Simple nomograms to calculate sample size in diagnostic studies

S Carley, S Dosman, S R Jones, M Harrison

Methods: Using a spreadsheet, we derived nomograms for calculating the number of patients required to determine the precision of a test’s sensitivity or specificity.

Results: The nomograms could be easily used to determine the sensitivity and specificity of a test.

Conclusions: In addition to being easy to use, the nomogram allows deduction of a missing parameter (number of patients, confidence intervals, prevalence, or sensitivity/specificity) if the other three are known. The nomogram can also be used retrospectively by the reader of published research as a rough estimating tool for sample size calculations.

Figure 1: (A) Specificity plot for p \( = 0.05 \). Example: \( P = 0.55, \ C_I = 0.04, \ SP = 0.90 \) giving \( N = 480 \). (B) Sensitivity plot for \( p = 0.05 \). Example: \( P = 0.55, \ C_I = 0.04, \ SN = 0.90 \) giving \( n = 393 \). A larger version of fig 1 is available on the EMJ website (http://emjonline.com/supplemental).
previous paper. In order to simplify the nomogram, and by convention, we fixed the probability of finding a false positive result at 5% or less. This figure is taken at the conventional level from therapeutic studies; no agreed convention currently exists for diagnostic tests. The nomograms were created using a Microsoft Excel spreadsheet.

This method should only be used if more than five subjects have each possible outcome (true positive, false positive, true negative, false negative).

RESULTS
Use of the nomograms
Fig 1 shows nomograms for the calculation of sensitivity (A) and specificity (B). For both nomograms the following method is used.

1. Use a straight edge to draw a horizontal line from the estimated prevalence to the required confidence interval (for example you estimate that a test has 80% sensitivity; you want to have a fairly precise estimate and so set your confidence intervals for 5%).
2. Draw a line from that intersection vertically until it meets the expected sensitivity or specificity.
3. Draw a horizontal line from that intersection to the right hand axis where the number of patients required may be estimated.

An example of how to use the nomograms is shown as a grey, arrowed line. Simple movement of the rule between different values on each axis can illustrate how a change in any single parameter may influence the precision of the results.

DISCUSSION
The nomogram has four elements to it (number of patients, confidence intervals, prevalence and sensitivity/specificty). If the researcher knows any three of these, they will be able to estimate the fourth. This allows the nomogram to be used retrospectively by the reader of published research as a rough estimating tool for sample size calculations. However, we must again stress the importance of the a priori sample size calculation when planning a study.

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LETTERS

Is morphine indicated in acute pulmonary oedema

Recent referrals to our intensive care unit have led us to question the indication for morphine in acute pulmonary oedema. Acute pulmonary oedema is a common, life-threatening emergency. Appropriate prompt therapy can provide rapid improvements in symptoms by reducing pre-load and after-load, or increasing myocardial contractility. Oxygen, loop diuretics, and nitrates are well-established therapeutic options. Most textbooks of acute medicine also recommend that intravenous morphine (or diamorphine in the UK) is given to cause systemic vasodilatation and sedate the patient, in the UK) is given to cause systemic vasodilatation and sedate the patient, despite the absence of evidence supporting its efficacy. Treatment with morphine may be associated with respiratory depression in an already hypoxic patient, potentially exacerbating cardiac insufficiency. Respiratory failure secondary to opiates in pulmonary oedema has previously been reported elsewhere.

In vivo experiments have confirmed that intravenous morphine results in significant peripheral vasodilatation and reduction in systemic vascular resistance. Further studies reveal that these effects are mediated via histamine receptors rather than opiate receptors, and directly correlate with the rise in plasma histamine concentrations in associated with morphine administration.

In view of the potential iatrogenic morbidity and non-specific pharmacological action of morphine in acute pulmonary oedema, we question the recommendation of its use. There are more potent vasodilators available without the side-effects of respiratory depression. We suggest that it is only used in acute pulmonary oedema, with caution, when analgesia is required in association with acute myocardial infarction. The use of titrated intravenous diuretics and nitrates to promote vasodilatation is preferable.

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References


Emergency rooms differ in the detail

I read with interest the article by Schull. I have recently moved to Trinidad and find that the problems in A&E are the same as the UK: overcrowding, waiting times, lack of facilities of trained staff. Each of these problems differ in detail.

Overcrowing and waiting times are less severe in Trinidad than the UK. In my department (a paediatric facility seeing 40,000 patients per year) our average time to see a doctor is less than half an hour. Is this a reflection of good practice? In most departments in Trinidad, staffing is at a junior level. Doctors in the Emergency Room provide limited care for patients before referral. This leads to shorter waiting times, but patients suffer through multiple referrals before receiving definitive care. This is more in the adult departments, where the average waiting time is less than that quoted, while the admission rate is higher (40% for adult departments compared to 10% for the children’s hospital). Quicker care is not necessarily better care.

