Information in practice

Using epidemiological data to guide clinical practice: review of studies on cardiovascular disease and use of combined oral contraceptives

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Abstract

Objective: To explore the usefulness of epidemiological data to guide clinical practice by seeking an answer to the question "What is the risk of cardiovascular disease among users of currently available, low dose, combined oral contraceptives who are aged less than 35 years, do not smoke, and do not have a medical condition known to increase the risk of vascular disease?"

Design: Review of all relevant published studies identified from the library of references held by Royal College of General Practitioners' Manchester Research Unit, checking of reference lists of identified studies, and Medline search.

Main outcome measures: Identification of methodologically sound studies able to address the specific clinical question.

Results: Our literature search identified 74 papers about the relation between current use of combined oral contraceptives and cardiovascular disease: 23 papers reporting risk of venous thromboembolism, 22 on ischaemic stroke, 13 on haemorrhagic stroke or subarachnoid haemorrhage, 13 on all stroke, and 33 on myocardial infarction. Only five papers provided information that directly addressed our clinical question; all related to the risk of venous thromboembolism. Fourteen of the discarded papers probably had the potential to answer our clinical question.

Conclusions: Much of the epidemiological data about the risk of cardiovascular disease in users of combined oral contraceptives is not useful to clinicians. Some of the discarded data could be made more useful to clinicians by reanalysis. This situation is unlikely to be unique to use of contraceptives.

Introduction

Epidemiology is the study of the distribution and determinants of health related states or events within a specified population,[1] its purpose being to inform decisions about the control of health problems. This population perspective usually results in epidemiologists being interested in looking at overall, average effects within the groups under investigation. In a randomised trial this would be the average effect (usually benefit) of a treatment, and in an observational study it would be the average effect (often risk) associated with a factor. Subgroup analyses looking at effects in individuals with specific characteristics tend to be treated with circumspection, even in systematic reviews, in which the quantity of data is greater.[2] Clinicians, on the other hand, are not interested in average effects; they need information about specific risks and benefits faced by the individual patients consulting them. Difficulties arise when clinicians try to use epidemiological data to guide clinical decisions.

In October 1995 the Medicine Control Agency of the United Kingdom announced that new epidemiological data indicated that users of certain brands of combined oral contraceptives might have a higher risk of venous thromboembolism than women using other types of combined contraceptive pill. At the same time, tentative evidence was emerging that the contraceptive pills associated with an increased risk of venous thrombosis might have a lower risk of myocardial infarction. In the following few weeks, thousands of users of combined oral contraceptives attended their doctors for information about their particular risk of cardiovascular disease. For most women, the specific clinical question that needed an answer was: "What is the risk of cardiovascular disease among users of currently available, low dose, combined oral contraceptives who are aged less than 35 years, do not smoke, and do not have a medical condition known to increase the risk of vascular disease?" In order to see if this question could be answered by available epidemiological data, we reviewed all published studies of cardiovascular disease in users of combined oral contraceptives, adopting an approach similar to that of a systematic reviewer.

Methods

Identification of studies

We identified studies from papers in the extensive library of reprints held by the Royal College of General Practitioners' Manchester Research Unit, by searching the reference lists of each paper, and by conducting a computerised literature search of Medline. We considered papers that provided a risk estimate for current use of combined oral contraception (or with sufficient raw data to enable us to calculate it). We were not interested in studies which examined only former users since it is generally agreed that the risk of

Full details of references w1-w43 appear on our website

cardiovascular disease associated with combined oral contraceptives is confined to current users.[3] We used only the most recently published report from each study unless an earlier paper contained information that was not available in the later report.

Selection of studies

We both assessed the identified papers using the following inclusion criteria.

Was the evidence relevant to our clinical question?

- Did the study examine currently available combined oral contraceptives?
- Did the study examine apparently healthy women?
- Did the study compare users with non-users?

Were there obvious problems with the remaining evidence?

- Did the studies of stroke and myocardial infarction collect information about smoking?
- Were data for healthy women presented specifically for low dose formulations?

Results

Our search identified 74 papers about the relation between current use of combined oral contraceptives and cardiovascular disease, some of which reported on more than one vascular outcome. Thus, 23 reported on venous thromboembolism,[4–10 w1-w16] 22 on ischaemic stroke,[11–16 w1-w4 w17-w28] 13 on haemorrhagic stroke or subarachnoid haemorrhage,[12 16–20 w1 w12 w18 w22 w23 w25 w27] 13 on all stroke,[12 17 21 w9 w13 w18 w26 w29-w33] and 33 on myocardial infarction.[17 22–34 w1-w3 w6 w9 w11-w13 w23 w34-w43]

Selection criteria

Did study examine currently available combined oral contraceptives?

