

## Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

Supplement to: Thwaites GE, Bang ND, Dung NH, et al. Dexamethasone for the treatment of tuberculous meningitis in adolescents and adults. *N Engl J Med* 2004;351:1741-51.

Table 1. Baseline Characteristics of Study Population.*				
Variable	Allocated Dexamethasone (N=274)		Allocated Placebo (N=271)	
	N or Median	Percent or Range	N or Median	Percent or Range
Recruited in HTD	48	17.5%	45	16.6%
Recruited in PNT hospital for tuberculosis	226	82.5%	226	83.4%
Age distribution (yr)				
15 to 17	12	4.4%	11	4.1%
18 to 30	93	33.9%	96	35.4%
31 to 50	94	34.3%	96	35.4%
51 to 65	40	14.6%	34	12.5%
>65	35	12.8%	34	12.5%
Definite diagnosis†	98	35.8%	89	32.8%
Smear positive, culture negative	16	5.8%	5	1.8%
Smear positive, culture positive	22	8.0%	22	8.1%
Smear negative, culture positive	60	22.0%	62	22.9%
Previous tuberculosis treatment	22	8.5%	25	9.9%
Temperature (°C)	38.0	37.0–40.6	38.0	36.8–41.0
Extrapulmonary/neural tuberculosis	58	21.2%	56	20.7%
Chest radiography				
Active nonmiliary tuberculosis	110	40.1%	104	38.4%
Miliary tuberculosis	75	27.4%	80	29.5%
Investigations				
Hematocrit (%)	36.1	17.6–53.6	36.7	9.0–66.4
Blood leucocyte count (×10 <sup>6</sup> /ml)	10100	2490–26300	10200	1050–39200
Plasma sodium (mmol/l)	131	102–152	130	107–155
Hepatitis B surface antigenaemia	30	11.8%	30	12.3%
Aspartate aminotransaminase (U/ml)	32	10–191	30	3–1145
Alanine aminotransferase (U/ml)	35	10–763	30	28–1001
Cerebrospinal fluid				
Opening pressure (cm H <sub>2</sub> O)	23	4–41	21	2–41
Leucocyte count (×10 <sup>3</sup> /ml)	117	1–1880	111	1–3990
Percentage neutrophils	10	0–96	10	0–96
Percentage lymphocytes	90	4–100	90	4–100
Protein (mg/dl)	156	10–3000	133	12–4700
Cerebrospinal fluid:plasma glucose	0.29	0.04–0.78	0.29	0.02–0.96
Lactate (mmol/l)	5.7	1.5–12.1	5.1	1.9–9.4
Treatment				
Mannitol given	100	36.5%	99	36.8%
Initial antituberculosis regimen				
Rifampicin, isoniazid, pyrazinamide, streptomycin	203	74.1%	196	72.9%
Rifampicin, isoniazid, pyrazinamide, ethambutol	46	16.8%	52	19.3%
Rifampicin, isoniazid, pyrazinamide, ethambutol, streptomycin	23	8.4%	20	7.4%
Isoniazid, pyrazinamide, ethambutol	1	0.4%	1	0.4%
Streptomycin, ethambutol	1	0.4%	0	
Initial doses of regimen (mg/kg)				
Rifampicin	9.4	6.0–13.3	9.4	3.6–15.0
Isoniazid	6.0	4.0–8.1	6.0	2.4–10.0
Pyrazinamide	26.3	12.5–26.3	26.6	3.6–45.5
Streptomycin	16.7	7.5–26.3	16.7	6.7–33.3
Ethambutol	18.6	10.0–25.8	20.0	13.8–40.0

\* Missing observations change the denominator in each treatment group (dexamethasone, placebo) for the following variables: hematocrit (261,264), blood leucocyte count (263,266), plasma sodium (234,239), aspartate aminotransaminase (222,217), alanine aminotransferase (222,217), cerebrospinal fluid opening pressure (104,121), cerebrospinal fluid leucocyte count (273,269), cerebrospinal fluid percentage neutrophils (272,268), cerebrospinal fluid percentage lymphocytes (272,268), cerebrospinal fluid protein (273,268), cerebrospinal fluid:plasma glucose (273,264), cerebrospinal fluid lactate (43,41), rifampicin dose (272,268), isoniazid dose (273,269), pyrazinamide dose (273,269), streptomycin dose (227,216), ethambutol dose (71,73).

† Smear positive=acid-fast bacilli seen by Ziehl–Neelsen stain of the cerebrospinal fluid; culture positive=*Mycobacterium tuberculosis* cultured from the cerebrospinal fluid.

**Table 2. Baseline Variables Independently Associated with Death, by Logistic Regression.\***

Variable	Hazard Ratio	95% CI	P Value
Admission Glasgow coma score $\leq 10$	3.33	2.27–5.00	<0.001
HIV infection	2.33	1.56–3.19	<0.001
Hemiplegia on entry to the study	1.66	1.11–2.49	0.014
Previous tuberculosis treatment	2.15	1.39–3.34	0.001
Extraneural/pulmonary tuberculosis	1.56	1.10–2.22	0.01
Total CSF white cell count ( $\times 10^6/\text{ml}$ )	0.99	0.998–0.999	0.02
Cerebrospinal fluid:blood glucose ratio	5.27	1.63–16.98	0.005
Hematocrit (%)	0.96	0.94–0.99	0.002
Adverse event requiring alteration in anti-tuberculosis drug dose or regimen	2.44	1.56–3.81	<0.001
Treatment with placebo	1.67	1.22–2.30	0.001

\* Variables were selected to the final model by a forward stepwise variable selection procedure with an entry significance level of 0.05. Five possible interactions within the model were examined and none were significant: treatment allocation and an adverse event ( $P=0.92$ ), HIV infection and an adverse event ( $P=0.44$ ), cerebrospinal fluid leucocyte count and cerebrospinal fluid:plasma glucose ( $P=0.81$ ), adverse event and hematocrit ( $P=0.25$ ), and previous tuberculosis treatment and HIV infection ( $P=0.48$ ).