

Ethical challenges associated with prediction and early detection of dementia

Dr Richard Milne

The promise of prediction

Right to know

Support ability to plan, manage health

Maximise treatment possibilities,

Obtain early access to care and support

Right to access a diagnosis

The problems of prediction

Right not to know

Limited predictive power

Limited options for action

Risk of harm

Potential for overtreatment and medicalisation

Stigma, employment and insurance implications

Unequal access

Prediction in practice

FDA allows 23andMe to sell genetic tests for 10 diseases

Guidance on ApoE recommends against general clinical use in asymptomatic population

- limited clinical utility
- poor predictive value (Goldman et al. 2011)

Amyloid guidance similar (Johnson et al. 2013)

Challenges:

- *Direct to consumer and interest* (Horton et al. 2019)
- *Research/clinic boundary*
- *Clinical trial recruitment*



Ethics in EPAD and beyond

EPAD/AMYPAD workgroup on ethical, legal and social implications of move to prevention and early detection in Alzheimer's disease

Empirical ethics study of emerging diagnostic technologies (SPACE)

Recruitment

Informed (staged) consent

Incidental findings

Communicating biomarker results

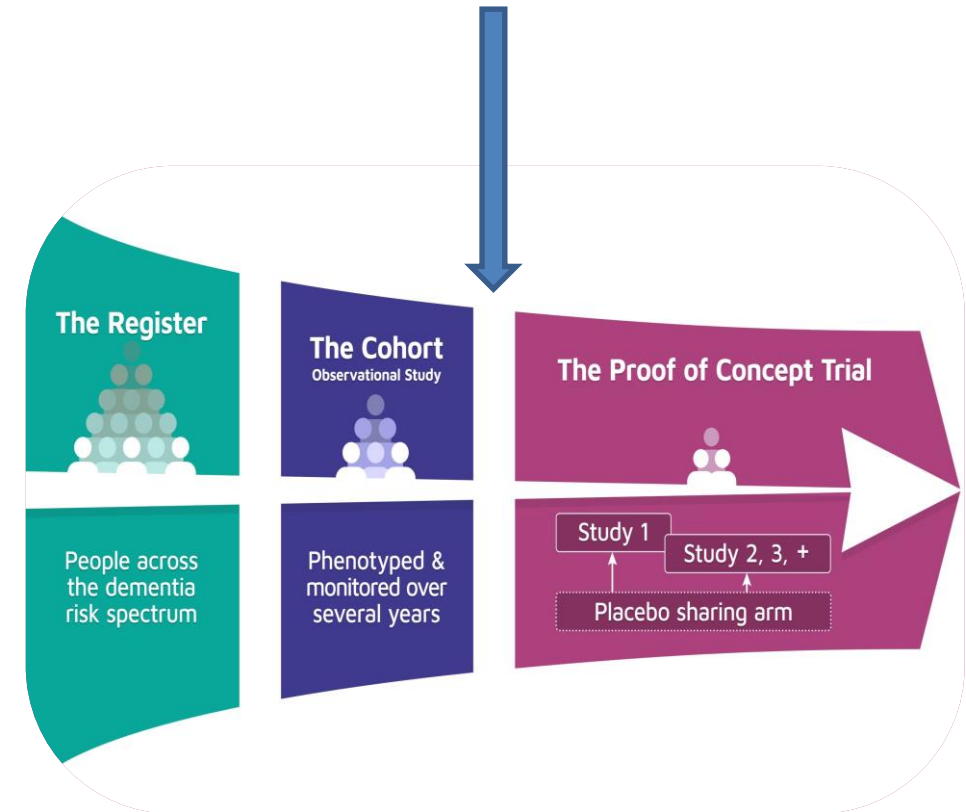
Participant representation

The clinical trial platform

EPAD involves recruitment from a cohort study to a phase II clinical trial targeting 'high risk' populations

Individual research results should be returned to research participants only when clinically valid and actionable.

