Correspondence

To the Editor:

Canada Night at the American Academy of Neurology Annual Meeting, Boston honouring Dr. Robert T. Ross

I have recently been honoured by the Canadian Neurological Society at the "Canada Night" on the occasion of the 49th Meeting of the American Academy of Neurology in Boston on April 15th. The honour was with respect to the Founding, Editing and Publishing of the Canadian Journal of Neurological Sciences in the early days and I was truly treated royally. I am writing to thank all Members of the the Canadian Neurological Society for this honour. I appreciate it very much and would hope that this short letter could be made available to the general membership in the Journal.

R.T. Ross
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To the Editor:

What Effect Does an Untreated Aneurysm Have on Life Expectancy?

If a patient is found to have a cerebral aneurysm that is asymptomatic should the surgeon operate or leave well alone? At first I thought the article by Leblanc and Worsley[1] was an admirably clear and interesting account of answering this. But I gradually became concerned about their assumption that "rupture will occur, on the average, when half of the life expectancy has expired". This is accurate if (a) everyone lives for their life expectancy (no shorter and no longer), and (b) the risk of aneurysm rupture is very low. But not otherwise.

In the case of the young, the first assumption is approximately true, but the second is not: life expectancy might be 60 years, say, with a standard deviation that is comparatively small (10 years, say); however, other risks of death are sufficiently low that the risk of aneurysm rupture is not negligible in comparison. The opposite is true for the elderly – it is the first assumption that breaks down: the distribution of lifetimes is very skewed in shape, with a standard deviation almost as great as the mean. (As to the second assumption, the higher risks of death from various natural causes, and the consequent small expected lifetime, mean that the risk of death from aneurysm rupture is small in comparison.) So for neither the young nor the elderly are both assumptions met.

NUMERICAL RESULTS

I will use the same notation as Leblanc and Worsley: r is the rate of aneurysm rupture, and L is expected lifetime. In addition, I will need a symbol for the standard deviation of lifetimes: σ. I will assume that aneurysm rupture necessarily leads to death. (It would be easy to bring in a probability of death or disability, as Leblanc and Worsley did, but it would only cloud the present discussion.)

I have two criticisms of what Leblanc and Worsley did: they ignored the variability of lifetimes (this will be important chiefly for the elderly); and though they attempt to allow for rL not being small compared to unity, in fact their method is an overcorrection (this will be important chiefly for the young). The result is that their calculations understate the years of life lost from aneurysm rupture; and this is so for both the young and the elderly, though for different reasons.

The derivations of the formulae to be compared are relegated to the Appendix. As explained there, unless the whole distribution of lifetimes in the absence of aneurysm rupture is known, an exact answer is impossible. The Table gives a numerical comparison of

three approximations. The first three columns define the patients under consideration, by their values of L, σ, and r. Then come three columns respectively giving results according to expression [2] (taken to be the nearest to correct), Leblanc and Worsley's method, and expression [3].

To give perspective to the figures, the patient who would otherwise have a life expectancy of 15 years would have an expected loss of 1 year if surgery is undertaken that has a 6.5% mortality rate; if surgery is not carried out, the expected loss if aneurysm rupture has 73% mortality is 1.4 years (= 1.9 x 0.73) according to Leblanc and Worsley's formula or 1.8 years if formula [2] is correct. Thus Leblanc and Worsley's formula understates the benefit of surgery by about 50%. (The figures of 6.5% and 73% are taken from their paper.)

It is not for me to say whether the corrections proposed here are sufficiently large to be considered clinically important. But my impression of the literature is that they probably are worth knowing

Table: Years of Life Lost if Fatal Aneurysm Ruptures Occur at a Rate r Per Year.

