Statistical aspects of health and medical research & policy

Keith R Abrams, *Department of Statistics*

March 18, 2024

WARWICK
THE UNIVERSITY OF WARWICK

About me …

- BSc MORSE in mid-1980s
- MSc in Medical Statistics (U of Leicester)
- PhD in Medical Statistics (U of Liverpool)

- Post-doctoral Fellow - King's College London & London School of Hygiene & Tropical Medicine
- Academic at U of Leicester for 27 years (joined UoW in June 2021)

- Teaching – Medical Statistics module to 3rd/4th UG & MSc Statistics
- Research – developing & applying statistical methods in medical applications
- Consultancy with pharmaceutical companies
- External roles, mainly National Institute for health & Care Excellence (NICE)

Statistics & Data Science

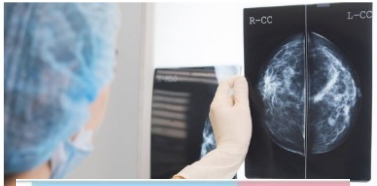
BBC NEWS

Health

AI 'outperforms' doctors diagnosing breast cancer

Fergus Walsh
Medical correspondent
@BBCFergusWalsh

2 January 2020



NHS

Health A-Z | Live Well | Care and support

Home › Behind the Headlines › Pregnancy and child

Once a month contraceptive pill in development

Thursday 5 December 2019

NEWS EXTRA

THALIDOMIDE

Has the horror drug of the '60s become hereditary?

The wonder that faded

NICE National Institute for Health and Care Excellence

Guidance | Standards and indicators | Life sciences | British National Formulary (BNF) | British National Formulary for Children (BNFC)

Home › NICE Guidance › Conditions and diseases › Cancer › Skin cancer

Melanoma: assessment and management

NICE guideline [NG14] Published: 29 July 2015 Last updated: 27 July 2022

Guidance | Tools and resources | Information for the public | Evidence | History

Guardian

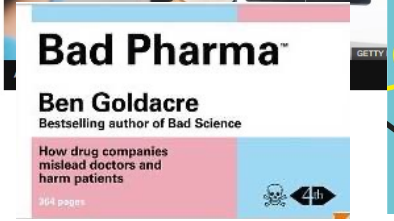
Sport | Culture | Lifestyle | More

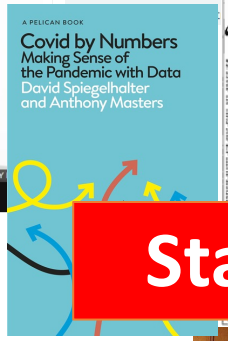
Environment UK politics Education Society Science Tech Global development Cities

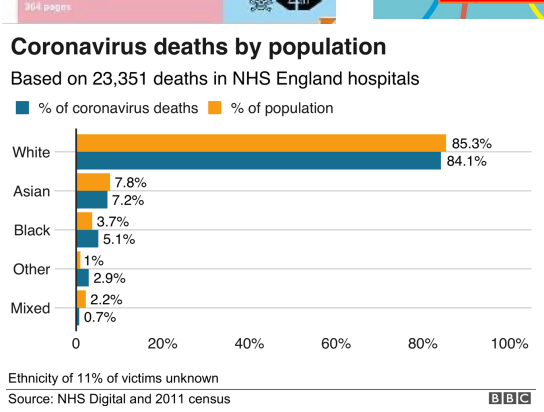
This article is more than 1 month old

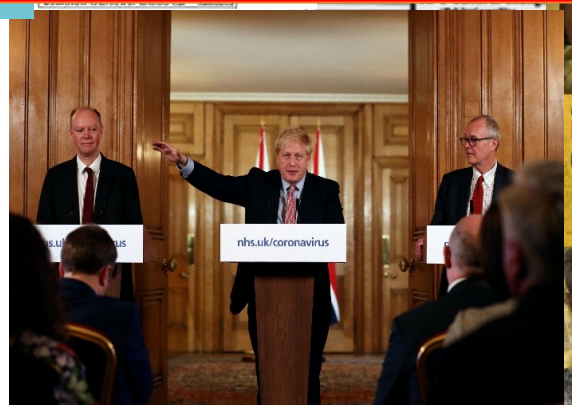
Smoking may increase risk of mental health problems – study

Researchers find link between tobacco cigarettes and depression and schizophrenia









BBC NEWS

Home | Cost of Living | War in Ukraine | Coronavirus | Climate | UK | World | Business | Politics | Tech | Science

UK | England | N. Ireland | Scotland | Alba | Wales | Cymru | Isle of Man | Guernsey | Jersey | Local News

Mould at home: How dangerous is it and what can be done?

