The use of analgesic antipyretics (ANAP) in children have long been a matter of controversy. Data on their practical use on an individual level has, however, been scarce. There are indications of possible effects on glucose homeostasis and immune function related to the use of ANAP. The aim of this study was to analyze patterns of analgesic antipyretic use across the clinical centers of The Environmental Determinants of Diabetes in the Young (TEDDY) prospective cohort study and test if ANAP use was a risk factor for islet autoimmunity. Data were collected for 8542 children in the first 2.5 years of life. Incidence was analyzed using logistic regression with country and first child status as independent variables. Holm's procedure was used to adjust for multiplicity of intercountry comparisons. Time to autoantibody seroconversion was analyzed using a Cox proportional hazards model with cumulative analgesic use as primary time dependent covariate of interest. For each categorization, a generalized estimating equation (GEE) approach was used. Higher prevalence of ANAP use was found in the U.S. (95.7%) and Sweden (94.8%) compared to Finland (78.1%) and Germany (80.2%). First-born children were more commonly given acetaminophen (OR 1.26; 95% CI 1.07, 1.49; p = 0.007) but less commonly Non-Steroidal Anti-inflammatory Drugs (NSAID) (OR 0.86; 95% CI 0.78, 0.95; p = 0.002). Acetaminophen and NSAID use in the absence of fever and infection was more prevalent in the U.S. (40.4%; 26.3% of doses) compared to Sweden, Finland and Germany (p< 0.001). Acetaminophen or NSAID use before age 2.5 years did not predict development of islet autoimmunity by age 6 years (HR 1.02, 95% CI 0.99-1.09; p = 0.27). In a sub-analysis, acetaminophen use in children with fever weakly predicted development of islet autoimmunity by age 3 years (HR 1.05; 95% CI 1.01-1.09; p = 0.024). ANAP use in young children is not a risk factor for seroconversion by age 6 years. Use of ANAP is widespread in young children, and significantly higher in the U.S. compared to other study sites, where use is common also in absence of fever and infection.