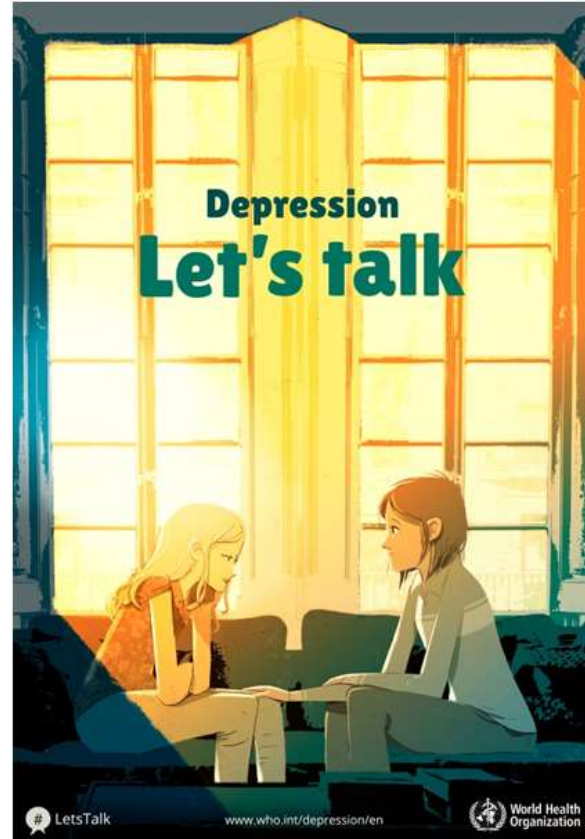


How UK Biobank is helping us to understand mental illness better

Daniel Smith
Professor of Psychiatry

Depression is now the leading cause of disability worldwide

(World Health Organisation, 2017)



Mental health assessments in UK Biobank:

Everyone (0.5 million people):

- Current psychiatric medication use
- Family history of mental illness
- Self-reported mental health problems and alcohol use
- Neuroticism assessment
- Linkage to hospital admission records
- Linkage to primary care (GP) records

About 175,000 people:

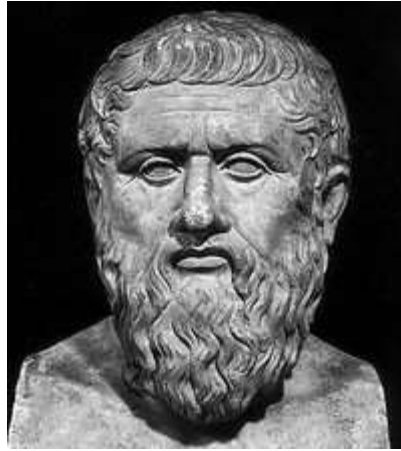
- Features of depression and bipolar disorder (*Smith et al, 2013*)

About 160,000 people:

- Online “*Thoughts and Feelings*” questionnaire (*Davis et al, in press*)

