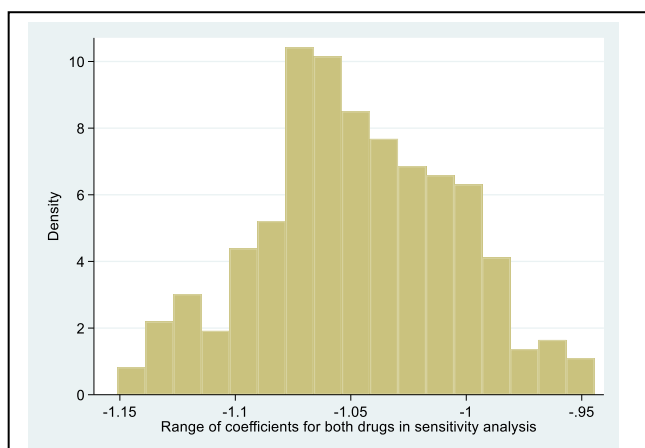
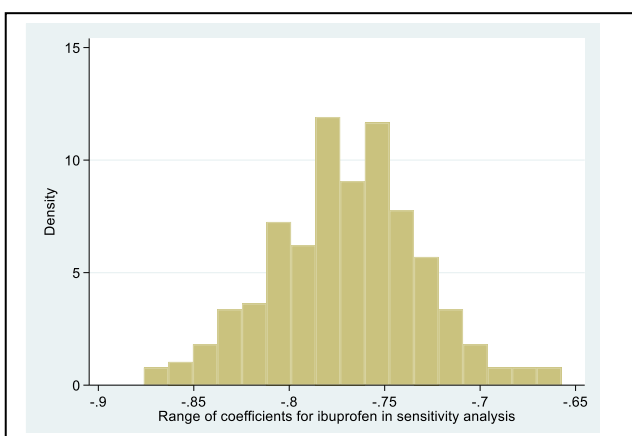
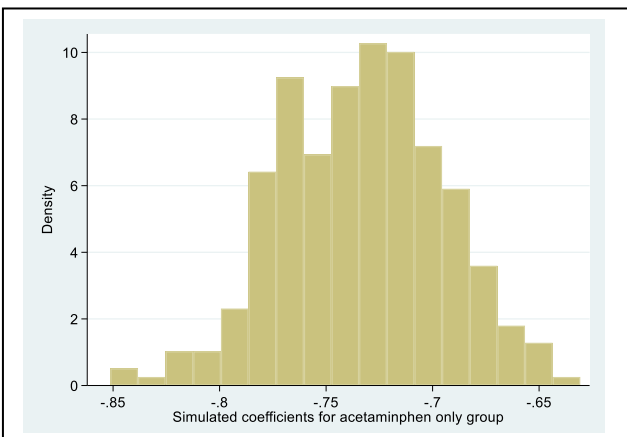


