General practice by numbers:

presentation to final outcome

This article explores ways in which numbers may be used in general practice to inform and guide decisions relating to the probabilities of illness, and the harms as well as the benefits of investigations and treatment, both for individual patients and for populations.

NUMBERS FOR THE INDIVIDUAL AND THE POPULATION

The numerical approach in the consultation requires an estimate of the probability that the patient with a particular symptom, sign, or test result has a particular disease. This can be expressed as the positive predictive value (PPV) (Figure 1). Once a disease is diagnosed, the additional benefit of treatment compared to no treatment may be expressed as a number needed to treat (NNT) for one person to gain that benefit (Figure 1). An additional term, the number needed to harm, similarly calculated represents the number of individuals treated for one to be harmed by the intervention. The information that provides the basis for these numbers comes from studies in large groups of participants. Increasingly, for diseases in which reduction of the risk of death is not the only criterion of effective care, the quality-adjusted life-year (QALY) or disability-adjusted life-year (DALY) are used as outcome measures.

For people who are asymptomatic, and for whom systematic population-based screening for a particular condition is proposed, or for patients in highly-selected well-defined groups who reflect participants in randomised controlled trials, NNTs and QALYs can provide the basis for policy decisions on treatment and commissioning. In everyday practice, where the presenting individual is self-selected, has poorly-defined symptoms, and falls between these other two types of populations, different means of measuring and assessing the benefits and harms of pursuing a diagnosis are required.

PRESENTATION IN PRIMARY CARE: NUMBERS NEEDED TO BENEFIT

The presentation of patients early in the 'organisation of their illness'[1] is recognised in the training of GPs.[2] The Read[3] alphanumeric computer coding system used in primary care in the UK contains a diagnostic chapter of 'vague diagnoses', representing symptoms and signs for which a more specific diagnosis cannot initially be made. In these circumstances we propose that a more appropriate measure of risk or benefit be used, in which the PPV of the vague diagnosis for a more specifically defined and diagnosed disease[4] is combined with the NNT, or other absolute measure of effectiveness of the treatment of the diagnosed disease, to produce an overall estimate of the effectiveness of pursuing a diagnosis, the 'number needed to benefit' (NNB). Since the diagnosis of the disease in itself is not the end point, the assessment of benefit in patients presenting with the initial problem needs to incorporate the effect of pursuing a diagnosis on patients who do not have the disease, who will often constitute the majority of patients presenting with a particular symptom. The NNB is the NNT divided by the PPV (Figure 1).

