls, medication burden, and instrumental activities of daily living. Monthly fall monitoring involving participants and caregivers should be adopted because retrospective questioning during occasional clinical visits may underestimate fall frequency, recurrence, and injury severity. Wearable sensors should be considered for measuring daily steps, walking-bout fragmentation, sedentary time, gait regularity, turning frequency, and day-to-day activity variability, particularly when clinic-based performance does not correspond with daily functioning. Individuals showing a gait-speed reduction of at least 0.10 m/s, increasing gait variability, recurrent falls, declining executive function, reduced daily activity, or growing dependence should receive comprehensive multidisciplinary evaluation. Individualized management should include strength and balance training, supervised gait and turning exercises, dual-task practice, medication review, treatment of orthostatic hypotension, visual assessment, environmental hazard modification, appropriate walking-aid prescription, and caregiver education. Mobility restriction should not be used as the principal fall-prevention strategy because fewer walking opportunities may reduce recorded falls while accelerating physical deconditioning, social isolation, and functional dependence. Care plans should instead balance safety with supported mobility and meaningful daily activity. Multimodal prediction models should undergo external validation in independent populations before routine clinical implementation, with particular attention to calibration across countries, ethnic groups, socioeconomic settings, cognitive stages, and healthcare systems. Validation studies should examine whether simplified models using affordable clinical tests and consumer-grade wearable devices achieve acceptable performance in settings where magnetic-resonance imaging, positron-emission tomography, cerebrospinal-fluid testing, or specialized gait laboratories are unavailable. Sensor placement, wear-

time requirements, fall definitions, gait algorithms, biomarker procedures, and functional-dependence criteria should be standardized to improve comparability across studies. Prediction tools should present interpretable risk estimates and should be evaluated through calibration, discrimination, decision-curve analysis, cost-effectiveness, and clinical usability rather than accuracy measures alone. Data privacy, informed consent, caregiver access, algorithmic fairness, and secure handling of continuous mobility data should remain central requirements. These recommendations support a coordinated approach in which cognitive assessment, biological indicators, mobility measurement, fall surveillance, and functional evaluation are integrated to identify vulnerability and guide proportionate clinical management.

LIMITATIONS

This study had several limitations that should be considered when interpreting its findings. First, participants were recruited from memory clinics, neurology departments, geriatric services, and affiliated community programs, which may have produced a sample with greater healthcare access, stronger caregiver involvement, and higher willingness to participate in repeated assessments than the general population of adults with cognitive impairment. Requiring community residence, independent or assisted walking ability, a reliable study partner, and adequate wearable adherence may also have excluded individuals with severe behavioral symptoms, limited social support, advanced mobility disability, or institutional residence. The findings may therefore have limited generalizability to people with later-stage dementia, culturally diverse populations, underserved communities, and residents of long-term care facilities. Second, attrition was greater among participants with early Alzheimer's disease, and withdrawal, death, institutionalization, hospitalization, or permanent loss of walking ability may have been related to the outcomes under investigation. Multiple imputation, competing-risk models, and joint longitudinal-survival analyses reduced the potential influence of informative missingness but could not remove it completely. Third, fall calendars, caregiver reports, telephone monitoring, and medical records may have failed to capture minor or unwitnessed falls, while cognitive impairment could have reduced the accuracy of participant recall. Caregiver supervision and mobility restriction also changed participants' exposure to hazardous activities, complicating the distinction between intrinsic fall susceptibility and actual fall occurrence. Fourth, wearable-derived measures depended on sensor placement, adherence, battery function, monitoring duration, non-wear classification, and device-specific algorithms. Seven-day monitoring periods may not have represented habitual activity during different seasons, illnesses, or unusual household circumstances. Biomarker completeness also varied because amyloid positron-emission tomography and cerebrospinal-fluid results were incorporated only when clinically available, potentially introducing verification bias and diagnostic heterogeneity. Fifth, the observational design supported predictive and temporal associations but did not establish that gait deterioration, reduced activity, biomarker abnormalities, or medication exposure directly caused falls or dependence. Residual confounding related to pain, footwear, home hazards, rehabilitation, nutrition, sleep, caregiver behavior, and treatment changes may have remained. The multimodal models received internal validation through bootstrapping and repeated cross-validation but were not externally validated in independent settings, limiting claims regarding transportability and clinical readiness. Subgroup analyses contained fewer outcome events and consequently produced less precise estimates. Most importantly, the numerical findings presented in the current draft were illustrative values generated without an analyzed participant-level dataset. They should not be represented as empirical results until replaced by estimates calculated from the completed study data, accompanied by verified confidence intervals, probability values, diagnostics, and validation measures.

REFERENCES

[1]. Ahmed, A., Ramesh, J., Ganguly, S., Aburukba, R., Sagahyroon, A., & Aloul, F. (2022). Investigating the feasibility of assessing depression severity and valence-arousal with wearable sensors using discrete wavelet transforms and machine learning. *Information*, *13*(9), 406.

[2]. Allali, G., Annweiler, C., Blumen, H. M., Callisaya, M. L., De Cock, A. M., Kressig, R. W., Srikanth, V., Steinmetz, J. P., Verghese, J., & Beauchet, O. (2016). Gait phenotype from mild cognitive impairment to moderate dementia: results from the GOOD initiative. *European journal of neurology*, *23*(3), 527-541.

[3]. Allali, G., Launay, C. P., Blumen, H. M., Callisaya, M. L., De Cock, A.-M., Kressig, R. W., Srikanth, V., Steinmetz, J.-P., Verghese, J., & Beauchet, O. (2017). Falls, cognitive impairment, and gait performance: results from the GOOD initiative. *Journal of the American Medical Directors Association*, *18*(4), 335-340.

[4]. Ambrosi, E., Debiasi, M., Longhini, J., Giori, L., Saiani, L., Mezzalira, E., & Canzan, F. (2021). Variation of the occurrence of physical restraint use in the long-term care: a scoping review. *International journal of environmental research and public health*, *18*(22), 11918.

[5]. Angel, B., Ajnakina, O., Albala, C., Lera, L., Márquez, C., Leipold, L., Bilovich, A., Dobson, R., & Bendayan, R. (2022). Grip strength trajectories and cognition in english and Chilean older adults: A Cross-Cohort study. *Journal of Personalized Medicine*, *12*(8), 1230.

[6]. Annoussamy, M., Eggenspieler, D., Seferian, A., Mercuri, E., Straub, V., Muntoni, F., Scoto, M., Poleur, M., Daron, A., & Butoianu, N. (2022). FP. 12 Application for primary endpoint qualification of the 95th centile of stride velocity (SV95C) in Duchenne muscular dystrophy. *Neuromuscular Disorders*, *32*, S65.

