Supplementary Table . Current and emerging biomarkers for differentiating dementia syndromes

Biomarker	Specimen/ modality	Clinical use	Current use in research
Alzheimer's disease			
Current clinical biomarkers			
Cell count	CSF	Unchanged in AD: useful to exclude neuroinfection	
CSF:serum albumin ratio	CSF/blood (paired samples)	Unchanged in AD: increased when integrity of blood brain barrier is compromised (vascular/neuroinfection/neuroinflammation)	
Aβ1-42	CSF	Reduced in AD	
t-tau	CSF	Increased in AD (non-specific marker of neuronal damage/death)	
p-tau	CSF	Increased in AD (specific marker of AD)	
	Structural MRI	Hippocampal and whole brain atrophy predates symptom onset	
	Amyloid PET	Radioisotope marker of amyloid deposition. Several ligands available International guidelines available for clinical use	
Future/ emerging biomarkers			
BACE-1	CSF		βsecretase enzyme involved in cleaving amyloid precursor protein; may be elevated in earliest stages of AD
sAPPα/sAPPβ	CSF		Marker of amyloid precursor protein metabolism – Not useful diagnostically but may be used to monitor response to treatment in clinical trials
Aβ isoforms	CSF		Markers of amyloid metabolism but require mass spectrometric techniques not suitable for clinical routine work at present
Neurofilament	CSF		Marker of axonal damage; may reflect subcortical/white matter damage across a

			range of neurodegenerative/neuroinflammatory and infectious diseases including AD; can be normal in pure AD
F_2-Isoprostanes	CSF		Marker of oxidative stress/ neuroinflammation elevated in AD
YKL-40	CSF, Plasma		Marker of neuroinflammation
VLP-1	CSF		Marker of neuronal injury
Neurogranin	CSF		Marker of synaptic degeneration
Frontotemporal dementia			
Current clinical biomarkers			
Aβ1-42	CSF	Aβ1-42 normal in non-AD dementia. Aβ1-42:tau ratio used to exclude diagnosis of AD	
t-tau	CSF	Often increased tau levels compared to normal controls; typically lower than in AD	
	Structural MRI	Specific structural patterns associated with clinical phenotypes	Associations developing between genetic mutations, pathology and imaging structural changes. Possible development prior to disease onset.
	PET	FDG PET used in early disease duration cases to demonstrate hypometabolism in frontal/ temporal lobes when structural imaging is normal. Amyloid binding ligands can differentiate AD from non-AD pathology	FDG/Amyloid PET may be useful in presymptomatic diagnosis tau binding ligands – currently under investigation
Future/ emerging biomarkers			
t-tau and p-tau	CSF	t-tau may be normal or elevated p-tau typically normal in FTD; elevated in AD	Decreased p-tau to t-tau ratio suggestive of TDP-43 pathology.
TDP-43	Plasma/ CSF		Increased levels found in plasma and CSF in FTD and MND.
Phosphorylated TDP-43	Plasma/ CSF		Increased levels in *C9ORF72* repeat expansion and *progranulin* mutation patients
Progranulin	serum		Low levels in serum of patients with *progranulin* mutation

Neurofilament light	CSF		Marker of axonal damage: increased levels found to correlate with disease severity and in TDP-43 cases
Inflammatory biomarkers TNF-alpha, TNK-beta, IL-15, IL-17, IL-23	CSF		Possible marker of underlying inflammatory process. Not specific to FTD given possible role of inflammation in other neurodegenerative conditions.
	DTI MRI		White matter damage may differentiate tau from TDP-43 pathology
	Functional MRI		Patterns of change in default and salience networks may differ between AD and FTD and between FTD subtypes.
Dementia with Lewy bodies			
Current clinical biomarkers			
	MRI	Global atrophy with relative hippocampal sparing has some (albeit imperfect) predictive value for DLB vs AD	Possible reduced volume of putamen in DLB compared to AD
	SPECT/PET	PET and SPECT imaging showing striatal dopamine loss. FDG PET showing parieto-occipital hypoperfusion	Ongoing research into use of cholinergic markers. Amyloid imaging not useful in differentiating DLB from AD
Tau	CSF		Variable levels of tau, typically lower than AD, but in rapid cases can be elevated
Aβ1-42	CSF		Aβ1-42 levels similar to AD.
Future/ emerging biomarkers			
Alpha-synuclein	CSF		Contrasting results found in DLB. Both reduced levels and no change.