On the trail of necrotizing fasciitis in children

Tauyee Hsieh and colleagues are to be commended for their attempt to define the pediatric presentation and outcome of necrotizing fasciitis versus cellulitis, using a case–control study design.[1] One major limitation of their study is the paucity of cases of necrotizing fasciitis (8 cases in total), despite a 16-year period for the retrospective analysis. This raises a question about the accuracy of the ICD-9 coding system for identifying cases of necrotizing fasciitis or similar entities. The answer is that it is not particularly accurate. For example, the sensitivity of ICD-9-CM codes appears to be at most 58.3% for laboratory-confirmed pneumococcal pneumoniae and tends to be much lower than that.[2] Identification of common occurrences such as adult stroke,[3] myocardial infarction,[4] childhood accidents[5] and reportable communicable diseases[6] via ICD-9 and ICD-9-CM codes is often equally poor, especially among pediatricians.[7] Furthermore, coding discrepancies are greater with more complex medical cases,[8] such as necrotizing fasciitis.[9] I do not criticize the authors for this limitation, but feel that it may help explain why so few cases were identified over such a long study period.

I am concerned that the authors did not estimate a study sample size that would have enabled them to address their question(s) with greater study power and precision. Sample size estimation is an important part of any study design, especially in a case–control study that attempts to examine a rare occurrence like pediatric necrotizing fasciitis.[10] Accordingly, a colleague and I developed a practical paper to assist clinician-researchers in the difficult task of estimating sample size for such studies.[10] As Hsieh and colleagues pointed out, they may have identified a greater number of cases by embarking on a multicentre study, which is often required when rare diseases are studied. It was for this purpose that the Ontario Group A Streptococcal Study Group was formed.[9,11] During 1992 and 1993 alone, this group identified 323 cases of invasive group A streptococcal disease in Ontario; the highest rates were among children and elderly people. However, necrotizing fasciitis occurred in only 6% of all patients, highlighting the rarity of this disease and its high rate of associated morbidity and mortality.[9]

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I read with interest the article by Tauyee Hsieh and colleagues describing a case–control study of necrotizing fasciitis in children.[1] The authors indicated that they enrolled control subjects who were "matched to the case subjects" by date of admission and by date of birth. Although it was not specifically stated, one might assume by the wording that the control subjects were individually matched to the case subjects. The authors also noted that, for the multivariate analysis, they were unable to obtain odds ratios from conditional logistic regression (which would take the matching into account) but verified their estimates by an alternative approach that did adjust for matching.

However, it is not clear whether appropriate analyses that take matching into account were utilized in their univariate comparisons, and whether the comparisons displayed in their Table 1 represent univariate or multivariate comparisons. They indicated that they analyzed their data using Fisher's exact test for categorical variables and the Wilcoxon rank-sum test for continuous variables. If the authors did not use matching, would the comparisons in Table 1 have been different if they had? Would this have altered the "significant" risk factors included in the multivariate analysis?

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[The authors respond:]

We agree with Joel Ray that the ICD-9 coding system may not adequately ensure retrieval of all relevant cases. To ensure that we captured

all relevant charts, we also reviewed other diagnostic categories such as myositis, gangrene, gas gangrene and erysipelas.[1] We also reviewed all charts of children with group A β-hemolytic *Streptococcus* cultured from sterile sites during the time period of the study.

With respect to doing a sample size calculation, our goal was to collect all of the possible cases of necrotizing fasciitis at our institution over the last 16 years. Our problem was not with the sample size but with the power to discern major factors associated with necrotizing fasciitis, because of the small number of cases (8). For this reason, the reported results only suggested a trend and did not confirm it. Consequently we did not do a retrospective power calculation.

Gary Liss refers to a multivariate analysis and the fact that we were unable to obtain odds ratios from conditional logistic regression. To clarify, we did not do a multivariate analysis. Because of the small number of patients, odds ratios could not be obtained from a conditional logistic regression. Instead, we verified each estimate using a logit estimate of the odds ratio, adjusting for matching.

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First-line drugs for hypertension

In his recent series of *CMAJ* articles on choosing a first-line drug in the management of elevated blood pressure, James Wright repeatedly uses the phrase "low cost."[1–3] Unfortunately, what he is referring to is purchase price, not all-in system costs. Because purchase decisions are being restricted by third-party payers (such as the British Columbia Ministry of Health, to which Wright's Therapeutics Initiative is advisory), it is important to understand the difference.

Hypertension is well controlled for only 16% of Canadians with high blood pressure.[4] This lack of good blood pressure control has an enormous avoidable cost associated with stroke, renal failure, heart failure and coronary artery disease.

Hughes and McGuire reported that in the British National Health Service the total cost of treating hypertension was £76.5 million per annum, of which £26.9 million was attributed to the costs of discontinuation or switching of therapy.[5]

It is thus very important to recognize that there is much less persistence in actual practice than in clinical trials. Cheaper drugs that are not taken be-