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REVIEW ARTICLE

Early detection of diseases causing dementia using digital navigation and gait measures: A systematic review of evidence

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Abstract

Wearable digital technologies capable of measuring everyday behaviors could improve the early detection of dementia-causing diseases. We conducted two systematic reviews following Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guidelines to establish the evidence base for measuring navigation and gait, two everyday behaviors affected early in AD and non-AD disorders and not adequately measured in current practice. PubMed and Web of Science databases were searched for studies on asymptomatic and early-stage symptomatic individuals at risk of dementia, with the Newcastle–Ottawa Scale used to assess bias and evaluate methodological quality. Of 316 navigation and 2086 gait records identified, 27 and 83, respectively, were included in the final sample. We highlight several measures that may identify at-risk individuals, whose quantifiability with different devices mitigates the risk of future technological obsolescence. Beyond navigation and gait, this review also provides the framework for evaluating the evidence base for future digital measures of behaviors considered for early disease detection.

KEYWORDS
ambulation, digital technology, gait, navigation, preclinical dementia, prodromal dementia, smartphones, virtual reality, wearables

1 | INTRODUCTION

The widespread use of wearable digital devices in the general population—most notably smartphones, smartwatches, and activity trackers—provides a hitherto unavailable opportunity to collect data on everyday functions and behaviors that may aid the early detection of dementia-causing diseases.[1] In principle, such an approach would overcome several major limitations of current diagnostic approaches. In contrast to the pen-and-paper cognitive tests used currently in clinical diagnostic practice, digital testing of this kind would have high ecological validity, given the tracking of real-life activities, and would be less affected by the educational and cultural confounds that at present restrict the utility of cognitive tests when applied to diverse populations. Separately, wearable devices would permit disease detection at a scale beyond that possible with current positron emission tomography (PET)– and cerebrospinal fluid (CSF)–based biomarker tests, which are expensive, invasive, and very restricted in their global availability. Although the imminent blood biomarker tests will do away with many of the drawbacks of current biomarker tests, their arrival does not alter the requirement to identify impaired brain functionality alongside biomarker evidence of molecular pathology in order to determine the presence of a disease state.

However, the future success of any digital approach of this kind is critically dependent on the selection of those functions, out of all

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possible functions potentially measurable with current and next generation devices, that are most relevant for early disease detection. Although the overarching requirement is that selected functions to be measured are sensitive to early disease, the need to distinguish between different diseases causing dementia—the clinical importance of which is magnified by the advent of pathology-specific immunotherapies—also requires that those functions to be measured have specificity for individual diseases. Beyond these core determinants of sensitivity and specificity there are operational requirements for the tools chosen to measure the functions of interest. Given the size of the population worldwide at risk of dementia, selected tools need to be low in cost but high in ease of use for both clinicians and affected individuals, and be applicable across diverse communities and cultures independent of language and demographic differences.

Spatial navigation and gait represent two behavioral domains that together illustrate this new approach to disease detection. Spatial navigation comprises behaviors that utilize the brain's representation of space to encode and recall the spatial layout of environments in order to guide wayfinding between places.[2] Different navigational strategies exist; allocentric navigation uses the spatial relationships between environmental features, whereas egocentric navigation represents a person-centered strategy based on the spatial relationship between the person and the environment features.[3] Finally, path integration is a form of navigation in which integration of linear and angular self-motion cues is used to update one's spatial location within an environment.[4]

The medial temporal lobe regions, notably the entorhinal cortex and hippocampus, are considered central to allocentric spatial navigation and path integration, whereas the medial parietal regions, in particular the retrosplenial cortex, are more involved with egocentric navigation and egocentric-to-allocentric transformations in spatial processing.[5] These behaviors are underpinned by neurons with spatially-modulated firing activity, such as grid cells, place cells, and head direction cells.[6] Given that these regions are implicated in the earliest stages of Alzheimer's disease (AD), with deposition of amyloid and tau pathology identified in the initial Braak pathological staging, recent work has focused on spatial navigation as a potential initial behavioral marker of AD.[7] Various studies indicate that alterations in navigation precede impairments in other cognitive domains, including episodic memory, in people at risk of AD.[8–10]

In contrast to navigation and its specific association with early AD, the distributed nature of gait and balance control in the brain means that disorders of gait (here "gait" is used as an umbrella term to encompass both gait and balance disorders) may be observed across a range of diseases causing dementia. It is unsurprising that impaired gait is a central early feature of diseases with prominent locomotor impairments, such as dementia with Lewy bodies (DLB), vascular dementia (VaD), and Parkinson's disease dementia (PDD).[11–13] However, the complexity involved in the maintenance of normal gait also makes it vulnerable to other dementia-causing diseases, including AD and frontotemporal dementia (FTD).[14,15]

Knowledge of the mechanics of gait is required to understand its involvement in diseases causing dementia. During a gait cycle, the legs alternate between swing and stance phases.[16] Double support, when both feet are touching the walking surface, takes up only 20% of a regular gait cycle.[16] This creates a need for constant online fine-tuning of posture and bodily movements to compensate for the shifting center of gravity during locomotion and the unpredictable dynamic environment, replete with stationary and moving obstacles, uneven walking surfaces, and changing elevation. In addition, gait needs to match internal goals. These adjustments are carried out through multiple feedback and feedforward loops encompassing many brain areas—including the primary motor, posterior parietal, and prefrontal cortex, and the thalamus, basal ganglia, cerebellum, and brainstem (Figure 1)[17–19]—that are vulnerable to a range of neurodegenerative and vascular pathologies.[20–22] The distributed nature of brain regions involved in gait control and their complex interactions make it difficult to clearly map changes in certain gait subdomains, such as pace or variability[23–28] to the decline in specific brain regions across different diseases. However, the type and early staging of pathology in DLB[29] reveals that impaiments in gait asymmetry, postural control, and balance observed across multiple studies[30–32] may indeed be specific to the early stages of this disorder, making gait an attractive domain for both early detection and differentiation of diseases causing dementia.

In summary, navigation and gait represent behaviors that are not captured by traditional cognitive diagnostic assessments but whose measurement may deliver added value for early detection of both AD and non-AD disorders. Given that both navigation and gait

RESEARCH IN CONTEXT

1. **Systematic review**: Following the Preferred Reporting Items for Systematic reviews and Meta–Analyses (PRISMA) guidelines, two structured reviews of literature from PubMed and Web of Science aimed to determine the evidence base for inclusion of digital measures related to navigation and gait domains in digital toolkits targeting early detection of dementia-causing diseases.
2. **Interpretation**: Navigation and gait measures may help detect asymptomatic and early-stage symptomatic individuals at high risk of dementia diseases. A mixture of digital devices and real-world tools were used that varied in scalability and user burden; however, we highlight measures that appear agnostic to the tool used.
3. **Future directions**: As one of the first reviews to systematically assess the potential of measures and digital tools targeting everyday behaviors to remotely detect dementia-causing diseases, this study provides a framework by which future digital measures may be evaluated against principles of clinical evidence, scalability, and inclusion before implementation in disease- detection toolkits.