The availability and use of inpatient facilities has an impact on throughput. In most departments in Trinidad, overcrowding on the wards is a part of life. Space is ‘made’ on wards by accommodating patients two to a bed, or making room for trolleys. The only area in which this policy is not feasible is ICU. The availability of ICU beds is much less than in developing countries and threshold for admission much higher.

Finally, staffing is a problem. Juniors with no specific interest in Emergency Medicine staff most departments. An audit of our paediatric emergency room suggests that senior staff can reduce both the admission rate and waiting time, but patients stay longer while receiving more comprehensive care.

In summary, the problems of all Emergency Rooms are similar, but vary in detail. Achieving better waiting times in the Emergency Room may be at the expense of the quality of care in the entire system, if managed in isolation.

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Glucagon use in β blocker overdose

The Best Evidence Topic Reports series is intended to provide evidence-based answers to clinical questions. The recent best evidence topic report by Boyd concluded that there is not enough evidence to support the use of glucagon in β blocker overdose. However, clinical toxicology is an area in which the evidence basis is often lacking and one therefore needs to rely on a combination of practical experience, case reports and assessment of biological plausibility. There is a sound theoretical basis for the use of glucagon in the cardiovascularly compromised patient who has taken a β blocker overdose. Glucagon activates adenyl cyclase and exerts an inotropic and chronotropic effect by a pathway that bypasses the β receptors.

Each of us has personal experience of the dramatic improvement in cardiovascular parameters that can occur following the administration of glucagon in this clinical situation.

Patients seldom take an overdose solely of a β blocker and the purist evidence base sought by Boyd is unlikely to be achievable. There is a wealth of clinical experience in support of administration of glucagon. Nobody would suggest that naloxone should not be used for opioid overdose yet the evidence base for its use is as flimsy as that of glucagon in β blocker overdose. We suggest that to attempt to undertake a randomised clinical trial of the use of glucagon in the compromised β blocker overdosed patient would be unethical.

By acting on the recommendation of this best evidence topic report, the unwary reader may deny patients a potentially life-saving treatment, which is universally recommended by toxicologists.

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Survey of blood gas interpretation

Hospital clinicians frequently request arterial blood gas (ABG) analysis to aid in the diagnosis and management of patients.

We carried out a one-day, survey to see how well ABG’s were interpreted. We asked participants to complete a written questionnaire during their normal working duties. No one declined to take part. Respondents were asked to give the normal ranges for ABG parameters. Five different ABG results were presented and respondents asked to describe (free text) the findings and to give any number

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References

It seemed at first sight to be a very useful collection of data but on closer examination it was most disappointing. The laboratory and other normal values are not quoted in SI units. The American values for things like blood glucose will be of little value to those working in the UK and much of the rest of the world.

Much of the detail is specific to the hospital concerned giving details of the colour of top for the blood sample required for each parameter. The section on blood transfusion has an administration check list, which has details that are specific to the procedures at the hospital concerned and are not generic.

There is a whole section on mnemonics and other aide memoirs. A few of these could be helpful, in the majority I would find easier to remember the lists rather than the mnemonic!

There are old favourites like C3,4,5, keeps the diaphragm alive and PEA ITTT VOD being the differential cause of pulseless electrical activity, namely; Potassium, Embolus, Acidosis, Ischaemia, Temperature, Tamponade. Tension pneumothorax, Volume Oxygen, Drugs; which I personally find most unhelpful.

My overall impression was sadly, that there are other similar products on the market which are more user friendly, and which have more material relevant to the field without confusion with American normal values.

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Forensic Medicine: clinical and pathological aspects


I do acknowledge some personal bias, but I believe that it really would be quite hard to write a boring book on forensic medicine. The subject matter is so interesting. And what interests most people, fascinates many. This hefty tome comprises 51 chapters written by an assorted collection of international authors. Given the diversity of the subjects covered and the contributing authors, the editors have done well to maintain a uniform style throughout. They should be particularly congratulated for managing to avoid an excess of photographs, which might be construed in some way as voyeuristic.

The relationship between the specialties of A&E and Forensic Medicine has sometimes been somewhat awkward, particularly in the UK. This was typified by some heated correspondence which occurred in the BMJ a few years ago about a wound which had been described as a "neatly incised laceration". Many of the chapters of this book are of direct relevance to A&E. The A&E specialist may wish to skip some subjects, such as the history of Forensic Medicine or the forensic investigation of war crimes. However, there is a wealth of material on injury, toxicology, and legal medicine. References, whilst not exhaustive, are reasonably representative.

Weighing in at 3.2 kilograms, this book will not easily find its way into the pocket of a busy clinician. With its attractive design and interesting content, it does deserve a place on the bookshelf. Take care though, if you open it to quickly look something up, you might easily find yourself distracted and become engrossed within the pages.

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