**1** Imagine you are trying to estimate, from imperfect observations of $F$ and $C$, the values of the two coefficients $B_0$ and $B_1$ in the temperature relation $F = B_0 + B_1 \times C$.

For each of the following situations (i)-(iii), and using the true values of $B_0 = 32$ and $B_1 = 9/5 = 1.8$, simulate[1] 1000 datasets and investigate the behaviour of 1000 estimates, $b_0$ and $b_1$, of $B_0$ and $B_1$. In each simulation, use samples of size $n = 4$, with temperatures of $C = 14$, 16, 18 and 20.

i. $C$ measured perfectly, $F$ measured with $\epsilon_F \sim$ Gaussian($\mu = 0$, $\sigma_{\epsilon_F} = 1$) errors that are independent of $F$. Check – formally, using a test based on the mean of the 1000 estimates – for evidence of bias in $b_1$. Also check whether the empirical variance of $b_1$ agrees with that given by the theoretical formula for Var($b_1$).

ii. $F$ measured perfectly, $C$ measured with $\epsilon_C \sim$ Gaussian($\mu = 0$, $\sigma_{\epsilon_C} = 1$) errors that are independent of $C$ [*Classical type* error: someone else chose situations when $C$ was indeed exactly 14, 16, etc, but didn't tell you what $C$ was, and instead asked you to independently record $C$ using your own imperfect instrument, and to use *your* recordings of $C$ in your estimation of the equation]. Again, formally test for evidence of bias in $b_1$.

iii. {*optional*} $F$ measured perfectly, $C$ measured with $\epsilon_C \sim$ Gaussian($\mu = 0$, $\sigma_{\epsilon_C} = 1$) errors that are independent of $C^* = C + \epsilon_C$, *and thus correlated with* $C$ [2]

In (i)-(ii), do your findings line up with the predictions in the Notes? If the patterns are difficult to see, you might change the number of simulations, the sizes of the errors, the range of $C$ or the sample size.

[1] If new to simulations, see "Computer code to simulate datasets with measurement error" at the bottom of the Resources webpage for measurement/surveys. It gives some 'starter' computer code, which you can modify to suit.

[2] This is an example of *Berkson type* error: you are relying on an instrument such as a thermostat that is set to 14, 16, etc, but in which the actual temperature is allowed to range below/above the setting before it is corrected upwards/downwards to stay near the setting. Rounding errors (binning of observations) are another example of Berkson-type errors: if you are told the rounded (error-containing) value $X^*$, you cannot predict the value of the error $\epsilon_X = X^* - X$; but if you are told $X$ you can tell the value of $\epsilon_X$.

**2.** This story "Is Scouting Safe?" is from The (Scouting) Leader 1991.

> Over the past year, leaders have been showing a growing commitment to provide each member a safe and enjoyable Scouting experience. In support of efforts in the field, we conducted a study to establish baseline data on scouting accident and injury trends so that we can make informed decisions about activity precautions or the need for higher safety standards. This column highlights the findings The first question we asked ourselves was, "Is Scouting a safe program for members?"
>
> Statistics Canada, Health Division, told us that 11 out of every 1,000 males aged 5-19 are hospitalized for at least one night a year. When we compared similar information taken from Scouting accident forms, we found our members are hospitalized at a rate of only one per thousand a year. Given that we run active programs and heavily use the outdoors, Scouting falls far below the average rate for daily living risk to males in this age group...

i. Since it is not clear how the Statistics Canada data that went into this calculation were collected, it is not clear how the 1.1% was arrived at. For the sake of this exercise, assume they used the formula

$$CI_{jan1-dec31} = 1 - \exp\left[ - \int_0^{365} ID(t)\delta t \right] = 0.011,$$

where ID(t), the incidence density [for the event of (1st) hospitalization during 1990] is *assumed (for this exercise)* constant over the year[3].

From this equation, calculate the value of $ID(t)$, and express it as the average number of hospitalizations per $10^5$ child-days or per $24^6$ child-hours [making the simplifying assumption that children are at the same risk of hospitalization for each of the 24 hours of every day].

ii. If Scouting members spend 2 hours per week in activities during the course of a normal 30-week Scouting year, and 2 weeks (24/7) in summer camps, how many Scouting-activity hours (SA-hrs) are contributed by 1000 scouts over the course of 1 year? Calculate an incidence density *ratio*, i.e.,

$$\frac{\text{1 hospitalization } \div \text{ SA-hrs}}{\text{incidence density obtained in (i)}}$$

(you can also call it a *rate ratio*). Comment.

