

information on these groups would be valuable.

The second question relates to comparative embryo survival rates. Jansen gives the number of live births per egg retrieval procedure, and fresh and frozen embryo transfer is combined in the live-birth result. Separating live embryo transfer from frozen embryo transfer, which is done in the Victorian *Infertility Treatment Authority annual reports 1998–2001*, would indicate that the transfer of a fresh embryo has about a 9.5% chance of resulting in a live birth, and the transfer of a frozen embryo has about a 3.1% chance of resulting in a live birth. In the current discussion of embryos being available for research, this information about embryo survival rates would be informative.

Competing interests: I am a member of the Ethics Panel of the Victorian Infertility Treatment Authority.

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IN REPLY: The pregnancies and live births I reported are all attributable to IVF intervention. The physiological and pharmacological reasons for this certainty follow.

Firstly, neither an egg-retrieval treatment nor an embryo-transfer treatment (both of which require hormone administration from the start of menstruation) can be embarked on if a woman is pregnant. This is established not just by the fact of menstrual bleeding, but by showing low levels of oestradiol and progesterone. Thus, no treatment cancellations or retrieval failures were for reasons of pregnancy.

In an egg-retrieval treatment cycle, preovulatory eggs are removed from

mature follicles with high efficiency, and so are not available to be ovulated, which virtually precludes natural conception in the retrieval cycle.

As described in my article, transfer of cryostored embryos occurs during a month in which the ovaries are suppressed by the cyclical regimen of ethinyl oestradiol and a progestin (used to develop the endometrium predictably). The effect is that of the sequential oral contraceptive regimens of the 1960s,¹ and ovulation is reliably inhibited.

Tonti-Filippini's estimate of a 25%–30% annual natural pregnancy likelihood with just 12 months' infertility would be more or less correct for couples in their 20s, but does not pertain to our population (median age, 36 years; median duration of infertility, 3.5 years). The arithmetic that predicts an expected, approximately 5% annual natural conception for such a population is given in Jansen.²

The time during which natural pregnancy could have occurred began with the month after the egg-retrieval cycle and ended, as reported, with the month before either (a) an embryo transfer resulted in a live birth, or (b) the last stored embryo from that retrieval was transferred. There were no natural conceptions that we know of, but, even if there were, such pregnancies would not and could not have been attributed to IVF treatment. Thus, the published figures are reliable.

I reported the implantation rate per embryo for women under the age of 35 as 24.7%. Subtracting the reported 10.5% miscarriage risk yields a live-birth rate of 24.7% minus (24.7% × 0.105), or about 22% per embryo transferred, which is indistinguishable from the expected 20% natural monthly fertility rates among normal couples of this age group.³ Similar calculations yield 11%

live births per embryo for those 35–39 years, and 4% live births for those over 40 years. With present practices at Sydney IVF (Day 5 blastocyst transfers, generally single embryos), the chance of a baby per embryo transferred is 41% (<35 years), 24% (35–39 years) and 12% (>40 years).

The embryo implantation and live birth data Tonti-Filippini reveals for live births per embryo in Victoria are therefore very low compared with the IVF results I report.

Competing interests: As stated with my article, I am a Director of Sydney IVF Limited and own shares in the company.

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The effect of recalling paracetamol on hospital admissions for poisoning

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TO THE EDITOR: Paracetamol availability is an important public health issue. Kisely et al have further investigated the impact of two paracetamol recall periods on analgesic poisoning using a dataset derived from hospital admissions.¹ We are concerned about the robustness of data that uses ICD codes, because of significant coding problems that occur with poisoning admissions.

Correspondents

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There should be no more than 5 references. The reference list should not include anything that has not been published or accepted for publication. Reference details must be complete, including: names and initials for up to 4 authors, or 3 authors et al if there are more than 4 (see mja.com.au/public/information/uniform.html#refs for how to cite references other than journal articles).