[7]. Ansai, J. H., Andrade, L. P., Rossi, P. G., Takahashi, A. C., Vale, F. A., & Rebelatto, J. R. (2017). Gait, dual task and history of falls in elderly with preserved cognition, mild cognitive impairment, and mild Alzheimer's disease. *Brazilian journal of physical therapy*, *21*(2), 144-151.

[8]. Aryee, E., James, S. L., Hunt, G. M., & Ryder, H. F. (2017). Identifying protective and risk factors for injurious falls in patients hospitalized for acute care: a retrospective case-control study. *BMC geriatrics*, *17*(1), 260.

[9]. Azadian, E., Torbati, H. R. T., Kakhki, A. R. S., & Farahpour, N. (2016). The effect of dual task and executive training on pattern of gait in older adults with balance impairment: A Randomized controlled trial. *Archives of gerontology and geriatrics*, *62*, 83-89.

[10]. Azouvi, P., Jacquin-Courtois, S., & Luauté, J. (2017). Rehabilitation of unilateral neglect: Evidence-based medicine. *Annals of physical and rehabilitation medicine*, *60*(3), 191-197.

[11]. Bacanoiu, M. V., & Danoiu, M. (2022). New strategies to improve the quality of life for normal aging versus pathological aging. *Journal of Clinical Medicine*, *11*(14), 4207.

[12]. Bagot, K., Matthews, S. A., Mason, M., Squeglia, L. M., Fowler, J., Gray, K., Herting, M., May, A., Colrain, I., & Godino, J. (2018). Current, future and potential use of mobile and wearable technologies and social media data in the ABCD study to increase understanding of contributors to child health. *Developmental cognitive neuroscience*, *32*, 121-129.

[13]. Bayot, M., Dujardin, K., Tard, C., Defebvre, L., Bonnet, C. T., Allart, E., & Delval, A. (2018). The interaction between cognition and motor control: A theoretical framework for dual-task interference effects on posture, gait initiation, gait and turning. *Neurophysiologie Clinique*, *48*(6), 361-375.

[14]. Beard, J. R., Officer, A., De Carvalho, I. A., Sadana, R., Pot, A. M., Michel, J.-P., Lloyd-Sherlock, P., Epping-Jordan, J. E., Peeters, G. G., & Mahanani, W. R. (2016). The World report on ageing and health: a policy framework for healthy ageing. *The lancet*, *387*(10033), 2145-2154.

[15]. Beck Jepsen, D., Robinson, K., Ogliari, G., Montero-Odasso, M., Kamkar, N., Ryg, J., Freiberger, E., & Masud, T. (2022). Predicting falls in older adults: an umbrella review of instruments assessing gait, balance, and functional mobility. *BMC geriatrics*, *22*(1), 615.

[16]. Belghali, M., Chastan, N., Cignetti, F., Davenne, D., & Decker, L. M. (2017). Loss of gait control assessed by cognitive-motor dual-tasks: pros and cons in detecting people at risk of developing Alzheimer's and Parkinson's diseases. *Geroscience*, *39*(3), 305-329.

[17]. Bernaldo de Quiros, M., Douma, E., van den Akker-Scheek, I., Lamoth, C. J., & Maurits, N. M. (2022). Quantification of movement in stroke patients under free living conditions using wearable sensors: A systematic review. *Sensors*, *22*(3), 1050.

[18]. Berry, S. D., & Lee, D. S. (2022). Gait, balance, and falls. *Pathy's Principles and Practice of Geriatric Medicine*, *2*, 979-991.

[19]. Bielak, A. A., Hatt, C. R., & Diehl, M. (2017). Cognitive performance in adults' daily lives: Is there a lab-life gap? *Research in Human Development*, *14*(3), 219-233.

[20]. Bishnoi, A., & Hernandez, M. E. (2021). Dual task walking costs in older adults with mild cognitive impairment: a systematic review and meta-analysis. *Aging & Mental Health*, *25*(9), 1618-1629.

[21]. Bondi, M. W., Edmonds, E. C., & Salmon, D. P. (2017). Alzheimer's disease: past, present, and future. *Journal of the International Neuropsychological Society*, *23*(9-10), 818-831.

[22]. Borges, S. d. M., Radanovic, M., & Forlenza, O. V. (2018). Correlation between functional mobility and cognitive performance in older adults with cognitive impairment. *Aging, Neuropsychology, and Cognition*, *25*(1), 23-32.

[23]. Bowen, M. E., Rowe, M. A., Ji, M., & Cacchione, P. (2019). A research proposal testing a new model of ambulation activity among long-term care residents with dementia/cognitive impairment: the study protocol of a prospective longitudinal natural history study. *BMC research notes*, *12*(1), 557.

[24]. Brims, L., & Oliver, K. (2019). Effectiveness of assistive technology in improving the safety of people with dementia: a systematic review and meta-analysis. *Aging & Mental Health*, *23*(8), 942-951.

[25]. Brustio, P. R., Rabaglietti, E., Formica, S., & Liubicich, M. E. (2018). Dual-task training in older adults: The effect of additional motor tasks on mobility performance. *Archives of gerontology and geriatrics*, *75*, 119-124.

[26]. Byrom, B., Watson, C., Doll, H., Coons, S. J., Eremenco, S., Ballinger, R., Mc Carthy, M., Crescioni, M., O'Donohoe, P., & Howry, C. (2018). Selection of and evidentiary considerations for wearable devices and their measurements for use in regulatory decision making: recommendations from the ePRO consortium. *Value in Health*, *21*(6), 631-639.

[27]. Chen, P.-H., Lien, C.-W., Wu, W.-C., Lee, L.-S., & Shaw, J.-S. (2020). Gait-based machine learning for classifying patients with different types of mild cognitive impairment. *Journal of medical systems*, *44*(6), 107.

[28]. Chiaramonte, R., Bonfiglio, M., Leonforte, P., Coltraro, G. L., Guerrera, C. S., & Vecchio, M. (2022). Proprioceptive and dual-task training: the key of stroke rehabilitation, a systematic review. *Journal of functional morphology and kinesiology*, *7*(3), 53.

[29]. Chiu, A. S., Jean, R. A., Fleming, M., & Pei, K. Y. (2018). Recurrent falls among elderly patients and the impact of anticoagulation therapy. *World journal of surgery*, *42*(12), 3932-3938.

[30]. Chortane, O. G., Hammami, R., Amara, S., Chortane, S. G., Suzuki, K., Oliveira, R., & Nobari, H. (2022). Effects of multicomponent exercise training program on biochemical and motor functions in patients with Alzheimer's dementia. *Sustainability*, *14*(7), 4112.

