1998, does not reflect recent advances with more modern chemotherapy drugs, although again their impact on survival is modest.

The article did not aim to address quality of life or other benefits from chemotherapy, or any parameters relating to palliation, which after all is the aim of the great majority of chemotherapy. It also does not discuss the curative benefit of other drugs in the medical oncology armamentarium, such as hormone therapy or 'targeted' drugs, such as bevacizumab or trastuzumab. One should not throw the baby out with the bath water, so to infer that medical oncology has no role in the management of cancer patients would be mischievous. Similarly, the article discusses issues to be considered in the formation of public policy, rather than making any statements on the management of individual patients.

Individual patients are concerned about their own chance of survival. Many patients will accept chemotherapy despite the small absolute benefit in survival.[3] A useful tool for adjuvant therapy for breast and bowel cancer, which uses a mathematical model for working out the benefit of chemotherapy, is Adjuvant! (www.AdjuvantOnline.com). Although such a model may show the small benefit, the patients and their families are often seeking a cure if at all possible. Their concerns are individual and immediate. They want to know the 'worth' of chemotherapy, but it is unlikely that the cost of the treatment is ever raised as a factor in an individual patient decision. Cost only becomes a significant issue if the treatment is not subsidised and the patient has to pay.

We are still left with the finding that the overall contribution of cytotoxic chemotherapy to survival in the 22 cancers reviewed in the study is less than 3%. Is this apparent heresy merely sour grapes from our radiation colleagues (who have previously shown a 16% survival benefit for radiation therapy[4]), or could it actually represent something close to the truth? At 2% or 6%, surely the message is the same. Modern Western society, with its obsession with cure at all costs and the focus on the outcome for an individual, has a track record of subverting community welfare on issues relating to 'big picture' sustainability.

Failure to come to terms with rationalisation of high cost medicine and the inability to convince multinational pharmaceutical corporations to provide drugs at a sustainable price will mean that our treatments are likely to have less, not more impact in the future, as only a portion of society will be able to afford them. Let us rise to the challenge rather than shrink from the spotlight. We have to hope that in the decades to come the contribution of chemotherapy to survival and well-being is significantly increased. However, we must realise that until we as prescribers, and the community as consumers, recognise our limitations and rationalise our resource utilisation, we may never achieve this goal.

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Conflict of interest: none declared

Letters

Letters, which may not necessarily be published in full, should be restricted to not more than 250 words. When relevant, comment on the letter is sought from the author. Due to production schedules, it is normally not possible to publish letters received in response to material appearing in a particular issue earlier than the second or third subsequent issue.

Assessment of thyroid function in pregnancy

Editor, – Some further points on testing thyroid function need to be added to the useful information in Associate Professor Tran's review, 'Biochemical tests in pregnancy' (Aust Prescr 2005;28:98–101). First, a small but significant decrease in the concentration of serum free T4, most marked in the third trimester, has been clearly documented.[1,2] In addition, albumin-dependent methods of free T4 estimation show marked negative bias, relative to the non-pregnant reference interval; in the late third trimester, such methods may give subnormal free T4 estimates in up to 50% of samples.[3] These methods are unsuitable for assessing thyroid status during pregnancy[4], unless results are evaluated in relation to reference intervals that reflect method-specific bias at various stages of pregnancy. Clinical chemists need to be aware of this issue when choosing an appropriate free T4 method for obstetric practice and by indicating appropriate reference intervals.

Professor Tran's counsel that 'Graves' disease needs to be rigorously controlled' in pregnancy goes beyond interpretation of test results. This advice must be tempered by the fact that any degree of maternal hypothyroidism in

the first trimester can have an adverse effect on fetal brain development[5,6], and that overtreatment in the third trimester can be associated with fetal goitre.[6] As thyrotoxicosis of immune origin often becomes less severe during pregnancy, it is often advisable to decrease the dose of antithyroid drug to minimise the chance of these adverse effects.[6] As pointed out by Professor Tran, the exact cause of newly-diagnosed thyrotoxicosis can be difficult to establish in early pregnancy. When the disorder is mild, as judged by clinical rather than laboratory criteria, it may be best followed without treatment for several months until there is a clear indication for active treatment.[6]

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Associate Professor H.A. Tran, author of the article, comments:

Professor Stockigt's comments are appreciated. As usual, they are incisive and informative. The small but significant decrease in serum free tetra-iodothyronine (fT4) can, in part, be explained by the peak of thyroid binding globulin concentrations in the third trimester, although these remain within the reference range in most cases.[1]

Selecting a special method for the obstetric population serviced by the relevant laboratory would always be a challenging task given the large scope of services imposed upon large laboratories by the current practice of pathology. The nuances of such a task are probably best reserved within the realm of clinical biochemists' practice.