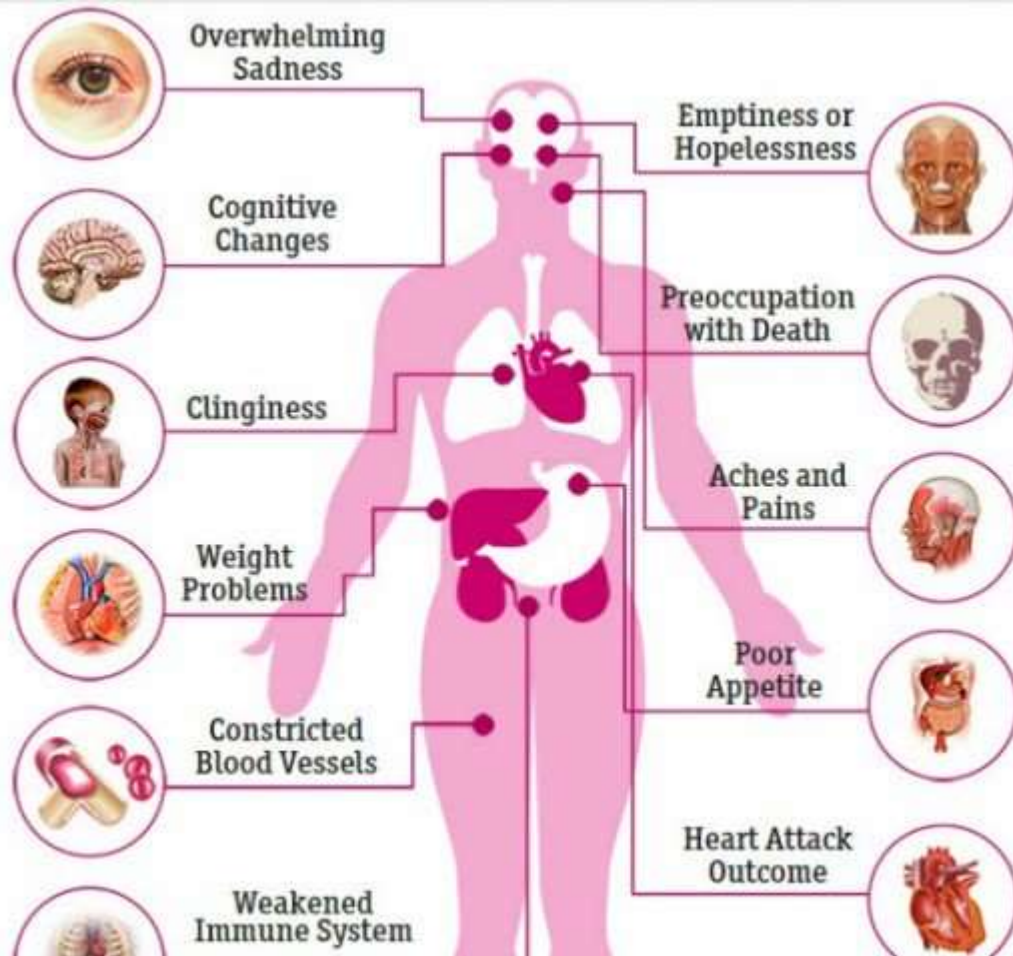


1. Understanding the overlap between mental and physical health
2. Discovering genes for neuroticism and depression
3. Circadian rhythms and mental illness



“The greatest mistake in the treatment of diseases is that there are physicians for the body and physicians for the soul, although the two cannot be separated.”

Plato, c370BC



Depression is a 'whole body' disorder

Cardiometabolic disease and features of depression and bipolar disorder: population-based, cross-sectional study

Daniel J. Martin, Zia Ul-Haq, Barbara I. Nicholl, Breda Cullen, Jonathan Evans, Jason M. R. Gill, Beverly Roberts, John Gallacher, Daniel Mackay, Andrew McIntosh, Matthew Hotopf, Nick Craddock, Ian J. Deary, Jill P. Pell and Daniel J. Smith

Individuals with **depression** had an increased risk of:

- high blood pressure
- diabetes
- heart disease (angina or myocardial infarction)
- stroke

These risks were even higher in those with **bipolar disorder**



“Most of the time I don't have much fun. The rest of the time I don't have any fun at all.”

Neuroticism:

- A heritable personality trait which describes a tendency to respond to stress with anxiety and/or low mood
- Associated with:
 - major depressive disorder, anxiety disorders, substance misuse disorders, personality disorders and schizophrenia
 - premature mortality
 - considerable public health and economic costs

