Chapter 13
Diagnostic tests: novel biomarkers

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Key points

- Blood biomarkers for p-tau181, p-tau217 and p-tau231 reflecting brain tau and Aβ pathology have been developed and validated in research and are being assessed through the appropriate channels for commercialisation and general clinical use.
- Novel biomarkers of non-Alzheimer's disease pathology are needed for research and clinical care.

This is a chapter of the *World Alzheimer Report 2021, Journey to a Diagnosis of Dementia* which can be accessed in full at: https://www.alzint.org/resource/world-alzheimer-report-2021/

Background for clinicians

The scientific community is developing cost-effective tests (or biomarkers) to diagnose the cause of dementia. It is expected that these tests will allow physicians to precisely identify and monitor the accumulation of abnormal proteins in the brain using affordable blood tests. This will pave the way for forthcoming therapies designed to remove the accumulation of proteins that can cause dementia.

> **Biomarkers are expected to advance clinical care by providing information regarding the underlying causes of dementias.**

Why are new biomarkers needed?

Biomarkers are expected to advance clinical care by providing information regarding the underlying causes of dementias. Today, biomarkers estimate brain concentrations of amyloid plaques and neurofibrillary tangles which are the hallmarks of Alzheimer's disease. However, there is a need to expand the biomarker repertoire to other proteinopathies involving aggregation of alpha-synuclein, transactive response DNA binding protein 43 kD (TDP-43), and tau aggregates involved in Picks's disease (3R-tau), or tauopathies like progressive supranuclear palsy (4R-tau), among others.

The global accessibility to these biomarkers will open unprecedented opportunities for personalised dementia prevention. As most biomarkers involve expensive infrastructure such as positron emission tomography (PET) scanners, cyclotrons or cerebrospinal fluid facilities, affordable blood biomarkers are needed to disseminate advances in early diagnostic and therapy to low- and middle-income countries.

Table 1 summarises examples of this new generation of biomarkers

Biomarker	
NfL	Neurofilament light chain
p-tau-181	Hyperphosphorylated tau
p-tau-217	Hyperphosphorylated tau
p-tau-231	Hyperphosphorylated tau
GFAP	Inflammation
YLK40	Inflammation
sTREM2	Inflammation

Blood based biomarkers

This new generation of biomarkers results from technological advances in mass spectroscopy and the introduction of high sensitivity immunoassays such as the single-molecule array (SIMOA), which is many orders of magnitude more sensitive than conventional immunoassays.

These technological advances allow detection, in peripheral blood, of the accumulation of amyloid and neurofibrillary tangles in the brain. In addition, the same techniques allow for quantifying downstream effects such as inflammatory responses, neuronal injury, and synaptic depletion.

Plasma fragments of amyloid-beta species quantified, thanks to innovations in immunoprecipitation and high-resolution mass spectrometry techniques, permit detection of brain amyloidosis based on the plasma concentrations of amyloid-beta species. Although these techniques are accurate and constitute significant progress in the field, they are neither affordable nor mature for large-scale utilisation. (1,2).

Plasma species of tau phosphorylated are considered biomarkers of tau pathology. Recently, species of tau phosphorylated on the epitopes 181, 217 and 231 have been measured in plasma using the SIMOA technology. Preliminary studies conducted in observational cohorts have shown excellent performance to identify individuals with pathologic load of neurofibrillary tangles in the brain, with specificity to Alzheimer's disease. As these phosphorylated tau species are also highly associated with pathological levels of amyloid, they constitute an excellent biomarker for Alzheimer's disease pathophysiology (3–7).

Neurofilament light (NFL) is an axonal protein sensitive to a wide range of neuronal insults. Although this biomarker of neuronal injury is not specific for any disease process, it is particularly increased in frontotemporal dementia when compared to Alzheimer's disease. Serum NFL correlates closely with CSF levels, suggesting that blood measurements reflect brain alterations. NFL increases with ageing and in familial Alzheimer's disease, blood NFL levels increase before its clinical onset. A recent multicentre validation supports the use of this biomarker as a screening test for neurodegeneration (8,9).

Biomarkers for non-Alzheimer's disease dementias constitute an important gap in the diagnosis of neurodegenerative conditions. Although quantification of alpha-synuclein remains challenging, progress has been achieved on the detection of pathological alpha-synuclein. Real-time quaking-induced conversion (RT-QuIC), which has been used in the diagnosis of Creutzfeldt-Jakob disease, has shown the ability to detect pathological forms of α-synuclein in CSF with high accuracy (10–12). A growing body of literature suggests that tau imaging agents such as PET with the tracers PI2620 and PBB3 detects 4R aggregates (13–15).

Research on biomarkers for neuroinflammation suggests potential clinical applications to help in the differential diagnosis of dementia. Preliminary results indicate that neuroinflammation biomarkers provide signatures of brain inflammatory responses secondary to the accumulation of abnormal protein aggregates. Changes in YLK40 and sTREM2 mean activation of microglial brain cells, while GFAP indicates astrocyte activation (16–22). Although several PET imaging agents can quantify neuroinflammation responses, they are exclusively used in research.

Biomarkers of synaptic depletion are being developed to quantify cerebrospinal fluid as synapse dysfunction constitutes a common target in all neurodegenerative conditions. However, such biomarkers remain in the early phase of development (23–25).

Survey results

The survey indicates that clinicians foresee an increase in the number of patients seeking a dementia diagnosis and that options such blood tests would facilitate their practice in combination with cognitive assessment and their own clinician judgement or national guidelines.

