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Disease impact number and population impact number: population perspectives to measures of risk and benefit

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The number needed to treat statistic is a clinically useful measure of treatment effect, conveying both statistical and clinical importance to the treating doctor.[1 2] This information, however, is limited to clinical decision making and lacks a public health perspective. We propose two new statistics, which should allow the impact of an intervention to be seen in the context of the broader population.

The number needed to treat is defined as the number of patients who must be treated to prevent one patient from experiencing the adverse effects of the disease being studied.[3] For example, treating five diabetic patients with intensive therapy may result in one fewer patient who dies or has a macrovascular event.[4] This gives an immediate and simple understanding of the impact of the intervention. The number needed to treat statistic, however, relates only to those people actually treated and does not give an appreciation of how many people with the disease in question, or of the total population, will benefit from applying the intervention. Our proposed new statistics offer this population perspective to the number needed to treat.

We propose two statistics, the disease impact number and the population impact number. The disease impact number provides a population perspective by taking account of the number of people in the population with the disease, not just those eligible for the intervention according to the entry criteria for the trial from which the evidence of benefit is derived or those who actually have access to treatment. It is defined as "the number of those with the disease in question among whom one event will be prevented by the intervention." It is given by the formula 1/(absolute risk reduction × proportion of people with the disease who are exposed to the intervention) where the absolute risk reduction is the absolute difference in event rates between experimental and control patients in a trial.[5] The number needed to treat is 1/absolute risk reduction, hence the disease impact number is analogous to the number needed to treat for all the people with disease.

The population impact number provides a population perspective by taking into account the number of people in the population from which the patients with the disease are drawn. It is defined as "the number of those in the whole population among whom one event will be prevented by the intervention." It is given by the formula 1/(absolute risk reduction × proportion of people with the disease who are exposed to the intervention × proportion of the total population with the disease of interest). Hence the population impact number is analogous to the disease impact number for the total population.

Summary points

The number needed to treat statistic is a clinically useful measure but lacks a population perspective

The disease impact number takes account of the number of people with the disease and is "the number of those with the disease in question among whom one event will be prevented by the intervention"

The population impact number takes account of the number of people in the population from which the patients with the disease are drawn and is "the number of those in the whole population among whom one event will be prevented by the intervention"

The disease impact number and population impact number allow an assessment of the wider impact of a treatment or service on the generality of people with the disease and the population from which they are drawn

Number needed to treat from a population perspective

Interventions after stroke and thrombolysis after acute myocardial infarction are examples of how these new statistics provide an interpretation of the results of interventions in clinical trials from a population perspective.

Interventions after stroke

Several interventions have been shown to improve the outcome after stroke.[6] Among these, thrombolysis has the largest efficacy in reducing death or dependency in terms of relative risk reduction, although it may be feasible for only around 4% of the population of people with stroke.[7] Aspirin, however, has a lower efficacy but could be used for about 70% of patients with stroke[6] (because some patients die before coming to medical attention and others have contraindications to aspirin). Table 1 shows how combining this information can help us understand the impact of these interventions from different perspectives.

For each intervention, the disease impact number and the population impact number are higher than the number needed to treat. Where the proportion of the stroke population who can access treatment is high, the disease impact number is not much higher than the number needed to treat. Where only a small proportion of the population can access the treatment—for example, for thrombolysis—the disease impact number (158) is considerably higher than the number needed to treat (7). A particular intervention may prevent one death or disability from ischaemic stroke from among many thousands of the population—the population perspective of the value of thrombolysis after stroke changes from a number needed to treat of 7 to a population impact number of over 120 000.

Benefits of thrombolysis after acute myocardial infarction

The efficacy of thrombolysis after acute myocardial infarction differs by age.[9] Because the rate of the disease is also heavily age dependent, it is likely that the impact of thrombolysis will have different implications for different age groups. Table 2 shows that the proportion of patients with acute myocardial infarction who are likely to receive thrombolysis is lower in the highest age category—this results in a high number of older patients with the disease among whom current treatment policies would be expected to save one life (disease impact number). Conversely, the low disease mortality in the youngest age group produces a high number of the population among which one life will be saved (population impact number). By considering the components of the disease impact number and population impact number, the effects of alternative treatment policies can be assessed. For example, if the proportion of patients aged 65-74 who receive thrombolysis were increased from 40% to 50%, the disease impact number would decrease from 93 to 75, and the population impact number would decrease from 6100 to just over 4800. If more aggressive secondary prevention were able, however, to reduce the event rate in this age group to, for example, that in the age group below (760/100 000) and 40% received thrombolysis, the population impact number would increase to over 12 000.