During the past three decades there have been major changes in the composition of combined oral contraceptives and the characteristics of women using them.[35] In view of these changes, we decided to include only studies that completed data collection after 1980 unless an earlier study supplied data about the risk associated with low dose products (that is, those containing <50 µg oestrogen). Of the 74 studies, 28 failed to meet this criterion.[16–19 22–26 w1-w10 w18 w23 w30 w31 w34-w38] Another study was conducted between 1980 and 1982, but 65% of its periods of observation related to use of combined oral contraceptives containing ≥ 50 µg oestrogen, and the authors did not provide separate risk estimates for lower dose preparations.[w11] We therefore also excluded this paper.

Did study examine apparently healthy women?

Sometimes it was difficult to determine the characteristics of subjects in a study. If a study of venous thromboembolism was reported to have excluded events that occurred in women with a history of this problem or during or soon after surgery or pregnancy, we assumed that it studied an apparently healthy group of women. Failure to make these exclusions in any analyses resulted in our rejecting five papers from our assessment of the risk of venous thromboembolism.[6 7 w12-w14] Similarly, we rejected 15 studies of stroke for failing to exclude events occurring in women with a history of stroke, other arterial disease, hypertension, or diabetes mellitus,[12–15 20 w17 w19 w20 w22 w24-w29] and we rejected nine studies of myocardial infarction for failing to exclude events occurring in women with a history of this condition, other arterial disease, hypertension, or diabetes mellitus.[28–30 32 33 w12 w40-w42]

Did study compare users with non-users?

Four studies were excluded because they lacked an adequate control group.[21 w15 w21 w32] Another paper provided estimates of the risk of venous thromboembolism in users of different combined oral contraceptives but did not have a comparison group of non-users.[w16] Since it was uninformative about whether users of these preparations have a different risk to that of non-users, we rejected it.

Did studies of stroke and myocardial infarction collect information about smoking?

This was a particular concern because smoking is an important confounder of the relation between the risk of arterial disease and the use of combined oral contraceptives. We rejected one paper that used data from a cohort of women in the group health cooperative of Puget Sound and was unable to collect any information about smoking.[w40]

Were data presented specifically for low dose formulations?

Four papers provided risk estimates for healthy women using combined oral contraceptives of any dose.[6 31 34 w44] None reported separate results for use of low dose preparations and so were unable to address our question.

Eligible studies

After excluding the rejected studies, we were left with seven papers; five relating to risks of venous thrombosis,[4 5 8–10] one to risks of stroke,[11] and one to risks of myocardial infarction.[27]

Venous thrombosis

There was reasonable evidence that currently available combined oral contraceptives are associated with an increased risk of venous thrombosis in healthy users (table). The more recent studies included many events, so the risk estimates had reasonably tight 95% confidence intervals. The World Health Organisation's study reported separate risk estimates for venous thromboembolism in healthy users living in different geographical areas (Europe and developing countries) and in separate age groups (<35 and ≥ 35).[8] Information was also given about the risk in women who smoked, who were overweight, and who had a history of hypertension in pregnancy, but only as an overall risk among users of any type of combined contraceptive pill, not separately for low dose preparations. Three studies provided separate risk estimates associated with low dose formulations containing specific progestogens.[8–10]

Two cohort studies provided data that could be used to estimate the incidence of venous thromboembolic disease in healthy users of low dose combined oral contraceptives and in non-users.[5 9] Vessey et al found that the crude incidence of possible, probable, or certain deep vein thrombosis or pulmonary embolism was $12.2/10^5$ woman-years in non-users (never and past users combined) compared with $39.4/10^5$ woman-

Current best evidence of cardiovascular risk among apparently healthy users of available low-dose combined oral contraceptives

Study	Years data relate to	Age range (years)	Study design	Events studied	Current use of contraceptives: No of users	Risk estimate (95% CI)	Subgroups analysed
Helmrich et al[4]	1976-83	18-49	Case-control	Non-fatal deep venous thromboembolism and pulmonary embolism	5	11.0 (3.7 to 32.0)	
Vessey et al[5]	1968-85	25-56	Cohort	Fatal and non-fatal superficial venous thrombophlebitis, deep venous thromboembolism, and pulmonary embolism	3	3.3 (0.9 to 11.4)*	
WHO[8]	1989-93	15-49	Case-control	Non-fatal deep venous thromboembolism and pulmonary embolism	132	4.3 (2.9 to 6.5)	European, aged <35
					42	3.9 (2.3 to 6.6)	European, aged ⩾35
					93	3.2 (2.3 to 4.5)	From developing country, aged <35
					28	2.5 (1.5 to 4.3)	From developing country, aged ⩾35
Jick et al[9]	1991-4	<40	Cohort	Non-fatal deep venous thromboembolism and pulmonary embolism	75	6.1 (2.5 to 15.1)*	
Lewis et al[10]	1993-5	16-44	Case-control	Fatal and non-fatal deep venous thromboembolism and pulmonary embolism	334	4.4 (3.4 to 5.8)	

