

isoflavones were extracted within four months of purchase (and before their stated use-by date) from 500 mg of each specimen after dissolution in 70% methanol. Glycosylated and free isoflavones were assayed in duplicate by gradient high-pressure liquid chromatography, with detection of isoflavones at 254 nm using a Waters 996 series photodiode detector with a limit of detection of 0.2 µg/mL. The identity of chromatogram peaks was confirmed by UV–V spectral analysis, and by comparison with standards. The mobile phase was acetonitrile, and adequate peak separation, linearity, accuracy and reproducibility were demonstrated. The total amount of available aglycone isoflavones in each sample was estimated (see Table).

Only two products (Phytolife and Promensil) had total isoflavone contents close to the stated amount, and the content of the Phytolife product was variable. Estimated aglycone contents of preparations demonstrated that glycosylated isoflavones contributed substantially to the stated content of the product. A previous study of isoflavone-containing preparations marketed in the United States produced similar results to ours.¹ Consumers may wish to consider not only whether an alternative therapy is of use, but also whether the product they purchase contains what they expect.

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Screening for gestational diabetes: the time of day is important

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TO THE EDITOR: The 50 g glucose challenge test (GCT) is widely recommended as a screening test for gestational diabetes (GD).¹ The test consists of a 50 g oral glucose load given at any time of the day, followed one hour later by the measurement of the plasma glucose concentration.² This test is recognised as imperfect for screening, as sensitivity and specificity are not 100%.^{2,3} It is known that glucose tolerance deteriorates in the afternoon,⁴ which raises the question of whether time of day influences the response to the 50 g GCT.

Screening for gestational diabetes (GD): the effect of screening time

	Time	
	Morning (0930–1200)	Afternoon (1205–1710)
Number screened	176	470
Age in years (mean ± SD)	31.2 ± 4.7	31.7 ± 5.0
Weight (mean ± SD)	59.4 kg ± 10.5 kg	60.8 kg ± 12.9 kg
Family history of diabetes	27	24
Past history of gestational diabetes	1	3
% White/Asian/Middle Eastern	62.6/28.0/9.0	67.5/25.9/5.8
Positive result, 50 g glucose challenge test	30 (17.0%)	146* (31.1%)
Abnormal result, 75 g glucose tolerance test	12 (6.8%)†	46‡ (9.8%)†

* $P < 0.001$, χ^2 . †% Of number screened. ‡ $P = 0.15$, χ^2 .

At Royal North Shore Hospital, screening for GD is performed at the 26–28-week visit by means of the 50 g GCT. In 2000, screening for GD was introduced into a morning midwives antenatal clinic, whereas previously it had only been performed in the afternoon. The population attending the clinic at the 26–28-week visit includes many women receiving shared care, and is regarded as being at low obstetric risk.

The Table shows the results of screening at the morning clinic compared with screening in the afternoon over the same time period. The two groups were identical in terms of age, weight, ethnicity, and family history of diabetes or past history of GD. The percentage of women with a positive screening test result during the morning clinic (17.0%) was significantly lower than that during the afternoon clinic (31.1%). Positive screening results were followed up with a diagnostic 75 g glucose tolerance test, and GD was diagnosed according to the Australian Diabetes in Pregnancy Society criteria.⁵ Women with a positive screening test result confirmed with a 75 g glucose tolerance test in the afternoon were less likely to have GD than those with a positive test in the morning (31.5% v 40.0%). Despite the fact that a smaller percentage of women who screened positive in the afternoon had GD, a greater percentage of the total number screened in the afternoon had GD than in the morning group. In this cohort, the difference (9.8% v 6.8%) was not significant (Table; $P = 0.15$).

These results are consistent with the hypothesis that a 50 g GCT test performed in the afternoon results in a greater number of positive results, a greater number of women undergoing diagnostic testing and a greater number of women identified with GD. The morning GCT appears to increase

specificity, with an associated decrease in sensitivity.

These results need to be taken into consideration when designing or implementing a screening program.

