# Dementia biomarkers: too soon for ‘mainstreaming’.

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Dementia biomarkers are valuable research tools, providing glimpses of brain pathology and function previously only available post-mortem. Prior to large-scale adoption in clinical practice, however, these technologies should demonstrate that they contribute meaningfully, cost-effectively and sustainably to patient care and experience.

In *The Lancet Neurology*, Chételat and colleagues present a ‘Personal view’ on the order in which PET-enabled dementia biomarkers should be offered in clinical practice.1 The authors promote the use of these biomarkers largely on the basis of diagnostic specificity established in controlled research conditions, rather than added value for patient outcomes in real-life settings. Moreover, the paper has the effect of expanding current use of PET-biomarkers in two ways. Firstly, by presenting the implementation of biomarkers beyond tertiary (research) centres as simply a matter of practical feasibility. Secondly, by suggesting that biomarkers might be indicated in populations beyond those covered by current “appropriate use criteria”.2 Consequently, the paper contributes to further ‘mainstreaming’ of biomarkers from research tools to routine diagnostic tests, which in our view is premature. It reinforces the shift towards a biological definition of dementia, a development that does not automatically benefit patients and carers and introduces several hazards.3

Firstly, it is unclear to what extent dementia patients benefit from a biomarker-based diagnosis. As Chételat and colleagues indicate, biomarkers facilitate an *aetiological* diagnosis, which is indicated when pathobiological information “is desired and considered meaningful for individual clinical reasons”. The crucial question here is who decides what is desired and meaningful: the patient (and her/his carer), the clinician, or the clinician-researcher? Unfortunately, insights into whether patients value having access to biomarker knowledge are limited and often weakened by framing bias. Nonetheless, there are indications that patients, carers and citizens (as potential future patients) consider aetiological biomarker information relevant if it helps address a clear need, both in the context of pre-symptomatic and symptomatic diagnosis.4, 5 Diagnosis for them is a means, not an end in itself. In contrast, the authors’ framing of the desirability of biomarker testing in terms of a ‘right to know’, simply assumes that knowledge is always worth having.

In fact, evidence that biomarker results meaningfully impact disease management is extremely modest. Notably, IDEAS had no control arm, while research showing an increase in ‘clinician confidence’ is insufficient to establish patient benefit.

Secondly, extending the clinical use of biomarkers is not without risk. Over 40% of cognitively intact individuals in their 80s have abnormal amyloid-PET scans and over 50% demonstrate hypometabolism on FDG-PET. 6, 7 Given that average age at referral to UK community memory clinics is 79, extending biomarker testing to patients in non-tertiary centres will likely generate a significant number of false positive results. In view of the social meanings attributed to ‘dementia’ and ‘AD’, the iatrogenic harm associated with overdiagnosis could be substantial. If anti-amyloid treatment becomes available, further harms would likely follow from overtreatment.

Finally, the move towards a biological definition of dementia takes place in a larger societal dynamic in which the perpetual promise that treatment for dementia may be imminent plays an influential role. Pharmaceutical and medical imaging companies, clinician-researchers and third sector organisations reinforce this narrative, presenting clinical application of currently available biomarkers as a necessary step towards disease-modifying treatment. The track record of drug developers is poor, however, and the principal modifiers of the lived experience of dementia remain social, not medical. Thus, promoting clinical biomarker testing in anticipation of effective biomarker-based treatment conflates the value of research with benefit for individual patients. It also risks diverting attention and funding from non-biological strategies for living with dementia.8, 9 To support patients and families in navigating the manifold uncertainties thrown up by cognitive symptoms in later life we still need tools rooted in psychosocial models; contextualising symptoms in a broader understanding of people’s lives, preparing patients for a range of possibilities (none of which can be fully predicted or excluded by biomarker tests) and facilitating social interventions agnostic to dementia sub-type.10

Overall, greater modesty seems called for in biomarker development, acknowledging that there is work to be done before widespread clinical implementation of dementia biomarkers can be considered ‘responsible innovation’. Future biomarker research should engage with people in the 9th and 10th decades of life, who form the majority and the fastest growing cohort of those with dementia. No biomarker platform can yet report on the various combinations of neuropathology associated with dementia at this age. Moreover, before promoting further ‘mainstreaming’, the desirability and meaningfulness of biomarker-based diagnosis should be established in terms valued by patients.

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Declaration of interests

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