*Estimated from data presented in study.

years in users of low dose preparations.[5] Jick et al estimated that the crude incidence of venous thrombosis was $3.8/10^5$ woman-years in past users and $23.2/10^5$ woman-years in current users of any low dose combined contraceptive pill.[9]

Stroke

The one eligible study of ischaemic stroke found a significant near doubling of risk of disease among current users of combined oral contraceptives compared with never users.[11] Although data about smoking were collected, the author did not provide separate risk estimates for healthy women using low dose combined contraceptives who smoked and for those who did not smoke. Even this study, therefore, did not answer our specific clinical question.

Myocardial infarction

The eligible study of myocardial infarction included only eight women who were using a low dose combined oral contraceptive at the time of their infarction.[27] Furthermore, separate risk estimates were not provided for users who smoked and those who did not. This meant that we did not find any studies of myocardial infarction which addressed our specific clinical question.

Discussion

Our literature search found many studies of the risk of vascular disease in current users of combined oral contraceptives. Much of the information, however, was concerned with the effects of combined oral contraceptives which are no longer available, or was derived from studies with serious methodological problems. Many of the studies used statistical techniques such as multivariate analysis to control for the effects of factors (confounders) that might be alternative explanations for a study's findings. For instance, many studies adjusted for differences in the proportion of smokers among users and non-users of oral contraceptives. In effect, these adjustments level the epidemiological playing field so that the real effects of combined oral contraceptives can be determined, but at a cost of losing information about the effects of the adjusting factor (in this case smoking) among contraceptive users.

In order to determine the effects of oral contraceptives in women with particular characteristics, populations need to be divided into their various subgroups. This can be done when designing a study, by defining which women will be recruited from the population pool of contraceptive users into the study (for example, only healthy users). Alternatively, it can be done at the time of analysis by stratifying the study population into users with different characteristics.

In statistical terms stratification is less efficient than multivariate analysis, but it does allow the effects of oral contraceptives to be observed in different users. With reanalysis using stratification, one of the rejected papers might have provided more information about the risk of venous thromboembolism among healthy users of low dose combined oral contraceptives,[7] five papers might have given more information on the risk of stroke,[12–15 20] and five might have given more information on the risk of myocardial infarction.[28–30 32 33] Another three papers examined healthy women but did not provide specific risk estimates for low dose combined oral contraceptives, even though these preparations were used by almost all the users of combined oral contraceptives in the studies.[6 31 34]

Our clinical example suggests that clinicians who wish to confine themselves to studies conducted in populations that closely represent their practice population will rarely find many studies to guide their practice. A similar situation exists with much experimental research. The paucity of information requires clinicians to extrapolate results from study populations that do not closely match their practice population. Such extrapolations usually imply an equal distribution of risk across the population; an assumption which may be wrong. For example, in several of the studies reviewed the risk of myocardial infarction or stroke was found to be concentrated in users of combined oral contraceptives with other risk factors for vascular disease, notably smoking,[12 14 16 17 20–26 30 32] and users with a history of hypertension.[11 12 14 16 18–20 24 30] This means that the estimate of overall risk for arterial disease

Key messages

- Epidemiological studies investigate overall, average effects within populations, but clinicians need information about specific risks and benefits faced by the individual patients consulting them
- We explored the clinical usefulness of epidemiological data in defining the risk of cardiovascular disease associated with currently available low dose combined oral contraceptives for young, healthy women who do not smoke
- Our literature search identified 74 papers about the subject, but only five provided information that directly addressed our clinical question
- Fourteen other studies probably had the potential to answer our question if their data were reanalysed
- Clinicians need to be cautious when extrapolating results from epidemiological studies to guide their clinical practice

among all users of combined oral contraceptives grossly exaggerates the risk among healthy non-smoking users.

In order to avoid making any assumptions about the distribution of risk, we need empirical data about the risk of cardiovascular disease in healthy users of combined oral contraceptives. This has been difficult to obtain because cardiovascular disease is uncommon in young women. Thus, even studies with large catchment areas and prolonged periods for recruitment have difficulty recruiting a large number of current users experiencing vascular problems, particularly arterial ones. At present, however, little of the epidemiological data about the risk of cardiovascular disease in users of combined oral contraceptives is of use to clinicians, although more could become available if the some data were reanalysed. This situation is unlikely to be unique to oral contraceptives.

