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Epidemiology and ocular disease

OPHTHALMIC PUBLIC HEALTH PART 2 C-18111 O

Professor Darren Shickle and Dr Ruth Hogg

The previous article in this series made it clear that epidemiology plays a key role in public health, particularly in determining health problems within a community. This article will outline the main concepts relating to epidemiology and provide examples of how these have been applied in improving our understanding of ocular disease.

Human epidemiology has been defined as “the study of the distribution and determinants of disease frequency” in populations.¹ It can be split into two categories, which relate to the underlying assumptions that govern it, namely that disease does not occur at random and that causal and preventative factors can be identified by careful analysis:

1. **Descriptive epidemiology** deals with the distribution of disease within a population and takes into account information regarding time (eg, year, season, day, hour), place (geographic variation – national, regional, local) and person (eg, age, race, sex, class, occupation, behaviours).

2. **Analytical epidemiology** involves

identifying possible causes for diseases.

Figure 1 shows the basic study designs used in epidemiological research depending on whether they are descriptive or analytical. Although they all represent different ways of harvesting information, each study design has particular strengths and limitations. Descriptive studies provide information on the occurrence and distribution of morbidity or mortality within a population according to the characteristics of the people affected, characteristics of place and characteristics of time. It may provide the first clues as to the determinants of a disease, and deliver insights that can be useful for healthcare providers planning

prevention programs or allocating resources. However, because a control or comparison group is not evaluated they cannot be used to definitively identify determinants of a given disease, instead, descriptive studies tend to be used to formulate hypotheses, which are then tested using an analytical strategy.

Analytical studies can be classified according to the role of the investigator; in an observational study the investigator follows the natural course of events and records who is exposed and non-exposed and whether subjects develop the disease or not. In an interventional study the investigator allocates which subjects receive the intervention and records who subsequently develops the disease.

In a case-control study a group which has the disease is compared with an appropriately matched group which does not have the disease, and exposure to factors of interest is then compared. Appropriate matching is crucial to the validity of such designs and participants are usually matched by age and gender. However, it is also important to look at the origin of the two populations to assess whether the level of matching is appropriate, eg, if the case population is recruited from a hospital clinic and the control population is recruited from university staff and students, there may be other important factors such as economic or education status that may influence the results; therefore matching should account for these factors as well so that the control population is as similar to the case population as possible. However, this may be logistically difficult as it is usually easier to recruit study participants who have the disease, as they are keen for research to be undertaken, in comparison with control participants who don't have the same incentive to take part.

An example of such a study is Lin et al.² who compared co-morbid conditions

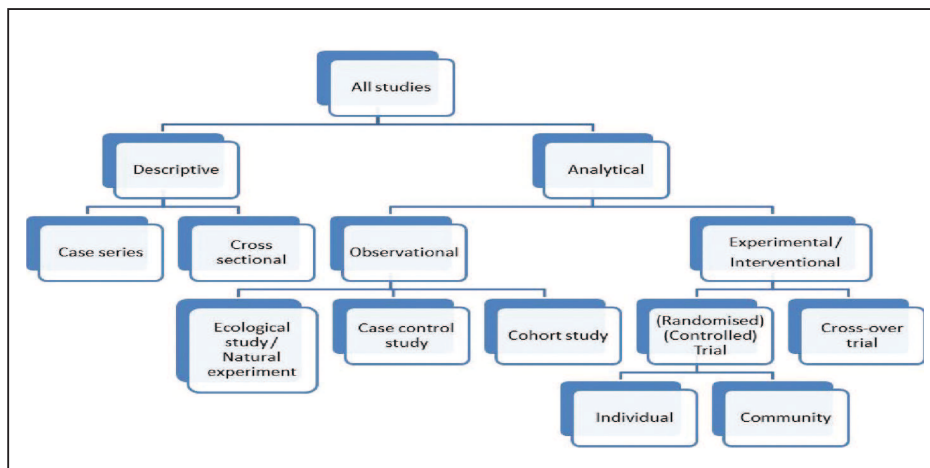


Figure 1
Classification of epidemiology study designs

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between patients with open angle glaucoma (OAG) and those in a control cohort in a case-control study. This study used data from an administrative database and compared 76,673 patients with a diagnosis of OAG to 230,019 randomly selected control patients who were matched in terms of age, gender, urbanisation level and monthly income. The presence or absence of 31 medical comorbidities was compared between the two groups and the prevalence of 28 out of the 31 conditions was found to be higher in the OAG group than the control group. Given the association between deprivation and common illnesses such as diabetes and cardiovascular disease, it is obvious that careful matching on characteristics such as urbanisation level and monthly income was essential in this study.