The aim of their study was as a follow-up to our own,² to look at the impact of removing paracetamol tablets from the shelf during a recall period. Availability is reported to be the most common reason for patients choosing to take paracetamol in overdose³ and, as such, has the potential to affect acute deliberate self-poisoning. However, Kisely et al recognised that it was difficult for them to distinguish between intentional and unintentional ingestions because of the limitations of their dataset¹ and hence they considered both of these together. This is inappropriate if the aim is to assess the effect of availability on paracetamol deliberate self-poisoning. For example, there is no evidence that presentations with therapeutic errors in dosing are related to availability and these should be excluded. This is not possible by using ICD codes and was therefore not done by Kisely et al.¹

In addition, it is only relevant to include accidental ingestions of tablet formulations of paracetamol, because only these were affected by the recall. There are significant numbers of presentations of children, who accidentally ingest liquid formulations of paracetamol (hence not related to the recall period), that are coded as paracetamol admissions. This introduces a further significant potential bias in the Kisely study.

A more concerning problem is the reliability of ICD coding in separating out different analgesics. Poisoning with prescription products such as paracetamol-codeine combination analgesics, which were not affected by the recall period, are also likely to be included in the study being coded as T39.1 (paracetamol overdoses).¹

There are significant limitations in using ICD codes, resulting in the dataset analysed not being a true reflection of the impact of the recall of paracetamol tablets. Our study took into account only tablet formulations of the paracetamol alone compounds.² Paracetamol ingestions following therapeutic error were excluded and accidental ingestions of only tablet formulations were included. While the numbers in the study were small for the hospital presentations, the data set for the NSW Poisons Information Centre was much larger and showed

significant increases in intentional and accidental ingestions of ibuprofen, the next most available analgesic.²

In an environment where paracetamol restriction is a hotly debated topic, particularly in light of recent coroners' cases, it is vital to consider the impact of paracetamol restriction on all types of deliberate self-poisoning by using an appropriate dataset that reflects the measures taken to reduce availability. The challenge for state and federal health departments is to fund appropriate postmarketing toxicovigilance for accidental and intentional self-poisoning in order to clarify these important public health issues.

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TO THE EDITOR: We read with interest the study of Kisely et al,¹ which showed a decrease in admissions for poisoning with paracetamol, but no coincident increase in use of other agents, as a result of the paracetamol recalls. We had noticed there was an unusually high number of presentations (18) to the Paediatric Emergency Department at the Women's and Children's Hospital, Adelaide (WCH), for poisoning with aspirin in 2000, compared with one presentation in 2001 and one in 2002. We wondered if the presentations in 2000 were temporally associated with the paracetamol recalls.

We extracted all WCH presentations with a primary diagnosis of paracetamol poisoning (ICD-9 code 965.4), aspirin poisoning (965.1), nonsteroidal anti-inflammatory drugs (965.6) and poisoning with all other drugs (960-979.9) for the two recall periods (16 March 2000 to 21 May 2000; 6 June 2000 to 23 August 2000)² and the same periods in 2001 and 2002. It could not be determined whether an over-the-coun-

Presentations (P) and admissions (A) for poisoning with paracetamol, aspirin, NSAIDs and other drugs at the Women's and Children's Hospital, Adelaide

	2000 restricted available		2001 available		2002 available	
	P	A	P	A	P	A
Aspirin	15	13	1	0	0	0
Paracetamol	23	6	34	13	34	14
NSAID	3	1	0	0	1	0
Other drugs	86	43	89	35	60	23

NSAID = non-steroidal anti-inflammatory drug.

ter preparation of a nonsteroidal anti-inflammatory drug had been taken. The results are shown in the Box.

These data show that the number of paracetamol poisoning presentations and admissions was lower during the recalls than in the same period in subsequent years, but there was a higher number of presentations and admissions for poisoning with aspirin.

All the aspirin poisoning presentations and admissions during the period when paracetamol was recalled were during the second recall (affecting SmithKline Beecham products). The other three aspirin poisoning presentations in 2000 occurred within 10 days of the end of the second recall. All but one of the 18 patients with aspirin poisoning who presented during 2000 were adolescents (17 females). Most of these exposures were likely to be due to intentional self-poisoning.