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Contributors: PCH coordinated the identification of studies, helped in their interpretation, wrote the draft paper, and contributed to its revision. VO-S helped with the interpretation of the studies and contributed to the revision of the draft paper. Both authors approved the final version and are guarantors for the paper.

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Transferring medical images on the world wide web for emergency clinical management: a case report

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Although the ability to transmit radiographs over the telephone has been feasible since 1929,[1] more advanced systems have been slow in introduction. We describe a simple system for transmitting medical images across a system based on personal computers and the internet's world wide web.

Methods and results

A system for transfer of medical images was set up in our orthopaedic department (fig 1). Clinical photographs were taken with an Apple Quicktake 150 digital camera, and radiographs were scanned on an Epson GT9000 flat bed scanner. The resulting digital images were converted to Joint Photographic Experts Group (JPEG) format at maximum quality using Adobe Photoshop on an Apple Power Macintosh computer. The files were saved onto a password protected area of the departmental website, which is maintained on an IBM compatible Pentium computer running the Microsoft programs Windows NT Server 4.0 and Internet Information Server. The server is connected to the internet via the University of Manchester. The minimum requirement for viewing images is a computer able to display 640×480 pixels in 256 colours and which must be connected to the internet and have installed web browser software capable of displaying JPEG files.

The system was tested when a 44 year old man presented with an isolated closed fracture of the right distal tibia and fibula (fig 2). The on call resident thought that urgent stabilisation was required but wished to perform this without compromising subsequent treatment. With the system described, two colour photographs of the patient's ankle and two scanned radiographs were placed on the departmental website. The JPEG files ranged in size from 640×480 pixels in 24 bit colour (clinical photographs) to 616×754 pixels in 8 bit grey scale (radiographs). The files took a total of 243 Kb (range 50-78 Kb) of disk space. The time taken to acquire and place the images on the website was 10 minutes.

The case was discussed with the consultant on call, who accessed the departmental website using a Power Macintosh computer with 28 800 bps modem via an internet service provider (CompuServe). The four images were downloaded over the internet in 70 seconds, after the password protection system had been cleared (fig 2). It was decided to apply calcaneal traction, and definitive fixation was performed several days later.

Comment

The ability to obtain advice from a non-resident senior doctor can be invaluable in an emergency situation. When clinical information is supplemented with medical images errors may be reduced. Although this method of consultation cannot replace direct patient contact, it can allow the correct treatment to be instituted more quickly.

