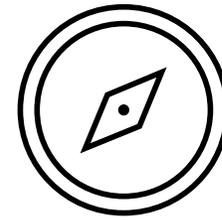# Disease modifying drugs in dementia – what is our role?

Panel discussion

Welcome and thank you…

Personal perspectives on our role re DMTs

o Will be complex – at the start

o Inside & shaping > outside?

o Dementia experts – future career pathways?

o Look outside of OAP – magnify health inequalities?

Disclosures

What?

NHS/NIHR roles

Commercial & non-commercial clinical trials in dementia

donepezil, memantine, dimebon, minocycline, losartan, semaglutide, bapineuzumab, crenezumab, aducanumab, gantenerumab.

CRN DeNDRoN Specialty Lead NE /NC & Industry Lead Dementia.

Advisory ad hoc roles Roche & Biogen – nil active

No involvement with Lecanemab or Donanemab

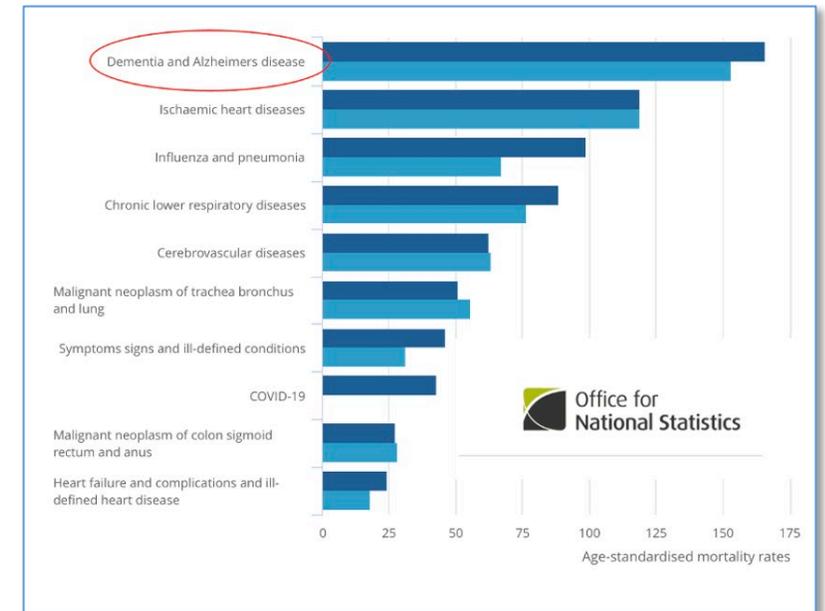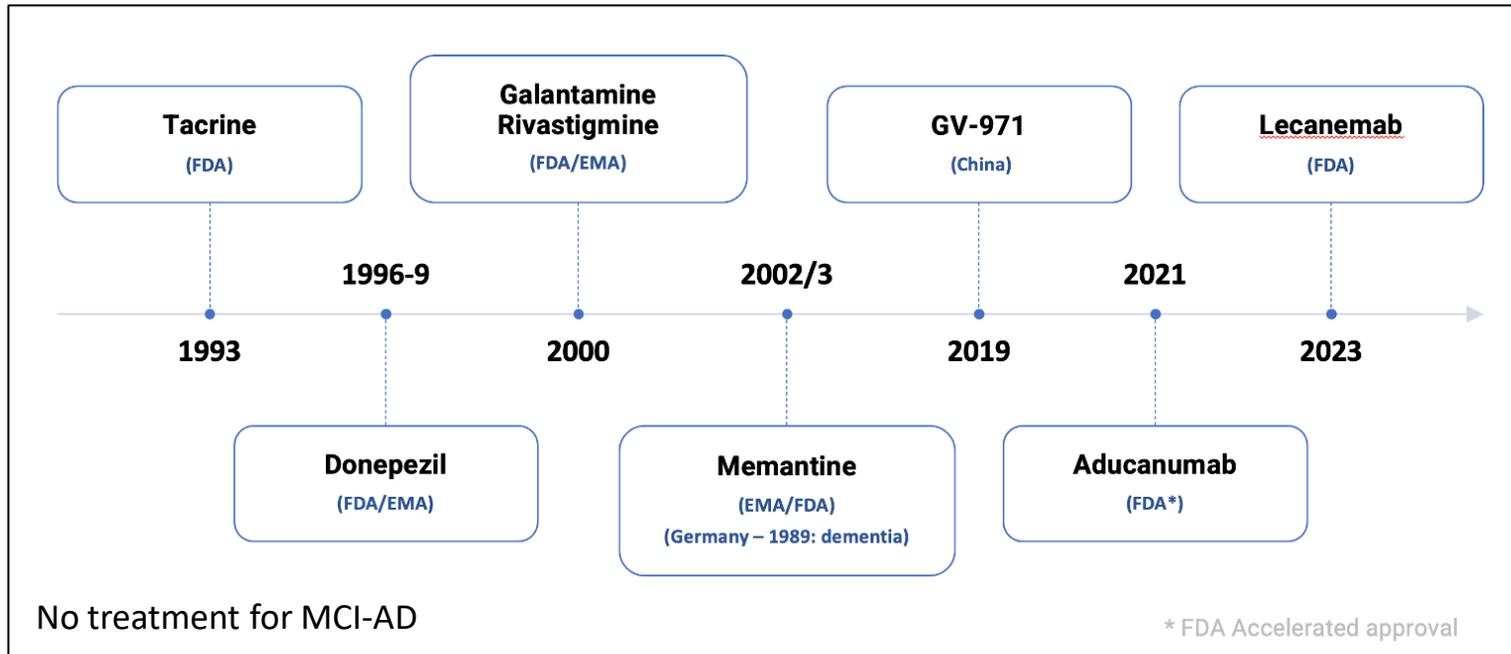**Why?**