3 days ago

By James Gregory
BBC News

And the risk is …

WARWICK
THE UNIVERSITY OF WARWICK

- Consider the (lifetime) risk of bowel cancer and the eating of processed meat ….

And the risk is …

WARWICK
THE UNIVERSITY OF WARWICK

- Consider the (lifetime) risk of bowel cancer and the eating of processed meat ….
- Overall risk of bowel cancer = 5.6%
- Eating of processed meat increases risk (in absolute terms) by 1%, i.e. 6.6%

https://www.eufic.org/en/understanding-science/article/absolute-vs.-relative-risk-infographic

And the risk is …

WARWICK
THE UNIVERSITY OF WARWICK

- Consider the (lifetime) risk of bowel cancer and the eating of processed meat ….
- Overall risk of bowel cancer = 5.6%
- Eating of processed meat increases risk (in absolute terms) by 1%, i.e. 6.6%
- Relative to (overall population) people who eat processed meat have a 6.6/5.6 = 1.18, i.e. 18% increased (relative) risk
- We need to know both absolute & relative risks to make decisions

https://www.eufic.org/en/understanding-science/article/absolute-vs.-relative-risk-infographic

Which treatment is better …

	Open Surgery	Non Surgical Treatment
Overall Success	273/350 = 78%	289/350 = **83%**

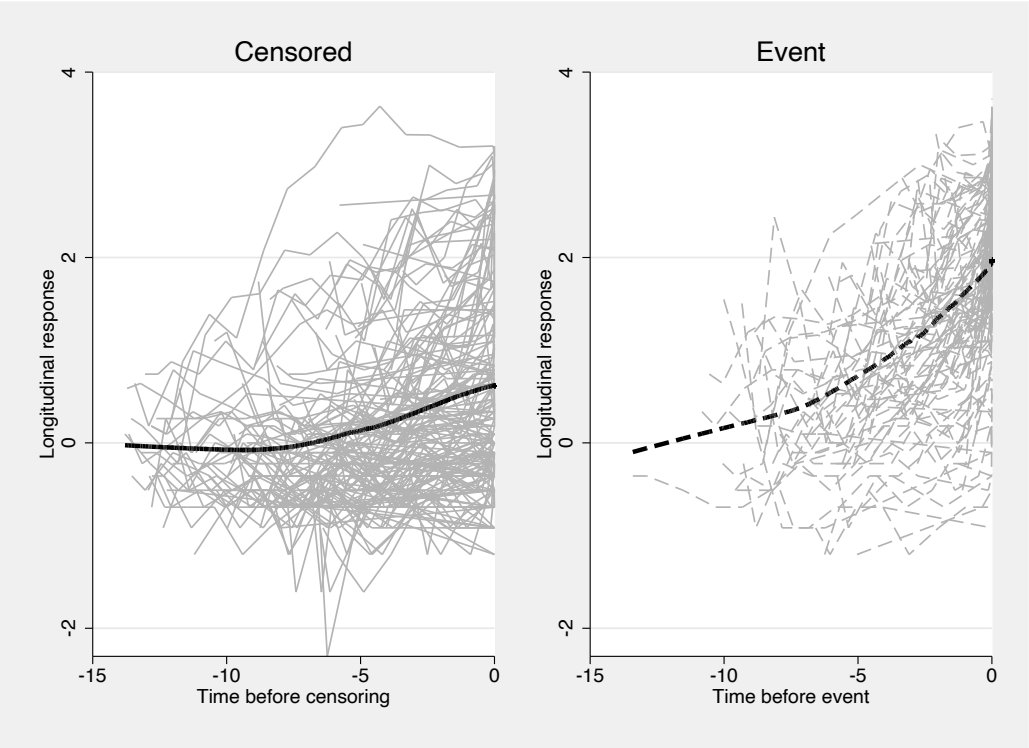
*C. R. Charig; D. R. Webb; S. R. Payne; J. E. Wickham (29 March 1986). "Comparison of treatment of renal calculi by open surgery, percutaneous nephrolithotomy, and extracorporeal shockwave lithotripsy". Br Med J (Clin Res Ed). **292** (6524): 879–882. doi:10.1136/bmj.292.6524.879. .*

Which treatment is better …

	Open Surgery	Non Surgical Treatment
Small kidney stones	81/87 = **93%**	234/270 = 87%
Large Kidney Stones	192/263 = **73%**	55/80 = 69%
Overall Success	273/350 = 78%	289/350 = **83%**