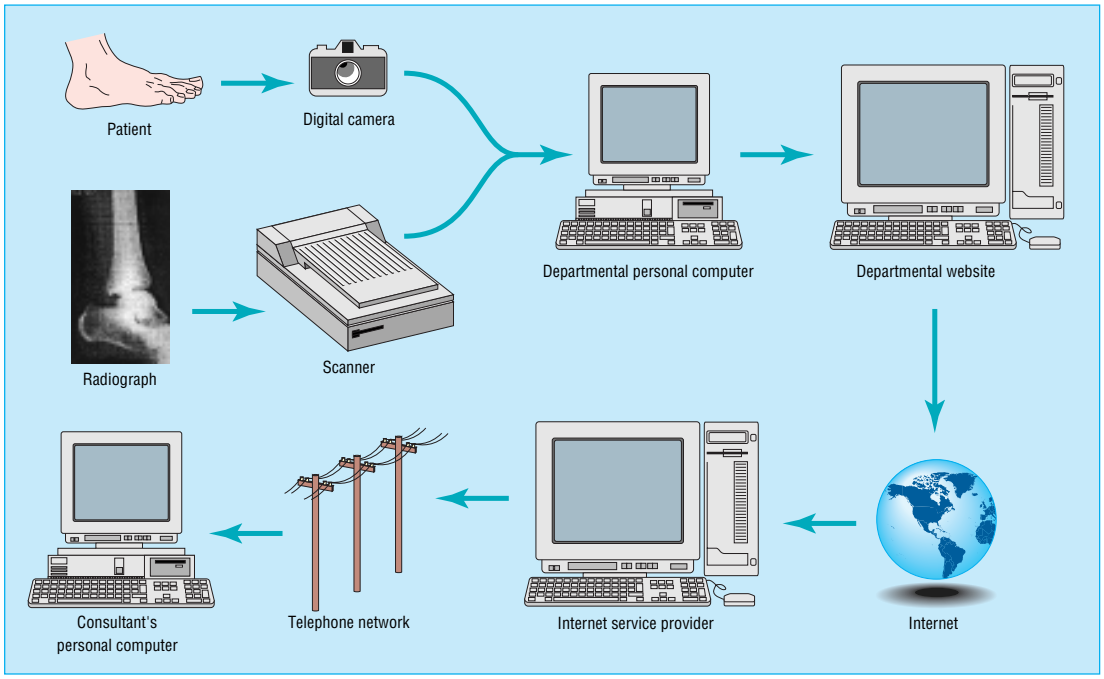

Fig 1 System for transfer of medical images across the world wide web

A longer version of this article is available on our website

Our system can be adapted for use by any specialty. Unlike other systems, no custom built equipment or software is required and learning to use it is easy. Although the internet has been used to transmit medical images,[2] this is the first report of using the world wide web in an emergency that we are aware of.

Image quality is paramount to the success of such a system. Previous reports, of similar quality images, have indicated that interpretation of transmitted images is satisfactory.[3–5] However, we recommend that any department adopting this approach to patient care should audit its use, as well as ensuring compliance with the Data Protection Act and its principles.

Contributors: PB set up the computer system and software necessary for the project. DSJ and PH tested the system described. The paper was written jointly by DSJ, RPG, PB, and PH. DSJ is guarantor for the paper.

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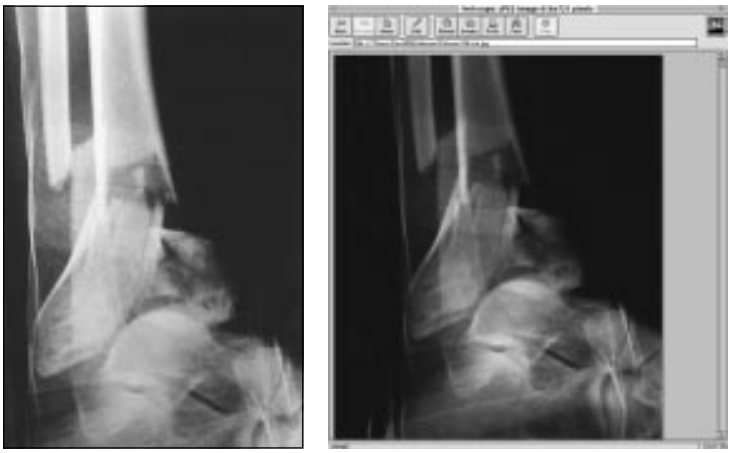

Fig 2 Lateral radiograph of patient's right ankle (left) and as viewed in a web browser (right)

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When can odds ratios mislead?

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Odds ratios are a common measure of the size of an effect and may be reported in case-control studies, cohort studies, or clinical trials. Increasingly, they are also used to report the findings from systematic reviews and meta-analyses. Odds ratios are hard to comprehend directly and are usually interpreted as being equivalent to the relative risk. Unfortunately, there is a recognised problem that odds ratios do not approximate well to the relative risk when the initial risk (that is, the prevalence of the outcome of interest) is high.[1 2] Thus there is a danger that if odds ratios are interpreted as though they were relative risks then they may mislead.

The advice given in many texts is unusually coy on the matter. For example: "The odds ratio is approximately the same as the relative risk if the outcome of interest is rare. For common events, however, they can be quite different."[3] How close is "approximately the same," how uncommon does an event have to be to qualify as "rare," and how different is "quite different"?

This short note quantifies the discrepancy between odds ratios and relative risks in different circumstances, and assesses whether such a discrepancy may seriously mislead if an odds ratio is used as an estimate of the relative risk.

Summary points

If the odds ratio is interpreted as a relative risk it will always overstate any effect size: the odds ratio is smaller than the relative risk for odds ratios of less than one, and bigger than the relative risk for odds ratios of greater than one

The extent of overstatement increases as both the initial risk increases and the odds ratio departs from unity

However, serious divergence between the odds ratio and the relative risk occurs only with large effects on groups at high initial risk. Therefore qualitative judgments based on interpreting odds ratios as though they were relative risks are unlikely to be seriously in error

In studies which show reductions in risk (odds ratios of less than one), the odds ratio will never underestimate the relative risk by a greater percentage than the level of initial risk

In studies which show increases in risk (odds ratios of greater than one), the odds ratio will be no more than twice the relative risk so long as the odds ratio times the initial risk is less than 100%

Odds and risk

There is a problem with odds: unlike risks, they are difficult to understand. The risk of an event happening is

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Table 1 Comparing risks and odds

Risk	Odds
0.05 or 5%	0.053
0.1 or 10%	0.11
0.2 or 20%	0.25
0.3 or 30%	0.43
0.4 or 40%	0.67
0.5 or 50%	1
0.6 or 60%	1.5
0.7 or 70%	2.3
0.8 or 80%	4
0.9 or 90%	9
0.95 or 95%	19

simply the number of those who experience the event divided by the total number of people at risk of having that event. It is usually expressed as a proportion or as a percentage. In either case the meaning is usually clear.