As emphasised, the management of thyrotoxicosis in pregnancy is not a simple task. It should not be simply a matter of medication adjustment according to biochemical results, which are never error proof. The literature is littered with, sometimes fatal, adverse reactions[2] where laboratory results as given, are acted upon, when instead a considered and competent clinical assessment is warranted. As inferred by Professor Stockigt, it is best to first do no harm; a caveat that is not applicable to pregnancy alone.

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Antibiotics for unapproved indications

Editor, – I would like to revisit the use of various antibiotics for 'orphan' indications. One example is rifampicin for deep infections due to methicillin-resistant *Staphylococcus aureus* (MRSA). There are few oral antibiotics available for the treatment of MRSA infections, but the combination of rifampicin and fusidic acid is commonly used and is recommended in Therapeutic Guidelines: Antibiotics.

In 1994, *Australian Prescriber* published a response to a query (Aust Prescr 1994;17:95) asking why rifampicin was not subsidised for osteomyelitis. The response said that no application had been submitted for the use of rifampicin for this indication.

Would it be possible for the Therapeutic Goods Administration to approve an 'orphan' indication for well-known drugs where they are recommended by recognised guidelines? Perhaps for such indications, a simplified application to the Australian Drug Evaluation Committee could be made by clinicians or their representative bodies.

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Dr Leonie Hunt, Director, Drug Safety & Evaluation Branch, Therapeutic Goods Administration, comments:

The Therapeutic Goods Administration (TGA) is able to approve indications for extensions of use of medicines, including antibiotics, after it has received an application from a sponsoring company, supported by data to establish quality, safety and efficacy for the intended use.

For an extension of indication, quality will usually have been established and the focus is on safety and efficacy. In order to

facilitate the lodgement of applications for the treatment of rare conditions, which may otherwise not be cost-effective, the TGA has introduced an Orphan Drug Scheme, whereby all evaluation fees are waived provided the sponsor obtains designation for the product for the indication. The usual criteria for determining a disease is rare are the orphan criteria that it is not likely to affect more than 2000 people.

The TGA has also adopted a number of modifications to data packages to facilitate applications for older, off-patent or orphan products. These include literature based submissions, whereby companies can submit published papers as the basis for an approval of a product or an extension of use of a product. Unfortunately, the TGA has no power to approve products for new indications in the absence of an application, but it is always happy to discuss with sponsors the modified data requirements for products where there is a demonstrated clinical need.

Top 10 drugs

These tables show the top 10 subsidised drugs in 2004–05. The tables do not include private prescriptions.

Table 1

Top 10 drugs supplied by DDD/1000 pop/day *

Drug	PBS/RPBS †
1. atorvastatin	98.173
2. simvastatin	55.967
3. ramipril	33.741
4. diltiazem hydrochloride	30.097
5. omeprazole	20.628
6. irbesartan	20.169
7. salbutamol	18.844
8. frusemide	18.775
9. aspirin	18.162
10. sertraline	17.604

Table 2

Top 10 drugs by prescription counts

Drug	PBS/RPBS †
1. atorvastatin	8,074,202
2. simvastatin	6,275,577
3. paracetamol	4,772,865
4. omeprazole	4,411,857
5. irbesartan	3,370,315
6. atenolol	3,247,475
7. salbutamol	3,062,355
8. esomeprazole	2,983,645
9. irbesartan with hydrochlorothiazide	2,938,448
10. ramipril	2,903,048

Table 3

Top 10 drugs by cost to Government

Drug	Cost to Government ($A)	DDD/1000/day PBS/RPBS †	Prescriptions PBS/RPBS †
1. atorvastatin	460,930,251	98.173	8,074,202
2. simvastatin	369,659,052	55.967	6,275,577
3. omeprazole	177,075,832	20.628	4,411,857
4. fluticasone with salmeterol	165,690,424	– ‡	2,764,969
5. clopidogrel	151,235,466	7.551	1,925,546
6. olanzapine	149,497,256	2.892	710,453
7. esomeprazole	143,233,727	11.465	2,983,645
8. pravastatin	119,587,717	13.983	2,102,171
9. alendronic acid	108,587,183	8.543	2,115,898
10. pantoprazole	104,291,272	10.971	2,586,383

* The defined daily dose (DDD)/thousand population/day is a more useful measure of drug utilisation than prescription counts. It shows how many people, in every thousand Australians, are taking the standard dose of a drug every day.

† PBS Pharmaceutical Benefits Scheme, RPBS Repatriation Pharmaceutical Benefits Scheme

‡ Combination drugs do not have a DDD allocated

Source: Drug Utilisation Sub-Committee (DUSC) Drug Utilisation Database, as at 10 Oct 2005.