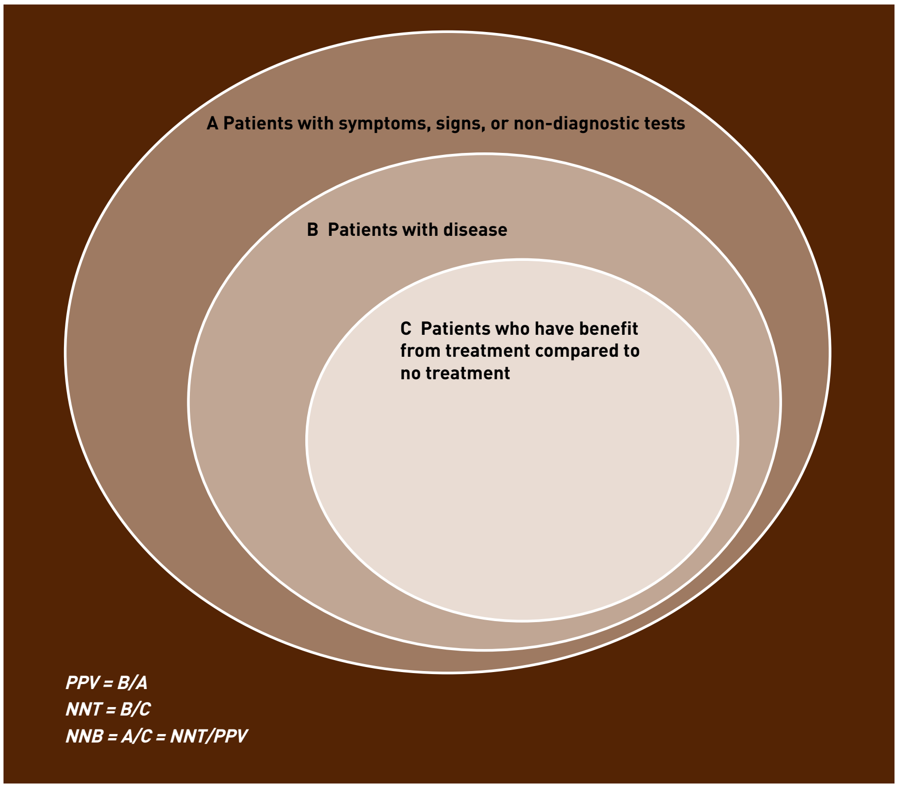

Figure 1. Positive Predictive Value (PPV), Number Needed to Treat (NNT) and Number Needed to Benefit (NNB).

PRESENTATION IN PRIMARY CARE: NUMBERS NEEDED TO DAMAGE

The corresponding measure of overall harm done if all patients presenting with a symptom were investigated to establish diagnosis and treatment, is the 'number needed to damage' (NND). There are three components of NND consisting of three 'numbers needed to harm' (NNH): NNH from investigation (NNH_1), NNH from treatment (NNH_2), and NNH from both investigation and treatment (NNH_3). The overall NND is then represented by: $1/([1/NNH_1] + [PPV/NNH_2] - [1/NNH_3])$.

At present there is rarely sufficient data to calculate such figures as clinical trials do not in general cover all parts of the pathway, but a hypothetical example can be used to illustrate the calculation. Consider 100 people presenting with a symptom

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(S), 10 of whom are given a diagnosis (D) (that is, PPV = 0.1). Of the 100 patients, 20 are harmed in some way by investigation, 18 of whom do not have D (that is, NNH_1 = 5); two people with D are harmed by the treatment, one of whom has also been harmed by the investigation (that is, NNH_2 = 5; NNH_3 = 100). Out of 100 people investigated, 21 people have been harmed in total (NND = 4.76).

THE OVERALL PICTURE: NNB AND NND TOGETHER

As the path from PPV to NNT usually involves stages with significant physical or psychological distress, morbidity, mortality, and/or economic cost, we suggest that the NNB, informed by the NND when data are available, is a better measure for policy decisions and for risk communication to individuals in primary care, and may help to promote more efficient decision making, improve patient satisfaction, and avoid some unnecessary or risky health care. NNBs should be available for outcomes of interest to those managing populations and for outcomes of interest to individuals.

APPLYING THE NNB

As an example of the calculation of NNB, the PPV for lung cancer in males with a Read Code entry of haemoptysis in a GP consultation is 7.5%,[5] thus for every 13 males with a haemoptysis code who are investigated one will have cancer. The 5-year absolute survival in England for lung cancer in males is 5.6%.[6] This is equivalent to an NNT, if it is assumed that those with lung cancer who present to primary care and are not registered have a 5-year survival of 0%, and that being diagnosed, registered, and treated carries benefits reflected by the higher probability of survival. The 5.6% 5-year absolute survival rate indicates that for every 18 males diagnosed with lung cancer one will be saved from dying from cancer in the next 5 years by registration and treatment. The calculation of the NNB (1/[0.075 x 0.056]) shows that, for every 238 males presenting with haemoptysis who are referred, one will be saved from dying from cancer in the next 5 years.

Age and sex-specific lung cancer PPVs for symptoms, signs, and non-specific diagnoses, and 5-year absolute survival rates following cancer diagnosis, show that NNBs are above 500 for haemoptysis and lung cancer in people aged <55 years, and fall with age until the age of 75 years when they begin to rise. The NNB figure of 238 represents a crude overall figure. In general NNBs for any cancer symptoms, signs, and non-specific diagnoses are high in younger people, fall in middle age and increase in older people. This is because the PPVs of cancer symptoms are dependent on the incidence of cancer in the population, which usually increases with age, in contrast to absolute survival, which falls with age. The middle years are often the time of maximal gain in survival.

