CONFLICTING EVIDENCE: A CONCERN NOT ONLY FOR CYCLE HELMET RESEARCH

Conflicts of evidence

The study of cycle helmets is beset by conflicts between case-control studies, which infer large benefits from helmet use by comparing injuries of cyclists who chose to wear helmets with those who did not, and data from entire cyclist populations when substantial increases in cycle helmet use (sometimes as a result of legislation) show that the benefits, if any, fall far short of those predicted by case-control studies.

Cycle helmet research is not the only area of research where such conflicts exist, as evidenced by an increasing number of papers in epidemiological journals drawing attention to this problem. There have been issues with studies of the effect of hormone replacement therapy on heart disease, vitamin supplements, antibiotics and the MMR triple vaccine. Findings that had appeared robust subsequently turned out to be unreliable or simply wrong.

Hormone replacement therapy

Over a number of years, evidence accumulated through observational studies that combined hormone replacement therapy (HRT) conferred significant protection against coronary heart disease (CHD). The studies compared women receiving HRT with those who didn't; it was noted that those receiving HRT were up to 50% less likely to suffer CHD than the other women. These observational studies were taken by many to be reliable evidence of a causal link and credible mechanisms were advanced to explain this [1]. However, subsequent randomised controlled trials showed that in fact HRT did not protect from CHD, rather the effect was either null or slightly negative [2] [3].

Randomised control trials are considered the most reliable form of evidence because they assign treatment options at random to those taking part. So any differences between the control group and those given HRT are due purely to chance and can be quantified by the law of averages.

But why did the different types of study produce contradictory results?

Some commentators had already pointed out that case-control studies could be used to show that HRT apparently conferred protection against violent death. Such an improbable result suggested a socio-economic bias in women who took HRT. Later investigations revealed that doctors tended to be risk-averse in how they prescribed HRT, avoiding women who already exhibited risk factors for CHD, such as hypertension and diabetes. Also, women who requested HRT were generally more health-conscious than those who did not, and were generally of higher socio-economic status. When the data were analysed, these biasing effects were not adequately accounted for, and this probably led to the misleading conclusions.

Vitamins, antibiotics and MMR

Leading epidemiologists have also questioned the findings of several observational studies suggesting that anti-oxidant vitamins confer longer life and protection against CHD and cancer [4]. As with HRT, randomised controlled trials have failed to repeat these findings [4]. Re-analysis of the original data suggested that the differences originally attributed to vitamin supplementation were probably due to socio-economic differences between those who chose to take supplements and those who did not. Although the observational studies tried to adjust for these differences, their conclusions were nonetheless incorrect and misleading.

There may be other examples of this problem. For example, the association between cannabis use and psychosis has been questioned [5]. Several observational studies showing an apparent link between antibiotic use in early life and a subsequent risk of asthma have also been questioned; time-trend data show no association [6].

Finally, some researchers claimed observational data show the MMR triple vaccine increases the risk of autism. The scare was sustained long after the association was refuted and may have reduced public confidence in an important public health programme.

Smoking: a case of non-conflicting evidence

Comparison with the science on smoking and lung cancer is informative. Here the predictions of case-control studies were matched by population-level statistics which showed that levels of lung cancer tracked the growth in smoking. Two independent sources of evidence agreed, and were further supported by animal-based testing, leading to a robust conclusion regarding the link between smoking and cancer. The contrast with cycle helmet research is stark: for helmets the different study types disagree on both the magnitude and the direction of any relationship.

Snowball effect

A similarity between these now controversial areas of epidemiological research has been the existence of a 'snowball effect', where observational studies have led to further similar studies in which the researchers have overlooked and repeated the methodological shortcomings of the earlier studies in their keenness to find a solution to a perceived problem.

Meta-analyses are also published, which summarise the state of present knowledge on a subject without actually adding any new data. As these various studies cite each other in turn, the list of references in support of the intervention builds up without necessarily adding to the sample base under consideration. In a relatively short period of time, acceptance of the need for and effectiveness of the intervention becomes the conventional wisdom in the medical profession and beyond.