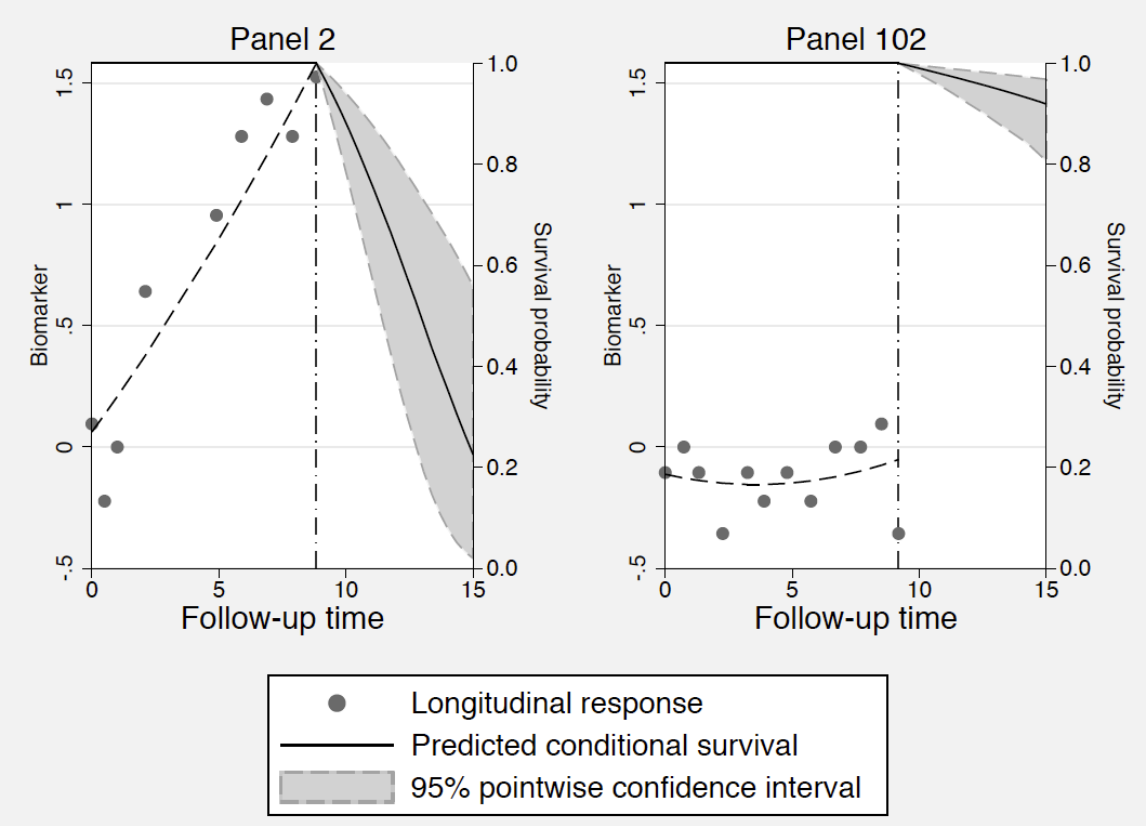
*C. R. Charig; D. R. Webb; S. R. Payne; J. E. Wickham (29 March 1986). "Comparison of treatment of renal calculi by open surgery, percutaneous nephrolithotomy, and extracorporeal shockwave lithotripsy". Br Med J (Clin Res Ed). **292** (6524): 879–882. doi:10.1136/bmj.292.6524.879. .*

Joint Modelling – 1



- 312 patients with primary biliary cirrhosis
- Cirrhosis is a slowly progressing disease in which healthy liver tissue is replaced with scar tissue, eventually preventing the liver from functioning properly
- 1945 repeated measures of serum bilirubin, a measure of liver function
- Outcome of all-cause death, where 140 (44.8%) patients died

Joint Modelling – 2



UK TAVI Trial – Intermittent Missing Data & Missing Data due to Death

JAMA | Original Investigation

Effect of Transcatheter Aortic Valve Implantation vs Surgical Aortic Valve Replacement on All-Cause Mortality in Patients With Aortic Stenosis
A Randomized Clinical Trial

The UK TAVI Trial Investigators

IMPORTANCE Transcatheter aortic valve implantation (TAVI) is a less invasive alternative to surgical aortic valve replacement and is the treatment of choice for patients at high operative risk. The role of TAVI in patients at lower risk is unclear.

OBJECTIVE To determine whether TAVI is noninferior to surgery in patients at moderately increased operative risk.