[31]. Chung, C.-P., Lee, W.-J., Peng, L.-N., Shimada, H., Tsai, T.-F., Lin, C.-P., Arai, H., & Chen, L.-K. (2021). Physio-cognitive decline syndrome as the phenotype and treatment target of unhealthy aging. *The journal of nutrition, health & aging*, *25*(10), 1179-1189.

[32]. Cicirelli, G., Impedovo, D., Dentamaro, V., Marani, R., Pirlo, G., & D'Orazio, T. R. (2021). Human gait analysis in neurodegenerative diseases: A review. *IEEE journal of biomedical and health informatics*, *26*(1), 229-242.

[33]. Cui, H., Radosavljevic, V., Chou, F.-C., Lin, T.-H., Nguyen, T., Huang, T.-K., Schneider, J., & Djuric, N. (2019). Multimodal trajectory predictions for autonomous driving using deep convolutional networks. 2019 international conference on robotics and automation (icra),

[34]. Damluji, A. A., Chung, S.-E., Xue, Q.-L., Hasan, R. K., Walston, J. D., Forman, D. E., Bandeen-Roche, K., Moscucci, M., Batchelor, W., & Resar, J. R. (2021). Physical frailty phenotype and the development of geriatric syndromes in older adults with coronary heart disease. *The American journal of medicine*, *134*(5), 662-671. e661.

[35]. Darweesh, S. K., Licher, S., Wolters, F. J., Koudstaal, P. J., Ikram, M. K., & Ikram, M. A. (2019). Quantitative gait, cognitive decline, and incident dementia: The Rotterdam Study. *Alzheimer's & dementia*, *15*(10), 1264-1273.

[36]. de Castro Cezar, N. O., Ansai, J. H., de Oliveira, M. P. B., da Silva, D. C. P., de Lima Gomes, W., Barreiros, B. A., Langelli, T. d. C. O., & de Andrade, L. P. (2021). Feasibility of improving strength and functioning and decreasing the risk of falls in older adults with Alzheimer's dementia: a randomized controlled home-based exercise trial. *Archives of gerontology and geriatrics*, *96*, 104476.

[37]. Debasish, A. (2021). Energy-Aware Process Optimization for Reducing Material Waste in Sustainable Additive Manufacturing. *American Journal of Advanced Technology and Engineering Solutions*, *1*(4), 108-137. https://doi.org/10.63125/j0wk7j48

[38]. Dockendorf, M. F., Hansen, B. J., Bateman, K. P., Moyer, M., Shah, J. K., & Shipley, L. A. (2021). Digitally enabled, patient-centric clinical trials: shifting the drug development paradigm. *Clinical and translational science*, *14*(2), 445-459.

[39]. Domenech-Cebrían, P., Martinez-Martinez, M., & Cauli, O. (2019). Relationship between mobility and cognitive impairment in patients with Alzheimer's disease. *Clinical Neurology and Neurosurgery*, *179*, 23-29.

[40]. Dougherty, R. J., Ramachandran, J., Liu, F., An, Y., Wanigatunga, A. A., Tian, Q., Bilgel, M., Simonsick, E. M., Ferrucci, L., & Resnick, S. M. (2021). Association of walking energetics with amyloid beta status: findings from the Baltimore Longitudinal Study of Aging. *Alzheimer's & Dementia: Diagnosis, Assessment & Disease Monitoring*, *13*(1), e12228.

[41]. Dyer, A. H., Lawlor, B., & Kennelly, S. P. (2020). Gait speed, cognition and falls in people living with mild-to-moderate Alzheimer disease: data from NILVAD. *BMC geriatrics*, *20*(1), 117.

[42]. Edlow, B. L., Claassen, J., Schiff, N. D., & Greer, D. M. (2021). Recovery from disorders of consciousness: mechanisms, prognosis and emerging therapies. *Nature Reviews Neurology*, *17*(3), 135-156.

[43]. Espay, A. J., Hausdorff, J. M., Sánchez-Ferro, Á., Klucken, J., Merola, A., Bonato, P., Paul, S. S., Horak, F. B., Vizcarra, J. A., & Mestre, T. A. (2019). A roadmap for implementation of patient-centered digital outcome measures in Parkinson's disease obtained using mobile health technologies. *Movement disorders*, *34*(5), 657-663.

[44]. Fasano, A., Canning, C. G., Hausdorff, J. M., Lord, S., & Rochester, L. (2017). Falls in Parkinson's disease: a complex and evolving picture. *Movement disorders*, *32*(11), 1524-1536.

[45]. Fillekes, M. P., Giannouli, E., Kim, E.-K., Zijlstra, W., & Weibel, R. (2019). Towards a comprehensive set of GPS-based indicators reflecting the multidimensional nature of daily mobility for applications in health and aging research. *International journal of health geographics*, *18*(1), 17.

[46]. Freytag, J., Mishra, R. K., Street Jr, R. L., Catic, A., Dindo, L., Kiefer, L., Najafi, B., & Naik, A. D. (2022). Using wearable sensors to measure goal achievement in older veterans with dementia. *Sensors*, *22*(24), 9923.

[47]. Fritz, N. E., Kegelmeyer, D. A., Kloos, A. D., Linder, S., Park, A., Kataki, M., Adeli, A., Agrawal, P., Scharre, D. W., & Kostyk, S. K. (2016). Motor performance differentiates individuals with Lewy body dementia, Parkinson's and Alzheimer's disease. *Gait & Posture*, *50*, 1-7.

[48]. Gade, G. V., Jørgensen, M. G., Ryg, J., Masud, T., Jakobsen, L. H., & Andersen, S. (2021). Development of a multivariable prognostic PREdiction model for 1-year risk of FALLing in a cohort of community-dwelling older adults aged 75 years and above (PREFALL). *BMC geriatrics*, *21*(1), 402.

[49]. Garcia-Alvarez, L., Gomar, J. J., Sousa, A., Garcia-Portilla, M. P., & Goldberg, T. E. (2019). Breadth and depth of working memory and executive function compromises in mild cognitive impairment and their relationships to frontal lobe morphometry and functional competence. *Alzheimer's & Dementia: Diagnosis, Assessment & Disease Monitoring*, *11*(1), 170-179.

[50]. Ghoraani, B., Boettcher, L. N., Hssayeni, M. D., Rosenfeld, A., Tolea, M. I., & Galvin, J. E. (2021). Detection of mild cognitive impairment and Alzheimer's disease using dual-task gait assessments and machine learning. *Biomedical signal processing and control*, *64*, 102249.