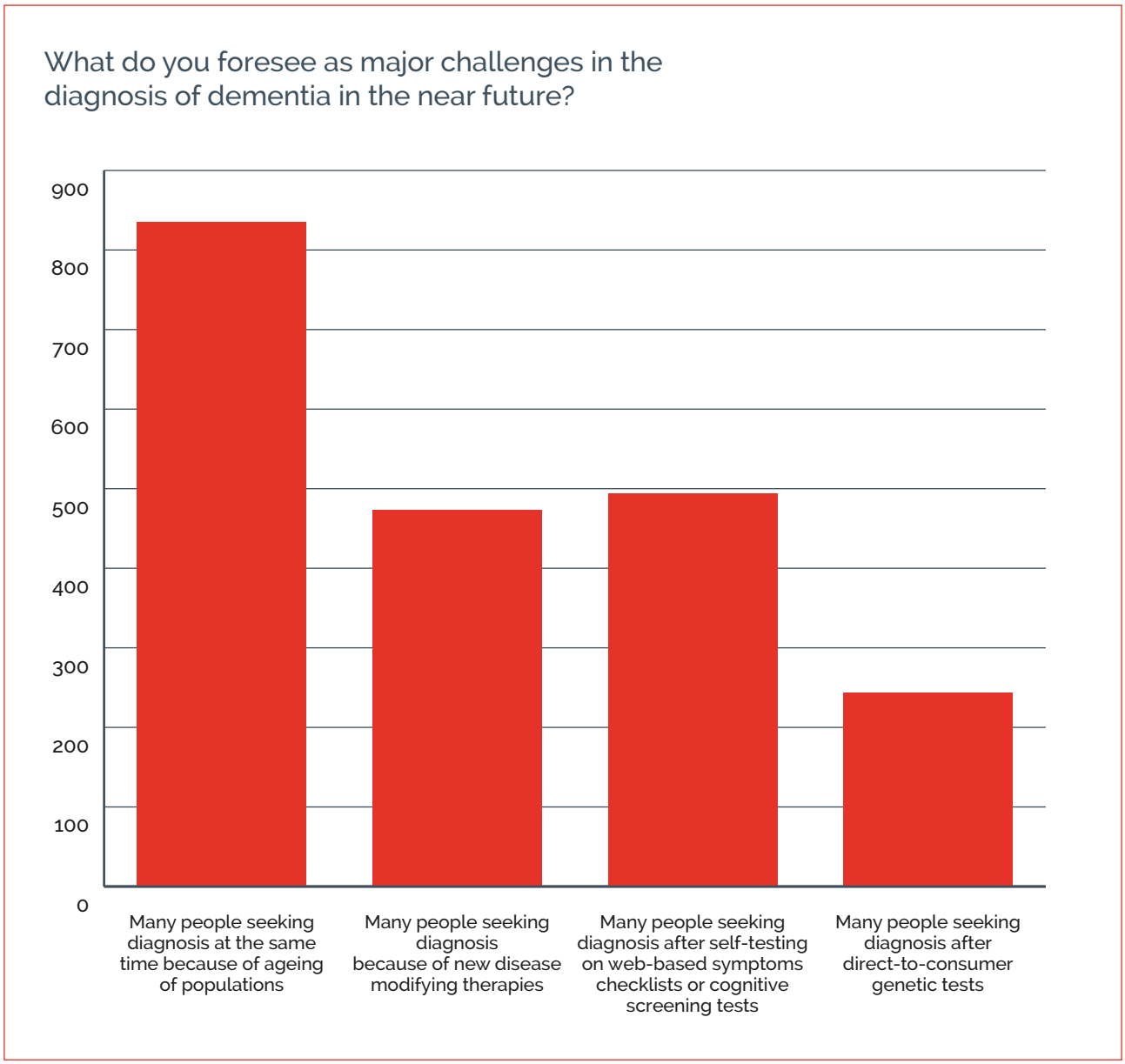

Chart 1. Clinician responses (multiple answers selected).

