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CLINICAL STUDY

Monte–Carlo simulation of random clustering of endophthalmitis following cataract surgery

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Abstract

Background **Endophthalmitis remains a serious and potentially blinding complication of cataract surgery with an overall incidence of ∼0.14% or one in 700 operations. Despite this knowledge of overall frequency, health-care providers find themselves confronted with clusters of cases where the appropriate level of response to the cluster is uncertain.**
Aim **To illustrate, by means of Monte–Carlo simulation models, the likelihood of random clustering of cases arising in units within a healthcare setting resembling the NHS and separately within the practices of individual surgeons.**
Method **Simulation models were constructed within a programming language in which individual cataract operations were simulated with a one in 700 likelihood of each operation resulting in a 'case of endophthalmitis'. Random clustering of 'cases of endophthalmitis' was observed in the models and 'outbreaks' were noted and tracked for various outbreak definitions.**
Results **The model outputs are presented graphically as the proportion of 'simulated units' affected by an 'outbreak' in a year and separately as the proportion of surgeons affected for a range of 'outbreak definitions'.**
Conclusion **These data presentations are easy to use and should facilitate a better understanding of shifts from endemic to epidemic rates of endophthalmitis with appropriate investigation of situations where a remediable common cause may exist.**

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Introduction

Endophthalmitis remains a serious and sight damaging complication of cataract surgery[1] with estimates of its incidence having varied between 0.055 and 0.49%.[2,3] The recent British Ophthalmological Surveillance Unit study reported an overall UK incidence rate of 0.14% or one in 700 operations[4], a rate very similar to the 0.13% found in both a meta-analysis of 90 published series[5] and a recent systematic review of 215 published studies.[6] Of some concern is the observation that rates may be rising, the systematic review noted an upward trend after 1992 with a significant increase since 2000 compared with previous decades (relative risk, 2.44, 95% CI, 2.27–2.61). The overall rate of endophthalmitis in the 2000–2003 period was 0.27%, a shift which may reflect changes in surgical technique.[6] While it is true that every individual case deserves reflection, a cluster of cases may require closure of an operating suite with a full investigation and search for a common cause.[7–9] Deciding when to initiate a full investigation can be difficult and an improved understanding of the likelihood of a cluster occurring purely by chance can be helpful. Inevitably numerical considerations play an important part but other factors also need to be considered. Frequently, no specific common source of an infectious agent is identified,[8,9] but the process of investigation may focus attention on generic infection control measures with a beneficial effect.[9] Monitoring surgical activity by means of statistical process control charts[10,11] has been used to detect excessive variation around an expected distribution for the occurrence of postoperative infections,[12] although a relatively high level of technical expertise and IT support is required for routine use of this technique. Whatever

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detection technique is used, knowing when incident infections shift from an endemic rate to an epidemic rate is essential to making an appropriate response to an outbreak or suspected outbreak of endophthalmitis. Not infrequently surgical teams find themselves faced with a situation where a cluster of infections seems to have occurred, yet they are ill equipped to decide whether closure and investigation of a surgical facility can be justified or not. Deciding a policy prior to any outbreak on which rates of infection deserve investigation and how intensive the investigation should be seems common sense.[13] The numerical question then becomes: Under which clustering condition should an outbreak be declared? This may for instance be defined as two cases in 270, two cases in 50, three cases in 630, four cases in 200, some other definition, or a combination of numeric definitions. Appropriate planning as to which definition should trigger which level of response requires a knowledge of the sort of random clustering which can be expected to occur due to chance alone.

Aim

The purpose of this report is to illustrate, by means of Monte–Carlo Simulation models, the likelihood of random clusters of endophthalmitis cases occurring in an ophthalmic surgical unit over a simulated period of 1 year in the UK. A secondary objective is to model clustering in surgical practice at the level of an individual surgeon.

Method: Model description, parameters and assumptions

Monte–Carlo Simulation models provide a flexible method for estimation of the likelihood of an event within a complex simulated environment. Although the binomial distribution can be used to estimate probabilities, the advantages of Monte–Carlo simulation are simplicity and flexibility. Binomial probabilities were used in this study to check on the basic functioning of the models as part of a validation exercise. Models were constructed within the Quick Basic programming language, were stochastic, and were run repeatedly to provide reasonably stable averages of the parameters of interest.