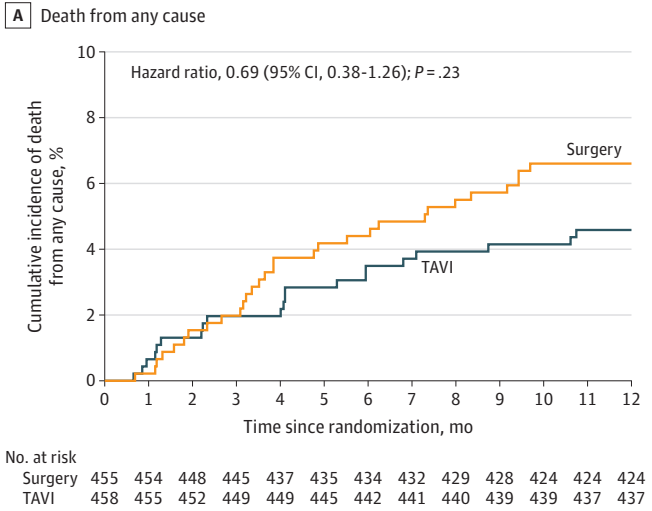
DESIGN, SETTING, AND PARTICIPANTS In this randomized clinical trial conducted at 34 UK centers, 913 patients aged 70 years or older with severe, symptomatic aortic stenosis and moderately increased operative risk due to age or comorbidity were enrolled between April 2014 and April 2018 and followed up through April 2019.

INTERVENTIONS TAVI using any valve with a CE mark (indicating conformity of the valve with all legal and safety requirements for sale throughout the European Economic Area) and any access route (n = 458) or surgical aortic valve replacement (surgery; n = 455).

MAIN OUTCOMES AND MEASURES The primary outcome was all-cause mortality at 1 year. The primary hypothesis was that TAVI was noninferior to surgery, with a noninferiority margin of 5% for the upper limit of the 1-sided 97.5% CI for the absolute between-group difference in mortality. There were 36 secondary outcomes (30 reported herein), including duration of hospital stay, major bleeding events, vascular complications, conduction disturbance requiring pacemaker implantation, and aortic regurgitation.

RESULTS Among 913 patients randomized (median age, 81 years [IQR, 78 to 84 years]; 424 [46%] were female; median Society of Thoracic Surgeons mortality risk score, 2.6% [IQR, 2.0% to 3.4%]), 912 (99.9%) completed follow-up and were included in the noninferiority analysis. At 1 year, there were 21 deaths (4.6%) in the TAVI group and 30 deaths (6.6%) in the surgery group, with an adjusted absolute risk difference of −2.0% (1-sided 97.5% CI, −∞ to 1.2%; $P < .001$ for noninferiority). Of 30 prespecified secondary outcomes reported herein, 24 showed no significant difference at 1 year. TAVI was associated with significantly shorter postprocedural hospitalization (median of 3 days [IQR, 2 to 5 days] vs 8 days [IQR, 6 to 13 days] in the surgery group). At 1 year, there were significantly fewer major bleeding events after TAVI compared with surgery (7.2% vs 20.2%, respectively; adjusted hazard ratio [HR], 0.33 [95% CI, 0.24 to 0.45]) but significantly more vascular complications (10.3% vs 2.4%; adjusted HR, 4.42 [95% CI, 2.54 to 7.71]), conduction disturbances requiring pacemaker implantation (14.2% vs 7.3%; adjusted HR, 2.05 [95% CI, 1.43 to 2.94]), and mild (38.3% vs 11.7%) or moderate (2.3% vs 0.6%) aortic regurgitation (adjusted odds ratio for mild, moderate, or severe [no instance of severe reported] aortic regurgitation combined vs none, 4.89 [95% CI, 3.08 to 7.75]).

Visual Abstract
Editorial page 1870
Multimedia
Supplemental content



- Used a Joint Model to adjust longitudinal Patient Reported Outcomes (e.g. Health-related Quality of Life) for both intermittent missing data and all-cause mortality

Modelling trajectories of disease in multimorbidity using “Big Data”

WARWICK
THE UNIVERSITY OF WARWICK

Effect on life expectancy of temporal sequence in a multimorbidity cluster of psychosis, diabetes, and congestive heart failure among 1·7 million individuals in Wales with 20-year follow-up: a retrospective cohort study using linked data

Rhiannon K Owen, Jane Lyons, Ashley Akbari, Bruce Guthrie, Utkarsh Agrawal, Daniel C Alexander, Amaya Azcoaga-Lorenzo, Anthony J Brookes, Spiros Denaxas, Carol Dezateux, Adeniyi Francis Fagbamigbe, Gill Harper, Paul D W Kirk, Eda Bilici Özyiğit, Sylvia Richardson, Sophie Staniszewska, Colin McCowan, Ronan A Lyons, Keith R Abrams

