Off 34 tranexamic acid errors (from 13 countries), 7 occurred in India. 8 European union countries reported 15 (out of 28) potassium chloride errors. Neuromuscular blocking drugs related events were widespread (21 errors from 13 countries). Cardiovascular drug incidents were increased at the expense of an increased profile of side-effects. However, a dose of 100µg represents a ceiling dose for analgesia and a threshold dose for increased rate of PONV.

### Background and Aims
Widespread adoption of intrathecal morphine into clinical practice is hampered by concerns of its potential side-effects. We undertook a systematic review, meta-analysis and trial sequential analysis with the primary objective of determining the efficacy and safety of intrathecal morphine. Our secondary objective was to determine the dose associated with greatest efficacy and safety.

### Methods
We systematically searched the literature for any trials comparing intrathecal morphine with a control group in patients undergoing hip, knee arthroplasty under spinal anaesthesia. Our primary efficacy outcome was rest pain score at 8–12h; our primary safety outcome was the rate of PONV within 24h.

### Results
Twenty-nine trials including 1814 patients were identified. Rest pain score at 8–12h was significantly reduced in the intrathecal morphine group with a mean difference (95%CI) of -1.7(-2.0,-1.3), I²=71%, p<0.0001, without subgroup difference between doses (p=0.35). Intrathecal morphine increased postoperative nausea and vomiting with a risk ratio (95%CI) of 1.4(1.2,1.6), I²=4%, p<0.0001. However, a subgroup analysis according to doses revealed that rates of PONV within 24h was similar between groups with doses of 100µg, while the risk significantly increased with doses above (p value for subgroup difference=0.03). The quality of evidence for our two primary outcomes was high and moderate-to-high for the secondary outcomes.

### Conclusions
There is high level evidence that intrathecal morphine provides effective analgesia after lower limb arthroplasty but at the expense of an increased profile of side-effects. However, a dose of 100µg represents a ceiling dose for analgesia and a threshold dose for increased rate of PONV.