



# On the personal utility of Alzheimer's disease-related biomarker testing in research

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# What is a biomarker?

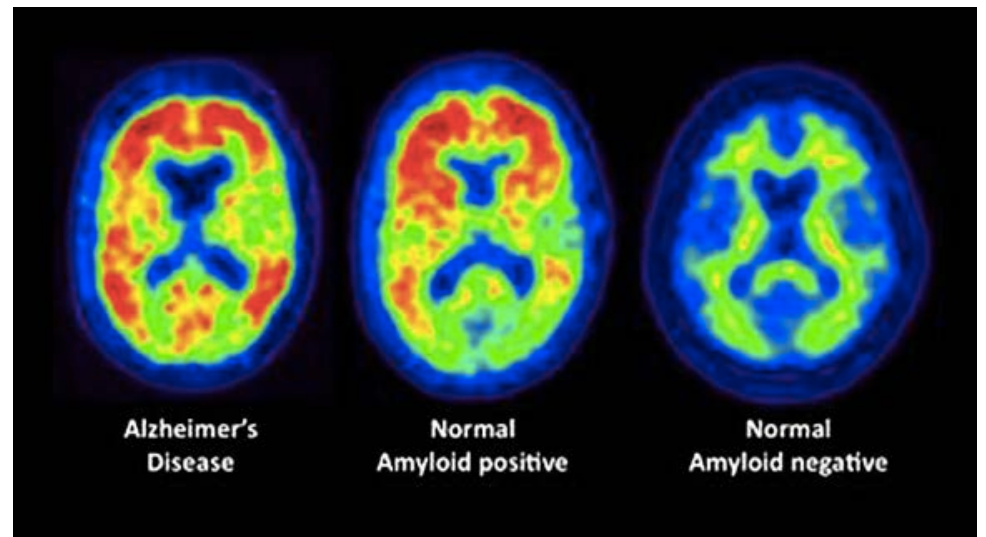
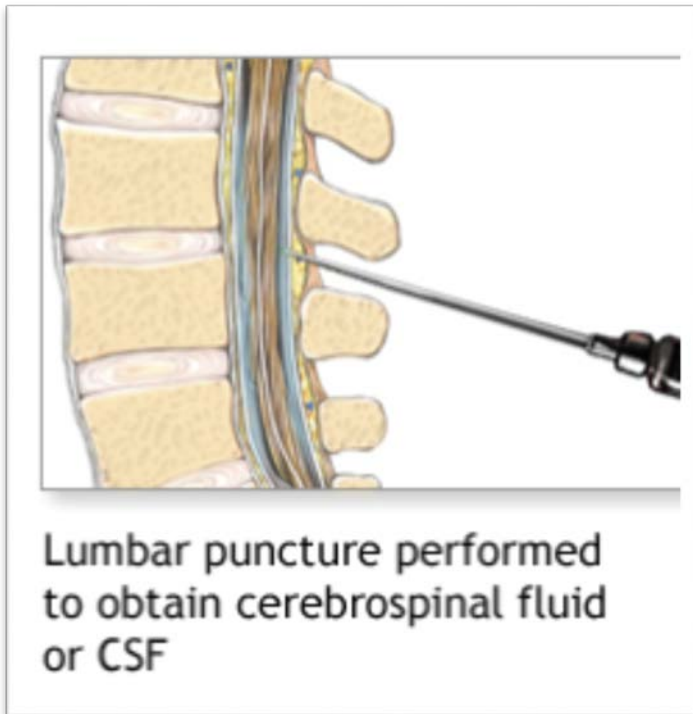
“a characteristic that is objectively measured and evaluated as an indicator of [...] pathogenic processes.”

(National Institutes of Health (NIH) Biomarkers Definitions Working Group, 1998)

