

Correspondence

Benefits and limitations of pathology databases to cancer registries

In a recent article, Brewster *et al*¹ presented data on estimated completeness of case ascertainment for 2335 cases of malignancy. Results are given for all subjects and for each of 36 anatomical sites. In each case, the observed percentage completeness is given, together with what purports to be a 95% confidence interval. A glance at these intervals is sufficient to suggest they are so narrow as to constitute wishful thinking.

On closer examination, it is evident that the authors intended to use the simplest method for calculating a confidence interval for a proportion, $p = r/n$, viz. $p \pm z (p(1-p)/n)$ where $z = 1.96$ for a 95% interval. In fact they have failed to take the n appearing in the denominator inside the square root, with the result that the intervals are narrower than intended, by a factor n , which can be large.

Moreover, this method is a very poor one,^{2,3} in several respects: it gives an inappropriate zero width interval when p is 0 or 1 (as in the article); when the numerator r is very small, the calculated lower limit can be an absurd value less than 0, with corresponding violation of the boundary at 1 when $n - r$ is very

small; and the average coverage of what is claimed to be a 95% interval is only around 88%.

The accompanying table shows confidence intervals calculated by the currently accepted standard method.⁴ These intervals may be obtained from Geigy scientific tables for small to moderate n ; they are not as yet particularly accessible to researchers, but can be accessed by statistical software including Minitab and SAS indirectly via the inverse of the β integral. An alternative, accepted method that is of closed form and thus readily programmed is $(2np + z^2 \pm z(z^2 + 4np(1-p))/(2(n+z^2)))$.⁵

Furthermore, it is difficult to appraise whether the heterogeneity of observed completeness rates is any greater than would be expected on the basis of chance variation; it is noteworthy that the lowest rates tend to have small denominators. A hypothesis test would be helpful here—it would necessitate a judicious, anatomically or pathologically meaningful combination of groups into broad categories each containing 100 cases or more.

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Dr Brewster comments:

We are grateful to Robert Newcombe for drawing our attention to the error in our calculation of confidence intervals which was replicated by the use of a spreadsheet and which, in retrospect, we should have identified ourselves. We are also persuaded by his arguments for using other methods of calculating confidence intervals in this situation. Nevertheless, the recalculation of confidence intervals, by whatever method, does not alter the substance or conclusions of our paper.

Histological patchiness and sparing of the rectum in ulcerative colitis: refuting the dogma

We were delighted to see that Levine *et al*¹ have confirmed the findings of our prospective study reported in 1995.² Thus, refuted is the conventional wisdom that ulcerative colitis is always diffuse and most severe in the rectum, and that it tapers in severity proximally. Our findings were welcomed by many of our colleagues who knew this from their clinical experience but were often dismayed

Estimated completeness of case ascertainment by the Scottish Cancer Registration Scheme, based on an independent comparison with pathology data, 1992

ICD-9 code	Site	No of cases (x)	No of completely "missed" cases (y)	Estimated % completeness (x/(x+y)×100)	95% Confidence intervals	
					Lower	Upper
140-149	Lip, oral cavity, and pharynx	39	1	97.5	86.8	99.9
150	Oesophagus	58	0	100.0	93.8	100.0
151	Stomach	89	1	98.9	94.0	100.0
153, 154	Colon, rectum	192	20	90.6	85.8	94.1
155, 156	Liver, gall bladder	30	0	100.0	88.4	100.0
157	Pancreas	57	1	98.3	90.8	100.0
152, 158, 159	Small intestine, retroperitoneum, other digestive sites	14	0	100.0	76.8	100.0
160	Nasal cavities, middle ear, sinuses	1	1	50.0	1.3	98.7
161	Larynx	21	1	95.5	77.2	99.9
162	Trachea, bronchus, lung	360	2	99.4	98.0	99.9
163	Pleura	10	0	100.0	69.2	100.0
170, 171	Bone, connective tissue	9	0	100.0	66.4	100.0
172	Skin (melanoma)	41	0	100.0	91.4	100.0
173 (M-807)	Skin (squamous cell)	103	12	89.6	82.5	94.5
173 (M-809)	Skin (basal cell)	330	46	87.8	84.0	90.9
173 (M-8832)	Skin (dermatofibrosarcoma)	1	1	50.0	1.3	98.7
174, 175	Breast (female/male)	247	13	95.0	91.6	97.3
179	Uterus	2	1	66.7	9.4	99.2
180	Cervix uteri	33	6	84.6	69.5	94.1
182	Corpus uteri	24	2	92.3	74.9	99.1
183	Ovary	46	1	97.9	88.7	99.9
184	Other, unspecified genital organs	11	0	100.0	71.5	100.0
185	Prostate	86	6	93.5	86.3	97.6
186	Testis	11	0	100.0	71.5	100.0
187	Penis	2	0	100.0	15.8	100.0
188	Bladder	115	2	98.3	94.0	99.8
189	Kidney	29	0	100.0	88.1	100.0
190	Eye	2	0	100.0	15.8	100.0
191, 192	Brain, central nervous system	30	0	100.0	88.4	100.0
193	Thyroid gland	6	1	85.7	42.1	99.6
194	Endocrine glands	1	0	100.0	2.5	100.0
196-199	Secondary sites	83	0	100.0	95.7	100.0
200, 202	Non-Hodgkin's lymphoma	53	8	86.9	75.8	94.2
201	Hodgkin's disease	8	1	88.9	51.8	99.7
203	Multiple myeloma	16	2	88.9	65.3	98.6
204-208	Leukaemia	42	4	91.3	79.2	97.6
140-208	All malignant sites	2202	133	94.3	93.3	95.2

when: pathologists used this finding of patchiness as a strong mandate for the diagnosis of Crohn's disease; or surgeons became reluctant to do proctocolectomies in ulcerative colitis cases that were indicated clinically, because they were fearful that patchiness of involvement meant Crohn's disease. As the armamentarium of immunomodulatory drugs expands, more specific to one disease than the other, it is critical to recognise this important diagnostic feature of ulcerative colitis.