Simulated events, 'cataract operations', were modelled individually such that each simulated 'operation' carried an equal risk (probability), one in 700, of resulting in an 'endophthalmitis' occurrence. Sequential 'operations' were observed and the occurrences of 'endophthalmitis cases' tracked in the model. A variety of definitions of a cluster were modelled, for example two or more cases within runs of say 10, 20, 50, 500 operations; or three or more cases within runs of say 20, 100, 1000 operations, etc. up to nine or more cases within runs of say 100, 1000, 2000 operations. For each definition, 'clusters of endophthalmitis cases' were modelled and tracked at the 'surgical unit' level. The model also simulated and had a 'memory' of 'endophthalmitis cases' which occurred towards the end of the 'preceding year' in each 'surgical unit', the number of 'remembered' operations depending on the particular definition of an 'endophthalmitis outbreak' under consideration in that simulation. Individual 'surgical unit' throughput was distributed such that it resembled closely the throughput for units in England and Wales based on the number of consultants in the various units. Individual unit throughput was further varied by a random $+/-$ 10% around that distribution. The combined 'surgical throughput' for all 150 'units' was around 300 000 'operations' per year, similar to the overall throughput for England.[14] Simulations represented a year of activity, each year being simulated 50 times to increase precision of estimates by averaging. Thus for each 'cluster definition', for example five cases or more in 1500 operations, the model reported back an estimate based on over 15M individually simulated 'cataract operations'. The estimated figure reported back by the model refers to the proportion of 'surgical units' which would experience an 'outbreak' in a year under the specific cluster definition being modelled. The method of counting cases is such that for each definition the reported figure includes not only the specified case number but also all more extreme case definitions. Five cases in 1500 therefore includes the likelihood of 6,7,8…etc. For simplicity and to avoid confusion, the convention used in the presentation of the results and discussion below will drop the repeated use of the term 'cases or more' in favour of 'cases'. The estimates presented in this version of the model illustrate, for each cluster definition, the proportion of 'surgical units' that would experience a 'spurious outbreak' in a year in a service delivery structure resembling the NHS.

Information of interest to individual surgeons would be the likelihood of clusters of infections within a run of their own surgical cases. A second (simplified) version of the model was constructed to simulate this alternative scenario. This model included the same outbreak definitions but was restricted to a maximum of 2000 cases, a sufficient number to cater for the personal throughput of the vast majority of cataract surgeons over a number of years.

Validation checks were performed on the models to confirm that expected parameters could be recovered from simulated data. A typical simulation run on over 150M 'cataract operations' resulted in a mean incidence rate of 'endophthalmitis' of one case in 699.9 or

0.001428736 or 1.4 per 1000. In addition, the expected number of clusters were calculated from the binomial distribution for all 'outbreak' definitions presented. These included an *'a priori'* adjustment for the floating boundary used by the simulation model, that is, the first case in a cluster could occur at any point within a run of operations. For all definitions, the agreement between the binomial prediction and the simulated data were near perfect ($R^2 \geqslant 0.9999$; 0.999 $<$slope $<$1.005 for all, linear regressions through origin).

Results

For each outbreak definition (eg two in 270), a single point is produced on the graphs in Figures 1 and 2, and definitions based on the same number of 'cases' occurring within a specified number of sequential 'operations' form a 'line'. Since there are around 250 points on each line, the total number of simulated 'operations' depicted in Figure 1 is of the order of 3×10^{10}. From Figure 1 it can be seen that for a definition of an outbreak of endophthalmitis based on two cases

