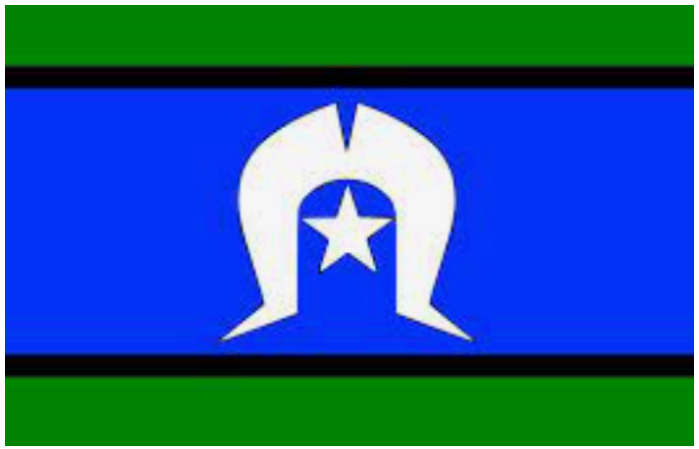
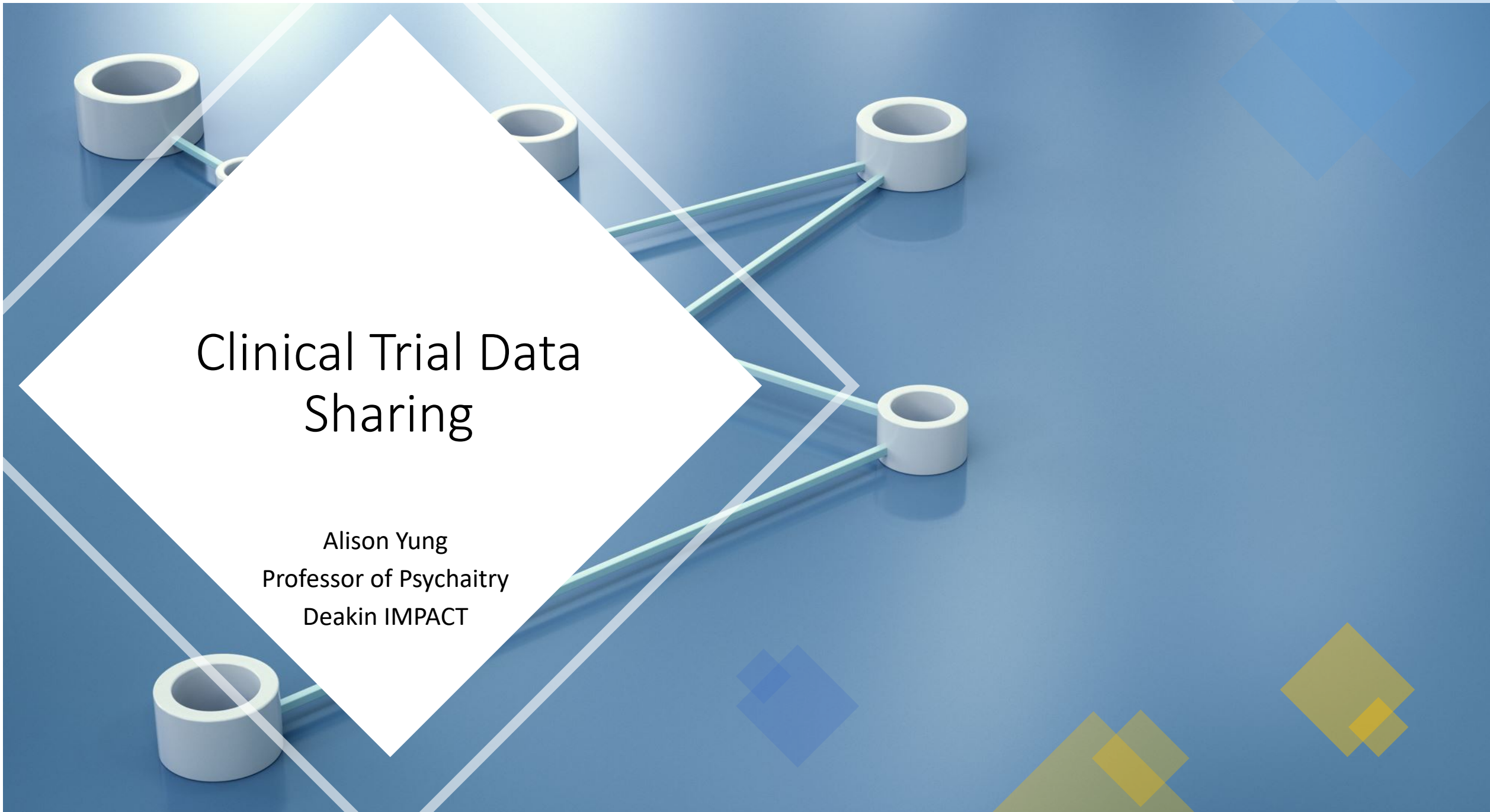