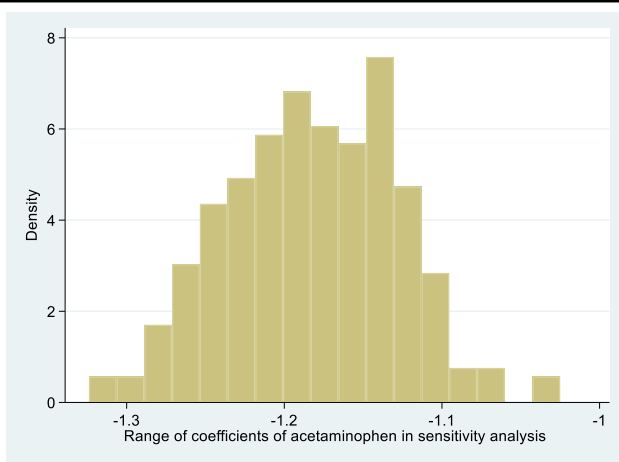
## S1 Appendix



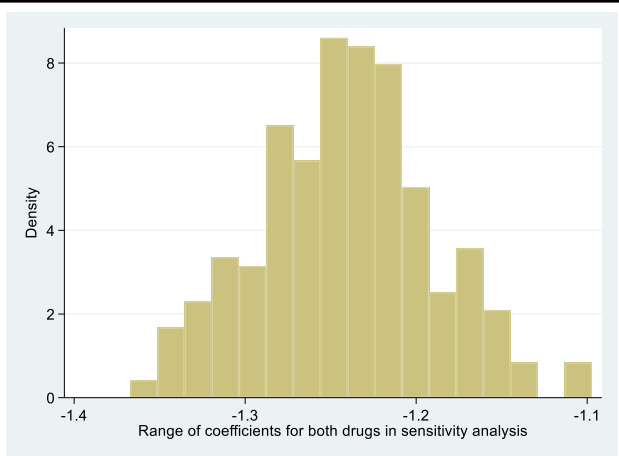
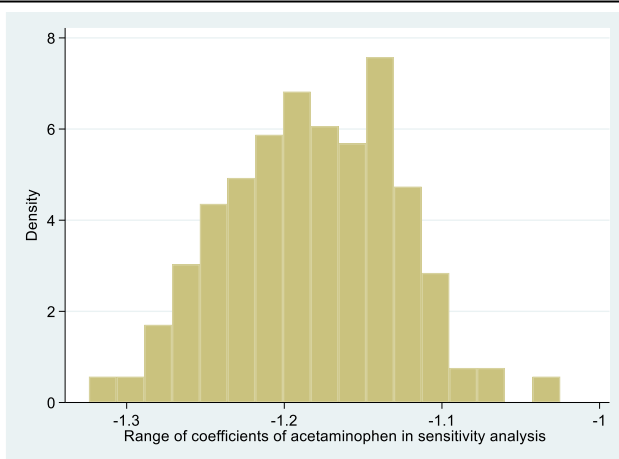
These graphs show the range of possible coefficients for each drug group in 300 simulations. This is for the 1 year follow up

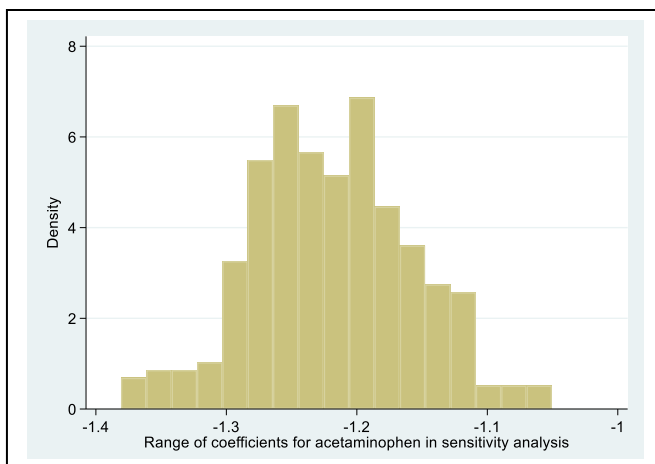
In the sensitivity analysis we assumed that some children who were not prescribed ibuprofen or acetaminophen at their inception visit nonetheless were administered it at home. We randomly assigned a new treatment group i.e. none/acetaminophen/ibuprofen or both drugs to children who were prescribed neither drug at their inception visit.

The sensitivity analysis coefficients continue to show a benefit if effect favoring antipyretics although the effect is much more modest. We now report the median of these alongside the original estimates in the main manuscript.