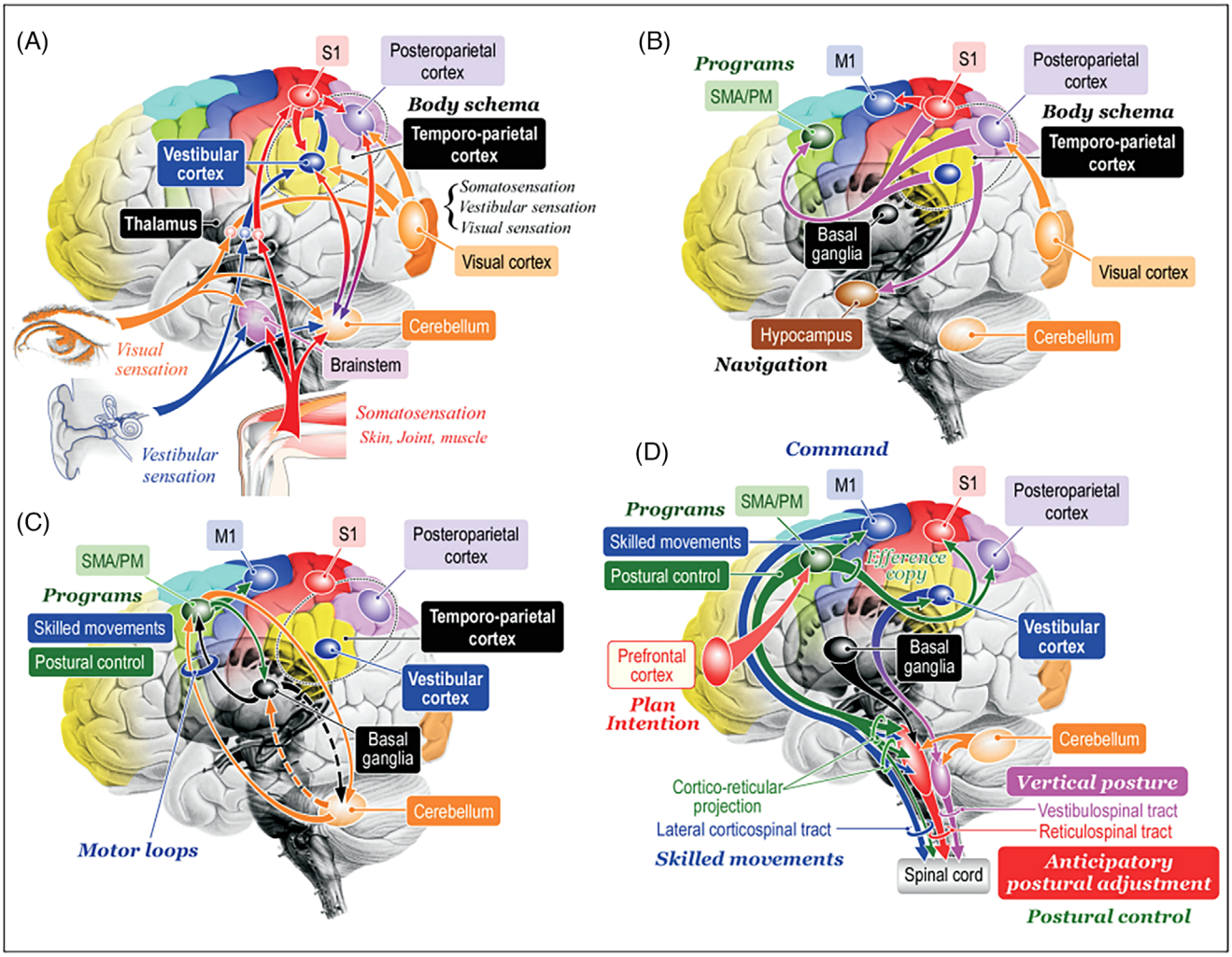

FIGURE 1 Brain mechanisms of gait control. Figure from Ref. 19

represent natural human activities, their inclusion in future diagnostic practice would provide an ecological validity and real-life relevance that is absent from current pen-and-paper tests. Finally, and of crucial importance given the global impact of dementia, both are language- and culture-invariant behaviors, meaning that tools used for their measurement may be applied across diverse populations without the educational, linguistic, and cultural confounds that limit the use of legacy cognitive tests.

However, to justify any future implementation of any measures in medical practice, it is crucial to establish the evidence base for use from a clinical perspective, and also to identify tools not only capable of measuring these behaviors in routine clinical practice but also of meeting operational requirements for future large-scale deployment, such as low cost and high ease of use for both clinicians and patients.

The aim of this systematic review, therefore, was to establish a structured approach to identifying: (1) measures reported in the literature to date in relation to preclinical and prodromal detection of diseases causing dementia, and (2) the technologies used to capture these measures, with navigation and gait as exemplar behaviors for the reasons provided. Although the criteria for preclinical and prodromal stages of AD is well established,[33,34] pre-dementia stages of other dementias are much harder to define due to a lack of reliable biomarkers.[35–39] Therefore, in this systematic review, we aimed to use a broader multi-disease definition of preclinical and prodromal stages based on established dementia risk factors and the presence of clinical cognitive symptoms. For example, we used "asymptomatic at-risk" to collectively describe either cognitively healthy biomarker-positive individuals or apolipoprotein E (*APOE*) ε4 carriers for AD, patients with polysomnography-confirmed idiopathic rapid eye movement (REM) sleep behavior disorder (iRBD) for DLB, and cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL) for VaD (the full list of conditions and their groupings are shown in Table 1).[35–39] Similarly, individuals with mild cognitive impairment (MCI) that were positive for AD biomarkers or carried *APOE* ε4 were considered to belong to the symptomatic at-risk group for AD. These groupings allowed us to holistically consider measures according to a key disease inflection point across dementia diseases (namely, the asymptomatic to symptomatic transition) in line with the need for a scalable but specific approach to dementia detection.

TABLE 1 Grouping of early disease stages based on the stage of progression and risk factors used in the review.

Category	Disease risk factor	Disease	Established term
Asymptomatic	*APOE* ε4	AD	n/a
	Biomarker positive (CSF, plasma, PET)	AD	Preclinical AD
	iRBD	DLB	n/a
	PD + iRBD	PDD	n/a
	CADASIL	VaD	n/a
	Progession to dementia	Any	n/a
Symptomatic	*APOE* ε4	AD	n/a
	Biomarker positive (CSF, plasma, PET)	AD	Prodromal AD
	iRBD	DLB	n/a
	PD + iRBD	PDD	n/a
	Progression to dementia	Any	n/a

Abbreviations: AD, Alzheimer's disease; *APOE*, apolipoprotein E; CADASIL, cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy; CSF, cerebrospinal fluid; DLB, dementia with Lewy Bodies; iRBD, idiopathic rapid eye movement sleep behavior disorder; PD(D), Parkinson's disease (dementia); PET, positron emission tomography; VaD, vascular dementia.

2 | METHODS

The systematic review was carried out following Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guidelines.

2.1 | Eligibility criteria

Published studies were included on adults 18 years of age and older which reported navigation or gait measures that were either i) predictive of the occurrence of dementia or ii) in cross-sectional studies were able to discriminate asymptomatic and early symptomatic individuals at risk of dementia disorders from their respective controls. This encompassed the following groups:

- AD: Preclinical AD (asymptomatic biomarker-positive or presymptomatic familial AD) or prodromal AD (biomarker-positive patients with MCI)
- VaD: (CADASIL patients prior to dementia onset)
- PDD (PD patients found to develop PDD within longitudinal follow-up, carry *APOE* ε4, be positive for AD biomarkers, or have comorbid RBD)
- DLB (polysomnography-confirmed iRBD patients)
- FTD (individuals found to develop FTD within longitudinal follow-up or have pre-symptomatic familial FTD)
- Individuals with increased genetic risk of sporadic forms of dementia (*APOE* ε4 carriers for AD, and individuals with high dementia risk scores as determined by genome-wide association studies)
- Individuals found to develop dementia within longitudinal studies of aging (including mixed dementia)

For navigation, studies using measures related to egocentric or allocentric spatial processing were included, that is, egocentric and allocentric spatial orientation, navigation or spatial memory, reference frame translation, wayfinding, route learning. Studies with measures focused on visuospatial or object-memory–based processing were excluded if the tests did not involve any significant egocentric or allocentric spatial processing. Studies reporting navigation changes in young *APOE* ε4 carriers (ages <30 years) were excluded as wrong study population, given the potential confounding effect of developmental factors in these younger individuals.[9] For gait, studies using measures related to walking, gait, posture, and balance were included.

Intervention, case, and uncontrolled studies were excluded due to their limited generalizability. Studies on established dementia were included only if they reported findings from individuals in the preclinical or prodromal stages of diseases meeting the criteria outlined earlier. Finally, only studies written in English were included.

2.2 | Information sources and search strategy

Searches were conducted on PubMed and Web of Science databases and limited to studies published before October 6, 2022, for navigation and before August 18, 2022 for gait. Any systematic reviews that were identified were also screened for relevant references. PubMed searches were restricted to human studies only. Because this filter is not available on the Web of Science, no filters were applied for searches on this database.

Search terms were constructed using a combination of keywords and spelling variants, as well as Medical Subject Headings (MeSH) for PubMed, connected using Boolean operators. Literature searches were divided into the following categories:

1. Preclinical and prodromal dementias: defined using search terms for dementias ("Alzheimer Disease"[MeSh], "Alzheimer's disease", "Frontotemporal Dementia"[MeSh], "Frontotemporal dementia", "Lewy Body Disease"[MeSh], "Dementia with Lewy bodies", "Dementia, Vascular"[MeSh], "vascular dementia",

"mixed dementia", "Parkinson's disease dementia"), followed by keywords for pre-clinical and prodromal detection: (preclinical, "pre-clinical", prodromal, presymptomatic, "pre-symptomatic", "early detection", "pre-dementia", predementia).
2. Genetic risk and disorders that increase the risk of developing dementia with two separate searches for APOE and CADASIL, and RBD:
   a. ("apolipoprotein E", APOE, CADASIL, "Cerebral Autosomal Dominant Arteriopathy with Subcortical Infarcts and Leukoencephalopathy")
   b. ("REM Sleep Behavior Disorder"[MeSh], "rapid eye movement sleep behaviour disorder", "REM sleep behaviour disorder", "rapid eye movement sleep behavior disorder", "REM sleep behavior disorder")
3. Prodromal AD: Amnesic mild cognitive impairment: ("Cognitive Dysfunction"[MeSh], "mild cognitive impairment") with biomarkers (biomarker OR amyloid OR tau)

Search terms in all categories were followed by AND terms defining either navigation or gait measures of interest:

1. Navigation terms used included: (navigat* OR allocentric OR egocentric OR wayfinding OR "path integration") with additional MeSH terms in PubMed searches (("Spatial Navigation"[MeSh] OR navigat*) OR allocentric OR egocentric OR wayfinding OR 'path integration')
2. Gait terms used included: (gait, balance, postur*, walking)

2.3 | Selection process

Records were first screened for duplicates using EndNote, which was followed by manual removal. Another screening was then carried out using Rayyan software, with the remaining duplicates removed either automatically by the software or manually by the reviewers. Two reviewers (G.C. and C.N.) independently screened titles and abstracts within Rayyan environment. Full-text screening was then performed on all potentially relevant records that could be retrieved by the same two reviewers, also independently. Any disagreements were resolved by discussion.