L	σ	r	[2]	L&W	[3]
60	14	0.02	25.6	21.0	–
40	12	0.02	13.1	11.0	–
25	10	0.02	5.9	4.9	–
15	8	0.02	2.5	1.9	3.5
10	6	0.02	1.2	0.9	1.7
6	4	0.02	0.5	0.3	0.6

Notes: (a) If aneurysm rupture is not necessarily fatal, the results need to be multiplied by the probability of this. (b) The choices of values of σ are guesses as to what might be appropriate at the various values of L. (c) Expression [3] is not intended for use when life expectancy is great.

about, particularly since [2] is simple enough to be evaluated using a hand-held calculator. Turning now to screening programs, in this context, death is a rare possibility that has a high cost. Hence I presume it is important to accurately evaluate its probability, so that it is given its appropriate weight, but not more, in the decision.

Expression [2] has been presumed here to be the most accurate. But it makes an assumption – that lifetimes have a gamma distribution in the absence of aneurysm rupture. I would like to suggest to Leblanc and Worsley, and to others expert in this subject, that they calculate exact results using expression [1] and real data on the probabilities of dying at different ages, in order to make a better comparison of the accuracy of various formulae.

APPENDIX

An extra risk (aneurysm rupture) is added to all the existing ones. This extra risk is assumed to be constant through time, and to be independent of all the other risks. The time elapsing before an aneurysm ruptures therefore has cumulative distribution $1 - e^{-rt}$, and probability density $r e^{-rt}$.

Let t be the time at which the aneurysm ruptures (if indeed this happens before death from any other cause), and x be the time of death from any other cause (if the aneurysm does not rupture first). As aneurysm rupture is taken to be independent of any other cause of death, the joint probability density of t and x is the product of their respective individual probability densities, $r e^{-rt} f(x)$. The life-

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time lost from aneurysm rupture is evidently $x - t$ (provided $x > t$). Thus the expected lifetime lost is

$$\int_{\chi=0}^{x=\infty} \int_{t=0}^{t=x} (x - t)\, re^{-rt} f(x)\, dt\, dx$$

$$= \int_0^{\infty} \left(x - \frac{1}{r} + \frac{1}{r} e^{-rx} \right) f(x)\, dx.$$

Unfortunately, therefore, we need to know the whole distribution of lifetimes, not just a few parameters like the mean and standard deviation, in order to calculate the answer.

We can, if we wish, write the answer in a compact form. Define

$$\ell(s) \text{ by } \ell(s) = \int_0^{\infty} e^{-sx} f(x)\, dx.$$

This is called the Laplace transform of $f(x)$. Then the expected lifetime lost is

$$L - \frac{1}{r} + \frac{1}{r} \ell(r). \tag{1}$$

Gamma Distribution of Lifetimes

To obtain something that is usable, we might be willing to assume the distribution has some convenient mathematical form. The gamma distribution may be familiar to readers. It is a skewed distribution having probability density proportional to $x^{\alpha-1} e^{-x/\beta}$. The Laplace transform takes a simple form, $(1 + \beta r)^{-\alpha}$. Hence the expected lifetime lost is $L - r^{-1} + r^{-1} (1 + \beta r)^{-\alpha}$. The parameters α and β of the gamma distribution may be written in terms of its mean L and s.d. σ as follows: $\beta = \sigma^2/L$ and $\alpha = L^2/\sigma^2$. Consequently, the expected lifetime lost is

$$L - \frac{1}{r} + \frac{1}{r} \left(1 + \frac{\sigma^2 r}{L} \right)^{-L^2/\sigma^2}. \tag{2}$$

This is simple enough for use on a hand-held calculator.

A special case of the gamma distribution is the exponential. In this case, $\alpha = 1$ and $\sigma = L$. Beck et al.[2,3] have argued for its usefulness in the present context. For this special case, [2] simplifies to

$$\frac{rL^2}{1 + rL}. \tag{3}$$

To take $\sigma = L$ may be appropriate for patients whose life expectancy is short (because of age or conditions other than the aneurysm), but otherwise [3] will overstate the loss of lifetime.