Although it is not possible to reach any definite conclusion from these observations, we share the concerns of Balit et al² that limiting the availability of paracetamol could result in an increase in poisonings with potentially more acutely dangerous agents such as aspirin, particularly for adolescents. There needs to be further consideration of the motivation of patients in choosing paracetamol and the source of the drug when taken for intentional self-poisoning before measures are taken to restrict access to paracetamol.

1. Kisely SR, Lawrence D, Preston NJ. The effect of recalling paracetamol on hospital admissions for poisoning in Western Australia. *Med J Aust* 2003; 178: 72-74.
2. Balit CR, Isbister GK, Peat J, et al. Paracetamol recall: a natural experiment influencing analgesic poisoning. *Med J Aust* 2002; 176: 163-166. □

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IN REPLY: Balit et al raise the problem of distinguishing between intentional and unintentional ingestions. As stated in our article, we did look at deliberate and accidental poisonings separately, but space restrictions, not limitations of our dataset, prevented us from presenting the results.¹ Of 2266 paracetamol poisonings, 1731 (76%) were coded as deliberate, 433 (19%) were accidental and in 103 (4.5%) the intention could not be determined. Restricting the analysis to the deliberate cases yields almost identical results.

Our dataset may have contained poisonings with liquid or combination formulations of paracetamol that were not recalled. This factor would have operated before, during and after the recall and would only serve to reduce the magnitude of any effect, rather than accentuating it.

We considered 2663 admissions for over-the-counter analgesic poisoning,¹ as opposed to 143 in the NSW study.² We did not look at telephone calls, as reliance on data from calls to a poisons information centre raises far more concerns about data quality than hospital statistics do. How reliable was the informant? How serious was the poisoning? Do telephone data contain less serious cases that do not require admission?

Hender et al report the findings of an observational study restricted to a single paediatric emergency department attached to the Women's and Children's Hospital, Adelaide. Unfortunately, data for only three years are presented, with no information for the years before the recall. Neither do we know how many were intentional or unintentional. By definition, their data exclude adults. As they state themselves, it is not possible to reach any definite conclusions from their observations. We should not prematurely dismiss the possible benefits of restrictions on the availability of paracetamol. If there are concerns that restricting the availability of paracetamol might increase the use of other

over-the-counter analgesics in poisonings, we should be investigating the effectiveness of restrictions on the availability of these as well.

Who precisely benefits from continued sales of over-the-counter analgesics in catering pack sizes?

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2. Balit CR, Isbister GK, Peat J, et al. Paracetamol recall: a natural experiment influencing analgesic poisoning. *Med J Aust* 2002; 176: 162-165. □

Whither pathology in medical education?

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TO THE EDITOR: All established disciplines that have contributed to medical curricula in the past should play, as Weedon¹ argued recently for pathology, a pivotal role in contemporary medical curricula. Indeed, students should be able to acquire better knowledge of a discipline through a problem-based learning (PBL) approach than through traditional teaching methods.

The crux of the PBL approach is that knowledge, skills and the other professional attributes are learnt in a way that puts them into context and thus makes them meaningful and better remem-

bered by medical students. The trouble is, as Weedon pointed out, the number of academics in the discipline of pathology is dwindling. The scarcity of academic pathologists, combined with the increased workloads of private pathologists, means that their input into designing and developing curricula and into pathology teaching may be increasingly inadequate.

Pathology is not the only discipline to be underserved in today's medical schools. In response to concerns about the medical curriculum, the Royal College of Pathologists of Australasia and other Colleges and interest groups have developed core syllabuses for use in medical programs. These developments are most welcome in view of the diminishing resources available for teaching in universities. In a PBL-oriented curriculum, teaching staff work in a multidisciplinary team in which the aspirations and limitations of each group are acknowledged, respected and acted upon in the context of realistic expectations of what is possible and what is necessary for medical graduates in the 21st century.

Currently, in Queensland, a series of pathology modules for students to use during their clinical rotations would be well received. The use and interpretation of pathology tests are already built into PBL case studies, and could be extended into a module set as prerequisite learning for an attachment to a public or private pathology laboratory.

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