CLAIMS

1. A method for identifying a subject as a candidate for further diagnostic testing and/or a therapeutic intervention for an amyloidosis disorder, the method comprising:
   (a) providing the age of the subject;
   (b) detecting an ApoE peptide and measuring the concentration of Aβ42 and Aβ40 and optionally a marker of neurodegeneration in a blood sample obtained from the subject, and then determining ApoE ε4 status, wherein the ApoE e4 status is the presence of epsilon 4 allele on an apolipoprotein E gene, calculating the Aβ42/Aβ40 value and optionally determining the concentration of the marker of neurodegeneration; and
   (c) identifying the subject as a candidate for further diagnostic testing and/or a therapeutic intervention for the amyloidosis disorder when
      (i) the subject is ApoE ε4 positive, and
         (1) the subject is at least 55 years old and the blood sample has an Aβ42/Aβ40 value of 0.1032 or less;
         (2) the subject is at least 60 years old and the blood sample has an Aβ42/Aβ40 value of 0.1094 or less;
         (3) the subject is at least 65 years old and the blood sample has an Aβ42/Aβ40 value of 0.1156 or less;
         (4) the subject is at least 70 years old and the blood sample has an Aβ42/Aβ40 value of 0.1218 or less;
         (5) the subject is at least 75 years old and the blood sample has an Aβ42/Aβ40 value of 0.128 or less;
         (6) the subject is at least 80 years old and the blood sample has an Aβ42/Aβ40 value of 0.1342 or less; or
         (7) the subject is at least 85 years old and the blood sample has an Aβ42/Aβ40 value of 0.1404 or less, or
      (ii) the subject is ApoE ε4 negative, and
         (1) the subject is at least 60 years old and the blood sample has an Aβ42/Aβ40 value of 0.1032 or less;
         (2) the subject is at least 65 years old and the blood sample has an Aβ42/Aβ40 value of 0.1094 or less;

(3) the subject is at least 70 years old and the blood sample has an Aβ42/Aβ40 value of 0.1156 or less;

(4) the subject is at least 75 years old and the blood sample has an Aβ42/Aβ40 value of 0.1218 or less;

(5) the subject is at least 80 years old and the blood sample has an Aβ42/Aβ40 value of 0.128 or less; or

(6) the subject is at least 85 years old and the blood sample has an Aβ42/Aβ40 value of 0.1342 or less.

2. A method for detecting Aβ amyloidosis, the method comprising:

(a) providing the age of the subject;

(b) detecting an ApoE peptide and measuring the concentration of Aβ42 and Aβ40 and optionally a marker of neurodegeneration in a blood sample obtained from the subject, and then determining ApoE ε4 status, wherein the ApoE e4 status is the presence of epsilon 4 allele on an apolipoprotein E gene, calculating the Aβ42/Aβ40 value and optionally determining the concentration of the marker of neurodegeneration; and

(c) identifying the subject as having or at risk of developing Aβ amyloidosis when

(i) the subject is ApoE ε4 positive, and

(1) the subject is at least 55 years old and the blood sample has an Aβ42/Aβ40 value of 0.1032 or less;

(2) the subject is at least 60 years old and the blood sample has an Aβ42/Aβ40 value of 0.1094 or less;

(3) the subject is at least 65 years old and the blood sample has an Aβ42/Aβ40 value of 0.1156 or less;

(4) the subject is at least 70 years old and the blood sample has an Aβ42/Aβ40 value of 0.1218 or less;

(5) the subject is at least 75 years old and the blood sample has an Aβ42/Aβ40 value of 0.128 or less;

(6) the subject is at least 80 years old and the blood sample has an Aβ42/Aβ40 value of 0.1342 or less; or

(7) the subject is at least 85 years old and the blood sample has an Aβ42/Aβ40 value of 0.1404 or less, or

(ii) the subject is ApoE ε4 negative, and

(1) the subject is at least 60 years old and the blood sample has an Aβ42/Aβ40 value of 0.1032 or less;

(2) the subject is at least 65 years old and the blood sample has an Aβ42/Aβ40 value of 0.1094 or less;

(3) the subject is at least 70 years old and the blood sample has an Aβ42/Aβ40 value of 0.1156 or less;

(4) the subject is at least 75 years old and the blood sample has an Aβ42/Aβ40 value of 0.1218 or less;

(5) the subject is at least 80 years old and the blood sample has an Aβ42/Aβ40 value of 0.128 or less; or

(6) the subject is at least 85 years old and the blood sample has an Aβ42/Aβ40 value of 0.1342 or less.