2.4 | Data collection process and data items

Data extraction was completed using a custom-made form by the two reviewers independently and then cross-reviewed with any information that was missing added. We sought to extract size, cognitive status, and demographic characteristics of the study sample (age, sex, and racial and ethnic background), medication status in the case of studies on PD, country(-ies) the sample was derived from, study type (longitudinal, i.e., case–control or cohort, or cross-sectional), all measures related to the domains of interest assessed in the study, digital devices (if applicable) used to record these measures, experimental procedures, study setting (in-person or remote), results derived from the relevant groups of participants, measures that showed promise in predicting dementia onset or differentiating between pre-dementia and control groups, and information on the quality of model predictions (area under the curve [AUC], sensitivity, and specificity), where available. Missing or unclear information was listed as "n/a."

2.5 | Study risk of bias assessment

The quality and risk of bias were evaluated for each study by two independent reviewers (C.N. and G.C.) using the Newcastle–Ottawa Scale (NOS) and its adapted version for cross-sectional studies.[40,41] This tool was selected based on its availability for case–control, cohort, and cross-sectional studies, enabling direct comparisons despite differences in design. The scales enable evaluation of studies based on the selection of study groups, comparability of study groups, and ascertainment of exposure or outcomes. Any disagreements between reviewers were solved by discussion. We excluded the question on non-respondents from the modified version of the scale, as it was not applicable to most gait and navigation studies. This led to a maximum of nine points awarded to studies meeting all criteria, regardless of the study design. We also awarded full points for the ascertainment of exposure or outcome question if the study used an objective quantitative assessment of gait, balance, posture, and navigation, independently of whether the assessment was carried out blindly.

2.6 | Effect measures

All relevant effect measures reported in the studies were gathered. Due to the heterogeneity among studies, only qualitative synthesis of results was performed.

3 | RESULTS

3.1 | Navigation

3.1.1 | Study selection

From 316 records identified through the systematic searches, 114 were duplicates and 143 were removed after title and abstract screening. Of the remaining 59 articles, 57 were screened at full-text stage, with 23 meeting the inclusion criteria. A further 5 articles were identified from references with one ineligible, resulting in a total of 27 studies included in the systematic review (see Figure 2 for the flow diagram).

3.1.2 | Study characteristics

Individual study characteristics are presented in Table S1, covering either prospective cohort (n = 6) or cross-sectional (n = 21) study

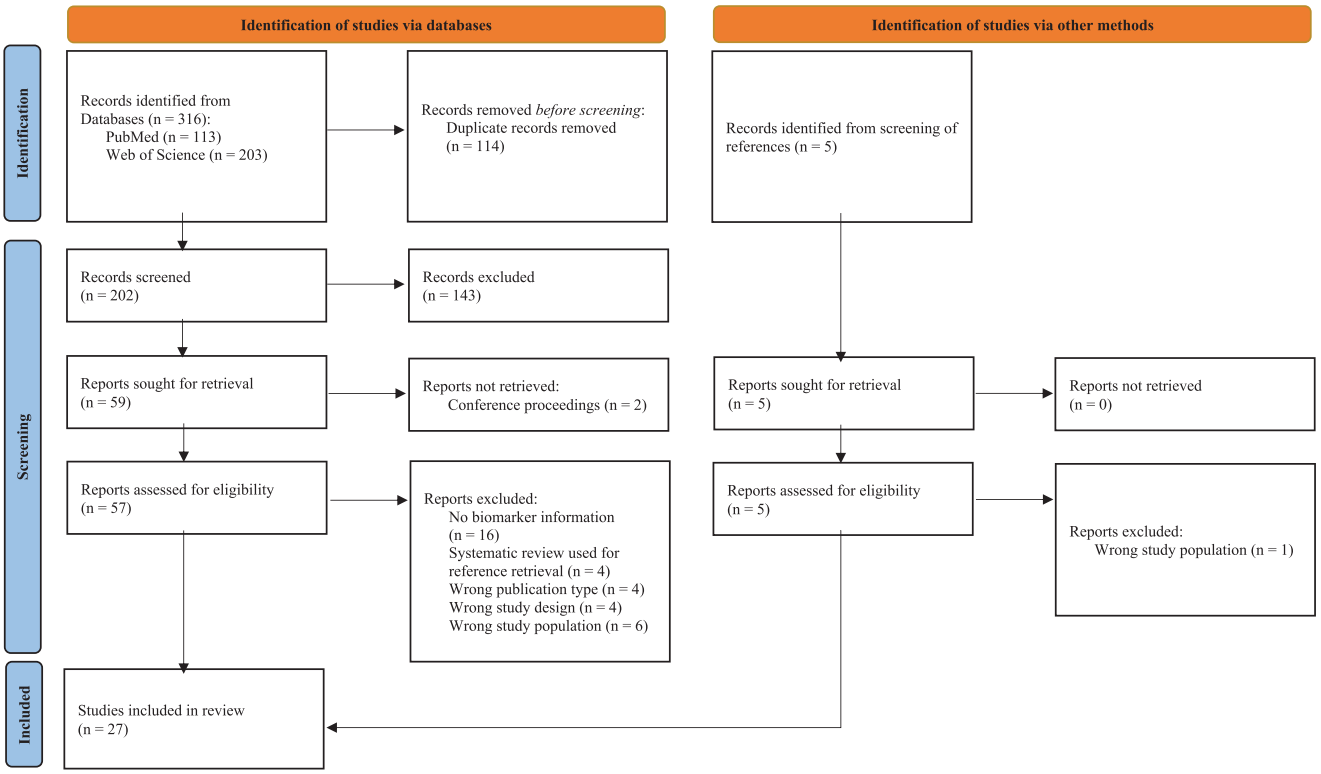

FIGURE 2 PRISMA flow diagram for navigation studies.

designs. No studies meeting the inclusion criteria investigated dementia disorders other than AD, and for AD, the majority of these were in the asymptomatic space ($n = 15$) covering mean ages of 37–82 years. Individuals within these studies were stratified mostly by genetic risk (*APOE* 4, $n = 8$),[9,42–47] biomarker status (cerebrospinal fluid [CSF] or positron emission tomography [PET], $n = 5$),[10,48–51] longitudinal clinical progression on the Clinical Dementia Rating (CDR) scale with biomarkers ($n = 1$),[10] by a clinician-confirmed dementia diagnosis ($n = 1$),[52] or by the Cardiovascular Risk Factors, Aging, and Incidence of Dementia (CAIDE) risk score ($n = 1$).[53] Studies in the symptomatic space ($n = 13$; of which one investigated a asymptomatic population in parallel), covering ages 68–75 years, were more frequently stratified by biomarker status (CSF or PET, $n = 8$),[54–61] followed by genetic risk (*APOE* ε4, $n = 4$)[62–65] or longitudinal progression to a clinician confirmed AD diagnosis ($n = 3$).[55,60,66]

All studies were conducted in Europe ($n = 18$) or the United States ($n = 9$), with only five studies reporting racial or ethnic distributions. The mean proportion of female participants across individual risk and control sub-groups was 49%, with a median sample size of 17 for risk groups and 28 for control groups. Studies were published from 2007, with the majority from 2015 onward (Figure 3A).

3.1.3 | Measures

In total, 143 unique measures of navigation were reported ($n = 189$ with duplicates; Table S2), of which 51 showed early diagnostic potential (36%). Of these, 23 related to passive recording of global positioning system (GPS) location data of individuals remotely during everyday car-driving behaviors, whereas the remaining 28 related to active cognitive tasks probing navigation behaviors that were performed by participants during in-person study visits at a research site. Within these active cognitive tasks, the predominantly examined behaviors were wayfinding, spatial memory, or path integration, with either allocentric or egocentric environmental spatial cues. Given the heterogeneity in reporting and assessment of these behaviors, a qualitative synthesis was performed and detailed below (Figure 3B).