An alternative strategy is a cohort study in which subjects are classified according to the presence or absence of an exposure (eg, smoking) and then followed-up over time to describe development of the disease in each group. This has the disadvantage that long follow-up times and large numbers of subjects are required so that enough subjects develop the disease to enable meaningful comparisons to be made. Examples of such studies include the Beaver Dam Eye Study in America, the Blue Mountains Eye Study in Australia and the Rotterdam Eye Study in Holland, which have all investigated the prevalence, incidence and progression of age-related macular degeneration (AMD).³

In these studies cohorts were drawn from defined geographical areas and participants underwent ophthalmological examination, anterior and posterior segment photography and

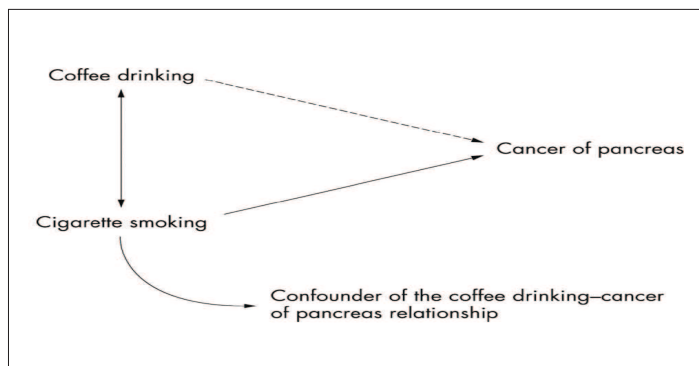


Figure 2

Cigarette smoking as a confounder of the relationship between coffee drinking and cancer of the pancreas. Reproduced with permission from the *Postgraduate Medical Journal* (2004;80:140-147), licence number: 2774111031680

gave blood samples for the purpose of genetic and biochemical analysis. Large amounts of data were also collected regarding medical history, diet and lifestyle via questionnaires, together with important clinical variables such as height, weight, and blood pressure. Although these studies have contributed hugely to our understanding of the prevalence of AMD, identification of important risk factors and progression of the disease, analysis identifying factors related to the incidence and progression of advanced AMD tended to lack statistical power due to the relatively small numbers of participants who either had advanced AMD at study commencement or developed it during follow-up.

Two large meta-analyses combining the data from all three studies provided a powerful way to circumvent the inadequacies of the studies on their own and provided useful information on risk factors for both prevalent and incident disease.^{4,5} Meta-analysis is a statistical procedure in which the results of several studies are mathematically combined in order to improve the reliability of the results and the ability to detect associations by increasing the power of the study. Studies chosen for inclusion in a meta-analysis must be

satisfactorily similar in order to accurately combine their results. For example, the studies on AMD found that age and smoking were the only risk factors that were statistically significant when the studies were combined for meta-analysis for the presence of late stage AMD. When the analysis looked over time at the numbers of people who developed late AMD, smoking and serum cholesterol were statistically significant in the meta-

analysis. Smoking was associated with an increased risk of developing AMD while serum cholesterol showed a strange relationship that the authors of the study could not easily explain; high cholesterol was associated with geographic atrophy and low cholesterol was associated with neovascular disease. Although a meta-analysis has many advantages it is prone to publication bias⁶ as the process is heavily reliant on published studies and it is well-recognised that it is very hard to publish studies that show no significant outcomes, therefore a meta-analysis that is based solely on published data, particularly in the case of observational studies should be interpreted with caution.⁶ For a fuller explanation of sources of biases in published research and how to avoid these see Song et al.⁷

