Alzheimer’s research

1. Notes from [In-depth insights into Alzheimer’s disease by using explainable machine learning approach | Scientific Reports (nature.com)](https://www.nature.com/articles/s41598-022-10202-2)

On the model:

 “The data set used is medium sized with average number of features allowing to experiment with more complex algorithms. Hence, the classifier built in this research uses **XGBoost** algorithm. Proven to show several advantages above other classification algorithms[47](https://www.nature.com/articles/s41598-022-10202-2#ref-CR47), XGBoost requires less feature engineering, meaning there is no need for scaling and normalizing data. It is less prone to overfitting if the hyperparameters are tuned properly.“

We must pay “special attention to the hyperparameters tuning.”

“XGBoost produced a f1-score of 0.84 and as such is considered to be highly competitive among those published in the literature. “

On the predictor variables:

Biomarkers and medical imaging are used in all the best models, so we can’t hope to get state of the art results without real medical measurements. ☹

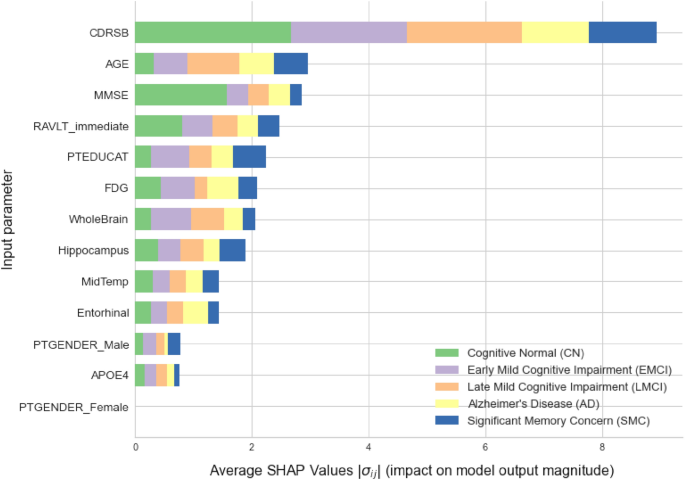
They emphasize that some of the most important measurements are from gene expression and MRI brain scans.

Some of their selected predictor variables are:

* *Age*–starting at about age of 65, the probability of getting AD doubles every 5 years[21](https://www.nature.com/articles/s41598-022-10202-2#ref-CR21),[22](https://www.nature.com/articles/s41598-022-10202-2#ref-CR22).
* *Gender*
* *Years of education- More important than (Age + Gender) \*2*
* *Race*
* *Cognitive tests*:
  + *CDRSB*: Clinical Dementia Rating Scale - Sum of Boxes.
  + *ADAS11*: Alzheimer’s Disease Assessment Scale 11.
  + *MMSE*: Mini-Mental State Examination.
  + *RAVLT\_immediate*: Rey Auditory Verbal Learning Test (sum of scores from 5 first trials).

*Some suspected influences are*:

* *Medical conditions*–type 2 diabetes, high blood pressure, high cholesterol, obesity[25](https://www.nature.com/articles/s41598-022-10202-2#ref-CR25), or depression[26](https://www.nature.com/articles/s41598-022-10202-2#ref-CR26) are known to increase the risk of developing dementia.
* *Lifestyle factors*–physical inactivity[27](https://www.nature.com/articles/s41598-022-10202-2#ref-CR27), smoking[28](https://www.nature.com/articles/s41598-022-10202-2#ref-CR28), unhealthy diet[29](https://www.nature.com/articles/s41598-022-10202-2#ref-CR29), excessive alcohol[30](https://www.nature.com/articles/s41598-022-10202-2#ref-CR30), or head injuries[31](https://www.nature.com/articles/s41598-022-10202-2#ref-CR31).



In order of correlation: Clinical Dementia Rating Scale - Sum of Boxes

Age

Mini-Mental State Examination.

Rey Auditory Verbal Learning Test (sum of scores from 5 first trials).

Years of education

measure cell metabolism, where cells affected by AD show reduced metabolism.

On imputation:

“Considering the data imputation methods applied, as it can be seen from the bar chart presented in Fig. [6](https://www.nature.com/articles/s41598-022-10202-2#Fig6), Extra Trees Regressor and Bayesian Ridge estimated values are closest to the original data. Both of them are multivariate algorithms. On the other hand, univariate algorithms using mean and median failed to do the estimation very accurately, which is somewhat expected considering the fact that the data set contains features represented by sensitive data values where simple average does not solve the problem.”