In contrast, the odds of an event is the number of those who experience the event divided by the number of those who do not. It is expressed as a number from zero (event will never happen) to infinity (event is certain to happen). Odds are fairly easy to visualise when they are greater than one, but are less easily grasped when the value is less than one. Thus odds of six (that is, six to one) mean that six people will experience the event for every one that does not (a risk of six out of seven or 86%). An odds of 0.2 however seems less intuitive: 0.2 people will experience the event for every one that does not. This translates to one event for every five non-events (a risk of one in six or 17%).

A second problem with odds is that, although they are related to risk, the relation is not straightforward. The table shows the odds for various risks. For risks of less than about 20% the odds are not greatly dissimilar to the risk, but as the risk climbs above 50% the odds start to look very different.

Relative risks and odds ratios

The relative risk of one group compared with another is simply the ratio of the risks in the two groups. Thus the relative risk tells us how much risk is increased or decreased from an initial level. Again it is readily understood: a relative risk of 0.5 shows that the initial risk has been halved; a relative risk of 3 shows that the initial risk has been increased threefold.

The odds ratio is calculated in a similar way: it is simply the ratio of the odds in the two groups of interest. We know that if the odds ratio is less than one then the odds (and therefore the risk too) has decreased, and if the odds ratio is greater than one then they have increased. But by how much? How do we interpret an odds ratio of, say, 0.5 or an odds ratio of 3? A lack of familiarity with odds means that many people have no intuitive feel for the size of the difference when expressed in this way.

When the risks (or odds) in the two groups being compared are both small (say less than 20%) then the odds will approximate to the risks and the odds ratio will approximate to the relative risk. Then interpretation is easy. But as the risk in either group rises above 20% the gap between the odds ratio and the relative risk will widen. A recent article in *Bandolier* concluded that "as both the prevalence [initial risk] and the odds ratio increase, the error in the approximation quickly becomes unacceptable."[2] But is this the case? In what circumstances will interpreting an odds ratio as though it were a relative risk lead to serious errors in interpretation?

Odds ratio as an approximation of relative risk

When faced with an odds ratio, we want to know the discrepancy between that odds ratio and the relative risk. Figures 1 and 2 show the extent to which the reported odds ratio underestimates or overestimates the relative risk for different odds ratios and a given level of initial risk (see appendix for calculations).

Figure 1 shows the underestimation of the relative risk by the odds ratio in studies that report odds ratios of less than one (typically studies of benefit from treatment or exposure). Even with initial risks as high as 50% and very large reductions in this risk (odds ratios of about 0.1), the odds ratio is only 50% smaller than the relative risk (0.1 for the odds ratio compared with a true value for the relative risk of 0.2). In fact, the discrepancy between the odds ratio and the true relative risk will never be greater than the initial risk (see appendix for proof).

Figure 2 shows the discrepancy between the odds ratio and the relative risk for studies which report odds ratios of greater than one (typically studies showing harm). Although large discrepancies between the odds ratio and the relative risk are possible, the odds ratio overstates the relative risk by less than 50% for a wide range of both initial risks and effect sizes. For initial risks of 10% or less, even odds ratios of up to eight can reasonably be interpreted as relative risks; for initial

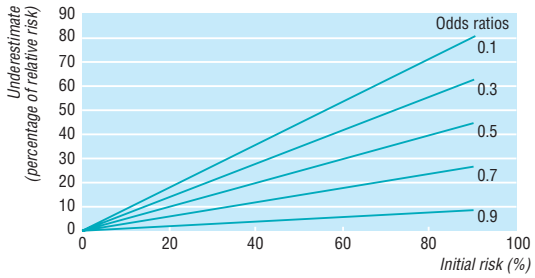

Fig 1 Amount by which odds ratios of <1 underestimate relative risk, for different odds ratios and different levels of initial risk

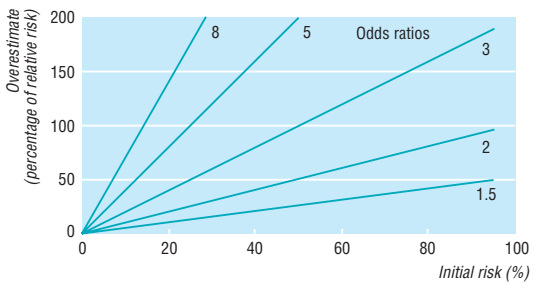

Fig 2 Amount by which odds ratios of >1 overestimate relative risk, for different odds ratios and different levels of initial risk