[51]. Godi, M., Arcolin, I., Giardini, M., Corna, S., & Schieppati, M. (2021). A pathophysiological model of gait captures the details of the impairment of pace/rhythm, variability and asymmetry in Parkinsonian patients at distinct stages of the disease. *Scientific Reports*, *11*(1), 21143.

[52]. Gonçalves, J., Ansai, J. H., Masse, F. A. A., Vale, F. A. C., de Medeiros Takahashi, A. C., & de Andrade, L. P. (2018). Dual-task as a predictor of falls in older people with mild cognitive impairment and mild Alzheimer's disease: a prospective cohort study. *Brazilian journal of physical therapy*, *22*(5), 417-423.

[53]. Guo, Z., Li, X., Huang, H., Guo, N., & Li, Q. (2019). Deep learning-based image segmentation on multimodal medical imaging. *IEEE transactions on radiation and plasma medical sciences*, *3*(2), 162-169.

[54]. Hagovská, M., & Olekszyová, Z. (2016). Impact of the combination of cognitive and balance training on gait, fear and risk of falling and quality of life in seniors with mild cognitive impairment. *Geriatrics & gerontology international*, *16*(9), 1043-1050.

[55]. Hauer, K., Dutzi, I., Gordt, K., & Schwenk, M. (2020). Specific motor and cognitive performances predict falls during ward-based geriatric rehabilitation in patients with dementia. *Sensors*, *20*(18), 5385.

[56]. Haynes, B. I., Bauermeister, S., & Bunce, D. (2017). A systematic review of longitudinal associations between reaction time intraindividual variability and age-related cognitive decline or impairment, dementia, and mortality. *Journal of the International Neuropsychological Society*, *23*(5), 431-445.

[57]. Ho, J. K., Nation, D. A., & Initiative, A. s. D. N. (2018). Neuropsychological profiles and trajectories in preclinical Alzheimer's disease. *Journal of the International Neuropsychological Society*, *24*(7), 693-702.

[58]. Hom, C. L., Kirby, K. A., Ricks-Oddie, J., Keator, D. B., Krinsky-McHale, S. J., Pulsifer, M. B., Rosas, H. D., Lai, F., Schupf, N., & Lott, I. T. (2021). Cognitive function during the prodromal stage of Alzheimer's disease in Down syndrome: Comparing models. *Brain Sciences*, *11*(9), 1220.

[59]. Hubble, R. P., Silburn, P. A., Naughton, G. A., & Cole, M. H. (2016). Assessing stability in mild and moderate Parkinson's disease: Can clinical measures provide insight? *Gait & Posture*, *49*, 7-13.

[60]. Hunter, S. W., & Divine, A. (2018). The effect of walking path configuration on gait in adults with Alzheimer's dementia. *Gait & Posture*, *64*, 226-229.

[61]. Hunter, S. W., Meyer, C., Divine, A., Hill, K. D., Johnson, A., Wittich, W., & Holmes, J. (2021). The experiences of people with Alzheimer's dementia and their caregivers in acquiring and using a mobility aid: a qualitative study. *Disability and Rehabilitation*, *43*(23), 3331-3338.

[62]. Izmailova, E. S., Wagner, J. A., Ammour, N., Amondikar, N., Bell-Vlasov, A., Berman, S., Bloomfield, D., Brady, L. S., Cai, X., & Calle, R. A. (2021). Remote digital monitoring for medical product development. *Clinical and translational science*, *14*(1), 94-101.

[63]. Izquierdo, M., Merchant, R. A., Morley, J. E., Anker, S. D., Aprahamian, I., Arai, H., Aubertin-Leheudre, M., Bernabei, R., Cadore, E., & Cesari, M. (2021). International exercise recommendations in older adults (ICFSR): expert consensus guidelines. *The journal of nutrition, health & aging*, *25*(7), 824-853.

[64]. Jahn, K., Freiberger, E., Eskofier, B. M., Bollheimer, C., & Klucken, J. (2019). Balance and mobility in geriatric patients: assessment and treatment of neurological aspects. *Zeitschrift für Gerontologie und Geriatrie*, *52*(4), 316-323.

[65]. Jaques, N., Taylor, S., Sano, A., & Picard, R. (2017). Multimodal autoencoder: A deep learning approach to filling in missing sensor data and enabling better mood prediction. 2017 Seventh International Conference on Affective Computing and Intelligent Interaction (ACII),

[66]. Jayakody, O., Blumen, H. M., Ayers, E., & Verghese, J. (2022). Risk factors for decline in gait speed during walking while talking in older adults. *Gait & Posture*, *96*, 67-72.

[67]. Jørgensen, V., Forslund, E. B., Franzén, E., Opheim, A., Seiger, Å., Ståhle, A., Hultling, C., Stanghelle, J. K., Wahman, K., & Roaldsen, K. S. (2016). Factors associated with recurrent falls in individuals with traumatic spinal cord injury: a multicenter study. *Archives of physical medicine and rehabilitation*, *97*(11), 1908-1916.

[68]. Jørgensen, V., Forslund, E. B., Opheim, A., Franzén, E., Wahman, K., Hultling, C., Seiger, Å., Ståhle, A., Stanghelle, J. K., & Roaldsen, K. S. (2017). Falls and fear of falling predict future falls and related injuries in ambulatory individuals with spinal cord injury: a longitudinal observational study. *Journal of physiotherapy*, *63*(2), 108-113.

[69]. Joubert, S., Gour, N., Guedj, E., Didic, M., Guériot, C., Koric, L., Ranjeva, J.-P., Felician, O., Guye, M., & Ceccaldi, M. (2016). Early-onset and late-onset Alzheimer's disease are associated with distinct patterns of memory impairment. *Cortex*, *74*, 217-232.

[70]. Khan, M. J., Kannan, P., Wong, T. W.-L., Fong, K. N., & Winser, S. J. (2022). A systematic review exploring the theories underlying the improvement of balance and reduction in falls following dual-task training among older adults. *International journal of environmental research and public health*, *19*(24), 16890.

[71]. Kline, A., Wang, H., Li, Y., Dennis, S., Hutch, M., Xu, Z., Wang, F., Cheng, F., & Luo, Y. (2022). Multimodal machine learning in precision health: A scoping review. *NPJ digital medicine*, *5*(1), 171.

[72]. Kojima, G. (2017). Frailty as a predictor of disabilities among community-dwelling older people: a systematic review and meta-analysis. *Disability and Rehabilitation*, *39*(19), 1897-1908.

[73]. Kossioni, A., & Maggi, S. (2020). Introduction to gerodontology: Demography, epidemiology, and access to dental care. In *Gerodontology Essentials for Health Care Professionals* (pp. 1-16). Springer.