An example of an interventional study within ophthalmology is the Age-Related Eye Disease Study (AREDS), a multi-centre randomised control trial in which approximately 3,600 participants were assigned to receive either a vitamin supplement or a placebo and were then followed up for five years, during which the progression of AMD was assessed. This was a double blind trial in which neither the investigator nor the participant knew whether the



supplement or the placebo had been allocated.⁸ An intervention study of this type is often considered to provide the most reliable form of evidence in epidemiology because participants are allocated to a particular intervention group at random, thereby reducing the risk that factors unrecognised at the time of study design may distort the results. However, when evaluating evidence, it is important to recognise that research questions can be addressed using a variety of approaches and from a pragmatic perspective the design chosen is often influenced by availability of time and resources as well as scientific consideration of the characteristics of the disease and gaps that need to be filled in our current knowledge. For a more detailed discussion of study designs see Hennekens and Buring.¹

The analytical process in epidemiology usually begins with the suspicion that a particular factor influences the pattern of occurrence of a disease, followed by the formulation of a specific hypothesis (eg, smoking causes cancer), which is then tested within a study which includes both individuals with the disease and a suitable comparison group to determine whether a statistical association exists. Even when this is achieved, it is vital to carefully consider alternative explanations, such as chance, bias (errors in the collection and interpretation of data) and confounding. Confounding occurs when a relationship between a risk factor and disease is caused by another variable that may not have been measured within the study but is associated with both the measured outcome and the risk factor.

Figure 2 shows an example in which coffee drinking is shown to be statistically associated with pancreatic cancer; if smoking, which is significantly associated with both coffee drinking and pancreatic cancer,

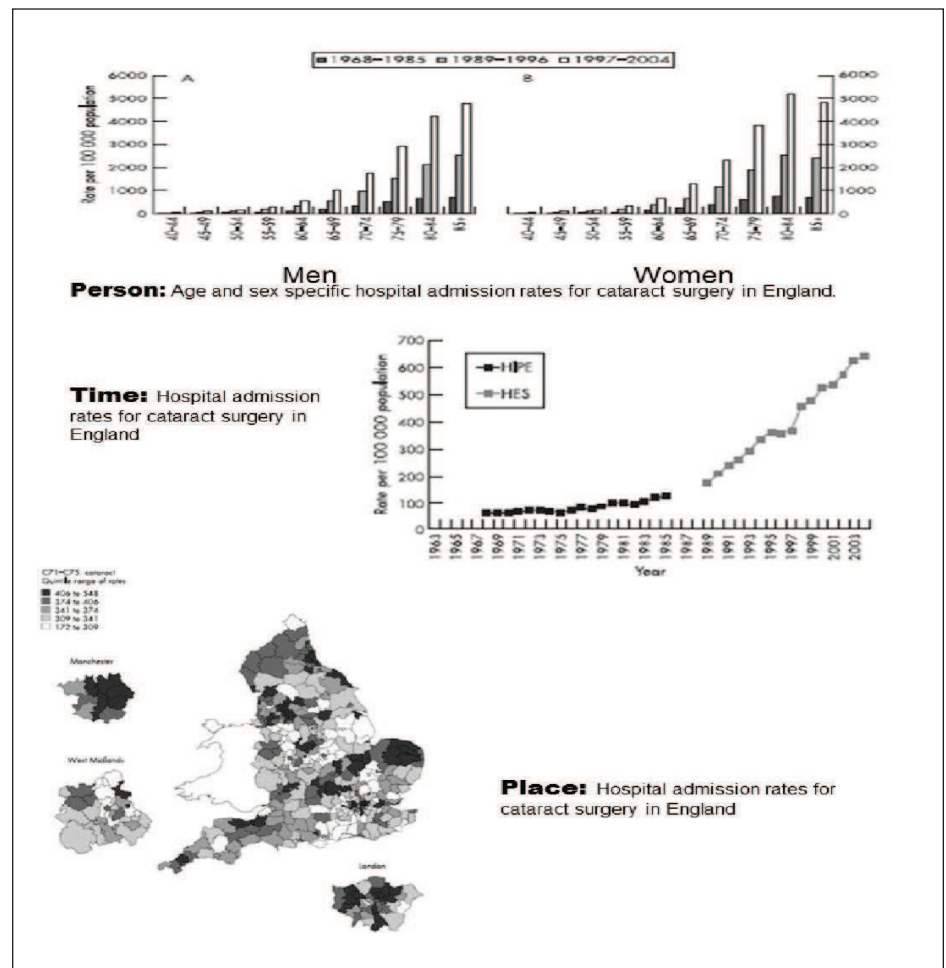


Figure 3

Data relating to hospital admissions for cataract surgery in England. Reproduced with permission from the *British Journal of Ophthalmology* (2007;91:901-904), licence number: 2795281307379

is not taken into account, the strength of the association between coffee drinking and cancer would be erroneously large. Therefore, when reading the latest news report or journal article it is vital that the reader considers whether any important factors have not been accounted for in the design and/or analysis phase of a study, based on an understanding of the natural history of the disease.

