# Solutions 8: Case-control studies

## Study 1: Childhood asthma

**Question 1:** The study hypothesis was that there is an association between dampness in the home and asthma in children.

**Question 2:**

a. Paediatric clinic at Kuopio University Hospital (or Kuopio University Hospital's allergy unit).

b. Incident hospital-based cases.

c. Parents of children with ongoing asthma may make changes to the exposure as a result of the disease, including eliminating dampness in the house, to protect the child from asthma. As cases change their behaviour or environment, it becomes more difficult to assess certain exposure-disease associations. In this case, moisture damage may have been repaired by parents before the visit by the building engineer. In contrast, newly diagnosed cases (usually) yet not have changed their environment as a result of disease diagnosis.

d. There are several sources of bias. It is possible that some children were not referred to the paediatric clinic by the GP or that children were not brought to the GP by parents. If there was under representation of children from lower socio-economic families because of unaware parents or unaware GPs (less likely) then the cases in the hospital might be biased with respect to the main exposure. Children with residence less than 2 years were excluded. Again, this may reflect socio-economic bias if poorer families were more likely to move around, and low socio-economic status is associated with living in damp homes. The name for this type of bias is selection bias.

**Question 3:**

a. Controls were randomly sampled from the population register of the area from which the cases were drawn and matched on municipality, age and sex.

b. One of the key and most difficult decisions in designing a case-control study is the choice of controls. An advantage for community controls in this study is that all the cases that arise in the population served by Kuopio University Hospital had to go to that hospital to be diagnosed as having asthma. That would not be the case in many places. Thus, these controls are more likely to reflect the exposure distribution in the source population that gave rise to the cases than perhaps a hospital control group. For example, hospital controls might be more likely to be from low socio-economic status families with poor housing. Therefore, the prevalence of the exposure (damp housing) in the hospital controls might not represent the exposure distribution in the population from which the cases derived.

   This is an example of selection bias. If the prevalence of damp housing was higher in hospital controls compared to population controls the odds ratio would be biased towards the null (no association). It should be noted however that there is no such thing as an "optimal" control group for all situations. Selection of an appropriate control group depends upon a number of factors including the characteristics and source of cases, the methods required for ascertaining exposure (and the need for obtaining comparable information from cases and controls), as well as logistic considerations.

c. Information on the response rate and characteristics of responders and non- responders would help to assess how representative the controls were. If the response rate was low

and the participation in the study was associated with socio-economic status this also might lead to a bias in the prevalence of exposure.

**Question 4:**

a. They wanted a more valid and objective assessment of dampness than asking parents about damp housing. In particular there may be information bias as the parents of children with asthma might be more likely to consider and recall their house damp compared to the parents of the controls.

b. Knowing the hypothesis could lead to observer bias. If the occupants of the houses informed the engineers that their child had asthma, the engineers might be more likely to assess the house very carefully for signs of moisture especially in the child's bedroom.

   The ascertainment of exposure was not retrospective (i.e. it is not possible to know whether the parents had made alterations to reduce moisture in the house after the diagnosis of asthma). This could lead to reverse causality, if for example the parents changed the housing environment when the child first developed symptoms of asthma but before the diagnosis (for this bias to occur the parents would have had to be aware that dampness and moisture might be associated with asthma); note regarding the direction of association: in this is scenario, the odds of asthma in children living in a damp house would be lower than those not living in a damp house. However, as the study used incident cases and the children were young this is less likely.

c. Possible ways to improve the validity of the exposure measurement:

   - Use of standard protocol
   - Training of observers (building engineers)
   - Testing of inter and intra observer variation
   - Objective measures of dampness

   In fact, the study investigators did some of these: standard protocol, measured agreement between the building engineers (kappa score) in a random 15 households, used a surface moisture recorder.

d. Children with asthma had 2.6 times the odds of living in a house with visible mould in the living areas, compared to children without asthma. Since the confidence interval does not include 1.0, it is unlikely that this association was observed by chance. Note that we can also interpret this OR as "The odds of asthma in children living in a house with visible mould in the living areas was 2.6 times that of children living in a house without visible mould in the living areas".

## Study 2: HIV and male circumcision

**Question 5:**

a. The unadjusted (or crude) odds ratio (OR) for the association of circumcision and HIV was = (48/101)/(121/272) = **1.07.** In other words, in crude analysis, the odds of circumcision among HIV-positive men was 1.07 times the odds of circumcision among HIV-negative men.

b. The authors believed that these factors were potential confounders. For occupation:

   - First, the authors believed that occupational status was proxy for HIV risk. For example, different jobs have different norms relating to sexual behaviour, and different levels of opportunity to have multiple partners. These are known risk factors for exposure to HIV.
   - Second, authors believed that occupational status was associated with circumcision. Again, this is plausible in rural areas that occupations might be affected by

membership in different ethnic groups, and circumcision is certainly related to ethnicity.

- Third, is not plausible to believe that circumcision affects occupational status.

Thus, after controlling for potential confounders (i.e. age, occupation, marital status, sexual history and sexually transmitted infections), the adjusted OR was 0.65. Assuming the authors were correct about these factors being confounders, it means the adjusted OR of 0.65 is closer to estimating the true exposure-disease relationship than the crude OR of 1.07 was. Whereas the crude OR suggests circumcision slightly elevates HIV infection risk, the adjusted OR provides evidence that circumcision is strongly protective.

**Question 6:**

Recall bias is unlikely to explain the association between circumcision and HIV status, as most of the cases and controls were unaware of their HIV status. Furthermore, circumcision status is likely to be well known to the individual respondent.

**Question 7 (Optional: to do in your own time):**

Other considerations may include:

Bias: Was there information bias in the reporting of the exposure? e.g. if some groups were more or less likely to report circumcision, for example due to social perception (e.g. social desirability). Was there selection bias? For example, were HIV positive circumcised men or HIV negative uncircumcised men under-represented, or HIV negative circumcised men or HIV positive uncircumcised men over-represented?

Chance: We would need to see the 95% confidence intervals before coming to a conclusion about this association. In the example of being circumcised the upper CI should be below 1 to indicate a protective effect.

Unmeasured confounding: were there other unmeasured confounders of the association e.g. religion, cultural factors etc. also consider if some confounders were not measured accurately (i.e. how is occupation grouped, how is sexual history measured etc.)