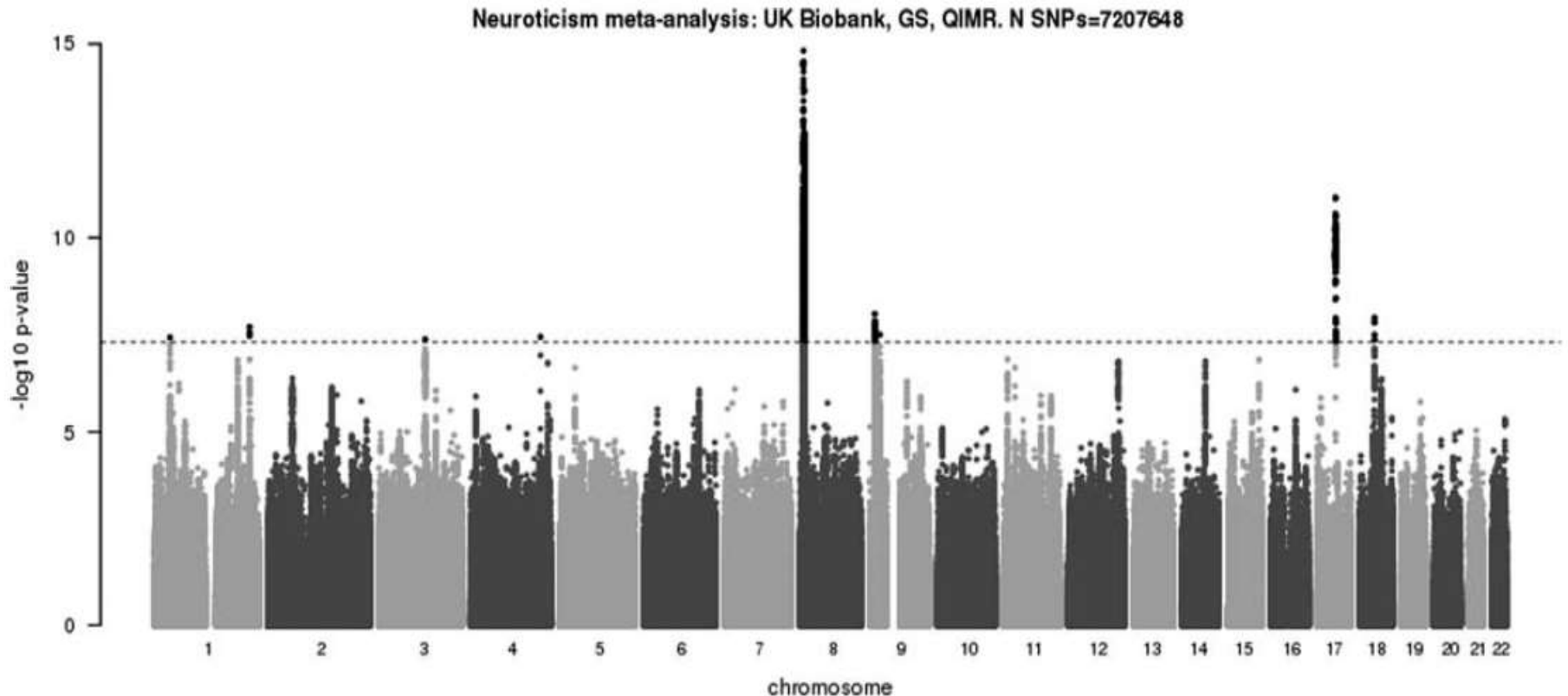
Assessment of Neuroticism in UK Biobank:

1. Does your mood often go up and down?
2. Do you ever feel 'just miserable' for no reason?
3. Are you an irritable person?
4. Are your feelings easily hurt?
5. Do you often feel 'fed-up'?
6. Would you call yourself a nervous person?
7. Are you a worrier?
8. Would you call yourself tense or 'highly strung'?
9. Do you worry too long after an embarrassing experience?
10. Do you suffer from 'nerves'?
11. Do you often feel lonely?
12. Are you often troubled by feelings of guilt?

IMMEDIATE COMMUNICATION

Genome-wide analysis of over 106000 individuals identifies 9 neuroticism-associated loci

DJ Smith^{1,15}, V Escott-Price^{2,15}, G Davies^{3,15}, MES Bailey⁴, L Colodro-Conde⁵, J Ward¹, A Vedernikov², R Marioni^{3,5,6}, B Cullen¹, D Lyall¹, SP Hagenaars³, DCM Liewald³, M Luciano³, CR Gale^{3,7}, SJ Ritchie³, C Hayward^{6,8}, B Nicholl¹, B Bulik-Sullivan^{9,10,11}, M Adams¹², B Couvy-Duchesne⁵, N Graham¹, D Mackay¹, J Evans¹, BH Smith^{8,13}, DJ Porteous^{3,8,14}, SE Medland⁵, NG Martin⁵, P Holmans², AM McIntosh^{3,8,12}, JP Pell^{1,16}, IJ Deary^{3,8,16} and MC O'Donovan^{2,16}



Genome-wide association analysis identifies 44 risk variants and refines the genetic architecture of major depression

(Psychiatric Genomics Consortium)

- 130,664 MDD cases and 330,470 controls
- 44 independent loci associated with MDD
- Genetic risk for MDD was correlated with lower educational attainment, higher body mass and schizophrenia
- New insights into the nature of MDD: primarily a disorder of the brain



“Early to bed, early to rise makes a man healthy, wealthy and wise.”