It is possible that low ascertainment will result in underestimates of the true NNB for some less aggressive cancers which have significant 5-year survival even if untreated. For example, 5-year survival figures for all diagnosed and treated cancer of the prostate in males will underestimate overall NNT if the significant survival in the absence of referral or treatment is not taken into account. The calculation of NNB for referral of males for investigation of prostate cancer in relation to symptoms such as nocturia (PPV estimated by Hamilton *et al* as 2.2%[7]) will be an underestimate if based on such 5-year survival figures.

COMPLEX CLINICAL PATHWAYS

Clinical pathways are multifaceted and other benefits and harms may occur, unrelated to cancer diagnosis. For example, the entry of a Read Code for rectal bleeding in a male during a consultation has a PPV of 2.4% for colorectal cancer,[5] and patients with this diagnosis have a 5-year absolute survival of 38%,[6] making a NNB of 110 symptomatic males referred to save one individual from dying of cancer. The low PPV reflects the high number of such presentations that are not caused by underlying cancer. Colonoscopy may diagnose other causes of rectal bleeding such as premalignant polyps and inflammatory bowel disease, the management of which may produce significant benefit not contained within the calculation based on survival alone. For example, in one study from general practice, the PPV of rectal bleeding in patients aged ≥45 years for premalignant polyps was 5%.[8] However such figures, even when made more inclusive of wider benefits, must also be balanced against the potential for the test itself to do damage, for example an associated rate of perforation of 0.13% and mortality of 0.065% from colonoscopy[9] and the difficult-to-quantify adverse psychological and physical effects of a chain of events initiated by an inconclusive result.[10]

Large datasets such as the Clinical Practice Research Datalink (CPRD) (www.cprd.com) and QResearch® (http://www.qresearch.org) or indeed individual practitioners' computerised clinical records, have potential use in a variety of conditions where clinical trials have established NNTs. For example, if the proportion of individuals presenting with an otalgia who go on to have otorrhoea, bilateral disease, or serious complications were estimated from such databases (allowing a calculation of a PPV), a calculated NNB (derived from the PPV and known NNTs[11]) could inform national and practice policy concerning the provision of antibiotics, tailored to individuals with differing risks of complications.

NUMBERS FOR THE CONSULTATION

How may such information be used in clinical general practice? Cardiovascular disease stands as an example of where a cut-off point of risk for serious disease in a population has been established and subsequently applied by GPs to individuals in the consulting room.[12] Should similar thresholds be calculated for cancer?

GPs have understandable concerns about the routine application of cut-off points. The reasons for delaying referral in an individual with a symptom of possible cancer suggest that clinicians recognise a policy based on populations but use individual characteristics to stratify risk and to balance risks and benefits. Intermediate levels of risk cause the greatest concern to clinicians, yet the evidence base for decisions often does not stratify by risk and may not provide a true estimate of risks and benefits for patients who deviate from the average risk in a trial.[13]

Computer software and prompts for serious illness have potential usefulness in managing symptoms and presentations in the consultation,[14] but the presence of multiple end points for benefit and damage in patients with complex problems, and the crucial importance of incorporating the beliefs and values of the individual patient

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in decision making, provide challenges in defining a universally acceptable cut-off point for action. Other problems include the use of outdated cancer survival statistics[6] and the shortcomings of some of the clinical trial evidence on which survival data are based.

Incorporating numbers into policy-making and individual patient care in general practice is complex. We have proposed measures of absolute benefit (NNB) and damage (NND) as useful when the final outcome after an intervention is the clearest measure of clinical and patient-defined importance. However, while numbers may be useful in the consultation, they can only provide an estimate for the individual patient.

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