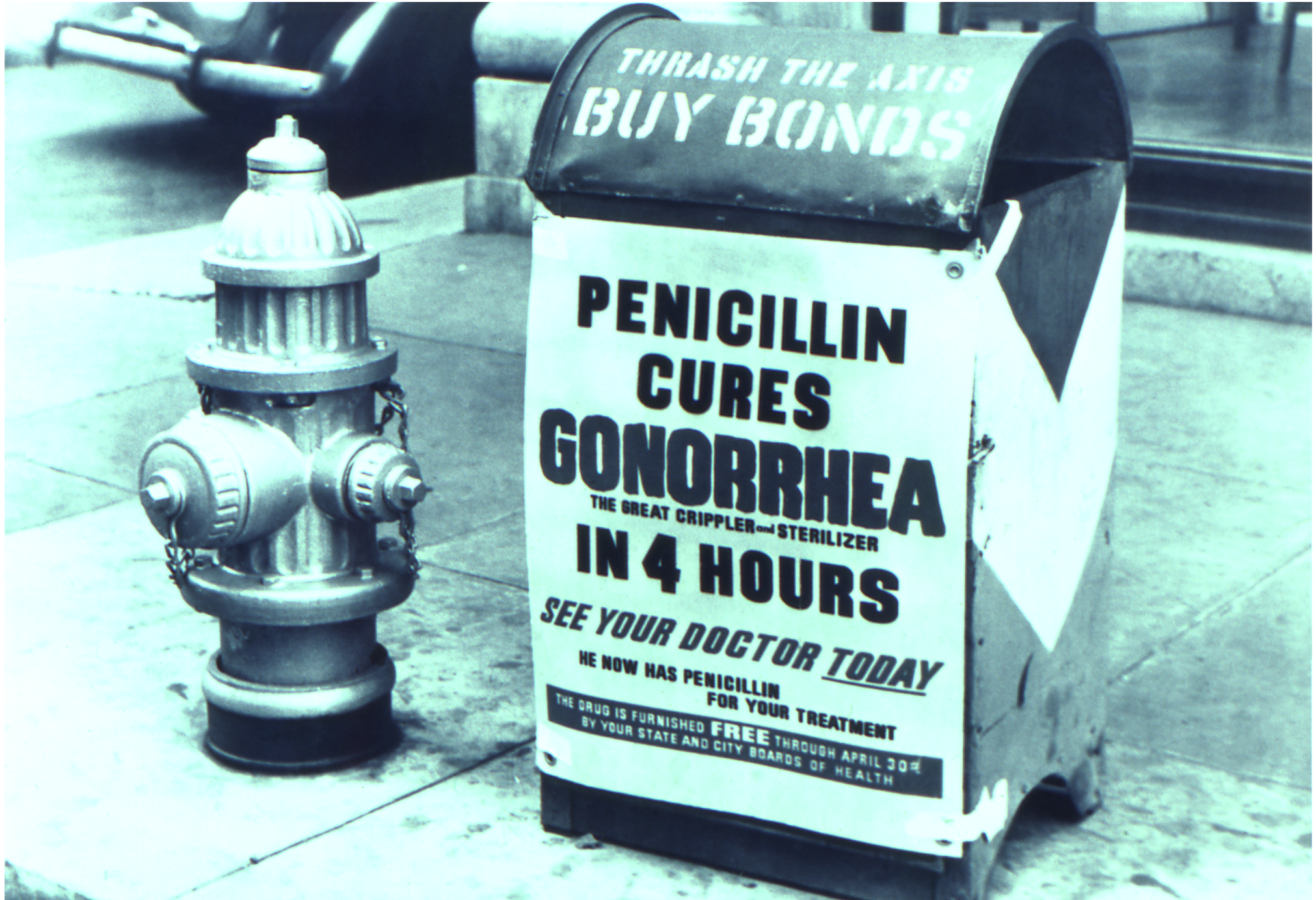


Clinical Trial Data Sharing

Alison Yung
Professor of Psychaitry
Deakin IMPACT

- Back in the day- mid 1940s to early 1970s:
- Antibiotics, such as penicillin and streptomycin, were incredibly successful at treating infectious diseases

Poster from 1944



Thinking in the 1960s and 1970s

- This led doctors to expect that a drug's efficacy would become obvious if it was tested on a few hundred patients.
- Medical researchers conducted trials to search for treatments for cardiovascular disease using very small sample sizes
- Nothing found to be effective, no treatments for AMI (heart attack), high death rate

Breakthroughs

- Richard Peto: statistician, methodologist realized that for something as common as heart disease, a drug that was effective in only a few percent of cases would still save many thousands of lives.
- Peto reveiwed evidence for the effect of the clot-busting drug streptokinase
- Small studies, no significant effect,
- Peto analysed them together: when combined they revealed a 20% reduction in the number of deaths in those allocated streptokinase.
- Next step was to conduct a definitive trial

Breakthroughs in thinking and CVD treatment

- Peto set up a Clinical trials Service Unit
- Collaborated with Peter Sleight, cardiologist
- Sleight – brought clinical credibility
- Essential for recruitment and translation of findings into practice
- Cardiologists on board

Breakthroughs

- Result: streptokinase became a mainstays of treatment for people following AMI (heart attack) for many years
- Heart muscle and many lives saved

So data sharing is good

- And it is happening a lot now, right?