Example of use of odds ratios

The fortnightly review by Dennis and Langhorne, "So stroke units save lives: where do we go from here?" (*BMJ* 1994;309:1273-7) reported outcomes after stroke (death or living in an institution) for patients managed in specialist stroke units compared with patients managed on general medical wards. Specialist stroke units had the better outcomes, with a reported odds ratio of 0.66. The authors advised that an "odds ratio of <1.0 indicates that outcome of care in a stroke unit is better," and concluded that "patients with stroke treated in specialist units were less likely to die than those treated in general medical wards." No further guidance was given on interpreting the quoted odds ratio.

Because the frequency of a poor outcome was very high (about 55%) there might be concern that the odds ratio is a poor estimate of the relative risk. In fact, the odds ratio of 0.66 corresponds to a relative risk of 0.81—that is, the odds ratio underestimates the relative risk by just 19%. In other words, interpreting the odds ratio as a relative risk suggests a reduction in deleterious outcomes after stroke (death or living in an institution) of about a third compared with a more likely true reduction of about a fifth. Clearly, in either case this represents a substantial reduction in poor outcomes for a patient group with a large initial risk.

risks up to 30% the approximation breaks down when the effect size gives odds ratios of more than about three. As a conservative rule of thumb, if the initial risk multiplied by the odds ratio is less than 100% then the odds ratio will overestimate the relative risk by less than twofold.

Does the discrepancy influence our interpretation?

The figures show that the odds ratio will always exaggerate the size of the effect compared with a relative risk. That is, if the odds ratio is less than one then it is always smaller than the relative risk. Conversely, if the odds ratio is greater than one then it is always bigger than the relative risk. Thus interpreting an odds ratio as though it were a relative risk could mislead us into believing that an effect size is bigger than is actually the case.

Crucially, however, large discrepancies are seen for only large effect sizes. Suppose an odds ratio of, say, 0.2 reflects a true relative risk of 0.4. Such a discrepancy is unlikely to alter your view: this is a large reduction in risk whichever way you look at it. This is particularly so as large discrepancies occur only when the initial risk is high and thus even modest changes in the relative risk will mean substantial gains. So, for studies which show reductions in risk, the odds ratio is unlikely to mislead: either it will be close in value to the relative risk or it represents a substantial effect for groups at high initial risk. Thus any qualitative judgment is unaltered by the discrepancy between the odds ratio and the relative risk (see box).

The same logic holds for studies which show increases in risk. The discrepancy between the odds ratio and the relative risk becomes large only when there are large effects (a twofold or threefold increase in risk) for groups already at a large initial risk. Although the odds ratio may diverge quite sharply from the relative risk, by the time it does so the message conveyed by the different measures is the same: these are large effects.

Of course, although qualitative judgments may be unaltered by the odds ratio deviating from the relative risk, quantitatively we can still be led astray. Thus if we are interested in assessing the impact of interventions quantitatively (for example, for a cost effectiveness analysis) then, for larger initial risks and substantial odds ratios, the actual relative risk should still be calculated.

Conclusion

The difference between the odds ratio and the relative risk depends on the risks (or odds) in both groups. So for any reported odds ratio, the discrepancy between that odds ratio and the relative risk depends on both the initial risk and the odds ratio itself. This is possibly why textbooks are coy about giving a single figure for risk beneath which it is acceptable to interpret odds ratios as though they were relative risks.

Odds ratios may be non-intuitive in interpretation, but in almost all realistic cases interpreting them as though they were relative risks is unlikely to change any qualitative assessment of the study findings. The odds ratio will always overstate the case when interpreted as a relative risk, and the degree of overstatement will increase as both the initial risk increases and the size of any treatment effect increases. However, there is no point at which the degree of overstatement is likely to lead to qualitatively different judgments about the study. Substantial discrepancies between the odds ratio and the relative risk are seen only when the effect sizes are large and the initial risk is high. Whether a large increase or a large decrease in risk is indicated, our judgments are likely to be the same—they are important effects.