“Evaluation results suggest that the SMOTE oversampling algorithm provides the best results”

1. Notes from [A Machine Learning‐Based Approach for Classification of Alzheimer’s Disease and its Risk Prediction - Kasani - 2022 - Alzheimer's & Dementia - Wiley Online Library](https://alz-journals.onlinelibrary.wiley.com/doi/10.1002/alz.064066)

“Based on the performance evaluation, the XGBoost classifier significantly outperformed all other models and achieved 82.55% accuracy followed by the Bagging classifier (81%). According to the XGBoost model, calculating risk factors to predict performance, the Consortium to Establish a Registry for AD (CERAD) subsets is among the highest ranked feature. It was intriguing that the parameters including job, job levels and retirement achieved a minimal, if any, impact in the final performance.”

From some random study: “some of the measures, in particular delayed recall of the word list, could efficiently distinguish persons with dementia from those with normal cognition.”

1. Notes from [International Journal of Geriatric Psychiatry | Wiley Online Library](https://onlinelibrary.wiley.com/doi/10.1002/gps.6007)

“Higher levels of depression and anxiety are consistently associated with subjective cognitive decline (SCD),[22](https://onlinelibrary.wiley.com/doi/10.1002/gps.6007#gps6007-bib-0022) aMCI,[23](https://onlinelibrary.wiley.com/doi/10.1002/gps.6007#gps6007-bib-0023),[24](https://onlinelibrary.wiley.com/doi/10.1002/gps.6007#gps6007-bib-0024) and AD[25](https://onlinelibrary.wiley.com/doi/10.1002/gps.6007#gps6007-bib-0025) and may be used as predictors for these cognitive states. Comparisons of affective symptoms between SCD/MCI and SCD/AD have yielded inconsistent results, but higher prevalence of depressive symptoms is observed compared to healthy controls.[22](https://onlinelibrary.wiley.com/doi/10.1002/gps.6007#gps6007-bib-0022) Higher anxiety and depression levels increase the risk of converting from (a)MCI to AD[26](https://onlinelibrary.wiley.com/doi/10.1002/gps.6007#gps6007-bib-0026)-[29](https://onlinelibrary.wiley.com/doi/10.1002/gps.6007#gps6007-bib-0029) and treatment of these conditions might potentially reduce the conversion rate.[30](https://onlinelibrary.wiley.com/doi/10.1002/gps.6007#gps6007-bib-0030) Additionally, the rate of cognitive decline is reported to be influenced by the age of depression onset.[31](https://onlinelibrary.wiley.com/doi/10.1002/gps.6007#gps6007-bib-0031) There is ongoing debate regarding whether depression constitutes a risk factor or an initial manifestation of AD, or both.[32](https://onlinelibrary.wiley.com/doi/10.1002/gps.6007#gps6007-bib-0032)-[34](https://onlinelibrary.wiley.com/doi/10.1002/gps.6007#gps6007-bib-0034)”

They found that personality, prevalence of depression and anxiety were useful for prediction.

4.) Tips for reducing your risk and reducing impact:

For those diagnosed with dementia, there are things that can help manage symptoms:

* Stay physically active.
* Eat healthily.
* Stop smoking and drinking alcohol.
* Get regular check-ups with your doctor.
* Write down everyday tasks and appointments to help you remember important things.
* Keep up your hobbies and do things that you enjoy.
* Try new ways to keep your mind active.
* Spend time with friends and family and engage in community life.

Plan ahead of time. Over time, it may be harder to make important decisions for yourself or your finances:

* Identify people you trust to support you in making decisions and help you communicate your choices.
* Create an advance plan to tell people what your choices and preferences are for care and support.
* Bring your ID with your address and emergency contacts when leaving the house.
* Reach out to family and friends for help.
* Talk to people you know about how they can help you.
* Join a local support group.

Common risk factors include:

* age (more common in those 65 or older)
* high blood pressure (hypertension)
* high blood sugar (diabetes)
* being overweight or obese
* smoking
* drinking too much alcohol
* being physically inactive
* being socially isolated
* depression.
* cholesterol
* low educational attainment
* cognitive inactivity
* air pollution

[Reduce your risk of dementia | Alzheimer's Society (alzheimers.org.uk)](https://www.alzheimers.org.uk/about-dementia/managing-the-risk-of-dementia/reduce-your-risk-of-dementia)

[Preventing Dementia | Stanford Health Care](https://stanfordhealthcare.org/medical-conditions/brain-and-nerves/dementia.html)

From Harvard Medical School:

Healthy habits may help ward off Alzheimer's. Consider the following steps to help prevent Alzheimer’s.