When research participants are invited to take part in a clinical trial, they should be informed about the reason why they were selected.



What are the consequences of risk communication

Sunday Review

What if You Knew Alzheimer's Was Coming for You?

Simple blood tests may soon be able to deliver alarming news about your cognitive health.

By PAGAN KENNEDY NOV. 17, 2017

ApoE

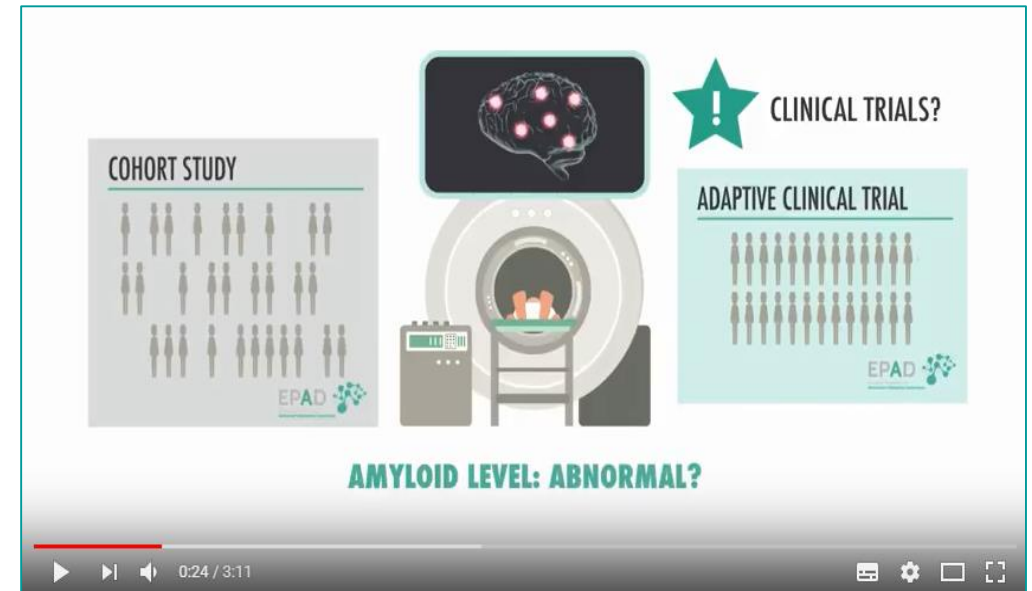
Among cognitively healthy research participants disclosure of ApoE ϵ 4-positivity in a trial setting:

- does not lead to elevated anxiety and depression levels,
- does increase test-related distress
- some evidence of a nocebo effect (Lineweaver et al. 2014)
- results in behaviour changes concerning insurance and health (Chao et al. 2008)
- does not reliably effect individual's baseline risk perception
- but does affect people's perception of the benefits and drawbacks of genotype-based risk information (Christensen et al. 2011)
- Dominated by REVEAL and US context

- Studies of abnormal **amyloid disclosure** to cognitively normal individuals **in a trial setting** suggest low risk of psychological harm (cf de Wilde et al. 2018; Burns et al. 2017)
- Very few studies yet published, predominantly attached to clinical trials
- Interest in results drops when uncertainties made clear (Gooblar et al. 2016; Milne et al. 2017)
- Importance of clarity about terminology and communication
 - Not a clear binary result

The importance of communication

- Link between impact of risk and quality of communication (cf REVEAL II)
- Protocols for amyloid disclosure developed for clinical trials (A4, EARLY, EPAD) often derived from HD/genetics experience
- Involve stages of education/information, screening and informed consent, disclosure discussion, follow up
- Challenges in terms of discussing uncertainty and availability of resource



Available in English, French, Spanish, German, Italian, Dutch, Swedish at <http://bit.ly/amyloidvideos>

Living with risk

Zallen (2016) qualitative interview study with 26 members of the ApoE4.info community