Against this background, research that comes to a different conclusion can have difficulty making an impact. When the randomised control studies into HRT were published, reactions were mixed. Some researchers tried to rework their data to fit the results of the trials, in effect to 'prove' that they were right all along. Others denied the validity of the new data. Some tried to explain the discrepancy by reference to differences in the study groups.

Implications for helmet research

The recognition that case-control and other observational studies may be fallible is valuable in the context of evidence for and against the efficacy of cycle helmets. The parallels with the examples given above are compelling.

Case-control studies reported high levels of protection from serious head injury, although many were conducted at a time when helmet use was low - only 3% in the case of the most widely cited paper [7]. However, time-trend studies have repeatedly shown little or no reduction in serious head injuries even where helmet wearing has increased sharply because of helmet legislation [14]. Given the universal failure of time-trend data to show any benefit from increasing helmet use, it is difficult to accept that cycle helmets confer significant protection at the individual level.

So why did the case-control helmet studies report very high levels of protection, up to 75% in the Addenbrooke's Hospital study in Cambridge in 1993 [8]? Serious head injuries to cyclists are fairly rare and the rate of helmet use was at that time low (11%). Thus the figure of 75% is not really as robust as it may look, being hedged by large error limits. The 95% confidence limits ranged from 6% to 90% protection.

Was this result also distorted by confounding socio-economic factors? There are often large differences in socio-economic factors between groups of cyclists who choose to wear helmets and those who do not. It was noted in Australia that those most resistant to helmet use appeared to be from the lower socio-economic groups. More formal study from Canada has shown that children of well-off parents are 2-3 times more likely to use helmets than those from poorer homes [9]. It has also long been noted that children from families without a car are many times more likely to be killed or seriously injured in road crashes than those from better off homes [10]. These two factors affecting lower socio-economic groups – lower helmet use, but greater risk of serious head injury– provide one plausible explanation as to why case-control studies have yielded excessive estimates of helmet efficacy.

A particular problem with cycle helmet research is that randomised control trials are not possible, for ethical and practical reasons. Moreover, the observational studies are usually published in the medical academic press and the conflicting evidence may be published in entirely different journals, outside the academic press, or not at all (being accumulated by ongoing and more widely based data collection processes involving civil servants rather than academics). In this way considerable momentum may be built up before the medical establishment becomes aware of the existence of the conflicting evidence. The medical press is also dominated by an interventionist approach, which may not always be the most appropriate. For example, some recent road safety innovations have taken the opposite direction, removing the effects of decades of interventions to produce a road environment devoid of paint and signage with, it seems, very positive results. In cycling, convincing evidence has been published that the most effective way to improve cycling safety is to encourage more people to cycle [11] [12].

Paralleling the experience with MMR, important public health benefits will be lost if cycling is discouraged by publicity trying to convince cyclists that, despite its relatively low injury rate per hour of activity, riding a bike is dangerous and helmets should be worn at all times. It is poor science to ignore the substantial body of evidence concerning head injury rates when legislation has increased helmet-wearing rates by 40-50 percentage points. These studies show beyond doubt that even very large increases in helmet use have little or no tangible benefit, and the best way to reduce injuries to cyclists is to try and prevent accidents from happening in the first place.

Lessons for the future

In an examination of the controversy that now surrounds observational studies, the editor of the International Journal of Epidemiology writes [13] that:

> *"It is, at the very least, clear that observational epidemiology may be more fallible than some have suggested".*

Also that:

> *"There is … at least as much to be learned from studies that have reached what now appear to be the wrong conclusions, as those that got it right. In many cases these will have been carried out to the highest standards, yet somewhere along the line, the authors were misled."*

Furthermore:

> *"An important clue as to whether the findings of individual-level associations in observational epidemiological studies are likely to be causal can come from time-trend or ecological data."*

Drawing four lessons from the HRT controversy, Pettiti recommends [2]:

- Do not turn a blind eye to contradictory evidence (such as from whole population time-series data) and especially do not repudiate it, but try instead to understand the reasons behind the contradictions.
- Do not be seduced by mechanism. Even where a plausible mechanism exists, do not assume that we know everything about that mechanism and how it might interact with other factors.
- Suspend belief. Of researchers defending observational studies, Pettiti says this: "Belief caused them to be unstrenuous in considering confounding as an explanation for the studies".
- Maintain scepticism.

References

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