AlzID™
Take control.

Program Highlights Page

PRODUCT DESCRIPTION

AlzID is a blood test that measures the levels of three key ethanolamine plasmalogens (PlsEtn) and one key phosphatidylethanolamine (PtdEtn) from which five phospholipid ratios are determined. Two of these ratios are a measure of the relative PlsEtn composition in blood and three of the ratios are a measure of PlsEtn biosynthesis. These five ratios are combined to create a single quantitative value called the Plasmalogen Biosynthesis Value (PBV). Persons with a low PBV are at increased risk of Alzheimer's Disease (AD) and persons with a high PBV are at a decreased risk of AD.

CLINICAL UTILITY

AlzID has several clinical uses:

- Identifying high-risk individuals who should consider known AD risk reducing diet and lifestyle behaviors.
- Identifying candidates for plasmalogen restoration therapy .

CLINICAL STUDIES

AlzID has been evaluated in numerous clinical studies including:

- Multiple independent case-control cohorts around the world, which consistently showed a PBV reduction in AD patients compared to controls. Most of these studies are described in our publications. Most recently:
- A NIH-sponsored longitudinal clinical trial involving over 1,000 elderly subjects performed at Rush University in Chicago determined that, on average, the incidence of AD occurred 10 years later in subjects with a high PBV and 10 years earlier in subjects with a low PBV. Subjects with a high PBV had a 62% lower incidence of AD than subjects with an average or low PBV after 6 years of follow-up.
- The NIH-sponsored Alzheimer's Disease Neuroimaging Initiative further confirmed that a high PBV was associated with a lower odds of AD and a reduced risk of future cognitive decline.
- Two random large population studies of people aged 30 to > 90 confirmed that PlsEtn levels decrease with advancing age

PBV MECHANISM

Plasmalogens make up a large proportion of the ethanolamine phospholipid portion of cellular membranes. They are structurally differentiated from other phospholipids by their vinyl ether bond which gives them their unique physiochemical and biological functions. Plasmalogen deficient membranes exhibit altered protein function resulting in increased production of Aβ-42, the pathological protein found in AD plaques and decreased vesicular fusion, the mechanism responsible for nerve transmission. Plasmalogens do not survive the human digestive tract so they cannot be obtained from the diet in appreciable amounts. They are made in the liver and distributed throughout the body. When the production of plasmalogens is less than what the body needs to maintain homeostasis, membrane levels decrease. When levels decrease below critical levels, pathological protein accumulation and reduced cognition is observed.

TEST METHOD

The current AlzID test is performed on 15µL of serum, collected using conventional phlebotomy. The assay is based on tandem mass spectrometry, and has been optimized to run on PDI's custom platform that can process up to 1000 samples per day. A proof-of-concept blood-spot version of AlzID has recently been developed to eliminate the need for conventional phlebotomy and improve distribution. The prototype product is based on a helical serum-separator technology that requires approximately two drops of blood from a finger-prick that can be performed in a person's home and mailed back to a central lab for analysis.

REGULATORY STATUS

AlzID is approved for use in Canada by Health Canada. The test is currently performed at Phenomenome Laboratory Services Inc (PLSI), a licensed medical laboratory in Saskatoon that is CLIA-compliant and certified by the College of American Pathologists (CAP) and the College of Physicians and Surgeons of Saskatchewan (SPSS).

INTELLECTUAL PROPERTY

Methods for the Diagnosis of Dementia and other Neurological Disorders. Issued: Canada, USA, France, Germany, Netherlands, Sweden, Switzerland, UK, Japan, New Zealand, Singapore. Expires: February 28, 2027;

PUBLICATIONS

- Goodenowe DB, Cook LL, Liu J, Lu Y, Jayasinghe DA, Ahiahonu PW, Heath D, Yamazaki Y, Flax J, Krenitsky KF et al: Peripheral ethanolamine plasmalogen deficiency: a logical causative factor in Alzheimer's disease and dementia. Journal of lipid research 2007, 48(11):2485-2498.
- Wood PL, Mankidy R, Ritchie S, Heath D, Wood JA, Flax J, Goodenowe DB: Circulating plasmalogen levels and Alzheimer Disease Assessment Scale-Cognitive scores in Alzheimer patients. J Psychiatry Neurosci 2010, 35(1):59-62.
- Wood PL, Khan AM, Mankidy R, Smith T, Goodenowe D: Plasmalogen Deficit: A New and Testable Hypothesis for the Etiology of Alzheimer's Disease. In: Alzheimer's Disease Pathogenesis-Core Concepts, Shifting Paradigms and Therapeutic Targets. Edited by De la Monte S: InTech; 2011.