Applying the principles of epidemiology to data on rates of hospital admission for cataract surgery in England (Figure 3), there appears to be a dramatic increase in cataract surgery between 1960 and 2000. Having observed this pattern we can then begin to consider various possible causes of

this increase, including an increase in the elderly population in England, the introduction of new technology (eg, phacoemulsification and day case surgery), or a change in the threshold at which interventions were carried out (eg, considering cataract extraction in patients with VA of 6/9 but experiencing visual problems, compared with only considering cataract extraction in patients with VA of 6/12 or worse, regardless of visual problems experienced), or a change in the system for documenting surgical procedures, eg, a change from HIPE (hospital inpatient enquiry) to HES (hospital episode statistics). Figure 3 also appears to show that there is considerable variation in

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the number of surgeries carried out in different regions in England. Once again the public health professional has to think through the possible causes of this pattern, which may be due to an increased prevalence of cataract in areas of deprivation, where there is likely to be higher levels of smoking, poorer diet (containing fewer antioxidants) and increased prevalence of diabetes mellitus. Alternatively the variation may be due to differing referral patterns or differing thresholds for intervention across regions, a “postcode lottery”.

In both of these cases, several plausible reasons can be proposed to account for the pattern observed. The public health professional would then have to consider each of these in turn, acquire the appropriate analytical data and decide in each case which factor is driving the pattern. It is clear that in order to do so successfully, a huge breadth of knowledge is required in terms of the disease under consideration (incidence, prevalence, risk factors),

the treatment (methods used, the introduction of new methodologies and thresholds for intervention), healthcare policies (waiting list initiatives, local commissioner policies, public/private uptake), social demographics (population, age demographics, deprivation, education etc.) and political policies. Methodologies such as these are increasingly being applied to health needs assessments, which aim to identify the health issues facing a particular population, determine the priorities, and inform appropriate resource allocation leading to improved health and reduced inequalities. A future article in this series will consider the data available to an optometrist which may be useful for such an endeavour, while the next article will focus on the role of the optometrist in detection of systemic disease and its implications for public health.

About the authors

Darren Shickle is professor in public

health and head of the Academic Unit of Public Health in the Institute of Health Sciences at the University of Leeds. He is also an honorary consultant in public health medicine, Bradford Hospitals NHS Trust and honorary consultant in public health medicine, NHS Leeds. His population eye research analyses data on uptake of NHS-funded eye tests, and reasons for poor uptake, to explore health inequalities. Dr Ruth Hogg is a lecturer at the Centre for Vision and Vascular Science at Queen’s University Belfast. She qualified as an optometrist in 2000 from the University of Ulster and was awarded a PhD from Queen’s University Belfast in 2005. Her research is focused on the early detection and prevention of advanced AMD, and through this she is also involved in working with the RNIB to promote ophthalmic public health.

References

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1. A cohort study is:

- a) descriptive and observational
- b) analytical and observational
- c) descriptive and experimental
- d) analytical and experimental

2. Confounding represents:

- a) an outcome measure that is significantly correlated with a measured risk factor
- b) too many variables that are measured in the study
- c) an unmeasured variable that is associated with both the outcome and a risk factor
- d) two measured risk factors that are correlated with each other

3. The process of “matching” ensures that:

- a) an equal number of cases and controls are recruited into a study
- b) study participants are matched with the correct treatment modality
- c) cases and controls are matched in terms of demographic variables
- d) confounding is eliminated within the study

4. A meta-analysis:

- a) improves the results by eliminating confounding
- b) can only be undertaken for descriptive studies
- c) eliminates publication bias
- d) improves reliability by combining results mathematically from several studies

5. All of the following have been identified as risk factors for AMD EXCEPT:

- a) a Lutein-rich diet
- b) Smoking
- c) Age
- d) High cholesterol

6. The gold standard in clinical study design to provide reliable evidence is a:

- a) case control study
- b) cohort study
- c) randomised controlled trial
- d) cross-sectional study