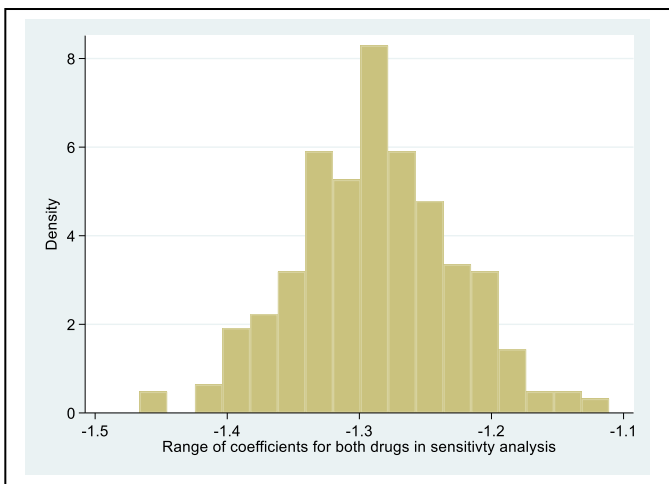
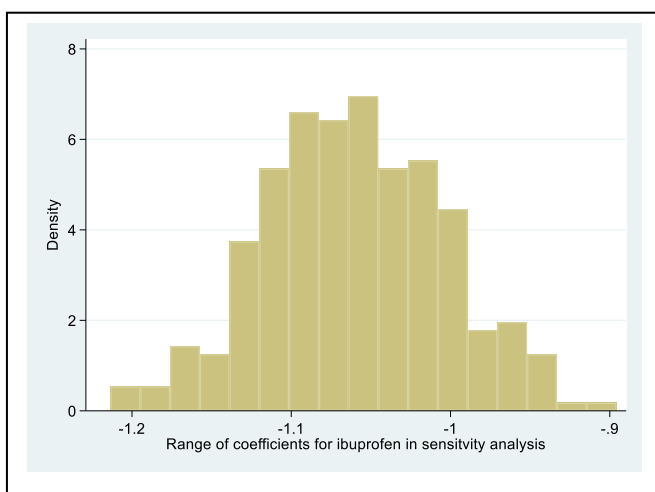


These graphs show the range of possible coefficients for each drug group in 300 simulations. This is for the 30-day follow up





These graphs show the range of possible coefficients for each drug group in 300 simulations. This is for the 14-day follow up



# Alternative models

## Effect of not adjusting for subsequent antipyretic use in selected models

Doctor visits for subsequent wheezing at 14-day follow up

| Adjusted for subsequent antipyretics |       |       |       |       | Not adjusted for subsequent antipyretics |       |       |
|--------------------------------------|-------|-------|-------|-------|--|-------|-------|
| Drug group                           | aIRR  | 95%lb | 95%ub |       | aIRR                                     | 95%lb | 95%ub |
| APAP only                            | 1     | -     | -     | -     | 1  | -     | -     |
| Ibuprofen +/- APAP                   | 1.021 | 0.789 | 1.323 | 0.872 | 1.042                                    | 0.800 | 1.358 |
| Ibuprofen only                       | 0.966 | 0.723 | 1.291 | 0.817 | 0.974                                    | 0.729 | 1.302 |
| Ibuprofen + APAP                     | 1.282 | 0.790 | 2.080 | 0.315 | 1.377                                    | 0.779 | 2.435 |

| Adjusted for subsequent antipyretics |       |       |       |   | Not adjusted for subsequent antipyretics |       |       |
|--------------------------------------|-------|-------|-------|---|--|-------|-------|
| Drug group                           | aIRR  | 95%lb | 95%ub |   | aIRR                                     | 95%lb | 95%ub |
| APAP only                            | 1     | -     | -     | - | 1  | -     | -     |
| Ibuprofen +/- APAP                   | 1.283 | 1.039 | 1.583 |   | 0.949                                    | 0.779 | 1.156 |
| Ibuprofen only                       | 1.209 | 0.958 | 1.152 |   | 0.916                                    | 0.735 | 1.141 |
| Ibuprofen + APAP                     | 1.662 | 1.081 | 2.554 |   | 1.110                                    | 0.741 | 1.662 |

Doctor visits for subsequent (episodes of) wheezing at 365-day follow up

| Adjusted for subsequent antipyretics |       |        |        |  | Not adjusted for subsequent antipyretics |        |        |
|--------------------------------------|-------|--------|--------|--|--|--------|--------|
|                                      | aIRR  | 95% lb | 95% ub |  | aIRR                                     | 95% lb | 95% ub |
| APAP only                            | 1     | -      | -      |  | 1  | -      | -      |
| Ibuprofen +/- APAP                   | 0.883 | 0.774  | 1.019  |  | 0.828                                    | 0.718  | 0.951  |
| Ibuprofen only                       | 0.853 | 0.733  | 0.992  |  | 0.864                                    | 0.761  | 0.982  |
| Ibuprofen + APAP                     | 1.005 | 0.781  | 1.414  |  | 0.999                                    | 0.913  | 1.095  |

All other adjustment as per models in manuscript.