[3] One possibility is that they divided the number of (first-for-the-child-that-year) hospitalizations in 1990 for persons in the aged 5-19 age-group by ( $365\times$ the estimated mid-1990 population of persons in that age-group)

**3.** The reported percutaneous Injury (PI) rate for obstetrics/gynecology (OB/GYN) residents (Table 1 of Ayas et al, "Extended work duration and the risk of self-reported percutaneous injuries in interns" – available, if interested, in the resources for Surveys) was 0.0975 injuries/Intern-Month.

i. Using this incidence rate, calculate the probability that an average-risk ob/gyn resident would have no (or the complement, at least one), percutaneous Injury by the end of (a) 1 month (b) 12 months of experience? i.e. what is the probability of 'surviving' these amounts of experience without a PI? The complement is often referred to as 'cumulative incidence' or 'risk'. Hint: either use the (more general) formula for the relationship between incidence density (or event rate) and cumulative incidence, or in this case (since the rate is assumed to be constant over time), by treating the number of events in the (say 12 month) interval in question as a Poisson random variable with expectation $\mu = 12 \times 0.0975$, and calculating the probability of 0 events in that time interval.

ii. What would the 6- and 12-month 'injury-free-survival' be if the incidence density varied linearly from: (a) 0.070 at $t = 0$ to 0.013 at $t = 12$ (b) 0.013 to 0.007 (c) 0.0007 to 0.0013?

What approximation suggests itself for (c)? Can you make it into a rule-of-thumb?

**4.** The following questions (relating to discrete-in-time acts, similar to repeated 'Russian roulette') are based on part of a letter to Editor of The Lancet, May 21, 1994:

> Mastro estimated the probability of HIV-1 transmission, per sexual contact, from female prostitutes to male military prostitutes in Northern Thailand. His conservative estimate of the transmission probability, based on all men, was 0.031 (95% CI 0.025 - 0.040). In a subgroup of men not reporting a history of other sexually transmitted diseases (STDs) his estimate was 0.012 (0.006 - 0.025). He attributes this unexpectedly high value to the possible presence of STDs in female prostitutes (which may have enhanced HIV transmission) and/or high levels of infectivity among the prostitutes who are likely to be at an early stage of HIV infection.
>
> Mastro apparently overlooks these explanations and assumes that the probability of transmission of HIV between regular partners would be the same as that in prostitute-client contacts. He then used this probability of 0.031 to calculate that over 90% of initially uninfected regular partners of seropositive persons would acquire infection over 1 year. This is inconsistent with data from prospective studies in developing countries suggesting seroconversion rates among HIV-discordant partners of about 10% per year. If it is assumed that couples on average have two sexual contacts per week, then on the basis of simple probability calculations, this gives an average transmission probability per sexual contact of about 0.001 (over 30 times smaller than the conservative estimate of Mastro)

i. Carry out the calculation using the 0.031 to arrive at an estimate of "over 90%" [paragraph 2]; assume two sexual contacts per week

ii. Assuming again two contacts per week, do the reverse calculation that produces an estimate of "about 0.001" [paragraph 3].

iii. The 'per-act' transmission probability for HPV is thought to be much higher [cf Pubmed for work of Ann Burchell]. Assuming a frequency of sexual intercourse of 2 /week with an infected partner, what would the 3-month cumulative incidence (seroconversion risk) be if (a) the per-act transmission probability was 10%? (b) this per-act transmission probability could be halved by condom use?

**5.** Breslow and Day used the 1968-1972 incidence[4] rates in table 2.3 to arrive at, in Table 2.4[5], the cumulative incidence (risk) for 4 cancers over various age spans.

For these same age spans, and also the age span 0-85 (close to "lifetime"), calculate the risk of dying from (a) lung cancer (b) breast cancer (c) any cause. Use as input to these risk calculations the cancer-specific and all-cause mortality rates[6] observed for Québec females in 2002.[7] For (a) and (b) ignore competing mortality, i.e., assume that one cannot die of another cause first.

[4] In epidemiology, incidence is typically used in relation to receiving a diagnosis of a illness; although deaths from an illness do, strictly speaking, pertain to a type of incidence, epidemiologists use the term mortality rates, rather than incidence rates, in this context.

[5] Note that what we (and survival analysis texts) call the 'integrated hazard' ($\Lambda$), Breslow & Day call a 'cumulated rate'.

[6] Calculate the mortality rates as no. of deaths ÷ (mid-year population size × 1 year). {Had the numbers of deaths for say each of the years 2001-2003 been available to you, you could have aggregated them in order to arrive at a more stable rate, namely the combined number of deaths ÷ (2002 population size × 3 years), or ÷ (sum of the person years in the 3 years in question).}

[7] The data are provided in a Excel file, and a .csv file that can be read into R or SAS, both located under the heading 'Datasets and programs' at the bottom of the Resources webpage for epidemiology/concepts/measures.