- Well…

Secondary user case study

Individual patient data meta-analyses of risk factors for onset of psychosis in the Ultra High Risk group

Yung et al HTA 17/31 *A refined prognostic tool to better identify individuals at high risk of developing psychosis*

Background – the Ultra High Risk group

- It is possible to identify individuals at high and imminent risk of developing a first episode of psychosis through use of the Ultra High Risk (UHR).

Ultra High Risk criteria

- Age: adolescence to young adulthood: age range at highest risk for onset of a psychotic disorder
- Attenuated psychotic features, and/or
- BLIPS: Brief Limited Intermittent Psychotic Symptoms and/or
- Family history of psychotic disorder or schizotypal personality disorder in a first degree relative PLUS a significant decline in functioning
- Yung et al 1996, 2003

What we know

- The Ultra High Risk criteria detect a group at high risk of developing a psychotic disorders
- Meta-analysis : 22% of UHR individuals developed psychotic disorder in I year, 29% in 2 years and 36% after 3 years
- Fusar-Poli et al 2012

- However, currently it is not possible to predict which UHR individuals will develop a psychotic disorder and which will not.
- This means that some UHR individuals are having unnecessary treatment, and may be told that they are at high risk of psychosis when they are not. It also means that services may be using a costly treatment, (eg CBT), in people who may not need it.
- Thus we need research to improve the ability to predict people most at risk of psychosis, over and above the existing UHR criteria, through the development of a refined prognostic tool.