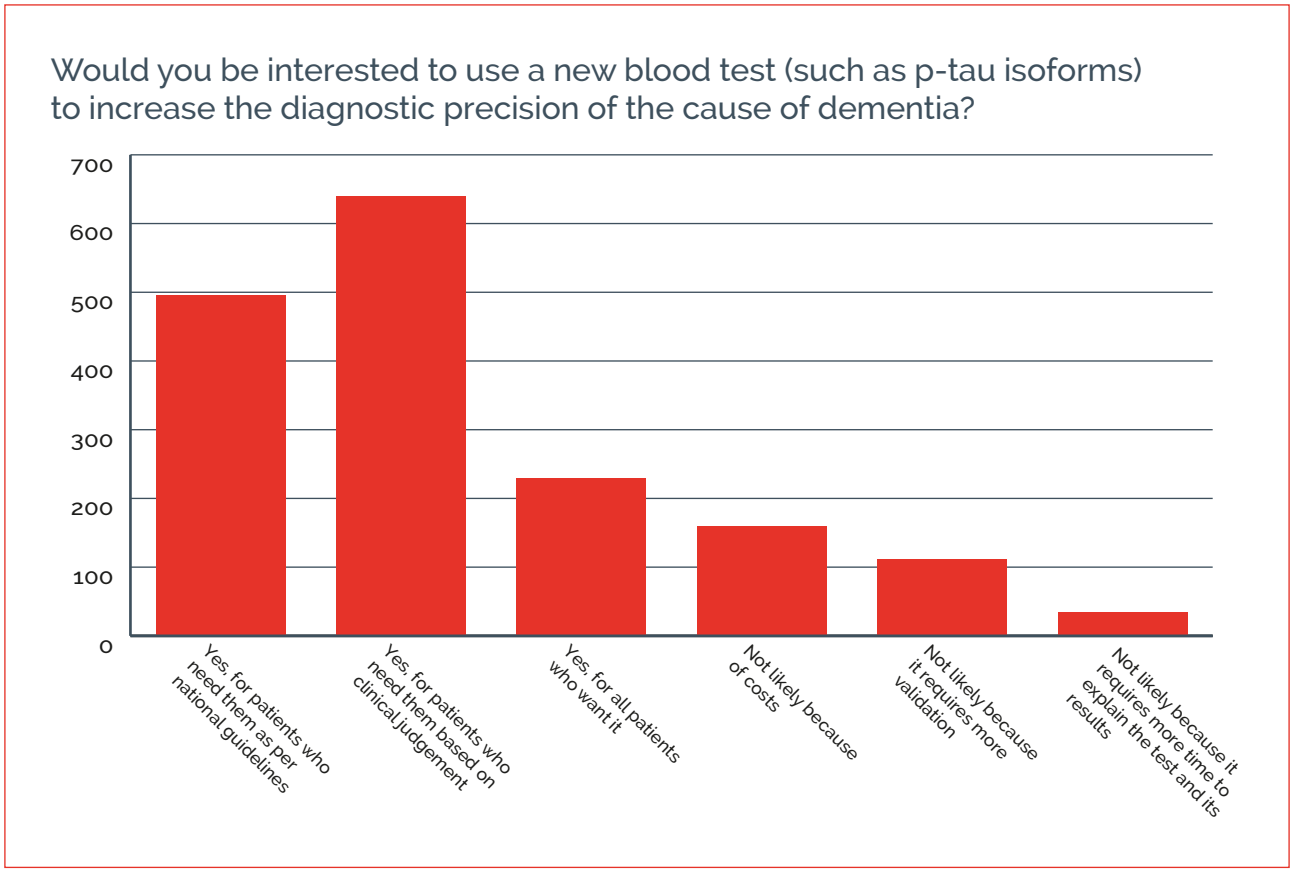

Chart 2. Clinician responses.

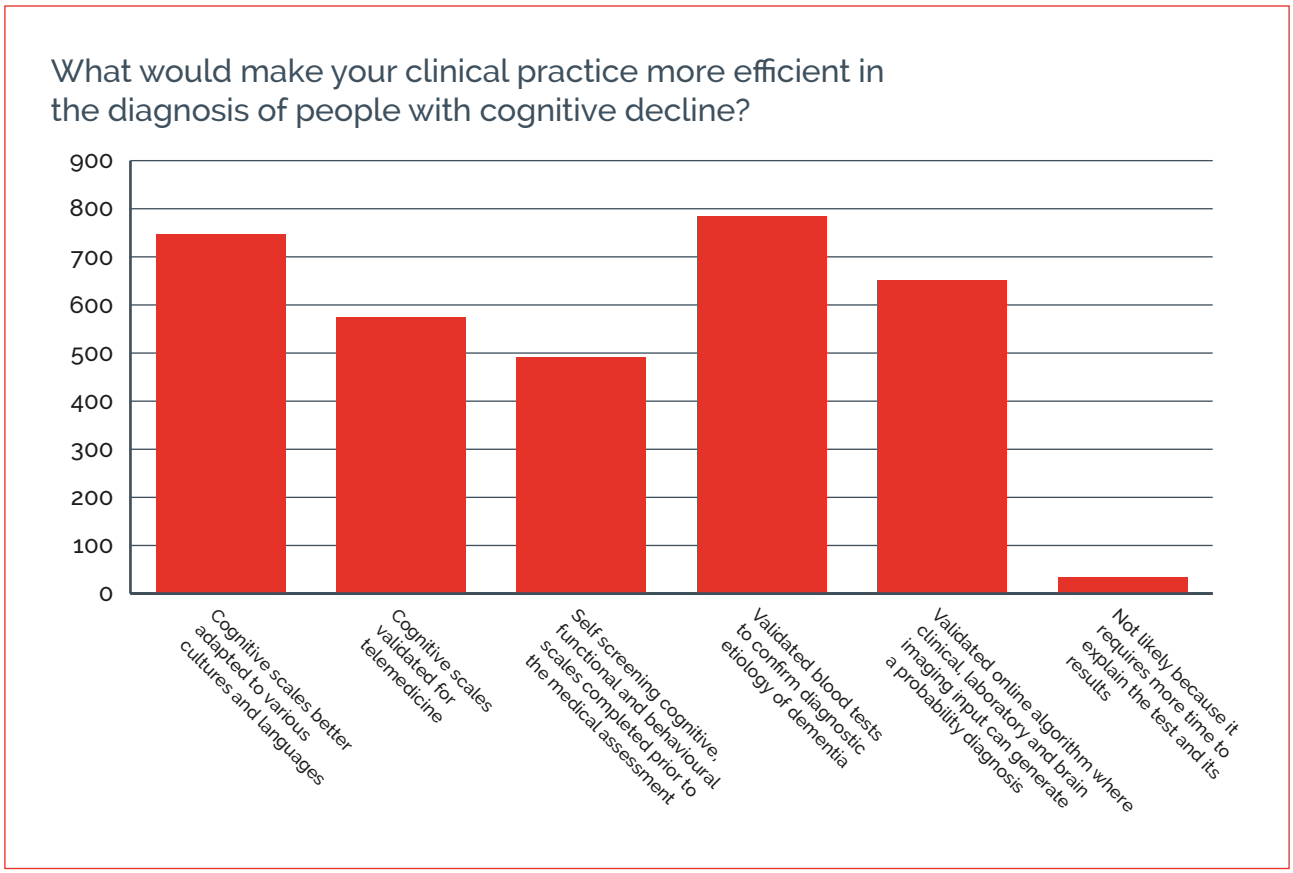

Chart 3. Clinician responses (multiple answers selected).