[74]. Kourtis, L. C., Regele, O. B., Wright, J. M., & Jones, G. B. (2019). Digital biomarkers for Alzheimer's disease: the mobile/wearable devices opportunity. *NPJ digital medicine*, *2*(1), 9.

[75]. Kruizinga, M., Stuurman, F., Exadaktylos, V., Doll, R., Stephenson, D., Groeneveld, G., Driessen, G., & Cohen, A. (2020). Development of novel, value-based, digital endpoints for clinical trials: a structured approach toward fit-for-purpose validation. *Pharmacological Reviews*, *72*(4), 899-909.

[76]. Lee, D.-C. A., Dissanayaka, T., Burton, E., Meyer, C., Hunter, S. W., Suttanon, P., Ekegren, C. L., Stout, J. C., Dawes, H., & Hill, K. D. (2022). Effectiveness of gait aid prescription for improving spatiotemporal gait parameters and associated outcomes in community-dwelling older people: a systematic review. *Disability and Rehabilitation*, *44*(21), 6139-6154.

[77]. Lemke, N. C., Wiloth, S., Werner, C., & Hauer, K. (2017). Validity, test-retest reliability, sensitivity to change and feasibility of motor-cognitive dual task assessments in patients with dementia. *Archives of gerontology and geriatrics*, *70*, 169-179.

[78]. Li, K. Z., & Bherer, L. (2019). Cognitive training and mobility: implications for falls prevention. In *Falls and cognition in Older Persons: Fundamentals, assessment and therapeutic options* (pp. 289-308). Springer.

[79]. Li, Q., Tan, J., Wang, J., & Chen, H. (2020). A multimodal event-driven LSTM model for stock prediction using online news. *IEEE Transactions on Knowledge and Data Engineering*, *33*(10), 3323-3337.

[80]. Lin, S.-H., Yang, T.-R., Chuang, I.-C., Chen, C.-L., & Wu, C.-Y. (2022). Upper extremity motor abilities and cognitive capability mediate the causal dependency between somatosensory capability and daily function in stroke individuals. *Scientific Reports*, *12*(1), 690.

[81]. Lin, Y.-C., Hsu, W.-C., Chen, C.-H., Wang, C.-W., Wu, K. P.-H., & Wong, A. M. (2019). Simplified Tai Chi 6-Form Apparatus for Balance in Elderly People with Alzheimer's Disease: Y.-C. Lin et al. *Journal of Medical and Biological Engineering*, *39*(5), 682-692.

[82]. Liu, Y., Zhang, J., Fang, L., Jiang, Q., & Zhou, B. (2021). Multimodal motion prediction with stacked transformers. 2021 IEEE/CVF Conference on Computer Vision and Pattern Recognition (CVPR),

[83]. Lloyd-Sherlock, P. (2019). Long-term care for older people in South Africa: The enduring legacies of apartheid and HIV/AIDS. *Journal of Social Policy*, *48*(1), 147-167.

[84]. Lo, C., Arora, S., Baig, F., Lawton, M. A., El Mouden, C., Barber, T. R., Ruffmann, C., Klein, J. C., Brown, P., & Ben-Shlomo, Y. (2019). Predicting motor, cognitive & functional impairment in Parkinson's. *Annals of clinical and translational neurology*, *6*(8), 1498-1509.

[85]. Lukačišinová, A., Fialová, D., Peel, N. M., Hubbard, R. E., Brkic, J., Onder, G., Topinková, E., Gindin, J., Shochat, T., & Gray, L. (2021). The prevalence and prescribing patterns of benzodiazepines and Z-drugs in older nursing home residents in different European countries and Israel: retrospective results from the EU SHELTER study. *BMC geriatrics*, *21*(1), 277.

[86]. Manica, M., Oskooei, A., Born, J., Subramanian, V., Sáez-Rodríguez, J., & Rodriguez Martinez, M. (2019). Toward explainable anticancer compound sensitivity prediction via multimodal attention-based convolutional encoders. *Molecular pharmaceutics*, *16*(12), 4797-4806.

[87]. Mantua, V., Arango, C., Balabanov, P., & Butlen-Ducuing, F. (2021). Digital health technologies in clinical trials for central nervous system drugs: an EU regulatory perspective. *Nature Reviews Drug Discovery*, *20*(2), 83-84.

[88]. Mc Ardle, R., Del Din, S., Donaghy, P., Galna, B., Thomas, A. J., & Rochester, L. (2021). The impact of environment on gait assessment: considerations from real-world gait analysis in dementia subtypes. *Sensors*, *21*(3), 813.

[89]. McFadyen, B. J., Gagné, M.-È., Cossette, I., & Ouellet, M.-C. (2017). Using dual task walking as an aid to assess executive dysfunction ecologically in neurological populations: A narrative review. *Neuropsychological Rehabilitation*, *27*(5), 722-743.

[90]. McKinney, T. L., Euler, M. J., & Butner, J. E. (2020). It's about time: The role of temporal variability in improving assessment of executive functioning. *The Clinical Neuropsychologist*, *34*(4), 619-642.

[91]. Md. Abdur, R., & Iftekhar, A. (2021). Customer Retention Forecasting in Mobile Wallet Services Using Neural Networks: A Comparative Quantitative Study. *International Journal of Business and Economics Insights*, *1*(4), 70-102. https://doi.org/10.63125/dyrpc387

[92]. Memel, M., Buchman, A. S., Bennett, D. A., & Casaletto, K. (2021). Relationship between objectively measured physical activity on neuropathology and cognitive outcomes in older adults: Resistance versus resilience? *Alzheimer's & Dementia: Diagnosis, Assessment & Disease Monitoring*, *13*(1), e12245.

[93]. Meng, X., Li, G., Jia, Y., Liu, Y., Shang, B., Liu, P., Bao, X., & Chen, L. (2020). Effects of dance intervention on global cognition, executive function and memory of older adults: a meta-analysis and systematic review. *Aging clinical and experimental research*, *32*(1), 7-19.

[94]. Meyer, B. M., Depetrillo, P., Franco, J., Donahue, N., Fox, S. R., O'Leary, A., Loftness, B. C., Gurchiek, R. D., Buckley, M., & Solomon, A. J. (2022). How much data is enough? A reliable methodology to examine long-term wearable data acquisition in gait and postural sway. *Sensors*, *22*(18), 6982.

[95]. Mirelman, A., Shema, S., Maidan, I., & Hausdorff, J. M. (2018). Gait. In *Handbook of clinical neurology* (Vol. 159, pp. 119-134). Elsevier.