3. A method for grading a subject for a stage of an amyloidosis disorder, the method comprising:

(a) providing the age of the subject;

(b) detecting an ApoE peptide and measuring the concentration of Aβ42 and Aβ40 and optionally a marker of neurodegeneration in a blood sample obtained from the subject, and then determining ApoE ε4 status, wherein the ApoE e4 status is the presence of epsilon 4 allele on an apolipoprotein E gene, calculating the Aβ42/Aβ40 value and optionally determining the concentration of the marker of neurodegeneration; and

(c) identifying the subject as having or at risk of developing the amyloidosis disorder when

(i) the subject is ApoE ε4 positive, and

(1) the subject is at least 55 years old and the blood sample has an Aβ42/Aβ40 value of 0.1032 or less;

(2) the subject is at least 60 years old and the blood sample has an Aβ42/Aβ40 value of 0.1094 or less;

(3) the subject is at least 65 years old and the blood sample has an Aβ42/Aβ40 value of 0.1156 or less;

(4) the subject is at least 70 years old and the blood sample has an Aβ42/Aβ40 value of 0.1218 or less;

(5) the subject is at least 75 years old and the blood sample has an Aβ42/Aβ40 value of 0.128 or less;

(6) the subject is at least 80 years old and the blood sample has an Aβ42/Aβ40 value of 0.1342 or less; or

(7) the subject is at least 85 years old and the blood sample has an Aβ42/Aβ40 value of 0.1404 or less, or

(ii) the subject is ApoE ε4 negative, and

(1) the subject is at least 60 years old and the blood sample has an Aβ42/Aβ40 value of 0.1032 or less;

(2) the subject is at least 65 years old and the blood sample has an Aβ42/Aβ40 value of 0.1094 or less;

(3) the subject is at least 70 years old and the blood sample has an Aβ42/Aβ40 value of 0.1156 or less;

(4) the subject is at least 75 years old and the blood sample has an Aβ42/Aβ40 value of 0.1218 or less;

(5) the subject is at least 80 years old and the blood sample has an Aβ42/Aβ40 value of 0.128 or less; or

(6) the subject is at least 85 years old and the blood sample has an Aβ42/Aβ40 value of 0.1342 or less.

4. A method of selecting subjects for a clinical trial for treating Aβ amyloidosis, the method comprising:

(a) detecting an ApoE peptide and measuring the concentration of Aβ42 and Aβ40 and optionally a marker of neurodegeneration in a blood sample obtained from the subject, and then determining ApoE ε4 status, wherein the ApoE e4 status is the presence of epsilon 4 allele on an apolipoprotein E gene, calculating the Aβ42/Aβ40 value and optionally determining the concentration of the marker of neurodegeneration; and

(b) identifying the subject as a candidate for the clinical trial when

(i) the subject is ApoE ε4 positive, and

(1) the subject is at least 55 years old and the blood sample has an Aβ42/Aβ40 value of 0.1032 or less;

(2) the subject is at least 60 years old and the blood sample has an Aβ42/Aβ40 value of 0.1094 or less;

(3) the subject is at least 65 years old and the blood sample has an Aβ42/Aβ40 value of 0.1156 or less;

(4) the subject is at least 70 years old and the blood sample has an Aβ42/Aβ40 value of 0.1218 or less;

(5) the subject is at least 75 years old and the blood sample has an Aβ42/Aβ40 value of 0.128 or less;

(6) the subject is at least 80 years old and the blood sample has an Aβ42/Aβ40 value of 0.1342 or less; or