Expert essay

Will the use of blood-based biomarkers become standard practice in Alzheimer's disease?

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There is great enthusiasm within the fields of Alzheimer's disease care and research for blood-based biomarkers. Biomarkers (short for 'biological markers') are signs of disease pathology that can be measured using laboratory or imaging tests. Blood-based biomarkers have the potential to offer reliable, inexpensive, and widely available means of screening for Alzheimer's disease, tracking disease progression, and accelerating the development of disease-modifying therapies.

Historically, Alzheimer's disease has been diagnosed based on the detection of dementia with a characteristic onset and pattern of impairments as well as the exclusion of alternative causes of cognitive impairment. This diagnosis was confirmed post-mortem via autopsy. More recently, there has been a move away from this syndromal definition of Alzheimer's disease toward a biological definition. Biomarkers have been, and are currently being developed, to be used to identify the neuropathological changes characteristic of Alzheimer's disease in living individuals independent of clinical symptoms, if any.

Researchers have identified numerous promising blood-based biomarkers for Alzheimer's disease. These biomarkers are in various stages of validation, and it is necessary to ensure that any tests for blood-based biomarkers are reliable and their results are reproducible before widespread adoption. Blood-based biomarkers will offer many advantages over CSF and PET biomarkers. Blood tests are commonly used in clinical and research settings around the world, meaning that necessary clinical competencies and infrastructure are already well established. Blood draws are safer, less invasive, and less expensive than either lumbar puncture or PET imaging. Moreover, blood draws are easily repeated over time.

There have been notable advances in the use of cerebrospinal fluid (CSF) and positron emission tomography (PET) to measure biomarkers that are proxies for the neuropathologic changes of Alzheimer's disease, including accumulation of extracellular amyloid-ß plaques and tangles of tau protein. CSF is the clear fluid surrounding the brain and spinal cord and can be obtained through a lumbar puncture. PET imaging uses a radioactive substance called a tracer to visualise activity or proteins in the brain. Biomarker evidence of abnormalities in both amyloid-ß and pathological tau should be present to diagnose Alzheimer's disease (1). Magnetic resonance imaging (MRI) can be used to measure neurodegeneration, a loss of neurons that is part of the classification system for Alzheimer's disease. Neurodegeneration is not, however, specific to Alzheimer's disease and thus not considered equivalent to biomarker evidence of amyloid-ß deposition and pathologic tau accumulation.

> **"Blood tests are commonly used in clinical and research settings around the world, meaning that necessary clinical competencies and infrastructure are already well established.**

Various CSF and PET biomarkers are now widely used in Alzheimer's disease research (2). Unfortunately, the cost, burdensomeness, and infrastructure demands of CSF and PET biomarkers has greatly limited their use – and thus their utility – in clinical practice.

Assuming that one or more blood-based biomarkers is validated, we can speculate about the impact they may have on Alzheimer's disease research and, eventually, clinical practice. They may be used alone or in combination with other modalities to provide diagnostic information, assess the severity of disease, offer prognostic information, or provide insight into the efficacy of treatment (5,6).

In research

Blood-based biomarkers for Alzheimer's disease hold significant promise as an approach to population-based screening. They can be used as an initial screening tool to identify prospective research participants who then undergo

further assessment, for instance using CSF or PET biomarkers and neuropsychological testing to verify study eligibility. Adoption of a multi-step process that begins with a simple blood draw will enable the study of Alzheimer's disease in larger populations more quickly, with less cost and burden.

These advantages are likely to be particularly pronounced in prevention trials that enrol individuals with preclinical Alzheimer's disease, a stage of the disease characterised by the presence of neuropathological changes in the absence of cognitive or functional impairment. Preclinical Alzheimer's disease cannot be identified without testing for biomarkers, and screen failures are common in prevention trials due to the lower frequency of neuropathological changes in cognitively unimpaired adults (7). Difficulty recruiting enough suitable research participants is a barrier to completing prevention trials. Researchers should, therefore, actively be using blood-based biomarkers as a screening mechanism to advance the urgent goal of identifying disease-modifying therapies for Alzheimer's disease.

In clinical care

Regrettably, older adults are often inadequately assessed for cognitive decline during primary care visits due to limitations on clinician time as well as lack of clinician expertise. Availability of a blood-based biomarker test will aid in addressing persistent issues of missed and delayed diagnoses. People who do not have blood-based biomarkers indicative of Alzheimer's disease will also benefit from the availability of a blood test, as a negative result may aid in differential diagnosis and suggest other avenues for intervention. Blood-based biomarkers could potentially be used to reduce the number of unnecessary referrals for specialised care and needless diagnostic procedures, which could shorten waiting times and reduce healthcare costs (8).

