



QResearch News Update Spring 2021

In this edition

- ◆ QResearch breast cancer prediction model gets the green light
- ◆ Blog: Finding the Vulnerable Before COVID Does
- ◆ Project case study: QCovid-19 risk stratification
- ◆ QResearch PPI Recruitment marks increase in member diversity
- ◆ QResearch Scientific Committee member focus: Madhurima Bhadra
- ◆ New QResearch Pancreatic Cancer project aims for earlier diagnosis
- ◆ Research Project Summary—characteristics of Hepatitis B associated with Cirrhosis and Cancer
- ◆ Risk of severe Covid-19 from asthma, respiratory conditions

Next Issue

We hope that you are enjoying our newsletters. We think that they are a great opportunity to feature some of the wide-ranging projects that have been enabled by access to QResearch data.

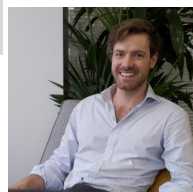
To feature your research news here, please email Claire Meadows at pa-Julia.hippisley-cox@phc.ox.ac.uk

QResearch Breast Cancer Prediction Model Project Gets the Green Light

Breast cancer is the most common form of cancer affecting women in the UK, and mammography screening is an approach used in many countries to detect breast cancers at an earlier stage. In the UK, for the majority of women that do not have known high-risk mutations such as BRCA, this involves mammograms for women aged 50–70 years every three years. However, the individual levels of risk for women vary widely, and there is increasing interest in 'personalising' or stratifying screening based on individual predicted risk, rather than using the 'one size fits all' approach. Risk prediction models have been developed for breast cancer incidence, but the evidence regarding their suitability to guide risk-stratified screening is not yet clear. Furthermore, there is growing interest in the possible applications of 'machine learning' algorithms to clinical risk prediction.

This project is using anonymised electronic health record data for over 11.6 million women, linked at the individual level to GP, hospital, cancer registry and death registry records, to develop and robustly evaluate a set of modelling approaches to estimate risk of developing breast cancer, the combined risk of developing and then dying from breast cancer, and also the risk of dying after being diagnosed with breast cancer. Aside from being the largest ever study undertaken in risk prediction modelling in breast cancer, this project has a strong focus on methodological aspects, such as assessing whether developed models work equally well across ethnic groups, whether they 'transport' to different regions and time periods, and performing fair, transparent comparisons between regression and machine learning approaches.

A protocol was submitted for consideration of publication, with data cleaning and preliminary analyses starting in January 2021. Interim results using Cox modelling on 'complete case' and multiply imputed samples of data are encouraging in terms of discrimination, calibration and transportability, and we look forward to sharing the final results for several models by Summer.



This work is being undertaken by Ash Clift (pictured) as part of his DPhil in Cancer Science under supervision from Julia Hippisley-Cox, Gary Collins, David Dodwell, Simon Lord, Mike Brady and Stavros Petrou. It is funded by Cancer Research UK.



Blog: Finding the Vulnerable Before COVID Does

Lee Gathercole, Technical Architect for NHS Digital writes

At the beginning of the pandemic, the Chief Medical Officer for England asked leading academics, clinicians and scientists to create a way of predicting who may be at high risk of serious illness if they catch coronavirus (COVID-19).

From this, the COVID-19 Risk Stratification programme was commissioned by the New and Emerging Respiratory Virus Threats Advisory Group to produce a data-driven mathematical model.

The University of Oxford led the work and used anonymised GP data to build a model, QCovid[®], that identified combination of factors such as sex, age, BMI, ethnicity and underlying medical conditions to determine an individual's risk of hospitalisation and death from COVID-19.

Historically, risk tools such as QCovid[®] were given to GP system suppliers to integrate into the GP system and used locally to identify those at high risk. However, the Chief Medical Officer for England wanted this risk stratification tool to be executed centrally.

Read more here

<https://f.ls/bsspj>

Project case study: QCovid: COVID-19 risk stratification

With very little data to work with, early efforts to identify those at risk of poor COVID-19 outcomes were based on expert opinion and consensus, which underpinned development of the shielded patient list. As more cases were reported, it became clear that a more diverse range of patients were dying of COVID-19, and a team led by Professor Julia Hippisley-Cox was tasked with developing a 'living prediction' model that could incorporate new data as it emerged to better identify those at highest risk of poor outcomes.