Summary

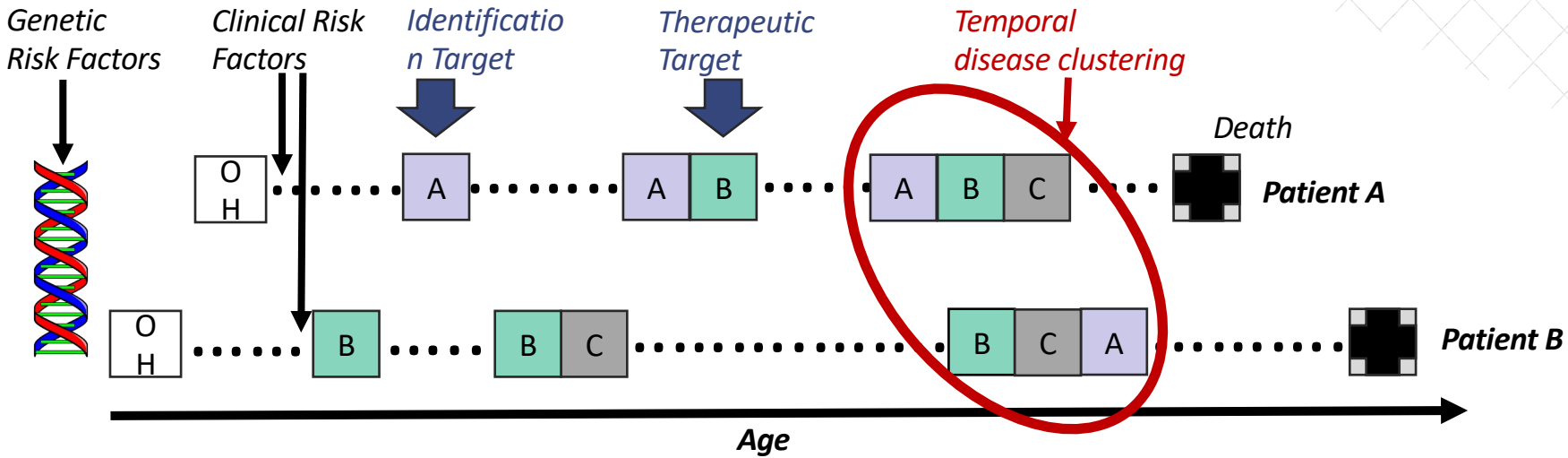
Background To inform targeted public health strategies, it is crucial to understand how coexisting diseases develop over time and their associated impacts on patient outcomes and health-care resources. This study aimed to examine how psychosis, diabetes, and congestive heart failure, in a cluster of physical–mental health multimorbidity, develop and coexist over time, and to assess the associated effects of different temporal sequences of these diseases on life expectancy in Wales.

Methods In this retrospective cohort study, we used population-scale, individual-level, anonymised, linked, demographic, administrative, and electronic health record data from the Wales Multimorbidity e-Cohort. We included data on all individuals aged 25 years and older who were living in Wales on Jan 1, 2000 (the start of follow-up), with follow-up continuing until Dec 31, 2019, first break in Welsh residency, or death. Multistate models were applied to these data to model trajectories of disease in multimorbidity and their associated effect on all-cause mortality, accounting for competing risks. Life expectancy was calculated as the restricted mean survival time (bound by the maximum follow-up of 20 years) for each of the transitions from the health states to death. Cox regression models were used to estimate baseline hazards for transitions between health states, adjusted for sex, age, and area-level deprivation (Welsh Index of Multiple Deprivation [WIMD] quintile).

Lancet Public Health 2023; 8: e535–45

Population Data Science, Health Data Research, Swansea University Medical School, Faculty of Medicine, Health and Life Science, Swansea University, Swansea, UK (R K Owen PhD, J Lyons MSc, A Akbari MSc, Prof R A Lyons MD); **Advanced Care Research Centre, Usher Institute, University of Edinburgh, Edinburgh, UK** (Prof B Guthrie PhD); **Nuffield Department of Primary Care Health Sciences, University of Oxford, Oxford, UK** (U Agrawal PhD); **Centre for**