For differentiating asymptomatic at-risk populations, the median AUC value reported in included studies was 0.81. A maximum of 0.96 (95% confidence interval [CI] 0.90–0.98) was achieved for cross-sectionally differentiating cognitively normal individuals with and without CSF AD biomarkers using navigational metrics derived from passive GPS tracking of driving behaviors in combination with age and *APOE* ε4 status.[50]

For symptomatic populations, the median AUC value reported was 0.90, with a maximum of 0.98 (95% CI not reported) for differentiating MCI patients with and without CSF AD biomarkers using an allocentric spatial memory metric.[56]

The classification ability of navigation testing was compared with that of other cognitive tests in 23 of the 27 studies (Table S1). In 17 of these, comparator metrics did not show statistically significant AUC classification. In the remaining six that did, for two studies the comparator metrics had lower AUC values than either navigation metrics alone or in combination. Where comparator metrics showed similar or

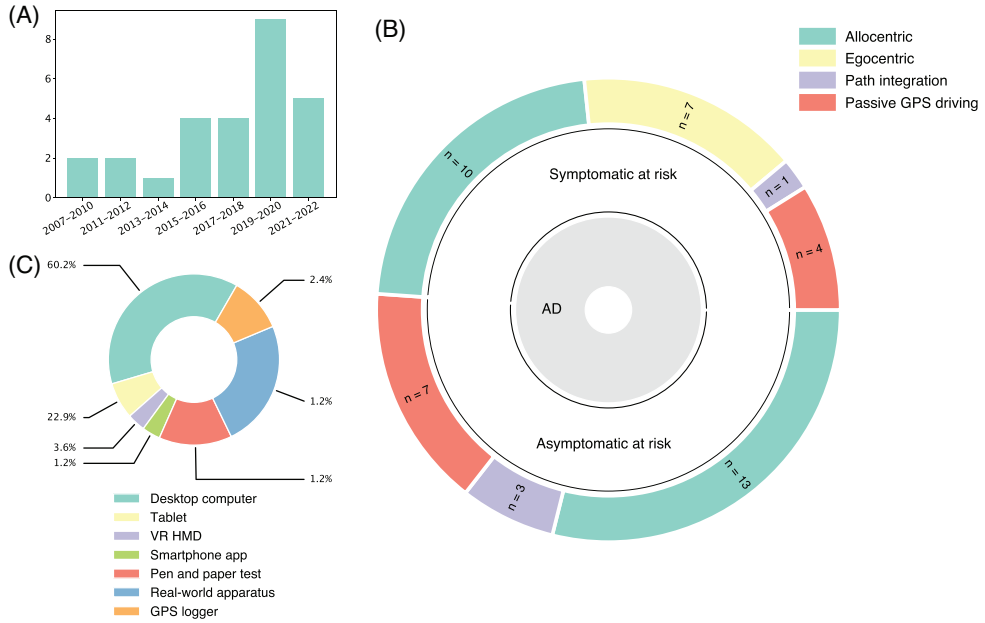

FIGURE 3 Descriptive information for navigation studies. (A) The number of navigation studies published between 2007 and 2022 included in the systematic review. (B) Navigation metrics with a potential for early detection in asymptomatic and symptomatic at-risk individuals. (C) Tools used to assess navigation across studies.

better AUC values, all studies were in prodromal stage AD, by which point more widespread neurodegenerative changes may be apparent and related to these multidomain impairments.

3.1.4 | Tools

Twenty-nine different tools were reported, of which there were seven different types (see Figure 3C). All studies investigating passive navigation behaviors during driving ($n = 3$) used data-logger devices fitted in participants' own vehicles to remotely collect GPS data during everyday life. Devices for active tasks included desktop computers with either keyboard- or joystick-controlled movement ($n = 11$), touchscreen tablets or smartphones ($n = 3$), or immersive virtual reality ($n = 1$). Ten studies used artificial constructs including a tape-marked floor maze ($n = 1$), pen-and-paper–based materials such as printed images or two-dimensional (2D) route drawing ($n = 4$), a set of indoor rooms and corridors within a building that were physically navigated ($n = 2$), and a life-size cylindrically enclosed purpose-built test arena in the style of a Morris water maze paradigm ($n = 4$).

3.1.5 | Results of qualitative syntheses

Across the 51 measures found to have early disease-detection capability, a qualitative synthesis was performed to better compare different types of measures and summarize the range of behaviors explored (Table S3). This generated 17 summary metrics across four key domains of navigation task type: seven allocentric, three egocentric, three path integration, and four passive GPS tracking metrics. However, frequency of reporting may relate either to frequency of investigation or frequency of significant effects across the included studies, which cannot be determined here without conducting a meta-analysis of both differentiative and non-differentiative metrics.

The most reported summary metric was related to linear distance error from a target goal location, especially in allocentric tasks. Increased allocentric distance error was observed in both asymptomatic[42,65] and symptomatic[62–64] *APOE* ε4 carriers, as well as biomarker-positive, prodromal AD patients.[58] Increased distance error from a target goal was also reported in egocentric tasks for symptomatic *APOE* ε4 carriers,[62–64] and in path-integration tasks for asymptomatic *APOE* ε4 carriers[9] and biomarker-positive, prodromal AD patients.[61]

The next most-reported spatial outcomes were allocentric measures of spatial memory for topographic scenes, reported mostly in symptomatic AD at-risk stages,[54–56] and time taken to find target goals, reported in asymptomatic *APOE* ε4 carriers,[42] biomarker-positive, preclinical individuals,[48] and individuals that progressed clinically over time to AD dementia.[10]

For passive GPS tracking devices in cars, the most frequently reported metrics showing differentiation of both asymptomatic and symptomatic risk groups were related to length of car journeys made (e.g., total number of miles traveled/month), frequency of journeys made (e.g., number of trips/month), and the complexity of journey trajectories (e.g., total area covered, number of trips <5 miles vs trips >15 miles).[50–52]

When we summarized according to pre-dementia stage (Figure 3B), allocentric metrics were roughly evenly reported between asymptomatic and symptomatic at-risk stages, whereas egocentric metrics were reported exclusively for symptomatic stages. Both path

integration and passive GPS tracking were reported more frequently for asymptomatic stages.

3.1.6 | Risk of bias in studies

The mean (SD) NOS rating of included cross-sectional studies was 6.7 (1.4) and of included cohort studies was 7.5 (1.6) of a nine-point maximum, indicating good overall methodological quality (Tables S4 and S5). However, specifically regarding the selection and comparability criteria, there was evidence of bias in some studies. Only 2 of the 21 cross-sectional studies justified the choice of sample sizes. The representativeness of included samples was questionable in five cross-sectional studies due to insufficient methodological detail or selection of pre-identified participants.

For between-group comparisons, proper adjustment for multiple confounding variables (including the major factor of age) was present in 17 studies, with a further 2 studies including moderate adjustment and the remaining 8 studies no adjustment, suggesting a need for cautious interpretation of AD effects. Finally, from the studies evaluated, two prospective cohort studies with dementia and/or MCI as an outcome included only one follow-up time point, which may not be considered as evidence of stable decline.

Within the 27 included studies, 3 reported null findings for navigation, suggesting a slight bias toward positive reporting.

3.1.7 | Discussion

Across the 27 studies meeting criteria for inclusion, several measures of navigation were identified that cross-sectionally differentiated asymptomatic and symptomatic at-risk AD groups from controls, or were predictive of clinical progression, with high AUC, sensitivity, and specificity. The median AUC of the six relevant asymptomatic at-risk studies was 0.81, whereas for the seven relevant symptomatic studies it was 0.90. In those studies where comparisons were made with other cognitive measures, the other cognitive measures were not observed to have similar classification accuracy. This has particular relevance for future clinical practice, since these comparator cognitive domains invariably included episodic memory, testing of which is central to AD diagnostic assessments worldwide. These findings illustrate that testing of spatial navigation may deliver added value, on top of current cognitive assessments, for the diagnosis of preclinical and prodromal stages of AD.[7,67]

In keeping with previous reports, and critical for informed digital tool selection, different navigation measures appeared differentially sensitive to stages of AD.[7] Egocentric metrics differentiated early symptomatic at-risk AD groups exclusively, whereas allocentric, path integration, and passive GPS metrics differentiated both asymptomatic and symptomatic populations. This may relate to a compensatory switch in preferred strategy from allocentric to egocentric cues with increasing disease progression,[58] which has also been explored in rodent models of AD.[68] This also reflects the neurobiology of navigation; more allocentric changes are associated with hippocampal-focused pathologies, whereas egocentric changes are more associated with parietal pathologies.[7]

In active navigation tasks, which were all conducted in-person in laboratory or clinic-based settings, the most widely examined metric was the continuous measure of distance error from a target goal in virtual reality environments. These tasks targeted either allocentric, egocentric, or path integration behaviors, with movement in desktop tests controlled either via a joystick, keyboard arrow keys, or screen tapping. In immersive virtual reality or real-world tasks, distance error was calculated from actual participant locomotion. Although digital virtual environment paradigms are advantageous in creating objective performance measures in highly controlled settings,[69,70] they increase the risk of digital exclusion, such as usability in older demographics, and in-person testing lacks clinical scalability for the purposes of earlier digital detection. One exception to the in-person tools was Sea Hero Quest, a citizen science smartphone navigation game app with over 4 million global downloads that was remotely played by participants.[71] Initiatives such as this exemplify the potential power of remote collection of different navigation-based metrics, which are independent of other cognitive abilities,[72] usable across multiple countries and cultures,[73] show sensitivity to preclinical genetic AD risk,[43] and can predict the real-world navigation ability of both young[74] and older users.[75]

In contrast to the active metrics, all passive GPS driving metrics were collected remotely using loggers fitted in participant personal cars. Passive collection of GPS data provides a low-burden, scalable approach to collecting navigation-related metrics. Although it remains to be seen how well passive-navigation metrics such as traveling frequency or trajectory complexity relate to active-navigation task performance or real-world navigation performance, these studies are currently underway. Recent studies have explored personal GPS devices[76] or smartphone app[77] tracking of location in dementia populations, which would enable wider participation and less reliance on personal vehicles.

