DESIGNING A CLINICAL STUDY FOR PANCREATIC CANCER RISK FACTORS

1 Introduction

Pancreatic cancer is the 10th most common cancer with 10,449 people diagnosed with pancreatic cancer in the UK in 2018. It has the lowest survival of all common cancers, with five-year survival less than 7%.

Early diagnosis is crucial to improve survival outcomes, with one-year survival in those diagnosed at an early stage six times higher than one-year survival in those diagnosed at stage four. However, most people with pancreatic cancer are diagnosed at a late stage (UK statistics on https://www.pancreaticcancer.org.uk/).

Patients usually experience no specific symptoms until the cancer is in a late stage. Currently there is no screening programme for pancreatic cancer in the UK, nor are there data to show reduced mortality from pancreatic cancer from any screening test. The diagnosis is usually made by imaging, after late symptoms such as jaundice and weight loss have already developed. Some data provide preliminary support for use of imaging methods (endoscopic ultrasound and MRI) if patients screened are **at increased risk** of pancreatic cancer. Therefore an accurate, non-invasive way to identify people at sufficiently high risk could enable the development of pancreatic cancer screening.

Known risk factors for pancreatic cancers include age, sex, smoking, high body mass index (BMI), diabetes, certain chemicals, ethnicity, and family history. There have also been investigations on the utility of a variety of **biomarkers** to identify those at sufficiently increased risk of pancreatic cancer to justify screening using imaging.

Cohort studies have a long history, but a recent development has been the use of biobanks from large population cohorts (such as UK Biobank - https://www.ukbiobank.ac.uk), that record data on participants from traditional questionnaires, in addition to biological samples, for instance to help evaluate the association between genetic variation, environmental exposures for risk of disease. Disease-specific biobanks have also been developed. One such at Barts Cancer Institute is the Pancreatic Cancer Research Fund Tissue Bank (PCRF, for further details see https://www.thepancreastissuebank.org). Set up in 2016, it has collected:

- Blood samples from 2,200 consenting patients who underwent biopsies or surgery for pancreatic diseases, including pancreatic cancers (also urine, saliva and tissue samples);
- Large numbers of healthy control blood (also urine and saliva).

2 Group activity

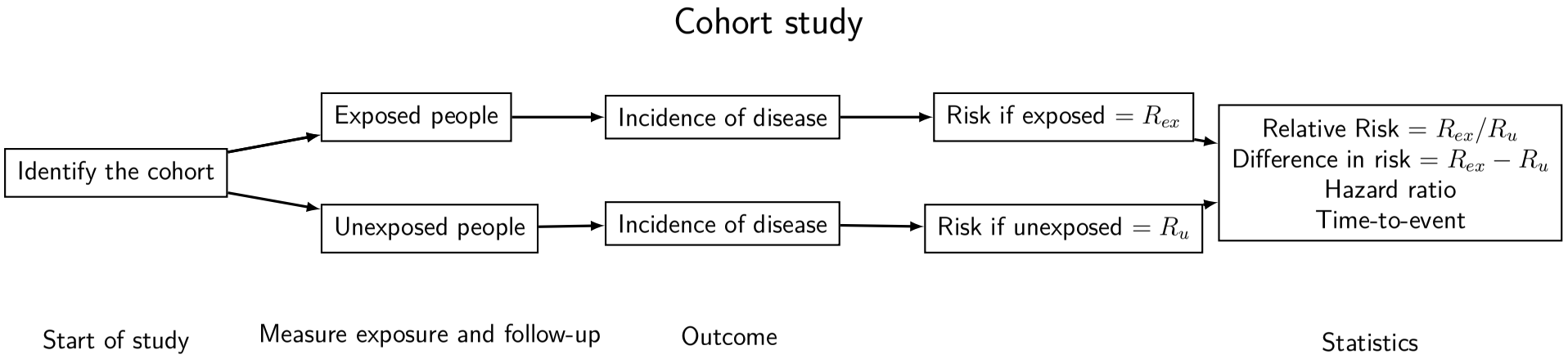
Assume that Cancer Research UK is going to fund two different studies to investigate whether your research group's biomarker panel can help stratify risk of pancreatic cancer, and enable early detection that might lead to improvements in public health outcomes. One will be a case-control study, that will report its results within 3 years and the second group they need to design a cohort study which will report its results within 13 years.

