

## **Appendix 1 (as supplied by the authors): Definitions of potency and sensitivity analyses**

### **Definitions of potency**

#### Group I: weak

Hydrocortisone

#### Group II: moderately potent

Triamcinolone, clobetasone, hydrocortisone butyrate, fluprednidene, alclometasone, hydrocortisone butyrate, flumetasone

#### Group III: potent

Budesonide, betamethasone, fluocortolone, desoximetasone, fluocinolone acetone, diflucortolone, fluocinonide, diflorasone, mometasone furoate, fluticasone

#### Group IV: very potent

Clobetasol, halcinolide

### **Sensitivity analyses**

We evaluated the effect of corticosteroid use before pregnancy start and late in pregnancy. Mothers using corticosteroids in the 4 weeks until pregnancy start were not significantly more likely to bear children with cleft lip ± palate (odds ratio, 1.21 (95% confidence interval, 0.77–1.99) or cleft palate alone (odds ratio, 1.07, (95% confidence interval, 0.51–2.26). When looking specifically at dermatologicals, results were similar to those associated with use in the 1st trimester – cleft lip ± palate odds ratio, 1.50 (95% confidence interval, 0.90–2.51) and cleft palate alone odds ratio,

1.46 (95% confidence interval, 0.65–3.26), but failed to reach statistical significance. Mothers using corticosteroids in the 2nd and 3rd trimester were not significantly more likely to bear children with cleft lip  $\pm$  palate (odds ratio, 1.03 (95% confidence interval, 0.84–1.27)) or cleft palate alone (odds ratio, 0.93, (95% confidence interval, 0.66–1.30)). For dermatological use late in pregnancy no increased risks were observed for neither cleft lip  $\pm$  palate (odds ratio, 1.07 (95% confidence interval, 0.80–1.45) or cleft palate alone (odds ratio, 1.08, (95% confidence interval, 0.68–1.72)). We further evaluated the robustness of the dermatological effect by comparing women using only dermatological corticosteroids in the 1st trimester to women using no corticosteroids in the period 4 weeks before pregnancy start and until birth. Results were similar to the main analysis, cleft lip  $\pm$  palate (odds ratio, 1.53 (95% confidence interval, 0.99–2.37)) and cleft palate alone (odds ratio, 1.79 (95% confidence interval, 0.95–3.37)), but failed to reach statistical significance. Using the 2nd and 3rd month of pregnancy (the primary critical period of cleft lip  $\pm$  palate development) instead of the 1st trimester as the main period of exposure we found no increased risk of cleft lip  $\pm$  palate associated with corticosteroid use (odds ratio, 1.05 (95% confidence interval, 0.76–1.45)). Using the 3rd and 4th month of pregnancy (the primary critical period of cleft palate alone development) instead of the 1st trimester as the main period of exposure we found no increased risk of cleft palate alone associated with corticosteroid use (odds ratio, 0.71 (95% confidence interval, 0.39–1.29)).