Finally, no navigation studies examined non-AD diseases in their early stages, which likely reflects the focus on AD, given the knowledge of early AD neuropathological involvement of medial temporal and parietal lobe regions subserving navigation and the absence of similar knowledge in non-AD disorders. Although a small number of studies have assessed navigation in vascular cognitive disorder[78] and FTD,[79] these involved patients with established dementia and as such fell outside the inclusion criteria of this review.

3.2 | Gait

3.2.1 | Study selection

From 2086 records identified through the systematic searches, 679 were found to be duplicates, and 1252 were removed after title and abstract screening. Of the remaining 154 articles, 153 were screened at the full-text stage, with 72 meeting the inclusion criteria. A further 29 articles were identified from references, of which 11 were

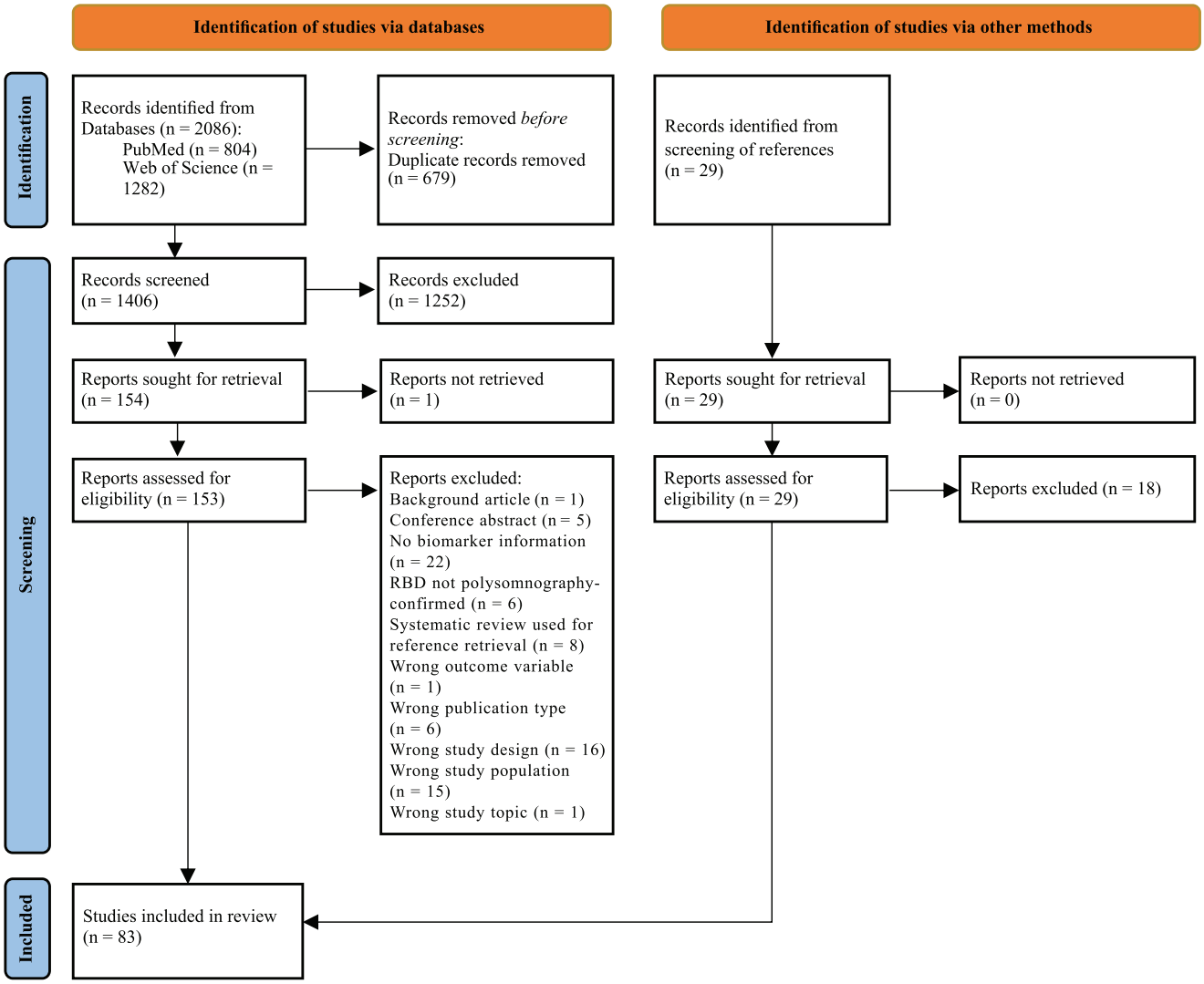

FIGURE 4 PRISMA flow diagram for gait studies.

suitable for inclusion, with a total of 83 studies included in the systematic review (see Figure 4).

3.2.2 | Study characteristics

Individual study characteristics are presented in (Table S6). The studies included in the systematic review were published between 2000 and 2022 (Figure 5A). Most studies investigated gait in association with risk of AD ($n = 35$),[26,27,80–112] DLB ($n = 16$),[11,28,30–32,113–123] and PDD ($n = 9$).[13,24,124–130] Very few studies were conducted in relation to FTD ($n = 1$) or VaD ($n = 2$) risk, with one combining asymptomatic and symptomatic individuals who progressed to FTD with those who later developed AD (AD/FTD group), and asymptomatic and symptomatic cases of future VaD with individuals who later progressed to DLB diagnosis (VaD/DLB group), as the two groups in each pair were similar in their gait characteristics.[23,131] Finally, 22 studies utilized the term "dementia," combining different dementia etiologies.[14,25,80,132–150]

Most studies reported findings from longitudinal assessments ($n = 49$, with $n = 46$ cohort studies and $n = 3$ case-control studies), whereas 34 studies were cross-sectional. The sample size across studies ranged from 10 to 69,150 (median = 102, IQR = 272), with sex balance varying from 100% female to 100% male (median = 50.8% female, IQR = 25). Participants were middle-aged or older (average age per comparison group for every study is provided in Table S6). The majority of studies were conducted on North American and European samples ($n = 71$), with only eight studies from Asia and four from Oceania (all were Australian). The reporting of participants' racial background was limited, with only 25 of 83 studies explicitly stating the racial distribution of their samples. The majority of participants in these studies were White.

The vast majority of studies included in the review were carried out within in-person settings (either in a laboratory, clinic, or at home with researchers present), with only one study collecting data both in-person and remotely and two studies remote-only.[28,85,113] Of the three studies, only one focused on gait alone and reported a number

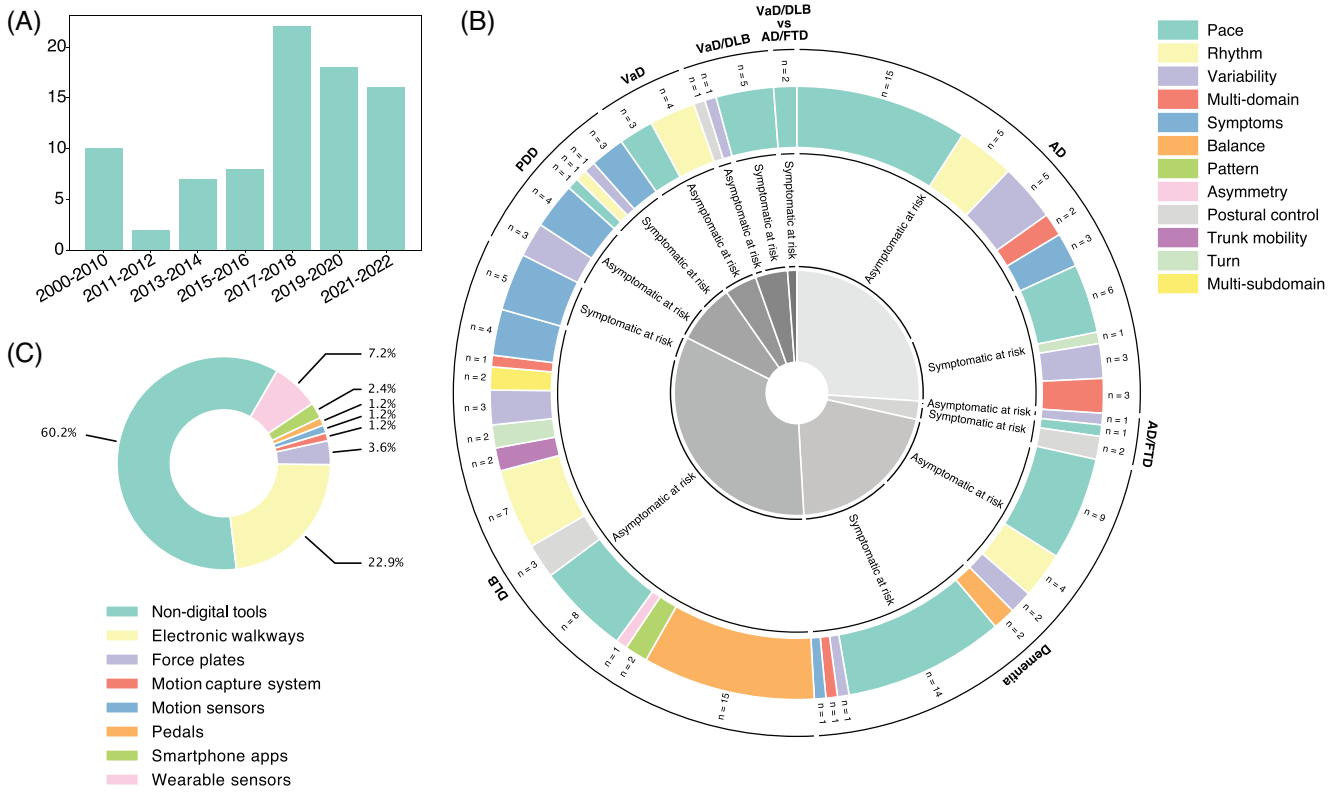

FIGURE 5 Descriptive information for gait studies. (A) Gait studies published between 2000 and 2022. (B) Gait metrics with a potential for early detection in asymptomatic and symptomatic at-risk individuals. (C) Tools used to assess gait across studies.

of quantitative gait measures,[28] with the other two studies providing composite scores that assesed other functions (e.g., resting tremor or memory) in addition to gait. This study was also the only study identified through systematic searches that collected data passively while participants were performing their normal daily activities.[28] In the remaining 82 studies, gait was assessed using a variety of active tasks (e.g., a 10-m walk at fast pace).

