Version history

Version	Date	Changes
V0.0	**30**	**First internal draft**

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Title

Influence of COVID-19 on burden of cardiovascular disease in England

Lay summary (<200 words)

Healthcare planners need use important epidemiological metrics for cardiovascular diseases like heart attack and stroke. To plan services, they need to know how often people develop diseases of different types ('incidence'), how severe these diseases are ('case fatality'), and how many people are living with different diseases ('prevalence'). The COVID 19 pandemic has influenced all of these measures through a combination of direct and indirect impacts on cardiovascular diseases. We aim to see how a range of diseases changed before, during, and after the COVID-19 pandemic.

We will calculate the incidence, case fatality and prevalence for a wide range of cardiovascular diseases. We will also see whether the estimates for commoner diseases like stroke and heart attack are different in people of different ethnicities, ages, levels of deprivation and sex in different regions of England. We will look at epidemiological metrics by years prior to the pandemic (before 2020), by months during the main phase of the pandemic (2020, 2021, 2022) and by years after the pandemic.

Background

Healthcare, third sector and research organisations would benefit from standardised, easily accessible epidemiological metrics for a comprehensive range of cardiovascular disorders. Of these metrics, only cause-specific mortality data are available at a national level, although these are not regularly reported by region, deprivation or age. Whilst overall mortality is important, these figures are difficult to use for healthcare planning because they substantially underestimate disease incidence, do not measure the effect of care (best measured simply with case fatality), and do not measure total community burden (best measured with disease prevalence). Although individual organisations can make estimates of their hospitalisation rates, it is difficult for a single organisation to compare its figures with others, because small differences in methods can lead to substantial differences in estimates across regions. A standardised, national approach using all available health data is needed in order to estimate the effect of the pandemic across a range of cardiovascular diseases.

These metrics are very valuable for planning of provision of research, healthcare, and third sector services. During and after the COVID pandemic, change in cardiovascular disease hospitalisations were a 'canary in the coalmine' for the effects of COVID-19 on the delivery of health services in the UK. For the monitoring and planning for future health emergencies, and care of cardiovascular disease into the future, the rapid and repeated deployment of standardised estimates from all available health care resources (primary, secondary care and ancillary datasets) would be a critical and easily delivered step.

Research aims

This application will leverage phenotyping, code, linked datasets and the multidisciplinary group fostered by the productive and collaborative CVD-COVID-UK group, to:

- Define clinically recognised important cardiovascular conditions with ICD-10 and SNOMED-CT focussing on four common conditions (stroke, MI, heart failure and peripheral vascular disease) and four rare conditions (arterial dissection, intracranial venous thrombosis, myocarditis and Taksubo cardiomyopathy) using the 'I' chapter of ICD-10 as an ontology.
- Estimate major epidemiological metrics (incidence, prevalence, recurrence rate and case fatality) of a comprehensive range of cardiac, cerebral and peripheral vascular disorders at a national level by age, sex, ethnicity, deprivation and multi-morbidity.
    - For rare cardiovascular conditions, estimate these metrics by year
    - For common major cardiovascular conditions (stroke, myocardial infarction (MI), heart failure and peripheral vascular disease), estimate these metrics by month
    - For the whole 'I' chapter, estimate these metrics by year
- Map at regional level the major epidemiological metrics for four major cardiovascular conditions (stroke, MI, heart failure and peripheral vascular disease) by age, sex, deprivation, multi-morbidity and ethnicity).

The key deliverable will be phenotyping, code, novel interactive visualisation, and a template for regular reporting of these metrics in the years to come. Our estimates will be influential for healthcare improvement, research and the third sector by revealing hidden inequalities across services, regions, and individuals with different socio-demographic characteristics.