Once a disease-modifying therapy for Alzheimer's disease is identified and approved for clinical use, it will be necessary to identify those individuals who might respond to therapy. In particular, if a drug is indicated for use in preclinical Alzheimer's disease, use of blood-based biomarkers to screen cognitively unimpaired adults is likely to become a standard of care. Blood-based biomarkers might also be used to monitor the efficacy of treatment and promote precision medicine, an approach to patient care that takes into account an individual's characteristics to identify the treatments that could work best for him or her (4).

Advances in the science of biomarkers should be paired with robust study of the ethical, legal, and social implications about learning one's biomarker results (9). This will include designing patient education and disclosure materials, tackling Alzheimer's disease stigma and discrimination, and evaluating whether the clinical use of biomarkers addresses or exacerbates health disparities. Further, efforts are needed on a global level to build the capacity to care for people living with Alzheimer's disease and Alzheimer's disease-related dementias.

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Expert essay

Blood biomarkers for Alzheimer's disease: a fast-growing promise

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There are well-established cerebrospinal fluid (CSF) and neuroimaging biomarkers that report on the underlying biology of Alzheimer's disease (1–2). Why then do we need blood biomarkers? CSF collection requires lumbar puncture, an invasive procedure with contra-indications and requiring specialised personnel to perform. Imaging biomarkers require position emissions tomography (PET) scanning, which is expensive, with accessibility limited to a few specialised hospitals (3). Therefore, while CSF and molecular neuroimaging techniques are excellent biomarkers, they lack the scalability, throughput, and simplicity for widespread routine clinical applications. This is where blood biomarkers come in: initially envisaged as first-line pre-screening tools, blood biomarkers now show immense diagnostic promise given their practical, scalable, and economic advantages.

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Following years of methodological advancements, we now have candidate blood-based methods to quantify amyloid (Aβ42/40) and tau pathologies (phosphorylated tau, p-tau), the two cardinal features of Alzheimer's disease, as well as neurodegeneration (with neurofilament light, NfL) (1,2). Similar to CSF biomarkers, characteristic blood changes include decreased Aβ42/40, and increased p-tau and NfL in Alzheimer's disease individuals as compared with controls. Blood Aβ42/Aβ40 modestly separates individuals with and without brain Aβ pathology (4,5). However, this biomarker is only marginally decreased in Alzheimer's disease (compared with more definite decreases in CSF Aβ42/Aβ40) regardless of the method used. Potential reasons for this observation include significant Aβ levels in peripheral tissues, large overlaps between diagnostic groups, and increases in normal ageing. Despite immunoprecipitation-mass spectrometry (IP-MS) methods showing modestly better performances, the low-throughput and extensive pre-analytical steps limit inter-laboratory transferability, and consequently, suitability of this method for routine use at this time (1). There are also substantial cohort differences in the optimal cut-points used to separate amyloid-positive from -negative individuals, also when a high-performance method is used (6), suggesting that the biomarker as such may lack in robustness. Glial fibrillary acid protein (GFAP), a marker of astrocytic activation, is another emerging blood marker related to amyloid pathology. GFAP is already increased in preclinical Alzheimer's disease (namely, cognitively normal adults with evident amyloid pathology), and predicts incident dementia (7). Blood GFAP increases proportionally with amyloid pathology – indexed by PET imaging and its combination with plasma Aβ42/Aβ40 detects cerebral amyloidosis. However, GFAP was also found to be elevated in other neurodegenerative diseases including frontotemporal dementia, traumatic brain injury and stroke. Given their analytical and disease-specificity limitations, blood Aβ42/Aβ40 and GFAP are candidate prognostic blood biomarkers that may best be used in combination with others to provide disease-specific information.

Blood p-tau continues to show promise as a marker of tau pathology in Alzheimer's disease. Concentrations of different p-tau analytes (for example, p-tau181, p-tau217 or p-tau231) gradually increase in the course of Alzheimer's disease; the levels are lowest in cognitively unimpaired adults, slightly increased in preclinical Alzheimer's disease, further elevated in mildly cognitively impaired elderly with amyloid pathology (Aβ+ MCI), and highest in Alzheimer's disease dementia (8–10). This time course is similar to those of CSF p-tau. Blood p-tau biomarkers predict current and future brain amyloid and tau accumulation, and correlate well with CSF biomarkers, and cognitive function. In longitudinal studies, blood p-tau increased according to disease severity: amyloid positive individuals had higher concentrations at baseline and at follow-up when compared with amyloid negative groups at identical clinical stages. Furthermore, those with increased p-tau baseline levels showed greater odds for worsening disease. In patients with autopsy-verified diagnosis and