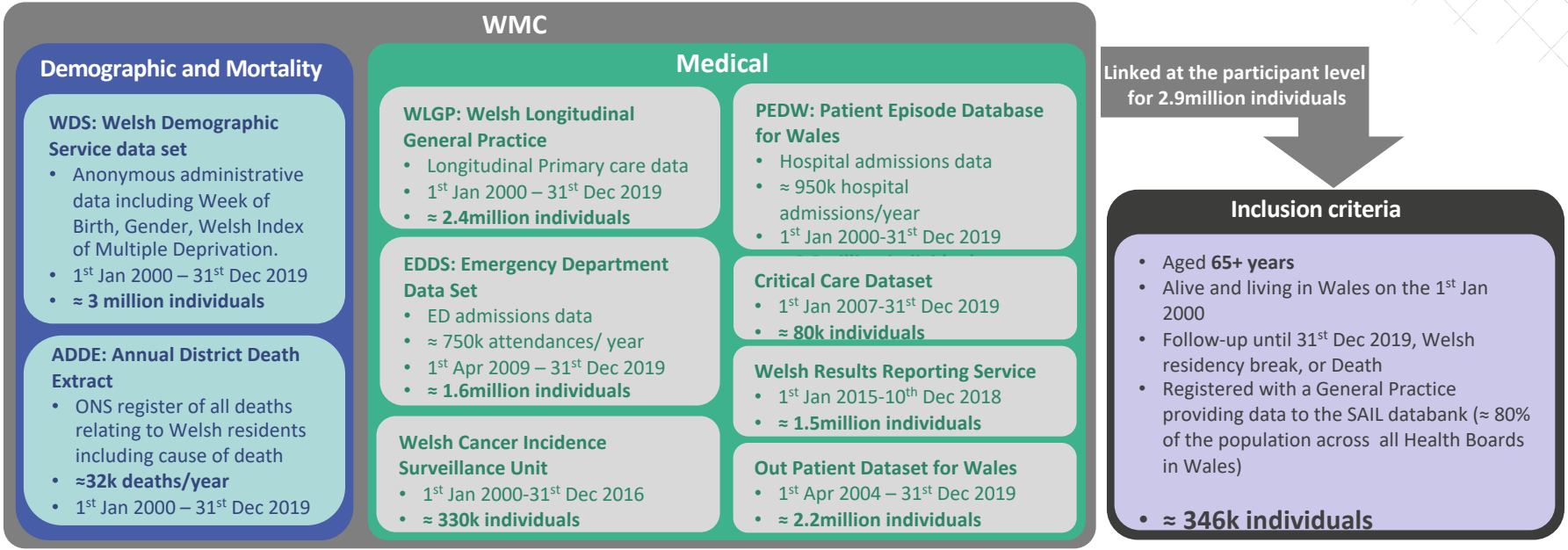
Objectives



- To analyse how diseases in multimorbidity develop over time in terms of disease sequencing, and time intervals (trajectories).
- To compare the associated impact of different disease trajectories on patient outcomes such as mortality.
- Assess the impact of identification and therapeutic targets.
- Identify risk factors for different disease trajectories.

The Wales Multimorbidity e-cohort (WMC)

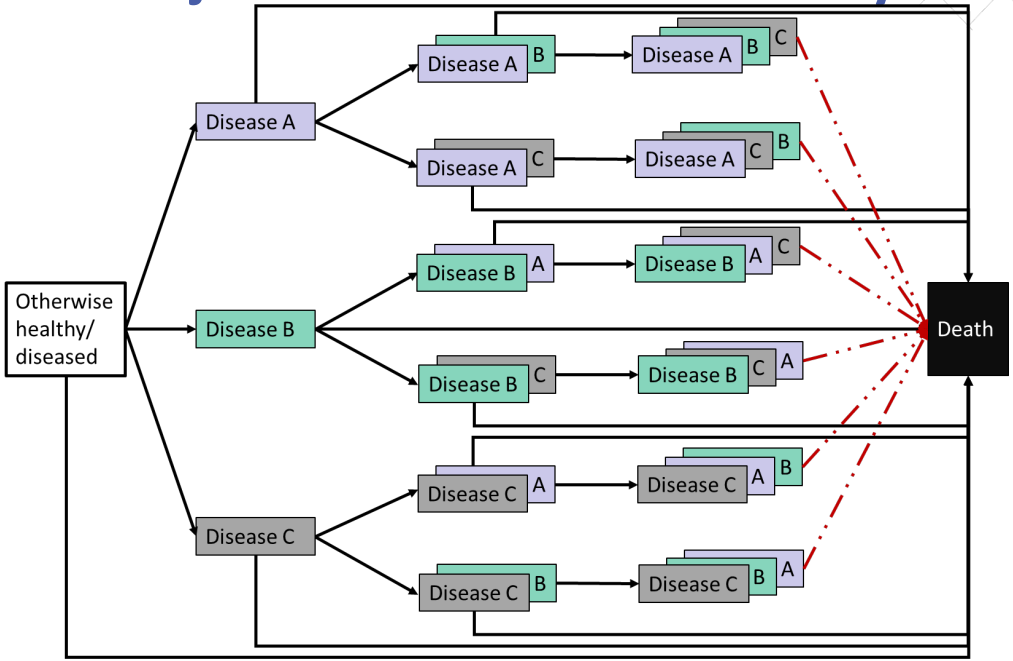
- Using the Secure Anonymised Information Linkage (SAIL) databank (www.saildatabank.com)
- For more information, please see Lyons J, et al. BMJ Open 2021;11:e047101. doi:10.1136/bmjopen-2020-047101



