# THE EFFECTS OF FLUOXETINE ON FRACTURE RISK AFTER STROKE

## FURTHER ANALYSES FROM THE FOCUS TRIAL

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The FOCUS trial showed that 20mg of fluoxetine daily, for six months, started 2-15 days post stroke had no effect on the modified Rankin scale (mRS), reduced the risk of new depression (Risk diff 3.8%) but increased the risk of bone fractures (Risk diff 1.4%). Further analyses aimed to explore the factors associated with bone fractures.

Sixty five of the 3127 (2.1%) patients enrolled had a fracture within six months of randomisation. Of these 59 (90.8%) resulted from a fall and 26 (40%) affected the neck of femur.
Cox proportional hazards modelling of the risk of fracture showed that only age >70yr (Hazard Ratio (HR)=1.97(95% CI 1.13 to 3.45;p=0.017), female sex (HR =2.13 (1.29-3.51; p=0.003) and fluoxetine treatment (HR =2.00 (1.20-3.34; p=0.008) were independent predictors.

Stroke pathology, severity, type of deficit, prior fractures, other medication affecting blood pressure, bone density and balance had no significant effect.

Furthermore, removing patients with a fracture from the primary analysis did not significantly alter the effect on mRS (Common odds ratio 0.951 with fractures, 0.961 without),

| | Fracture by 6 months | | | | |
|---|---|---|---|---|---|
| | No | | Yes | | |
| | N | % | N | % | Log –rank statistic |
| **Total randomised** | 3062 | 100.0 | 65 | 100.0 | |
| Fluoxetine | 1521 | 49.7 | 43 | 66.2 | 0.0084 |
| Placebo | 1541 | 50.3 | 22 | 33.9 | |
| **Sex** | | | | | |
| Female | 1167 | 38.1 | 38 | 58.5 | 0.0005 |
| Male | 1895 | 61.9 | 27 | 41.5 | |
| **Age group** | | | | | |
| ≤70 years old | 1313 | 42.9 | 17 | 26.2 | 0.0043 |
| >70 years old | 1749 | 57.1 | 48 | 73.9 | |

Only increasing age, female sex and fluoxetine were independent predictors of fracture risk. Most fractures resulted from falls. Although many of the fractures were serious, and are likely to have impaired patients' function, the increased fracture risk did not explain the lack of observed effect of fluoxetine on mRS.

A future individual patient data meta-analysis including the patients from the ongoing AFFINITY and EFFECTS trials may clarify the mechanism of fractures due to fluoxetine.