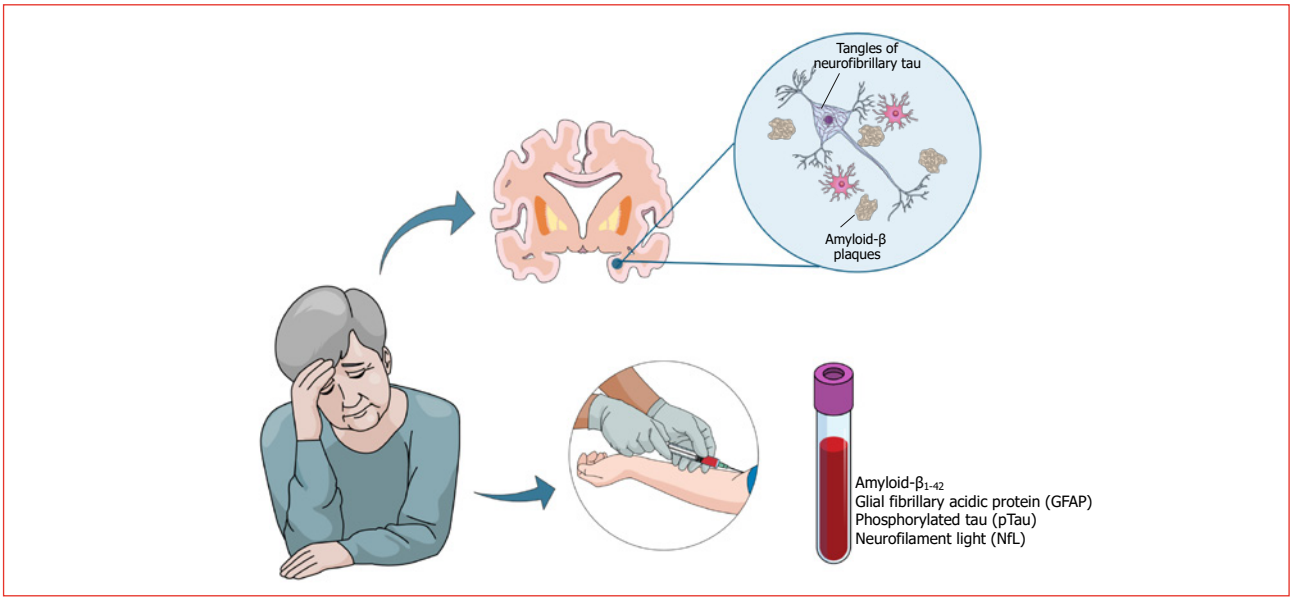

Figure 1. Schematic representation of blood-based plasma biomarkers. Novel biomarkers quantify in the peripheral blood, pathophysiological processes happening in the brain tissue.

ante mortem blood, p-tau elevations were most obvious 4–8 years prior to death, and distinguished pathology-confirmed Alzheimer's disease from non-ADs regardless of clinical diagnosis during life. Furthermore, p-tau concentrations agreed more strongly with diagnosis given at autopsy than during life. Notably, similar blood p-tau levels were found in people with pure Alzheimer's disease and those with concomitant disease, indicating that the biomarker is uniquely specific to the presence of Alzheimer's disease pathology.

Blood NfL is a candidate neurodegeneration biomarker that increases according to clinical diagnosis in Alzheimer's disease (11). However, compared with blood p-tau, these increases are not specific to Alzheimer's disease when associated with brain changes at the anatomical level (12). For instance, while longitudinal changes in blood p-tau associate specifically with amyloid-PET accumulation in Alzheimer's disease-characteristic brain regions, blood NfL increases are more wide-ranging. In agreement, blood NfL is increased in multiple neurodegenerative conditions (as a general marker of neuronal damage/injury) and may therefore be used together with other more-specific biomarkers (for example, p-tau) when evaluating for Alzheimer's disease. Commercial NfL methods are now measured as part of a routine clinical assessment in several European countries, including Sweden and the Netherlands; the first Alzheimer's disease-related blood biomarker to come this far. Other prospective blood-based neurodegeneration biomarkers, including total-tau and neutrophin 1 precursor (NT1), have shown prognostic potential but their performances do not appear suited for diagnostic use just yet.

Although blood-based Alzheimer's disease biomarkers have recently shown highly encouraging findings in research settings, efforts to standardise measurements to ensure transferability and reproducibility between laboratories are in their infancy. The different methodologies to quantify amyloid pathology in the blood are still poorly correlated, suggesting they do not measure the same analytes. Recently some methodological improvements have been introduced, still warranting updated comparisons between them. For p-tau, preliminary method comparisons have shown high correlations and similar performances between biomarker assays, especially in symptomatic Alzheimer's disease, but still a lot of work is required to validate assays for clinical use. NfL has been proven to be a very robust blood biomarker, with highly associated measures in samples processed using standard and unconventional methods. However, further method comparison is needed for harmonisation of techniques and readings to support interpretation in clinical practice.

Although blood-based Alzheimer's disease biomarkers have recently shown highly encouraging findings in research settings, efforts to standardise measurements to ensure transferability and reproducibility between laboratories are in their infancy.

In conclusion, blood biomarkers have shown very promising diagnostic performances, and were associated with key disease features in Alzheimer's disease, reinforcing their great potential for routine clinical evaluations, research studies, and therapeutic trials. With further development of reliable assays

on fully automated instruments, these blood tests are expected to transform Alzheimer's disease care by greatly simplifying access to timely and cost-effective diagnostic and prognostic screening, which will not only immediately benefits patients, families and clinicians, but will also enable the development and evaluation of new disease-modifying therapies.