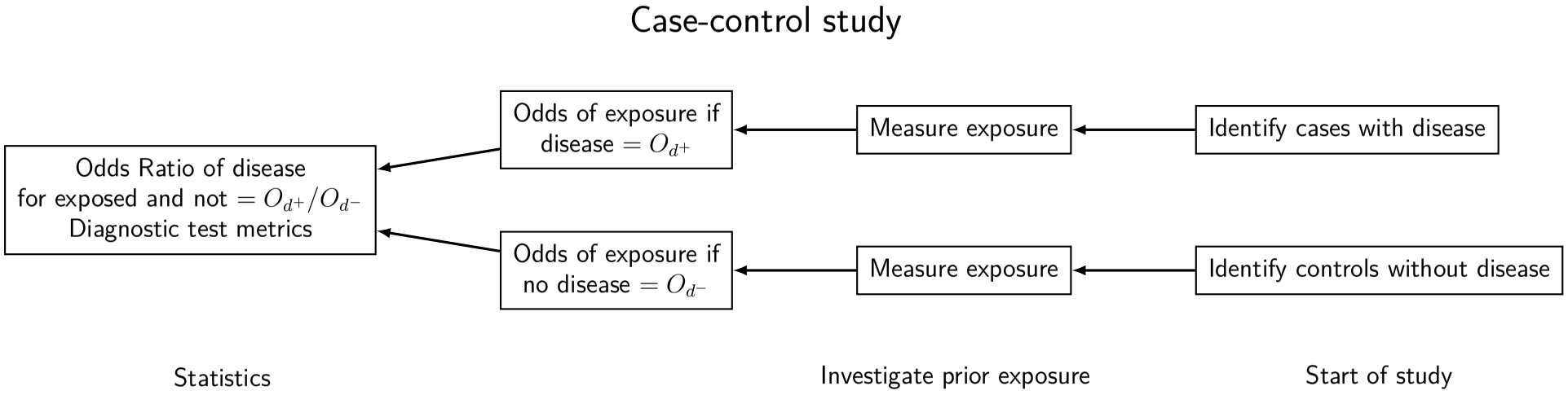
Group A (and multiples) needs to design a case-control study that reports results within 3 years;

Group B design a cohort study that reports results within 13 years.

3 Annotated students' materials

3.1 Cohort and case control studies and possible metrics





A: Case-control study with results in 3 years	**B: Cohort study with results in 13 years**
What are your entry criteria for **cases**?	What characteristics of the cohort will make the follow up easier and enable you to obtain useful results? Think about who will you recruit - what type of people, for where and how, how many?
Most case-control studies match cases and controls. What would you match on and what are your entry criteria for **controls**?	
Describe how you will recruit to the case control study (remember you can use a biobank)	

What is a simple binary risk factor or exposure?

How else could you measure the risk factor (biomarker)?

Briefly describe how you would collect information on the risk factor.

Give the most accurate and useful simple binary measure of outcome for your study.

Who will the actual results be representative of?

Who will these results be useful for?

What other results could your get from your study group?

Could the age of the participants affect the interpretation of your results? If so how?

What biases could occur from your study design?

Give an example of a study of an exposure and a disease that would be unsuitable for your type of study but suitable for the other. Explain the characteristics of the exposure or disease that make it unsuitable

Summarise the advantages in general of your type of study?

Summarise the disadvantages in general of your type of study?

Table 1: Fill in the side corresponding to your group.

Further reading:

- Early detection of pancreatic cancer: https://pubmed.ncbi.nlm.nih.gov/32135127/
- Description of the UROPANC trial: https://www.bartscancer.london/centre-for-experimental-cancer-medicine/clinical-trial-portfolio/uropanc/
- A combination of urinary biomarker panel and PancRISK score for earlier detection of pancreatic cancer: A case–control study: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7758047/
- Germline BRCA2 K3326X and CHEK2 I157T mutations increase risk for sporadic pancreatic ductal adenocarcinoma: https://onlinelibrary.wiley.com/doi/10.1002/ijc.32127
- Noninvasive Diagnosis of Pancreatic Cancer Through Detection of Volatile Organic Compounds in Urine: https://pubmed.ncbi.nlm.nih.gov/29129714/
- Biomarkers in molecular medicine: cancer detection and diagnosis: https://www.future-science.com/doi/10.2144/05384SU04
- Empirical Evidence of Design-Related Bias in Studies of Diagnostic Tests: https://jamanetwork.com/journals/jama/fullarticle/191668
- Statistical Hypothesis Testing versus Machine Learning Binary Classification: Distinctions and Guidelines: https://www.sciencedirect.com/science/article/pii/S2666389920301562