Leblanc and Worsley

Here, I will make explicit why Leblanc and Worsley's method overcorrects for rL not being small compared to unity. Suppose that anyone not suffering an aneurysm rupture lives for exactly time L. Further, suppose aneurysm rupture is extremely rare. (That is, we are assuming that both σ/L and rL are close to zero.) Then the proportion of people suffering aneurysm rupture is rL, on average this

happens midway through their life so they lose $L/2$ years of life each, and the average over the whole population of years of life lost is $rL^2/2$. Now, if rL is not small, the proportion of people suffering aneurysm rupture is not rL, but $1 - e^{-rL}$. Leblanc and Worsley have this. (They actually write $1 - (1 - r)^L$ instead, but the difference is unimportant.) But it is not now correct to say the average over the whole population of years of life lost is $(1 - e^{-rL})L/2$.

For a proportion $r\, e^{-rt}\, dt$ of people, their aneurysm ruptures between time t and time $t+dt$ (for small dt). The length of life they lose is $L-t$. The average for the population is $\int_0^L r e^{-rt} (L-t)\, dt$, which works out to be $L - r^{-1} + r^{-1} e^{-rL}$. Expanding the exponential as an infinite series in rL, we get $\tfrac{1}{2}rL^2 (1 - \tfrac{1}{3}rL + \ldots)$. In contrast, Leblanc and Worsley's expression $\tfrac{1}{2}L(1 - e^{-rL})$ becomes $\tfrac{1}{2}rL^2(1 - \tfrac{1}{2}rL + \ldots)$. Because the term that multiplies $\tfrac{1}{2}rL^2$ is approximately $1 - \tfrac{1}{2}rL$ rather than $1 - \tfrac{1}{3}rL$, the correction is greater in magnitude than it should be.

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1. Leblanc R, Worsley KJ. Surgery of unruptured, asymptomatic aneurysms: a decision analysis. Can J Neurol Sci 1995; 22: 30-35 (Correction, p 172)
2. Beck JR, Klassirer JP, Pauker SG. A convenient approximation of life expectancy (the "DEALE"), I. Validation of the method. Am J Med 1982; 73: 883-888.
3. Beck JR, Pauker SG, Gottlieb JE, Klein K, Kassirer JP. A convenient approximation of life expectancy (the "DEALE"), II. Use in medical decision-making. Am J Med 1982; 73: 889-897.

Reply from the Authors:

Hutchinson challenges our assumption that aneurysm "rupture will occur, on the average, when half the life expectancy has expired". As we stated in our paper this is true if "the annual rate of rupture is constant over the patient's life expectancy so that rupture will occur, on average, when half the life expectancy has expired if 'r' (the annual risk of rupture) is small".[1] This point was previously made in our paper in *Neurosurgery* addressing angiographic screening and elective surgery of familial cerebral aneurysms, and by Levey et al. in their paper addressing *Occult Intracranial Aneurysms and Polycystic Kidney Disease*.[2,3] The detailed derivation and the implications of this assumption are detailed in the Appendix to our paper in *Neurosurgery* and were referenced in the paper in question in the *Canadian Journal of Neurological Sciences*.[1,2]

The reader should note that our analysis was made conditional on the observed natural lifetime L. We made no assumptions about the distribution of L. What our results tell the patient and the surgeon is the expected years of life lost *if* the patient's lifetime is L. The patient and the surgeon are then free to average these results over whatever distribution the lifetimes might have, be it a gamma distribution (as Hutchinson has assumed, to get [2]), or a more realistic distribution taken from life tables that might depend on age, sex, health, smoking habits, weight, cholesterol level, daily exercises, medical history, etc. (to get [1]). The patient and the surgeon are free to choose this. The *expected* years of life lost, under the gamma distribution, is usually greater than the *conditional* years of life lost evaluated at L - *life expectancy* because the conditional years of life lost is concave in L. This is the essence of Hutchinson's comment. Whether one chooses to use our formula or Hutchinson's depends on his or her choice of assumption with regard to the distribution of L.