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Expert essay

CSF and blood biomarkers for non-Alzheimer's dementias

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Primary neurodegenerative disorders (NDDs) are characterised by aggregates of abnormal proteins in the central nervous system. Six hallmark proteins enable the classification of most NDDs: two of them form extracellular aggregates, amyloid-β (Aβ) and the prion protein (PrPsc), while four aggregate intracellularly: tau, alpha-synuclein (α-synuclein), TAR DNA-binding protein 43 (TDP-43) and fused in sarcoma (FUS), leading to amyloidopathies, prionopathies, tauopathies, α-synucleinopathies, TDP43-proteinopathies and FUS inclusions, respectively (1). The neurodegenerative pathologies often coexist, and additional vascular changes are also prevalent causing clinical and neuropathological heterogeneity. The presenting clinical manifestations and syndromes vary between NDDs but are related to the severity, type, and regional distribution of the proteinopathies. Alzheimer's disease is typically characterised by memory impairment, aphasia, apraxia, and agnosia, related to the involvement of medial temporal lobe and parietal cortex. In contrast, the frontotemporal dementias are characterised by behavioural and language changes, and Lewy body dementias (Parkinson disease dementia and dementia with Lewy bodies) by executive, attentional, and visuospatial impairment, and non-cognitive symptoms such as parkinsonism, REM-sleep behaviour disorder, autonomic symptoms and visual hallucinations. The neuroanatomical distribution of proteinopathy pathology help to establish consensus protocols for neuropathological assessment and diagnosis. The clinico-pathological correlation is however difficult to establish. In addition, most neurodegenerative disorders are heterogeneous diseases, namely combinations of proteinopathies, thus biomarkers, such as imaging and biofluid analysis, are crucial for accurate diagnosis which may allow detection in early prodromal or even pre-clinical stages for early interventions when available. With the exception of Alzheimer's disease, where the most recent diagnostic criteria (2) include biomarkers to establish the typical proteinopathy, non-Alzheimer's disease neurodegenerative disorders are mainly diagnosed by clinical features. In Alzheimer's disease, there is already excellent imaging (3), cerebrospinal fluid (CSF) (4) and promising blood biomarkers (5) being developed. In contrast, fluid biomarkers in non-Alzheimer's dementia remain in their infancy but will greatly benefit from the developments in the Alzheimer's disease field.

The core CSF biomarkers for Alzheimer's disease (Aβ42/40, T-tau and P-tau), reflecting the defining Aβ and tau pathologies as well as neurodegeneration, consistently demonstrate diagnostically significant changes across studies (6). However, the concentrations of these core Alzheimer's disease biomarkers are largely normal in the majority of dementias outside of the Alzheimer's disease continuum (7). This can be of great utility in the differential diagnosis of individuals with cognitive symptoms. There are isolated exceptions to this rule; Aβ42 is abnormally decreased in approximately half of dementia with Lewy body cases and many patients with Parkinson's disease dementia (8), which highlights the overlapping pathologies with Alzheimer's disease found at post-mortem. Furthermore, marked increases of T-tau in Creutzfeldt-Jakob disease (CJD) is a common observation, whereas the concentration of P-tau remains normal or only marginally changed in CJD (9) – this makes a ratio of P-tau/T-tau an excellent biomarker in the diagnosis of CJD (10). An unpredicted finding is that levels of CSF t-tau and p-tau are largely normal in frontotemporal dementia. The same holds true for other primary tauopathies (for example, primary progressive supranuclear palsy [PSP]). Neurofilament light chain (NFL) is the smallest of the neurofilament triplet proteins that are the structural components of the axons. NFL is released from the axons throughout life and increasingly in normal ageing; however, in response to axonal injury, NFL release into the extracellular space, CSF and blood is accelerated. Several studies have shown that CSF NFL levels are highest in brain disorders with subcortical pathology, such as vascular dementia (VaD) and normal pressure hydrocephalus (11). Notably, CSF NFL concentrations are clearly higher in frontotemporal dementia than in pure Alzheimer's disease without concomitant cerebrovascular disease (12), which supports that NFL aids in this differential diagnostic specific situation. In addition, CSF NFL also shows a very marked increase in CJD (correlating with CSF T-tau), due to the very extreme level of neurodegeneration (13). Importantly, while CSF NFL is relatively normal in Parkinson's

disease, several studies have shown a very marked increase in CSF NFL in atypical parkinsonian disorders, specifically in corticobasal syndrome (CBD), multiple systemic atrophy (MSA), and PSP (14). Measurements of total α-synuclein in CSF has been proposed as a biomarker for Parkinson's dementia and dementia with Lewy bodies, but most studies only show minor reductions in Parkinson's dementia, with considerable overlap between controls and other patient groups. Recent developments in real-time quaking-induced conversion (RT-QuIC) technology, which explores the self-replicating property of proteinopathic proteins, show great promise in accurate diagnosis of α-synucleinopathies (15), and potentially also TDP-43 (16). As mentioned in the previous essay, biomarkers reflecting post- and presynaptic pathology (for example, neurogranin, GAP-43, SNAP25 and synaptotagmin-1) are specifically increased in individuals with amyloid pathology.

The development of blood biomarkers for non-Alzheimer's disease dementias has not had the same recent success as for Alzheimer's disease (17). α-Synuclein and TDP-43 can be detected and quantified in blood, but their concentrations do not associate well with CSF or neuropathological findings and are likely confounded by high peripheral expression. However, Alzheimer's disease blood biomarkers, specifically p-tau, are extremely useful in differentiating Alzheimer's disease from non- Alzheimer's disease dementias with very high accuracy (18–20). In addition, they can also detect co-pathology in disorders such as dementia with Lewy bodies (21,22). As a close correlation exists between CSF and plasma NfL, CSF findings have been largely replicated in blood (23). While plasma NfL has limited specificity for an accurate diagnosis, it is a robust marker for ongoing neurodegeneration. Nonetheless, plasma NfL is clinically useful in identifying atypical parkinsonian disorders (for example, CBD, MSA and PSP) in individuals with parkinsonism, dementia in individuals with Down syndrome, dementia among psychiatric disorders, and frontotemporal dementia in people with cognitive impairment (23). GFAP is a marker of astrogliosis and is increased in the brains of non- Alzheimer's disease dementia individuals and it is also increased in the CSF of several dementias. However, GFAP changes in blood in non-Alzheimer's disease neurodegenerative disorders appear relatively minor; when measured in blood, the marker appears particularly sensitive to Alzheimer's disease-related Aβ pathology.