Acknowledgements

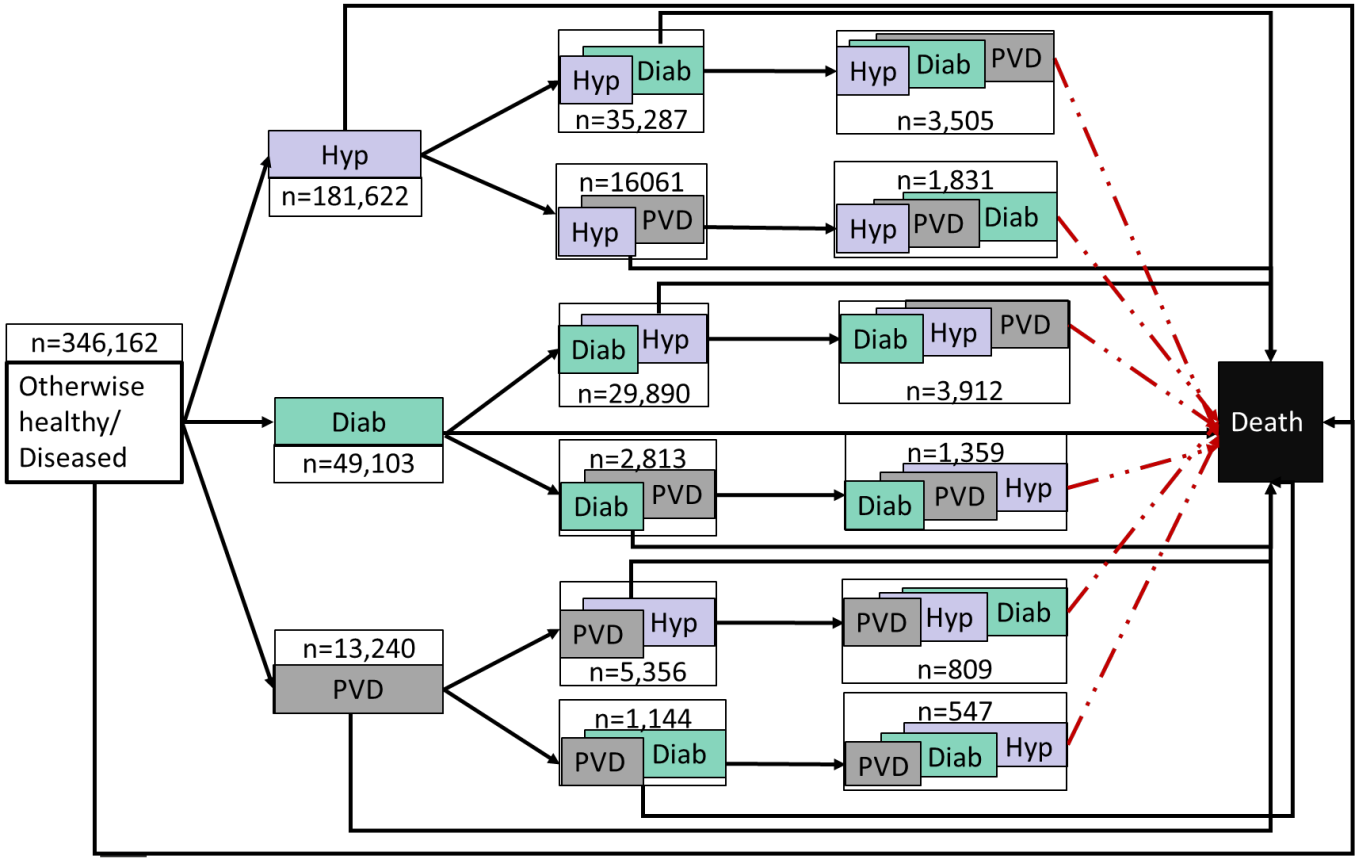
We would like to acknowledge all data providers who make anonymised data available for research. We wish to acknowledge the collaborative partnership that enabled acquisition and access to the de-identified data, which led to this output. We would like to extend our gratitude and acknowledgement to the NHS, the SAIL Consumer panel and the SAIL independent Information Governance Review Panel (IGRP) who approved this project under project number 0911.