3.2.3 | Measures

In total, 363 gait measures were reported across studies (Table S6). Of these, 165 (45.4%) reported across 65 studies were shown to have early diagnostic potential in asymptomatic (n = 112) and symptomatic (n = 53) at-risk groups (Figure 5B). Most of these measures (n = 121) characterized gait alone, while the remaining assessed balance (n = 17), multiple domains (n = 7), or symptoms and qualitative gait characteristics using standard clinical motor assessment tools, such as the Unified Parkinson's Disease Rating Scale (UPDRS) (n = 20). The most commonly occurring measures across these categories are summarized below (see Figure 6 and Table 2 for definitions). All remaining measures and tasks used to record them are presented in Table S7, with the direction of quantitative gait change shown in Table S8. With only 11 of the quantitative measures with early diagnostic potential recorded passively in the real world, the majority were captured using active tasks (n = 134) under single-task (n = 96; e.g., walk 10 m) or the more challenging dual-task conditions (n = 36; e.g., walk 10 m while counting backwards from 100 by three). Often, data acquired under single- and dual-task conditions were combined into a single measure of dual-task cost, which represented the difference in performance between conditions. Finally, two measures were collected using virtual reality tasks.

Gait measures with early diagnostic potential could be further subdivided into those characterizing its macrostructure (n = 2) and microstructure (n = 120). Two macrostructural gait measures—both reflecting the pattern of walking and recorded as part of a single study measuring gait passively in the real world—differed between asymptomatic individuals at risk of DLB and healthy controls (Figure 5B).[28] Most microstructural gait metrics with disease-detection capabilities fell under the pace (n = 65), rhythm (n = 21), and variability (n = 20) sub-domains, with one metric describing gait asymmetry, six postural control, two truncal mobility, three turn properties, and three multiple sub-domains at the same time (Figure 5B).

The most frequently encountered measure in the pace subdomain was gait speed (n = 39), found to discriminate between individuals at risk of developing dementias across the spectrum (asymptomatic and symptomatic at risk of AD, symptomatic at risk of AD/FTD, asymptomatic and symptomatic at risk of dementia, asymptomatic at risk of DLB, symptomatic at risk of PDD and symptomatic at risk of VaD/DLB) and their respective control groups.[14,23–26,80,87,88,91,96,98,101,105,106,108–110,117,133,135–142,144,145,147,150] In the only study that compared individuals across the preclinical and prodromal

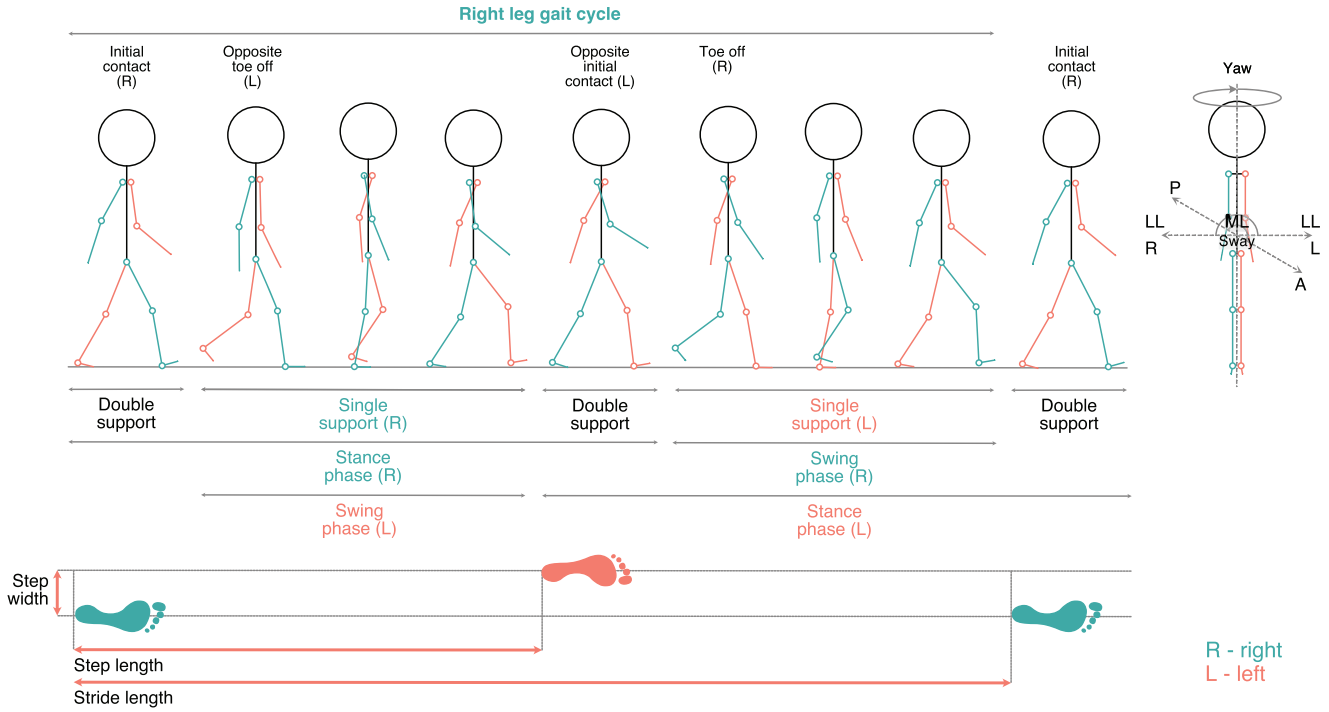

FIGURE 6 A diagram showing the sources of main quantitative gait metrics. A normal gait cycle of each leg consists of swing and stance phases. A, anterior; L, left; LL, lateral; ML, medial; P, posterior; R, right;.

TABLE 2 A glossary of metrics used in text.

Subdomain	Measure	Definition
Asymmetry	Step time asymmetry	Difference in step time between L and R steps
Balance	Jerk (A-P, ML-LL, overall)	Jerkiness of sway in A-P and ML-LL directions and overall
	RMS acceleration (A-P, overall)	Root mean square acceleration in A-P direction and overall
Pace	Gait speed	Ratio between distance traveled and time taken to travel that distance
	Step length	Distance between two consecutive initial contacts
Posture	Dual-task cost in step width	Difference in step width between double- and single task conditions
	Step-length asymmetry	Difference in step length between L and R steps
	Step width	Lateral distance between the midlines of R and L heels
Rhythm	Cadence	Steps per minute
	Double support time	Time spent in double support phase, which is the time between the initial contact of one foot and toe off of the opposite foot
	Stance time	Time spent in stance phase, which is the time from the initial contact to toe off of the same foot
	Step time	Average time taken to make a single step
	Swing time	Time spent in swing phase, during which foot moves forward in the air
Trunk	Range of motion of trunk (A-P)	Angular range of the thoracic spine in the AP plane (i.e., moving back and forth)
Turn	Peak angular velocity of trunk (A-P)	The peak angular speed of thoracic spine motion in the A-P plane (i.e., moving back and forth)
	Turn yaw score	Composed of rotation duration and amplitude measures along the vertical axis
Variability	Cycle-time variability	Variance in the time interval between two successive occurrences of initial contact of the same foot (gait cycle)
	Stride-length variability	Variance in the length between two consecutive heel strikes of the same foot (stride length)

Abbreviations: A, anterior; L, left; ML, medial; LL, lateral; P, posterior; R, right.

stages of different diseases, two pace measures, namely, gait speed and step length, were shown to differentiate symptomatic individuals who progressed to VaD/DLB from those who progressed to AD/FTD.[23]

In the rhythm subdomain, the most common measures were cadence (n = 4), double support time (n = 4), swing time (n = 4), stance time (n = 3), and step time (n = 3). Both cadence and double support time could discriminate between asymptomatic individuals at risk of AD and healthy controls.[83,109,110] In addition, alterations in these two measures were found in asymptomatic individuals who progressed to dementia during follow-up as well as asymptomatic participants at risk of PDD (both cadence) or VaD (double support time) as compared to their respective control groups.[24,131,145] Finally, measures of swing, stance, and step time could discriminate between controls and asymptomatic individuals who progressed to dementia (stance and swing time) or were at risk of DLB (all three) or VaD (swing time).[28,116,145]