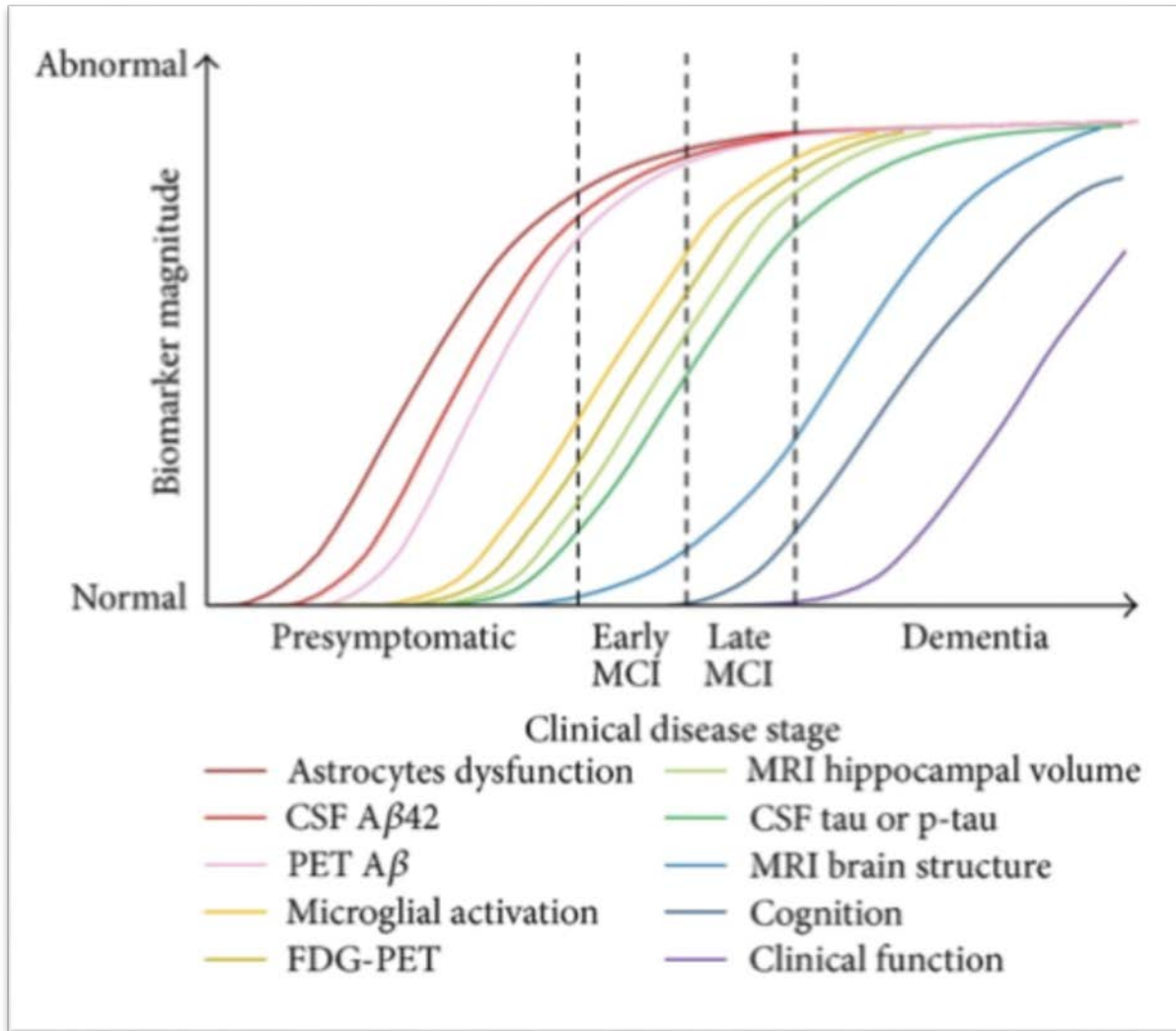
- A biomarker is a measurable sign of disease (or of a risk factor for disease)