Scale and impact of Alzheimer's disease and other dementias

Absence of treatments that change the course of the illness

Q1: Need for DMT?

Drugs approved for Alzheimer's disease

No treatment for MCI-AD
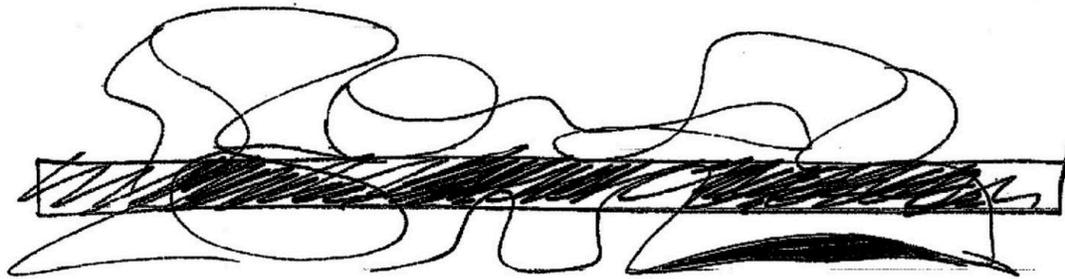
* FDA Accelerated approval

○ ARUK: public No 1 research priority   ○ Health inequalities: unmet needs   ○ Advocacy

Q2: Achieving disease modification will require service modification ?

Zaha Hadid – Phaeno Science Center | Architect Sketches

Sketches & Photos: www.zaha-hadid.com/architecture/phaeno-science-centre/

New to us…..time dimension….now….future…?

To guide and inform conversations....

o Common ground

o Consensus

Are we ready to deliver disease modifying treatments?

Old Age Psychiatrists' views on diagnosing and treating Alzheimer's disease before dementia.
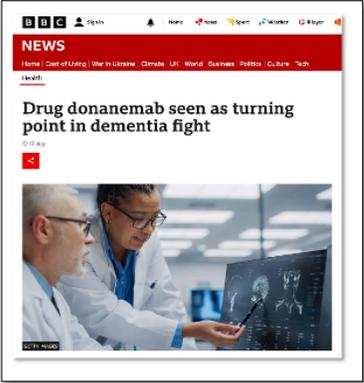
May 2021

o Collaboration

o Connecting

o Commissioners

Q3: Current landscape for DMT?