Testing did produce adverse psychological reactions in participants who hadn't received pre-test counselling or for whom it was unexpected

Nearly all (23/26) concluded that they had benefited in the long term although a small number continued to regret



I definitely was emotionally traumatized ... The emotional impact so high, it was strong and huge; it was almost as if I was imagining I was already having to find a way to have an exit strategy, something that really gave me comfort

(Participant F: homozygous, tested for a different health problem)

In the end I'm glad I did it ... And, yes, I'm glad I know because I think I am doing things that I might not do. But, obviously, I wish I didn't have it.
(Participant F)

I wish I never knew about this. There's really nothing I can do at my age. It's like a cloud, hanging over my head. I'm basically, I think, optimistic and happy, and I pulled myself out of that really down period. But, it's just a terrible thing hanging over me.

(Participant N: homozygous, tested for general interest)

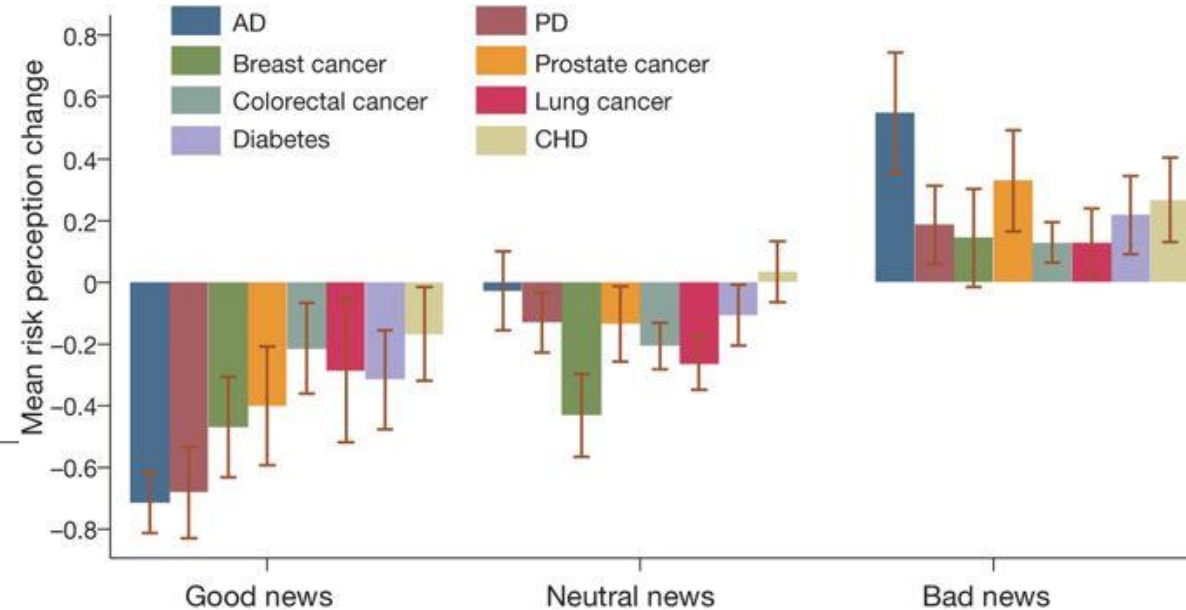
DTC

















- >26 million people have had some form of DTC
- Little data on emotional impact
- Effect on baseline risk perception greatest for Alzheimer's disease
- Problems of false positive/false negatives