In the variability subdomain, cycle-time variability and stride-length variability were the most commonly reported metrics (n = 3 each). Although cycle-time variability could distinguish asymptomatic individuals at risk of AD, AD/FTD, or VaD/DLB from controls,[23,27] stride-length variability was altered in symptomatic participants at risk of AD, and both asymptomatic and symptomatic individuals who developed dementia during follow-up as compared to controls.[102,135,145]

Few measures of postural control, gait asymmetry, truncal mobility, and turn properties were reported. Postural control measures, such as step-width (n = 1) and step-length asymmetry (n = 1), showed potential for discriminating between controls and asymptomatic or symptomatic individuals at risk of DLB and asymptomatic individuals at risk of VaD/DLB.[23,31,32] However, there was also some evidence that dual-task cost in step width, another postural measure, could distinguish between symtomatic individuals at risk of AD/FTD and controls at both middle and older age.[23] Step-time asymmetry, the only measure of asymmetry identified by the review, showed an ability to distinguish asymptomatic participants at risk of DLB from controls.[31] Truncal mobility, measured in terms of the range of motion of the trunk in the anterior-posterior plane, was found to discriminate between asymptomatic individuals at risk of developing DLB and controls under both single- and dual-task conditions.[118] Finally, the two measures describing turn properties—namely, the peak angular velocity of the trunk in the anterior-posterior plane while turning, and turn yaw score, composed of yaw duration and amplitude measures—were able to distinguish controls from asymptomatic individuals at risk of DLB and symptomatic cases at risk of AD, respectively.[84,118]

Quantitative balance measures of sway jerk (anterior-posterior, medial-lateral, and overall) as well as root mean square acceleration (RMS, anterior-posterior and overall) were recorded under different task conditions of the same study and found to distinguish asymptomatic participants at risk of DLB from healthy controls.[30] Such measures, apart from two performance-based examples, such as a score on a standing balance test, that were found to distinguish participants who later progressed to dementia from those who did not, were generally lacking of dementia risk groups outside of DLB (Figure 5B).

Many metrics reported in relation to impending synucleinopathies, such as DLB and PDD, were qualitative and collected as part of a clinical assessment (Figure 5B). Of these, incidence of freezing of gait (FOG, n = 2) and fall frequency (n = 2), as well as presence of rigidity (n = 2) were associated with PDD and DLB risk in both asymptomatic and symptomatic individuals.[11,115,124,127,128]

Twelve of the 83 studies reported AUC values that described the ability of different gait metrics to predict future dementia risk or classify at-risk versus control groups (Table S6).[11,28,85,93,99,113,114,119,120,130,135,137,151] The models varied from univariate to multivariate, and sometimes included measures from other domains, such as memory, voice, and tremor. The lowest identified AUC value was that for a univariate model that used gait speed measured during a 4-m walk to predict dementia risk (AUC = 0.59).[137] Other studies reported higher AUC values, in particular for quantitative gait measures (e.g., a combination of micro gait measures could discriminate iRBD patients from healthy controls with an AUC of 0.70[28]), and especially when assessed in combination with other, non-gait measures (e.g., neuromotor index could predict conversion from MCI to AD with an AUC of 0.94).[85] Similar values were reported for sensitivity and specificity of these models.

3.2.4 | Tools

Most studies (n = 50) did not use any digital technologies to capture gait measures (Figure 5C). In these studies, performance was quantified either by measuring time to complete the test with a stopwatch or by rating quality of performance using a standardized motor scale. In the remaining studies, electronic walkways that allow capture of bilateral foot placement as participants walk were the most common tool (n = 19 studies, Figure 5C).[23,24,31,83,94,102,103,108–111,122,129,131,135,141,145,146,152] Three studies utilized force plates to measure alterations in posture,[32,119,125] whereas one study used a motion capture system,[27] which is used as the gold standard in gait research and allows for movement capture of the whole body as participants walk (Figure 5C). None of these technologies are scalable for widespread clinical use due to their cost, size, and operational complexity. Another study utilized passive motion sensors,[136] which could be implemented at home to measure gait speed, but only in single-person households, as it is impossible to distinguish who activates the sensors with additional wearable technologies. Wearable sensors that enable measurement of linear acceleration and angular velocity while participants move were utilized in six studies (Figure 5C).[28,30,84,97,114,118] They included one- (n = 3), four- (n = 1), and six- (n = 2) sensor systems. Although multi-sensor systems are potentially hard to implement in real-world settings because they increase the set-up time and reduce comfort, one-sensor alternatives, with the sensor fixed on the lower back, may provide a good balance between user acceptability and signal quality.[28,30,84] Only two studies utilized custom smartphone-based applications that employed internal phone sensors to measure gait and balance

(Figure 5C).[85,113] Whether these apps have been validated against gold standard tools was not described.

3.2.5 | Quality and risk of bias in studies

The mean (SD) NOS rating for cross-sectional studies on gait was 7.0 (1.4) of 9, whereas longitudinal cohort studies were rated 8.1 (0.9) of 9 (Tables S9 and S10). Only three case–control studies met the criteria for inclusion and received an average of 7.3 (1.2) stars of 9 (Table S11). This indicated that the general quality of studies that met the inclusion criteria was relatively high.

In relation to recruitment bias, only 19 (56%) of 34 cross-sectional studies reported information that warranted representativeness of the sample as compared to the average in the target population. In contrast, the selection of samples for longitudinal studies appeared to be less biased, with 42 (91%) of 46 studies being rated as having a representative target cohort, and 44 (96%) of 46 studies having selected an adequate control cohort. Similarly, two out three case–control studies were rated as having adequate case definition and good representativeness of the cases, as well as adequate selection and definition of controls.

Comparability of participants was generally high within studies, with 26 of 34 (76%) cross-sectional, 41 of 46 (89%) cohort, and all 3 case–control studies fully adjusting for age and sex, two important factors that have been found to affect gait, in their design or analysis.

Ascertainment of exposure and outcome was generally carried out objectively across studies, with all 34 cross-sectional studies, 43 of 46 (93%), and all 3 case–control studies reporting unbiased exposure and outcome assessments.

In terms of attrition bias in cohort studies, 15 of 46 (33%) studies either reported large attrition rates of more than 20% or failed to adequately explain the reasons behind attrition or exclusion. This indicated a risk of bias in these studies.

3.2.6 | Discussion

The 83 studies included in this systematic review provide evidence for the value of gait in early detection of dementias. In line with predictions based on the overlap between brain networks controlling gait and early pathophysiology underlying different dementia-causing diseases, these measures were able to discriminate between asymptomatic and symptomatic individuals at risk of developing dementias and healthy controls. In addition, models including these measures were able to predict the onset of clinical symptoms with moderate to high AUC, sensitivity, and specificity, although, notably, only 12 studies used such models. Most measures focused specifically on gait, with pace, rhythm, and variability subdomains affected in asymptomatic and symptomatic individuals at risk of all dementias investigated.[23,24,80,87,88,91,117,133,135–138] By comparison, gait asymmetry, truncal mobility, and balance measures may help to distinguish individuals at risk of DLB from health controls regardless of the stage of disease progression.[23,31,32,84] More evidence is required to establish the ability of these measures to detect preclinical or prodromal AD, FTD, and VaD. Similarly, only one study attempted to compare gait in at-risk individuals across the dementia spectrum and found more severe impairments in the pace subdomain in participants who later progressed to VaD/DLB as compared to AD/FTD.[23] This finding is consistent with those from a study that recruited participants at more advanced disease stages and found disproportionate changes in gait speed and balance in DLB as compared to AD.[153] However, additional studies using objective quantitative gait and balance measures captured using analogous protocols to compare at-risk individuals at asymptomatic and symptomatic stages of different disorders are required to verify which gait measures can not only predict development of dementias but also distinguish among dementia-causing diseases in their earlier stages.

The review also evaluated the tools used in the measurement of gait and balance to date and their suitability for remote deployment at-scale. Most studies included in the systematic review utilized research-grade technologies, which were ill-suited to routine clinical use due to high cost and/or operational complexity.[24,83,135] Several studies utilized wearable accelerometer sensors, including three that used a single, multi-axial sensor. Although multi-sensor systems are potentially difficult to implement in real-world settings due to the increased user burden, one-sensor systems, if validated against gold standard tools, may provide a good balance between user acceptability and signal quality.[154] In contrast, the use of smartphone applications for harnessing accelerometer, gyroscope, and (in many cases) magnetometer sensors to measure gait was also limited, with only two studies utilizing such applications as part of active tasks. The authors of neither study mentioned validation of their apps against gold standard tools.[85,113] Given the widespread use of smartphones, this may be the most scalable and acceptable option to measure gait, although the variable positioning of smartphones (e.g., in the hand, pocket, or a bag) may pose challenges to signal extraction and data quality.[155,156] Only three studies recorded gait remotely and only one also collected gait data passively while participants carried out their normal daily activities. [28] Active intermittent assessment of gait may be less valuable than continuous passive monitoring, since it may result in participants exerting maximum effort for only a short period and, therefore, may mask any real difficulty with walking experienced in the dynamic real-world settings.[157] Therefore, both passive recording of everyday gait and the utilization of smartphones for this purpose should be explored in future studies, as they provide an unparalleled opportunity to reveal sensitive, specific, inexpensive, and ecologically valid early disease signatures without the need for complex task instructions and expensive research-grade tools.[158]

Few studies were identified on preclinical and prodromal VaD and FTD. This limitation was likely caused by the low prevalence of CADASIL and FTD in the general population as compared to other dementia-causing diseases. As a result, measures with the highest sensitivity and specificity to detect VaD- and FTD-causing diseases identified in future studies may differ from those presented here.