CLARITY-AD Study:
Lecanemab in Early Alzheimer's disease.
N Engl J Med. 2022 (Eisai)

The TRAILBLAZER-ALZ 2:
Donanemab in Early Symptomatic Alzheimer's Disease
JAMA. 2023 (Eli Lilly)

- **Finishing or starting line for current monoclonal antibodies? But if yes….**
  - **(DMT future will evolve….could be very different…)**

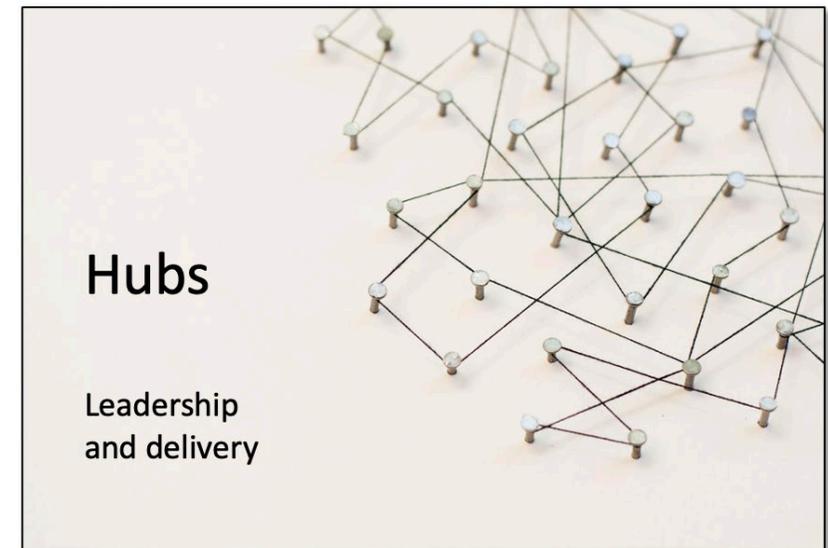# On the inside or outside service redesign and delivery....?

Expertise	**Capacity and integration**	**Care pathways**	**Future facing**	Hub
multi-professional / broad based	biomarker access, workforce, training, safety	primary and secondary care	research and registry	

Starting position?:
- acknowledging where we are....
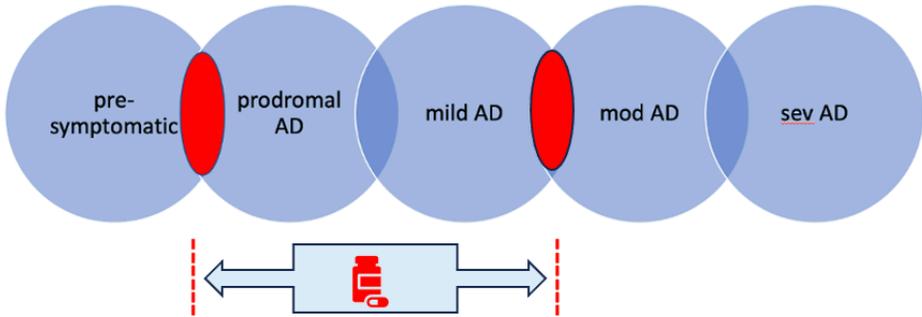- given complexities delivering mAbs....

Geographically strategic "hubs":
- model to provide leadership and skills to deliver DMTs safely, effectively & fairly by understanding local needs, strengths & gaps??
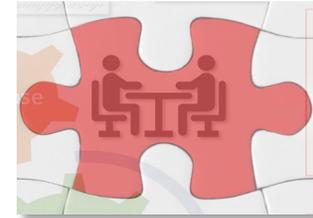

Hubs

Leadership and delivery

Key: we ensure offered to the right person, in the right way, at the right time to maximise benefit and minimise risk...

Diagnostic algorithms

pre-symptomatic — prodromal AD — mild AD — mod AD — sev AD

Biomarker Toolkit

"shot in the dark to a shot on target"

Imaging   CsF   Blood

○ Right way – dementia experts - skill set of Old Age Psychiatrists: B-P-S broad based

Do you have access to, and confidence in the interpretation of, the following diagnostic and biomarker tests?