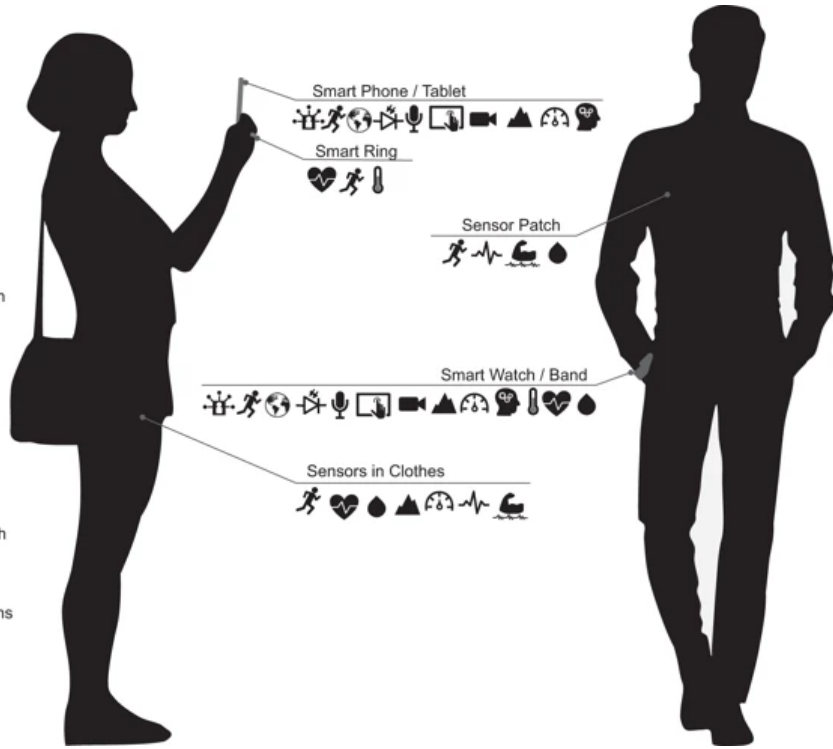
Type of information	Responses, % endorsing out of <i>n</i> = 1,648		
	not interested	somewhat interested	very interested

<i>General</i>			
Ancestry	3.9	22.5	73.7
Traits ^a	2.3	25.5	72.2
Disease risk	1.9	26.2	71.9
Drug response	9.1	38.8	52.1
Carrier status	43.0	26.1	30.9

<i>Disease-specific risks</i>			
Alzheimer disease	6.8	26.9	66.3
Arthritis	16.9	42.0	41.1
Asthma	31.1	39.2	29.7
Bipolar disorder	25.9	36.4	37.7
<i>Cancer</i>			
Breast	5.8	27.3	66.9
Colon	11.2	36.1	52.7



-  Microphone
-  Touch Screen
-  Camera
-  Altimeter
-  Barometer
-  PPG
-  ElectroCardioGraph
-  IMU
-  Geo-Positioning
-  Light Sensor
-  Thermometer
-  ElectroMyoGraph
-  ElectroDermoGraph
-  Logic
-  Wireless Interactions
-  Social Network



Google Home



The future of prediction: DTC 2.0?

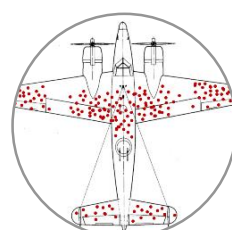
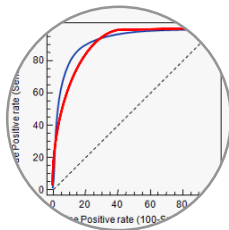
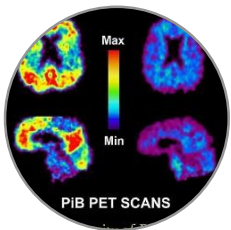