4 | GENERAL DISCUSSION

Digital measures capturing real-life activities are central to next-generation approaches to earlier dementia detection, given their potential to overcome several inherent limitations of current pen-and-paper cognitive tests such as ecological validity and applicability across diverse populations irrespective of demographic differences. However, to deliver added diagnostic value, it is crucial that these approaches select those activities with robust evidence of involvement in early disease and that are measurable using methods with the potential for future widespread use in clinical practice.

Navigation and gait represent activities that meet these selection requirements. Their testing has complementary value for dementia disorders in general, given that navigation is subserved by brain regions selectively vulnerable to early AD, whereas gait is controlled by a distributed network of brain regions that are variously affected in AD as well as non-AD disorders, such as FTD, PDD, VaD, and DLB. Both can be measured remotely and applied across diverse populations irrespective of differences in education, language, and culture. By conducting this systematic review, we established the utility of digital navigation and gait measures for detecting dementia risk and provided examples of technologies used to capture these measures in unsupervised settings. Furthermore, we created a framework for evaluating the evidence base for the inclusion of measures in digital toolkits aimed at early detection of dementia in the future.

Eligibility criteria for studies were deliberately stringent to ensure a high quality of results with greater certainty of evidence, including only cross-sectional studies where participants had either biomarker-confirmed preclinical or prodromal dementia or a higher risk for future disease based on established genetic (*APOE* ε4 for AD) and other risk factors (iRBD for DLB and PDD and CADASIL for VaD), or cohort studies with evidence of dementia outcomes. The terms "asymptomatic at-risk" and "symptomatic at-risk" were used to refer collectively to preclinical and prodromal stages of different dementias beyond AD for which there is no accepted definition.

4.1 | Measures

The results identified a number of measures in both modalities that differed between symptomatic and asymptomatic at-risk individuals and controls, some of which also showed high classification accuracy. Measures were collected either actively through tasks or passively during routine behaviors, and either in-person during research visits or remotely during everyday life. It is important to note that several consistent findings across different methods of acquisition and task design highlighted the potential of identified measures to provide accurate read-outs of incipient disease effects. For navigation, these related to measures of distance error in goal-finding paradigms, using allocentric or path-integration focused prompts for earlier asymptomatic at-risk AD stages and egocentric prompts for symptomatic stages. For gait, measures of pace, rhythm, and variability, which were affected in individuals at risk of all dementias investigated, and asymmetry, truncal mobility, and balance, which were altered in asymptomatic and symptomatic individuals at risk of DLB, showed promise for use in early disease detection.

The sensitivity and reliability of these measures likely relate to their grounding in cognitive and movement neuroscience (see Section 3.2.6), and subsequently the ability to tailor the task designs in such a way that enables very subtle changes in cognitive ability associated with early pathology manifestation to be detected. For example, the navigation measure of distance error under path integration conditions was only differentiative of asymptomatic at-risk groups in the most difficult task condition; namely, when supportive spatial cues that provided directional cues to participants were removed from the environment, whereas baseline performance was unchanged.[9] Similarly for gait, many measures sensitive to asymptomatic at-risk stages were acquired under dual-task conditions, with walking and balancing exercises performed while participants were carrying out a second cognitive task to disproportionately impair performance in the former.[28] Improved understanding of brain mechanisms underlying the sensitivity of these measures can help refine tasks for clinical implementation and harness their full potential for early disease detection.[132]

4.2 | Devices

Across navigation and gait, a mixture of digital devices and real-world tools were used which varied in scalability and user burden. Most assessment approaches employed (including the assessment of navigation using a desktop computer with a virtual reality environment or gait using an electronic walkway) were not scalable or implementable remotely for widespread clinical use, despite their diagnostic potential.

Some studies, however, used tools that could address this issue, while at the same time capturing similar measures of interest. For navigation, the smartphone navigation game app Sea Hero Quest collected measures of allocentric distance error, angular path integration, and object-location memory while participants played at home. In addition, metrics captured passively through GPS loggers in personal cars could differentiate asymptomatic at-risk groups, with more scalable wearable sensors being explored (see Section 3.1).

For gait, a single multiaxial wearable Axivity accelerometer placed on the lower back was employed to collect data on pace, rhythm, variability, asymmetry, and postural control subdomains over a week-long period while participants performed their normal everyday activities. Measures derived could distinguish participants at risk of DLB from controls, suggesting that real-world settings are sufficiently challenging to reveal subtle deficits or adaptations resulting from early changes in the brain.[28]

These examples highlight the future potential of rapidly developing technologies that enable measures derived from neuroscientific understanding to be captured in a device-agnostic manner. Newer iterations of increasingly ergonomic virtual, augmented, and mixed-reality devices, allow real-world simulating test paradigms to be delivered in ever more-scalable and user-friendly ways while behavioral assessments previously confined to desktop computers or pen-and-paper

formats are being redesigned as tablet or phone apps.[134] Although device transferability in gait is more complex owing to the difficulties caused by the variable smartphone positioning, small wearable sensors that can be temporarily fixed to the body and developments in signal extraction algorithms for smartphone data may in the future provide the means for remote measurement of motoric behaviors of this kind.[155,156]

Passive sensing of behaviors has many advantages over active testing, including lower user burden and high ecological validity[28,159–162]; however, this approach also has several drawbacks, such as lower signal quality and issues with compliance and participant engagement. Passively captured signal varies depending on environmental factors, such as terrain, weather conditions, and rural as opposed to urban settings. Unless such information can be gathered from other passive sensors (e.g., location data may enable tracking of environmental factors for the purposes of gait analysis, while abrupt and severe changes in gait may indicate that alterations in navigation may be due to factors other than AD) or diaries, which increase user burden, it may be difficult to compare passive measures across individuals and establish population norms. Nevertheless, tracking decline within individuals over time may still be possible with good quality signal extraction algorithms. Finally, one of the most important drawback of passive sensing is its privacy risks, given the close association of measures to participant personal information.[163] GPS data, especially, pose a privacy risk, with data breaches potentially resulting in identification of private addresses and even an individual's location in real time. For future clinical application, robust privacy-preserving methods, such as the use of on-device analytics that minimize or eliminate transfer of potentially privacy-sensitive data from users' own devices, will need to be deployed.

4.3 | Limitations and strengths of the study

Although stringent inclusion criteria were employed, and the overall NOS ratings indicated good methodological quality of studies, there was evidence of bias in some studies, where sample representativeness and the extent of comparability was questionable or insufficiently reported. Specifically, the majority of gait and all of navigation studies included in this review were conducted with participants of European or North American descent, and in only 30% of gait studies and 18% of navigation studies were the racial or ethnic demographic breakdowns provided. For navigation, in the three passive GPS tracking studies, purposive sampling was used to include only individuals with access to a personal car. These factors may limit the geographical and socioeconomic generalizability to other populations, cultures, or nations. The most valuable evidence is often derived from large-scale longitudinal cohort studies, which are expensive to conduct and may disproportionately exclude countries with limited research funding. Although navigation and gait are activities common to all human communities, these limitations mean that, at present, the study results summarized cannot be considered generalizable across populations.

Regarding comparability, in navigation studies, median group sizes were 15 and 29 for risk and control groups, respectively, whereas for gait studies they varied from 7 to 69,150 (median = 102). Although relatively small sample sizes may introduce the risk of false-positive results,[164] the absence of effect sizes may hinder the interpretation of findings in very large studies. Similarly, age was not adjusted for in 32% of navigation and ≈10% of gait and balance studies, which is the largest confounding variable. Ultimately, more research with larger-scale samples is needed before these measures can be validated for clinical use.

4.4 | Conclusions and future directions

The measurement of navigation and gait may improve early detection of diseases causing dementia and overcome several limitations of legacy tests including real-world relevance and freedom from linguistic and cultural confounds. This systematic review summarizes the evidence of the ability of navigation and gait measures to identify asymptomatic and symptomatic individuals at risk of dementia and also evaluates digital and non-digital measurement devices with the potential for future clinical use at scale. Although the review has provided a clinical evidence base for measuring navigation and gait, it has also identified areas of bias in work undertaken to date, which will need to be addressed if such tools are to meet inclusivity and diversity requirements in any future clinical application. Finally, although focusing on navigation and gait as exemplar behaviors of high disease-detection value, the methodology used in this systematic review can be used as a framework for future evaluation of other measures and measurement devices that may also have utility in the early detection of dementia disorders.

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CONFLICT OF INTEREST STATEMENT

The authors have no conflicts of interest to declare. Author disclosures are available in the supporting information.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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