- The first step in developing such a tool is an evidence synthesis.
- One part of this was to conduct an IPD meta-analysis

IPD – inclusion criteria

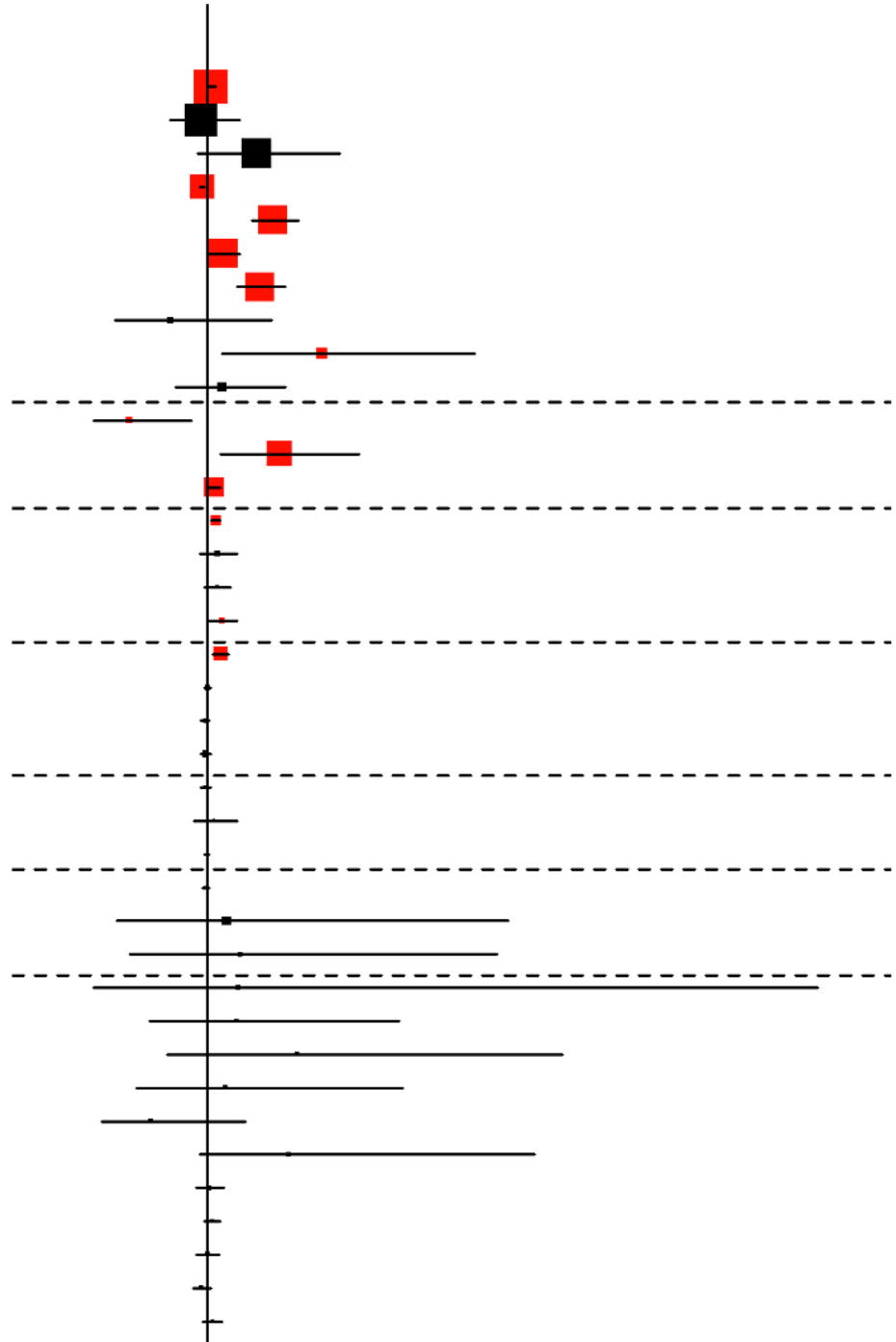
- To be included, studies had to include individuals meeting UHR criteria
- Intake criteria operationalised using the CAARMS or SIPS or equivalents
- Study design: Any prospective study (i.e. cohort studies as well as randomised controlled trials of preventive interventions)
- Studies must have included a baseline assessment, at least 12-month follow-up longitudinal assessments, and analyses aimed at identifying prognostic factors for psychosis transition in UHR individuals.