The QCovid model was conceived as a tool to support communication with patients about their relative level of risk and to stratify and prioritise populations for interventions, including vaccination. It could also stratify patient groups for clinical trials.

The QCovid model was based on data from a representative sample of GPs' electronic health records, covering 20% of the UK population. These data were linked to multiple other data sources, from disease registries, intensive care units, test data and other sources.

The data were divided into two sets, one being used to develop the model and one being used as a validation data set. A further validation was carried out on an independent data set, the ONS public health data asset, generated in response to COVID-19, which covers 40 million people.

The model showed excellent predictive power, with the top 5% of the population identified as being at highest risk accounting for 75% of all deaths, and the top 20% making up 94% of all deaths.

QCovid has been incorporated into a living systematic review of COVID-19, and was identified as having particularly low risk of bias. It has placed great emphasis on transparency, and a web-based calculator has been developed that implements the algorithm and is available for research use (<https://qcovid.org>). An NHS version with linkage to other data sources is in routine clinical use. The model is updated as new data emerge, and as factors change the risk of disease (such as the roll-out of vaccination).

The QCovid is an extension of other similar tools developed by the team for other conditions, and the approach adopted for COVID-19 could be applied to additional diseases to support patient stratification and aid clinician decision-making.

For more information see here

<https://digital.nhs.uk/coronavirus/risk-assessment/clinical-tool>

and

<https://www.emishealth.com/news-events/news/nhs-uses-qcovid-risk-model-to-fast-track-vaccinations-for-the-vulnerable/>

About QResearch

QResearch is a large consolidated database derived from the anonymised health records of over 35 million patients.

The data currently come from approximately 1500 general practices using the EMIS clinical computer system.

The practices are spread throughout the UK and include data from patients who are currently registered with the practices as well as historical patients who may have died or left.

Historical records extend back to 1989, making it one of the largest and richest general practice databases in the world.

Founder Julia Hippisley-Cox is based at Nuffield Department of Primary Health Sciences, Medicine Sciences Division, University of Oxford.

www.qresearch.org

In this new pancreatic cancer study, the researchers will evaluate:

- (1) association between type 2 diabetes and related illnesses with pancreatic cancer,
- (2) quantify referrals for pancreatic cancer scans amongst patients diagnosed with type 2 diabetes in primary care in line with NICE guidance, and
- (3) identify potential markers to predict pancreatic cancer among type 2 diabetes patients diagnosed in primary care.

QResearch PPI Recruitment Marks Increase in Member Diversity

Following the guidance of the QResearch Advisory Board to embed PPI within all aspects of our research we sought members of the public and patients to recruit for the QResearch Scientific Committee. In order to review an increasingly diverse range of research applications we sought academics and clinicians from a range of research and primary care specialties.

To work towards the membership of our committee being more diverse and more representative of the patients whose data we hold, we carried out recruitment in a way that we hoped would enable and encourage a diversity of applications.

QResearch Scientific Committee Member Focus: Madhurima Bhadra

Madhurima Bhadra is a project management professional with wide-ranging experience in primary care research, fund-raising in non-governmental organisations, renewable energy management and over 15 years in general practice management. She has represented practices on information governance panels, including as administrator on the multi-professional Newham GP Reference Panel which ensured requests to access patient data to provide health care services or undertake research were fit for purpose and met Data Protection and ethical standards.

New QResearch Pancreatic Cancer Project Aims for Earlier Diagnosis

Despite improvements in treatment and care, pancreatic cancer remains to be a very deadly disease. This is mainly due to patients presenting at late stages of disease as it mostly shows no or vague symptoms in early stages. About 25-50% of patients who develop pancreatic cancer have some form of diabetes.

However, currently, pancreatic cancer has only been found in approximately 1% of new-onset type 2 diabetes, and hence, there remains an important need for GPs to better identify at-risk patients. Patients with pancreatic cancer who are diagnosed at an earlier stage have more treatment options and may be able to undergo surgery and have better outcomes.