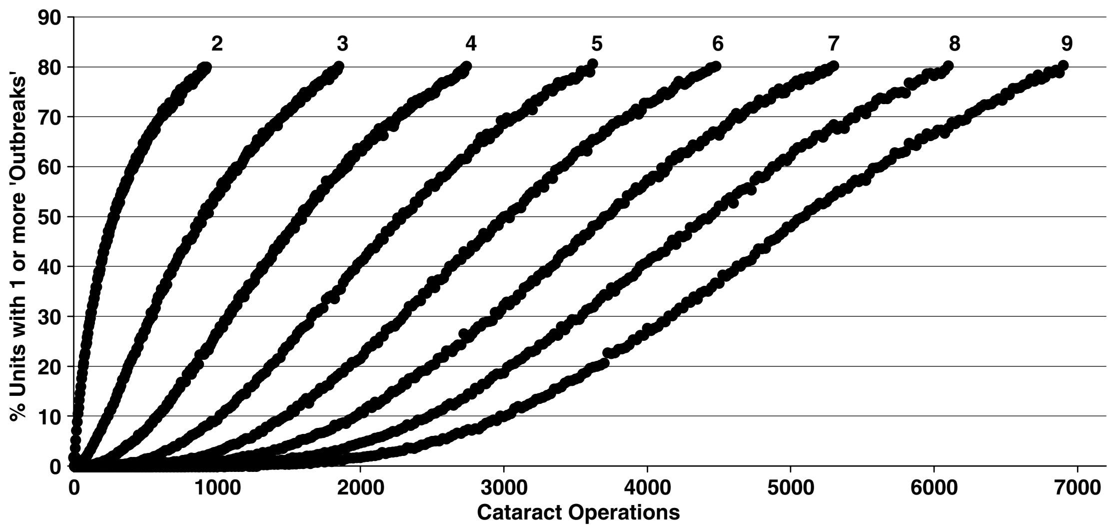

Figure 1 Expected annual frequency of endophthalmitis 'outbreaks' in surgical units to be expected as a result of random clustering alone. Each line represents a class of outbreak definition (ie 2, 3, … 9 endophthalmitis cases) and each point indicates the percentage of UK units affected each year (*Y*-axis) per number of cataract operations performed (*X*-axis). See text for further details.

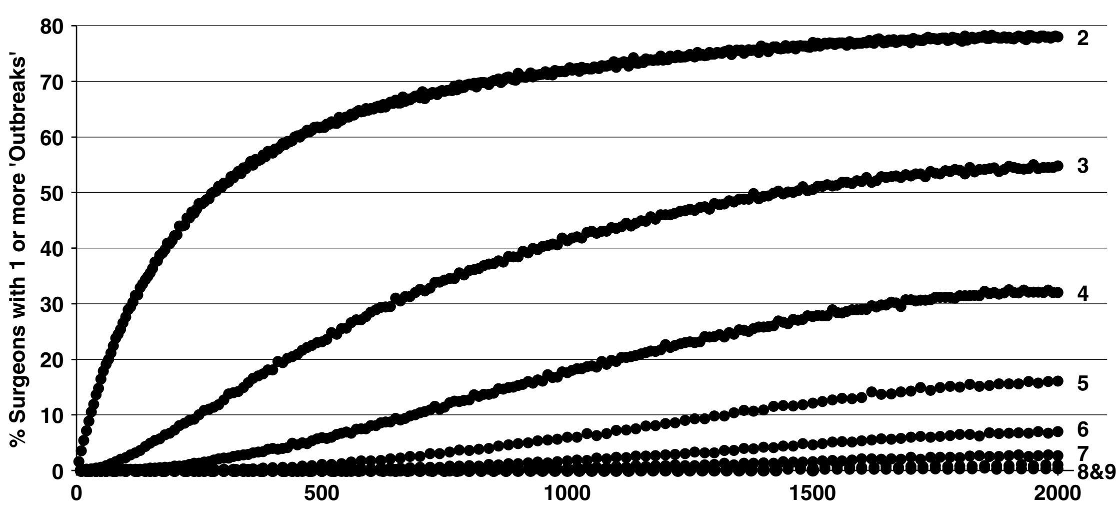

Figure 2 Expected frequency of endophthalmitis 'outbreaks' to be expected for individual surgeons as a result of random clustering alone. Each line represents a class of outbreak definition (ie 2, 3, … 9 endophthalmitis cases) and each point indicates the percentage of surgeons affected (*Y*-axis) per number of cataract operations performed (*X*-axis). See text for further details.

occurring within 270 operations around 50% of 'surgical units' would experience an 'outbreak' in a year purely due to random clustering. A more stringent definition of two cases in 25 operations would result in around 10% of 'units' experiencing a spurious outbreak. With a definition of two cases in 900 operations around 80% of units would be experiencing a 'spurious outbreak' each year. Clearly the latter definition lacks utility and models with outbreak frequency greater than 80% are not presented.