Modelling disease trajectories in multimorbidity



- Multistate modelling using age as a time scale.
- Allows simultaneous estimation of disease trajectories via estimation of all possible transitions between health states.
- Individuals were censored on date of break in Welsh residency, cohort end (31 December 2019) or date of death when death is a competing risk.
- Models were adjusted for gender and socioeconomic status (using Welsh Index of Multiple Deprivation, WIMD).

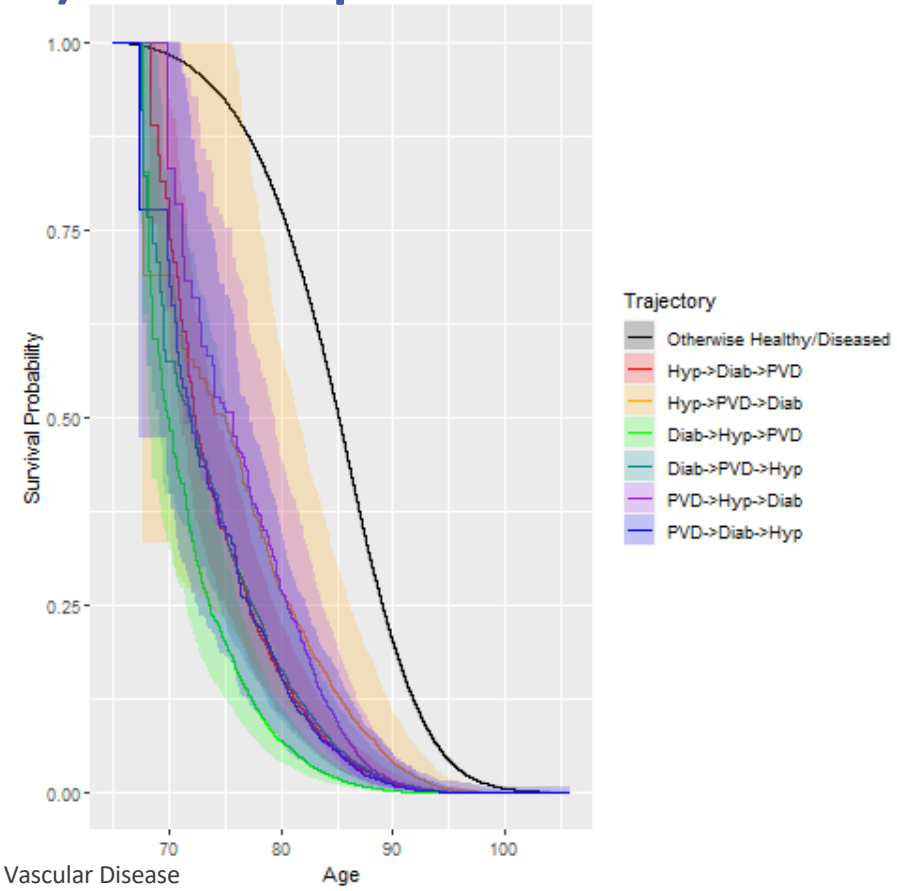
Example in Diabetes, Hypertension and Peripheral Vascular Disease (PVD)



Mortality from transition	n
Otherwise healthy/diseased	72,232
Hypertension	88,867
Diabetes	12,398
PVD	5,816
Hyp->Diab	19,381
Hyp->PVD	11,116
Diab->Hyp	19,020
Diab->PVD	1,286
PVD->Hyp	3,674
PVD->Diab	510
Hyp->Diab->PVD	2,513
Hyp->PVD->Diab	1,272
Diab->Hyp->PVD	3,171
Diab->PVD->Hyp	1,141
PVD->Hyp->Diab	593
PVD->Diab->Hyp	446

Diab; Diabetes, Hyp; Hypertension, PVD; Peripheral Vascular Disease

Example in Diabetes, Hypertension and Peripheral Vascular Disease (PVD): Survival probabilities



Diab; Diabetes, Hyp; Hypertension, PVD; Peripheral Vascular Disease

WARWICK
THE UNIVERSITY OF WARWICK

Thank you

Email: Keith.Abrams@warwick.ac.uk

Webpage: www.warwick.ac.uk/krabrams

A pdf copy of these slides is available via **QR code**