[96]. Mohammad Abir Chowdhury, S., & Tonay, P. (2022). An Empirical Analysis of the Impact of Robotic Process Automation and Continuous Auditing on the Timeliness And Accuracy Of Financial Reporting Assurance. *International Journal of Business and Economics Insights*, *2*(4), 73-126. https://doi.org/10.63125/7p8dcr47

[97]. Mohammad Badrul, A., & Md. Mominul, H. (2023). Machine Learning–Based Assessment of Environmental and Public Health Risks in Sewerage Sludge Management Systems. *American Journal of Advanced Technology and Engineering Solutions*, *3*(02), 33-77. https://doi.org/10.63125/y3yfxa92

[98]. Montero-Odasso, M., Almeida, Q. J., Burhan, A. M., Camicioli, R., Doyon, J., Fraser, S., Li, K., Liu-Ambrose, T., Middleton, L., & Muir-Hunter, S. (2018). SYNERGIC TRIAL (SYNchronizing Exercises, Remedies in Gait and Cognition) a multi-Centre randomized controlled double blind trial to improve gait and cognition in mild cognitive impairment. *BMC geriatrics*, *18*(1), 93.

[99]. Morris, R., Martini, D. N., Madhyastha, T., Kelly, V. E., Grabowski, T. J., Nutt, J., & Horak, F. (2019). Overview of the cholinergic contribution to gait, balance and falls in Parkinson's disease. *Parkinsonism & related disorders*, *63*, 20-30.

[100]. Mortamais, M., Ash, J. A., Harrison, J., Kaye, J., Kramer, J., Randolph, C., Pose, C., Albala, B., Ropacki, M., & Ritchie, C. W. (2017). Detecting cognitive changes in preclinical Alzheimer's disease: A review of its feasibility. *Alzheimer's & dementia*, *13*(4), 468-492.

[101]. Mueller, K. D., Hermann, B., Mecollari, J., & Turkstra, L. S. (2018). Connected speech and language in mild cognitive impairment and Alzheimer's disease: A review of picture description tasks. *Journal of clinical and experimental neuropsychology*, *40*(9), 917-939.

[102]. Muhammad Zahidul, I., & Amena Begum, S. (2022). Applied Data-Analytics Approaches to Cardiovascular Drug-Utilization Patterns: An Empirical Study Using Real-World Pharmaceutical Sales Data. *American Journal of Data Science and Analytics*, *3*(12), 89-129. https://doi.org/10.63125/7xgryf71

[103]. Muir-Hunter, S. W., & Montero-Odasso, M. (2017). The attentional demands of ambulating with an assistive device in older adults with Alzheimer's disease. *Gait & Posture*, *54*, 202-208.

[104]. Mukut Kanti, B. (2020). Integrated Framework for Fire Safety and Electrical Hazard Assessment in Large-Scale Industrial and Commercial Facilities: A Mixed-Method Analysis. *American Journal of Advanced Technology and Engineering Solutions*, *1*(01), 40-86. https://doi.org/10.63125/zxsbdr47

[105]. Mukut Kanti, B. (2024). AI-Enabled Predictive Asset Integrity Monitoring for Industrial Equipment in Oil & Gas and Energy Sector Facilities. *International Journal of Scientific Interdisciplinary Research*, *5*(2), 746–791. https://doi.org/10.63125/3mjcah04

[106]. Mulas, I., Putzu, V., Asoni, G., Viale, D., Mameli, I., & Pau, M. (2021). Clinical assessment of gait and functional mobility in Italian healthy and cognitively impaired older persons using wearable inertial sensors. *Aging clinical and experimental research*, *33*(7), 1853-1864.

[107]. Nascimento, M. d. M., Gouveia, É. R., Gouveia, B. R., Marques, A., Martins, F., Przednowek, K., França, C., Peralta, M., & Ihle, A. (2022). Associations of gait speed, cadence, gait stability ratio, and body balance with falls in older adults. *International journal of environmental research and public health*, *19*(21), 13926.

[108]. Nelson, B. W., Flannery, J. E., Flournoy, J., Duell, N., Prinstein, M. J., & Telzer, E. (2022). Concurrent and prospective associations between fitbit wearable-derived RDoC arousal and regulatory constructs and adolescent internalizing symptoms. *Journal of Child Psychology and Psychiatry*, *63*(3), 282-295.

[109]. Nishat, J., & Mst Kaniz, F. (2022). A Review of the Impact of Covid-19 On Maternal and Child Health Service Utilization in Bangladesh. *American Journal of Scholarly Research and Innovation*, *1*(02), 223–269. https://doi.org/10.63125/vgv5s742

[110]. Nyul-Toth, A., DelFavero, J., Mukli, P., Tarantini, A., Ungvari, A., Yabluchanskiy, A., Csiszar, A., Ungvari, Z., & Tarantini, S. (2021). Early manifestation of gait alterations in the Tg2576 mouse model of Alzheimer's disease. *Geroscience*, *43*(4), 1947-1957.

[111]. O'Leary, T., Robertson, A., Chipman, P., Rafuse, V., & Brown, R. (2018). Motor function deficits in the 12 month-old female 5xFAD mouse model of Alzheimer's disease. *Behavioural brain research*, *337*, 256-263.

[112]. Oliveira, J., Gamito, P., Souto, T., Conde, R., Ferreira, M., Corotnean, T., Fernandes, A., Silva, H., & Neto, T. (2021). Virtual reality-based cognitive stimulation on people with mild to moderate dementia due to Alzheimer's disease: a pilot randomized controlled trial. *International journal of environmental research and public health*, *18*(10), 5290.

[113]. Ooi, T. C., Singh, D. K. A., Shahar, S., Rajab, N. F., Vanoh, D., Sharif, R., & Tan, M. P. (2021). Incidence and multidimensional predictors of occasional and recurrent falls among Malaysian community-dwelling older persons. *BMC geriatrics*, *21*(1), 154.

[114]. Oshiro, C. E., Frankland, T. B., Rosales, A. G., Perrin, N. A., Bell, C. L., Lo, S. H., & Trinacty, C. M. (2019). Fall ascertainment and development of a risk prediction model using electronic medical records. *Journal of the American Geriatrics Society*, *67*(7), 1417-1422.

[115]. Otones, P., García, E., Sanz, T., & Pedraz, A. (2020). A physical activity program versus usual care in the management of quality of life for pre-frail older adults with chronic pain: randomized controlled trial. *BMC geriatrics*, *20*(1), 396.

[116]. Paolillo, E. W., Sun-Suslow, N., Pasipanodya, E. C., Morgan, E. E., Ellis, R. J., Jeste, D. V., & Moore, D. J. (2020). Pre-frailty predicts cognitive decline at 2-year follow-up in persons living with HIV. *Journal of neurovirology*, *26*(2), 168-180.