# Alzheimer's disease biomarkers

1. Biomarkers in cerebrospinal fluid (CSF)
2. Imaging biomarkers (MRI, PET)
3. Genetic biomarkers (ADAD genes, ApOE)



# Alzheimer's disease cascade hypothesis



# Secondary prevention studies

In AD biomarker positive research participants in the very early stages of AD

These can be healthy volunteers free from cognitive complaints

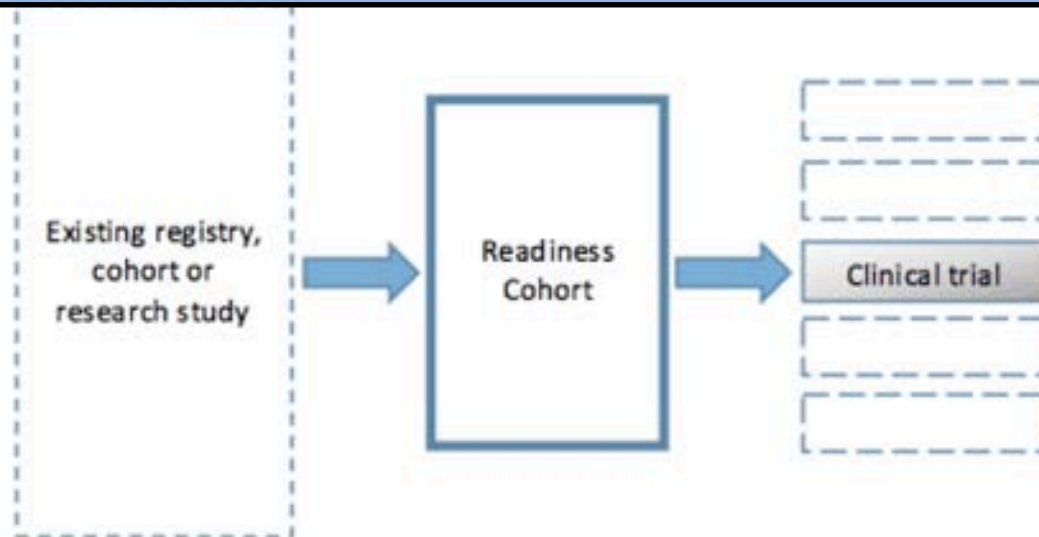


Figure 1. Simplified model of a readiness cohort drawn from existing studies and leading to one or several clinical trials

# Disclosure of AD biomarkers

- Should these volunteers (routinely) be informed about AD biomarker test results?
- There is a right to access personal data
- What are good reasons (not) to actively disclose?

Risk of harm



“Personal utility”

# Little is known about the risk of harm



## Alzheimer's Research & Therapy

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ABOUT

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### Psychological, behavioral and social effects of disclosing Alzheimer's disease biomarkers to research participants: a systematic review

S. A. S. A. Bemelmans, K. Tromp, E. M. Bunnik, R. J. Milne, S. Badger, C. Brayne, M. H. Schermer and E. Richard 

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# What does personal utility mean?

As an alternative/as complementary to *clinical utility*

Examples:

- changing one's life
- arranging one's financial affairs (e.g. life insurance)
- advance care planning
- preparing oneself or one's family members for the possibility of AD
- making altruistic contributions to scientific research

(Grosse et al. 2009, Kopits et al. 2011, Roberts et al. 2013)



# Modelled on clinical utility

A biomarker test should:

- Inform clinical management
  - Improve health or well-being
    - > options should be available, accessible and effective
    - > options should be more (cost-)effective than existing options
- Likewise, biomarker tests should change and improve one's life

# What is utility?

**'util-i-ty**  *noun* \yü-ti-lə-tē\  
A blue rounded rectangle containing the word 'utility' with a speaker icon, the word 'noun', and the phonetic transcription '\yü-ti-lə-tē\'. Below the word are three definitions.

: the quality or state of being useful

: a service (such as a supply of electricity or water) that is provided to the public

: a company that provides electricity, water, etc.

*plural* **util-i-ties**

**Full Definition of UTILITY** .....



**1** : fitness for some purpose or worth to some end

**2** : something useful or designed for use

**Origin of UTILITY** .....

Middle English *utilite*, from Anglo-French *utilité*, from Latin *utilitat*, *utilitas*, from *utilis* useful, from *uti* to use

First Known Use: 14th century

# A definition of personal utility

Two preconditions:

- Clinical validity
  - Reasonable personal use (including: an answer to a question)
- Personal utility is not the same as a subjective experience of value
- People can be mistaken about personal utility

PAPER

## Personal utility in genomic testing: is there such a thing?

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### ABSTRACT

In ethical and regulatory discussions on new applications of genomic testing technologies, the notion of 'personal utility' has been mentioned repeatedly. It has been used to justify direct access to commercially offered genomic testing or feedback of individual research results to research or biobank participants. Sometimes research

ests have given rise to ethical and regulatory discussions, in which concerns are expressed with regard to quality assurance, psychological and social risks and implications of testing, and informed consent. Moreover, commercially offered genomic testing does not appear to lead to any health benefit.<sup>1</sup> Lately, however, health benefit no longer seems to

# Are AD biomarkers personally useful?

Open Access Research

BMJ open

## MRI and cerebrospinal fluid biomarkers for predicting progression to Alzheimer's disease in patients with mild cognitive impairment: a diagnostic accuracy study