Research objectives

- To define clinically recognisable phenotypes of cardiovascular disorders, based on chapter 'I' of ICD-10 in discussion with relevant clinical specialities (cardiology, neurology, vascular surgery) with phenotypes developed as part of CVD-COVID-UK (where possible).
- To define and calculate epidemiological metrics for cardiovascular conditions (incidence, case fatality, recurrence and prevalence) for each time period.
- For major cardiovascular conditions (stroke, MI, heart failure and peripheral vascular disease), to calculate how the epidemiological metrics vary
    - by age, sex, ethnicity, deprivation, multi-morbidity and region across England;
    - by age, sex, ethnicity, deprivation, multi-morbidity between regions.
- To present statistics using data-visualisations

Data sources

- GPES data for Pandemic Planning and Research (GDPPR)
- Hospital Episodes Statistics (HES)
- Sentinel Stroke National Audit Programme (SSNAP)
- Myocardial Ischaemia National Audit Project (MINAP)
- National Heart Failure Audit (NHFA)
- Death records
- Prescription records
- Emergency Care Data Set (ECDS)

Datasets for analysis

Population of England organised in 1-year rolling cohorts; and in 1-month rolling cohorts for four major cardiovascular conditions (stroke, MI, heart failure and peripheral vascular disease) for the period of the public health emergency of international concern declaration by the WHO for COVID (1/2020 to 5/2023)

Cohort	Start date	End date
One-year periods	1st January of earliest full year available in the NHS England SDE	31st December of each full year available in the NHS England SDE
One-month periods	First day of each calendar month, beginning 1/2020	Last day of each calendar month

Phenotype definition

We will define phenotypes using the ICD-10 'I' chapter (https://spiros.github.io/disease_atlas/tree_simplified.html#8). We will consult with a neurologist, cardiologist, and peripheral vascular specialist to define recognised clinical conditions within this chapter (or adapt similar work), and then define each condition using ICD-10 codes (suitable for HES and death records) and SNOMED (suitable for ECDS and GPES), with existing code-lists defined by CVD-COVID-UK members and beyond. We will use data from SNNAP, MINAP and NHFA to define stroke, MI and heart failure, with the definitions used by each audit.

We have predefined four common conditions: all stroke, myocardial infarction, heart failure and peripheral vascular diseases; and four rare conditions: arterial dissection, intracranial venous thrombosis, myocarditis and Taksubo cardiomyopathy.

Characteristic definitions

We will define non-time varying exposures (date of birth, sex, ethnicity) once, and for ethnicity we will use the first defined ethnicity over the whole period of follow up to reduce the amount of missing data in this key demographic variable.

We will define time varying exposures (deprivation, region and multi-morbidity) using the latest information available on the 1st January of each year. We define multi-morbidity as the presence of two or more long term conditions ascertained in any data source (see appendix 1)

Statistical methods for each target disease and for each time period (calendar year or month)

Absolute and standardised incidence

Numerator: count of people with at least one event of the target cardiovascular disease in the follow up period

Denominator: count of people alive with no prior target cardiovascular disease at the beginning of each time period from GDPPR estimates, with sensitivity analyses using ONS estimates

Follow up: time in each period

For the four defined common conditions, incidence will also be calculated standardised to the whole UK population age structure.

30 day case fatality

Numerator: count of deaths of any cause within 30 days from the first incident target cardiovascular disease

Denominator: count of people alive with no prior target cardiovascular disease with at least one incident event of the target disease in each time period

Follow up: 30 days from the first incidence of each person in the denominator

For the four defined common conditions, case fatality will also be calculated standardised to the whole UK population age structure.

Annual secondary cardiovascular disease rate in 30 day survivors

Numerator: count of people with any record of myocardial infarction or stroke more than 30 days after a first incident target condition

Denominator: count of people alive with no prior target cardiovascular disease with at least one incident event of the target disease in each time period who survive 30 days

Follow up: 365 days from the first incidence of each person in the denominator

For the four defined common conditions, incidence will also be calculated standardised to the whole UK population age structure.

