Drug therapy, imaging, and other aspects of clinical management change after Alzheimer's biomarker testing in routine practice: Findings from the IMPACT-AD BC study

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Background

- Alzheimer's disease (AD) CSF biomarkers (amyloid-beta peptides and tau proteoforms) have demonstrated high diagnostic accuracy[1,2]; however, we have a limited understanding of how testing alters clinical management
- To assess utility and optimal utilization in routine medical care in Canada, we assessed the impact of testing on clinical management

Methods

- 'Investigating the Impact of Alzheimer's Disease Diagnostics in British Columbia' (IMPACT-AD BC) study is an observational, longitudinal study examining the impact of AD CSF testing on clinical management, health care utilization, and patients and their care partners
- Eligible participants: AD CSF biomarker testing ordered as part of routine care and meeting the Appropriate Use Criteria[3]

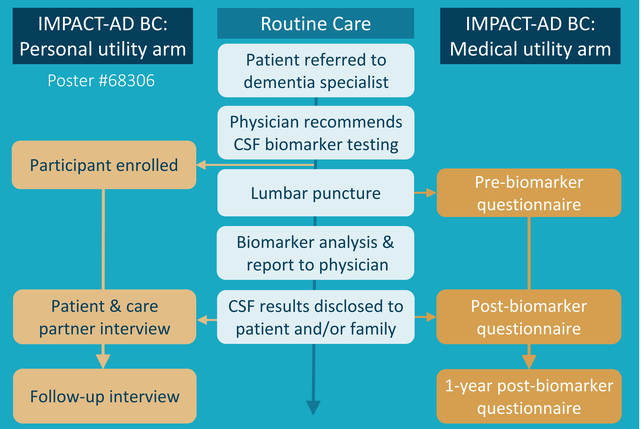


Figure 1. IMPACT-AD study flowchart.

References: (1) DeMarco ML et al. An automated clinical mass spectrometric method for identification and quantification of variant and wild-type amyloid-beta peptides 1-40 and 1-42 in CSF. *Alzheimers Dement.* 2020;e12036. (2) Forgrave LM et al. Establishing pre-analytical requirements and maximizing peptide recovery in the analytical phase for mass spectrometric quantification of amyloid-ß peptides 1-42 and 1-40 in CSF. *Clin Chem & Lab Med.* 2022;60(2):198-206. (3) Shaw LM, et al. Appropriate use criteria for lumbar puncture and CSF testing in the diagnosis of Alzheimer's disease. *Alzheimers Dement.* 2018;14(11):1505-1521.

Conclusions

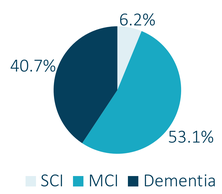
- Substantial changes in clinical management as a direct result of Alzheimer's disease biomarker testing were observed
- Use of costly imaging diagnostics was greatly reduced
- Alzheimer's disease drug therapy increased for biomarker-positive patients, and decreased for biomarker-negative patients
- Findings demonstrate value of early diagnosis in guiding medical care, even in the absence of disease-modifying therapeutics

Results

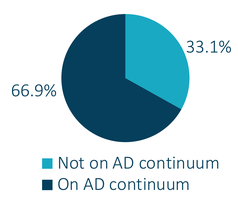
Demographics

Participants	Age	Sex
145	64 years (IQR: 59-69)	52.4% ♂ 47.6% ♀

Cognitive impairment at baseline



Biomarker interpretation



Change in Overall Clinical Management

Table 1. Changes in composite clinical management plans.

	Overall (n = 142*)	SCI (n = 9)	MCI (n = 77)	Dementia (n = 56)
Primary Outcome, No. (%)				
Overall change	127 (89.4)	6 (66.7)	68 (88.3)	53 (94.6)
Changes by Component, No. (%)				
AD drugs	56 (39.4)	2 (22.2)	32 (41.6)	22 (39.3)
Other relevant drugs	27 (19.0)	2 (22.2)	15 (19.5)	10 (17.9)
Other diagnostic procedures	92 (64.8)	3 (33.3)	51 (66.2)	38 (37.9)
Referral and counselling	81 (57.0)	6 (66.7)	43 (55.8)	32 (57.1)

* Three participants pending post-biomarker data completion.

Terms: SCI, subjective cognitive impairment; MCI, mild cognitive impairment; AD, Alzheimer's disease; ND: neurodegenerative disease; FTD: frontotemporal dementia.

Biomarkers increase appropriate use of AD drug therapies & long-term care counseling

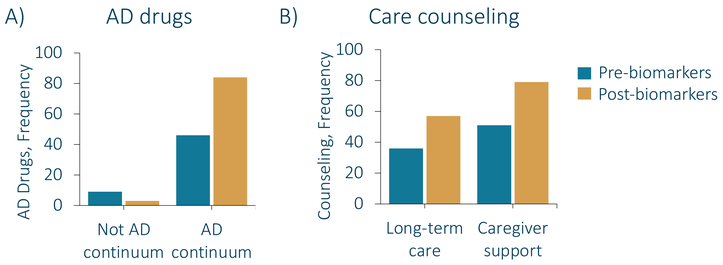


Figure 2. (A) Change in prescription of memantine and/or cholinesterase inhibitors, grouped by AD CSF biomarker findings. (B) Change in counseling.

Biomarkers decrease need for costly brain imaging diagnostics

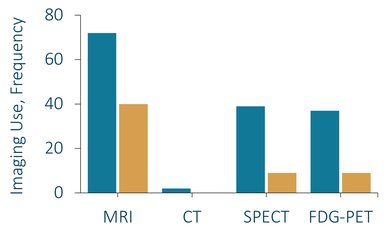


Figure 4. Change in use of imaging diagnostics from pre-biomarkers to post-biomarkers.

Increased Diagnostic Confidence

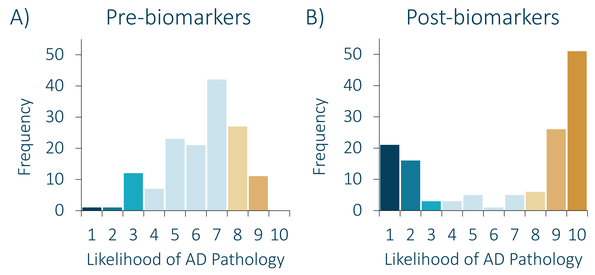


Figure 3. Likelihood of AD pathology as rated by the participant's physician (A) pre- and (B) post-biomarkers.

↑ Diagnostic certainty: cases in diagnostic gray zone pre-biomarkers (4-7 scale) substantially reduced from 65.5% to 9.9% post-biomarkers

Change in Diagnosis

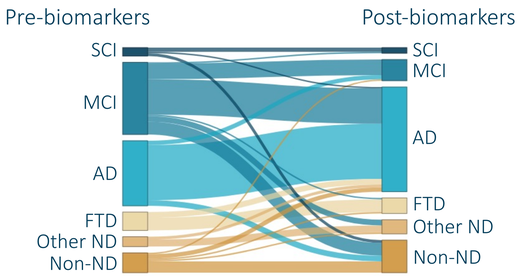


Figure 5. Change in diagnosis as a result of biomarker testing.

- 15.2% with AD diagnosis changed to non-AD
- 38.5% with non-AD diagnosis changed to AD

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