**Table S1** Cross-classified results of IWG-1, IWG-2, and AT(N) criteria for diagnosing AD

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| IWG-1 | IWG-2=1 | |  | IWG-2=0 | |
| AT(N)=1 | AT(N)=0 |  | AT(N)=1 | AT(N)=0 |
| IWG-1=1 | 19 | 58 |  | 0 | 22 |
| IWG-1=0 | 0 | 0 |  | 209 | 600 |

**Notes:** “1” represents a patient diagnosed with AD, “0” represents a patient diagnosed with non-AD.

**Table S2** Cross-classified results of IWG-2 and AT(N) criteria for diagnosing preclinical AD

|  |  |  |
| --- | --- | --- |
| AT(N) | IWG-2 | |
| IWG-2=1 | IWG-2=0 |
| AT(N)=1 | 329 | 28 |
| AT(N)=0 | 151 | 114 |

**Notes:** “1” represents a patient diagnosed with preclinical AD. “0” represents a patient diagnosed with non-preclinical AD.

**Latent class model with fixed effect dependent**

We used the latent class model with fixed effect dependent to evaluate the diagnostic accuracy of the IWG-1, IWG-2 and AT(N) criteria for the diagnosis of AD in the absence of a gold standard.

Let *T*1, *T*2, *T*3 denote the diagnostic results of the IWG-1, IWG-2, and AT(N) criteria, where *T*1, *T*2, and *T*3 =0,1, with "1" indicating the presence of AD, and "0" indicating the absence of AD. let *D* denote the true status of the person with AD, which is not observed in the study. The parameters of interest include: the prevalence of AD in the population, *π*, defined as *π = P(D=1)*; the sensitivity of the *i*th diagnostic criteria for detecting AD, *Sei*, defined as *Sei* = *P(Ti=1|D=1)*; and the specificity of the *i*th diagnostic test for detecting AD, *Spi*, defined as *Spi = P(Ti=0|D=0)*, where *i* = 1,2,3.

Assume that there are *n* participants in the sample and three diagnostic criteria results for every subject. We represent the observed data as *Y* = (*Yt1, t2, t3*), where *Yt1, t2, t3* is the number of subjects with *T*1= *t1*, *T*2 = *t2*, and *T*3 = *t3*; here *t1*, *t2*, *t3* = 0, 1. For example, Y111 denotes the number of subjects whose diagnostic results for all three criteria indicate that the AD is present.

IWG-2 was revised on the base of IWG-1 criteria, the diagnostic results of these two criteria might be correlated in detecting AD. Therefore, it is reasonable to assume that IWG-1 and IWG-2 are conditionally dependent given the true disease status. We model the pairwise dependence using the covariance between tests, such as *covDp* and *covDn*, which measured the dependence of IWG-1 and IWG-2 among the AD or non-AD subject, respectively.

Let *Y = (Y111, Y110, Y101, Y100, Y011, Y010, Y001, Y000)*, the observed data, and *θ = (Se1, Sp1, Se2, Sp2, Se3, Sp3, π, covDp, covDn)*, which represents the set of parameters in the model. The likelihood function based on the observed data is:

To estimate these parameters using Bayesian methods, we need to specify a prior distribution for them. The prevalence, sensitivities and specificities are assumed to follow a *beta* prior distribution. The informative priors were obtained by relevant literature, which has been mentioned in the manuscripts (**Table S3**). To be valid covariances, *covDp* and *covDn* need to ensure that the probability of each combination is between 0 and 1. Therefore, necessary constraints as follows.

It was difficult to directly obtain the posterior estimator of each parameter through a numerical integration method in the Bayesian model. we used the MCMC algorithm

to draw a random sample from the joint posterior distribution. We then computed the sample median of the randomly drawn sample to estimate θ and its components of

interest. In this study, the WinBUGS package was used to perform this MCMC process.

**Latent class model with independent assumption**

The latentclass model with independent assumption for assessing the diagnostic accuracy of IWG-2 and AT(N) in detecting preclinical AD without a gold standard was similar to the above model. In this model, IWG-2 and AT(N) were independent, it was the simplified version of the latent class model with fixed effect dependent. We will not repeat the details.

**Table S3** Prior information of the parameters in latent class models for evaluating the performance of IWG-1, IWG-2, and AT(N) criteria in diagnosing AD, and assessing the performance of IWG-2and AT(N) criteria in detecting preclinical AD

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | AD | | Preclinical AD | |
|  | mode value | Distribution | mode value | Distribution |
| Prevalence | 0.01 | Beta (661.36,10.38) | 0.22 | Beta (196.56,54.47) |
| *Se* IWG-1 | 0.86 | Beta (42.91,7.82) | - | - |
| *Se* IWG-2 | 0.84 | Beta (111.48,30.37) | 0.80 | Beta (75.65,19.78) |
| *Se* AT(N) | 0.67 | Beta (84.25,16.86) | 0.96 | Beta (102.29,5.22) |
| *Sp* IWG-1 | 0.96 | Beta (28.31,9.82) | - | - |
| *Sp* IWG-2 | 0.76 | Beta (25.59,13.11) | 0.93 | Beta (175.25,15.13) |
| *Sp* AT(N) | 0.75 | Beta (72.93,24.98) | 0.81 | Beta (40.81,16.10) |
| *Cd* | - | Unif (lc, uc) | - | Unif (lc, uc) |
| *Cn* | - | Unif (ls, us) | - | Unif (ls, us) |

Abbreviations:AD, Alzheimer's disease; *Se*, sensitivity; *Sp*, Specificity; *Cd*, the covariance between IWG-1 and IWG-2 under true disease status; *Cn*, the covariance between IWG-1 and IWG-2 under true non-disease status; Beta: Beta distribution; Unif: Uniform distribution; lc=-(1-*Sp* IWG-1) (1-*Sp* IWG-2); uc=min(*Sp* IWG-1,*Sp* IWG-2) - *Sp* IWG-1\* *Sp* IWG-2; ls=-(1-*Se* IWG-1) (1-*Se* IWG-2); us=min(*Se* IWG-1,*Se* IWG-2) - *Se* IWG-1\* *Se* IWG-2.

ADNI-1, ADNI-GO, ADNI-2, and ADNI-3

(n=908)

(n=908)

IWG-1

Non-AD

(n=809)

IWG-2

Non-AD

(n=831)

AD

(n=77)

AT(N)

Non-AD

(n=641)

AD

(n=267)

AD

(n=99)

**Figure S1** Classification of subjects with AD according to IWG-1, IWG-2 and AT(N) criteria

Abbreviations:AD, Alzheimer's disease; IWG, International Working Group.

IWG-2

Preclinical AD

(n=480)

AT(N)

Preclinical AD

(n=357)

Non-preclinical AD

(n=265)

Non-preclinical AD

(n=142)

ADNI-1, ADNI-GO, ADNI-2, and ADNI-3

(n=622)

**Figure S2** Classification of subjects with preclinical AD according to IWG-2 and AT(N) criteria

Abbreviations:AD, Alzheimer's disease; IWG, International Working Group.