

# Letters Correspondance

## Concerns about what constitutes clinical evidence

We read with great interest the article by Soltani and Moayyeri<sup>1</sup> in the November 2005 issue of *Canadian Family Physician*. We fully agree with the authors that probabilistic reasoning (as opposed to a deterministic approach) is the optimal use of available evidence in estimating the likelihood of a diagnosis.

Nevertheless, we have serious hesitations about the validity of what the authors define as the dynamic properties of likelihood ratios (LRs) and about their argument that LRs can be easily used in a sequence of tests. An important advantage of LRs is that they can combine the results of multiple tests, in which the LR of the whole set of findings is the product of the LR of each individual test.<sup>2</sup> A necessary assumption for this approach, however, is the conditional independence between tests.<sup>3</sup> Two tests are independent if knowing the result of one test does not change the probability of the result of the other one. This condition is often not met in reality, constituting an obstacle against using sequential LRs without proper adjustment for test dependency.

In the example given in the article, the authors have multiplied 5 LRs attributable to 5 items in the medical history, physical examination, and para-clinical evaluation of a hypothetical patient. This approach resulted in a change in the probability of cancer from 0.7% to around 20%. The problem of dependence, however, arises. In this instance, for example, history of cancer and age are very likely to be correlated because patients with previous history of cancer are generally older than patients without such history. The combined LR of these 2 findings for the diagnosis of cancer is, therefore, different from the product of individual LRs.

Similar arguments hold for several other combinations of tests in Table 1 of the article (eg, dependence between the duration of pain and weight loss and between the history of cancer and radiographic findings). Consequently, the estimated posterior probability of 20% is probably inaccurate. No further refinement of this estimation is possible unless some measure of conditional dependence is at hand.

Dealing with test dependency is a statistical issue. Some methods have been proposed to account for test dependence,<sup>4,5</sup> none of which are simple enough to be used in routine clinical practice.

Notwithstanding all the advantages of evidence-based reasoning, physicians should be aware of the pitfalls involved in implementing such approaches

without considering the underlying assumptions and limitations.

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## References

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## Response

Sadatsafavi and Ganjizadeh have correctly pointed to a prerequisite of dynamic decision making using likelihood ratios (LRs). Independence of the tests should be considered for accurate use of LRs in a series of clinical tests, but this should not be taken as a disadvantage of this approach.

First, there is usually some kind of dependency between clinical presentations. For instance, in our scenario there might also be some dependency between age and erythrocyte sedimentation rate.<sup>1</sup> No one can be sure about absence of correlation between different clinical signs and symptoms, but these correlations can generally be ignored in the case of presentations from different body systems. As Sadatsafavi and Ganjizadeh note, statistical methods for adjustment of such dependencies are not applicable clinically. Several authorities have emphasized evidence for this prerequisite of clinical decision making sufficiently, and, as a general approach, suggest that no more than 5 LRs be multiplied for a diagnosis.<sup>2</sup> These tests should reflect different body organs or systems.

Second, consideration of confidence intervals (CIs) for probability and for any measurement in clinical practice is an indispensable part of probabilistic reasoning and dynamic decision making. Family physicians have to appreciate the presence of uncertainty for estimates of pretest probability of diseases and LRs of different tests, and they should notice that they are dealing with ranges of values instead of single numbers. In this context, multiplication of more LRs will result in numbers with wider CIs, and perceived dependency between tests will lose its importance.

Third, it is necessary to note that even diagnostic and therapeutic thresholds have CIs. Degree

of uncertainty for a diagnosis is inversely related to the overlapping section of CIs for the diagnostic threshold and the posttest probability of the disease. If the posttest probability is sufficiently distant from the threshold, then you can easily distinguish between presence or absence of the disease. If the distance between posttest probability and diagnostic threshold is not large enough, however, you should suspend judgment until receiving additional information from other possible sources. Dependence or independence of the tests might have some effect for transition of the point estimates, but little effect for shift of the situation. In our scenario, for instance, if posttest probability of cancer in the patient was lower than 5% or more than 50%, physicians could decide between follow-up or therapeutic intervention. With the estimate of 20% (or somewhat lower considering dependence of the tests), however, physicians must pursue diagnosis using a paraclinical test with highly significant positive and negative LR.

Although consideration of independence of clinical tests is proposed as an essential step before application of multiple LR, this problem is usually resolved by using a few tests from independent body systems. Clinicians can increase their diagnostic efficiency by using tests with significant and independent LR

derived from valid research evidence instead of their own intuition or personal experience.

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## Family physicians are generalists!

*"If any organization is to remain healthy, it must have a balance between generalists and specialists."*

—Ian McWhinney<sup>1</sup>

Family doctors are the ultimate generalists in Canadian medical practice. They care for people of all ages and both sexes, from preconception to grief; apply medical knowledge and basic technical skills for common problems; and coordinate referrals and consultations for complex problems requiring specialists' expertise. Knowledge of the breadth of medicine, committing to continuing personal relationships, and