○ Sufficient access
○ Confident in interpretation

CT   MRI   SPECT   PET-FDG   PET-amyloid   CSF

○ Clinical symptom-focused and inherently late-stage diagnosis & management of AD to the next-generation pathway

- biomarker-guided & digitally facilitated decision-making algorithms
- for risk stratification, early detection, timely diagnosis, and preventative or therapeutic interventions
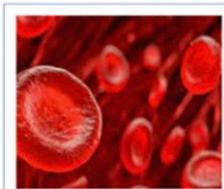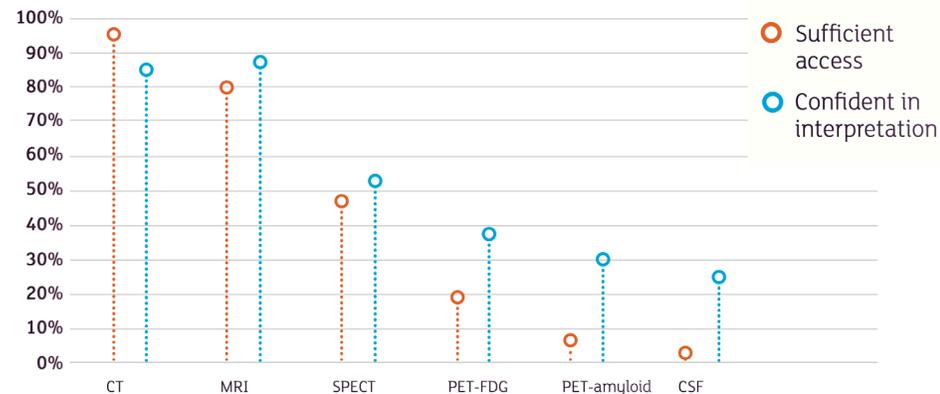
Hampel et al Nat Ageing 2022

Translating new medicines into clinical practice requires patience – manage expectations - but change possible & happening all around us!

Doubtful: "one-drug/one-target/one-disease" approach for AD

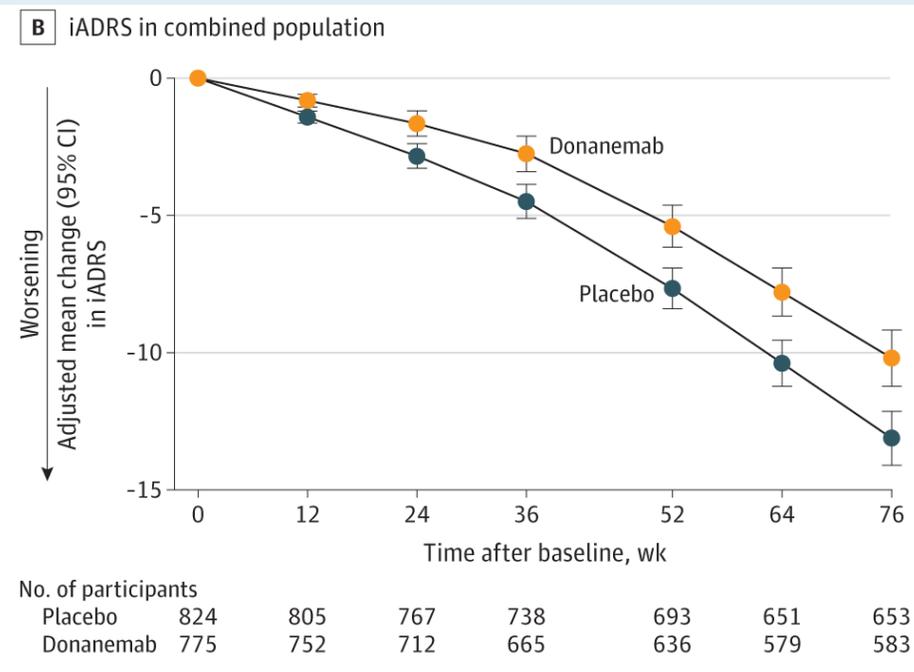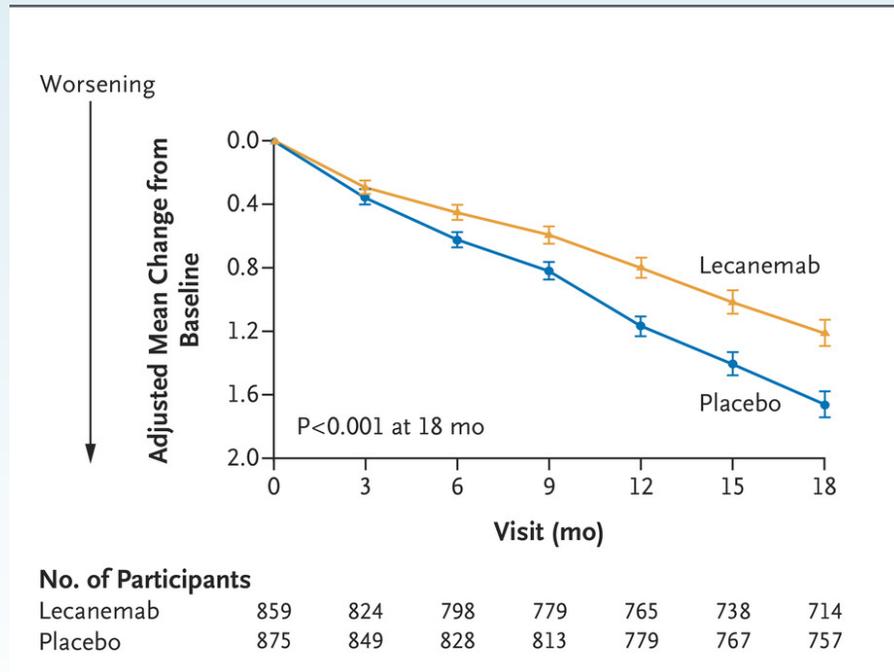# Disease modifying drugs in dementia – what is our role?

