Background
In 2003, in the largest randomised trial of its kind, this team found that haloperidol + promethazine IM was safe and effective for rapid tranquilisation of aggressive people with psychosis (n=301, 99% follow up).1

In 2004, our second team showed haloperidol + promethazine IM to be considerably more effective and safe than lorazepam for a similar population (n=200, 99% follow up).2

In 2005 these two trials were described as follows:

In 2005, the Brazil-UK team wished to compare the haloperidol + promethazine mix, now the most evaluated approach for rapid tranquillisation, with another APA and NICE recommendation for acutely disturbed people thought to have psychosis – the use of haloperidol alone.

TREC-Rio*
*Tranquilização Rápida-Ensaio Clínico
[Translation: Rapid Tranquillisation-Clinical Trial]

Design
- Pragmatic, randomised
- Real-world participants
- Regularly used, available interventions
- Routinely recorded outcomes
- Designed with the help of staff of the Psychiatric Emergency Rooms of Rio, carers and advocate groups in Rio, trialists with experience in the area of emergency medicine

Protocol
Eligible if the person needs acute intramuscular sedation because of disturbed and dangerous behaviour and clinician is uncertain about the benefits and risks of haloperidol plus promethazine versus haloperidol alone.

Exclude if clinician believes that one treatment represents an additional risk for the patient.

Trial entry treatment allocated by taking consecutive TREC boxes stored in the emergency drug cupboard. The box has two questions on the outside.

- Either haloperidol (2 X 5mg ampules) + promethazine (2 X 50mg ampules) OR haloperidol (2 X 5mg ampule). All doses are at the discretion of the doctor.
- One syringe, one needle, two swabs, one plaster.
- TREC form to be filled out by the attending doctor/nurse.
- TREC stickers for the patient's notes.

Outcomes
Primary outcome is tranquil or sedated at 20 minutes. Data for up to two weeks were extracted from the notes on clinical state, hospital status, sedation, use of additional medications and adverse reactions.

Results
The Data Monitoring Committee (DMC) recommended that the Steering Committee halt the trial early.
- 316 randomised
- 99% follow up

IM haloperidol + promethazine is again shown to be rapid and safe.

The high incidence of adverse effects for the haloperidol alone group is not related to use of higher doses of the drug.

Because of the clear findings the Brazilian DMC felt it unethical to continue using the APA-NICE recommended intervention.

Conclusions
More acutely aggressive psychotic people have been randomised to IM haloperidol/promethazine than any other approach to rapid tranquillisation.

The trials are recognised to be of the highest quality.

Although haloperidol may often be given with other drugs, the use of haloperidol alone is one of the recommendations of the APA and NICE.

In the light of these new data these recommendations should be amended.

References
2. BJPsych 2004; 185: 63-9