The researchers (including Dr Pui San Tan, pictured below) will use primary care information from QResearch. This will be linked to hospital records, cancer registry and death records to search for individual new-onset diabetes patient characteristics (e.g. age, gender, lifestyle) that are associated with a later diagnosis of pancreatic cancer. These linkages will be used to generate estimates using standard statistical procedures to better understand how pancreatic cancer can be diagnosed earlier among type 2 diabetes patients presenting in GP clinics.



This study will help better understand the association between diabetes and pancreatic cancer and identify potential opportunities for earlier detection of pancreatic cancer by GPs in the primary care setting.

Risk of severe Covid-19 from asthma and other respiratory diseases only modestly increased, new analysis suggests

People with asthma have only a modestly increased risk of developing severe Covid-19 and requiring admission to hospital from the illness, finds an analysis of 8.3 million electronic health care records in England led by University of Oxford researchers.

Published in *The Lancet Respiratory Medicine*, the study examined routine patient data collected between January 2020 to April 2020 to generate risk assessments for severe Covid-19 in people with chronic respiratory diseases. Unlike previous studies of people hospitalised with Covid-19, which suggest large increases in risk associated with underlying respiratory disease, this analysis demonstrates that the risk of severe Covid-19 is only modestly raised over the risk in people without such conditions.

The analysis reviewed several respiratory diseases and included data from 1.09 million people with asthma, 193,520 people with chronic obstructive pulmonary disease and 5,677 people with other interstitial lung disease. It compared the risks in these groups to 7 million people without respiratory diseases.

When adjusted for age, sex, demographic factors, underlying health conditions and compared with those without respiratory diseases, people with active asthma and severe asthma were at 26% and 29% higher relative risk of hospital admission with Covid-19, respectively, and around 30% higher relative risk of admission to intensive care.

There was no evidence that asthma was associated with an increased absolute risk of death from Covid-19, and the risks appeared similar for all ethnicities.

Having chronic obstructive pulmonary disease (COPD) was associated with a 50% increased risk of hospitalisation and 54% increased risk of death from Covid-19, which was higher in those with white ethnicity.

In patients with interstitial disease, a group of less common lung diseases which cause scarring of the lung tissue, the analysis shows a 30–50% increased relative risk of developing severe Covid-19 requiring hospital admission or leading to death. Patients in this group are currently advised to shield.

Though a concern for many, the risk of long-covid in people with respiratory disease was not determined in this study.

Lead researcher Professor Paul Aveyard, a general practitioner and Professor of Behavioural Medicine in the University of Oxford's Nuffield Department of Primary Care Health Sciences said: 'At the start of the pandemic, the assumption that pre-existing respiratory disease would lead to an increased risk of serious Covid-19 illness was reasonable.'

For more information see here <https://digital.nhs.uk/coronavirus/risk-assessment/clinical-tool>

QResearch Project Summary – Characteristics of Chronic Hepatitis B Associated with Cirrhosis and Cancer

Researcher Cori Campbell writes

Nearly 300 million individuals are infected with hepatitis B virus (HBV) worldwide, and HBV is the leading global cause of primary liver cancer (PLC) death. However, HBV population demographics and risk factors for PLC have not been well characterised.

We have established a cohort of 7952 patients with chronic HBV infection (CHB) using ICD/READ codes in the QR database. The majority of patients in the cohort are male (61%). At baseline (time of CHB diagnosis), 74% of patients were aged < 45 years, 44% were residing in the most deprived geographical regions, and > 50% were non-white. In this cohort, we report significantly increased odds of PLC in patients with diabetes mellitus type 2 (T2DM) (OR 1.70, 95% CI 1.01–2.80) and reduced odds associated with statin use (OR 0.63, 95% CI 0.42–0.94) in multivariable models adjusted for age, sex, demographics and other T2DM treatment.

The researchers plan to develop a prognostic PLC risk score in our cohort, and we will be submitting an application to the NIHR Research for Patient Benefit scheme to support this ongoing program of work.