DTC 2.0

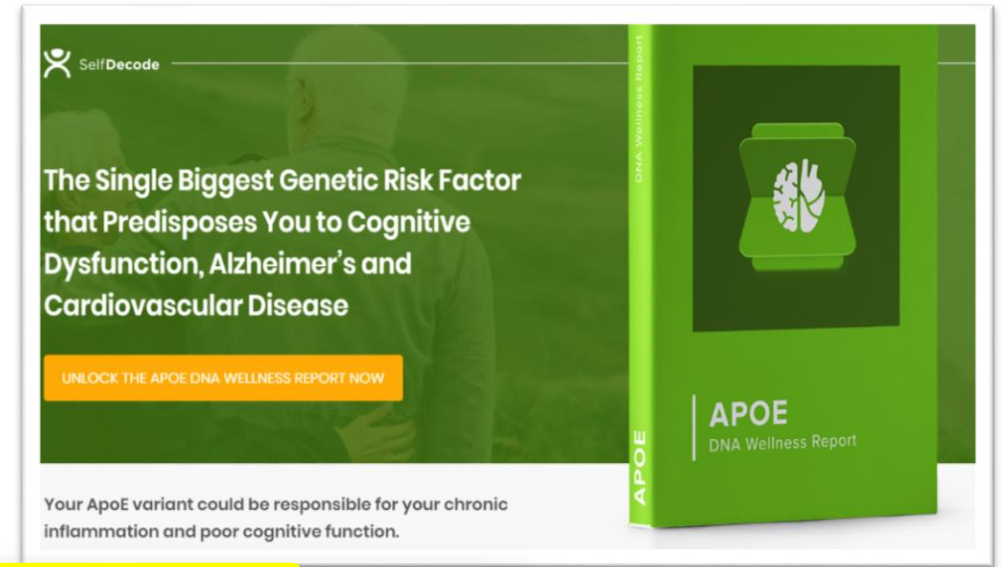
Clinical oversight vs autonomy

Specific challenges associated with data-driven detection based on 'edge' data

- Consent
- Transparency
- Fairness
- Accountability
- Governance
- Commercialisation

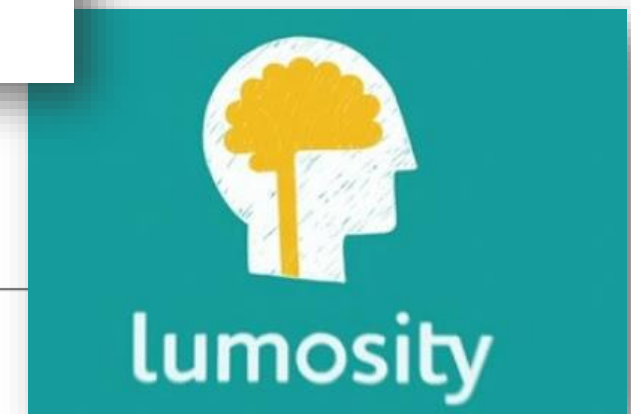


The political economy of risk



“Lumosity preyed on consumers’ fears about age-related cognitive decline,

suggesting their games could stave off memory loss, dementia, and even Alzheimer’s disease,” said Jessica Rich, director of the FTC’s Bureau of Consumer Protection, in a statement. “But Lumosity simply did not have the science to back up its ads.”



Conclusions

- In absence of clear clinical benefit and accuracy, arguments in favour of communicating risk predictions rely on autonomy and personal utility
- Arguments against emphasise potential psycho-social harms
- Understanding impact can help with discussion of when it is right to return prediction results and how
 - Information about risk predictions doesn't cause harm to the majority of people, in controlled settings - **focus on what key features of communication are and how and to whom they are made available**
- Wider social and economic consequences of detection and prevention less considered
- Including fair and equitable access to prevention

Thank you

EPAD ELSI workpackage

Shirlene Badger

Sonja Bemelmans

Carol Brayne

Eline Bunnik

Dianne Gove

Edo Richard

Marthe Smedinga

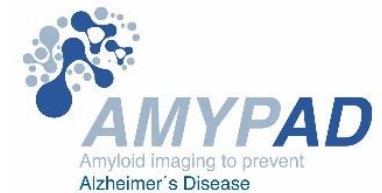
Maartje Schermer

Krista Tromp

Luc Truyen

Wellcome SPACE study

Alessia Costa



References and further reading

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