Our findings were in patients with documented ulcerative colitis whereas Levine *et al* found predominately normal or borderline biopsies among patients with ulcerative proctitis (10 of 11 cases) rather than ulcerative colitis. Although we have shown that over time rectal biopsies from patients with ulcerative proctitis are indistinguishable from biopsies from patients with ulcerative colitis,³ it remains a possibility that these diseases may have different pathophysiology. Nonetheless, it is important to realise that in ulcerative proctitis, rectal biopsies may normalise over time. The presence of frankly normal rectal histology in patients with longstanding diagnoses of ulcerative colitis or proctitis often raises the issue of the accuracy of the initial diagnoses. We support Levine *et al* in their contention that these diseases are dynamic in their expression patterns, and this fact should now be accepted into the new diagnostic dogma of ulcerative colitis.

Why has the conventional wisdom of absolute rectal involvement, and absolute disease continuity in ulcerative colitis persisted so long? We believe that it points to the selectivity of human observation. We only look for what we believe we should find. Patchy rectosigmoid involvement in ulcerative colitis is one example, but an even more compelling one is how *Helicobacter pylori* could be missed in gastric biopsy tissue sections for so long, by so many!

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Rights of possession in human corpses

English law fails to recognise any right to possession of a corpse as the corpse is not a *chose in action*. This means—for example, it cannot be stolen.¹

However, what is not commonly recognised is that the executors may have the right to dispose of the body according to the terms

of the deceased's will. Any interference in this right—such as removing the body (or as we laymen might say, "stealing it") may raise a cause of action under the Law of Property Act 1925. This point has been made at least since Glazebrook lectured on criminal law at Cambridge in the early '70s.

The legal rule that a body cannot be stolen commonly generates a belief that no other cause of action can possibly arise, although the example above shows that it can. The editorial team of the *Journal of Clinical Pathology* is to be congratulated in disabusing their readership of this common misconception.

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Proliferation indexes—a comparison between cutaneous basal and squamous cell carcinomas

We read with interest the article by Al-Sader *et al* that compared cell proliferation indexes in cutaneous basal cell carcinomas (BCC) and squamous cell carcinomas (SCC).¹ We have evaluated silver-stained nucleolar organiser region (Ag-NOR) protein quantity, proliferating cell nuclear antigen (PCNA) labelling index, and mitotic index in the corresponding spontaneous canine cutaneous tumours obtaining comparable results.^{2,3} However, more recently, in an attempt to explain the paradoxical clinical behaviour of canine cutaneous BCC, we obtained interesting results studying the combined behaviour of mitotic index, apoptotic index, and mitotic phase distribution in the aforementioned tumours.⁴ In fact, in accordance with Brown and Gatter for human BCC,⁵ our results strongly suggest that a prolonged "M phase" of the cell cycle plays an important role in maintaining a slow rate of growth in canine BCC. The strong similarity between canine and human BCC and SCC support the opinion that spontaneous animal tumours could represent useful models for human disease.

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Brain tissue banks in psychiatric and neurological research

We welcomed the article by Cairns and Lantos on brain tissue banks.¹ The importance of such facilities in psychiatric and neurological research has not been adequately appreciated by the wider clinical community, perhaps because collection and storage of postmortem tissue for research is not as an emotive issue as requesting organs for donation. However, without such tissue banks little would be known about many debilitating conditions.

The South West Brain Bank in Bristol was established over 10 years ago to collect brain tissue from people suffering from dementia. It is from this experience that we write to emphasise certain points that are important not only to potential donors and their relatives but also to the physicians requesting the donation, and those using the tissue for research.

Making the decision to donate tissue for research can be a very difficult one for most people. This can be made even more difficult if it is left to the time when loved ones are close to death or have died. It is far preferable that all arrangements are made in advance of the event, and it is helpful if potential donors and their families can be given information about the procedures involved in a donation (perhaps in the form of a leaflet). The details can be assimilated and discussed within the family and with the coordinator of the facility at a time when bereavement does not cloud the issue. We have found the role of the brain bank coordinator to be a crucial one at this stage. We have one person acting as the coordinator, an MLSO trained in neuropathology. She deals with the donation from the initial arrangements through to processing of the tissue for histological assessment.

Before a histological diagnosis is made, the neuropathologist is provided with as complete a clinical history as possible. This is obtained, using a standardised protocol, from all available hospital and general practitioner notes.

The continuing acquisition of tissue for research purposes relies heavily on an understanding of the importance of such donations by the medical practitioners who must make the request and, perhaps more importantly, by their patients and relatives. The responsibility for giving potential donors and their families enough information and support regarding a donation lies with the brain banks who must approach this with compassion and sensitivity.

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