Method

Literature search, including snow balling

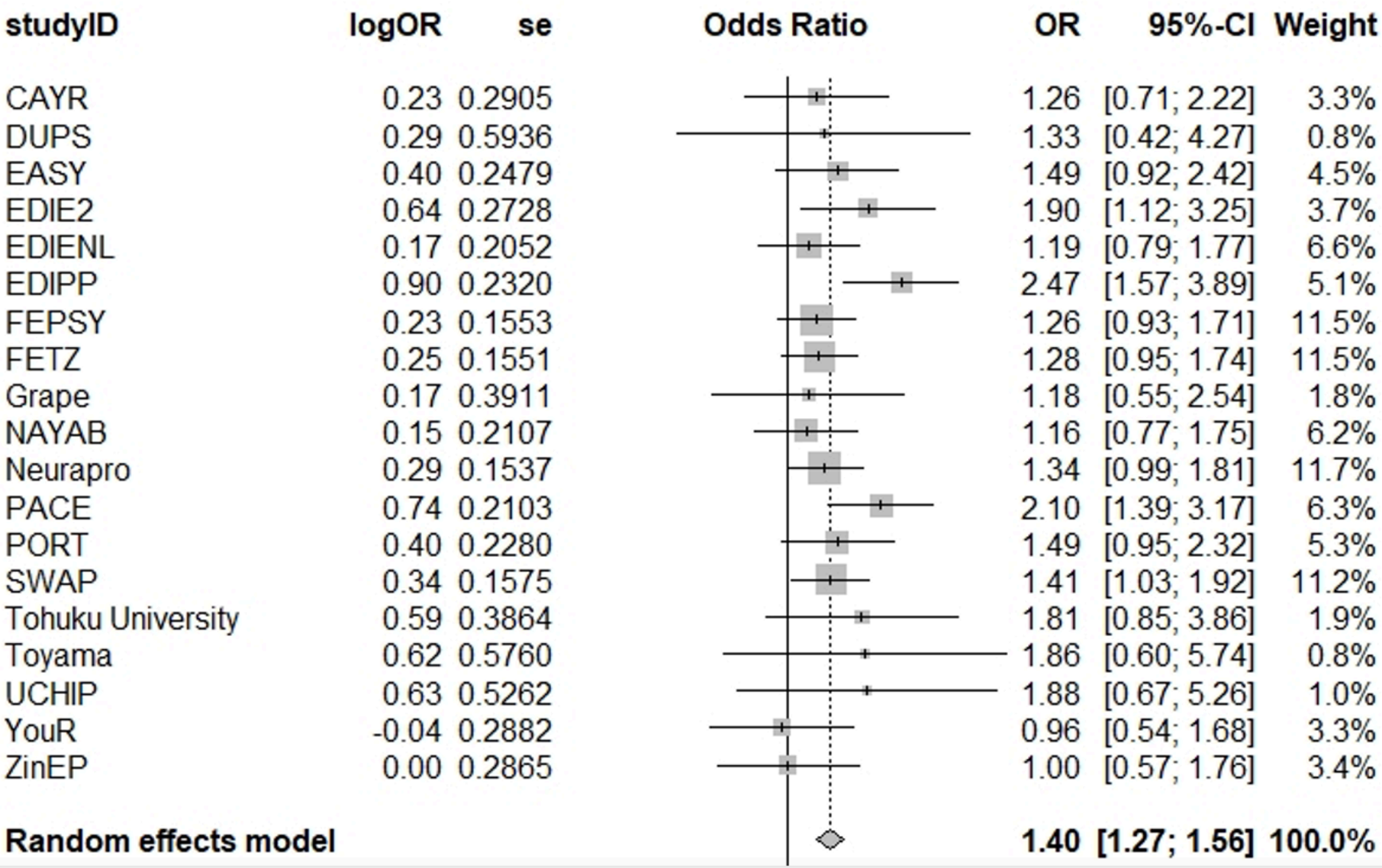
Contacting authors and data custodians

Prognostic Factor	Studies (n)	Participants (n)	I^2(%)
Age	26	3689	22
Gender	24	3612	0
Genetic risk	20	3300	0
Global functioning	20	2615	41
Disorders of thought content	19	3143	0
Perceptual abnormality	19	3143	29
Disorganised speech	20	3171	40
Antidepressants	7	756	0
Antipyshcotic medication	13	1207	0
Anxiety	4	1021	0
CBT	5	735	0
Depression: as binary	22	2751	0
Depression: as continuous	17	2126	17
Depression: depression specific	9	1113	15
Negative symptoms: PANSS	8	653	53
Negative symptoms: SANS	3	377	0
Negative symptoms: SIPS	7	638	64
Negative symptoms: Combined	16	1499	40
Neurocog: Processing speed	5	598	0
Neurocog: Verbal fluency	5	508	0
Neurocog: Verbal learning and memory	7	766	34
Neurocog: Executive function	5	476	37
Premorbid adjust: childhood	3	328	0
Premorbid adjust: early adolescent	3	324	0
Premorbid adjust: late adolescent	3	296	0
Substance abuse	6	1001	52
Cannabis abuse	3	569	0
Alcohol abuse	3	543	68
Trauma: PN (binary)	4	506	0
Trauma: EN (binary)	4	496	19
Trauma: PA (binary)	4	500	0
Trauma: EA (binary)	4	499	0
Trauma: SA (binary)	4	483	0
Trauma: PN (cts)	4	506	0
Trauma: EN (cts)	4	496	0
Trauma: PA (cts)	4	500	0
Trauma: EA (cts)	4	499	0
Trauma: SA (cts)	3	389	0



Variable	Studies (n)	Participants (n)	Pooled estimate OR (95% CI)	I^2 (%)
Age	26	3689	1.02 (1.00, 1.05)	22
Gender	24	3612	0.96 (0.77, 1.20)	0
Global functioning score	20	2615	0.97 (0.95, 0.98)	41
Disorders of thought content	19	3143	1.40 (1.27, 1.56)	0
Perceptual abnormality	19	3143	1.10 (1.00, 1.20)	29
Disorganised speech	20	3171	1.32 (1.18, 1.48)	40
Antidepressants	7	756	0.77 (0.43, 1.39)	0
Antipsychotic medication	13	1207	1.70 (1.09, 2.64)	0
Anxiety	4	1021	1.09 (0.80, 1.48)	0
CBT	5	735	0.52 (0.30, 0.90)	0
Depression				
As binary variable	22	2751	1.44 (1.08, 1.93)	0
As continuous Z-score	17	2126	1.04 (1.01, 1.08)	17
Depression specific metrics	9	1113	1.05 (1.02, 1.08)	15
Negative symptoms				
PANSS	8	653	1.06 (0.95, 1.18)	53