1. The Expert Committee on the Diagnosis and Classification of Diabetes Mellitus. Report of the Expert Committee on the Diagnosis and Classification of Diabetes Mellitus. *Diabetes Care* 1997; 20: 1183–1197.
2. American Diabetes Association. Gestational diabetes mellitus. *Diabetes Care* 2001; 24 Suppl 1: S77–S79.
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Changing demographics of cervical carcinoma

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TO THE EDITOR: We have recently noticed changes in the incidence of invasive cervical carcinoma in the Gippsland Health Region and would like to know whether other regions have noticed similar demographic changes.

During 24 months in 1999–2000, 19 women (median age, 59 years; range, 33–88 years) with squamous carcinoma were registered in our pathology practice. Based on information from the Victorian Cervical Cytology Register, almost half (10 women) had no previous cervical smear history whatsoever, while three had had smears, but at irregular intervals up to 14 years apart. The remaining six women had had regular Pap smears, with 1–3 negative smears preceding the diagnosis of cancer.

Sixteen of the women had consulted their general practitioner for some other ailment before the cervical cancer was discovered (median interval, 14 months), but no cervical smear had been obtained. Of particular interest is the fact that six of the 19 patients are in their seventh decade or older, with a median age of 80 years (range, 79–88 years).

The Victorian Department of Human Services reports that the cervical-smear participation rate for eligible women in the Gippsland region is 68%, a rate not much different from the other regions.¹ The two-yearly participation rate for the 60–69-years age group is 56%, and, although no official figure is available for women in their seventh or eighth decades, it is likely to be considerably lower. The Cancer Epidemiology Centre has recorded that, over a 16-year period, the incidence of cervical carcinoma in Victorian women aged over 70 years fell by 50%, and simultaneously there has been a shift in the peak incidence from the 70–74-years age group to one a decade older (Vicky Thursfield, Information Manager, personal communication).

Accordingly, we suspect that women over 70 years of age still have a significant incidence of invasive cervical carcinoma, but are not being offered cervical smears, even when the National Health and Medical Research Council guidelines indicate the necessity.

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Ethics and evidence-based medicine

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TO THE EDITOR: In response to Leeder and Rychetnik's article,¹ evidence-based medicine (EBM) also has significant potential to reduce the quality of patient care, with obvious ethical implications. I refer to two specific issues of concern.

The first relates to the increased expectation that clinicians, and especially trainees, not only understand the role of EBM in clinical practice, but actively contribute to its underlying database. Indeed, some of the professional colleges (eg, the Faculty of the Australian and New Zealand College of Anaesthetists) now include formal projects (which are often, but not necessarily, clinical trials) in their final assessment of trainees.² This is leading

to increasing numbers of poorly designed trials that are unlikely to make useful contributions to the clinical database. These commonly take two forms: studies which lack sufficient power to confirm the absence of a true difference between groups,^{3,4} or studies which use a placebo when effective therapeutic alternatives exist.⁵ Yet such studies are frequently published in reputable, peer-reviewed journals.⁶ Both of these types of studies are unethical, and both impact adversely on patient care.

Increasing the evidence base of clinical medicine is important, but our primary responsibility remains the maintenance of quality of care of all patients, especially those involved in clinical trials. Therefore, education of clinicians, and especially trainees, must emphasise the role and importance of statistics, epidemiology and study design in all areas of medicine to prevent unnecessary reductions in the quality of care of this subset of patients.

The second concern relates to the increase in "quality improvement" projects that are rarely submitted to ethics committees for approval. These activities also contribute to the evidence base, primarily at a local level, but patients are usually unaware that they are involved in these projects, and that these activities may have significant quality-of-care implications for them.

It is therefore important that internal hospital quality assurance activities undergo a similar level of scrutiny by ethics committees to that of clinical trials. Patients involved in any audit or project that has the potential to influence their care should be required to give informed consent. Only then can we reassure a patient that, while we are continually striving to improve the care we provide by developing the evidence base for clinical medicine, the care of each individual remains our primary concern.

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