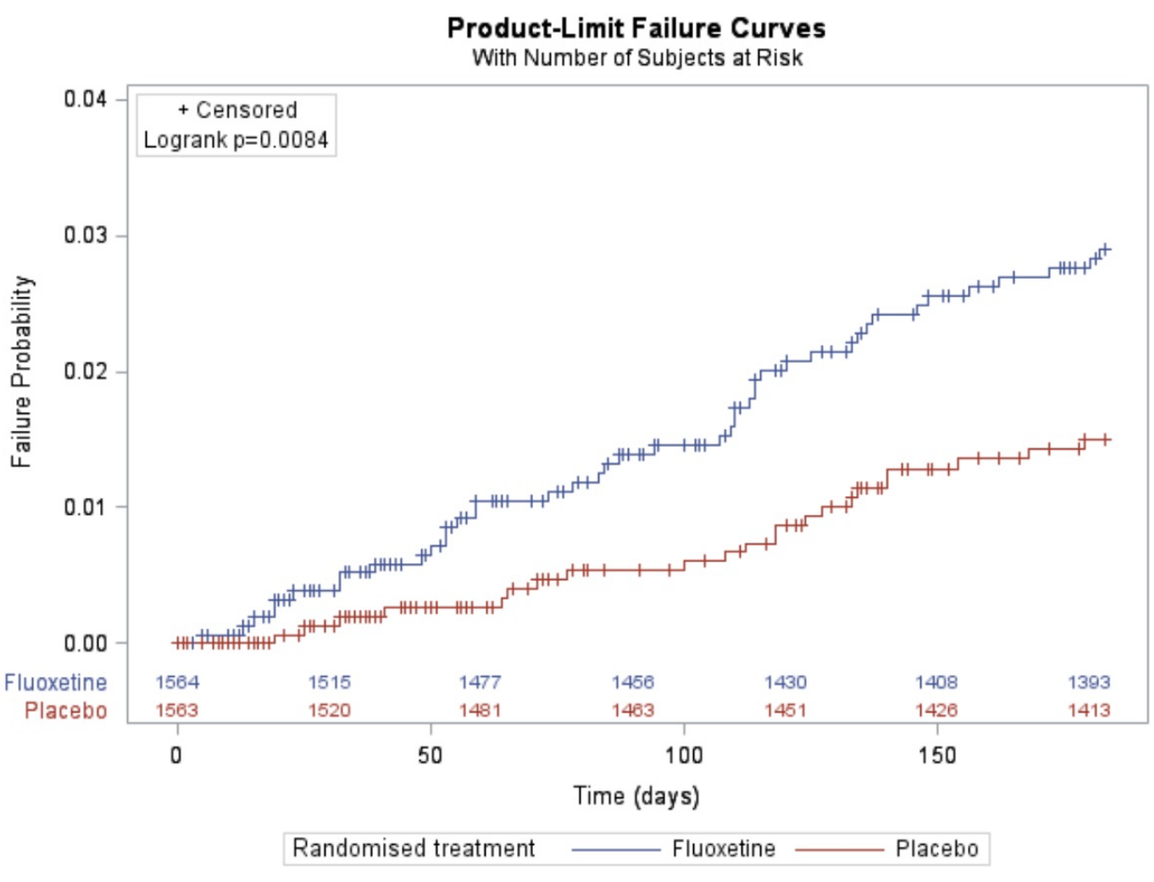


Figure 1. Kaplan Meier curves to six months comparing the risk of fracture in those allocated fluoxetine and placebo.

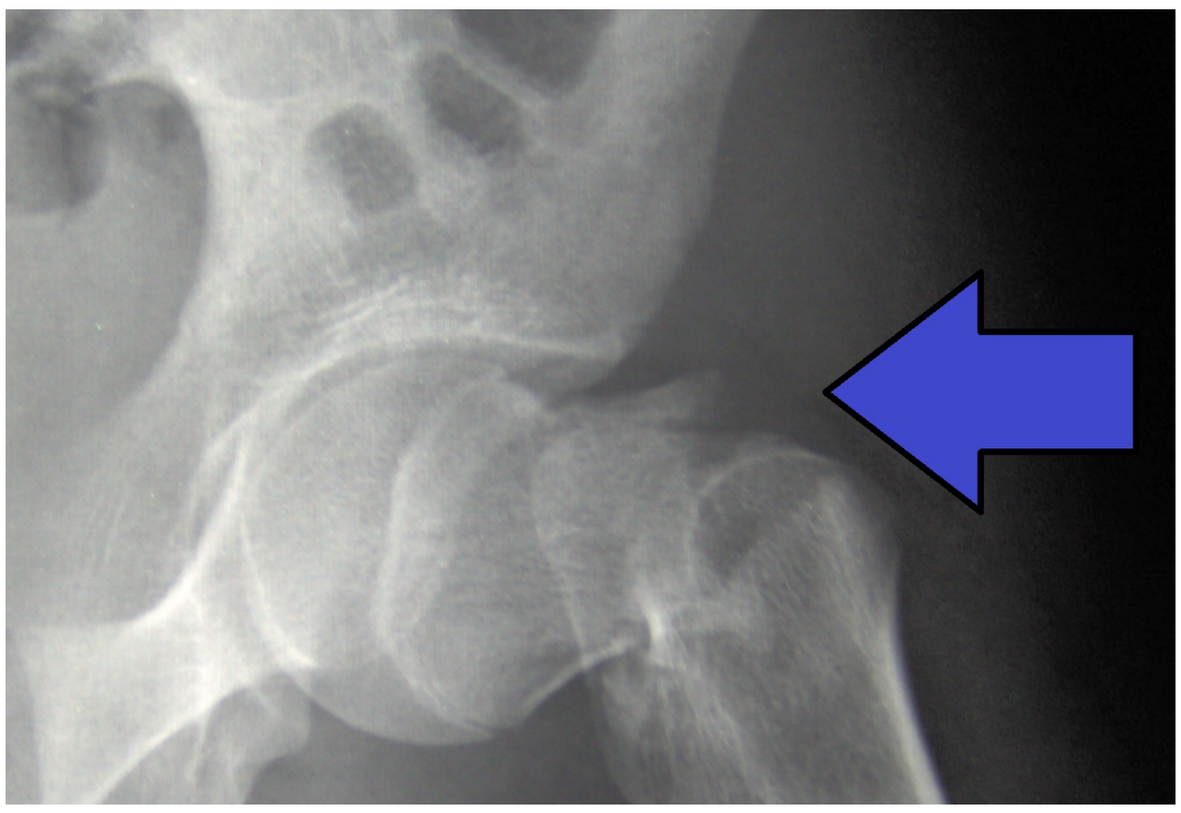

Figure 2. Femur neck fracture. From Wikipedia