should be required to treat the postmenopausal lack of estrogen.

Baumgartner's offer to discuss Premarin provides the opportunity to pose the following questions: Are precise figures currently available on the number of steroid components in Premarin? To what extent has their spectrum of effects been elucidated? Has it been established that all of the metabolites produce only beneficial effects?

According to our estimates, Premarin must contain considerably more steroid metabolites than have been reported in the literature. A report recently appeared on the occurrence of hitherto unknown metabolites such as δ-8-estrone.[2] It is particularly important in the case of long-term treatment with the preparation to know the effects of components that do not predominate quantitatively in the extract. We now know that estrogenic metabolites can produce a number of different effects;[3] some metabolites are thought to increase the risk of breast cancer.[4]

Competing interests: None declared.

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[The author responds:]

Premarin is a complex natural product comprised of multiple components. It has been the subject of more than 3500 citations and over 57 years of clinical use in Canada, the US and around the world. All of the estrogenic components that have been tested for biological activity have been found to be biologically active. As Theodor Lippert and Alfred Mueck state, different estrogens can produce different effects. An estrogen can be an agonist in one tissue and an antagonist in another; we know that these effects are tissue and cell dependent. Furthermore, we know that the effect of an estrogen can be different when administered acutely versus chronically and, perhaps most important, that its effect can be different, in fact opposite, when administered in conjunction with other estrogens.[1–4] Thus, the effects of Premarin cannot be ascribed to an individual metabolite or component or group of components. Effects are all too frequently ascribed to estrogens as a class by individuals whose knowledge in the area is limited; in any event the data are more often than not based on studies with Premarin. On the basis of current scientific and clinical knowledge of the mechanisms of estrogen action, an assumption that Premarin's effects apply or can be extrapolated to all estrogens is inappropriate.

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It's always a g'day to immunize, mate

Considering the recent adverse publicity that immunization has received in both the scientific and the lay press, I found a recent *CMAJ* piece on immunization by Barbara Sibbald[1] to be quite useful and timely. Your readers may also find an excellent brochure produced by the Australian government to be useful.[2] It can be downloaded in PDF format from the Web.

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Caring for patients with Alzheimer's disease in Italy

We read with interest the article by Margaret Hux and colleagues on the association between cognitive function and the cost of caring for patients with Alzheimer's disease.[1] We conducted a similar study in Italy.

We sampled 10 patients at each of 9 Italian centres for the care of patients with Alzheimer's disease. At each centre we collected information on the patients' degree of cognitive impairment, as indicated by the Mini-Mental State Examination,[2] and the levels of care associated with different levels of impairment. We also surveyed sociodemographic characteristics of family caregivers and asked them to estimate the time and money the family devoted to caring for the family member with Alzheimer's disease. Italian National Health Service tariffs[3,4] were used to estimate the cost of medical services and the replacement approach[5] was applied to estimate the costs of informal care provided.

We analysed the association between cognitive function (using the classification system used by Hux and colleagues) and costs using multiple linear regression. Cost was logarithmically transformed to better fit a Gaussian distribution.

Seventy-six (84%) of the patients and their caregivers agreed to participate. The patients had a mean Mini-