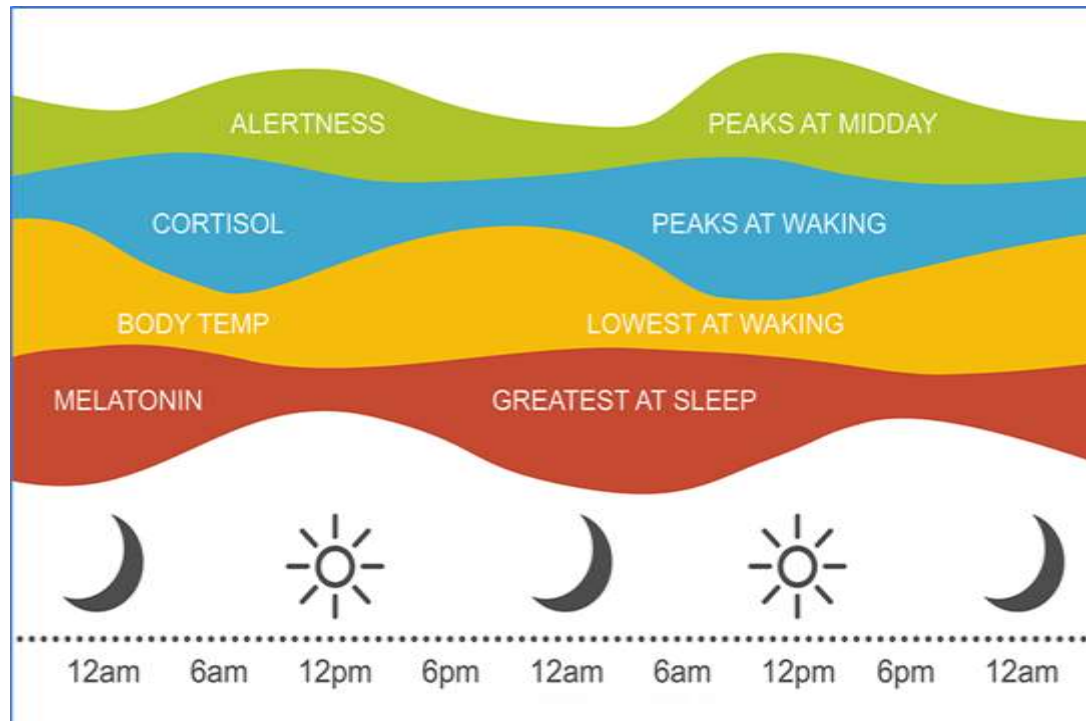
Benjamin Franklin
(1706 -1790)

Chronotype: Night Owl or Morning Lark?





Activity monitoring in UK Biobank
(100,000 participants)



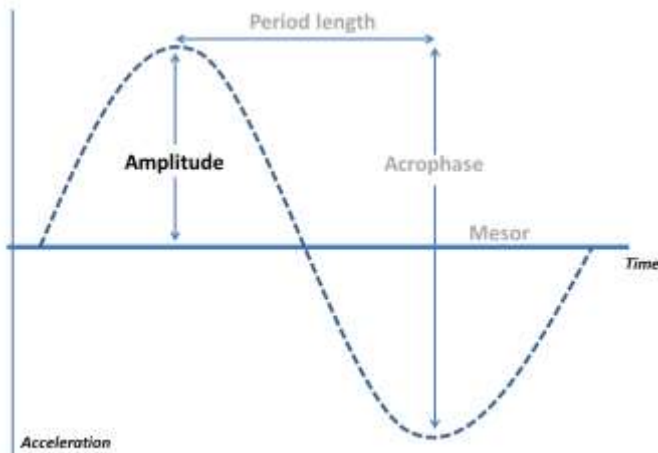
Circadian rhythms are vital for health and wellbeing, especially mental health



Circadian disruption:



Circadian rhythmicity within UK Biobank



Relative amplitude = difference between most active 10hrs and least active 5hrs, averaged over the week

Low relative amplitude:

- Higher neuroticism
- Lower overall happiness
- Lower health satisfaction
- Greater loneliness
- More smoking, more alcohol
- Greater mood instability
- Increased risk of depression
- Increased risk of bipolar disorder



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Thank you



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