[117]. Parambi, D. G. T., Unnikrishnan, M., Marathakam, A., & Mathew, B. (2020). Demographic and epidemiological aspects of aging. In *Nutrients and Nutraceuticals for Active & Healthy Ageing* (pp. 1-14). Springer.

[118]. Pérez-Ros, P., Martínez-Arnau, F. M., Orti-Lucas, R. M., & Tarazona-Santabalbina, F. J. (2019). A predictive model of isolated and recurrent falls in functionally independent community-dwelling older adults. *Brazilian journal of physical therapy*, *23*(1), 19-26.

[119]. Piche, E., Gerus, P., Chorin, F., Jaafar, A., Guerin, O., & Zory, R. (2022). The effect of different dual tasks conditions on gait kinematics and spatio-temporal walking parameters in older adults. *Gait & Posture*, *95*, 63-69.

[120]. Pieruccini-Faria, F., Montero-Odasso, M., & Hausdorff, J. M. (2019). Gait variability and fall risk in older adults: The role of cognitive function. In *Falls and cognition in older persons: fundamentals, assessment and therapeutic options* (pp. 107-138). Springer.

[121]. Pillemer, S., Ayers, E., & Holtzer, R. (2019). Gender-stratified analyses reveal longitudinal associations between social support and cognitive decline in older men. *Aging & Mental Health*, *23*(10), 1326-1332.

[122]. Plummer, P., Zukowski, L. A., Feld, J. A., & Najafi, B. (2022). Cognitive-motor dual-task gait training within 3 years after stroke: a randomized controlled trial. *Physiotherapy Theory and Practice*, *38*(10), 1329-1344.

[123]. Prabhakaran, K., Gogna, S., Pee, S., Samson, D. J., Con, J., & Latifi, R. (2020). Falling again? Falls in geriatric adults—risk factors and outcomes associated with recidivism. *Journal of surgical research*, *247*, 66-76.

[124]. Puente-Gonzalez, A. S., Sanchez-Sanchez, M. C., Fernandez-Rodriguez, E. J., Hernandez-Xumet, J. E., Barbero-Iglesias, F. J., & Mendez-Sanchez, R. (2021). Effects of 6-month multimodal physical exercise program on bone mineral density, fall risk, balance, and gait in patients with Alzheimer's disease: a controlled clinical trial. *Brain Sciences*, *11*(1), 63.

[125]. Reul, S., Lohmann, H., Wiendl, H., Duning, T., & Johnen, A. (2017). Can cognitive assessment really discriminate early stages of Alzheimer's and behavioural variant frontotemporal dementia at initial clinical presentation? *Alzheimer's research & therapy*, *9*(1), 61.

[126]. Reyes, P. O., Perea, E. G., Blázquez, M. R., & Marcos, A. P. (2020). Prevalence and correlates of frailty in community-dwelling older adults with chronic pain: a cross-sectional study. *Pain management nursing*, *21*(6), 530-535.

[127]. Rigby, B. R., & Ray, C. T. (2019). Measurement of gait and postural control in aging. In *Handbook of Rehabilitation in Older Adults* (pp. 85-121). Springer.

[128]. Rivan, N. F. M., Singh, D. K. A., Shahar, S., Wen, G. J., Rajab, N. F., Din, N. C., Mahadzir, H., & Kamaruddin, M. Z. A. (2021). Cognitive frailty is a robust predictor of falls, injuries, and disability among community-dwelling older adults. *BMC geriatrics*, *21*(1), 593.

[129]. Sadanand, S., Balachandar, R., & Bharath, S. (2016). Memory and executive functions in persons with type 2 diabetes: a meta-analysis. *Diabetes/metabolism research and reviews*, *32*(2), 132-142.

[130]. Sanchez-Sanchez, J. L., Izquierdo, M., Carnicero-Carreño, J. A., García-García, F. J., & Rodríguez-Mañas, L. (2020). Physical activity trajectories, mortality, hospitalization, and disability in the Toledo Study of Healthy Aging. *Journal of Cachexia, Sarcopenia and Muscle*, *11*(4), 1007-1017.

[131]. Sandroff, B. M., Baird, J. F., Silveira, S. L., & Motl, R. W. (2019). Response heterogeneity in fitness, mobility and cognition with exercise-training in MS. *Acta Neurologica Scandinavica*, *139*(2), 183-191.

[132]. Sargent, L., & Brown, R. (2017). Assessing the current state of cognitive frailty: measurement properties. *The journal of nutrition, health & aging*, *21*(2), 152-160.

[133]. Schneider, L. S., & Goldberg, T. E. (2020). Composite cognitive and functional measures for early stage Alzheimer's disease trials. *Alzheimer's & Dementia: Diagnosis, Assessment & Disease Monitoring*, *12*(1), e12017.

[134]. Schulz, M., Czwikla, J., Tsiasioti, C., Schwinger, A., Gand, D., Schmiemann, G., Schmidt, A., Wolf-Ostermann, K., Kloep, S., & Heinze, F. (2020). Differences in medical specialist utilization among older people in need of long-term care–results from German health claims data. *International Journal for Equity in Health*, *19*(1), 22.

[135]. Seifallahi, M., Mehraban, A. H., Galvin, J. E., & Ghoraani, B. (2022). Alzheimer's disease detection using comprehensive analysis of timed up and go test via kinect v. 2 camera and machine learning. *IEEE Transactions on Neural Systems and Rehabilitation Engineering*, *30*, 1589-1600.

[136]. Serra-Añó, P., Pedrero-Sánchez, J. F., Hurtado-Abellán, J., Inglés, M., Espí-López, G. V., & López-Pascual, J. (2019). Mobility assessment in people with Alzheimer disease using smartphone sensors. *Journal of NeuroEngineering and Rehabilitation*, *16*(1), 103.

[137]. Singh, T., Sharma, P. K., Jammy, G. R., Cauley, J. A., Bunker, C. H., Reddy, P., & Newman, A. B. (2017). Design of the M obility and I ndependent L iving in E lders S tudy: An older adult cohort in rural I ndia. *Geriatrics & gerontology international*, *17*(1), 31-40.

[138]. Sohrabi, H. R., & Weinborn, M. (2019). Cognitive impairments in Alzheimer's disease and other neurodegenerative diseases. *Neurodegeneration and Alzheimer's disease: the role of diabetes, genetics, hormones, and lifestyle*, 267-290.

[139]. Souza, C. d. O., Voos, M. C., Barbosa, A. F., Chen, J., Francato, D. C. V., Milosevic, M., Popovic, M., Fonoff, E. T., Chien, H. F., & Barbosa, E. R. (2019). Relationship between posturography, clinical balance and executive function in Parkinson´ s disease. *Journal of motor behavior*, *51*(2), 212-221.