Edo Richard,<sup>1</sup> Ben A Schmand,<sup>1,2</sup> Piet Eikelenboom,<sup>1,3</sup> Willem A Van Gool,<sup>1</sup> The Alzheimer's Disease Neuroimaging Initiative

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**ABSTRACT**  
**Objectives:** To assess the incremental value of MRI and cerebrospinal fluid (CSF) analysis after a short memory test for predicting progression to Alzheimer's disease from a pragmatic clinical perspective.  
**Design:** Diagnostic accuracy study in a multicentre prospective cohort study.  
**Setting:** Alzheimer Disease Neuroimaging Initiative participants with complete data on neuropsychological

**ARTICLE SUMMARY**  
**Article focus**  
■ Although often applied in practice, it is not known to what extent MRI and cerebrospinal fluid (CSF) analysis improve diagnostic accuracy.  
■ Reports on diagnostic accuracy of MRI and CSF-analysis in dementia in general do not address the topic from a pragmatic clinical

- After the administration of a brief test of memory, MRI or CSF does not substantially affect diagnostic accuracy for Alzheimer's disease in patients with mild cognitive impairment.

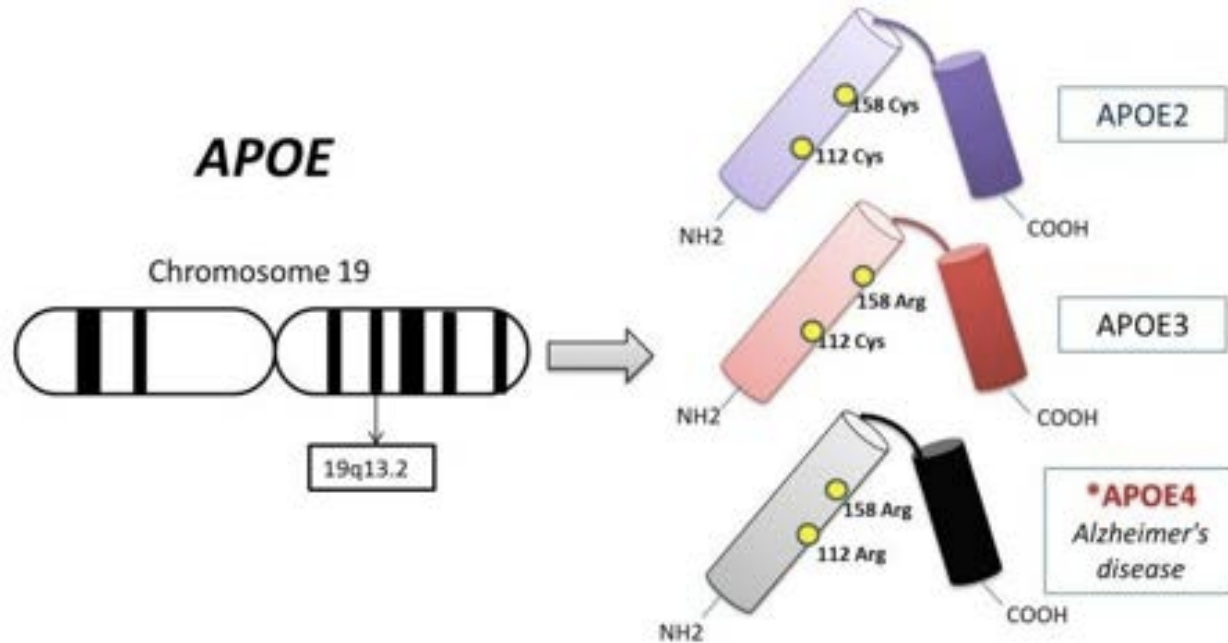
AD biomarkers (e.g. MRI, CSF, PET) are of little clinical validity: they do not distinguish those who will develop AD from those who will not, especially in healthy people.

## Are AD biomarkers personally useful? (II)

Because of its limited clinical validity, AD biomarker information:

- Does not answer a question
  - Cannot be used in any reasonable manner
- In healthy volunteers/people with SCD/MCI, AD biomarker information has little/no personal utility

# What about the ApoE gene?



# Conclusions

Personal utility does not equal a subjective experience of value

Recommendations for individuals:

- Not to use information of limited clinical validity, personally or clinically
- Learn how to deal with inherent uncertainty

Recommendations for researchers:

- No need to routinely disclose biomarker information
- Personal utility not always a reason to disclose
- Communicate that AD biomarker information is *not* a diagnosis
- Not to recommend clinical/personal actions

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