Currently considered drugs (amyloid MABs)

Understand/know what the trials have shown

Articulate benefits, risks and costs

Keep up to date with MHRA and NICE processes

1. Understand what the trials have shown

No. of Participants
Lecanemab	859	824	798	779	765	738	714
Placebo	875	849	828	813	779	767	757

No. of participants
Placebo	824	805	767	738	693	651	653
Donanemab	775	752	712	665	636	579	583

From Andrews et al (2019) MCID for CDR-SB—Overall and by Disease Severity.
Note. Clinically meaningful decline indicates clinician's assessment of meaningful decline in a patient's memory, nonmemory cognitive abilities, behaviour, ability to manage his/her affairs, or motor/movement changes since the previous visit.

Very latest data don't confirm or refute DCM
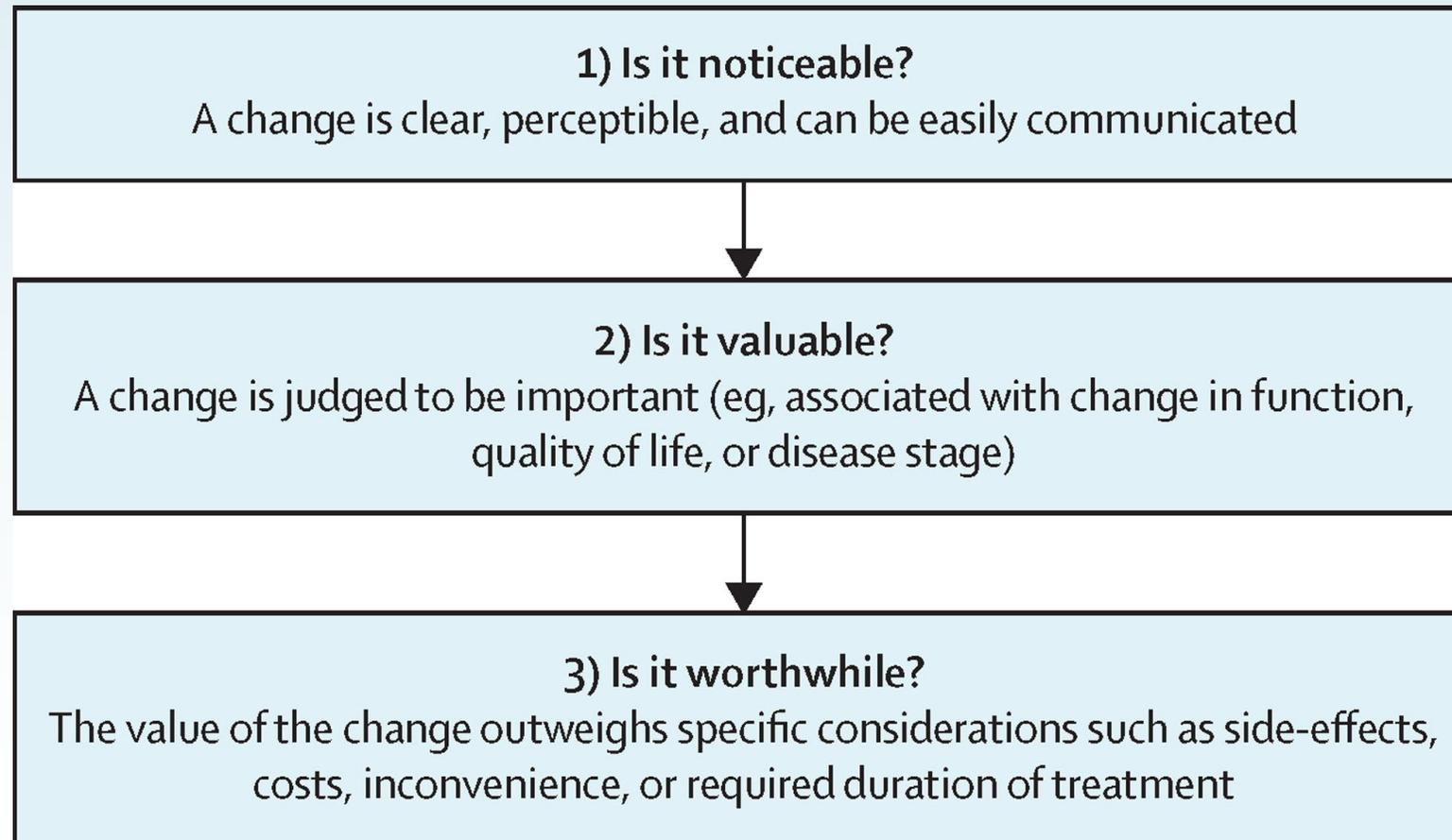
2. Articulate benefits, risks and costs

Drug-placebo differences at 18/12 consistently 50% MCID

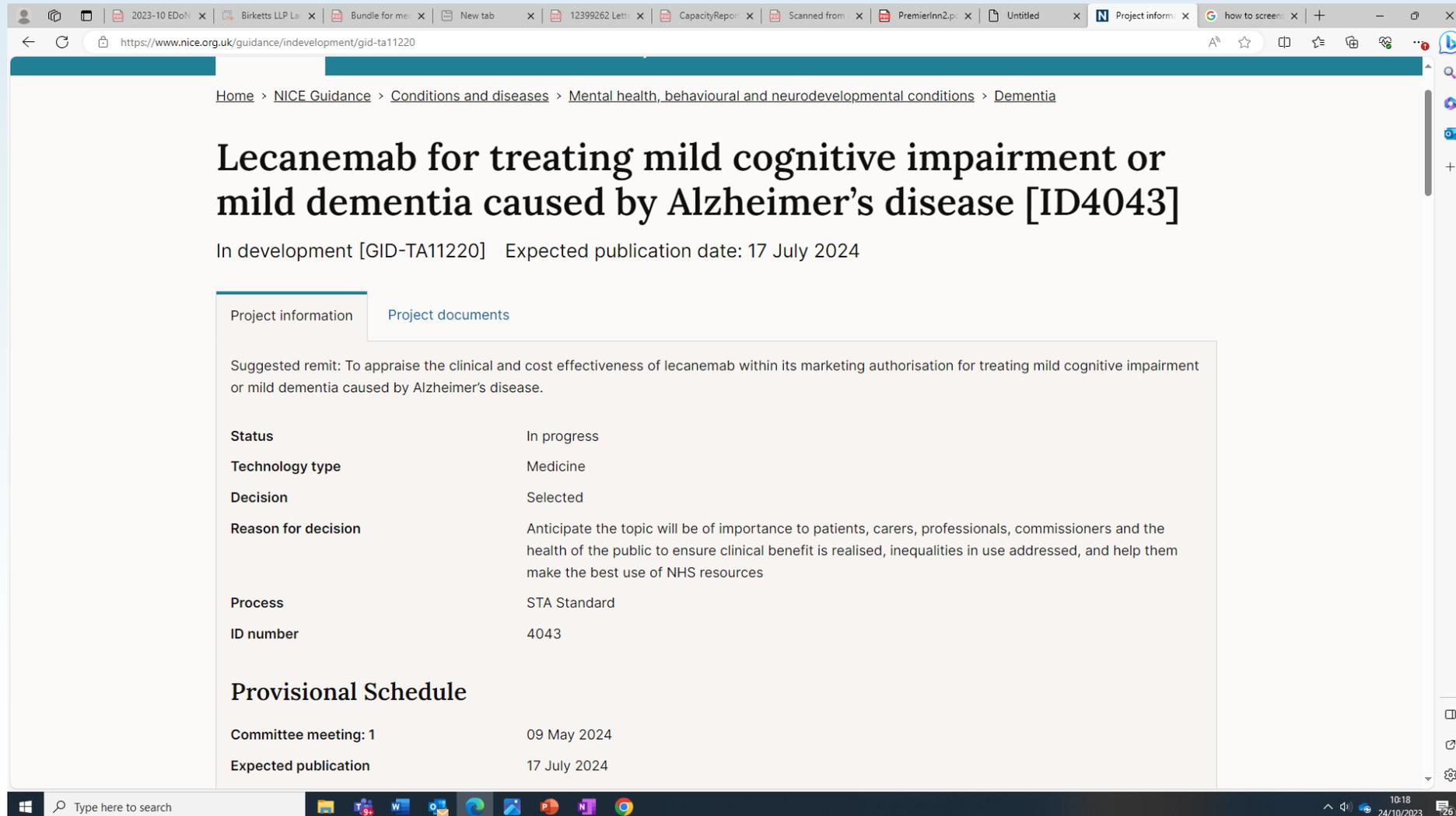**Trials not designed to establish disease course modification**