Prevalence

Numerator: count of people with a new or prior record of target cardiovascular disease

Population: count of people alive at middle of the time period

Follow up: beginning to mid-point of the time period

For the four defined common conditions, prevalence will also be calculated standardised to the whole UK population age structure.

Subgroup analyses

For all target diseases: calculation of the four metrics by age, sex, ethnicity, deprivation, region and multimorbidity in England.

For stroke, MI, heart failure and peripheral vascular disease: calculation of the four metrics by age, sex, ethnicity and multimorbidity and deprivation for each English region.

Variable	Levels
Sex	Male Female
Age	0-19 20-29 30-39 40-49 50-59 60-69 70-79 80-89 90+
Ethnicity	Asian or Asian British Black or Black British Mixed Other White
Deprivation	Quintiles from Index of Multiple Deprivation 2019
Region	East Midlands East of England London North East North West South East South West West Midlands Yorkshire and The Humber
Multimorbidity	Defined based on number of ICD-10 chapters available at the beginning of each study period: 0-1 2-3 4+

Appendix

Body system as defined by Delphi study	Delphi "always include" conditions	Delphi "usually include" conditions	Inclusion (including aggregation into higher-level condition) or exclusion (and rationale)
Cardiovascular system	Stroke	-	Included (as stroke AND transient ischaemic attack combined)
	Coronary artery disease	-	Included
	Heart failure	-	Included
	Peripheral arterial disease	-	Included
	-	Heart valve disorders	Included
	-	Arrhythmia	Included
	-	Venous thromboembolic disease	Included
	-	Aneurysm	Included
	-	Hypertension	Included
Metabolic and endocrine disease	Diabetes	-	Included
	Addison's disease	-	Included
	Cystic fibrosis	-	Included
	-	Thyroid disorders	Included
Respiratory disease	Chronic obstructive pulmonary disease	-	Included
	Asthma	-	Included
	-	Bronchiectasis	
Neurological disease	Parkinson's disease	-	Included
	Epilepsy	-	Included
	Multiple sclerosis	-	Included
	Paralysis	-	Included
	-	Transient ischaemic attack	Included (as stroke OR transient ischaemic attack combined)
	-	Peripheral neuropathy	Included
	-	Chronic primary pain	Excluded
Cancer	Solid organ cancers	-	Included (as cancer)
	Haematological cancers (included as cancer)	-	Included (as cancer)
	Metastatic cancers (included as cancer)	-	Included (as cancer)

	-	Melanoma (included as cancer)	Included (as cancer)
	-	Cerebral tumours that can cause disability	Excluded: it was decided to exclude based on difficulty in defining this population using code lists applied to routinely collected data
Mental and behavioural disorder	Dementia	-	Included
	Schizophrenia	-	Included
		Depression	Included
		Bipolar disorder	Included
		Drug or alcohol misuse	Included
		Eating disorder	Included
		Autism	Included
		Post-traumatic stress disorder	Included
Musculoskeletal disease	Connective tissue disease		Included
		Osteoarthritis	Included
	-	Long term musculoskeletal problems due to injury	Excluded:
	-	Osteoporosis	Included
	-	Gout	Included
Urogenital disorder	Chronic kidney disease		Included
	End stage kidney disease (included as chronic kidney disease)	-	Included
	-	Endometriosis	Included
	-	Chronic urinary tract infection	Excluded
Haematological disorder	-	Anaemia	Included
Eye disease	-	Vision impairment that cannot be corrected	Included
Ear disease	-	Hearing impairment that cannot be corrected	Included
	-	Meniere's disease	Included
Infectious disease	HIV	-	Included
		Chronic Lyme disease	Excluded
	-	Tuberculosis	Included
	-	Post-acute ~~covid~~COVID-19 (study pre-2020)	Excluded (too frequent)
Congenital disease	-	Congenital disease and chromosomal abnormalities	Included

Digestive disease	Chronic liver disease	-	Included
	Inflammatory bowel disease	-	Included
	-	Chronic pancreatitis	Included
	-	Peptic ulcer	Included