The Vision of Mirza [*and Incidence Density: cf. passage that begins with* •]

Joseph Addison [1672-1719]

> Omnem, qu nunc obducta tuenti
> Mortales hebetat visus tibi, et humida circum
> Caligat, nubem eripiam. 1
> Virgil, AEneid, ii. 604.

WHEN I was at Grand Cairo, I picked up several oriental manuscripts, which I have still by me. Among others I met with one entitled The Visions of Mirza, which I have read over with great pleasure. I intend to give it to the public when I have no other entertainment for them, and shall begin with the first vision, which I have translated word for word, as follows:

On the fifth day of the moon, which according to the custom of my forefathers I always keep holy, after having washed myself and offered up my morning devotions, I ascended the high hills of Baghdad, in order to pass the rest of the day in meditation and prayer. As I was here airing myself on the tops of the mountains, I fell into a profound contemplation on the vanity of human life, and passing from one thought to another, Surely, said I, man is but a shadow, and life a dream. Whilst I was thus musing, I cast my eyes towards the summit of a rock that was not far from me, where I discovered one in the habit of a shepherd, with a little musical instrument in his hand. As I looked upon him he applied it to his lips, and began to play upon it. The sound of it was exceeding sweet, and wrought into a variety of tunes that were inexpressibly melodious and altogether different from anything I had ever heard. They put me in mind of those heavenly airs that are played to the departed souls of good men upon their first arrival in Paradise, to wear out the impressions of the last agonies, and qualify them for the pleasures of that happy place. My heart melted away in secret raptures.

I had often been told that the rock before me was the haunt of a genius; and that several had been entertained with music who had passed by it, but never heard that the musician had before made himself visible. When he had raised my thoughts by those transporting airs which he played, to taste the pleasures of his conversation, as I looked upon him like one astonished, he beckoned to me, and by the waving of his hand directed me to approach the place where he sat. I drew near with that reverence which is due to a superior nature; and as my heart was entirely subdued by the captivating strains I had heard, I fell down at his feet and wept. The genius smiled upon me with a look of compassion and affability that familiarized him to my imagination, and at once dispelled all the fears and apprehensions with which I approached him. He lifted me from the ground, and taking me by the hand, Mirza, said he, I have heard thee in thy soliloquies; follow me.

He then led me to the highest pinnacle of the rock, and placing me on the top of it, Cast thy eyes eastward, said he and tell me what thou seest. • I see, said I, a huge valley and a prodigious tide of water rolling through it. The valley that thou seest, said he, is the Vale of Misery, and the tide of water that thou seest is part of the great tide of eternity. What is the reason, said I, that the tide I see rises out of a thick mist at one end, and again loses itself in a thick mist at the other? What thou seest, said he, is that portion of eternity which is called time, measured out by the sun, and reaching from the beginning of the world to its consummation. Examine now, said he, this sea that is thus bounded by darkness at both ends, and tell me what thou discoverest in it. I see a bridge, said I, standing in the midst of the tide. The bridge thou seest, said he, is human life; consider it attentively. Upon a more leisurely survey of it I found that it consisted of more than threescore and ten entire arches, with several broken arches, which, added to those that were entire, made up the number to about a hundred. As I was counting the arches, the genius told me that this bridge consisted at first of a thousand arches; but that a great flood swept away the rest, and left the bridge in the ruinous condition I now beheld it. But tell me further, said he, what thou discoverest on it. I see multitudes of people passing over it, said I, and a black cloud hanging on each end of it. As I looked more attentively, I saw several of the passengers dropping through the bridge into the great tide that flowed underneath it; and upon further examination, perceived there were innumerable trap-doors that lay concealed in the bridge, which the passengers no sooner trod upon, but they fell through them into the tide and immediately disappeared. These hidden pitfalls were set very thick at the entrance of the bridge, so that throngs of people no sooner broke through the cloud, but many of them fell into them. They grew thinner towards the middle, but multiplied and lay closer together towards the end of the arches that were entire.

There were indeed some persons, but their number was very small, that continued a kind of hobbling march on the broken arches, but fell through one after another, being quite tired and spent with so long a walk.

I passed some time in the contemplation of this wonderful structure, and the great variety of objects which it presented. My heart was filled with a deep melancholy to see several dropping unexpectedly in the midst of mirth and jollity, and catching at everything that stood by them to save themselves. Some were looking up towards the heavens in a thoughtful posture, and in the midst of a speculation stumbled and fell out of sight. Multitudes were very busy in the pursuit of bubbles that glittered in their eyes and danced before them, but often when they thought themselves within the reach of them their

footing failed and down they sunk. In this confusion of objects, I observed some with scimitars in their hands, and others with urinals, who ran to and fro upon the bridge, thrusting several persons on trap-doors which did not seem to lie in their way, and which they might have escaped had they not been thus forced upon them.