Exercise. "The most convincing evidence is that physical exercise helps prevent the development of Alzheimer's or slow the progression in people who have symptoms," says Dr. Marshall. "The recommendation is 30 minutes of moderately vigorous aerobic exercise, three to four days per week."

Eat a Mediterranean diet. "This has been shown to help thwart Alzheimer's or slow its progression. A recent study showed that even partial adherence to such a diet is better than nothing, which is relevant to people who may find it difficult to fully adhere to a new diet," says Dr. Marshall. The diet includes fresh vegetables and fruits; whole grains; olive oil; nuts; legumes; fish; moderate amounts of poultry, eggs, and dairy; moderate amounts of red wine; and red meat only sparingly.

Get enough sleep. "Growing evidence suggests that improved sleep can help prevent Alzheimer's and is linked to greater amyloid clearance from the brain," says Dr. Marshall. Aim for seven to eight hours per night.

## Not as certain

We have some—but not enough—evidence that the following lifestyle choices help prevent Alzheimer's.

Learn new things. "We think that cognitively stimulating activities may be helpful in preventing Alzheimer's, but the evidence for their benefit is often limited to improvement in a learned task, such as a thinking skills test, that does not generalize to overall improvement in thinking skills and activities of daily living," says Dr. Marshall.

Connect socially. "We think that greater social contact helps prevent Alzheimer's," explains Dr. Marshall, but so far, "there is only information from observational studies."

Drink—but just a little. There is conflicting evidence about the benefit of moderate alcohol intake (one drink per day for women, one or two for men) and reduced risk of Alzheimer's. "It is thought that wine in particular, and not other forms of alcohol, may be helpful, but this has not been proved," says Dr. Marshall.

From AARP:

Some of the methods doctors use to help diagnose dementia:

* **Cognitive and neuropsychological tests** assess language and math skills, memory, problem-solving and other types of mental functioning.
* **Blood tests** are [relatively new](https://www.aarp.org/health/conditions-treatments/info-2024/blood-test-for-alzheimers.html) when it comes to diagnosing dementia and are not yet widespread in﻿ clinical settings, though that could soon change. Doctors can order ﻿t﻿e﻿s﻿t﻿s to measure levels of beta-amyloid and p-tau217, hallmark﻿s of Alzheimer’s disease.
* **Brain scans** such as MRI or PET imaging can spot changes in brain structure and function. These tests also can identify strokes, tumors and other problems that can cause dementia.
* **Psychiatric evaluation** can determine whether a [mental health condition](https://www.aarp.org/health/conditions-treatments/info-2024/white-coat-syndrome.html) is causing or affecting the symptoms.
* **Genetic tests** may be helpful if someone is showing symptoms before age 60. The early-onset form of Alzheimer’s is strongly linked to a person’s genes, according to the Mayo Clinic. Talk with a genetic counselor before and after getting tested.​ ​

**In conclusion**

The predictor variables we should be looking for are:

1. Age
2. Education
3. Gender
4. Income
5. Social Life
6. Depression
7. Anxiety
8. Therapy
9. Family History(could be replaced by genes for greater accuracy, but less people will be able to answer)
10. Cognitive tests
    1. Rey Auditory Verbal Learning Test.
    2. Mini Mental-State Examination.
    3. Clinical Dementia Rating Scale - Sum of Boxes.
    4. Alzheimer’s Disease Assessment Scale 11.
11. Smoking
12. Exercise
13. Diet
14. Sleep
15. Alcohol
16. Weight
17. Blood pressure
18. Blood sugar
19. Cholesterol
20. Head Injuries

For prevention and mitigation, these are likely some of the steps people should take:

1. General Health
   1. Sleep
   2. Exercise (especially important)
   3. Smoking
   4. Therapy
   5. Weight
2. Mediterranean Diet [Mediterranean Full Text (biomedcentral.com)](https://bmcmedicine.biomedcentral.com/articles/10.1186/s12916-023-02772-3)
3. Mental Stimulation
   1. Learn new things (The languages thing is false)
   2. Social Life
   3. Higher level of Education (especially important)

The optimal model will likely be XGBoost.

The optimal imputation method will likely be SMOTE oversampling algorithm.