Appendix: Calculation of discrepancy between odds ratios and relative risks

If the proportions of subjects experiencing an event in two groups are P_1 (initial risk) and P_2 (post-intervention risk) then the relative risk is P_2/P_1 and the odds ratio is $(1-P_1)/(1-P_2)\times$ relative risk. Simple algebra leads this multiplier to be recast as $1-P_1+(P_1\times$ odds ratio). However, it is convenient to express the discrepancy between the odds ratio and the relative risk as a proportion of the relative risk. Therefore, for studies in which the odds ratio is <1, 1 minus this multiplier is the discrepancy ($P_1-(P_1\times$ odds ratio)). For studies in which the odds ratio is >1, the multiplier minus 1 gives the discrepancy (($P_1\times$ odds ratio) $-P_1$). Figures 1 and 2 plot these discrepancy values (as percentages) for various initial risks and odds ratios.

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Conflict of interest: None.

1 Sinclair JC, Bracken MB. Clinically useful measures of effect in binary analyses of randomized trials. *J Clin Epidemiol* 1994;47:881-9.
2 Deeks J. Swots corner: what is an odds ratio? *Bandolier* 1996;3(3):6-7.
3 Altman DG. *Practical statistics for medical research*. London: Chapman and Hall, 1991.

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Netlines

Lest we forget …

● Andrew Bamji has placed the Plastic Surgery Archives—a collection of material that documents the development of plastic surgery at the beginning of the 20th century, particularly after the first world war—on the web on **http://ourworld.compuserve.com/homepages/Andrew_Bamji/homepage.htm**. The site has links to other online material about the first world war, including a medical bibliography of the war (**http://raven.cc.ukans.edu/~kansite/ww_one/medical/medtitle.htm**).

Evidence based medicine

● There are ever more sources of evidence based medicine appearing on the web. The full text of the evidence based medicine journal *Bandolier* is available free on **http://www.jr2.ox.ac.uk/Bandolier/**, the Internet Database of Evidence-Based Abstracts and Articles (IDEA) can be found at **http://www.ohsu.edu/bicc-informatics/ebm/ebm_topics.htm**, and the NHS Centre for Reviews and Dissemination is at **http://www.york.ac.uk/inst/crd/**. For more comprehensive information, visit Netting the Evidence (**http://www.shef.ac.uk/uni/academic/R-Z/scharr/ir/netting.html**), an index of online sources of evidence based medicine, complete with commentaries, produced by Andrew Booth at the School of Health and Related Research (ScHARR), Sheffield.

Online journals: Highwire Press

● With production of the *BMJ* website all set to change over to Highwire Press next month, it is worth visiting the Highwire Press site (**http://highwire.stanford.edu/** in the United States or **http://intl.highwire.org** in Europe) to see how many online journals they are managing now—everything from the *American Journal of Respiratory and Critical Care Medicine* (**http://www.ajrccm.org**) to *Science* magazine (**http://www.sciencemag.org**). Future titles will include the Annual Reviews series and the journals of the American Society for Microbiology and the American Heart Association. All the journals are available as full text online both in HTML and Adobe Acrobat format (**http://www.adobe.co.uk/products/acrobat/main.html**) and come with fully searchable archives of past issues. The only snag is that, for most of them, you must have a subscription. In the near future the Highwire Press site will allow you to search all its journals in one go, and will also feature a Medline service.

ER online

● As *ER* is probably the best medical drama on British television, it is nice to see so much *ER* related stuff on the internet. A good starting place for exploring it all is the Alt.TV.ER site (**http://www.digiserve.com/er/erdex.html**), where you can pick up episode listings, summaries and reviews, and also commentaries on the medical conditions featured in each show. There is also an exhaustive set of links to other *ER* pages and sites. British viewers can discuss the show on the newsgroup uk.media.tv.er (news:uk.media.tv.er).

He@lth Information on the Internet

● *He@lth Information on the Internet* (**http://www.wellcome.ac.uk/healthinfo/**) is a new bimonthly newsletter from the Wellcome Trust and the Royal Society of Medicine, containing a range of contributed articles and regular features. The first issue is available in full on the web at **http://www.wellcome.ac.uk/healthinfo/be1.html**. I am on its editorial board.

Index to Theses

● The Index to Theses site (**http://www.theses.com/**) allows you to search an online database of theses accepted for higher degrees by the Universities of Great Britain and Ireland. Abstracts are available for recent theses. To use the site you must be in an institution that subscribes to the "dead-tree" version of the database.

Laparoscopy online

● The laparoscopy.com website (**http://www.laparoscopy.com**) features a feast of virtual laparoscopy, including multimedia walk-throughs of procedures, images, an online radio channel, and discussion forums.

The Visible Embryo

● The Visible Embryo (**http://visembryo.ucsf.edu/**) is an impressive online tour of the first four weeks of human life. For full appreciation of the site, however, you must have the Shockwave plug-in (available from **http://www.macromedia.com**) and plenty of memory allocated to your web browser.

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