In summary, CSF and blood biomarkers for non-Alzheimer's disease dementias still rely on negative Alzheimer's disease biomarkers (which have a very high diagnostic utility for amyloid and tau pathologies) and the non-specific increase of NfL, as supportive evidence alongside clinical assessments. While much work is needed to develop robust biological markers for TDP43 pathology and primary tauopathies, there is now great promise in characterizing α-synucleinopathies by RT-QuiC. This will greatly aid a broad spectrum of dementias but, in particular, in the early diagnosis of Parkinson's disease, Parkinsons' dementia and dementia with Lewy bodies.

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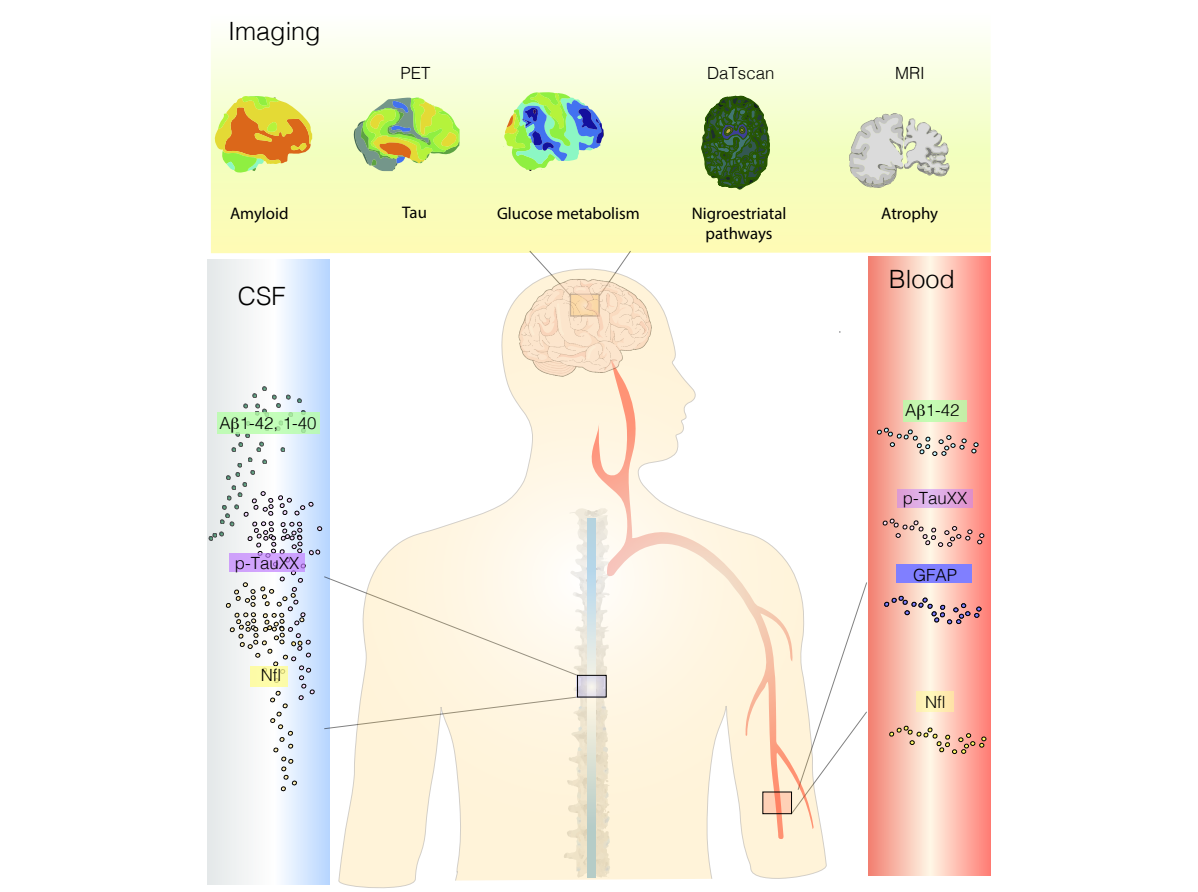
Conclusions

The emergence of biomarkers into the diagnosis of dementia is being hailed by physicians around the world as an inexpensive and effective method to identify and monitor the accumulation of abnormal proteins in the brain. Physicians are anticipating the widespread adoption of these blood tests into their everyday practice as high sensitivity techniques to quantify disease pathophysiology in peripheral blood samples will advance clinical care.

The image below image combines the laboratory evaluations for dementia articulated throughout Section II including imaging, cerebrospinal fluid and blood biomarkers. Not only do they help confirm the diagnosis, but also offer insight into the underlying cause of the syndrome. Specialised tests such as PET and SPECT allow for the visualisation of a host of biochemical processes. thus providing for increased diagnostic accuracy. A lumbar puncture is a safe and effective procedure that detects the presence of pathological processes in the brain and the novel biomarkers will allow for precise identification of accumulated abnormal proteins in the brain in a widespread and affordable way.

This is especially relevant as the population ages and more people will seek out a dementia assessment in the coming years. Though still in its infancy when it comes to standardisation, transferability and reproducibility, plasma biomarkers promise to accelerate diagnosis and permit a level of yet unseen personalised care on a global scale given their ease of use, affordability and adaptability.



Visual overview of biomarker testing reviewed throughout Part II.

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