ARIA common, uncommonly fatal, 1% "life changing"

Fortnightly infusions, monitoring MRIs, drug costs

Three-step guide for evaluation of treatment effects (Kathy Liu - Lancet Longevity November 2023)

1) Is it noticeable?
A change is clear, perceptible, and can be easily communicated

↓

2) Is it valuable?
A change is judged to be important (eg, associated with change in function, quality of life, or disease stage)

↓

3) Is it worthwhile?
The value of the change outweighs specific considerations such as side-effects, costs, inconvenience, or required duration of treatment

3. Keep up to date with MHRA and NICE

DISEASE MODIFYING DRUGS IN DEMENTIA – WHAT IS OUR ROLE? A TRAINEE'S PERSPECTIVE

JAMES HOTHAM

MENTAL DISORDER – WHO DEFINITION

- A mental disorder is characterized by a clinically significant disturbance in an individual's cognition, emotional regulation, or behaviour. It is usually associated with distress or impairment in important areas of functioning. There are many different types of mental disorders. Mental disorders may also be referred to as mental health conditions. The latter is a broader term covering mental disorders, psychosocial disabilities and (other) mental states associated with significant distress, impairment in functioning, or risk of self-harm.
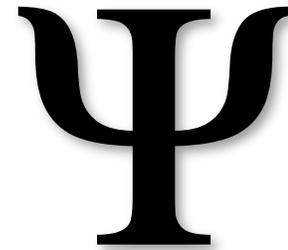

World Health Organization

WHAT IS BEST FOR PATIENTS? (IN MY OPINION)

- Receive accurate diagnosis and effective treatment in a timely manner

- Empowered at each step to understand their care and the options open to them

- Supported through the process

- Personalised care

WHAT IS BEST FOR PSYCHIATRY?

- Reducing stigma
- Hope
- Protect our professional scope
- Adapting to new treatments and learning new skills
- Attracting doctors to psychiatry

Ψ

WHAT WILL THE SYSTEM WANT?

- Get the new treatment to the right patients as efficiently and cost effectively as possible

- There are many barriers to delivering these new treatments within mental health services or by psychiatrists

- If we as a specialty feel that psychiatrists are the right doctors to be supporting patients through diagnosis and treatment of Alzheimer's dementia, then we need to be preparing now and address those barriers