Table 1 Benefits of different proved interventions for treatment of non-haemorrhagic first stroke on basis of death or dependency at six months

	Aspirin	Warfarin	Organised stroke unit	Thrombolysis
Absolute risk reduction*	0.031	0.042	0.050	0.159
Proportion of stroke population treated†	0.70	0.29	0.70	0.04
Number needed to treat	33	24	20	7
Disease impact number	46	83	29	158
Population impact number ‡	35 450	63 160	21 980	120 950

*From a systematic review.[6]
†Comprises those for whom treatment can be provided based on access, suitability, and availability (will vary according to economic and geographical setting[6]).
‡Annual rate of first cerebral infarction taken as 1.3/1000 (Oxford community stroke study).[8]

Table 2 Benefits of thrombolysis after acute myocardial infarction by age for men in Australia on basis of deaths from days 0-35

	Age (years)		
	<55	55-64	65-74
Absolute risk reduction[9]	0.011	0.018	0.027
Proportion of population with acute myocardial infarction eligible for treatment*	0.54	0.49	0.40
Event rate of acute myocardial infarction per 100 000†	137	760	1523
Number needed to treat	91	56	37
Disease impact number	169	113	93
Population impact number	123 000	14 900	6100

*Assumes 77%, 70%, and 66% of patients in each ascending age group are admitted to hospital (due to deaths occurring before reaching hospital: WHO MONICA project monitoring trends and determinants in cardiovascular disease study, unpublished) and proportions given thrombolysis in hospital are 0.7, 0.7, and 0.6 in each ascending age group (New South Wales acute cardiac care study, unpublished).
†Based on mortality data from Australian Institute of Health and Welfare[10] and morbidity data from Australian Institute of Health and Welfare national morbidity database.

Discussion

The number needed to treat statistic is sensitive to the absolute risk in the non-treated group, which may be misleading when the data are derived from a meta-analysis.[11 12] Our measures are also sensitive to this issue as our calculations start from the same basis as the number needed to treat. The actual numbers we have calculated depend on several other assumptions in terms of the proportions of the population with disease who can access treatment as well as the proportions of the total population with the disease of interest.

The number needed to treat statistic has been modified by Rembold who has suggested the number needed to screen.[13] He divided the number needed to treat by the prevalence of unrecognised or untreated disease. This has a similar goal to our statistics, in that it adds a population dimension to the number needed to treat statistic.

Public health implications

The number needed to treat has been developed for helping clinical decision making—that is, how many patients would have to be treated with the intervention in question to save one patient having the outcome of interest? These data can only come from an appropriately rigorous estimate of benefit, and this is usually a randomised controlled trial. For many reasons, only a subset of patients with the disease are usually evaluated by such a trial. Assume that of 100 patients with an acute myocardial infarction, 70 reach hospital as 30 have died before reaching medical assistance (table 2, age 55-64 years). Any intervention on these 70 patients that might save one or two lives, based on the number needed to treat of 56, is to be welcomed by the patient and doctor but should be seen in the public health context of the 30 who died before reaching hospital. These new statistics help to offer this public health perspective. Assume that there was a certain amount of resource to commit to the treatment of stroke. The number needed to treat statistic would provide attractive incentives for the funds to go to treatment with thrombolysis, as the clinician only has to treat seven patients to avoid death or dependency in one of them. The resources used in introducing thrombolysis (including urgent admission to hospital and computed tomography as well as the drug cost) will only save one person from a population of 120 000 from dying or becoming dependent (as identified by the population impact number statistic). This compares with the smaller amount of resources used in giving aspirin to stroke survivors, which would save one person from a population base one fifth of the size of that needed for thrombolysis.

These statistics can also be extended to examine disease causation, and we are separately presenting the way of calculating the statistics for cohort and case-control studies where the focus is on the number of people who need to be exposed to a risk factor to result in the development of disease in one person.

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Commentary: DINS, PINS, and things—clinical and population perspectives on treatment effects

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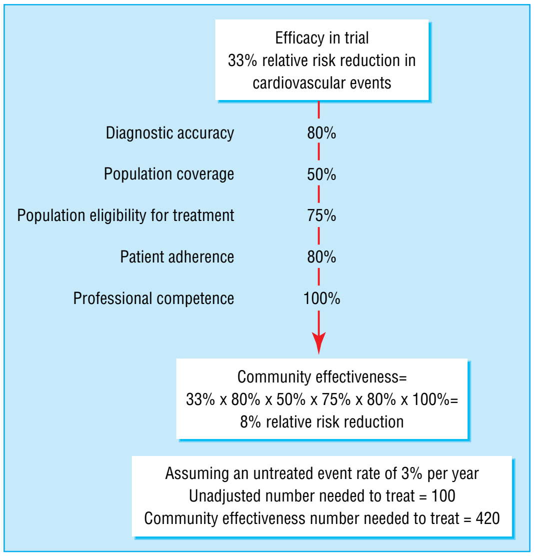
Both the proposed disease impact number and the population impact measure are derived from the number needed to treat, which is calculated from the difference in event rates in the control and intervention arms of clinical trials. In trials, however, participants often differ from non-participants, and this usually results in outcomes being less common in trials than in the population at large. Thus the event rates in trials—and therefore the number needed to treat, disease impact number, and population impact number—may bear little relation to those found in routine clinical practice. For example, in the Medical Research Council mild hypertension trial, cardiovascular event rates among hypertensive patients were comparable to those of normotensive patients in the general population, resulting in a trial derived number needed to treat of twice that of the population derived estimate.[1] Similar differences in magnitude arise in calculation of the disease impact number and population impact number.