The lines in Figure 1 represent outbreak definitions based on between two and nine cases of infection and the proportion of units affected by a 'cluster' or 'spurious outbreak' can be read from the graph for the relevant number of operations for any given outbreak definition. A medium-sized surgical unit may for instance have experienced six cases in 2600 operations and Figure 1 would indicate that this would be expected by chance in around 40% of units each year. Similarly if there were seven cases in 2600 operations, then this would be expected in just over 20% of units, if eight cases in 2600 around 12%, and if nine cases around 5% of units in a year.

Figure 2 provides information relevant to the practice of individual surgeons. Simulations were performed for runs up to 2000 operations. For a surgeon performing 10 cataract operations a week over 40 weeks per year, this would represent 5 years work. From Figure 2 it is clear that outbreaks involving more than six endophthalmitis cases would be unlikely to occur due to chance alone. On the other hand, clustering of smaller numbers of infections could arise by chance, for example, there would be a 30% chance of a surgeon encountering four cases within a run of 1600 operations or three cases in 630 operations. There would be around a 50% chance of encountering two cases in 270 and a 60% chance of encountering two cases in 450 operations. At a throughput of 10 cases a week over 40 weeks (400 operations annually), there would be just under a 5% chance of a surgeon experiencing four cases spread throughout a year, just under a 20% chance of three cases in a year, and just under a 60% chance of two cases in a year.

Discussion

The term 'spurious outbreak' is used with caution, and judgement will always be required when interpreting such numerical data. On the one hand, there is a risk that random clustering will result in unnecessary closure and over zealous investigation of surgical units and on the other hand, that there may be a temptation to passing an observed cluster of cases off as being due to random variation, with the loss of an opportunity to identify and eliminate a common infective or underlying cause. The choice of the background rate of one in 700 is based upon recent data from the BOSU Study,[4] backed up by the very similar findings of a meta-analysis of over 90 published series[5] and a recent systematic review of over 3 million reported operations.[6] Large samples across time and location are likely to provide a robust 'average rate' around which clustering may be investigated.

Perhaps the greatest utility of the simulations derives from epidemic scenarios that are rather unlikely to have occurred due to random clustering. Mandal *et al*.[9] reported their experience of investigating a cluster of seven endophthalmitis cases in a single surgeon's case series of 427 operations. From the graph in Figure 2 it can be seen that $<1\%$ of surgeons could expect to observe five cases in such a series. Had the surgeon been in possession of this information at the time, he may well have decided to discontinue operating on the occasion of the fifth case thus avoiding the sixth and seventh adverse outcomes. Anderson *et al*.[8] similarly reported on five cases in a multisurgeon series of 1000. From Figure 1 it is apparent that this would occur in just under 10% of units in a year due to random variation. In this example, the appropriate response seems less clear and a legitimate decision might have been to investigate while continuing to run the surgical facility. On that occasion, the surgical team involved chose the cautious option of closure of the theatre and a full investigation.

Conclusion

The data presented in these simulations have utility in facilitating identification of clusters of endophthalmitis which appear to have shifted from an endemic to an epidemic rate. The graphical presentations make this information accessible to relevant members of the surgical team without the need for an understanding of complex statistical issues. In conjunction with appropriate clinical judgement, these data will assist surgical units and individual surgeons to make correct decisions when considering the investigation of an endophthalmitis cluster which may have an underlying common cause. Relevant changes in practice should ultimately benefit patients with a reduction in avoidable morbidity from this potentially blinding surgical complication.

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