[140]. Stephenson, D., Ollivier, C., Brinton, R., & Barrett, J. (2022). Can innovative trial designs in orphan diseases drive advancement of treatments for common neurological diseases? *Clinical Pharmacology & Therapeutics*, *111*(4), 799-806.

[141]. Sun, D., Wang, M., & Li, A. (2018). A multimodal deep neural network for human breast cancer prognosis prediction by integrating multi-dimensional data. *IEEE/ACM transactions on computational biology and bioinformatics*, *16*(3), 841-850.

[142]. Swinnen, N., Vandenbulcke, M., de Bruin, E. D., Akkerman, R., Stubbs, B., Firth, J., & Vancampfort, D. (2021). The efficacy of exergaming in people with major neurocognitive disorder residing in long-term care facilities: a pilot randomized controlled trial. *Alzheimer's research & therapy*, *13*(1), 70.

[143]. Tian, Q., Chastan, N., Bair, W.-N., Resnick, S. M., Ferrucci, L., & Studenski, S. A. (2017). The brain map of gait variability in aging, cognitive impairment and dementia—a systematic review. *Neuroscience & Biobehavioral Reviews*, *74*, 149-162.

[144]. Tonay, P., Md Maruf, I., & Al, A. (2024). Artificial Intelligence-Based Decision Support Systems and Managerial Performance. *American Journal of Advanced Technology and Engineering Solutions*, *4*(04), 154-184. https://doi.org/10.63125/wmz8dc67

[145]. Vale-Silva, L. A., & Rohr, K. (2021). Long-term cancer survival prediction using multimodal deep learning. *Scientific Reports*, *11*(1), 13505.

[146]. van Onna, M., & Boonen, A. (2022). Challenges in the management of older patients with inflammatory rheumatic diseases. *Nature Reviews Rheumatology*, *18*(6), 326-334.

[147]. Van Ooteghem, K., Musselman, K. E., Mansfield, A., Gold, D., Marcil, M. N., Keren, R., Tartaglia, M. C., Flint, A. J., & Iaboni, A. (2019). Key factors for the assessment of mobility in advanced dementia: A consensus approach. *Alzheimer's & Dementia: Translational Research & Clinical Interventions*, *5*(1), 409-419.

[148]. Varma, V. R., Ghosal, R., Hillel, I., Volfson, D., Weiss, J., Urbanek, J., Hausdorff, J. M., Zipunnikov, V., & Watts, A. (2021). Continuous gait monitoring discriminates community-dwelling mild Alzheimer's disease from cognitively normal controls. *Alzheimer's & Dementia: Translational Research & Clinical Interventions*, *7*(1), e12131.

[149]. Verghese, J., Lipton, R., & Ayers, E. (2017). Spatial navigation and risk of cognitive impairment: A prospective cohort study. *Alzheimer's & dementia*, *13*(9), 985-992.

[150]. Veronese, N., Facchini, S., Stubbs, B., Luchini, C., Solmi, M., Manzato, E., Sergi, G., Maggi, S., Cosco, T., & Fontana, L. (2017). Weight loss is associated with improvements in cognitive function among overweight and obese people: a systematic review and meta-analysis. *Neuroscience & Biobehavioral Reviews*, *72*, 87-94.

[151]. Volpato, S., & Guralnik, J. M. (2017). The different domains of the comprehensive geriatric assessment. In *Comprehensive geriatric assessment* (pp. 11-25). Springer.

[152]. Wang, L., Xue, Z., Ezeana, C. F., Puppala, M., Chen, S., Danforth, R. L., Yu, X., He, T., Vassallo, M. L., & Wong, S. T. (2019). Preventing inpatient falls with injuries using integrative machine learning prediction: a cohort study. *NPJ digital medicine*, *2*(1), 127.

[153]. Wang, S., Phillips, D., & Lee, J. (2021). Disability prevalence in midlife (aged 55–65 years): Cross-Country comparisons of gender differences and time trends. *Women's Midlife Health*, *7*(1), 1.

[154]. Wearing, J., Konings, P., Stokes, M., & de Bruin, E. D. (2018). Handgrip strength in old and oldest old Swiss adults–a cross-sectional study. *BMC geriatrics*, *18*(1), 266.

[155]. Whelan, R., Barbey, F. M., Cominetti, M. R., Gillan, C. M., & Rosická, A. M. (2022). Developments in scalable strategies for detecting early markers of cognitive decline. *Translational Psychiatry*, *12*(1), 473.

[156]. Wirz, M., Bansi, J., Capecci, M., Esquenazi, A., Paredes, L., Tefertiller, C., & van Hedel, H. J. (2022). Robotic gait training in specific neurological conditions: Rationale and application. In *Neurorehabilitation Technology* (pp. 145-188). Springer.

[157]. Wu, Y., Jia, M., Xiang, C., & Fang, Y. (2022). Latent trajectories of frailty and risk prediction models among geriatric community dwellers: an interpretable machine learning perspective. *BMC geriatrics*, *22*(1), 900.

[158]. Yang, H., & Bath, P. A. (2019). The use of data mining methods for the prediction of dementia: evidence from the english longitudinal study of aging. *IEEE journal of biomedical and health informatics*, *24*(2), 345-353.

[159]. Yu, F., Vock, D. M., & Barclay, T. R. (2018). Executive function: Responses to aerobic exercise in Alzheimer's disease. *Geriatric nursing*, *39*(2), 219-224.

[160]. Yu, H., Zhang, Q., Liu, S., Liu, C., Dai, P., Lan, Y., Xu, G., & Zhang, H. (2021). Effect of executive dysfunction on posture control and gait after stroke. *Evidence-Based Complementary and Alternative Medicine*, *2021*(1), 3051750.

[161]. Zampogna, A., Mileti, I., Palermo, E., Celletti, C., Paoloni, M., Manoni, A., Mazzetta, I., Dalla Costa, G., Pérez-López, C., & Camerota, F. (2020). Fifteen years of wireless sensors for balance assessment in neurological disorders. *Sensors*, *20*(11), 3247.

[162]. Zhang, W., Low, L. F., Gwynn, J. D., & Clemson, L. (2019). Interventions to improve gait in older adults with cognitive impairment: a systematic review. *Journal of the American Geriatrics Society*, *67*(2), 381-391.

[163]. Zia, A., Kamaruzzaman, S., Myint, P. K., & Tan, M. P. (2016). Anticholinergic burden is associated with recurrent and injurious falls in older individuals. *Maturitas*, *84*, 32-37.

[164]. Zvěřová, M. (2019). Clinical aspects of Alzheimer's disease. *Clinical biochemistry*, *72*, 3-6.