Estimating a population impact number or disease impact number requires decisions to be made about the relevant number needed to treat and the level of risk or disease severity to use. An intervention may be beneficial among high risk populations, but small hazards can outweigh any benefits in low risk populations.[2] As disease risk shows notable sociodemographic, secular, and geographical variation, a disease impact number or a population impact number would vary greatly depending on the population studied. Ranges of population impact numbers and disease impact numbers are therefore required to reflect population variation, and even then they are insufficient to make public health decisions as issues of cost, patient



Trial efficacy to community effectiveness chain: hypothetical example taken from antihypertensive treatment in elderly people

preferences and adherence, professional competence, and potential harm are not considered. The disease impact number and population impact number are subject to greater random error than the number needed to treat or relative risk reduction, as errors occur in estimation of both the proportion of people exposed to a particular intervention and disease prevalence. Combining these random errors produces fairly wide confidence intervals, reflecting the greater uncertainty of these more complex measures.

Measures of relative risk have the virtue that they tend to be relatively stable between populations and over time.[3] Furthermore, the diminution of efficacy that occurs in application of interventions in the real world can be examined: inaccurate diagnosis, incomplete population coverage, patient adherence to treatment, and professional competence all tend to reduce efficacy found in trials—sometimes called community effectiveness or, in the context of hypertension, the "rule of halves."[4] This approach makes explicit the links in the chain that have the biggest impact on treatment effectiveness, and consequently are appropriate targets for clinical or public health action (figure). The "community" relative risk reduction obtained after taking account of each link can be converted into a number needed to treat by application of the relevant level of risk or prognosis in the population studied.

Do disease impact numbers and population impact numbers have a future? The potential hazards of generalising numbers needed to treat, the conceptual simplicity of community effectiveness, the usefulness of alternative population measures (particularly those embodying a cost dimension such as cost per quality adjusted life year), and the greater random error in the estimation of disease impact numbers and population impact numbers make them questionable public health policy tools. Their best role may be in communicating a population perspective to clinicians familiar with numbers needed to treat.

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When I use a word …

An/atomy

As I have mentioned before (*BMJ* 1999;319:1758), at one time the indefinite articles "a" and "an" were joined to the words that they governed—for example, aman or anoke. When the words were later split again, some spurious words were formed in error—for example, instead of a naranj we have an orange and instead of a noumpere we have an umpire. This process is called metanalysis, one casualty of which was "anatomy."

Anatomy is from the Greek ἀνά (ana, up) and τέμνω (temno, I cut). In addition to its current meaning, the study of the structures of the body or the structures themselves, at one time it also meant a skeleton. When the indefinite article was being restored to its separate existence, the word "atomy" was falsely coined from "anatomy" through aphaeresis, by the removal of the supposed indefinite article. Gay used it in *The Beggar's Opera* (2, i). When Matt of the Mint is asked what has happened to his brother, Tom, he says that he had an accident—in other words, was hanged—and having fallen into the hands of the dissectors "is among the otamies [*sic*] at Surgeon's Hall." By extension atomy also came to mean someone very thin; witness, for example, its appearance in Henry IV Part 2 (5, iv, 29): "… you starved bloodhound. … Thou atomy, thou!" Even Dickens used the word figuratively in *Dombey and Son* (Chapter IX): "Withered atomies of teaspoons."

I recently thought that I had come across a modern instance of the word, in Anthony Burgess's translation of *Cyrano de Bergerac*, which was used to subtitle Jean-Paul Rappeneau's 1990 film of Edmond Rostand's play. The couplet in question (which occurs in the famous balcony scene in Act 3) is about love:

Aussi l'ai-je tenté mais tentative nulle,
Ce nouveau-né, Madame, et un petit Hercule.

Burgess translated this as follows:

But the tough atomy I thought to seize
And crush, turned out an infant Hercules.

But there is another word "atomy," describing a property of the atom, smallness, or things that are tiny. Queen Mab, Mercutio tells us, is "Drawn with a little team of atomies/Athwart men's noses as they lie asleep" (*Romeo and Juliet*, 1, iv, 58). So did Burgess use atomy here in the sense of a tiny insignificant being (a metaphor that was coined long before the true power of the atom was known)? Well, if so, why did he choose to call it tough? It would have been more natural and accurate to have written:

But the tender infant that I thought to seize
And crush, turned out a pocket Hercules.

No, I think that Burgess, a consummate practitioner of logodaedaly, chose "atomy" for deliberate ambiguity, implying that the love borne for Roxane by Cyrano (her "almost brother" as she describes him in Act 2) had started out as a skeletal friendship but later became a grand Herculean passion. Neither anatomy nor an atomy.

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