

Letters

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Use of Doppler ultrasonography to predict pre-eclampsia

We enjoyed Jeltsje Cnossen and colleagues' systematic review of the use of uterine artery Doppler ultrasonography to predict pre-eclampsia.¹ They concluded that an increased pulsatility index with notching during the second trimester is the best predictor of pre-eclampsia and strongly recommended the routine use of these measurement parameters in clinical practice. However, this recommendation is based on only 2 studies, one of which included 1757 low-risk women and the other 351 high-risk women. As the incidence of pre-eclampsia is relatively low (0.4%–6.7%), screening tests require high likelihood ratios to adequately predict the disease's probability with positive test results and very low likelihood ratios to confidently exclude the disorder with negative test results.² An increased pulsatility index with notching produced sufficiently positive likelihood ratios (21.0) in high-risk women but it was inadequate in low-risk populations (7.5); importantly, the negative likelihood ratios were quite poor for both populations (0.59 and 0.82 respectively).

We also have methodologic concerns. First, a valid meta-analysis should be examined for heterogeneity before one considers pooling the results of primary studies to create summary estimates with enhanced precision.³ There is no indication in the review that

the heterogeneity of the study results was formally tested. Second, there is a substantial possibility of publication bias in this area of research,⁴ and there is no indication that this was assessed. Finally, although pooling of sensitivities and specificities instead of likelihood ratios has recently been encouraged,⁵ we are skeptical and agree with others⁶ that sensitivities and specificities are inappropriate for meta-analyses as they do not behave independently when pooled from primary studies to generate separate averages.

We therefore suggest that the authors' conclusions are premature. Doppler ultrasonography, although useful for monitoring high-risk pregnancies, should not currently be recommended for routine screening to predict pre-eclampsia.

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[Six of the authors respond:]

We thank Agustín Conde-Agudelo and Marshall Lindheimer for giving us the

opportunity to clarify the interpretation of our findings. We regret that they interpreted our words as a strong recommendation for routine use of Doppler ultrasonography in clinical practice. In the abstract we stated that "a pulsatility index, alone or combined with notching, is the most predictive Doppler index. These indices should be used in clinical practice."¹ Our intention was not to recommend the routine use of Doppler ultrasonography but rather to emphasize that if it is used then the pulsatility index, alone or combined with notching, is the best choice.

More generally, we do not think that firm clinical recommendations should be made on the basis of what might be called early-phase diagnostic studies or meta-analyses thereof.² A more formal economic modelling analysis on this topic, although still hampered by the use of early-phase diagnostic studies only, showed that the routine use of Doppler ultrasonography cannot currently be considered cost-effective.³

Conde-Agudelo and Lindheimer raise 3 methodologic concerns. First, the statistical test for heterogeneity has bad statistical properties, making such tests virtually superfluous. Although the I^2 statistic is an improvement,⁴ we agree with its inventors that "quantification of heterogeneity is only one component of a wider investigation of variability across studies, the most important being diversity in clinical and methodological aspects."⁵ We carefully dealt with methodologic diversity using predefined stratified analyses. Second, funnel-plot asymmetry may be caused by at least 6 different mechanisms, of which publication bias is just 1. This is why experts in the field now prefer the term small-study bias. Without firm criteria to distinguish the sources for the asymmetry, interpretation of such plots remains speculative.^{6,7} Finally, the non-independence of sensitivity and specificity is a phenomenon for which the bivariate method explicitly accounts.⁸ In conclusion, we concur with Conde-Agudelo and Lindheimer

that it is still too early to recommend routine use of Doppler ultrasonography to predict a pregnant woman's risk of developing pre-eclampsia and intrauterine growth restriction.

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Electronic medical records

We wish to comment on the editorial about electronic medical records.¹ Adoption of electronic health records has been slow in Canada. In some provinces fewer than 30% of medical practices use an electronic health record as their primary record-keeping

tool and many of these practices do not use essential features of the system. Perhaps the design and deployment of these systems could account for this disturbing statistic.

Vendors of electronic record-keeping systems tend to focus on the expedient addition of clinical data. However, the increasing quantity of longitudinal information that includes personal and family histories, detailed notes on clinical encounters, laboratory results and referral material can result in data overload. Thus, the electronic medical record can become a hindrance rather than a support.

The needs of all stakeholders must be carefully considered in the design of electronic medical record-keeping systems. To be relevant and useful to clinicians and their patients (the primary stakeholders), electronic health records need to be used at the point of care. Policy-makers in the health care system are important secondary stakeholders because data from electronic records can be collated for use in managing the health care system.

Software vendors and the provincial bodies responsible for electronic health record certification must understand the impact of the way in which information is presented on the usefulness and usability of electronic records. Rather than being a passive repository of information, the electronic record should be capable of revealing complex trends and patterns. As well, training methods must be adjusted so that health care providers are taught to understand that facts must be added to the health record in the context of continuing care and not only to provide a medicolegal historical record.

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Medical isotope production and nuclear terrorism

Two recent *CMAJ* news articles gave good insights into last December's medical isotope crisis.^{1,2} It was inspiring to read how our colleagues in nuclear medicine coped with the interruption in the isotope supply.

It may not be widely known that the manner in which medical isotopes are produced in Canada is unintentionally exacerbating the problem of nuclear terrorism. Uranium contains 2 isotopes, uranium 238 (U 238) and uranium 235 (U 235). Natural uranium consists of 0.7% U 235 whereas highly enriched uranium consists of more than 20% U 235. Most of the medical isotopes produced at the Chalk River facility are made from weapons-grade highly enriched uranium. Highly enriched uranium is one of the main ingredients in homemade nuclear bombs, and its theft and smuggling cannot reliably be detected.³

Canada's MDS Nordion, one of the 4 major international suppliers of medical isotopes, imports about 20 kg of weapons-grade highly enriched uranium from the United States annually to produce its isotopes. In the process of making medical isotopes, about 97% of the bomb-grade material remains unused. These ever-increasing leftovers, sufficient to make several Hiroshima-sized bombs, are deposited in commercial sites that constitute a long-term security risk.

There is another option. The production of medical isotopes can be converted from the use of highly enriched uranium to the use of low-enriched uranium (which cannot be used to make a nuclear bomb) without technical obstacles.⁴ This is being done successfully in smaller facilities in Argentina, Indonesia and Australia. For Canadian suppliers, the conversion would entail an initial cost for retooling, but thereafter the production costs would be comparable to those with highly enriched uranium.⁵ In the long term, there may actually be savings as the costs of storing weapons-grade highly enriched uranium would be eliminated. As the sole purchasers of medical isotopes, health