The genius, seeing me indulge myself on this melancholy prospect, told me I had dwelt long enough upon it, Take thine eyes off the bridge, said he, and tell me if thou seest anything thou dost not comprehend. Upon looking up, What mean, said I, those great flights of birds that are perpetually hovering about the bridge, and settling up it from time to time? I see vultures, harpies, ravens, cormorants, and among many other feathered creatures several little winged boys that perch in great numbers upon the middle arches, These, said the genius, are Envy, Avarice, Superstition, Despair, Love, with the like cares and passions that infest human life.

I here fetched a deep sigh. Alas, said I, man was made in vain: how is he given away to misery and mortality, tortured in life, and swallowed up in death! The genius being moved with compassion towards me, bid me quit so uncomfortable a prospect. Look no more, said he, on man in the first stage of his existence, in his setting out for eternity; but cast thine eye on that thick mist into which the tide bears the several generations of mortals that fall into it. I directed my sight as I was ordered, and (whether or no the good genius strengthened it with any supernatural force, or dissipated part of the mist that was before too thick for eye to penetrate) I saw the valley opening at the farther end, and spreading forth into an immense ocean that had a huge rock of adamant running through the midst of it, and dividing it into two equal parts. The clouds still rested on one half of it, insomuch that I could discover nothing in it; but the other appeared to me a vast ocean planted with innumerable islands, that were covered with fruits and flowers, and interwoven with a thousand little shining seas that ran among them. I could see persons dressed in glorious habits with garlands upon their heads, passing among the trees, lying down by the sides of fountains, or resting on beds of flowers; and could hear a confused harmony of singing birds, falling waters, human voices, and musical instruments. Gladness grew in me upon the discovery of so delightful a scene. I wished for the wings of an eagle that I might fly away to those happy seats; but the genius told me there was no passage to them except through the gates of death that I saw opening every moment upon the bridge. The islands, said he, that lie so fresh and green before thee, and with which the whole face of the ocean appears spotted as far as thou canst see, are more in number than the sands on the seashore; there are myriads of islands behind those which thou here discoverest, reaching farther than thine eye, or even thine imagination can extend itself. These

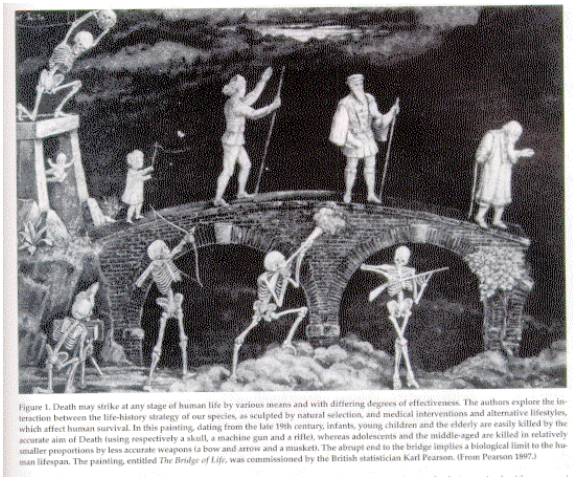

Figure 1. Death may strike at any stage of human life by various means and with differing degrees of effectiveness. The authors explore the interaction between the life-history strategy of our species, as sculpted by natural selection, and medical interventions and alternative lifestyles, which affect human survival. In this painting, dating from the late 19th century, infants, young children and the elderly are easily killed by the accurate aim of Death (using respectively a skull, a machine gun and a rifle), whereas adolescents and the middle-aged are killed in relatively smaller proportions by less accurate weapons (a bow and arrow and a musket). The abrupt end to the bridge implies a biological limit to the human lifespan. The painting, entitled *The Bridge of Life*, was commissioned by the British statistician Karl Pearson. (From Pearson 1897.)

Figure 1: The Bridge of Life. In Karl Pearson: The chances of death and other studies in evolution (1897). Based on Addison's allegory ???

are the mansions of good men after death, who, according to the degree and kinds of virtue in which they excelled, are distributed amount these several islands, which abound with pleasures of different kinds and degrees suitable to the relishes and perfections of those who are settled in them; every island is a paradise accommodated to its respective inhabitants. Are not these, O Mirza, habitations worth contending for? Does life appear miserable that gives thee opportunities of earning such a reward? Is death to be feared that will convey thee to so happy an existence? Think not man was made in vain who has such an eternity reserved for him. I gazed with inexpressible pleasure on these happy islands. At length, said I, Show me now, I beseech thee, the secrets that lie hid under those dark clouds which cover the ocean on the other side of the rock of adamant. The genius making me no answer, I turned me about to address myself to him a second time, but I found that he had left me; I then turned again to the vision which I had been so long contemplating; but, instead of the rolling tide, the arched bridge, and the happy islands, I saw nothing but the long valley of Baghdad, with oxen, sheep, and camels grazing upon the sides of it.