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KEY POINTS

DEMENTIA AND AGING

The association between PBV and dementia was investigated in a longitudinal study involving 1060 elderly subjects. During the follow-up period (3.6 years on average) 92 new cases of dementia were observed. At follow-up 148 (13.8%) of the subjects had dementia.

Gender	n	ApoE ε2ε3/ε3ε3/ε4	Age	Dementia No | Yes	Age	Dementia No | Yes
Female	830	96 | 511 | 192	80.2±7.5	786 | 44	83.8±7.7	715 | 115
Male	230	34 | 140 | 49	80.9±7.1	218 | 12	84.3±7.2	197 | 33
Total	1060	130 | 651 | 241	80.3±7.4	1004 | 56	83.9±7.6	912 | 148

ODDS OF DEMENTIA

Odds of Dementia at Follow-Up

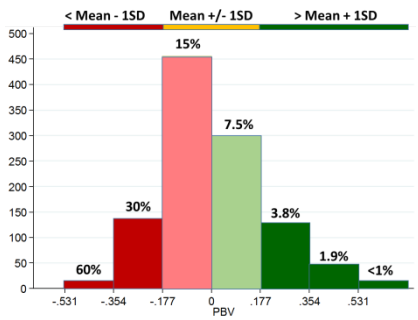
Variable	Odds Ratio	p
PBV	0.52	2.4e-08
APOE ε3ε3	Reference	
APOE ε2ε3	0.57	1.3e-01
APOE ε3ε4/ε4ε4	2.18	2.7e-04
Age	2.09	5.5e-11
Education	0.85	9.7e-01
Female	Reference	
Male	1.22	3.9e-01

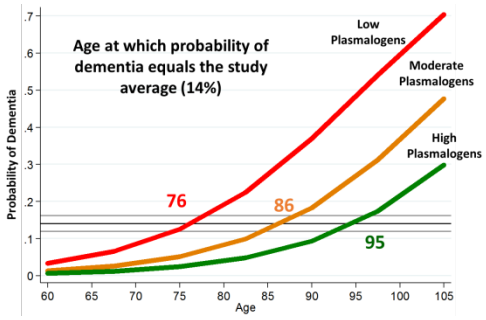
Odds of Becoming Demented

Variable	OR	p
PBV(BL)	0.57	2.9e-04
dPBV (BL-FU)	1.56	2.3e-03
ApoE ε3ε3	Reference	
ApoE ε2ε3	0.35	5.1e-02
ApoE ε3ε4/ε4ε4	2.27	1.5e-03
Age (BL)	1.91	2.7e-06
dAge (FU-BL)	1.67	2.0e-04
Education	0.95	6.6e-01
Female	Reference	
Male	1.28	3.8e-01

For each increase in PBV by one standard deviation the odds of having dementia decreased by approximately 50%. Furthermore, non-demented subject's with a high serum PBV were less likely to convert to dementia and non-demented subjects in which their PBV decreased from baseline during the follow-up period were more likely to develop dementia.

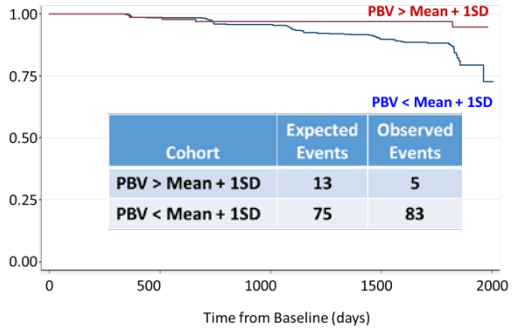
INCIDENCE OF DEMENTIA





For each increase in PBV by one standard deviation the incidence of dementia decreased by approximately 50%. Subjects with a high PBV have a very low incidence of dementia. Illustrated in a separate way, the age associated with the study incidence of dementia (13.8%) was 76 in subjects with a low PBV whereas subjects with a high PBV it was 95.

TIME TO AD



Cohort	Expected Events	Observed Events
PBV > Mean + 1SD	13	5
PBV < Mean + 1SD	75	83

Variable	Baseline All (n)	Baseline NCI	Baseline MCI	Baseline AD	At "Event" All (n)	At "Event" NCI	At "Event" MCI	At "Event" AD
Female	802	625	169	0	802	557	156	67
Male	225	159	62	0	225	157	42	23

1027 subjects without Alzheimer's Disease were followed for 6 years. During the follow-up period 90 new cases of AD were observed. However, the incidence of AD in subjects with a high PBV at baseline was 62% lower than subjects with a normal or a low PBV

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