SANS	3	377	1.06 (0.98, 1.14)	0
SIPS	7	638	1.09 (1.01, 1.18)	64
Combined	16	1499	1.08 (1.03, 1.13)	40

Disorders of Thought Content



New insights into risk for psychosis

- Negative symptoms – not previously included in prognostic models but a significant predictor in the IPD meta-analysis
- Neurocognitive variables not predictive – these have been included in previous prognostic models

New insights into data sharing

Most of the time and energy spent on the study was on contacting and re-contacting data custodians, drawing up agreements

We need a better method for data requesting, access and secure analysis

HeSANDA Initiative

Health Studies Australian National Data Asset

Aim: Improving access to health research data for maximum benefit.

HeSANDA Mental Health Node

A problem in mental health research is many trials and other studies with small sample sizes are under-powered to find meaningful effects.

Another issue is relative waste of data. Once the primary paper is written investigators need to move on to write and manage the next grant.

Deakin leads the HeSANDA “Mental Health Node”
Mental Health Node aims to develop processes and infrastructure to enable data sharing

Benefits of data sharing

Data sharing will enable

- Efficient use of data
- Aggregate, IPD, Network meta-analyses etc
- Pooling secondary outcomes and exposure not previously examined in detail

Benefits for secondary users

- Novel research without the need for expensive data collection
- High impact publications
- Impact on health practice and policy
- More funding

Benefits for data custodians

- New insights from working with secondary users
- Publications with secondary users
- Impact on health practice and policy

Why am I telling you this?

We need you!

Data custodians – to share data

Prospectively – to request permission from research participants by asking for unspecified or extended consent

Retrospectively – sharing meta-data with Mental Health Node

Secondary users to use search for meta-data via Health Data Australia

https://researchdata.edu.au/health/

Thanks!