(7) the subject is at least 85 years old and the blood sample has an Aβ42/Aβ40 value of 0.1404 or less, or

(ii) the subject is ApoE ε4 negative, and

(1) the subject is at least 60 years old and the blood sample has an Aβ42/Aβ40 value of 0.1032 or less;

(2) the subject is at least 65 years old and the blood sample has an Aβ42/Aβ40 value of 0.1094 or less;

(3) the subject is at least 70 years old and the blood sample has an Aβ42/Aβ40 value of 0.1156 or less;

(4) the subject is at least 75 years old and the blood sample has an Aβ42/Aβ40 value of 0.1218 or less;

(5) the subject is at least 80 years old and the blood sample has an Aβ42/Aβ40 value of 0.128 or less; or

(6) the subject is at least 85 years old and the blood sample has an Aβ42/Aβ40 value of 0.1342 or less.

5. The method of claim 1, wherein the further diagnostic test is selected from

(a) a cerebral spinal fluid (CSF) test that measures the concentration of one or more biomolecules in the CSF, wherein the one or more biomolecules are selected from Aβ peptide, tau, phospho-tau, neurofilament light chain, visinin-like protein one, or ApoE;

(b) a structural imaging test selected from magnetic resonance imaging (MRI) or computed tomography (CT);

(c) a functional imaging test selected from positron emission tomography (PET), functional magnetic resonance imaging (fMRI), or fluorodeoxyglucose (FDG)-PET; or

(d) a molecular imaging test selected from Pittsburgh compound B (PIB)-PET, florbetaben-PET, florbetapir-PET, or flutemetamol-PET.

6. The method of any one of claims 1-5, wherein the method is performed using immunoprecipitation and mass spectrometry (IP/MS)

7. The method of any one of claims 1-6, wherein the method is performed in a single assay.

8. The method of any one of the preceding claims, wherein the probability of diagnosing the disease is calculated using a receiver operating curve (ROC) area under the curve (AUC).

9. The method of any one of the preceding claims, wherein a predetermined threshold is determined by a data point of the highest specificity at the highest sensitivity on the ROC curve.

10. The method of any one of the preceding claims, wherein the marker of neurodegeneration is selected from one or more of neurofilament light chain (Nfl), a tau isoform, visinin-like protein 1, a neurogranin isoform, phosphorylated Tau, TDP-43, a-synuclein, SOD-1, FBP1, FUS, FKBP51, IRS-1, phosphorylated IRS-1, cathepsin D (CTSD), type 1 lysosome-associated membrane protein (LAMP1), a ubiquitinylated protein (UBP), heat-shock protein 70 (HSP70), neuron-specific enolase (NSE), CD9, CD63, CD81, CD171, BACE1, amyloid beta precursor protein, GHR, PD-1, APEX1, huntingtin, PRKN, or PSEN1.

11. The method of any one of the preceding claims, wherein the subject (a) was not previously diagnosed with Aβ amyloidosis, (b) is asymptomatic, (c) is a potential participant in a clinical trial for a disease associated with Aβ amyloidosis, (d) is a candidate for amyloid imaging, or (e) any combination of (a) through (d).

12. The method of claim 4 further comprising determining a treatment to be administered based on the grade of Aβ amyloidosis.

13. The method of claim 12, wherein the treatment to be administered is a non-pharmacological treatment, a pharmacological treatment, or treatment with an imaging agent followed by detection of the imaging agent.

14. The method of claim 13, wherein the imaging agent is a functional imaging agent or a molecular imaging agent.

15. The method of claim 12, wherein the treatment to be administered is a non-pharmacological treatment.

16. The method of claim 12, wherein the treatment to be administered is a pharmacological treatment.

17. The method of claim 13, wherein the treatment to be administered is administered through a clinical trial.

18. A kit, comprising

(a) a means for determining age, ApoE ε4 status, and/or an Aβ42/Aβ40 value in a subject in need thereof; and

(b) instructions for use according to the method of any one of claims 1-17.